JUDICIAL NOTICE

Numerical risk comparison of non-vaccination versus vaccination

TABLE OF CONTENTS

1. Introduction

This Notice is concerned with vaccinations that are presently mandated in the United States ("US") in certain circumstances and/or certain states for enrolment in institutions that provide childcare/preschool, elementary, secondary or tertiary education, for persons in the various age groups that are relevant and for which reasonably sufficient data is available, with the lower limit of 6 months and upper limit of 22 years.

This Notice presents, in relation to all infectious diseases that are notifiable in the US and subject to state mandates for conformation with recommendations for routine vaccinations for 0 to 18 year olds by the Centers for Disease Control and Prevention (CDC), an analysis of the overall level of benefit, compared to the risk, of an individual being vaccinated in accordance with those recommendations.

Those diseases ("the subject diseases") are diphtheria, tetanus, pertussis, poliomyelitis, measles, mumps, rubella, varicella, hepatitis A, hepatitis B (chronic), invasive *Haemophilus Influenzae* type b disease, invasive pneumococcal disease, invasive meningococcal disease, and pediatric influenza mortality.

"A case of infectious disease ought not be assumed to mean the same as a case of an infection, because there may be many cases of infection that are asymptomatic (and may culminate in the development of natural immunity), i.e. without suffering the disease ("dis" "ease"). This Notice will perhaps demonstrate that the most strongly in the case of diphtheria (paragraph 7.1), but that is not to say that the same does not apply to all of the other infectious diseases. A demonstrable ability to prevent such a disease in the unvaccinated by other measures, that are risk-free, undermines the necessity, or even benefit, of the targeting vaccination.

The risks analyzed (and ultimately compared) are the frequencies of serious adverse events (SAEs) that are judged to arise as a result of non-vaccination and from vaccination over a particular age range or set of age ranges (hereafter "subject age group(s)" or "subject age range(s)") in the population for that subject disease. Each subject age group is chosen in accordance with the age(s) at which doses of the subject vaccination are recommended by the CDC, within the limits of data availability. The lower limit of the subject age range is in all cases at least 6 months of age for any subject disease, because less than that is prior to the scheduled completion of the primary course of any of the subject vaccinations.

The analysis is for an infant, child or "adolescent" (up to 20 years old) who has not been diagnosed as being in any special category that the CDC names as at higher risk for harm from the relevant vaccine-targeted disease and/or from the vaccination.

A SAE is defined as where a patient is reported as having been hospitalized (or an existing hospitalization prolonged) or died or had any life-threatening or permanently disabling illness in association with the subject (targeted) disease or subject (targeting) vaccination.

Estimates are presented of the total differential frequencies of SAEs arising from non-vaccination (SRIU) or from vaccination (SRIV), and ultimately the relative difference between the total SRIU and SRIV for the relevant age range, to the extent that they are presently reasonably able to be estimated numerically, based upon the available published data.

The benefit of performing these analyses is based upon the precautionary principle at common law, which obliges every prospective administrator of any medical procedure to take the default position of favoring maintenance of the *status quo* - non-interference with his/her individual patient, and hence to not recommend the procedure for that individual, unless the prospective administrator is able to be properly satisfied, scientifically, that the procedure will not harm the patient, or at the least (if some level of risk is unavoidable either way), that the benefit for that individual significantly outweighs the risk. That obligation may be seen to especially apply in the case of a purely prophylactic procedure that is considered to be administered to a healthy patient, to whom there is no apparent imminent risk.

With respect to that overall level of benefit,

- the benefit that is appropriate to be determined and compared with the risk is only that which is supplementary to the total benefit that is achievable by application of all available alternative risk-free method(s). Accordingly, the analyses presented in this Notice seek to incorporate that refinement of the benefit to that extent that that is reasonably possible numerically, and
- the primary such benefit of concern addressed in this Notice is that to the individual patient. However, in relation to some vaccinations, the Notice also addresses the subject of impact upon the health of others.

For the purpose of addressing whether or not vaccination is of overall benefit to the individual patient, the Notice requests acceptance of documents containing numerical data that is relevant to calculations in relation to, and hence enabling a comparison between:

(1) the average serious risk arising from a vaccine-eligible individual not being vaccinated, and

(2) the average serious risk arising the same individual being vaccinated.

Accordingly,

- **PART 1 – DATA RELEVANT TO NON-VACCINATION AND VACCINATION RISK** starting on page 7 relates to documents and assumptions that are generally applicable to risk analyses for all of the vaccine-targeted diseases and/or vaccinations covered herein, and

- **PART 2 – RISK FROM NON-VACCINATION** starting on page 104 presents an analysis to determine the level of benefit from each vaccination, i.e. the differential (increased) serious risk for “vaccine-eligible” children arising from non-vaccination, and
- **PART 3 – RISK FROM VACCINATION** starting on page 354 presents an analysis to determine the level of serious risk from each vaccination,
- **PART 4 – COMPARISON OF RISK FROM NON-VACCINATION VS VACCINATION** starting on page 434 presents a comparison of the risks determined in PART 2 and PART 3 and independently published comparison(s) of risk from non-vaccination versus vaccination.

Notes:

- The use of *Italics* in this Notice denotes words or numbers quoted from the stated source.
- Every reference to “the above table” is to be interpreted to be to the nearest table to that particular reference, earlier in the text of the Notice, unless it is stated otherwise. Similarly, any reference to “the table below” is to be interpreted to be to the nearest table to that reference, later in the text of the Notice, unless it is stated otherwise.
- Every derived estimate is to be interpreted to apply specifically to residents of the United States or District of Columbia, unless stated otherwise.

PART 1 – DATA RELEVANT TO NON-VACCINATION AND VACCINATION RISK

2. Definition of Serious Adverse Events, and Serious Adverse Effects

2.1 Serious Adverse Event (SAE)

The Plaintiff hereby requests that the Court take judicial notice of the following document:

- CDC web page entitled "Vaccine Adverse Event Reporting System (VAERS), Vaccine Adverse Event Reporting System Summary", dated 1995, accessible at: https://wonder.cdc.gov/wonder/help/vaers.html
  (last accessed February 9, 2021)
  (hereafter "VAERS Definitions")
  A true and correct copy of the aforesaid document is attached hereto as **Exhibit 1.**

The VAERS Definitions states:

> *"Events are classified as serious when any of the following outcomes are associated with the event: Death, Permanent Disability, Life Threatening, Hospitalized, Existing Hospitalization Prolonged, Congenital Anomaly or Birth Defect. Prior to June 30, 2017, events were classified as serious when any of the following outcomes were associated with the event: Death, Permanent Disability, Life Threatening reaction, or Hospitalization."*

Based upon this excerpt, a serious adverse event (SAE) is defined in this Notice as any untoward medical occurrence that:

- results in death, or
- is life-threatening (at the time of the event), or
- requires inpatient hospitalisation or prolongation of existing hospitalisation, or
- results in permanent disability.

Therefore, complications or medically important conditions, even severe ones, that arise during the course of a targeted infectious disease or after vaccination, do not necessarily fall within the definition of a serious adverse event used in VAERS and in this Notice. This definition is also assumed to be the definition intended by the use of that term in exhibited documents except where they state otherwise.

2.2 Serious Adverse Effect

A serious adverse effect is defined in this Notice as a SAE that is judged by appointed clinical investigators (which may be the reporting health care professional or the sponsor or other appointed investigator) to have a certain or probable causal relationship to the associated infectious disease or vaccination.

Totalled over the material period, the probability of a serious adverse effect:

- arising from non-vaccination is abbreviated herein to SRIU, and
- arising from vaccination is abbreviated herein to SRIV.

The primary ultimate goal presented herein is to compare SRIU and SRIV in the case of each infectious disease or targeting vaccination that is covered by this Notice.

Any SAE that is cited herein in relation to any infectious disease is taken to be a serious adverse effect, whereas only a proportion of SAEs reported to have occurred in temporal association with a vaccination are judged to be vaccine-related.

3. Population

3.1 Total Resident US population

The Plaintiff hereby requests that the Court take judicial notice of the two documents entitled:

- "Midyear Population and Density - Custom Region - United States", selected for the years 1980 to 1999 and 2000 to 2018, which are respectively accessible at:

  https://www.census.gov/data-tools/demo/idb/region.php?T=6&RT=0&A=separate&Y=1980,1981,1982,1983,1984,1985,1986,1987,1988,1989,1990,1991,1992,1993,1994,1995,1996,1997,1998,1999&C=US&R=0 and

  https://www.census.gov/data-tools/demo/idb/region.php?T=6&RT=0&A=separate&Y=2000,2001,2002,2003,2004,2005,2006,2007,2008,2009,2010,2011,2012,2013,2014,2015,2016,2017,2018,2019&C=US&R=0
  (hereafter "Whole Population Data")
  (last accessed September 8, 2020)

  A true and correct copy of both of these documents is attached hereto as **Exhibit 2.**

Located below the tables in each of these documents is the following description of the data in the tables:

"United States data are based on official estimates and projections. All population estimates and projections are for the resident population. Population estimates for 2010-2018 are consistent with the 2010 Census provide the US resident population figures in each of the years 1980 – 2018."

The tables in the documents provide the following figures as the whole "*Midyear*" "*population estimates …for resident population*" in the "*United States*" for the respective years "*1980*" to "*2019*":

US Population, 1980-2019

Year	Population
1980	227,224,681
1981	229,465,714
1982	231,664,458
1983	233,791,994
1984	235,824,902
1985	237,923,795
1986	240,132,887
1987	242,288,918
1988	244,498,982
1989	246,819,230
1990	249,622,814
1991	252,980,941
1992	256,514,224
1993	259,918,588

Year	Population
1994	263,125,821
1995	266,278,393
1996	269,394,284
1997	272,646,925
1998	275,854,104
1999	279,040,168
2000	282,162,411
2001	284,968,955
2002	287,625,193
2003	290,107,933
2004	292,805,298
2005	295,516,599
2006	298,379,912
2007	301,231,207

Year	Population
2008	304,093,966
2009	306,771,529
2010	309,326,085
2011	311,580,009
2012	313,874,218
2013	316,057,727
2014	318,386,421
2015	320,742,673
2016	323,071,342
2017	325,147,121
2018	327,167,434
2019	330,268,840

(hereafter "Whole Population Table")

3.2 Five Year Age Group populations aged under 20 years

The Plaintiff hereby requests that the Court take judicial notice of the document entitled:

- "Midyear Population by Youth Age Groups and Sex - Custom Region - United States", selected for the years 2010 through 2019, accessible at: https://www.census.gov/data-tools/demo/idb/region.php?T=4&RT=0&A=separate&Y=2007,2008,2009,2010,2011,2012,2013,2014,2015,2016,2017,2018,2019&C=US&R=:
  (last accessed September 3, 2020)
  (hereafter "Five Year Age Group Data")

  A true and correct copy of the aforesaid document is attached hereto as **Exhibit 3.**

The table includes the following midyear US resident population data for the respective years 2010 to 2019 by five-year age group.

The table in the document states the following to be the "*Mid-year*" "*resident population*" in the "*United States*" for the years "*2010*" to "*2019*", totaled for each five-year age group under 20 years of age:

US Population by five year age group under < 20 years, 2010-2019

Year	*0 – 4 yrs*	*5 – 9 yrs*	*10 – 14 yrs*	*15 – 19 yrs*
2010	*20,188,815*	*20,331,229*	*20,680,642*	*21,981,217*
2011	*20,123,103*	*20,332,518*	*20,713,010*	*21,659,079*
2012	*19,976,066*	*20,467,161*	*20,670,087*	*21,370,267*
2013	*19,849,214*	*20,567,352*	*20,651,300*	*21,178,925*
2014	*19,872,353*	*20,515,054*	*20,666,075*	*21,054,605*
2015	*19,918,105*	*20,476,743*	*20,604,887*	*21,083,170*
2016	*19,922,365*	*20,432,396*	*20,620,680*	*21,135,528*
2017	*19,891,967*	*20,304,937*	*20,765,794*	*21,103,332*
2018	*19,810,275*	*20,195,642*	*20,879,527*	*21,097,221*
2019	*20,304,120*	*20,180,503*	*20,814,198*	*21,100,800*

(hereafter "Five Year Age Group Population Table")

3.3 Selected Single Age Group Populations up to Age 20 Years

The Plaintiff hereby requests that the Court take judicial notice of the table entitled:

"Midyear Population by Single Year Age Groups - Custom Region - United States", selected for the years 2006 through 2018, accessible at:
https://www.census.gov/data-tools/demo/idb/region.php?T=15&RT=0&A=separate&Y=2006,2007,2008,2009,2010,2011,2012,2013,2014,2015,2016,2017,2018,2019&C=US&R=0
(hereafter "Single Year Age Group Data")
(last accessed September 4, 2020)

A true and correct copy of the aforesaid table is attached hereto as **Exhibit 4**.

The table in Exhibit 4, hereafter "Single Year Age Groups Population Table", includes the midyear US resident population data for the respective years 2010 to 2018 for certain selected single year age groups.

That data for selected single year age groups is as follows:

US Population - selected single year age groups

Year	0 yrs	5 yrs	6 yrs	10 yrs	15 yrs	20 yrs
2010	3,951,430	4,064,521	4,072,904	4,186,957		
2011	3,963,092	4,087,054	4,074,533	4,135,289		
2012	3,926,570	4,131,049	4,096,633	4,045,469	4,143,301	4,546,565
2013	3,931,258	4,121,876	4,141,130	4,072,986	4,148,033	4,452,932
2014	3,954,786	4,004,571	4,133,374	4,114,582	4,163,079	4,411,460
2015	3,983,965	4,017,585	4,017,408	4,118,758	4,248,058	4,349,935
2016	3,955,192	4,034,325	4,030,894	4,144,072		
2017	3,893,945	4,002,285	4,046,625	4,190,254		
2018	3,848,208	4,010,118	4,015,259	4,184,077		
2019	4,095,614	4,023,461	4,012,057	4,064,631		

(hereafter "Selected Single Year Age Groups Population Table")

The Whole Population Table and Five Year Age Group Population Table and Selected Single Year Age Groups Population Table may be collectively referred to herein as the "Population Tables".

4. Vaccination Schedules

4.1 CDC-recommended vaccination schedules 2006-2020

The Plaintiff hereby requests that the Court take judicial notice of the following CDC-published documents containing vaccination schedules recommended by the Advisory Committee on Immunization Practices (ACIP) and approved by the Centers for Disease Control and Prevention (CDC) in the respective years (all accessible via: https://www.immunize.org/acip/acip_archive.asp)

- "Recommended Childhood and Adolescent Immunization Schedule --- United States, 2006 Harmonized Childhood and Adolescent Immunization Schedule, 2006"

  Citation: CDC MMWR, January 6, 2006, Vol.54(52):Q1-Q4, accessible at http://www.cdc.gov/mmwr/PDF/wk/mm5451.pdf
  (last accessed July 3, 2020)
  (hereafter "CDC Schedule 2006")

  A true and correct copy of this document is attached hereto as **Exhibit 5.**

- "Recommended Immunization Schedules for Persons Aged 0-18 Years --- United States, 2007"

  Citation: CDC MMWR, January 5, 2007, Vol. 55(51):Q1-Q4, accessible at http://www.cdc.gov/mmwr/PDF/wk/mm5551-Immunization.pdf

(last accessed July 3, 2020)
(hereafter “CDC Schedule 2007”)

A true and correct copy of this document is attached hereto as **Exhibit 6.**

- “Recommended Immunization Schedules for Persons Aged 0-18 Years--United States, 2008”

  Citation: CDC MMWR, January 11, 2008; 57(01):Q-1-Q-4, accessible at http://www.cdc.gov/mmwr/PDF/wk/mm5701-Immunization.pdf
  (last accessed July 3, 2020)
  (hereafter “CDC Schedule 2008”)

  A true and correct copy of this document is attached hereto as **Exhibit 7.**

- “Recommended Immunization Schedules for Persons Aged 0 Through 18 Years--United States, 2009”

  Citation: CDC MMWR, January 2, 2009; 57(51):Q-1-Q-4, accessible at https://www.cdc.gov/mmwr/PDF/wk/mm5751.pdf
  (last accessed July 3, 2020)
  (hereafter “CDC Schedule 2009”)

  A true and correct copy of this document is attached hereto as **Exhibit 8.**

- “Recommended Immunization Schedules for Persons Aged 0 Through 18 Years--United States, 2010”.

  Citation: CDC MMWR, January 8, 2010; 58(51&52):1-4, accessible at http://www.cdc.gov/mmwr/PDF/wk/mm5851-Immunization.pdf
  (last accessed July 3, 2020)
  (hereafter “CDC Schedule 2010”)

  A true and correct copy of this document is attached hereto as **Exhibit 9.**

- “Recommended Immunization Schedules for Persons Aged 0 Through 18 Years -- United States, 2011”.

  Citation: CDC MMWR, February 11, 2011; 60(5):1-4, accessible at http://www.cdc.gov/mmwr/pdf/wk/mm6005.pdf (pages 29–32),
  along with relevant Errata contained in MMWR, March 18, 2011;60(10), accessible at: https://www.cdc.gov/mmwr/PDF/wk/mm6010.pdf
  (both documents last accessed July 3, 2020)
  (hereafter these two documents combined “CDC Schedule 2011”)

A true and correct copy of these two documents combined is attached hereto as **Exhibit 10.**

- "Recommended Immunization Schedules for Persons Aged 0 Through 18 Years - United States, 2012"

  Citation: CDC MMWR, February 10, 2012; 61(5):1-4, accessible at http://www.cdc.gov/mmwr/pdf/wk/mm6105.pdf (pages 31–34)
  (last accessed July 3, 2020)
  (hereafter "CDC Schedule 2012")

  A true and correct copy of this document is attached hereto as **Exhibit 11.**

- "Advisory Committee on Immunization Practices (ACIP) Recommended Immunization Schedules for Persons Aged 0 Through 18 years and Adults Aged 19 Years and Older — United States, 2013".

  Citation: CDC MMWR Supplements, February 1, 2013; 62(01):1-21, accessible at http://www.cdc.gov/mmwr/pdf/other/su6201.pdf
  (last accessed July 3, 2020)
  (hereafter "CDC Schedule 2013")

  A true and correct copy of this document is attached hereto as **Exhibit 12**.

- the CDC web page headed "Recommended Immunization Schedules for Persons Aged 0 Through 18 Years UNITED STATES, 2014", located at https://www.cdc.gov/vaccines/schedules/downloads/past/2014-child.pdf
  (last accessed September 13, 2020)
  (hereafter "CDC Schedule 2014")

  A true and correct copy of this document is attached hereto as **Exhibit 13.**

  the CDC web page headed "Recommended Immunization Schedules for Persons Aged 0 Through 18 Years UNITED STATES, 2015", located at https://www.cdc.gov/vaccines/schedules/downloads/past/2015-child.pdf
  (last accessed September 13, 2020)
  (hereafter "CDC Schedule 2015")

  A true and correct copy of this document is attached hereto as **Exhibit 14.**

- the CDC web page headed "Recommended Immunization Schedules for Persons Aged 0 Through 18 Years UNITED STATES, 2016", located at https://www.cdc.gov/vaccines/schedules/downloads/past/2016-child.pdf

(last accessed September 13, 2020)
(hereafter “CDC Schedule 2016”)

A true and correct copy of this document is attached hereto as **Exhibit 15.**

- the CDC web page headed “Recommended Immunization Schedules for Persons Aged 0 Through 18 Years UNITED STATES, 2017”, located at https://www.cdc.gov/vaccines/schedules/downloads/past/2017-child.pdf
(last accessed September 13, 2020)
(hereafter “CDC Schedule 2017”)

  A true and correct copy of this document is attached hereto as **Exhibit 16.**

- the CDC web page headed “Recommended Immunization Schedules for Persons Aged 0 Through 18 Years UNITED STATES, 2018”, located at https://www.cdc.gov/vaccines/schedules/downloads/past/2018-child.pdf
(last accessed September 13, 2020)
(hereafter “CDC Schedule 2018”)

  A true and correct copy of this document is attached hereto as **Exhibit 17**.

- the CDC web page headed “Recommended Immunization Schedules for Persons Aged 0 Through 18 Years UNITED STATES, 2019”, located at https://www.cdc.gov/vaccines/schedules/downloads/past/2019-child.pdf
(last accessed September 13, 2020)
(hereafter “CDC Schedule 2019”)

  A true and correct copy of this document is attached hereto as **Exhibit 18.**

- the CDC web page headed “Recommended Immunization Schedules for Persons Aged 0 Through 18 Years UNITED STATES, 2020”, located at https://www.cdc.gov/vaccines/schedules/downloads/child/0-18yrs-child-combined-schedule.pdf
(last accessed September 13, 2020)
(hereafter “CDC Schedule 2020”)

  A true and correct copy of this document is attached hereto as **Exhibit 19.**

Hereafter this Notice may refer to all Exhibits 5 through 19 combined as the “CDC Schedules”.

4.2 Vaccine Trade names

CDC Schedule 2020 contains a table entitled “Vaccines in the Child and Adolescent Immunization Schedule*, which includes the following columns and selected rows:

Vaccines	***Abbreviations***	***Trade names***
Diphtheria, tetanus, and acellular pertussis vaccine	***DTaP***	*Daptacel®, Infanrix®*
Tetanus, diphtheria, and acellular pertussis vaccine	***Tdap***	*Adacel®, Boostrix®*
Poliovirus vaccine (inactivated)	***IPV***	*IPOL®*
DTaP and inactivated poliovirus vaccine	***DTaP-IPV***	*Kinrix®, Quadracel®*
Measles, mumps, and rubella vaccine	***MMR***	*M-M-R® II*
Measles, mumps, rubella, and varicella vaccine	***MMRV***	*ProQuad®*
Varicella vaccine	***VAR***	*Varivax®*
Hepatitis A vaccine	***HepA***	*Havrix®, Vaqta®*
Hepatitis B vaccine	***HepB***	*Engerix-B®, RecombivaxHB®*
Haemophilus influenzae type b vaccine	***Hib (PRP-T)*** ***Hib (PRP-OMP)***	*ActHIB®, Hiberix®, PedvaxHIB®*
Pneumococcal 13-valent conjugate vaccine	***PCV13***	*Prevnar13®*
Meningococcal serogroups A, C, W, Y vaccine	***MenACWY-D,*** ***MenACWY-CRM***	*Menactra®, Menveo®*
Influenza vaccine (inactivated)	***IIV***	*Multiple*
Influenza vaccine (live, attenuated)	***LAIV***	*FluMist® Quadrivalent*

In accordance with the contents in this table, the analyses of vaccine effectiveness and vaccine risks will focus on information available relating to the listed trade names. Any use in this Notice of abbreviations that are contained in this table are also defined to mean the associated vaccines in the table.

5. Vaccination Coverage

5.1 Coverage in infants

The Plaintiff hereby requests that the Court take judicial notice of the CDC-published report entitled:

"Vaccine Coverage for United States Infants at Milestone Ages: Missed Opportunities for Vaccination"

Citation: Gebremeskel BG, Zhang D, Goveia MG, Marshall GS, O'Brien MA. J Pediatric Infect Dis Soc. 2016;5(4):473-475. doi:10.1093/jpids/piw034, accessible at https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5181363/
(last accessed July 25, 2020)
(hereafter "Vaccination Coverage in Infants Report")

A true and correct copy of this document is attached hereto as **Exhibit 20.**

The Vaccination Coverage in Infants Report states:

> *"For infants born in 2011 and 2012, first dose coverage at 3 months of age for RV, DTaP, and PCV was 79%, 86%, and 82%, respectively. At 7 months of age, coverage for the last dose of RV (defined as the third dose of RV5 [RotaTeq, Rotavirus Vaccine, Live, Oral, Pentavalent, Merck & Co., Inc.] or the 2nd dose of RV1 [ROTARIX, Rotavirus Vaccine, Live, Oral, GlaxoSmithKline Biologicals]) and for 3 doses of DTaP and PCV, respectively, was 69%, 73%, and 69%. At 13 months of age, the respective coverage rates were 73%, 83%, and 84% (Figure 11)."*

5.2 Coverage in Daycare (1-4 years age range):

With respect to estimating children's vaccination status at age 1-4 years:

(a) 2006 – 2007:

The Plaintiff hereby requests that the Court take judicial notice of the CDC-published report entitled
"National, State, and Local Area Vaccination Coverage Among Children Aged 19--35 Months --- United States, 2007"

Citation: Darling N, M Kolasa M, Wooten KG. CDC MMWR Morb Mortal Wkly Rep 2008 (September 5); 57(35);961-966, accessible at https://www.cdc.gov/mmwr/preview/mmwrhtml/mm5735a1.htm
(last accessed June 30, 2020)
(hereafter "CDC Daycare Coverage Report 2006-2007")

A true and correct copy of the aforesaid report is attached hereto as **Exhibit 21.**

The CDC Daycare Coverage Report 2006-2007 states:

"The National Immunization Survey (NIS) provides vaccination coverage estimates among children aged 19--35 months for each of the 50 states and selected urban areas. This report describes the results of the 2007 NIS, which provided coverage estimates among children born during January 2004--July 2006."*

and

"National coverage was …for ≥4 doses of DTaP (84.5%); coverage with ≥3 doses of DTaP was 95.5%... National vaccination coverage estimates for PCV7 continued to increase, from 86.9% in 2006 to 90.0% in 2007 for ≥3 doses and from 68.4% to 75.3% for ≥4 doses. Among AI/AN children, coverage with the fourth dose of PCV7 increased significantly, from 62.7% to 80.4%."

and

"Coverage with ≥4 doses of PCV7 increased significantly to 75.3% in 2007, a substantial increase since PCV7 was first recommended in 2000."

and

"Despite record high coverage with MMR vaccine, nearly 8% of children aged 19--35 months surveyed for the 2007 NIS remained unvaccinated."

includes a table entitled:

*"**TABLE 1. Estimated vaccination coverage among children aged 19–35 months, by selected vaccines and dosages — National Immunization Survey, United States, 2003–2007***

whose column headings and selected rows are as follows:

	2006¶		2007**	
Vaccine and dosage	**%**	**(95% CI)**	**%**	**(95% CI)**
DTP/DT/DTaP§§				
≥3 doses	95.8	(±0.5)	95.5	(±0.5)
≥4 doses	85.2	(±0.9)	84.5	(±0.9)
Poliovirus	92.8	(±0.6)	92.6	(±0.7)
MMR¶¶ ≥1 dose	92.3	(±0.6)	92.3	(±0.7)
Hib* ≥3 dose**	93.4	(±0.6)	92.6	(±0.7)
Hepatitis B ≥3 doses	93.3	(±0.6)	92.7	(±0.7)
Varicella ≥1 dose	89.2	(±0.7)	90.0	(±0.7)
PCV7†††				
≥3 doses	86.9	(±0.8)	90.0	(±0.8)
≥4 doses	68.4	(±1.1)	75.3	(±1.2)

Below the table are the following abbreviation expansions and notes referenced by the table:

> ""¶ *Born during January 2003-June 2005 (2006 estimate based on National Immunization Survey dataset, which was rereleased on February 25, 2008....*
>
> ** *Born during January 2004-July 2006*
>
> †† *Confidence interval.*
>
> §§ *Diphtheria, tetanus toxoids and pertussis vaccines, diphtheria and tetanus toxoids, and diphtheria, tetanus toxoids and any acellular pertussis vaccine.*
>
> ¶¶ *Measles, mumps, and rubella vaccine.*
>
> *** Haemophilus Influenzae *type b (Hib) vaccine.*
>
> ††† *7-valent pneumococcal conjugate vaccine (PCV7)".*

The CDC Daycare Coverage Report 2006-2007 also states:

> *"Vaccination coverage with the fourth dose of DTaP and the fourth dose of PCV7 was lower among children living below the poverty level compared with children living at or above the poverty level, but this difference declined from 6.1% in 2006 to 4.8% in 2007 for ≥4 doses of DTaP and from 9.4% in 2006 to 3.5% in 2007 for ≥4 doses of PCV7"*

(b) 2008 – 2012:

The Plaintiff hereby requests that the Court take judicial notice of the CDC-published report entitled
"Vaccination Coverage Among Children Aged 19–35 Months — United States, 2012"

Citation: Black L, Yankey D, Kolosa M. CDC MMWR Morb Mortal Wkly Rep 2013 (September 13);62(36);733-740, accessible at
https://www.cdc.gov/mmwr/preview/mmwrhtml/mm6236a1.htm (html) or
https://www.cdc.gov/mmwr/pdf/wk/mm6236.pdf (pdf)
(last accessed June 30, 2020)
(hereafter "CDC Daycare Coverage Report 2008-2012")

A true and correct copy of the aforesaid table is attached hereto as **Exhibit 22**.

The report states:

"The National Immunization Survey (NIS) is a random-digit–dialed telephone survey used to monitor vaccination coverage among U.S. children aged 19–35 months. This report describes national, state, and selected local area vaccination coverage estimates…, based on results from the 2012 NIS."

and

"Children in families with incomes below the federal poverty level††† had lower coverage than children in families at or above the poverty level for ≥3 and ≥4 doses of DTaP, primary and full series of Hib, ≥3 and ≥4 doses of PCV, ≥2 doses of HepA, rotavirus vaccine, and the combined vaccine series (Table 2)."

and

"Vaccination coverage varied by state, with coverage for the combined vaccine series ranging from 59.5% in Alaska to 80.2% in Hawaii.…Variations in coverage were widest for …≥2 doses of HepA (ranging from 32.3% in Wyoming to 65.9% in Georgia), and rotavirus vaccine (ranging from 54.2% in the District of Columbia to 83.0% in New Hampshire)."

and includes a table entitled:

*"**TABLE 1. Estimated vaccination coverage among children aged 19–35 months, by selected vaccines and dosages — National Immunization Survey, United States, 2008–2012***

whose column headings and selected rows are as follows:

Vaccine and dosage	2008		2009		2010	
	%	(95% CI)	%	(95% CI)	%	(95% CI)
DTaP						
≥3 doses	96.2	(±0.5)	95.0	(±0.6)	95.0	(±0.6)
≥4 doses	84.6	(±1.0)	83.9	(±1.0)	84.4	(±1.0)
Poliovirus (≥3 doses)	93.6	(±0.6)	92.8	(±0.7)	93.3	(±0.7)
MMR (≥1 doses)	92.1	(±0.7)	90.0	(±0.8)	91.5	(±0.7)
Hib§						
Primary series	N/A		92.1	(±0.8)	92.2	(±0.8)
Full series	N/A		54.8	(±1.4)	66.8	(±1.3)
HepB						
≥3 doses	93.5	(±0.7)	92.4	(±0.7)	91.8	(±0.7)

Varicella (≥1 doses)	*90.7*	*(±0.7)*	*89.6*	*(±0.8)*	*90.4*	*(±0.8)*
PCV						
≥3 doses	*92.8*	*(±0.6)*	*92.6*	*(±0.7)*	*92.6*	*(±0.8)*
≥4 doses	*80.1*	*(±1.1)*	*80.4*	*(±1.2)*	*83.3*	*(±1.0)*
HepA**						
≥1 doses	*70.5*	*(±1.1)*	*75.0*	*(±1.1)*	*78.3*	*(±1.1)*
≥2 doses	*40.4*	*(±1.2)*	*46.6*	*(±1.4)*	*49.7*	*(±1.4)*
Rotavirus††	*N/A*		*43.9*	*(±1.4)*	*59.2*	*(±1.4)*

Vaccine and dosage	***2011***		***2012***	
	%	***(95% CI)***	***%***	***(95% CI)***
DTaP				
≥3 doses	*95.5*	*(±0.5)*	*94.3*	*(±0.7)†*
≥4 doses	*84.6*	*(±1.0)*	*82.5*	*(±1.2)†*
Poliovirus (≥3 doses)	*93.9*	*(±0.6)*	*92.8*	*(±0.7)†*
MMR (≥1 doses)	*91.6*	*(±0.8)*	*90.8*	*(±0.8)*
Hib§				
Primary series	*94.2*	*(±0.6)*	*93.3*	*(±0.7)*
Full series	*80.4*	*(±1.1)*	*80.9*	*(±1.2)*
≥3 doses	*91.1*	*(±0.7)*	*89.7*	*(±0.9)†*
Varicella (≥1 doses)	*90.8*	*(±0.7)*	*90.2*	*(±0.8)*
PCV				
≥3 doses	*93.6*	*(±0.6)*	*92.3*	*(±0.8)†*
≥4 doses	*84.4*	*(±1.0)*	*81.9*	*(±1.1)†*
HepA**				
≥1 doses	*81.2*	*(±1.0)*	*81.5*	*(±1.1)*
≥2 doses	*52.2*	*(±1.4)*	*53.0*	*(±1.5)*
Rotavirus††	*67.3*	*(±1.3)*	*68.6*	*(±1.4)*

Below the table are the following abbreviation expansions and notes referenced by the table:

*"**Abbreviations:** CI = confidence interval; DTaP = diphtheria and tetanus toxoids and acellular pertussis vaccine (includes children who might have been vaccinated with diphtheria and tetanus toxoids and pertussis vaccine or diphtheria and tetanus toxoids vaccine); MMR = measles, mumps, and rubella vaccine; Hib = Haemophilus influenzae type b vaccine; N/A = not available (estimate not available if the unweighted sample size for the denominator was <30 or 95% CI half width / estimate >0.588 or 95% CI half width >10); HepB = hepatitis B vaccine; HepA = hepatitis A vaccine; PCV = pneumococcal conjugate vaccine.*

** For 2008, includes children born during January 2005–June 2007; for 2009, children born during January 2006–July 2008; for 2010, children born during January 2007–July 2009; for 2011, children born during January 2008–May 2010; and for 2012, children born during January 2009–May 2011…*

§ Hib primary series: receipt of ≥2 or ≥3 doses, depending on product received. Full series: receipt of ≥3 or ≥4 doses, depending on product received (primary series and booster dose). Hib coverage for primary or full series not available until 2009…

*** HepA coverage not available before 2008.*

†† Rotavirus vaccine includes ≥2 or ≥3 doses, depending on the product received (≥2 doses for Rotarix [RV1] or ≥3 doses for RotaTeq [RV5]). Estimates of rotavirus vaccine coverage not available before 2009."

(c) 2013 – 2017:

The Plaintiff hereby requests that the Court take judicial notice of the CDC-published report entitled
"Vaccination Coverage Among Children Aged 19–35 Months — United States, 2017"

Citation: Hill HA, Elam-Evans LD, Yankey D, Singleton JA, Kang Y. CDC MMWR Morb Mortal Wkly Rep 2018;67:1123–1128, accessible at
http://dx.doi.org/10.15585/mmwr.mm6740a4 (html) or
https://www.cdc.gov/mmwr/volumes/67/wr/pdfs/mm6740a4-H.pdf (.pdf)
(last accessed June 30, 2020)
(hereafter "CDC Daycare Coverage Report 2013-2017")

A true and correct copy of the aforesaid table is attached hereto as **Exhibit 23**.

The report states:

"CDC used data from the 2017 National Immunization Survey-Child (NIS-Child) to assess vaccination coverage at national, state, territorial, and selected local levels among children aged 19–35 months in the United States."

and

"Differences in vaccination coverage by race/ethnicity and poverty status in 2017 were similar to those observed in previous years."

and

"the proportion of uninsured children who had received no vaccinations (7.1%) was higher than that among those with private insurance (0.8%)… Coverage was lower for most vaccines among uninsured and Medicaid-insured children ...These disparities were larger for vaccines that require a booster dose in the second year of life (e.g., DTaP, Hib, and PCV)… Unvaccinated children in the 2017 NIS-Child were disproportionately uninsured: 17.2% of unvaccinated children were uninsured, compared with 2.8% of all children."

and

"estimated rotavirus coverage ranged from 64.7% in California to 85.1% in Rhode Island. Coverage with MMR ranged from 85.8% in Missouri to 98.3% in Massachusetts; MMR coverage was <90% for 11 states in 2017."

and

"Measles was declared eliminated from the United States in 2000, yet outbreaks caused by imported *cases continue to occur each year"*

and includes a table entitled:

*"**TABLE 1. Estimated vaccination coverage among children aged 19–35 months, by selected vaccines and doses — National Immunization Survey-Child, United States, 2013-2017*"***

whose column headings and selected rows are as follows:

Vaccine/Dose	***Survey year % (95% CI)***				
	2013	***2014***	***2015***	***2016***	***2017***
DTaP†					
≥3 doses	*94.1 (93.2–95.0)*	*94.7 (94.0–95.4)*	*95.0 (94.4–95.5)*	*93.7 (92.8–94.5)*	*94.0 (93.3–94.7)*

≥4 doses	*83.1 (81.8–84.3)*	*84.2 (83.0–85.4)*	*84.6 (83.5–85.7)*	*83.4 (82.1–84.6)*	*83.2 (82.0–84.3)*
Poliovirus (≥3 doses)	*92.7 (91.6–93.6)*	*93.3 (92.5–94.1)*	*93.7 (93.0–94.3)*	*91.9 (90.9–92.9)*	*92.7 (91.9–93.5)*
MMR (≥1 dose)¶	*91.9 (90.9–92.7)*	*91.5 (90.6–92.4)*	*91.9 (91.0–92.7)*	*91.1 (90.1–92.0)*	*91.5 (90.6–92.3)*
Hib					
*Primary series***	*93.7 (92.7–94.5)*	*93.3 (92.5–94.1)*	*94.3 (93.7–94.9)*	*92.8 (91.8–93.6)§*	*92.8 (91.9–93.6)*
*Full series***	*82.0 (80.7–83.3)*	*82.0 (80.7–83.2)*	*82.7 (81.5–83.8)*	*81.8 (80.5–83.0)*	*80.7 (79.4–82.0)*
HepB…					
≥3 doses	*90.8 (89.7–91.7)*	*91.6 (90.7–92.4)*	*92.6 (91.9–93.3)*	*90.5 (89.3–91.5)§*	*91.4 (90.5–92.3)*
Varicella (≥1 dose)¶	*91.2 (90.2–92.1)*	*91.0 (90.1–91.9)*	*91.8 (91.0–92.5)*	*90.6 (89.6–91.5)*	*91.0 (90.1–91.8)*
PCV					
≥3 doses	*92.4 (91.4–93.3)*	*92.6 (91.8–93.4)*	*93.3 (92.5–94.0)*	*91.8 (90.8–92.7)§*	*91.9 (90.9–92.8)*
≥4 doses	*82.0 (80.6–83.3)*	*82.9 (81.6–84.2)*	*84.1 (83.0–85.2)*	*81.8 (80.4–83.1)§*	*82.4 (81.1–83.6)*
HepA					
≥1 dose	*83.1 (81.9–84.3)§*	*85.1 (84.0–86.2)§*	*85.8 (84.7–86.8)*	*86.1 (84.9–87.2)*	*86.0 (84.8–87.1)*
≥2 doses§§	*54.7 (53.1–56.3)*	*57.5 (55.9–59.1)§*	*59.6 (58.1–61.0)*	*60.6 (59.1–62.2)*	*59.7 (58.2–61.3)*
Rotavirus¶¶	*72.6 (71.1–74.0)§*	*71.7 (70.1–73.2)*	*73.2 (71.8–74.6)*	*74.1 (72.6–75.5)*	*73.2 (71.6–74.7)*

Below the table are the following abbreviation expansions and notes referenced by the table:

*"**Abbreviations:** CI = confidence interval; DTaP = diphtheria, tetanus toxoids, and acellular pertussis vaccine; HepA = hepatitis A vaccine; HepB = hepatitis B vaccine; Hib* = Haemophilus influenzae *type b conjugate vaccine; MMR = measles, mumps, and rubella vaccine; PCV = pneumococcal conjugate vaccine.*

† Includes children who might have been vaccinated with diphtheria and tetanus toxoids vaccine or diphtheria, tetanus toxoids, and pertussis vaccine…
¶ Includes children who might have been vaccinated with measles, mumps, rubella, and varicella vaccine.
*** Hib primary series: ≥2 or ≥3 doses, depending on product type received; full series includes primary series and booster dose, which includes receipt of ≥3 or ≥4 doses, depending on product type received…*
§§ Estimates of ≥2 doses of HepA are likely underestimates because a child could be on schedule but not receive a second dose of HepA until age 41 months. This dose would not be collected by NIS-Child, which includes children aged 19–35 months only.
¶¶ Includes ≥2 doses of Rotarix monovalent rotavirus vaccine (RV1), or ≥3 doses of RotaTeq pentavalent rotavirus vaccine (RV5)."

The report also includes a table entitled:

"TABLE 2. Estimated vaccination coverage among children aged 19–35 months, by selected vaccines and doses, metropolitan statistical area (MSA) status, and health insurance status† — National Immunization Survey-Child, United States, 2017§"*

whose selected column headings and selected rows are as follows:

Vaccine / Dose	***Private only (referent) (n = 8,536)***	***Other insurance (n = 644)***	***Any Medicaid (n = 5,714)***	***Uninsured (n = 439)***
DTaP¶				
≥3 doses	*96.5 (95.7–97.2)*	*93.7 (90.7–95.8)***	*92.6 (91.2–93.8)***	*78.2 (71.3–83.8)***
≥4 doses	*86.9 (85.2–88.5)*	*83.6 (79.3–87.2)*	*80.8 (78.9–82.5)***	*62.4 (55.0–69.1)***
Poliovirus (≥3 doses)	*95.2 (94.3–96.0)*	*92.7 (89.5–95.0)*	*91.2 (89.6–92.5)***	*77.9 (71.0–83.6)***
MMR†† (≥1 dose)	*93.7 (92.3–94.8)*	*91.0 (87.5–93.6)*	*90.4 (89.1–91.6)***	*74.6 (67.5–80.6)***
Hib				
Primary series§§	*95.5 (94.6–96.2)*	*92.2 (88.8–94.7)***	*91.1 (89.5–92.5)***	*78.0 (71.1–83.7)***
Full series§§	*85.1 (83.2–86.9)*	*78.8 (73.8–83.1)***	*77.7 (75.6–79.7)***	*62.0 (54.6–68.9)***
HepB				
≥3 doses	*93.3 (91.9–94.4)*	*92.5 (89.4–94.7)*	*90.4 (88.8–91.7)***	*78.6 (71.8–84.1)***
Varicella†† (≥1 dose)	*92.9 (91.5–94.1)*	*91.3 (88.0–93.8)*	*90.4 (89.1–91.6)***	*69.5 (62.2–76.0)***
PCV				
≥3 doses	*94.5 (92.9–95.7)*	*91.0 (87.6–93.5)***	*90.5 (88.9–91.8)***	*75.2 (67.9–81.2)***
≥4 doses	*87.6 (85.8–89.3)*	*81.3 (76.8–85.2)***	*78.9 (76.8–80.8)***	*59.0 (51.6–66.1)***
HepA				
≥1 dose	*88.1 (86.5–89.6)*	*86.1 (81.7–89.5)*	*85.3 (83.5–87.0)***	*63.3 (55.7–70.3)***
≥2 doses	*63.2 (61.0–65.2)*	*61.1 (55.2–66.7)*	*57.7 (55.2–60.2)***	*35.7 (29.1–42.9)***
*Rotavirus****	*81.8 (79.8–83.6)*	*67.4 (61.0–73.3)***	*66.8 (64.2–69.4)***	*51.5 (44.2–58.7)***
Combined 7-vaccine series †††	*76.0 (73.9–77.9)*	*69.2 (63.6–74.2)***	*66.5 (64.1–68.9)***	*48.5 (41.2–55.8)***
No vaccinations	*0.8 (0.6–1.1)*	*—§§§*	*1.0 (0.7–1.4)*	*7.1 (4.6–10.8)** ”*

hereafter “Vaccination Coverage in 19–35 month olds by Insurance Status Table 2017”

Below the table are the following abbreviation expansions and notes referenced by the table:

*"**Abbreviations:** CI = confidence interval; DTaP = diphtheria and tetanus toxoids and acellular pertussis vaccine; HepA = hepatitis A vaccine; HepB = hepatitis B vaccine; Hib = Haemophilus influenzae type b conjugate vaccine; MMR = measles, mumps, and rubella vaccine; PCV = pneumococcal conjugate vaccine…*

¶ Includes children who might have been vaccinated with diphtheria and tetanus toxoids vaccine or diphtheria, tetanus toxoids, and pertussis vaccine.

*** Statistically significant (p<0.05) difference compared with the referent group…*

§§§ Estimate not available because the 95% CI was ≥20."

Hereafter this Notice will refer to all of the reports referenced in this paragraph 5.2 as "CDC Daycare Coverage Reports".

It shall be assumed in this Notice that approximately the same coverage figures that appear in the CDC Daycare Coverage Report 2013-2017 for 2017 were equally applicable to each year since.

5.3 Coverage in Elementary School (5-10 years age range)

With respect to estimating children's vaccination status at age 5 years (in some reporting years combined with those aged 6 years):

(a) 1997-1998:

The Plaintiff hereby requests that the Court take judicial notice of the CDC-published report entitled
"Vaccination Coverage Among Children Enrolled in Head Start Programs or Day Care Facilities or Entering School"

Citation: J*iles* RB*, Fuchs* C*, Klevens* RM. In: CDC Surveillance Summaries (September 22). CDC MMWR 2000;49(no. SS-9);27-38, accessible at
https://www.cdc.gov/mmwr/PDF/ss/ss4909.pdf
(last accessed June 30, 2020)
(hereafter "CDC Elementary School Coverage Report 1997-1998")

A true and correct copy of the aforesaid report is attached hereto as **Exhibit 24**.

The report states:

"CDC's National Immunization Program administers grants to support 64 vaccination programs. These programs are in all 50 states, …and the District of Columbia. Grant guidelines require annual school vaccination surveys ….This system constitutes the only source of nationally representative vaccination coverage estimates for these populations."

and

"Kindergarten/First Grade:

Of the 64 reporting areas, 43 (67.2%) submitted coverage levels for children enrolled in kindergarten and first grade. …Four of the 43 programs reported coverage levels for the combined MMR. The mean vaccination coverage levels among the reporting areas were 96.7% for poliovirus vaccine (range: 82.8%–99.9%), 96.7% for DTP/DT/Td (range: 82.8%–99.8%), 96.0% for measles vaccine (range: 82.8%–99.9%), and 96.5% for mumps and rubella vaccines (range: 82.8%–99.9%)….

Interpretation: …because a high proportion of states and territories did not submit vaccination coverage reports to CDC, these estimated means may not reflect levels for all children in the United States."

and

"In six reporting areas, pertussis vaccination is not required; in at least three reporting areas, mumps vaccination is not required."

and

"data from school records can potentially reflect vaccination status of nearly all U.S. children because most children, regardless of race/ethnicity, socioeconomic status, and access to care, are enrolled in schools. Accuracy is also high because information regarding vaccinations is generally based on provider records and does not rely on parent recall (4)."

and

"The mean vaccination coverage levels among the reporting vaccination programs were 97.8% for poliovirus vaccine (range: 80.0%–100.0%), 97.0% for DTP/DT/Td (range: 87.7%–100.0%), 93.3% for measles vaccine (range: 91.4%–100.0%), and 93.2% for mumps and rubella vaccines (range: 91.4%–100.0%)."

The report includes a table entitled:

"TABLE 3. Estimated vaccination coverage among children enrolled in kindergarten and first grade, by reporting area and selected vaccine — 64 U.S. vaccination programs, 1997–98 school year"

whose selected column headings and rows are as follows:

Area	Grade	Polio # (%)	DTP / DT / Td† (%)	Measles§ (%)	Mumps¶ (%)	Rubella** (%)
United States (weighted mean)		**96.7**	**96.7**	**96.0**	**96.5**	**96.5**
Massachusetts††	K	97.0	96.8	97.3	97.3	97.3
Rhode Island§§	K	98.6	97.0	98.5	98.5	98.5
Ohio††	K	99.0	98.0	99.0	99.0	99.0
Minnesota††§§	K	95.9	95.5	98.3	98.3	98.3
Missouri†††	K	97.8	97.7	97.6	98.7	97.9
Kentucky§§§	K	—	—	84.9	84.9	84.9
Nevada¶¶¶	1	98.4	97.5	96.8	96.8	96.8
Alaska§§	K–1	96.5	96.5	96.5	96.5	96.5
California†† †††	K	96.2	96.6	94.3	94.3	94.3
Oregon§§	K–1	97.2	96.9	98.4	98.4	98.4
Washington****	K–1	95.0	97.0	98.0	98.0	98.0

Below the table are the following abbreviation expansions and notes referenced by the table:

*" * At least 3 doses of poliovirus vaccine.*

† At least 3 doses of diphtheria, tetanus toxoids, and pertussis vaccine (DTP); diphtheria and tetanus toxoids (DT); or tetanus toxoid (Td), unless otherwise noted.

§ One dose of measles vaccine, unless otherwise noted.

¶ One dose of mumps vaccine.

*** One dose of rubella vaccine.*

†† At least 4 doses of diphtheria, tetanus toxoids, and pertussis vaccine (DTP); diphtheria and tetanus toxoids (DT); or tetanus toxoid (Td).

§§ Measles, mumps, and rubella coverage reported for combined measles, mumps, and rubella vaccine (MMR). One dose of MMR, unless otherwise noted.

††† Two doses of measles vaccine.

§§§ Two doses of measles, mumps, and rubella vaccines.

¶¶¶ Two doses of MMR vaccine.

***** DTP/DT/Td doses unspecified."*

Included also in the report is the statement:

"overall weighted mean estimates presented in this report might not be representative of all U.S. children"

Regarding the reference in the above quoted footnote to "*tetanus toxoid (Td)*", the CDC Page About Diphtheria, Tetanus, and Pertussis Vaccines (Exhibit 73, cited in paragraph 7.1(c)0 herein), includes a heading "*Diphtheria and Tetanus (DT and Td) Only Vaccines*" and states:

"Each 0.5-mL dose of Td (MassBiologics) contains the following active ingredients: 2 Lf of tetanus toxoid and 2 Lf of diphtheria toxoid."

(b) 1999-2000:

The Plaintiff hereby requests that the Court take judicial notice of the CDC-published report entitled
"Vaccination Coverage Among Children Enrolled in Head Start Programs and Licensed Child Care Centers and Entering School --- United States and Selected Reporting Areas, 1999--2000 School Year"
Citation:. In: CDC MMWR 2001;50(39);847-855, accessible at
https://www.cdc.gov/mmwr/preview/mmwrhtml/mm5039a2.htm and
https://www.jstor.org/stable/pdf/23312331.pdf
(last accessed June 9, 2020)
(hereafter "CDC Elementary School Coverage Report 1999-2000")

A true and correct copy of the aforesaid report is attached hereto as **Exhibit 25**.

The report states:

"all states… conduct annual vaccination assessment surveys of coverage with basic vaccines among children …entering kindergarten or first grade."

and

"This report summarizes estimated coverage with the basic vaccines: >3 doses of polio virus vaccine, >3 tetanus containing doses (diphtheria and tetanus toxoids and acellular pertussis vaccine [DTaP]), diphtheria and tetanus toxoids (DT), or tetanus toxoids (Td), and 1 dose each of measles, mumps, and rubella vaccines for the September 1999-June 2000 school year."

and

"Kindergarten/First Grade

Of the 64 programs, 44 (68.8%) submitted vaccination coverage levels for children enrolled in kindergarten and/or first grade (Table 1). The mean level among programs was 97.3% for poliovirus vaccine (range: 85.6%-99.9%), 97.2% for DTaP/DT/Td (85.3%-99.9%), 97.1% for measles (range: 86%-100%), and 97.4% for mumps and rubella vaccines (range: 86%-100%); 38 (86.4%) programs reached the 2010 goal of >95% coverage for poliovirus vaccine and measles, mumps, and rubella vaccines, and 37 (84.1%) reached the goal for DTaP/DT/T."

The report includes a table entitled:

"TABLE 1. Estimated vaccination coverage among children in kindergarten and first grade, by reporting area and vaccine — 64 vaccination programs. United States and selected territories, 1999-2000 school year."

whose selected column headings and rows are as follows:

Reporting area	***% Grade****	***% Poliovirus §***	***% DTP/DT/ Td ¶***	***% M/M/R***
United States (weighted mean)		***97.3***	***97.2***	***97.1 / 97.4 / 97.4***
Maine †† §§ ¶¶	*K*	*88.0*	*88.0*	*88.0*
*New Hampshire****	*1*	*99.6*	*99.5*	*98.4*
*Rhode Island****	*K*	*98.7*	*98.2*	*96.9*
Vermont †††	*K-1*	*96.2*	*97.1*	*91.4*
Ohio§§§	*K*	*96.0*	*95.0*	*98.0*
*North Carolina****	*K-1*	*99.7*	*99.6*	*99.7*
*South Carolina****	*K*	*99.0*	*99.0*	*100.0*
*Kentucky****	*K*	*96.0*	*97.0*	*96.0*
*Alaska****	*K-1*	*96.0*	*96.0*	*95.9*
California ¶¶ §§§	*K*	*97.1*	*96.3*	*96.4*

Below the table are the following abbreviation expansions and notes referenced by the table:

*" * Coverage estimates are from states that reported data for children entering kindergarten and/or first grade only.*

† The proportion of eligible children included in the assessment survey.

§ At least 3 doses of poliovirus vaccine unless otherwise indicated.

¶ *At least 3 doses of diphtheria and tetanus toxoids and acellular pertussis vaccine (DTaP), diphtheria and tetanus toxoids (DT), or tetanus toxoid (Td) unless otherwise indicated.*

** *One dose of measles vaccine, 1 dose of mumps vaccine, and 1 dose of rubella vaccine. Each antigen reported separately unless otherwise indicated.*

†† *At least 4 doses of poliovirus vaccine.*

§§ *At least 5 doses of DTaP, DT, or Td.*

¶¶ *At least 2 doses of measles, 2 doses of mumps, and 2 doses of rubella vaccines.*

*** *Measles, mumps, and rubella coverage reported for combined measles, mumps, and rubella vaccine (MMR). One dose of MMR unless otherwise indicated.*

††† *Two doses of MMR.*

§§§ *At least 4 doses of DTap, DT, or Td."*

(c) 2002-2003:

The Plaintiff hereby requests that the Court take judicial notice of the CDC-published report entitled:
"Vaccination Coverage Among Children Entering School --- United States, 2002-03 School Year."

Citation: Shaw K, Stanwyck C, McCauley M. CDC MMWR August 22, 2003. 52(33);791-793, accessible at https://www.hsdl.org/?view&did=764457
(last accessed June 9, 2020)
(hereafter "CDC Elementary School Coverage Report 2002-03")

A true and correct copy of the aforesaid report is attached hereto as **Exhibit 26**.

The report states:

"This report presents data regarding vaccination coverage from the 50 states and the District of Columbia (DC) for the 2002–03 school year, which highlight high reporting rates and overall high coverage. Findings indicate that vaccines required by each state and the methods for surveying schools vary."*

and

"For the 2002–03 school year, 49 (96.1%) states submitted vaccination coverage levels for children enrolled in kindergarten and/or first grade. All 49 states reported coverage for ≥3 doses of poliovirus vaccine, ≥1 dose of measles-containing vaccine, ≥1 dose of mumps-containing vaccine, and >1 dose of rubella-containing vaccine (Table 1). For diphtheria and tetanus toxoids and acellular pertussis vaccine, 39 (76.5%) states reported coverage for ≥4 doses, and 10 (19.6%) reported coverage for >3 doses; 39 states also reported coverage for 3 doses of hepatitis B (HepB) vaccine…

A total of 18 states based reports on a census of children entering kindergarten and first grade, 15 states on surveys of >95% of children, and five states on surveys of <50% of children (range: 5.1%–42.2%)."

and includes a table entitled:

"TABLE. Estimated vaccination coverage among children enrolled in kindergarten (K) and first grade, by state and vaccine — United States, 2002–03 school year †."*

whose selected column headings and rows are as follows:

State	Grade §	≥ 3 Polio (%) **	3 DTP/ DTaP/ DT (%) ††	≥ 4 DTP/ DTaP/ DT (%)	Measles (%)§§	Mumps (%)¶¶	Rubella (%)***	3 HepB (%) †††
Total****	—	96.2	95.5	—	95.7	96.1	96.1	96.0

Below the table are the following abbreviation expansions and notes referenced by the table:

"* *For this report, the District of Columbia is included as a state.*

† *Required vaccination dosage among children varied by state. In addition to the states included in this report, several territories reported coverage; detailed reports are available at http://www2.cdc.gov/nip/schoolsurv/schoolrptg.asp*

§ *Coverage estimates are from state and local immunization programs that reported data for children entering kindergarten and/or first grade only.*

¶ *The proportion of eligible children included in the assessment survey.*

** *At least 3 doses of poliovirus vaccine.*

†† Three doses of diphtheria and tetanus toxoids and pertussis vaccine, diphtheria and tetanus toxoids and acellular pertussis vaccine, or tetanus toxoids.

§§ Measles-containing vaccine.

¶¶ Mumps-containing vaccine.

**** Rubella-containing vaccine.*

††† Three doses of hepatitis B vaccine.

***** Weighted average. Calculated by using estimates with ≥1 dose of measles, mumps, and rubella–containing vaccines; ≥3 doses of DTP, DTaP, or DT; and ≥4 doses of DTP, DTaP, or DT.*"

(d) 2003-2004:

The Plaintiff hereby requests that the Court take judicial notice of the CDC-published report entitled:
"Vaccination Coverage Among Children Entering School --- United States, 2003--04 School Year".

Citation: Lyons BH, Stanwyck C. CDC MMWR 2004 Nov 12;53(44):1041-4, accessible at https://www.cdc.gov/mmwr/preview/mmwrhtml/mm5344a4.htm and https://pubmed.ncbi.nlm.nih.gov/15538319/
(last accessed June 9, 2020)
(hereafter "CDC Elementary School Coverage Report 2003-04")

A true and correct copy of the aforesaid report is attached hereto as **Exhibit 27**.

The report states:

> *"To determine the percentage of vaccination coverage among children entering kindergarten, data on vaccination coverage were analyzed from reports submitted to the National Immunization Program by states, the District of Columbia (DC)*, … for the 2003--04 school year. This report summarizes the results of that analysis, which determined that coverage for all vaccines except hepatitis B (HepB) and varicella was reported at >90% in 45 areas."*

and

"For the 2003--04 school year, all states except one submitted reports of vaccination coverage levels for children entering kindergarten. Fifty reports included coverage for poliovirus vaccine, diphtheria and tetanus toxoids and pertussis vaccine, diphtheria and tetanus toxoids and acellular pertussis vaccine, or diphtheria and tetanus toxoids (DTP/DTaP/DT), measles vaccine, and rubella vaccines; 49 reports included coverage for mumps vaccine (Table 1). Coverage for HepB vaccine was included in 43 reports, and coverage for varicella vaccine was included in 33 state reports. DC reported on all of the vaccination coverages. When determining coverage, up-to-date (UTD) status was used rather than number of doses because the doses required to be UTD vary depending on timing of vaccinations, area requirements regarding number of doses, and brand of vaccines."

and

"The number of state reports based on 100% of children entering kindergarten increased …to 22 in 2003--04 (2). In an additional 21 states, coverage was assessed in surveys of >80% of eligible children. In the remaining seven states, coverage was assessed in surveys of <20% of eligible children (range: 0.5%--18.5%)."

and

"Coverage for all vaccines except HepB and varicella was reported at 90%--95% in 16 (31.3%) states and at >95% in 29 (56.9%) states (Table 1). Nationally, coverage was reported at >95% for all vaccines except varicella, for which coverage was 93.3%."

and

"this report is based only on coverage among children entering kindergarten, rather than on a mix of those children and first graders."

includes a table entitled:

"TABLE. Estimated vaccination coverage among children enrolled in kindergarten, by vaccine and state — Annual School Surveillance, United States, 2003–04 school year"*

whose selected column headings and rows are as follows:

State	Polio (%)	DTP/ DTaP / DT (%)§	Measles (%)	Mumps (%)	Rubella (%)	HepB ¶ (%)	Varicella (%)
Colorado	*84.0*	*84.0*	*84.0*	*84.0*	*84.0*	*84.0*	*84.0*
New Hampshire	*95.6*	*89.0*	*89.1*	*87.5*	*89.5*	*89.0*	*86.6*
Pennsylvania	*88.0*	*88.0*	*88.0*	*88.0*	*88.0*	*88.0*	*88.0*
Total	***95.6***	***95.5***	***95.4***	***96.0***	***95.9***	***95.7***	***93.3***

Below the table are the following notes referenced by the table:

*" * Includes District of Columbia.*

§ *Diphtheria and tetanus toxoids and pertussis vaccine, diphtheria and tetanus toxoids and acellular pertussis vaccine, or diphtheria and tetanus toxoids.*

¶ *Hepatitis B vaccine."*

(e) 2005-2006:

The Plaintiff hereby requests that the Court take judicial notice of the CDC-published report entitled:

"Vaccination Coverage Among Children Entering School --- United States, 2005-06 School Year"
Citation: CDC MMWR 2006 Oct 20;55(41):1124-6, accessible at
https://www.cdc.gov/mmwr/preview/mmwrhtml/mm5541a3.htm and
https://pubmed.ncbi.nlm.nih.gov/17060899/
(last accessed June 9, 2020)
(hereafter "CDC Elementary School Coverage Report 2005-06")

A true and correct copy of the aforesaid report is attached hereto as **Exhibit 28**.

The report states:

"For the 2005--06 school year, DC and all states except two (Illinois and Wyoming) submitted reports of vaccination coverage levels for children entering kindergarten. Of these, 49 reports included coverage for polio vaccine, DTP/DTaP/DT vaccine, measles-containing vaccine, and rubella-containing vaccine; 46 reports included coverage for mumps-containing vaccine; 43 reports included coverage for hepatitis B vaccine; and 41 reports included coverage for varicella vaccine (Table 2)."

and

"To determine coverage, state or territory up-to-date status was used rather than number of doses received because the number of doses required to be up-to-date varies depending on timing of vaccinations, area requirements regarding number of doses, and brand of vaccines."

and

"Coverage for the newest recommended vaccine included in the assessment, varicella, was reported as >95% in 29 (57%) states and DC and >90% in 36 (71%) states and DC (Table 1). Coverage for other vaccines was higher, ranging from 31 (61%) states with >95% coverage for measles and hepatitis B vaccines, to 34 (67%) states with >95% coverage for DTP/DTaP/DT vaccine."

and includes a table entitled:

"TABLE 2. Estimated vaccination coverage among children enrolled in kindergarten, by vaccine and state/territory — United States, 2005–06 school year"*

whose selected column headings and selected rows are as follows:

State	Polio (%)§	DTP/ DTaP/DT (%) ¶	Measles (%)**	Mumps (%)††	Rubella (%)§§	HepB (%)¶¶	Varicella (%)***
United States	**95.7**	**95.5**	**95.4**	**95.9**	**95.9**	**96.0**	**96.0**
Delaware	89.7	89.8	87.1	87.1	87.1	90.2	84.8
Pennsylvania	77.6	77.6	77.6	77.6	77.6	77.6	77.6
Washington	90.9	91.1	93.9	95.5	95.5	92.8	-

Below the table are the following notes referenced by the table:

"* *Includes District of Columbia*

§ *Three or more doses of any poliovirus vaccine*

¶ *Four or more doses of any diphtheria and tetanus toxoids and pertussis vaccine, diphtheria and tetanus toxoids and acellular pertussis vaccine, or diphtheria and tetanus toxoids vaccine.*

** *One or more doses of measles-containing vaccine.*

†† *One or more doses of mumps-containing vaccine.*

§§ *One or more doses of rubella-containing vaccine.*

¶¶ *Three or more doses of hepatitis b vaccine.*

*** *One or more doses of varicella vaccine or history of varicella disease."*

(f) 2006-2007:

The Plaintiff hereby requests that the Court take judicial notice of the CDC-published report entitled:

"Vaccination Coverage Among Children in Kindergarten - United States, 2006-07 School Year"

Citation: CDC MMWR 2007 Aug 17;56(32):819-821, accessible at https://www.cdc.gov/mmwr/preview/mmwrhtml/mm5632a3.htm and https://pubmed.ncbi.nlm.nih.gov/17703172/
(last accessed June 9, 2020)
(hereafter "CDC Elementary School Coverage Report 2006-07")

A true and correct copy of the aforesaid report is attached hereto as **Exhibit 29.**

The report states:

> *"To …determine vaccination coverage among children in kindergarten, data were analyzed from reports submitted to CDC by 49 states and the District of Columbia (DC) for the 2006--07 school year (2).* This report summarizes findings from that analysis"*

and

> *"To determine vaccination coverage, up-to-date status was defined by the vaccines and doses required for school entry in each state rather than by the number of doses recommended by ACIP; the number of doses required to be up to date varies by state depending on timing of vaccinations, state and local area requirements regarding number of doses, and vaccine brands used"*

and

> *"For the 2006--07 school year, all states except Nevada submitted reports of vaccination coverage levels for children entering kindergarten. All 49 reporting states and DC assessed vaccination rates in public schools; 44 states also assessed rates in private schools, and six states also assessed rates in home schools"*

and includes a table entitled:

> *"TABLE 2. Estimated vaccination coverage among children enrolled in kindergarten, by vaccine — United States, 2006–07 school year***"**

whose selected column headings and rows are as follows:

State/Area	Polio (%)	DTP/ DTaP/DT † (%)	MMR (%)§	Hepatitis B (%)	Varicella (%)
United States	96.3	96.0	95.6	96.8	96.5

Below the table are the following notes referenced by the table:

"† *Diphtheria and tetanus toxoids and pertussis vaccine, diphtheria and tetanus toxoids and acellular pertussis vaccine, or diphtheria and tetanus toxoids vaccine.*

§ *Measles, mumps, and rubella."*

(g) 2009-2010:

The Plaintiff hereby requests that the Court take judicial notice of the CDC-published report entitled:

"Vaccination Coverage Among Children in Kindergarten - United States, 2006-07 School Year"

Citation: Stokley S, Stanwyck C, Avey R, Greby S. CDC MMWR 2011 June 3, 2011 / 60(21);700-704, accessible at https://www.cdc.gov/mmwr/preview/mmwrhtml/mm6021a4.htm and https://www.cdc.gov/mmwr/pdf/wk/mm6021.pdf online
(last accessed July 26, 2020)
(hereafter "CDC Elementary School Coverage Report 2009-10")

A true and correct copy of the aforesaid report is attached hereto as **Exhibit 30**.

The report states:

> *"This report summarizes data from school assessment surveys submitted to CDC by 48 federal immunization program grantees (including 47 states and the District of Columbia) for the 2009--10 school year to describe vaccination coverage …rates."*

and

> *"The vaccination status of students was considered up-to-date if they had received all of the vaccine doses required for school entry in their state or area. All reporting grantees require 3 or 4 doses of poliovirus vaccine and 2 doses of MMR vaccine. School entry requirements for other vaccinations vary by state/area: 44 grantees require 4 or 5 doses of DTP/DTaP/DT, 41 grantees require 3 doses of HepB vaccine, and 25 grantees require 1 dose and 18 grantees require 2 doses of varicella vaccine"*

and includes a table entitled:

"TABLE 2. Estimated vaccination coverage among children enrolled in kindergarten, by vaccine and state/area --- United States, 2009--10 school year"
whose selected column headings and rows are as follows:

State/Area	Vaccine					
	Polio-virus (%)	DTP/DTaP/DT (%)	MMR (%)	Hepatitis B (%)	Varicella	
					1 dose (%)	2 doses (%)
Alabama	94	94	94	---†	96.8	---†
Arizona	95.5	95	95	96.8	97.5	---†
Arkansas	98	97.5	98.3	98.5	98.3	---†
California	93.6	93.1	93.6	96.1	96.6	---†
Connecticut	98.3	98.5	98.5	98.4	98.4	---†
Delaware	89.4	89.6	89.7	88.9	---†	89
District of	91.2	89.8	96.9	96.3	---†	90.6
Florida	91.3	91.3	91.3	91.3	---†	91.3
Georgia	100	99.9	99.6	100	---†	99.6
Hawaii	95.2	94.8	95	95.1	96.2	---†
Idaho	92.8	86.8	87	93	---†	62.9†
Illinois	95.8	95.6	94.5	---†	96.5	---†
Indiana	92.9	91.1	92.8	95.2	96	---†
Iowa	84.5	84.5	84.5	84.5	---†	84.5
Kansas	97.9	97.1	90.9	97	---†	85.3
Kentucky	94.1	93.2	92.2	93	NA	---†
Louisiana	98.9	98	96.9	98	---†	93.7
Maine	95.4	96.2	95.5	---†	95.9	---†
Maryland	99.8	99.6	98.9	99.7	99.5	---†
Massachusetts	92.9	92.4	93	97.7	98.6	---†
Michigan	96.6	96	95.3	97.3	97.3	---†
Minnesota	94.8	94.3	95.1	96.4	---†	94
Mississippi	99.7	99.7	99.7	99.7	---†	99.7
Missouri	98.1	97.1	97.3	97.4	98.8	---†
Montana	96.9	96.7	95.5	---†	---†	---†
Nebraska	98.7	98.7§	97.5	97.5	97.2	---†
Nevada	98.7	97.9	94.5	98	---†	76.5
New Mexico	99.3	99	97.6	99.1	---†	94.9
New York	98.4	98.3§	97.6	98.3	98.4	---†
North	97.3	97.2	97.3	98.2	98.3	---†
North Dakota	92.2	90.8	92.2	92.6	---†	89.6
Ohio	88.3	87.9	88.6	90.5	91.2	---†
Oklahoma	97.6	97.3	97.3	99.5	99.7	---†
Oregon	94.3	93.9	94.4	95	95.2	---†
Pennsylvania	94.4	90.8	86.9	93.5	NA	79.4**
Rhode Island	90.1	90.3	92.1	92.8	---†	86.9
South	87.7	86.7	87.2	87.6	91	---†
South Dakota	97.8	97.9	96.8	94.7†	---†	97.7
Tennessee	97.4	97.4	97.4	97.4	97.4	---†

Texas	*98.1*	*97.7*	*98.1*	*98.6*	*---†*	*96.8*
Utah	*97.9*	*97.5*	*97.7*	*98.6*	*99.3*	*---†*
Vermont	*92.1*	*91.8*	*91.8*	*94.8*	*---†*	*88.2*
Virginia	*99.1*	*98.4*	*92.1*	*97.6*	*98.3*	*---†*
Washington	*91.8*	*91.6*	*91.7*	*92.8*	*---†*	*88.6*
West Virginia	*91.5*	*91.9*	*91.2*	*92*	*---†*	*88.4*
Wisconsin	*98.2*	*97.3*	*94.2*	*97.4*	*---†*	*90.3*

Below the table are the following notes referenced by the table:

"Abbreviations: DTP = diphtheria and tetanus toxoids and pertussis; DTaP = diphtheria and tetanus toxoids and acellular pertussis; DT = diphtheria and tetanus toxoids; MMR = measles, mumps, and rubella; NA = not available.

† Vaccine not required for school entry.

§ Reported estimate is for 3 doses of DTP/DTaP/DT.

*** State requires 1 dose for school entry but could only report coverage for 2 doses."*

Average or median coverages are not included in the reported data. However, the medians can be determined to be as follows for each vaccination:

State/Area	Vaccine					
	Polio-virus (%)	DTP/DTaP/DT (%)	MMR (%)	Hepatitis B (%)	Varicella	
					1 dose (%)	2 doses (%)
Median	**95.65**	**95.3 §**	**94.75**	**97**	**97.4**	**90.3**

§ Nebraska and New York are excluded from the calculation of the median because the reported estimate of coverage in those states is for only 3 doses of DTP/DTaP/DT.

(h) 2011-2012:

The Plaintiff hereby requests that the Court take judicial notice of the CDC-published report entitled:

"Vaccination Coverage Among Children in Kindergarten — United States, 2011–12 School Year"

Citation: CDC MMWR 2012 Aug 24;61(33):647-652, accessible at https://www.cdc.gov/mmwr/preview/mmwrhtml/mm6133a2.htm and https://www.cdc.gov/mmwr/pdf/wk/mm6133.pdf
(last accessed June 9, 2020)
(hereafter "CDC Elementary School Coverage Report 2011-12")

A true and correct copy of the aforesaid report is attached hereto as **Exhibit 31**.

The report states:

"This report summarizes vaccination coverage, exemption rates, and reporting methods from the 2011–12 school year kindergarten vaccination assessments submitted by 56 grantees, including 49 states, DC, one city, and five other reporting areas. Median coverage with 2 doses of measles, mumps, and rubella (MMR) vaccine was 94.8% among 47 reporting states and DC."

and

"Generally, at the start of the school year, health department or school personnel conduct a vaccination coverage survey or census of enrolled students to determine compliance with school requirements established to protect children from vaccine-preventable diseases."

and

"Vaccination status of kindergarteners was considered up-to-date if they had received all of the vaccine doses required for school entry in their state or area. All reporting grantees required 2 doses of MMR vaccine and 3 or 4 doses of poliovirus vaccine. School entry requirements for other vaccinations varied by grantee: 52 grantees required 4 or 5 doses of DTaP vaccine, 50 grantees required 3 doses of HepB vaccine, and 13 grantees required 1 dose and 37 grantees required 2 doses of varicella vaccine. §"

and

"Overall, among grantees in the 47 states and DC that reported 2011–12 school vaccination coverage, median MMR vaccination coverage was 94.8%, with a range of 86.8% in Colorado to 99.3% in Texas; four jurisdictions of these grantees reported <90% MMR coverage (Table 1). Median coverage with 2 doses of varicella vaccine among 33 grantees reporting was 93.2%, with a range of 84.0% in Colorado to 99.2% in Mississippi and Texas. The median coverage levels for DTaP, poliovirus, and HepB vaccines all were at or above… 95%."

and includes this footnote:

"§ One state (South Dakota) assessed vaccination coverage for 3 doses of HepB vaccine, but HepB vaccination is not a requirement for school entry."

includes a table entitled:

"TABLE 1. Estimated vaccination coverage among children enrolled in kindergarten, by state/area, type of survey conducted, and selected vaccines — United States, 2012–13 school year"*

whose selected column headings and rows are as follows:

State/Area	MMR¶ (%)	DTaP/DT** (%)	Polio (%)	Hepatitis B (%)	Varicella 1 dose (%)	Varicella 2 doses (%)
**Median††††	**94.8**	**95.2**	**95.9**	**96.6**	**97.0**	**93.2**
District of Columbia	94.0	91.1¶¶	93	96.6	—§§	93.5
Hawaii	94.4	93.3¶¶	93.7	94.9	95.7	—††
Idaho	89.2	89.0¶¶	89.6	92.3	—§§	85.8
Indiana	93.3	90.2¶¶	90.4	93.2	—§§	91.9
Iowa	91.1	91.1	91.1	91.1	—§§	91.1
Kansas	88.2	88.0¶¶	96.9	95.8	—§§	85.9
Massachusetts	94.2	92.5¶¶	93.3	97.8	—§§	92.7
Minnesota	95.7	95.5¶¶	95.8	97.5	—§§	94.9
Mississippi	99.2	99.2¶¶	99.2	99.2	—§§	99.2
Nebraska	99.0	99.7***	99.5	99.3	—§§	96.8
New York State	96.9	97.9***	98.4	98.2	98.4	—††
Oklahoma	95.0	94.6¶¶	94.6	97.7	97.8	—††
Oregon	94.0	93.7¶¶	94	94.6	95.0	—††
Pennsylvania	86.9	91.1**	95.5	94.4	—§§	85.1
Rhode Island	91.7	93.4¶¶	92.6	93.1	—§§	91.3
South Dakota	97.4	97.5	97.2	95.4	—§§	95.5 “
Texas	99.3	99.3¶¶	99.3	99.7	—§§	99.2
Washington	91.8	90.9¶¶	91.0	93.0	—§§	90.4
Alabama	93.6	93.6	93.6	—††	93.2	—††
Arizona	94.7	94.9	94.9	96.3	96.9	—††
California	93.2	93.0	93.2	95.7	96.1	—††
Hawaii	94.4	93.3¶¶	93.7	94.9	95.7	—††
Illinois	97.3	96.4	96.2	—††	98.0	—††
Kentucky	92.0	93.7	95.0	93.3	75.7	—††
Maine	93.0	96.6	96.1	—††	94.9	—††
Maryland	98.7	99.6	99.7	99.6	99.7	—††
New York	96.9	97.9***	98.4	98.2	98.4	—††
North Carolina	97.2	97.0	97.3	98.0	98.1	—††
Oklahoma	95.0	94.6¶¶	94.6	97.7	97.8	—††
Oregon	94.0	93.7¶¶	94.0	94.6	95.0	—††
South Carolina	94.5	96.5	96.7	96.6	97.1	—††
Utah	98.0	97.7	98.1	99.1	99.5	—††
				Average where one dose required for varicella:	95.4	

Below the table are the following notes referenced by the table:

** Abbreviation: NA = not available.*

¶ Measles, mumps, and rubella.

*** Diphtheria and tetanus toxoids and acellular pertussis vaccine. DTaP vaccination coverage might include some DTP (diphtheria and tetanus toxoids and pertussis vaccine) or DT (diphtheria and tetanus toxoids) vaccinations if administered in another country or vaccination provider continued to use after 2000. Pertussis vaccine is not required in Pennsylvania; the estimate for Pennsylvania represents DT only.*

†† Vaccine not required for school entry.

§§ Coverage levels for 1 dose of varicella are not presented when coverage for 2 doses of varicella were reported.

¶¶ Reported estimate is for 5 doses of DTaP.

**** Reported estimate is for 3 doses of DTaP.*

†††† The center of the estimates in the distribution. The median is based on estimates for 49 states and the District of Columbia."

(i) 2012-2013:

The Plaintiff hereby requests that the Court take judicial notice of the CDC-published report entitled:

"Vaccination Coverage Among Children in Kindergarten - United States, 2012-13 School Year"

Citation: Seither R, Shaw L, Knighton CL, Greby SM, Stokley S. CDC MMWR 2013 Aug 2;62(30):607-612, accessible at https://www.cdc.gov/mmwr/preview/mmwrhtml/mm6230a3.htm and https://www.cdc.gov/mmwr/pdf/wk/mm6230.pdf
(last accessed June 9, 2020)
(hereafter "CDC Elementary School Coverage Report 2012-13")

A true and correct copy of the aforesaid report is attached hereto as **Exhibit 32**.

The report states:

"This report summarizes vaccination coverage from 48 states and DC and exemption rates from 49 states and DC for children entering kindergarten for the 2012–13 school year. Forty-eight states and DC reported vaccination coverage, with medians of 94.5% for 2 doses of measles, mumps, and rubella (MMR) vaccine; 95.1% for local requirements for diphtheria, tetanus toxoid, and acellular pertussis (DTaP) vaccination; and 93.8% for 2 doses of varicella vaccine among awardees with a 2-dose requirement."

and

"This report describes compliance with state regulations of 3, 4, or 5 doses of DTaP vaccine. Of the 51 awardees, only Nebraska, New York, and Pennsylvania report <4 doses of DTaP vaccine."

and

"Kindergarteners were considered up-to-date for each vaccination if they had received all of the doses required for school entry in their jurisdiction. School entry requirements varied by awardee: all reporting awardees required 2 doses of MMR vaccine; for DTaP vaccine, two awardees required 3 doses, 35 required 4 doses, and 20 required 5 doses; and for varicella vaccine, 13 required 1 dose, 41 required 2 doses, and three did not require varicella vaccination."

and

"Overall, among the 48 states and DC that reported 2012–13 school vaccination coverage, median 2-dose MMR vaccination coverage was 94.5% (range: 85.7% in Colorado to ≥99.9% in Mississippi); 20 reported coverage ≥95% (Table 1). Median DTaP vaccination coverage was 95.1% (range: 82.9% in Colorado and Arkansas to ≥99.9% in Mississippi); 25 reported coverage ≥95%. Median 2-dose varicella vaccination coverage among the 36 states and DC requiring and reporting 2 doses was 93.8% (range: 84.6% in Colorado to ≥99.9% in Mississippi); 14 reported coverage ≥95%."

and includes a table entitled:

"TABLE 1. Estimated vaccination coverage among children enrolled in kindergarten, by state/area, type of survey conducted, and selected vaccines — United States, 2012–13 school year"*

whose selected column headings and rows are as follows:

"State/Area	*MMR§ (%)*	*DTaP/DT¶ (%)*	*Varicella*	
			1 dose (%)	*2 doses (%)*
Median†††	*94.5*	*95.1*	*—*	*93.8"*
*Alabama***	*92.8*	*92.8*	*91.9*	*NReq*
Arizona	*94.5*	*94.6*	*96.8*	*NReq*
*California***	*92.7*	*92.5*	*95.6*	*NReq*
*Hawaii***	*97.3*	*98.0*	*99.3*	*NReq*
Illinois	*95.5*	*94.6*	*96.6*	*NReq*
*Maine***	*91.3*	*95.2*	*95.1*	*NReq*
*Maryland***	*98.2*	*99.4*	*99.6*	*NReq*
*New York***	*96.6*	*98.4*	*98.4*	*NReq*
North Carolina	*97.3*	*97.2*	*98.0*	*NReq*
Oklahoma	*90.5*	*90.2*	*92.8*	*NReq*
Oregon	*93.5*	*93.4*	*94.5*	*NReq*
Utah	*96.3*	*97.8*	*99.6*	*NReq*
Average where one dose required for varicella:			96.5	

Below the table are the following notes referenced by the table:

" Estimates are adjusted for nonresponse and weighted for sampling where appropriate, except where complete data were unavailable. Percentages for Delaware, Georgia, and Puerto Rico are approximations. Estimates for South Carolina and Colorado were provided by the awardee. Estimates based on a completed vaccine series (i.e., not antigen-specific) are designated by use of the ≥ symbol…*

§ Most awardees require 2 doses; California, Illinois, New York, and Oregon require 2 doses of measles, 1 dose of mumps, and 1 dose of rubella.

¶DTaP vaccination coverage might include some DTP (diphtheria and tetanus toxoids and pertussis) or DT vaccinations if administered in another country or vaccination provider continued to use after 2000. Most awardees require 4 doses of DTaP/DT vaccine; 5 doses are required for school entry in Colorado, District of Columbia, Hawaii, Idaho, Iowa, Kansas, Massachusetts, Minnesota, Mississippi, North Carolina, Oregon, Rhode Island, Texas (including Houston), Vermont, Washington, Wyoming, Northern Mariana Islands, and Puerto Rico; 3 doses are required by Nebraska and New York; 4 doses of DT and 2 doses of pertussis vaccine are required by the U.S. Virgin Islands. Pertussis vaccine is not required in Pennsylvania; the estimate for Pennsylvania represents DT only.

††† The median is the center of the estimates in the distribution. The median does not include Alaska, New Hampshire, Houston, Guam, the Commonwealth of the Northern Mariana Islands, Palau, Puerto Rico, and the U.S. Virgin Islands."

(j) 2013-2014:

The Plaintiff hereby requests that the Court take judicial notice of the CDC-published report entitled:

- "Vaccination coverage among children in kindergarten - United States, 2013-14 school year."

  Citation: Seither R, Masalovich S, Knighton CL, et al. CDC MMWR 2014;63(41):913-920, accessible at https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4584748/ and https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4584748/pdf/913-920.pdf (last accessed June 9, 2020)
  (hereafter "CDC Elementary School Coverage Report 2013-14")

  A true and correct copy of the aforesaid report is attached hereto as **Exhibit 33**.

The report states:

"This report describes vaccination coverage in 49 states and the District of Columbia (DC)… for children enrolled in kindergarten during the 2013–14 school year. Median vaccination coverage was 94.7% for 2 doses of measles, mumps, and rubella (MMR) vaccine; 95.0% for varying local requirements for diphtheria, tetanus toxoid, and acellular pertussis (DTaP) vaccine; and 93.3% for 2 doses of varicella vaccine among those states with a 2-dose requirement. The median total exemption rate was 1.8%."

and

"Vaccination requirements for school entry, as reported to CDC by the federally funded immunization programs, varied.[**] Kindergartners were considered up-to-date for any single vaccine if they had received all of the doses of that vaccine required for school entry in their jurisdiction. Nine states considered kindergartners up-to-date only if they had received all of the doses for all vaccines required for school entry in their jurisdiction.[††]"

and

"Among the 49 states and DC that reported 2013–14 school vaccination coverage, median 2-dose MMR vaccination coverage was 94.7% (range = 81.7% in Colorado to ≥99.7% in Mississippi); 23 reported coverage ≥95% (Table 1), and eight reported coverage <90% (Table 1, Figure). Median local requirement for DTaP vaccination coverage was 95.0% (range = 80.9% in Colorado to ≥99.7% in Mississippi); 25 reported coverage ≥95%. Median 2-dose varicella vaccination coverage among the 36 states and DC requiring and reporting 2 doses was 93.3% (range = 81.7% in Colorado to ≥99.7% in Mississippi); nine reported coverage ≥95% "

and these two footnotes:

"This report describes compliance with state regulations of 3, 4, or 5 doses of DTaP vaccine. Of the 49 states and DC, only Nebraska, New York, and Pennsylvania report <4 doses of DTaP vaccine. IID-10.2 sets a target of 95% of kindergartners receiving ≥2 doses of MMR vaccine. IID-10.5 sets a target of 95% of kindergartners receiving ≥2 doses of varicella vaccine."

and

"Among the 49 reporting states and DC, all programs required 2 doses of a measles-containing vaccine, of which MMR is the only one available in the United States. For local requirements for DTaP vaccine, two required 3 doses, 27 required 4 doses, 20 required 5 doses, and one state did not require pertussis. For varicella vaccine, 13 required 1 dose, 36 required 2 doses, and 1 did not require varicella vaccination"

and a table entitled:

"TABLE 1. Estimated vaccination coverage, among children enrolled in kindergarten, by state/area, type of survey conducted, and selected vaccines — United States, 2013–14 school year"*

whose selected column headings and rows are as follows:

State/Area	MMR§ (%)	DTaP/DT¶ (%)	Varicella	
			1 dose (%)	2 doses (%)
Median†††	**94.7**	**95.0**	**96.6**	**93.3**
California¶¶	92.3	92.2	95.3	NReq
Kansas§§¶¶	86.9	87.6		85.5
Maryland¶¶	97.6	99.0	99.0	NReq
Minnesota¶¶	93.4	96.6		92.6
Nebraska¶¶	96.6	96.8		94.9
New Mexico¶¶	95.9	97.4		93.4
Washington	89.7	90.3		88.4
Wisconsin¶¶	92.6	96.3		91.2
Pennsylvania††¶¶	85.3	NReq†††		84.0"

Below the table are the following notes referenced by the table:

*"**Abbreviations:** MMR = measles, mumps, and rubella vaccine; DTaP = diphtheria and tetanus toxoids and acellular pertussis vaccine; NA = not available; NReq = not required for school entry.*

** Estimates are adjusted for nonresponse and weighted for sampling where appropriate, except where complete data were unavailable. Percentages for Delaware, Houston, Virginia, and Puerto Rico are approximations. Estimates based on a completed vaccine series (i.e., not antigen-specific) are designated by use of the ≥ symbol….*

¶ Most states require 2 doses; Alaska, California, New York, and Oregon require 2 doses of measles, 1 dose of mumps, and 1 dose of rubella vaccine.

*** Pertussis vaccination coverage might include some DTP (diphtheria and tetanus toxoids and pertussis vaccine) vaccinations if administered in another country or if a vaccination provider continued to use DTP after 2000. Most states require 4 doses of DTaP vaccine; 5 doses are required for school entry in Colorado, District of Columbia, Hawaii, Idaho, Indiana, Iowa, Kansas, Massachusetts, Minnesota, New Jersey, New Mexico, North Carolina, North Dakota, Oregon, Rhode Island, Tennessee, Texas, Utah, Vermont, Washington, Northern Mariana Islands, Puerto Rico, and U.S. Virgin Islands; 3 doses are required by Nebraska and New York. Pertussis vaccine is not required in Pennsylvania. ..*

¶¶ Counts the vaccine doses received regardless of Advisory Committee on Immunization Practices recommended age and time interval; vaccination coverage rates shown might be higher than those for valid doses.

**** Does not include non-district-specific, virtual, and college laboratory schools, or private schools with fewer than 10 students.*

††† Pertussis is not required in Pennsylvania; coverage for diphtheria and tetanus was 88.3%.

§§§ The median is the center of the estimates in the distribution. The median does not include Houston, Guam, the Commonwealth of the Northern Mariana Islands, Puerto Rico, and the U.S. Virgin Islands."

(k) 2014-2015:

The Plaintiff hereby requests that the Court take judicial notice of the CDC-published report entitled:

"Vaccination coverage among children in kindergarten - United States, 2014-15 school year."

Citation: Seither R, Masalovich S, Knighton CL, et al. CDC MMWR 2015 Aug 28;64(33);897-904, accessible at https://www.cdc.gov/mmwr/preview/mmwrhtml/mm6433a2.htm and https://www.cdc.gov/mmwr/pdf/wk/mm6433.pdf
(last accessed June 9, 2020)
(hereafter "CDC Elementary School Coverage Report 2014-15")

A true and correct copy of the aforesaid report is attached hereto as **Exhibit 34**.

The report states:

"This report describes vaccination coverage estimates in 49 states and the District of Columbia (DC) and vaccination exemption estimates in 46 states and DC that reported the number of children with at least one exemption among kindergartners during the 2014–15 school year."

and

"State and local vaccination requirements for school entry varied.¶¶¶ Kindergartners were considered up-to-date for any vaccine if they received all doses required for school entry in their residence jurisdiction. In most jurisdictions, kindergartners with a ***history of varicella disease*** *are considered to be vaccinated against varicella, whereas in some jurisdictions they may be given a medical exemption. Eight states considered kindergartners up-to-date only if they had received all doses of all vaccines required for school entry in their jurisdiction.**** Coverage estimates were based on completed vaccination series in those jurisdictions."*

and

"Among the 49 reporting states and DC, median reported MMR coverage was 94.0% (range = 86.9% [Colorado] to 99.2% [Mississippi]); 17 areas reported MMR coverage ≥95%; and seven reported MMR coverage <90% (Table 1). Median reported DTaP coverage was 94.2% (range = 84.3% [Colorado] to 99.6% [Maryland]); 21 areas reported coverage ≥95%. Among the 39 states and DC requiring and reporting 2-dose varicella vaccination coverage, median reported coverage was 93.6% (range = 85.4% [Colorado] to 99.2% [Mississippi]); 17 areas reported coverage ≥95%"

and includes the following footnotes:

"§§§ …This report describes compliance with state regulations of 3, 4, or 5 doses of DTaP vaccine. Of the 50 states and DC, only Nebraska required and reported 3 doses of DTaP vaccine. IID-10.2 sets a target of ≥95% of kindergartners receiving ≥2 doses of MMR vaccine. Four states required 2 doses of measles-containing vaccine, but only 1 dose each of mumps and rubella vaccine. One state required 2 doses measles and mumps, but only 1 dose of rubella vaccine. One state required only 1 dose of MMR vaccine until age 7 years."

and

"¶¶¶ Among the 50 states and DC, all but New York State required 2 doses of a measles-containing vaccine, with MMR as the only measles-containing vaccine available in the United States. For local requirements for DTaP vaccine, one (Nebraska) required 3 doses, one (Virginia) required 4 doses, one (Pennsylvania) did not require pertussis, and all others required 5 doses unless the fourth dose was administered on or after the fourth birthday. For varicella vaccine, 10 areas required 1 dose, 40 required 2 doses, and one (Montana) did not require varicella vaccination"

and includes a table entitled:

"TABLE 1. Estimated vaccination coverage by state/area, vaccine, and survey methodology among children enrolled in kindergarten — United States, 2014–15 school year"*

whose selected column headings and rows are as follows:

State/Area	***MMR ¶ 2 doses (%)***	***DTaP** 5 doses (%)***	***Varicella 2 doses (%)***
Median ***	***94.0***	***94.2***	***93.6***
Arkansas§§	*88.4*	*85.6*	*88.0*
California§§	*92.6*	*92.4*	*NReq*
Florida††¶¶	*≥93.3*	*≥93.3*	*≥93.3*
Kentucky§§	*92.7*	*94.4*	*92.3*
Maine§§	*92.1*	*95.4*	*NReq*
Maryland§§	*99.1*	*99.6*	*98.8*
Massachusetts††§§	*94.7*	*92.9*	*94.1*
Nebraska††§§	*96.0*	*96.4*	*95.8*
New Jersey§§	*≥92.3*	*≥92.3*	*NReq*
New York State††§§	*98.2*	*97.5*	*96.4*
Oklahoma§§	*90.3*	*90.0*	*NReq*
Oregon†† §§	*94.1*	*93.8*	*NReq*
Pennsylvania§§	*91.7*	*NReq***	*92.0*
Rhode Island§§	*95.7*	*96.1*	*95.4*
Texas§§†††	*97.4*	*97.2*	*97.0*
Wyoming§§§	*96.8*	*96.7*	*96.5*
Kansas§§¶¶¶	*89.2*	*89.6*	*88.9*
Wisconsin§§	*91.6*	*96.5*	*90.9*

Below the table are the following notes referenced by the table:

*"**Abbreviations:** MMR = measles, mumps, and rubella vaccine; DTaP/DT = diphtheria, tetanus, and acellular pertussis vaccine/diphtheria and tetanus vaccine; NA = not available; NReq = not required for school entry.*

** Estimates are adjusted for nonresponse and weighted for sampling where appropriate. Percentages for Houston are approximations. Estimates based on a completed vaccine series (i.e., not antigen-specific) are designated by use of the ≥ symbol. Coverage may include history of disease and laboratory evidence of immunity….*

¶ Most states require 2 doses of MMR vaccine; Alaska, California, and Oregon require 2 doses of measles, 1 dose of mumps, and 1 dose of rubella vaccine. Pennsylvania requires 2 doses of measles and mumps, and 1 dose of rubella vaccine. New York requires 2 doses of measles and mumps vaccine and 1 dose of rubella vaccine by age 7 years but reports ≥1 dose of MMR.

*** Pertussis vaccination coverage might include some DTP (diphtheria, tetanus, and pertussis vaccine) vaccinations if administered in another country or vaccination provider continued to use after 2000. Most states require 5 doses of DTaP vaccine for school entry; Virginia requires 4 doses; Nebraska requires 3 doses. Pennsylvania requires 4 doses of diphtheria and tetanus vaccine, but pertussis vaccine is not required. Kentucky requires ≥5 but reports ≥4 doses of DTaP…*

**** Pertussis vaccine is not required in Pennsylvania. Coverage for diphtheria and tetanus was 93.9%.*

***** The median is the center of the estimates in the distribution. The median does not include Hawaii, Houston, New York City, Guam, the Commonwealth of the Northern Mariana Islands, Puerto Rico, and the U.S. Virgin Islands. Hawaii reported the number of children compliant with school vaccination requirements, either by being vaccinated or by having an exemption."*

(l) 2015-2016:

The Plaintiff hereby requests that the Court take judicial notice of the CDC-published report entitled:

"Vaccination Coverage Among Children in Kindergarten — United States, 2015–16 School Year."

Citation: Seither R, Calhoun K, Mellerson J, et al. CDC MMWR 2016;65:1057–1064. DOI: http://dx.doi.org/10.15585/mmwr.mm6539a3, accessible at https://www.cdc.gov/mmwr/volumes/65/wr/mm6539a3.htm (html) and https://www.cdc.gov/mmwr/volumes/65/wr/pdfs/mm6539a3.pdf (pdf)
(last accessed June 9, 2020)
(hereafter "CDC Elementary School Coverage Report 2015-16")

A true and correct copy of the aforesaid report is attached hereto as **Exhibit 35**.

The report states:

> *"This report describes vaccination coverage estimates in all 50 states and the District of Columbia (DC), and the estimated number of kindergartners with at least one vaccine exemption in 47 states and DC, during the 2015–16 school year."*

and

> *"Kindergartners were considered up-to-date for a vaccine if they received all doses required for school entry,[††] except in seven states[§§] that considered kindergartners up-to-date only if they had received all doses of all vaccines required for school entry. Kindergartners with a history of varicella disease were reported as either vaccinated against varicella or medically exempt, varying by program."*

and

"Among the 50 states and DC, median MMR coverage was 94.6% (range = 87.1% [Colorado] to 99.4% [Maryland and Mississippi]); 22 states reported coverage ≥95%, and three states and DC reported coverage <90% (Table 1). Among 49 states and DC that require DTaP vaccination, median coverage was 94.2% (range = 86.6% [Colorado] to 99.6% [Maryland]); 20 states reported coverage ≥95%, and four states and DC reported coverage <90%. Among 42 states and DC that required 2-dose varicella vaccination, median coverage was 94.3% (range = 85.7% [Colorado] to 99.4% [Mississippi]); 18 states reported coverage ≥95%, and five states and DC reported coverage <90%. The number of states requiring 2 doses of varicella vaccine for school entry increased from 39 in 2014–15 to 42 in 2015–16. Median 2-dose varicella coverage increased from 93.6% to 94.3%, in part because of high coverage in three states that added a requirement for 2 doses of varicella vaccine (Montana [93.6%]; North Carolina [97.0%]; and Utah [94.8%])."

and includes the following footnotes:

"†† All the 50 states and DC required 2 doses of a measles-containing vaccine, with MMR as the only measles-containing vaccine available in the United States. For local DTaP vaccine requirements, Nebraska required 3 doses, four states (Illinois, Pennsylvania, Virginia, and Wisconsin) required 4 doses, Pennsylvania did not require pertussis, and all other states required 5 doses unless the fourth dose was administered on or after the fourth birthday. Kentucky required 5 doses of DTaP by age 5, but reported 4-dose coverage for kindergartners. For varicella vaccine, eight states required 1 dose and 42 states and DC required 2 doses."

and

"§§ Alabama, Florida, Georgia, Iowa, Mississippi, New Hampshire, and New Jersey considered kindergartners up-to-date only if they had received all doses of all vaccines required for school entry."

and

"[¶¶¶] ...This report describes compliance with state requirements of 3, 4, or 5 doses of DTaP vaccine. Among the 50 states and DC, only Nebraska required and reported 3 doses of DTaP vaccine. …Four states required 2 doses of measles-containing vaccine but only 1 dose each of mumps and rubella vaccine. Four states required 2 doses measles and mumps but only 1 dose of rubella vaccine. One state required 2 doses of measles and rubella and zero doses of mumps."

and includes a table entitled:

"TABLE 1. Estimated vaccination coverage by state/area, vaccine, and survey methodology among children enrolled in kindergarten — United States, 2015–16 school year"*

whose selected column headings and rows are as follows:

State/Area	***MMR¶ 2 doses (%)***	***DTaP** 5 doses (%)***	***Varicella 1 dose (%)***	***2 doses (%)***
Median††	***94.6***	***94.2***	***96.1***	***94.3***
Alabama§§	*=93.1*	*=93.1*	*=93.1*	*NReq*
*Alaska¶¶,****	*93.5*	*92.8*	*NReq*	*92.6*
Florida§§,¶¶	*=93.7*	*=93.7*	*NReq*	*=93.7*
Iowa§§	*=91.8*	*=91.8*	*NReq*	*=91.8*
*Kansas¶¶,***,†††*	*89.4*	*89.4*	*NReq*	*87.9*
Kentucky¶¶,†††	*92.2*	*93.9*	*NReq*	*91.6*
Maryland†††	*99.4*	*99.6*	*NReq*	*99.2*
Massachusetts§§,†††	*96.4*	*94.9*	*NReq*	*95.8*
Minnesota¶¶	*92.8*	*93.0*	*NReq*	*92.3*
Mississippi§§	*=99.4*	*=99.4*	*NReq*	*=99.4*
Missouri§§,¶¶	*95.7*	*95.6*	*NReq*	*95.4*
Nebraska§§,†††	*95.6*	*96.8*	*NReq*	*97.3*
New Hampshire	*=91.9*	*=91.9*	*NReq*	*=91.9*
New Jersey§§	*=96.3*	*=96.3*	*=96.3*	*NReq*
North Carolina¶¶,†††	*97.3*	*97.1*	*NReq*	*97.0*
Oklahoma†††	*94.4*	*96.1*	*NA*	*NReq*
Oregon§§,†††	*93.9*	*93.5*	*95.2*	*NReq*
Pennsylvania	*95.5*	*NReq§§§*	*NReq*	*96.5*
Rhode Island§§,¶¶,†††	*96.4*	*96.8*	*NReq*	*96.0*
Tennessee§§,¶¶	*93.5*	*93.5*	*NReq*	*93.5*
Texas (including Houston)¶¶,†††	*97.6*	*97.4*	*NReq*	*97.2*
*Virginia¶¶,****	*95.7*	*98.3*	*NReq*	*93.7*
Washington¶¶	*91.0*	*91.1*	*NReq*	*89.4*
Wisconsin¶¶,†††	*93.2*	*96.9*	*NReq*	*92.5*
Wyoming¶¶	*96.9*	*96.6*	*NReq*	*96.5*

Below the table are the following abbreviation expansions:

> *"**Abbreviations:** DTaP/DT = diphtheria and tetanus toxoids (DT) and acellular pertussis vaccine; MMR = measles, mumps, and rubella vaccine; NA = not available (i.e., not collected or reported to CDC); NReq = not required for school entry."*

and the following notes referenced by the table:

> *"* Estimates are adjusted for nonresponse and weighted for sampling where appropriate. Estimates based on a completed vaccine series (i.e., not antigen-specific) are designated by use of the = symbol. (These have not affected median.) Coverage might include history of disease and laboratory evidence of immunity.*
>
> *¶ Most states required 2 doses of MMR; Alaska, California, New Jersey, and Oregon required 2 doses of measles, 1 dose of mumps, and 1 dose of rubella vaccines. Georgia, New York, New York City, North Carolina, Pennsylvania, and Virginia required 2 doses of measles and mumps, 1 dose of rubella vaccines. Iowa required 2 doses of measles and 2 doses of rubella vaccines.*
>
> *** Pertussis vaccination coverage might include some DTP (diphtheria and tetanus toxoids and pertussis vaccine) vaccinations if administered in another country or vaccination provider continued to use after 2000. Most states required 5 doses of DTaP vaccine for school entry; Illinois, Virginia, and Wisconsin required 4 doses; Nebraska required 3 doses. Pennsylvania required 4 doses of diphtheria and tetanus vaccine, but pertussis vaccine was not required. Kentucky required =5 but reported =4 doses of DTaP.*
>
> *†† Median calculated from data from the 50 states and the District of Columbia (i.e., does not include Houston, New York City, Guam, N. Mariana Islands, Puerto Rico, or U.S. Virgin Islands)…*
>
> *§§§ Pertussis vaccine was not required in Pennsylvania. Coverage for diphtheria and tetanus was 96.3%."*

(m) 2016-2017:

The Plaintiff hereby requests that the Court take judicial notice of the CDC-published report entitled:

"Vaccination Coverage for Selected Vaccines, Exemption Rates, and Provisional Enrollment Among Children in Kindergarten - United States, 2016-17 School Year."

Citation: Seither, Ranee et al. CDC MMWR. *V*ol. 66,40 1073-1080. 13 Oct. 2017, doi:10.15585/mmwr.mm6640a3, accessible at https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5657930/ (html) and https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5657930/pdf/mm6640a3.pdf (last accessed June 9, 2020)
(hereafter "CDC Elementary School Coverage Report 2016-17")

A true and correct copy of the aforesaid report is attached hereto as **Exhibit 36**.

The report states:

> *"This report summarizes 2016–17 school year MMR, DTaP, and varicella vaccination coverage reported by immunization programs in 49 states, exemptions in 50 states, and kindergartners provisionally enrolled or within a grace period in 27 states."*

and

> *"Kindergartners were considered up-to-date and included in the coverage estimate for a given vaccine if they received all doses required for school entry,§§ except in seven states¶¶ that considered kindergartners up-to-date only if they had received all doses of all vaccines required for school entry in those states. Kindergartners with a history of varicella disease were reported as either vaccinated against varicella or medically exempt, varying by immunization program."*

and

"Since the 2011–12 school year, median kindergarten MMR vaccination coverage has remained near 95%... Among the 49 states included in this analysis, median MMR coverage was 94.0% (range = 85.6% [DC] to 99.4% [Mississippi]); 20 states reported coverage ≥95%; and six states (Alaska, Colorado, Idaho, Indiana, Kansas, and DC) reported cover-age <90% (Table 1). Among the 48 states that required and reported DTaP vaccination, median coverage was 94.5% (range = 82.2% [DC] to 99.6% [Maryland]); 23 states reported coverage ≥95% and six states (Alaska, Arkansas, Colorado, Idaho, Kansas, and DC) reported coverage <90%. Among the 42 states that required and reported 2 doses of varicella vaccine, median coverage was 93.8% (range = 84.6% [DC] to 99.4% [Mississippi]); 15 states reported coverage ≥95%, and seven states (Alaska, Colorado, Idaho, Indiana, Kansas, Washington, and DC) reported coverage <90%."

and includes the following footnotes:

"† Median vaccination coverage was determined using estimates for 49 states; Oklahoma and Wyoming did not report data because of widespread problems with the quality of data reported by schools."

and

"§§All 50 states and DC required 2 doses of a measles-containing vaccine; MMR is the only measles-containing vaccine available in the United States. Local DTaP requirements varied. Nebraska required 3 doses, four states (Illinois, Maryland, Virginia, and Wisconsin) required 4 doses, Pennsylvania did not require pertussis vaccination, and all other states required 5 doses, unless the fourth dose was administered on or after the fourth birthday. The reported coverage estimates represent the percentage of kindergartners with the state-required number of DTaP doses, except for Kentucky, which required 5 doses of DTaP by age 5 years, but reported 4-dose coverage for kindergartners. Eight states required 1 dose of varicella vaccine and 42 states and DC required 2 doses."

and:

"¶¶Alabama, Florida, Georgia, Iowa, Mississippi, New Hampshire, and New Jersey considered kindergartners up-to-date only if they had received all doses of all vaccines required for school entry."

and includes a table entitled:

"TABLE 1. Estimated vaccination coverage for MMR, DTaP, and varicella vaccines among children enrolled in kindergarten, by vaccine and immunization program — United States and territories, 2016–2017 school year"*

whose selected column headings and rows are as follows:

	MMR**	DTaP††	Varicella	
Immunization program	**2 doses**	**5 doses**	**1 dose**	**2 doses**
Median§§	**94.0**	**94.5**	**96.5**	**93.8**
Alabama¶¶	≥93.8	≥93.8	≥93.8	NReq
Alaska***,†††	89.0	89.1	NA	88.9
Arizona¶¶	94.0	93.9	96.7	NReq
Arkansas§§§	91.9	89.2	NA	91.7
California§§§	97.3	96.9	98.5	NReq
Florida¶¶,***	≥94.1	≥94.1	NA	≥94.1
Georgia¶¶	≥93.3	≥93.3	NA	≥93.3
Iowa¶¶	≥92.6	≥92.6	NA	≥92.6
Kansas***,†††,§§§	89.5	88.7	NA	88.8
Kentucky***,§§§	90.8	92.5	NA	90.4
Maryland§§§	99.3	99.6	NA	99.0
Massachusetts¶¶,§§§	96.1	96.1	NA	95.7
Minnesota***	92.8	93.2	NA	92.3
Mississippi¶¶	≥99.4	≥99.4	NA	≥99.4
Nebraska¶¶,§§§,¶¶¶	96.7	97.2	NA	95.8
New Hampshire¶¶	≥91.5	≥91.5	NA	≥91.5
New Jersey¶¶	≥96.5	≥96.5	≥96.5	NReq
North Carolina***,§§§	96.2	96.1	NA	95.9
Oklahoma§§§,****	NA	NA	NA	NReq
Oregon¶¶,§§§	93.8	93.2	95.0	NReq
Pennsylvania	93.6	NReq††††	NA	94.6
Rhode Island***,§§§	95.1	95.6	NA	94.8
Tennessee¶¶,***	96.9	96.8	NA	96.7
Texas (including Houston)***,§§§	97.3	97.2	NA	96.6
Washington***	90.5	90.8	NA	89.3
West Virginia***	95.9	95.7	NA	92.6
Wisconsin***,†††,§§§	94.0	96.6	NA	92.8

Below the table are the following abbreviation expansions:

"Abbreviations: DTaP = diphtheria, tetanus, and acellular pertussis vaccine; MMR = measles, mumps, and rubella vaccine; NA = not available (i.e., not collected or reported to CDC); NReq = not required for school entry."

and the following notes referenced by the table:

"…Estimates based on a completed vaccination series (i.e., not vaccine specific) use the "≥" symbol. Coverage might include history of disease or laboratory evidence of immunity…*

*** MMR is the only measles containing vaccine available in the United States. Most states require 2 doses of MMR; Alaska, New Jersey, and Oregon require 2 doses of measles, 1 dose of mumps, and 1 dose of rubella vaccines. Georgia, New York, New York City, North Carolina, Pennsylvania, and Virginia require 2 doses of measles and mumps, 1 dose of rubella vaccines. Iowa requires 2 doses of measles and 2 doses of rubella vaccines.*

†† Pertussis vaccination coverage might include some diphtheria, tetanus toxoids, and pertussis vaccine (DTP) vaccinations if administered in another country or by a vaccination provider who continued to use DTP after 2000. Most states require 5 doses of DTaP for school entry; Illinois, Maryland, Virginia, and Wisconsin require 4 doses; Nebraska requires 3 doses. Pennsylvania does not require pertussis vaccine. The reported coverage estimates represent the percentage of kindergartners with the state-required number of DTaP doses, except for Kentucky, which requires ≥5 but reports ≥4 doses of DTaP…

§§ Median calculated from data from 48 states and the District of Columbia (i.e., does not include Oklahoma, Wyoming, Houston, New York City, Guam, Marshall Islands, Federated States of Micronesia, N. Mariana Islands, Palau, Puerto Rico, or U.S. Virgin Islands). Coverage data were reported for 3,973,172 kindergartners.…

†††† Pertussis vaccine is not required in Pennsylvania. Coverage for tetanus and diphtheria toxoids was 94.8%."

(n) 2017-2018:

The Plaintiff hereby requests that the Court take judicial notice of the CDC-published report entitled:

"Vaccination Coverage for Selected Vaccines and Exemption Rates Among Children in Kindergarten — United States, 2017–18 School Year."

Citation: Mellerson JL, Maxwell CB, Knighton CL, Kriss JL, Seither R, Black CL. CDC MMWR 2018;67:1115–1122. DOI: http://dx.doi.org/10.15585/mmwr.mm6740a3external icon, accessible at https://www.cdc.gov/mmwr/volumes/67/wr/mm6740a3.htm (html) and https://www.cdc.gov/mmwr/volumes/67/wr/pdfs/mm6740a3-H.pdf (last accessed June 9, 2020)
(hereafter "CDC Elementary School Coverage Report 2017-18")

A true and correct copy of the aforesaid report is attached hereto as **Exhibit 37**.

The report states:

> "*This report summarizes vaccination coverage and exemption estimates collected by state and local immunization programs* for children in kindergarten (kindergartners) in 49 states and the District of Columbia (DC) ….Median vaccination coverage† was 95.1% for the state-required number of doses of diphtheria and tetanus toxoids, and acellular pertussis vaccine (DTaP); 94.3% for 2 doses of measles, mumps, and rubella vaccine (MMR); and 93.8% for 2 doses of varicella vaccine*"

and

> "*Among the 49 states and DC included in this analysis, median 2-dose MMR coverage was 94.3% (range = 81.3% [DC] to ≥99.4% [Mississippi]), 23 states reported coverage ≥95%, and three states and DC reported coverage <90% (Table 1). Median DTaP coverage was 95.1% (range = 79.7% [DC] to ≥99.4% [Mississippi]), 25 states reported coverage ≥95%, and three states and DC reported coverage <90%. Among the 41 states and DC that required and reported 2 doses of varicella vaccine, median coverage was 93.8% (range = 80.5% [DC] to ≥99.4% [Mississippi]), 17 states reported coverage ≥95%, and four states and DC reported coverage <90%."*

and

"Reporting of varicella vaccination status among kindergartners with a history of varicella disease varied within and among states; some were reported as vaccinated against varicella and others as medically exempt."

and includes the following footnotes:

"†Median vaccination coverage was determined using estimates for 49 states and DC; Wyoming did not report data because of problems with the quality of data reported by schools. Data from cities were included with their state data. Data from territories were not included in median calculation."

and

*"***All 49 reporting states and DC required 2 doses of a measles-containing vaccine. Local DTaP requirements varied. Nebraska required 3 doses, four states (Illinois, Maryland, Virginia, and Wisconsin) required 4 doses, and all other states required 5 doses, unless the fourth dose was administered on or after the fourth birthday. The reported coverage estimates represent the percentage of kindergartners with the state-required number of DTaP doses, except for Kentucky, which required 5 doses of DTaP by age 5 years, but reported 4-dose coverage for kindergartners. Nine states required 1 dose of varicella vaccine; 41 states and DC required 2 doses"*

and:

"†††Alabama, Florida, Georgia, Iowa, Mississippi, New Hampshire, and New Jersey considered kindergartners up to date only if they had received all doses of all vaccines required for school entry."

and includes a table entitled:

"TABLE 1. Estimated vaccination coverage for MMR, DTaP, and varicella vaccines among children enrolled in kindergarten, by vaccine and immunization program — United States and territories, 2017–18 school year."*

whose selected column headings and rows are as follows:

Immunization program	MMR**	DTaP††	Varicella	
	2 doses	5 doses	1 dose	2 doses
Median§§	**94.3**	**95.1**	**96.2**	**93.8**
Alabama¶¶	≥92.7	≥92.7	≥92.7	NReq
Alaska***,†††	91.6	91.1	NA	91.3
Arkansas§§§	91.9	91.3	NA	91.6
California§§§	96.9	96.4	98.2	NReq
Florida¶¶,***	≥93.7	≥93.7	NA	≥93.7
Georgia¶¶	≥93.4	≥93.4	NA	≥93.4
Iowa¶¶	≥93.0	≥93.0	NA	≥93.0
Kansas***,†††,§§§	89.1	89.5	NA	88.3
Kentucky***,§§§	92.6	93.7	NA	91.7
Maryland§§§	98.6	99.0	NA	98.6
Massachusetts¶¶,§§§	96.3	96.4	NA	96.0
Minnesota***	92.5	92.8	NA	92.2
Mississippi¶¶	≥99.4	≥99.4	NA	≥99.4
Nebraska§§§	96.2	96.7	NA	95.5
New Hampshire	≥92.4	≥92.4	NA	≥92.4
New Jersey¶¶	≥96.1	≥96.1	≥96.1	NReq
North Carolina***,§§§	97.0	96.8	NA	96.8
Oklahoma***	92.6	93.9	96.8	NReq
Oregon¶¶,§§§	93.2	92.4	94.4	NReq
Rhode Island¶¶,***,§§§	96.4	96.2	NA	96.0
Tennessee¶¶,***	96.9	96.7	NA	96.8
Virginia†††	95.5	98.2	NA	93.3
Washington***	90.6	90.7	NA	89.4
West Virginia****	98.4	98.0	NA	98.1
Wisconsin***,†††,§§§	91.8	96.5	NA	91.2

Below the table are the following abbreviation expansions:

*"**Abbreviations:** DTaP/DT = diphtheria and tetanus toxoids (DT) and acellular pertussis vaccine; MMR = measles, mumps, and rubella vaccine; NA = not available; NReq = not required for school entry."*

** Estimates are adjusted for nonresponse and weighted for sampling where appropriate. Estimates based on a completed vaccine series (i.e., not vaccine-specific) use the "≥" symbol. Coverage might include history of disease or laboratory evidence of immunity…*

*** Most states require 2 doses of MMR; Alaska, New Jersey, and Oregon require 2 doses of measles, 1 dose of mumps, and 1 dose of rubella vaccines. Georgia, New York, New York City, North Carolina, and Virginia require 2 doses of measles and mumps and 1 dose of rubella vaccines. Iowa requires 2 doses of measles and 2 doses of rubella vaccines.*

†† …Most states require 5 doses of DTaP for school entry, or 4 doses if the fourth dose was received on or after the fourth birthday; Illinois, Maryland, Virginia, and Wisconsin require 4 doses; Nebraska requires 3 doses. The reported coverage estimates represent the percentage of kindergartners with the state-required number of DTaP doses, except for Kentucky, which requires ≥5 but reports ≥4 doses of DTaP.

§§ Medians calculated from data from 49 states and the District of Columbia …Coverage data were reported for 3,988,127 kindergartners…."

(o) 2018-2019:

The Plaintiff hereby requests that the Court take judicial notice of the CDC-published report entitled:

"Vaccination Coverage for Selected Vaccines and Exemption Rates Among Children in Kindergarten — United States, 2018–19 School Year."

Citation: Seither R, Loretan C, Driver K, Mellerson JL, Knighton CL, Black CL. Vaccination Coverage with Selected Vaccines and Exemption Rates Among Children in Kindergarten — United States, 2018–19 School Year. CDC MMWR 2019;68:905–912. DOI: http://dx.doi.org/10.15585/mmwr.mm6841e1, accessible at https://www.cdc.gov/mmwr/volumes/68/wr/mm6841e1.htm (html) and https://www.cdc.gov/mmwr/volumes/68/wr/pdfs/mm6841e1-H.pdf
(last accessed September 9, 2020)
(hereafter "CDC Elementary School Coverage Report 2018-19")

A true and correct copy of the aforesaid report is attached hereto as **Exhibit 38**.

The report states:

"*This report summarizes data collected by state and local immunization programs* on vaccination coverage among children in kindergarten in 49 states, exemptions for kindergartners in 50 states, and provisional enrollment and grace period status for kindergartners in 30 states. Nationally, vaccination coverage† was 94.9% for the state-required number of doses of diphtheria and tetanus toxoids, and acellular pertussis vaccine (DTaP); 94.7% for 2 doses of measles, mumps, and rubella vaccine (MMR); and 94.8% for the state-required doses of varicella vaccine*"

and

"*Nationally, 2-dose MMR coverage was 94.7% (range = 87.4% [Colorado] to ≥99.2% [Mississippi]). Coverage of ≥95% was reported by 20 states and coverage of <90% by two (Table). DTaP coverage was 94.9% (range = 88.8% [Idaho] to ≥99.2% [Mississippi]). Coverage of ≥95% was reported by 21 states, and coverage of <90% by one. Varicella vaccine coverage was 94.8% (range=86.5% [Colorado] to ≥99.2% [Mississippi]), with 20 states reporting coverage ≥95%, and four reporting <90% coverage."*

and includes the following footnotes:

"† National and median vaccination coverage was determined using estimates for 49 states; Alaska and DC did not report school coverage data."

and

"¶¶ All states required 2 doses of a measles-containing vaccine. Local DTaP requirements varied. Nebraska required 3 doses, four states (Illinois, Maryland, Virginia, and Wisconsin) required 4 doses, and all other states required 5 doses, unless the 4th dose was administered on or after the fourth birthday. The reported coverage estimates represent the percentage of kindergartners with the state-required number of DTaP doses, except for Kentucky, which required 5 doses of DTaP by age 5 years but reported 4-dose coverage for kindergartners. Seven states required 1 dose of varicella vaccine; 44 states required 2 doses"

and:

*"*** Alabama, Florida, Georgia, Iowa, Mississippi, New Hampshire, and New Jersey considered kindergartners up to date only if they had received all doses of all vaccines required for school entry."*

and includes a table entitled:

"TABLE. Estimated vaccination coverage† for measles, mumps, and rubella vaccine (MMR), diphtheria and tetanus toxoids and acellular pertussis vaccine (DTaP), and varicella vaccine …among children enrolled in kindergarten, by immunization program — United States, territories, and associated states, 2018–19 school year."*

whose selected column headings and rows are as follows:

Immunization program	MMR 2 doses (%)§§	DTaP 5 doses (%)¶¶	Varicella 2 doses (%)***
National estimate	**94.7**	**94.9**	**94.8**

Below the table are the following abbreviation expansions:

** Estimates are adjusted for nonresponse and weighted for sampling where indicated.*

§§ Most states require 2 doses of MMR; Alaska, New Jersey, and Oregon require 2 doses of measles, 1 dose of mumps, and 1 dose of rubella vaccines. Georgia, New York, New York City, North Carolina, and Virginia require 2 doses of measles and mumps, 1 dose of rubella vaccines. Iowa requires 2 doses of measles and 2 doses of rubella vaccines.

¶¶ Most states require 5 doses of DTaP for school entry, or 4 doses if the 4th dose was received on or after the 4th birthday; Illinois, Maryland, Virginia, and Wisconsin require 4 doses; Nebraska requires 3 doses. The reported coverage estimates represent the percentage of kindergartners with the state-required number of DTaP doses, except for Kentucky, which requires ≥5 doses but reports ≥4 doses of DTaP.

**** Most states require 2 doses of varicella vaccine for school entry; Alabama, Arizona, California, Hawaii, Maine, New Jersey, Oklahoma, and Oregon require 1 dose. Reporting of varicella vaccination status for kindergartners with a history of varicella disease varied within and among states; some were reported as vaccinated against varicella and others as medically exempt"*

Hereafter this Notice will refer to all of the reports referenced in this paragraph 5.3 as "CDC Elementary School Coverage Reports".

It shall be assumed in this Notice that approximately the same coverage levels stated in the CDC Elementary School Coverage Report 2018-19 to have applied when the survey for that year was conducted applied also in the following year.

5.4 Coverage in Secondary School (11-17 years age range)

With respect to estimating children's/adolescents' vaccination status at age 11-19 years:

(a) 2006:

The Plaintiff hereby requests that the Court take judicial notice of the CDC-published report entitled:

"National Vaccination Coverage Among Adolescents Aged 13--17 Years --- United States, 2006."

Citation: Jain N, Stokley S. CDC MMWR Vol. 56, No. 34 (August 31, 2007), pp. 885-888, accessible at
https://www.cdc.gov/mmwr/preview/mmwrhtml/mm5634a3.htm (html)
(last accessed August 9, 2020)
(hereafter "CDC Secondary School Coverage Report 2006")

A true and correct copy of the aforesaid report is attached hereto as **Exhibit 39.** The report states:

> *"since 2005, three new vaccines specifically for older children have been licensed and recommended in the United States: meningococcal conjugate vaccine (MCV4) for those aged 11--12 years and 15 years†; tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis (Tdap) vaccine for those aged 11--12 years (or at ages 13--18 years if not received at ages 11--12 years); and human papillomavirus (HPV) vaccine for girls aged 11--12 years (or at ages 13--18 years if not received at 11--12 years)."*

and

> *"NIS-Teen is a random-digit--dialed telephone survey …to determine vaccination coverage estimates (4,5). During October 2006--February 2007, a total of 5,468 household interviews were conducted with parents or guardians of adolescents aged 13--17 years.¶"*

and

"Coverage with >1 dose of either Td or Tdap vaccine after age 10 years was 60.1% (95% confidence interval [CI] = 57.8--62.4) (Table). Overall vaccination coverage with Td vaccine was 49.4% (CI = 47.0--51.7) and ranged from 35.7% among adolescents aged 13 years to 63.5% among those aged 17 years. In 2005, Tdap vaccine was licensed and recommended to replace a single dose of Td vaccine. Coverage with 1 dose of Tdap vaccine was 10.8% (CI = 9.4--12.3) and ranged from 5.1% among adolescents aged 17 years to 15.4% among those aged 14 years.

Coverage with >3 doses of hepatitis B vaccine among all adolescents aged 13--17 years was 81.3% (CI = 79.4--83.1);… Overall coverage with measles, mumps, and rubella (MMR) vaccine also was high (86.9% [CI = 85.2--88.5])….

MCV4 vaccination had been received by 11.7% (CI = 10.3--13.2) of adolescents aged 13--17 years; the highest coverage was among those aged 15 years (13.9% [CI = 10.9--17.6]). Adolescents aged 17 years had the lowest MCV4 coverage (7.1% [CI = 5.0--10.0]; p<0.05).

…for adolescents aged 13--15 years… coverage was 84.3% (CI = 82.0--86.4) for >3 doses of hepatitis B vaccine, 88.5% (CI = 86.4--90.3) for >2 doses of MMR vaccine, and 56.7% (CI = 53.7--59.7) for >1 dose of Td or Tdap booster; coverage was 70.9% (CI = 66.3--75.1) for >1 dose of varicella vaccine among those without a reported history of disease.

To assess receipt of Td or Tdap vaccinations at ages 10--12 years, vaccination coverage was determined for >1 booster dose by the year in which adolescents reached age 13 years. Receipt of Td or Tdap vaccination increased from 22.7% (CI = 18.4--27.6) of children who reached age 13 years in 2002 to 41.7% (CI = 36.4--47.3) of children who reached age 13 years in 2006 (Figure).. "

and includes a table entitled:

"TABLE. Estimated vaccination coverage among adolescents aged 13-17 years, by selected vaccines and age — National Immunization Survey-Teen, United States, 2006"*

whose selected column headings and rows are as follows:

	Age (yrs)			
	13 (n = 570)		14 (n = 566)	
Vaccine	%	(95% CI)†	%	(95% CI)
MMR§ ≥2 doses	87.0	(82.8-90.3)	90.1	(87.5-93.6)
Hepatitis B ≥3 doses	88.6	(84.5-91.6)	84.6	(88.5-94.4)
Td or Tdap since age 10 years				
≥1 dose Td or Tdap	48.3	(43.1-53.7)	57.1	(51.8-62.2)
≥1 dose Tdap	12.7	(9.6-16.5)	15.4	(11.8-19.8)
≥1 dose Td	35.7	(30.7-40.9)	41.7	(36.7-46.9)
MCV4 ≥1 dose	11.3	(8.6-14.8)	12.5	(9.4-16.5)

Below the table are the following notes referenced by the table (or title):

"† Confidence interval.

§ Measles, mumps and rubella…

*** Estimate might not be reliable if the confidence interval (CI) half width > 10 or the CI half-width / Estimate > 0.5.*

†† Tetanus and diphtheria toxoids vaccine (Td) or tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis (Tdap)…

¶¶ *Includes percentages receiving meningococcal conjugate vaccine (MCV4) and meningococcal-unknown type vaccine.*

§§ Meningococcal conjugate vaccine. Includes those receiving MCV4 or an unspecified type of meningococcal vaccine."

(b) 2007:

The Plaintiff hereby requests that the Court take judicial notice of the CDC-published report entitled:

"Vaccination Coverage Among Adolescents Aged 13-17 Years—United States, 2007."

Citation: Jain N, Stokley S, Yankey D. CDC MMWR Vol. 57, No. 40 (October 10, 2008), pp. 1100-1103, accessible at (html)
(last accessed June 12, 2020)
(hereafter "CDC Secondary School Coverage Report 2007")

A true and correct copy of the aforesaid report is attached hereto as **Exhibit 40**. The report states:

"Three new vaccines have been recommended for adolescents by the Advisory Committee for Immunization Practices (ACIP) since 2005: meningococcal conjugate vaccine (MCV4; 1 dose), tetanus, diphtheria, acellular pertussis vaccine (Tdap; 1 dose), and quadrivalent human papillomavirus vaccine (HPV4; 3 doses)"*

and

"Since 2006, CDC has conducted the National Immunization Survey--Teen (NIS--Teen) to estimate vaccination coverage from a national sample of adolescents aged 13--17 years. This report describes the findings from NIS--Teen 2007, which indicated substantial increases in receipt of new adolescent vaccinations compared with 2006, including Tdap (from 10.8% to 30.4%) and MCV4 (from 11.7% to 32.4%), and increases in coverage with childhood vaccinations, including measles, mumps, and rubella (MMR), hepatitis B (HepB), and varicella (VAR) (among those without disease history). An assessment of HPV4 coverage, which is reported for the first time, showed that 25.1% of adolescent females initiated the vaccine series (>1 dose) in 2007. "

and

"† NIS--Teen 2007 was conducted during the fourth quarter 2007"

and

"For HPV4 coverage…No significant differences were observed among age groups… Among HPV4 recipients, an estimated 32.3% (95% confidence interval [CI] = 26.5--38.7) had received 1 dose, 44.2% (CI = 37.8--50.8) had received 2 doses, and 23.5% (CI = 18.2--29.9) had received 3 doses by the interview date."

and

"Among adolescents aged 13--17 years, vaccination coverage with ≥1 dose of either tetanus and diphtheria toxoids vaccine (Td) or Tdap after age 10 years was 72.3%, a significant increase from the 60.1% coverage rate measured in 2006 ($p<0.05$) (Table). Coverage with 1 dose of Tdap increased from 2006 to 2007 (10.8% to 30.4%, $p<0.05$)….
Vaccination coverage with ≥3 doses of HepB was 87.6%, an increase from 81.3% in 2006 ($p<0.05$). Coverage with >2 doses of MMR was 88.9%, an increase of 2.0 percentage points compared with 2006 (Table)"

and includes a table entitled:

"TABLE 1. Estimated vaccination coverage among adolescents aged 13-17 years, by selected vaccines and age — National Immunization Survey-Teen, United States, 2007"*

whose selected column headings and rows are as follows:

	Age (yrs)			
	13 (n = 551)		14 (n = 627)	
Vaccine	%	(95% CI†)	%	(95% CI)
MMR§ ≥2 doses	88.8	(84.8-91.8)	91.0	(87.5-93.6)
Hepatitis B ≥3 doses	90.6	(86.5-93.5)	91.9	(88.5-94.4)
Td or Tdap since age 10 years				
≥1 dose Td or Tdap	64.0	(58.5-69.1)	70.4	(65.5-74.7)
≥1 dose Tdap	43.2	(37.7-48.8)	37.3	(32.2-42.7)
≥1 dose Td	20.8	(16.5-25.8)	33.0	(28.2-38.3)
MCV4 ≥1 dose	32.6	(27.5-38.0)	31.6	(26.9-36.6)
HPV4*** ≥1 dose	25.8	(19.1-33.9)	22.8	(17.6-28.9)

Below the table are the following notes referenced by the table (or title):

*" * Age and vaccination receipt determined at time of household interview. Vaccination coverage estimates include only adolescents who had adequately complete provider-reported immunization records.*

† Weighted percentage and 95% confidence interval.

§ Measles, mumps and rubella vaccine.

†† Estimate might not be reliable if the (CI half width)/estimate >0.5 or (CI half width) > 10.

§§ Tetanus and diphtheria toxoids vaccine (Td) or tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis vaccine (Tdap)., or diphtheria and tetanus toxoids vaccine.

¶¶ Includes percentages receiving meningococcal conjugate vaccine (MCV4) and meningococcal-unknown type vaccine.

*** Quadrivalent human papillomavirus vaccine. Percentages reported among females only (n=1,440); HPV4 vaccine is not recommended for males"*

(c) 2008:

The Plaintiff hereby requests that the Court take judicial notice of the CDC-published report entitled:

"National, State, and Local Area Vaccination Coverage Among Adolescents Aged 13-17 Years—United States, 2008."

Citation: CDC MMWR, Vol. 58, No. 36 (September 18, 2009), pp. 997-1001, accessible at https://www.cdc.gov/mmwr/preview/mmwrhtml/mm5836a2.htm (html) or https://www.jstor.org/stable/pdf/23319200.pdf (pdf)
(last accessed June 12, 2020)
(hereafter "CDC Secondary School Coverage Report 2008")

A true and correct copy of the aforesaid report is attached hereto as **Exhibit 41**.

The report states:

> *"Since 2006, CDC has conducted the National Immunization Survey-Teen (NIS-Teen) to estimate vaccination coverage from a national sample of adolescents aged 13-17 years (2).This report summarizes results from the 2008 NIS-Teen and, for the first time, includes estimates for each of the 50 states and selected local areas. Nationally, vaccination coverage for the three most recently recommended adolescent vaccinations and one childhood vaccination increased from 2007 to 2008: MCV4 (from 32.4% to 41.8%), Tdap (from 30.4% to 40.8%), >1 dose of HPV4 (from 25.1% to 37.2%) … However, substantial variability in vaccination coverage was observed in 2008 among state and local areas and by race/ethnicity and poverty status."*

and

> *"Among adolescents aged 13—17 years, vaccination coverage with >1 dose of tetanus, diphtheria toxoid vaccine (Td) or Tdap after age 10 years remained stable at 72.2%; however, coverage with >1 dose of Tdap increased from 30.4% in 2007 to 40.8% in 2008 (Table 1). Vaccination coverage with >1 dose of MCV4 increased from 32.4% in 2007 to 41.8% in 2008. For HPV4, 37.2% of adolescent females had initiated the vaccination series (>1 dose) in 2008, compared with 25.1% in 2007, and 17.9% of females had received >3 doses. Among adolescent females who initiated the HPV4 series, 79.4% had received their first dose at least 24 weeks before the interview date (the minimum period in which to complete the series) (4); of these, 59.6% (95% confidence interval [CI] = 55.5—63.5) had received >3 doses."*

and

"Healthy People 2010 established vaccination coverage targets of 90% for adolescents aged 13-15 years for ≥3 doses of HepB, ≥2 doses of MMR, ≥1 dose of Td or Tdap… For the first time, Healthy People 2010 targets were achieved for ≥3 doses of HepB (91.8%, CI = 90.7-92.8) and ≥2 doses of MMR (90.7%, CI = 89.6-91.8)"

and includes a table entitled:

"TABLE 1. Estimated vaccination coverage among adolescents aged 13--17 years, by age at interview and selected vaccines and doses --- National Immunization Survey--Teen, United States, 2008"*

whose selected column headings and rows are as follows:

	Age (yrs)			
	13 (n = 3,455)		14 (n = 3,641)	
Vaccines and doses	**%**	**(95% CI †)**	**%**	**(95% CI)**
Td or Tdap since age 10 years††				
≥1 dose Td or Tdap	*64.1*	*(61.0--67.2)*	*69.7*	*(66.5--72.7)*
≥1 dose Tdap	*51.9*	*(48.7--55.1)*	*47.3*	*(44.0--50.6)*
MCV4 ≤ [sic] 1 dose§§	*42.0*	*(38.8--45.1)*	*43.0*	*(39.8--46.4)*
MMR§ ≥2 doses	*90.3*	*(88.0--92.2)*	*91.8*	*(89.8--93.4)*
Hepatitis B ≥3 doses	*92.8*	*(91.2--94.1)*	*93.1*	*(91.5--94.3)*
HPV4¶¶				
≥1 dose	*35.2*	*(31.1-39.6)*	*33.8*	*(29.6-38.2)*
≥3 doses	*14.5*	*(11.9-17.5)*	*16.6*	*(13.6-20.2)*

Below the table are the following notes referenced by the table (or title):

"† Confidence interval.

§ Measles, mumps, and rubella vaccine…

†† Includes percentages receiving tetanus and diphtheria toxoids vaccine (Td), tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis (Tdap), or tetanus-unknown type vaccine.

§§ Includes percentages receiving meningococcal conjugate vaccine (MCV4) or meningococcal-unknown type vaccine."

¶¶ Quadrivalent human papillomavirus vaccine. Percentages reported among females only (n = 8,607); HPV4 vaccine is not recommended for males."

The report also states:

"Blacks … had lower vaccination coverage percentages than whites… for …Tdap (36.0% versus 41.7%)"

and

"those who live below the poverty level tend to have …higher rates of cervical cancer incidence and mortality"

and includes the following footnote:

*""""** Adolescents were classified as below poverty level if their total family income was less than the federal poverty level specified for the applicable family size and number of children aged <18 years. All others were classified as at or above the poverty level. Additional information is available at http://www.census.gov/hhes/www/poverty.html"*

(d) 2009:

The Plaintiff hereby requests that the Court take judicial notice of the CDC-published report entitled:

"National, State, and Local Area Vaccination Coverage Among Adolescents Aged 13-17 Years—United States, 2009."

Citation: CDC MMWR, Vol. 59, No. 32 (August 20, 2010), pp 1018-1023, accessible at https://www.cdc.gov/mmwr/preview/mmwrhtml/mm5932a3.htm (html) or https://www.cdc.gov/mmwr/pdf/wk/mm5932.pdf (pdf)
(last accessed June 12, 2020)
(hereafter "CDC Secondary School Coverage Report 2009")

A true and correct copy of the aforesaid report is attached hereto as **Exhibit 42**.

The report states:

"Since 2006, CDC has conducted the National Immunization Survey–Teen (NIS-Teen) to estimate vaccination coverage among adolescents aged 13–17 years. This report summarizes results from 2009 NIS-Teen and updates data from 2008 NIS-Teen (2)."

"Among those who initiated the HPV series, 90.1% had received their first dose at least 24 weeks before the interview date and had the minimum period needed to complete the series before the interview. Of these, 67.5% (95% confidence interval [CI] = 64.4–70.5) received ≥3 doses. Among males, 49.6% (CI = 47.8–51.4) received both ≥1 dose of Td/Tdap and ≥1 dose of MenACWY; among females, 33.6% (CI = 31.8–35.4) received ≥1 dose of Td/Tdap, ≥1 dose of MenACWY, and ≥1 dose of HPV."

"coverage with ≥2 doses of MMR was similar to coverage during 2008 at 89.1%; coverage with ≥3 doses of HepB increased from 87.9% to 89.9% (Table 1)."

"Coverage estimates varied by state and local area (Table 2) with rates ranging from 22.6% (Mississippi) to 76.6% (Colorado) for ≥1 doses of Tdap, from 19.3% (Mississippi) to 78.3% (District of Columbia) for ≥1 dose of MenACWY, and from 22.9% (Mississippi) to 69.0% (Massachusetts) for ≥1 dose of HPV. Four states (Connecticut, Massachusetts, New Hampshire, and Rhode Island) had coverage of >60% for all three routinely administered adolescent vaccines (Tdap, MenACWY, and HPV)."

and includes a table entitled:

"TABLE 1. Estimated vaccination coverage among adolescents aged 13--17 years in 2009, by age at interview and seleted* [sic] *vaccines and doses --- National Immunization Survey (NIS)--Teen, United States, 2009"*

whose selected column headings and rows are as follows:

Vaccines and doses	***Age at interview (yrs)***			
	13		***14***	
	(n = 3,915)		***(n = 4,203)***	
	%†	***(95% CI †)***	***%***	***(95% CI)"***
Td or Tdap since age 10 years				
≥1 dose Td or Tdap¶¶	*70.5*	*(67.9--73.0)*	*74.8*	*(72.4--77.1)*
≥1 dose Tdap	*65.2*	*(62.5--67.8)*	*63.5*	*(60.8--66.2)*
*MenACWY *** ≥1 dose*	*53.8*	*(51.0--56.5)*	*56.1*	*(53.3--58.9)*
MMR§ ≥2 doses	*91.2*	*(89.5--92.6)*	*89.3*	*(87.6--90.8)*
Hepatitis B ≥3 doses	*93.4*	*(92.1--94.5)*	*90.6*	*(88.9--92.1)*
HPV†††				
≥1 dose	*37.1*	*(33.5–40.9)*	*40.6*	*(36.8–44.6)*
≥3 doses	*19.5*	*(16.8–22.5)*	*23.2*	*(20.3–26.4)*

Below the table are the following notes referenced by the table (or title):

*" * Adolescents (N = 20,066) in the 2009 NIS-Teen were born during January 1991--February 1997…*

† Weighted percentage and confidence interval. Estimates with CI widths >20 might not be reliable.

§ ≥2 doses of measles, mumps, and rubella vaccine.

¶¶ Includes tetanus and diptheria [sic] *toxoid vaccine (Td); tetanus toxoid, reduced diptheria toxid* [sic]*, and acellular pertussis (Tdap); or tetanus-unknown vaccine at or after age 10 years.*

**** Meningococcal conjugate vaccine or meningococcal-unknown type vaccine.*

††† Human papillomavirus vaccine, either quadrivalent or bivalent, among females (n = 9,621)."

(e) 2010:

The Plaintiff hereby requests that the Court take judicial notice of the CDC-published report entitled:

"National and State Vaccination Coverage Among Adolescents Aged 13 Through 17 Years --- United States, 2010."
Citation: CDC MMWR, Vol. 60, No. 33 (August 26, 2011), pp 1117-1123, accessible at https://www.cdc.gov/mmwr/preview/mmwrhtml/mm6033a1.htm (html) or https://www.cdc.gov/mmwr/pdf/wk/mm6033.pdf (pdf)
(last accessed June 12, 2020)
(hereafter "CDC Secondary School Coverage Report 2010")

A true and correct copy of the aforesaid report is attached hereto as **Exhibit 43**.

The report states:

"CDC tracks vaccination coverage among adolescents aged 13 through 17 years through the National Immunization Survey–Teen (NIS-Teen). To provide updated vaccination coverage estimates, CDC analyzed 2010 NIS-Teen data and compared results with 2009 NIS-Teen estimates (2). This report summarizes the results of that analysis, which found that coverage increased for all three of the routinely administered adolescent vaccines: Tdap from 55.6% to 68.7%, MenACWY from 53.6% to 62.7%, (among females) ≥1 dose of HPV from 44.3% to 48.7%, and ≥3 doses of HPV from 26.7% to 32.0%."

"From 2007 to 2010, the average annual percentage-point increases for ≥1 dose of Tdap (12.8 points, 95% confidence interval [CI] = 12.1–13.4) and ≥1 dose of MenACWY (10.1 points, CI = 9.5–10.7) were significantly greater than that for ≥1 dose of HPV (7.9 points, CI = 7.0–8.7) (p≤0.05) (Figure)."

"From 2009 to 2010, vaccination coverage increased for all three vaccines. Tdap coverage increased from 55.6% to 68.7%, MenACWY from 53.6% to 62.7%, (among females) ≥1 dose of HPV from 44.3% to 48.7%, and ≥3 doses of HPV from 26.7% to 32.0% (Table 1). At least 24 weeks between the first and third doses of the HPV vaccine are needed to complete the series (1). Among females who initiated the HPV series, 94.3% met the minimum period needed to complete the series before the interview. Of these, 69.6% received ≥3 doses. Among adolescent males, 1.4% (CI =1.1–1.8) received ≥1 dose of HPV."

"Coverage estimates varied by state and reporting area (Table 3), with rates ranging from 29.0% (Mississippi) to 87.9% (New Hampshire) for ≥1 dose of Tdap and from 26.0% (Mississippi) to 89.5% (District of Columbia) for ≥1 dose of MenACWY."

and includes a table entitled:

"TABLE 1. Estimated vaccination coverage among adolescents aged 13 through 17 years, by age at interview and selected vaccines and doses --- National Immunization Survey--Teen (NIS-Teen), United States, 2010"*

whose selected column headings and rows are as follows:

Vaccines/Doses	Age at interview (yrs)		Overall (13-17 yr olds)
	13 (n = 3,914)	14 (n = 3,918)	2010 (N = 19,257)
	% (95% CI †)	% (95% CI)	% (95% CI)
Td or Tdap§			
≥1 dose Td or Tdap since age 10 yrs	78.0 (75.5--80.3)	82.5 (80.4--84.4)	81.2 (80.2–82.2)
≥1 dose Tdap since age 10 yrs	73.7 (71.2--76.2)	77.2 (74.8--79.3)	68.7 (67.5–69.8)
MenACWY†† ≥1 dose	63.8 (61.1--66.5)	66.6 (64.0--69.1)	62.7 (61.5–63.9)
MMR*** ≥2 doses	93.2 (91.9--94.3)	91.0 (88.9--92.8)	90.5 (89.6–91.3)
Hepatitis B ≥3 doses	94.8 (93.7--95.8)	93.0 (91.0--94.6)	91.6 (90.8–92.4)
HPV†††			
≥1 dose	38.9 (34.9–43.1)	48.5 (44.5–52.6)¶	48.7 (46.9–50.5)
≥3 doses	23.2 (20.1–26.6)	30.5 (26.9–34.3)¶	32.0 (30.3–33.6)
3-dose series completion¶¶	64.1 (55.9–71.5)	68.2 (61.7–74.0)	69.6 (66.8–72.2)

Below the table are the following notes referenced by the table (or title):

† Confidence interval. Estimates with confidence interval widths >20 might not be reliable.

§ Includes percentages receiving tetanus and diptheria [sic] *toxoid vaccine (Td) since age 10 years, or tetanus toxoid, reduced diptheria* [sic] *toxoid, and acellular pertussis (Tdap), or tetanus--unknown type vaccine since age 10 years…*

†† Includes percentages receiving meningococcal conjugate vaccine (MenACWY) or meningococcal-unknown type vaccine.

§§ ≥1 dose of human papillomavirus vaccine, either quadrivalent or bivalent. Percentage reported among females only (n = 9,220).

¶¶ Percentage of females who received 3 doses among those who had at least 1 HPV dose and at least 24 weeks between the first dose and the interview date.

**** ≥2 doses of measles, mumps, and rubella vaccine."*

(f) 2011:

The Plaintiff hereby requests that the Court take judicial notice of the CDC-published report entitled:

"National and State Vaccination Coverage Among Adolescents Aged 13–17 Years — United States, 2011."
Citation: CDC MMWR, Vol. 61, No. 34 (August 31, 2012), pp 671-677, accessible at https://www.cdc.gov/mmwr/preview/mmwrhtml/mm6134a3.htm (html) or https://www.cdc.gov/mmwr/pdf/wk/mm6134.pdf (pdf)
(last accessed June 12, 2020)
(hereafter "CDC Secondary School Coverage Report 2011")

A true and correct copy of the aforesaid report is attached hereto as **Exhibit 44**.

The report states:

> *"To assess vaccination coverage among adolescents aged 13–17 years,† CDC analyzed data from the National Immunization Survey-Teen (NIS-Teen). This report summarizes the results of that assessment, which indicated that, from 2010 to 2011, vaccination coverage increased for ≥1 dose Tdap on or after age 10 years (from 68.7% to 78.2%), ≥1 dose MenACWY (from 62.7% to 70.5%), and, among females, for ≥1 dose of HPV (from 48.7% to 53.0%) and ≥3 doses of HPV§ (from 32.0 to 34.8%)"*

and

> *"The average annual percentage point increase from 2007 to 2010 was 12.8 (95% confidence interval [CI] = 11.9–13.6) for ≥1 dose of Tdap, 10.1 (CI = 9.3–10.9) for ≥1 dose of MenACWY, and among females, 7.9 (CI = 6.7–9.0) for ≥1 dose of HPV. The percentage point increase from 2010 to 2011 was 9.5 for ≥1 dose of Tdap, 7.8 for ≥1 dose of MenACWY, 4.3 for ≥1 dose and 2.8 for ≥3 doses of HPV among females, 672 MMWR / August 31, 2012 / Vol. 61 / No. 34 and 6.9 for ≥1 dose of HPV among males (Table 1). Among females and males who initiated the HPV series, 70.7% and 28.1% received 3 doses, respectively."*

and

> *"Coverage estimates for ≥1 dose of Tdap ranged from 36.9% (Mississippi) to 95.0% (New Hampshire), and for ≥1 dose of MenACWY, from 27.6% (Arkansas) to 92.1% (Indiana) (Table 3)."*

and includes a table entitled:

"TABLE 1. Estimated vaccination coverage with selected vaccines and doses among adolescents aged 13–17 years, by age at interview — National Immunization Survey-Teen (NIS-Teen), United States, 2010 and 2011"*

whose selected column headings and rows are as follows:

	Age at interview (yrs)				Total (13-17 yr olds)	
	13		14		2011	
	(n = 4,763)		(n = 4,842)		(N = 23,564)	
Vaccines/Doses	%	(95% CI †)	%	(95% CI †)	%	(95% CI †)
Td or Tdap §						
≥1 dose Td or Tdap on or after age 10 yrs	83.9	(±1.8)	85.2	(±1.7)	85.3	(±0.8)
≥1 dose Tdap on or after age 10 yrs	81.0	(±2.0)	80.6	(±2.0)	78.2	(±0.9)
MenACWY †† ≥1 dose	71.4	(±2.1)	72.0	(±2.2)	70.5	(±1.0)
MMR* ≥2 doses**	92.0	(±1.3)	91.8	(±1.5)	91.1	(±0.7)
Hepatitis B ≥3 doses	93.7	(±1.2)	93.5	(±1.3)	92.3	(±0.7)
HPV§§						
Females						
≥1 dose	41.6	(±3.6)	45.5	(±3.6)	53.0	(±1.7)
≥3 doses	22.9	(±2.9)	29.2	(±3.2)¶	34.8	(±1.6)¶
3-dose series completion¶¶	63.6	(±5.7)	72.1	(±5.0)¶	70.7	(±2.3)¶
Males						
≥1 dose	9.8	(±2.4)	8.2	(±2.0)	8.3	(±1.0)
≥3 doses	1.6	(±0.8)	1.8	(±1.1)	1.3	(±0.3)
3-dose series completion¶¶	32.4	(±14.1)	35.7	(±16.6)	28.1	(±6.5)

Below the table are the following notes referenced by the table (or title):

" † *CI = confidence interval. Estimates with CI widths >20 might not be reliable.*

§ *Includes percentages receiving tetanus and diphtheria toxoid vaccine (Td) on or after age 10 years, or tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis (Tdap), or tetanus–unknown type vaccine on or after age 10 years…*

†† *Includes percentages receiving meningococcal conjugate vaccine (MenACWY) or meningococcal–unknown type vaccine.*

§§ Human papillomavirus vaccine, either quadrivalent or bivalent. Percentage reported among females (n = 11,236) and males (n = 12,328). Some adolescents might have received more than the 3 recommended HPV doses.

¶¶ Percentage of females or males who received 3 doses among those who had ≥1 HPV dose and ≥24 weeks between the first dose and the interview date.

**** ≥2 doses of measles, mumps, and rubella vaccine."*

(g) 2012:

The Plaintiff hereby requests that the Court take judicial notice of the CDC-published report entitled:

"National and State Vaccination Coverage Among Adolescents Aged 13–17 Years — United States, 2012."

Citation: CDC MMWR, Vol. 62, No. 34 (August 30, 2013), pp 685-693, accessible at https://www.cdc.gov/mmwr/preview/mmwrhtml/mm6234a1.htm (html) or https://www.cdc.gov/mmwr/pdf/wk/mm6234.pdf (pdf)
(last accessed June 12, 2020)
(hereafter "CDC Secondary School Coverage Report 2012")

A true and correct copy of the aforesaid report is attached hereto as **Exhibit 45**.

The report states:

"To monitor vaccination coverage among persons aged 13–17 years,† CDC analyzed data from the National Immunization Survey–Teen (NIS-Teen). This report highlights findings of that analysis. From 2011 to 2012, coverage increased for ≥1 Tdap vaccine dose§ (from 78.2% to 84.6%), ≥1 MenACWY vaccine dose (from 70.5% to 74.0%) and, among males, ≥1 HPV vaccine dose (from 8.3% to 20.8%)"

and

"During 2006–2012, coverage for ≥1 Tdap vaccine dose and ≥1 MenACWY vaccine dose increased steadily, with annual average increases of approximately 12.0 (95% confidence interval [CI] = 9.9–14.0) and 10.1 (CI = 7.5–12.6) percentage points, respectively."

and

"From 2011 to 2012, while ≥1 Tdap vaccine dose coverage increased 6.4 percentage points, coverage for ≥1 MenACWY vaccine dose increased only 3.5 percentage points. During 2007–2011, coverage for ≥1 HPV vaccine dose among females lagged behind estimates for Tdap and MenACWY vaccines, increasing on average 6.1 (CI = 3.3–8.9) percentage points each year. However, in 2011 and 2012, HPV vaccination rates among females did not increase (Figure, Table 1)."

and

"Compared with 2011 coverage rates, 2012 coverage estimates among males for HPV vaccine doses were higher (Figure, Table 1), but ≥1 dose coverage was lower ($p<0.05$) in 2012, the first survey year following the routine recommendation for males (3), than that achieved for females by 2007 (Figure) (7), the first survey year following licensure of the quadrivalent HPV vaccine for administration to females (2)."

and

"Among females, HPV vaccination coverage increased by an average of approximately 4–6 percentage points per year of age for ≥1, ≥2, ≥3 doses and series completion ($p<0.05$); however, even among females aged 17 years (the most highly vaccinated age group), only 44.5% had received ≥3 doses."

and

"Coverage estimates for Tdap, MenACWY, and HPV vaccines varied widely among states. Coverage for ≥1 Tdap vaccine dose ranged from 53.5% (Mississippi) to 96.3% (New Hampshire), and for ≥1 MenACWY vaccine dose, from 37.5% (Arkansas) to 94.3% (Rhode Island) (Table 3)."

and includes a table entitled:

"TABLE 1. Estimated vaccination coverage with selected vaccines among adolescents aged 13–17 years, by age when interviewed — National Immunization Survey–Teen (NIS-Teen), United States, 2011–2012"*

whose selected column headings and rows are as follows:

Vaccines/Doses	Age when interviewed (yrs) — 2012				Total (13-17 yr olds)	
	13		14		2012	
	(n = 3,937)		(n = 3,961)		(N = 19,199)	
	%	(95% CI)†	%	(95% CI)	%	(95% CI)
Tdap§ ≥1 dose	85.3	(±2.1)	85.7	(±2.1)	84.6	(±0.9)
MenACWY ** ≥1 dose	72.5	(±2.6)	73.4	(±2.6)	74.0	(±1.1)
MMR*** ≥2 doses	92.0	(±1.3)	91.8	(±1.5)	91.4	(±0.8)
Hepatitis B ≥3 doses	93.7	(±1.2)	93.5	(±1.3)	92.8	(±0.7)
HPV†† vaccine coverage						
Females						
≥1 dose	46.8	(±4.0)	49.4	(±4.2)	53.8	(±1.9)
≥2 doses	31.5	(±3.5)	36.8	(±4.0)	43.4	(±1.9)
≥3 doses	20.2	(±3.0)	28.7	(±3.8)§§	33.4	(±1.7)
Males						
≥1 dose	19.5	(±3.1)	22.2	(±3.6)	20.8	(±1.5)
≥2 doses	12.4	(±2.7)	13.0	(±2.8)	12.7	(±1.3)
≥3 doses	6.6	(±1.8)	5.9	(±2.1)	6.8	(±1.0)
HPV†† 3-dose series completion ¶¶						
Females	49.9	(±6.4)	64.4	(±6.9)§§	66.7	(±2.6)
Males	47.9	(±11.0)	40.2	(±11.6)	45.1	(±5.0)

Below the table are the following notes referenced by the table (or title):

*"**Abbreviations:** CI = confidence interval; Tdap = tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis; MenACWY = meningococcal conjugate; … MMR = measles, mumps, and rubella.*

** Adolescents (N = 19,199) in the 2012 NIS-Teen were born during January 6, 1994–February 18, 2000.*

† Estimates with 95% CI widths >20 might not be reliable.

§ Includes percentages receiving Tdap vaccine on or after age 10 years.

*** Includes percentages receiving MenACWY or meningococcal–unknown type vaccine.*

†† HPV vaccine, either quadrivalent or bivalent. Percentage reported among females (n = 9,058) and males (n =10,141). Some adolescents might have received more than the recommended 3 doses of HPV vaccine.

§§ Statistically significant difference (p<0.05) in estimated vaccination coverage by age; reference group was adolescents aged 13 years.

¶¶ The completion rate for the 3-dose HPV vaccination series represents the percentage of adolescents who received 3 doses among those who had ≥1 HPV vaccine dose and ≥24 weeks between the first dose and the interview date. The calculation was limited to 4,548 females and 1,414 males who met the criteria of having received ≥1 HPV vaccine dose and having ≥24 weeks between the first dose and the interview date.

**** ≥2 doses of MMR vaccine."*

(h) 2013:

The Plaintiff hereby requests that the Court take judicial notice of the CDC-published report entitled:

"National, regional, state, and selected local area vaccination coverage among adolescents aged 13-17 years--United States, 2013"

Citation: Elam-Evans, Laurie D et al. CDC MMWR 2014, Vol. 63(29): 625-33, accessible at https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5779424/ (html) or https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5779424/pdf/625-633.pdf https://www.cdc.gov/mmwr/pdf/wk/mm6234.pdf(pdf)
(last accessed June 12, 2020)
(hereafter "CDC Secondary School Coverage Report 2013")

A true and correct copy of the aforesaid report is attached hereto as **Exhibit 46**.

The report states:

"To assess vaccination coverage among adolescents aged 13–17 years, CDC analyzed data from the 2013 National Immunization Survey-Teen (NIS-Teen).§ This report summarizes the results of that analysis, which show that from 2012 to 2013, coverage increased for each of the vaccines routinely recommended for adolescents: from 84.6% to 86.0% for ≥1 Tdap dose; from 74.0% to 77.8% for ≥1 MenACWY dose; from 53.8% to 57.3% for ≥1 HPV dose among females, and from 20.8% to 34.6% for ≥1 HPV dose among males."

and

"During 2006–2013, NIS-Teen data show that coverage trends differed substantially for Tdap, MenACWY, and HPV vaccination (Figure). Coverage estimates for ≥1 Tdap dose and ≥1 MenACWY dose increased significantly each year from 2006 to 2013, with average increases of 10.4 percentage points (95% confidence interval [CI] = 7.8–13.1) for Tdap and 8.9 percentage points (CI = 6.5–11.3) for MenACWY. Coverage for ≥1 HPV dose increased an average of 4.5 percentage points (CI = 2.7–6.3) annually from 2007 to 2013 for females, and by 9.9 percentage points (CI = 4.8–15.0) from 2010 to 2013 for males. In 2013, Tdap and MenACWY coverage estimates were 86.0% and 77.8%, respectively (Table 1). From 2012 to 2013, coverage with ≥1, ≥2, and ≥3 HPV doses increased for both sexes. Coverage with ≥1 HPV dose in 2013 was 57.3% for females and 34.6% for males. No statistically significant changes occurred from 2012 to 2013 in coverage for ≥2 doses of MR vaccine or ≥3 doses of hepatitis B vaccine."

and

"Coverage with the second MenACWY dose was calculated as the proportion of adolescents aged 17 years on date of interview who received a second MenACWY dose on or after their 16th birthday, among those who had received a first dose before their 16th birthday (only second doses received on or after their 16th birthday and at least 8 weeks after the first dose were counted). All of these adolescents were aged 16 years after the MenACWY second dose was recommended by ACIP in October 2010 (n = 2,310) (6). The MenACWY 2-dose completion rate was 29.6% (CI = 26.4%–33.0%)."

and

"In 2013, there was wide variation among states in coverage (Table 3). Coverage for ≥1 Tdap ranged from 60.2% (Mississippi) to 95.5% (Rhode Island), whereas coverage estimates for ≥1 MenACWY ranged from 40.4% (Arkansas) to 93.7% (North Dakota)."

and

"Coverage for ≥2 MMR doses ranged from 83.2% (West Virginia) to 97.4% (New Hampshire and Louisiana)."

includes a table entitled:

"TABLE 1. Estimated vaccination coverage with selected vaccines among adolescents aged 13–17 years, by age at interview — National Immunization Survey–Teen (NIS-Teen), United States, 2013"*

whose selected column headings and rows are as follows:

Vaccines/Doses	Age at interview (yrs)				Total (13-17 yr olds)	
	13		14		2013	
	(n = 3,735)		(n = 3,841)		(N = 18,264)	
	%	(95% CI)	%	(95% CI)	%	(95% CI)
Tdap§ ≥1 dose	87.2	(±1.9)	87.0	(±2.1)	86.0	(±0.9)
MenACWY†† ≥1 dose	76.1	(±2.4)	78.2	(±2.3)	77.8	(±1.1)
MMR*** ≥2 doses	92.6	(±1.4)	93.1	(±1.4)	91.8	(±0.8)
Hepatitis B ≥3 doses	94.7	(±1.3)	94.0	(±1.3)	93.2	(±0.7)
HPV§§ vaccine coverage						
Females						
≥1 dose	50.6	(±4.1)	55.1	(±4.2)	53.8	(±1.9)
≥2 doses	39.2	(±4.2)	43.3	(±4.2)	43.4	(±1.9)
≥3 doses	25.8	(±3.8)	32.1	(±3.9)¶	33.4	(±1.7)
Males						
≥1 dose	33.5	(±4.5)	35.1	(±4.4)	20.8	(±1.5)
≥2 doses	23.4	(±4.3)	24.3	(±4.0)	12.7	(±1.3)
≥3 doses	11.7	(±2.7)	13.6	(±3.3)	6.8	(±1.0)
HPV§§ 3-dose series completion¶¶						
Females	56.1	(±6.7)	64.7	(±5.7)	70.4	(±2.5)
Males	41.6	(±9.4)	47.1	(±9.3)	48.3	(±4.0)

Below the table are the following notes referenced by the table (or title):

*"**Abbreviations:** CI = confidence interval; Tdap = tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis; MenACWY = meningococcal conjugate; … MMR = measles, mumps, and rubella.*

**Adolescents (N = 18,264) in the 2013 NIS-Teen were born January 11, 1995, through February 13, 2001…*

§ Includes percentages receiving Tdap vaccine at or after age 10 years

¶ Statistically significant difference (p<0.05) in estimated vaccination coverage by age: reference group was adolescents aged 13 years.

*** Statistically significant difference (p<0.05) compared with 2012 NIS-Teen overall estimates.*

†† Includes percentages receiving MenACWY or meningococcal-unknown type vaccine.

§§ HPV vaccine, either quadrivalent or bivalent may be used for females, and only quadrivalent may be used for males. Percentage reported among females (n = 8,710) and males (n = 9,554). Some adolescents might have received more than the recommended 3 doses of HPV vaccine.

¶¶ The completion rate for the 3-dose HPV vaccination series represents the percentage of adolescents who received ≥3 doses among those who had ≥1 HPV vaccine dose with at least 24 weeks between the first dose and the interview date. The calculation was limited to 4,611 females and 2,580 males who met the criteria of having received ≥1 HPV vaccine dose and having at least 24 weeks between the first dose and the interview date.

****≥2 doses of MMR vaccine."*

(i) 2014:

The Plaintiff hereby requests that the Court take judicial notice of the CDC-published report entitled:

"National, Regional, State, and Selected Local Area Vaccination Coverage Among Adolescents Aged 13–17 Years — United States, 2014"

Citation: CDC MMWR, Vol. 64, No. 29 (July 31, 2015), pp 784-792, accessible at https://www.cdc.gov/Mmwr/preview/mmwrhtml/mm6429a3.htm (html) or https://www.cdc.gov/mmwr/pdf/wk/mm6429.pdf (pdf)
(last accessed June 12, 2020)
(hereafter "CDC Secondary School Coverage Report 2014")

A true and correct copy of the aforesaid report is attached hereto as **Exhibit 47**.

The report states:

> *"To assess vaccination coverage among adolescents, CDC analyzed data collected regarding 20,827 adolescents through the 2014 National Immunization Survey–Teen (NIS-Teen).* From 2013 to 2014, coverage among adolescents aged 13–17 years increased for all routinely recommended vaccines: from 84.7% to 87.6% for ≥1 tetanus diphtheria-acellular pertussis (Tdap) vaccine dose, from 76.6% to 79.3% for ≥1 meningococcal conjugate (MenACWY) vaccine dose, from 56.7% to 60.0% and from 33.6% to 41.7% for ≥1 HPV vaccine dose among females and males, respectively.†"*

and

> *"Among males, coverage for ≥1 and ≥3 HPV doses increased approximately 8 percentage points from 2013 to 2014. In 2014, coverage with ≥2 MenACWY among adolescents aged 17 years was 28.5%; an additional 4.5% (95% confidence interval [CI] = 3.6%– 5.5%) of adolescents aged 17 years received their first MenACWY dose on or after their 16th birthday."*

and

> *"In 2014, vaccination coverage varied among the 50 states and DC (Table 3, Figures 2 and 3). Coverage for ≥1 Tdap dose ranged from 94.8% (Connecticut) to 70.8% (Idaho and Mississippi) and for ≥1 MenACWY dose from 95.2% (Pennsylvania) to 46.0% (Mississippi)."*

and

> *"Estimated coverage with ≥1 MenACWY dose continues to increase among adolescents, but geographic disparities are evident... Although 78.8% of adolescents aged 17 years received ≥1 dose of MenACWY, only 28.5% received the complete the 2-dose series."*

and includes a table entitled:

> *"TABLE 1. Estimated vaccination coverage with selected vaccines and doses among adolescents aged 13–17* years, by age at interview — National Immunization Survey–Teen (NIS-Teen), United States, 2014"*

whose selected column headings and rows are as follows:

Vaccine	Age at interview (yrs) (2014) 13 (n = 4,292) % (95% CI)	14 (n = 4,329) % (95% CI) "	Total (adolescents aged 13–17 yrs) 2014 (N = 20,827) % (95% CI)
Tdap§ ≥1 dose	87.5 (±2.1)	89.1 (±1.6)	87.6 (±0.9)
MenACWY ** ≥1 dose	78.0 (±2.5)	81.0 (±2.1)	79.3 (±1.1)
MMR ≥2 doses	90.2 (±1.8)	91.1 (±1.6)	90.7 (±0.8)
HepB ≥3 doses	91.3 (±1.8)	91.7 (±1.5)	91.4 (±0.7)
HPV§§ vaccine coverage			
Females			
≥1 dose	51.1 (±4.1)	56.6 (±3.9)	60.0 (±1.9)
≥2 doses	40.1 (±4.0)	46.4 (±4.0)¶¶	50.3 (±1.9)
≥3 doses	26.2 (±3.6)	35.9 (±3.9)¶¶	39.7 (±1.9)
Males			
≥1 dose	38.9 (±4.2)	42.6 (±4.0)	41.7 (±1.8)
≥2 doses	27.1 (±3.9)	30.9 (±3.8)	31.4 (±1.7)
≥3 doses	16.2 (±3.3)	20.9 (±3.5)	21.6 (±1.6)
HPV§§ 3-dose series completion¶¶			
Females	56.1 (±6.3)	66.8 (±5.2)¶¶	69.3 (±2.4)
Males	47.1 (±7.6)	56.6 (±6.6)	57.8 (±3.0)

Below the table are the following notes referenced by the table (or title):

*"**Abbreviations:** CI = confidence interval; Tdap = tetanus-diphtheria-acellular pertussis vaccine; MenACWY = meningococcal conjugate vaccine; …MMR = measles, mumps, and rubella vaccine; HepB = hepatitis B vaccine.*

** Adolescents (N = 20,827) in the 2014 NIS-Teen were born during the period January 1996–February 2002.*

† …A revised adequate provider data definition was implemented in 2014 NIS-Teen, and estimates might not be directly comparable to those previously published…

§ Includes percentages receiving Tdap at or after age 10 years….

*** Includes percentages receiving MenACWY or meningococcal-unknown type vaccine.*

†† ≥2 doses of MenACWY or meningococcal-unknown type vaccine. Calculated only among adolescents who were aged 17 years at time of interview. Does not include adolescents who received 1 dose of MenACWY vaccine at or after age 16 years."

(j) 2015:

The Plaintiff hereby requests that the Court take judicial notice of the CDC-published report entitled:

- "National, Regional, State, and Selected Local Area Vaccination Coverage Among Adolescents Aged 13–17 Years — United States, 2015."

  Citation: Reagan-Steiner S, Yankey D, Jeyarajah J, Elam-Evans L, Curtis C, MacNeil J, and Markowitz L, Singleton J. CDC MMWR 2016. Vol 65:850-858. 10.15585/mmwr.mm6533a4, accessible at https://www.cdc.gov/mmwr/volumes/65/wr/mm6533a4.htm (html) or https://www.researchgate.net/publication/306921947_National_Regional_State_and_Selected_Local_Area_Vaccination_Coverage_Among_Adolescents_Aged_13-17_Years_-_United_States_2015 (pdf)
  (last accessed June 12, 2020)
  (hereafter "CDC Secondary School Coverage Report 2015")

  A true and correct copy of the aforesaid report is attached hereto as **Exhibit 48**.

The report states:

"To assess vaccination coverage among adolescents in the United States, CDC analyzed data collected regarding 21,875 adolescents through the 2015 National Immunization Survey-Teen (NIS-Teen). During 2014–2015, coverage among adolescents aged 13–17 years increased for each HPV vaccine dose among males, including ≥1 HPV vaccine dose (from 41.7% to 49.8%), and increased modestly for ≥1 HPV vaccine dose among females (from 60.0% to 62.8%) and ≥1 quadrivalent meningococcal conjugate vaccine (MenACWY) dose (from 79.3% to 81.3%)."*

and

"National Vaccination Coverage

In 2015, among males, coverage with ≥1 HPV vaccine dose was 49.8% and with ≥3 doses was 28.1%; among females coverage with ≥1 dose was 62.8% and with ≥3 doses was 41.9% (Table 1) (Figure 1). During 2014–2015, among males, coverage with each HPV vaccine dose increased, with percentage point increases of 8.1 for ≥1 dose, 7.6 for ≥2 doses, and 6.5 for ≥3 doses. Among females, coverage with ≥1 HPV vaccine dose increased modestly (2.8 percentage points). Among all adolescents, coverage with ≥1 MenACWY dose increased 2.0 percentage points to 81.3%. Among adolescents aged 17 years, coverage with ≥2 MenACWY doses increased 4.8 percentage points to 33.3%; an additional 5.3% (95% confidence interval [CI] = 4.4%–6.4%) received their first MenACWY dose on or after their 16th birthday.

In 2015, among all adolescents (females and males combined), HPV vaccination coverage with ≥1 dose was 56.1% (95% CI = 54.9%–57.4%), with ≥2 doses was 45.4% (95% CI = 44.2%–46.7%), and with ≥3 doses was 34.9% (95% CI = 33.7%–36.1%). Among all adolescents, coverage with ≥1 HPV vaccine dose was 30.3 percentage points lower than coverage with ≥1 Tdap dose and 25.2 percentage points lower than coverage with ≥1 MenACWY dose.

includes a table entitled:

"TABLE 1. Estimated vaccination coverage with selected vaccines and doses among adolescents aged 13–17 years, by age at interview — National Immunization Survey–Teen (NIS-Teen), United States, 2015",*

whose selected column headings and rows are as follows:

Vaccine	Age (yrs) 13 (n = 4,476) % (95% CI)	14 (n = 4,567) % (95% CI)	Total 2015 (N = 21,875) % (95% CI)
Tdap† ≥1 dose	86.5 (±2.0)	88.7 (±1.7)	86.4 (±1.0)
MenACWY§			
≥1 dose	79.2 (±2.4)	81.9 (±2.4)	81.3 (±1.0)
≥2 doses	—	—	33.3 (±2.7)
MMR ≥ 2 doses	91.5 (±1.6)	91.4 (±1.7)	90.7 (±0.8)
Hepatitis B vaccine ≥3 doses	91.0 (±1.9)	91.8 (±1.7)	91.1 (±0.8)
HPV§§ vaccine coverage			
Females			
≥1 dose	56.4 (±4.2)	61.2 (±4.0)	62.8 (±1.8)
≥2 doses	42.6 (±4.2)	49.0 (±4.1)¶	52.2 (±1.8)
≥3 doses	29.5 (±3.9)	37.3 (±4.0)¶	41.9 (±1.8)
Males			
≥1 dose	48.7 (±3.9)	47.0 (±4.2)	49.8 (±1.8)
≥2 doses	36.7 (±3.8)	38.5 (±4.1)	39.0 (±1.7)
≥3 doses	24.9 (±3.5)	27.7 (±3.9)	28.1 (±1.6)

Below the table are the following notes referenced by the table (or title):

*"**Abbreviations:** CI = confidence interval;… MenACWY = quadrivalent meningococcal conjugate vaccine; MMR = measles, mumps, and rubella vaccine; Tdap = tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis vaccine.*

† Includes percentages receiving Tdap vaccine at or after age 10 years.

§ Includes percentages receiving MenACWY or meningococcal–unknown-type vaccine….

†† ≥2 doses of MenACWY or meningococcal–unknown-type vaccine. Calculated only among adolescents who were 17 years of age at interview (n = 3,984); does not include adolescents who received their first dose of MenACWY vaccine at or after age 16 years.

§§ HPV vaccine, 9-valent (9vHPV), quadrivalent (4vHPV), or bivalent (2vHPV). Percentages in the table are reported separately for females only (n = 10,508) and for males only (n = 11,367). Coverage with ≥1 HPV vaccine dose among all adolescents (females and males combined) aged 13–17 years was 56.1% (95% CI = 54.9%–57.4%); with ≥2 doses was 45.4% (95% CI = 44.2%–46.7%), and with ≥3 doses was 34.9% (95% CI = 33.7%–36.1%). 9vHPV, 4vHPV, or 2vHPV are recommended for females and 9vHPV or 4vHPV are recommended for males. Some adolescents might have received more than the 3 recommended HPV vaccine doses."

(k) 2016:

The Plaintiff hereby requests that the Court take judicial notice of the CDC-published report entitled:

- "National, Regional, State, and Selected Local Area Vaccination Coverage Among Adolescents Aged 13–17 Years — United States, 2016."

  Citation: Walker TY, Elam-Evans LD, Singleton JA, et al. CDC MMWR 2017;66:874–882. DOI: http://dx.doi.org/10.15585/mmwr.mm6633a2external icon, accessible at https://www.cdc.gov/mmwr/volumes/66/wr/mm6633a2.htm (html) or https://www.cdc.gov/mmwr/volumes/66/wr/pdfs/mm6633a2.pdf (pdf) (last accessed June 12, 2020)
  (hereafter "CDC Secondary School Coverage Report 2016")

  A true and correct copy of the aforesaid report is attached hereto as **Exhibit 49**.

The report states:

"To estimate adolescent vaccination coverage in the United States, CDC analyzed data from the 2016 National Immunization Survey–Teen (NIS-Teen) for 20,475 adolescents aged 13–17 years. During 2015–2016, coverage increased for ≥1 dose of Tdap (from 86.4% to 88.0%) and for each HPV vaccine dose (from 56.1% to 60.4% for ≥1 dose). Among adolescents aged 17 years, coverage with ≥2 doses of MenACWY increased from 33.3% to 39.1%. In 2016, 43.4% of adolescents (49.5% of females; 37.5% of males) were up to date with the HPV vaccination series, applying the updated HPV vaccine recommendations retrospectively.†."*

and includes in a footnote:

"† Adolescents were considered to be up to date with HPV vaccination if they had received ≥3 doses, or if each of the following applied: 1) they had received 2 doses; 2) the first dose was received before their 15th birthday; and 3) the difference between dates of first and second doses was ≥5 months minus 4 days, the absolute minimum interval between the first and second doses (https://www.cdc.gov/vaccines/programs/iis/cdsi.html)."

and states:

"National Vaccination Coverage

In 2016, ≥1-dose HPV vaccination coverage among teens was 60.4% (65.1% for females; 56.0% for males), and 43.4% were up to date with the recommended HPV vaccination series (49.5% for females; 37.5% for males) (Table 1). During 2015–2016, HPV vaccination coverage increased for ≥1 dose by 4.3 percentage points overall (6.2 for males), for ≥2 doses by 3.8 percentage points (2.8 for females; 4.6 for males), and for ≥3 doses by 2.2 percentage points (3.4 for males) (Table 1) (Figure 1). Also during 2015–2016, coverage with ≥1 Tdap dose increased by 1.6 percentage points to 88.0%; …coverage with ≥2 MenACWY doses increased by 5.8 percentage points to 39.1% (Table 1) (Figure 1)."

and includes a table entitled:

"*TABLE 1. Estimated vaccination coverage with selected vaccines and doses among adolescents aged 13–17* years, by age at interview — National Immunization Survey–Teen, United States, 2016****",***

whose selected column headings and rows are as follows:

Vaccine	% (95% CI) †		
	Age (yrs)		Total
	13 (n = 4,209)	14 (n = 4,256)	2016 (N = 20,475)
Tdap§ ≥1 dose	87.6 (85.4–89.6)	88.5 (86.3–90.4)	88.0 (87.1–88.9)
MenACWY**			
≥1 dose	81.7 (79.2–83.9)	83.3 (81.1–85.4)	82.2 (81.2–83.2)
≥2 doses††	—	—	39.1 (36.1–42.1)
MMR vaccine ≥2 doses	90.7 (88.6–92.4)	91.9 (90.3–93.3)	90.9 (90.1–91.6)
Hepatitis B vaccine ≥3 doses	91.7 (89.7–93.3)	92.5 (91.0–93.8)	91.4 (90.7–92.1)
HPV§§ vaccine			
All adolescents			
≥1 dose	53.5 (50.8–56.2)	59.2 (56.3–62.0)¶	60.4 (59.2–61.6)¶
≥2 doses	40.6 (37.9–43.4)	47.2 (44.2–50.2)¶	49.2 (47.9–50.4)¶
≥3 doses	27.0 (24.5–29.6)	34.9 (32.0–38.0)¶	37.1 (35.9–38.4)¶
HPV UTD***	33.7 (31.1–36.5)	42.5 (39.5–45.6)¶	43.4 (42.1–44.7)¶
Females			
≥1 dose	54.7 (50.9–58.4)	62.7 (58.5–66.7)¶¶	65.1 (63.3–66.8)¶¶
≥2 doses	42.9 (39.1–46.8)	50.2 (45.7–54.6)¶¶	55.0 (53.1–56.8)¶¶
≥3 doses	28.8 (25.2–32.6)	38.4 (34.1–42.9)¶¶	43.0 (41.1–44.9)¶¶
HPV UTD	36.1 (32.4–40.0)	46.1 (41.6–50.5)¶¶	49.5 (47.6–51.4)¶¶
Males			
≥1 dose	52.4 (48.5–56.3)	56.0 (52.0–59.9)	56.0 (54.3–57.7)
≥2 doses	38.4 (34.6–42.3)	44.5 (40.4–48.6)¶¶	43.6 (41.9–45.3)¶¶
≥3 doses	25.2 (21.9–28.8)	31.8 (27.9–36.0)¶¶	31.5 (30.0–33.2)¶¶
HPV UTD	31.4 (27.9–35.3)	39.3 (35.2–43.5)¶¶	37.5 (35.8–39.2)¶¶

Below the table are the following notes referenced by the table (or title):

*"**Abbreviations:** confidence interval; …MenACWY = quadrivalent meningococcal conjugate vaccine; MMR = measles, mumps, and rubella; …NIS-Teen = National Immunization Survey–Teen; Tdap = tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis vaccine; UTD = up to date.*

† Estimates with 95% CI half-widths >10 might not be reliable.

§ Includes percentages receiving Tdap vaccine at age ≥10 years…

*** Includes percentages receiving MenACWY or meningococcal-unknown type vaccine.*

†† ACIP recommends a booster dose at age 16 years. Estimates are provided for ≥2 doses of MenACWY or meningococcal-unknown type vaccine. Calculated only among adolescents who were aged 17 years at time of interview. Does not include adolescents who received 1 dose of MenACWY vaccine at age ≥16 years.

§§ HPV vaccine, nine-valent (9vHPV), quadrivalent (4vHPV), or bivalent (2vHPV). For ≥1, ≥2, and ≥3 dose measures, percentages are reported among females and males combined (N = 20,475) and for females only (n = 9,661) and males only (n = 10,814).

**** HPV UTD includes those who received ≥3 doses, and those who received 2 doses when the first HPV vaccine dose was initiated before age 15 years and the time between the first and second dose was at least 5 months minus 4 days."*

(l) 2017:

The Plaintiff hereby requests that the Court take judicial notice of the CDC-published report entitled:

- "National, Regional, State, and Selected Local Area Vaccination Coverage Among Adolescents Aged 13-17 Years - United States, 2017."

  Citation: Walker TY, Elam-Evans LD, Yankey D, et al. CDC MMWR 2018 (Aug 24);67(33):909-917. DOI: http://dx.doi.org/10.15585/mmwr.mm6733a1, accessible at https://www.cdc.gov/mmwr/volumes/67/wr/mm6733a1.htm (html) or https://www.cdc.gov/mmwr/volumes/67/wr/pdfs/mm6733a1-H.pdf (pdf)

  [published correction appears in CDC MMWR 2018 Oct 19;67(41):1164].
  (last accessed June 12, 2020)
  (hereafter "CDC Secondary School Coverage Report 2017")

  A true and correct copy of the aforesaid report is attached hereto as **Exhibit 50**.

The report states:

"To estimate U.S. adolescent vaccination coverage, CDC analyzed data from the 2017 National Immunization Survey–Teen (NIS-Teen) for 20,949 adolescents aged 13–17 years. During 2016–2017, coverage increased for ≥1 dose of HPV vaccine (from 60.4% to 65.5%), ≥1 dose of MenACWY (82.2% to 85.1%), and ≥2 doses of MenACWY (39.1% to 44.3%). Coverage with Tdap remained stable at 88.7%. In 2017, 48.6% of adolescents were UTD with the HPV vaccine series (HPV UTD) compared with 43.4% in 2016.†."*

and includes in a footnote:

† Adolescents were considered to be HPV UTD if they had received ≥3 doses, or if all of the following applied: 1) they had received 2 doses; 2) the first dose was received before the 15th birthday; and 3) the interval between the first and second doses was ≥5 months minus 4 days, the absolute minimum interval between the first and second doses https://www.cdc.gov/vaccines/programs/iis/cdsi.html."

and states:

"National Vaccination Coverage

In 2017, coverage with ≥1 dose of HPV vaccine was 65.5% among teens, an increase of 5.1 percentage points compared with 2016; 48.6% were HPV UTD with the recommended vaccination series, an increase of 5.2 percentage points from 2016 (Table 1) (Figure). Among adolescents surveyed during 2016–2017, HPV vaccination initiation by age 13 years increased an average of 5.9 percentage points for each birth year, from 19.6% (1998 birth cohort) to 56.3% (2004 birth cohort) (Supplementary Figure 1, https://stacks.cdc.gov/view/cdc/58071). HPV UTD status by age 13 years increased an average of 3.6 percentage points for each birth year, from 7.7% (1998 birth cohort) to 29.8% (2004 birth cohort)."

and includes a table entitled:

"**TABLE 1. Estimated vaccination coverage with selected vaccines and doses among adolescents aged 13–17* years, by age at interview — National Immunization Survey–Teen (NIS–Teen), United States, 2017**",

whose selected column headings and rows are as follows:

	Age (yrs), % (95% CI) †		Total % (95% CI) †
	13	14	2017
Vaccine	(n = 4,283)	(n = 4,429)	(N = 20,949)
Tdap§ ≥1 dose	86.4 (84.0–88.4)	89.9 (88.0–91.5)	88.7 (87.8–89.6)
MenACWY**			
≥1 dose	83.6 (81.2–85.8)	85.8 (83.8–87.6)	85.1 (84.2–86.1)
≥1 dose	—	—	44.3 (41.4–47.2)
MMR ≥2 doses	93.7 (92.4–94.8)	91.6 (89.6–93.3)	92.1 (91.3–92.8)
Hepatitis B vaccine ≥3 doses	93.0 (91.4–94.3)	92.4 (90.6–93.8)	91.9 (91.1–92.6)
HPV¶¶ vaccine – all adolescents			
≥1 dose	60.7 (57.9–63.5)***	65.1 (62.5–67.6)¶	65.5 (64.3–66.7)
UTD†††	39.0 (36.2–41.8)***	48.3 (45.5–51.2)¶	48.6 (47.3–49.9)
HPV¶¶ vaccine – females			
≥1 dose	64.5 (60.5–68.3)***	67.8 (63.8–71.6)	68.6 (66.9–70.2)
UTD	43.7 (39.6–47.8)***	52.7 (48.3–57.1)¶	53.1 (51.2–55.0)
HPV¶¶ vaccine – males			
≥1 dose	57.1 (53.1–61.0)	62.4 (59.1–65.6)¶	62.6 (60.9–64.2)
UTD	34.4 (30.8–38.2)	44.1 (40.6–47.6)¶	44.3 (42.6–46.0)

Below the table are the following notes referenced by the table (or title):

*"**Abbreviations:** confidence interval; …MenACWY = quadrivalent meningococcal conjugate vaccine; MMR = measles, mumps, and rubella vaccine; NA = not applicable, Tdap = tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis vaccine; UTD = up to date.*

† Estimates with 95% CIs >20 might be unreliable.

§ Includes percentages receiving Tdap vaccine at age ≥10 years….

*** Includes percentages receiving MenACWY or meningococcal vaccine of unknown type….*

§§ ≥2 doses of MenACWY or meningococcal vaccine of unknown type. Calculated only among adolescents who were aged 17 years at interview. Does not include adolescents who received one dose of MenACWY vaccine at age ≥16 years.

¶¶ HPV vaccine, nine–valent (9vHPV), quadrivalent (4vHPV), or bivalent (2vHPV). For ≥1 dose measures, percentages are reported among females and males combined (N = 20,949) and for females only (N = 9,845) and males only (N = 11,104)…

††† HPV UTD includes those with ≥3 doses, and those with 2 doses when the first HPV vaccine dose was initiated at age <15 years and at least 5 months minus 4 days elapsed between the first and second dose. This update to the HPV recommendation occurred in December of 2016."

(m) 2018:

The Plaintiff hereby requests that the Court take judicial notice of the CDC-published report entitled:

- "National, Regional, State, and Selected Local Area Vaccination Coverage Among Adolescents Aged 13–17 Years — United States, 2018."

  Citation: Walker TY, Elam-Evans LD, Yankey D, et al. CDC MMWR Morb Mortal Wkly Rep 2019;68:718–723. DOI: http://dx.doi.org/10.15585/mmwr.mm6833a2, accessible at https://www.cdc.gov/mmwr/volumes/68/wr/mm6833a2.htm (html) or https://www.cdc.gov/mmwr/volumes/68/wr/pdfs/mm6833a2-H.pdf (pdf) (last accessed June 12, 2020)
  (hereafter "CDC Secondary School Coverage Report 2018")

  A true and correct copy of the aforesaid report is attached hereto as **Exhibit 51**.

The report states:

"To estimate vaccination coverage among adolescents in the United States, CDC analyzed data from the 2018 National Immunization Survey–Teen (NIS-Teen) which included 18,700 adolescents aged 13–17 years. During 2017–2018, coverage with ≥1 dose of HPV vaccine increased from 65.5% to 68.1%, and the percentage of adolescents up-to-date† with the HPV vaccine series increased from 48.6% to 51.1%, although the increases were only observed among males. Vaccination coverage increases were also observed for ≥1 MenACWY dose (from 85.1% to 86.6%) and ≥2 MenACWY doses (from 44.3% to 50.8%).*

Coverage with tetanus and reduced diphtheria toxoids and acellular pertussis vaccine (Tdap) remained stable at 89%.†."

and includes in a footnote:

"† Adolescents were considered to be up to date with HPV vaccination if they had received ≥3 doses, or if all of the following applied: 1) they had received 2 doses; 2) the first dose was received before their 15th birthday; and 3) the difference between dates of first and second doses was ≥5 months minus 4 days, the absolute minimum interval between the first and second doses (https://www.cdc.gov/vaccines/programs/iis/cdsi.html)

and states:

"National Vaccination Coverage

In 2018, 51.1% of adolescents aged 13–17 years were up to date with the HPV vaccine series, and 68.1% had received ≥1 dose of HPV vaccine (Table 1) (Figure). During 2017–2018, the increase in HPV vaccination coverage was attributable to increases among males only (increase of 4.4 percentage points in males who were up to date versus 0.6 in females). Coverage with ≥1 MenACWY dose increased by 1.5 percentage points to 86.6%. Among persons aged 17 years, coverage with ≥2 MenACWY doses increased by 6.5 percentage points to 50.8%.."

includes a table entitled:

*"**TABLE 1. Estimated coverage with selected vaccines and doses among adolescents aged 13–17* years, by age at interview — National Immunization Survey–Teen (NIS-Teen), United States, 2018**",*

whose selected column headings and rows are as follows:

	Age at interview (yrs), % (95% CI)†		***Total (13-17 yr olds)***
	13	***14***	***2018***
Vaccine	***(n = 3,852)***	***(n = 3,875)***	***(n = 18,700)***
Tdap§ ≥1 dose	*87.1 (85.0–89.0)*	*87.7 (85.4–89.7)*	*88.9 (88.0–89.7)*
*MenACWY***			
≥1 dose	*86.3 (84.2–88.1)*	*86.2 (84.0–88.1)*	*86.6 (85.6–87.5)*
≥2 doses	—	—	*50.8 (47.7–53.8*
MMR ≥2 doses	*93.5 (92.1–94.7)*	*93.0 (91.6–94.2)*	*91.9 (91.2–92.6)*
Hepatitis B vaccine ≥3 doses	*93.1 (91.5–94.5)*	*93.0 (91.5–94.3)*	*92.1 (91.3–92.8)*
HPV¶¶ vaccine			
All adolescents			

*UTD***	*39.9 (37.0–42.9)*	*50.3 (47.3–53.2)¶*	*51.1 (49.8–52.5)*
≥1 dose	*62.6 (59.7–65.4)*	*66.9 (64.1–69.6)¶*	*68.1 (66.8–69.3)*
Females			
UTD	*38.9 (35.0–42.9)*	*52.7 (48.5–56.8)¶*	*53.7 (51.8–55.6)*
≥1 dose	*61.1 (56.9–65.2)*	*68.6 (64.4–72.5)¶*	*69.9 (68.1–71.6)*
Males			
UTD	*40.9 (36.5–45.3)*	*47.7 (43.6–51.8)¶*	*48.7 (46.8–50.6)*
≥1 dose	*64.0 (59.9–67.9)*	*65.1 (61.3–68.7)*	*66.3 (64.6–68.0)*

Below the table are the following notes referenced by the table (or title):

*"**Abbreviations:** confidence interval; …MenACWY = quadrivalent meningococcal conjugate vaccine; …MMR = measles, mumps, and rubella vaccine; NA = not applicable; Tdap = tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis vaccine; UTD = up-to-date.*

† Estimates with 95% CIs >20 might be unreliable.

§ Includes percentages receiving Tdap vaccine at age ≥10 years.
¶ Statistically significant difference (p<0.05) in estimated vaccination coverage by age; reference group was adolescents aged 13 years.

*** Includes percentages receiving MenACWY or meningococcal-unknown type vaccine….*

¶¶ HPV vaccine, 9-valent (9vHPV), quadrivalent (4vHPV), or bivalent (2vHPV). Percentages are reported among females and males combined (N = 18,700) and for females only (N = 8,928) and males only (N = 9,772).

**** HPV UTD includes those with ≥3 doses, and those with 2 doses when the first HPV vaccine dose was initiated at age <15 years, and there was at least 5 months minus 4 days between the first and second dose. This update to the HPV recommendation occurred in December 2016 (https://www.cdc.gov/mmwr/volumes/65/wr/mm6549a5.htm)."*

The report also includes a table entitled:

*"**TABLE 2. Estimated vaccination coverage with selected vaccines and doses among adolescents* aged 13–17 years by metropolitan statistical area† and health insurance status§ — National Immunization Survey–Teen (NIS-Teen), United States, 2018"***

whose selected column headings and selected rows are as follows:

Vaccine	Health insurance status % (95% CI)¶			
	Private insurance only (n = 10,404)	Any Medicaid (n = 5,999)	Other insurance (n = 1,516)	Uninsured (n = 781)
Tdap§ ≥1 dose	90.1 (89.0–91.2)	88.2 (86.6–89.6)††	85.6 (82.3–88.3)††	85.1 (80.7–88.6)††
MenACWY§§				
≥1 dose	87.6 (86.4–88.8)	86.5 (84.8–88.0)	84.3 (81.1–87.0)††	78.3 (72.7–83.0)††
≥2 doses¶¶	52.8 (48.6–56.9)	52.4 (46.9–57.8)	38.6 (30.0–48.0)††	34.1 (21.6–49.4)††
HPV*** vaccine				
UTD†††	50.2 (48.4–52.0)	55.7 (53.4–58.1)††	45.1 (40.9–49.3)††	35.5 (30.1–41.4)††
≥1 dose	65.6 (63.8–67.3)	74.4 (72.3–76.3)††	62.6 (58.5–66.5)	56.2 (50.1–62.2)††
MMR ≥2 doses	92.8 (91.9–93.6)	92.0 (90.6–93.1)	90.1 (87.3–92.3)††	84.2 (78.6–88.5)††
Hepatitis B ≥3 doses	93.0 (91.9–93.9)	92.1 (90.8–93.3)	90.5 (87.8–92.6)	84.1 (78.5–88.4)††

hereafter "Vaccination Coverage in 13-17 year olds by Insurance Status Table 2018"

Below the table are the following abbreviation expansions and notes referenced by the table:

*"**Abbreviations:** CI = confidence interval; HPV = human papillomavirus; MenACWY = quadrivalent meningococcal conjugate vaccine; MMR = measles, mumps, and rubella vaccine; MSA= metropolitan statistical area; Tdap = tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis vaccine; UTD = up-to-date.*

** Adolescents (N = 18,700) in the 2018 NIS-Teen were born January 2000–February 2006…*

§ Adolescents' health insurance status was reported by parent or guardian. "Other insurance" includes the Children's Health Insurance Program, military insurance, Indian Health Service, and any other type of health insurance not mentioned elsewhere.

¶ Estimates with CIs >20 might be unreliable.

*** Includes percentages receiving Tdap vaccine at age ≥10 years.*

†† Statistically significant difference (p<0.05) in estimated vaccination coverage …The referent groups were …adolescents with private insurance only….

§§ Includes percentages receiving MenACWY and meningococcal-unknown type vaccine.

¶¶ ≥2 doses of MenACWY or meningococcal-unknown type vaccine. Calculated only among adolescents aged 17 years at interview. Does not include adolescents who received 1 dose of MenACWY vaccine at age ≥16 years.

**** HPV vaccine, nine-valent (9vHPV), quadrivalent (4vHPV), or bivalent (2vHPV) in females and males combined.*

††† HPV UTD includes those with ≥3 doses, and those with 2 doses when the first HPV vaccine dose was initiated at age <15 years, and there was at least 5 months minus 4 days between the first and second dose. This update to the HPV recommendation occurred in December 2016 (https://www.cdc.gov/mmwr/volumes/65/wr/mm6549a5.htm)."

Hereafter this Notice will refer to all of the reports referenced in this paragraph 5.4 as "CDC Secondary School Coverage Reports".

Hereafter this Notice will refer to the group of reports referenced in this paragraph 5, as "Vaccination Coverage Reports".

PART 2 – RISK FROM NON-VACCINATION

6. Non-vaccination Risk (SRIU) – generally applicable information and notes

6.1 Basic formulae applicable for calculating non-vaccination risk

The Plaintiff hereby requests that the Court take judicial notice of the document entitled "On Sample Sizes to Estimate the Protective Efficacy of a Vaccine"

- article whose citation is:
  Citation: Robert T. O'Neill (FDA). Statistics in Medicine 1988, Vol. 7, 1279-1288, accessible at: https://onlinelibrary.wiley.com/doi/abs/10.1002/sim.4780071208
  (last accessed June 16, 2020)
  (hereafter "Efficacy Formula Article")

  A true and correct copy of the aforesaid article is attached hereto as **Exhibit 52**.

The Efficacy Formula Article refers to:

> *"vaccine protective efficacy, defined as VE = 1 — ARV/ARU where ARV is the disease attack rate in the vaccinated group and ARU is the disease attack rate in the controls".*

(a) Formulas for Disease Rate (DRU) and Serious outcome Rate in the Unvaccinated (SRU)

The following formula can be algebraically derived from the formula given in Exhibit 52 ("VE = 1 — ARV/ARU"),

DRU = DRP / (1 – (VC x VE)),

where DRU = Disease Rate in the Unvaccinated, and

DRP = Disease Rate in the Population, and

VC = Vaccination Coverage rate, and

VE = Vaccine Effectiveness rate.[1]

[1] Derivation method: Substitute the parameters in the first formula using the following relevant formulas: DRV = DV / PV, DV = D – DU, PV = P x VC, DU = DRU x PU, PU = P x (1 – VC), and D = DRP x P,
where DV = number of disease cases in the Vaccinated,
and PV = number of persons who are Vaccinated,
and DU = number of Disease cases in the unvaccinated,
and PU = number of persons who are unvaccinated,
and D = total number of Disease cases,
and P = total number of persons in the Population,
and DV = number of cases in the vaccinated,
and DU = number of cases in the unvaccinated,
and VC = Vaccination Coverage rate (proportion of persons vaccinated),
and DRP = Disease notification Rate in the Population.

(hereafter “Formula for Disease Rate in Unvaccinated”)

Similarly, the following calculation is able to be made:

SRU = SRP / (1 – (VC x VE)),

where SRU = Serious outcome Rate in the Unvaccinated, and

SRP = Serious outcome Rate in the Population,

(hereafter “Formula for Serious Outcome Rate in the Unvaccinated”),

where SRP is directly known.

In this Notice, as is necessary for those formulas to be valid, the description of those described as “Unvaccinated” in the population means not having received any dose, or portion of any dose, of the vaccine that is designed to target the particular disease that is the subject of the analysis, but otherwise having essentially the same characteristics those vaccinated, such as socioeconomic status and vaccine eligibility as well as age.

Accordingly, except where otherwise stated, the relevant calculations within this Notice will incorporate the following assumptions:

- that the percentage of the unvaccinated population who are ineligible for vaccination is negligible, and
- that in the case of vaccines of which multiple doses are given, the combination of:
  - the percentage of the population that is partly vaccinated, and
  - the differential disease rate in that group compared to that in those who are unvaccinated,

  is low enough such that it does not significantly affect the overall DRU calculation result. “Partly vaccinated” is defined to mean receipt of at least one, but not all, of the doses that form the basis of the VC figure that is used in the calculation of DRU.

(b) Formulae for differential (Increased) Disease Rate in the Unvaccinated

Basic formula:

Based upon the formula (for DRU) and assumptions in the previous paragraph, the following formula can be algebraically derived:

DRIU = DRU x VE,

where DRIU = Differential (increased) disease rate/risk for an unvaccinated person above that for a vaccinated person.

Incorporating the formula in paragraph 6.1(a) above results in the following formula for estimating DRIU:

DRIU = DRP x VE / (1 – (VC x VE)),

(hereafter "Formula for Differential Disease Rate for Unvaccinated")

(c) Formulae for differential risk of Serious outcome for Unvaccinated

The differential rate/risk of a disease-related serious adverse event ("SAE") occurring in a vaccine-eligible person as a result of his/her not being vaccinated, "SRIU", can hence be represented mathematically as:

i. where figure(s) available for serious outcome rate per disease case:

SRIU = DRIU x SRD

where SRIU = Differential (increased) serious outcome rate/risk for an unvaccinated person above that for a vaccinated person, and

SRD = disease-associated SAE Rate per disease case (e.g. case fatality rate) in an unvaccinated, vaccine-eligible person

OR

ii. where figure(s) available directly for serious outcome rate per person:

SRIU = SRP x VE / (1 – (VC x VE)),

where SRIU = Differential (increased) serious adverse event rate/risk for an unvaccinated person above that for a vaccinated person

(hereafter "Formula for Differential Serious Outcome Rate for Unvaccinated").

(d) Other factors affecting DRP and/or SRP, hence DRU and/or SRU

Since the value of DRU is dependent upon and directly proportional to DRP, any factor affecting DRP will also have a flow-on effect to DRU. Such a factor may, for example, be one that affects the chance of transmission and/or of the development of symptoms.

Similarly, since the value of SRU is directly proportional to SRP, then any factor affecting SRP will also have a flow-on effect to SRU. Such a factor may, for example, be one that affects the quality of medical care or one that affects the vitality, or efficiency, of the innate immune system for protecting against long term harm.

In the case of some vaccine-targeted diseases, it may be hypothesized that an important factor affecting DRP may be mandatory vaccination itself – that it causes a significant enough increase in the level of VC as to result in significant interruption of transmission and hence reduction in DRP. However, that relationship may be reasoned to be possible only to the extent that:

- the targeted disease is contagious between humans, and
- the vaccine is designed to prevent transmission of the causative pathogen, and
- the vaccine is effective at preventing that transmission, and
- VC is uniformly high across the US within individual local community groups consisting of persons of varying ages in contact with each other, rather than VC only being high as a national average, and
- other US state(s) and/or countries where the vaccination is not and/or has not been, mandatory, has/have had significantly lower VC, and a demonstrably causally associated significantly higher DRU.

6.2 Disease notifications in the Population

(a) 2007-2016:

The Plaintiff hereby requests that the Court take judicial notice of the CDC-published reports each entitled,

“Summary of Notifiable Infectious Diseases – United States, <Year>”,

where <Year> ranges from 2007 through 2018, all of which reports are accessible via this web page: https://www.cdc.gov/mmwr/mmwr_nd/.

Individually, the titles, citations and locations of the reports are respectively:

- "Summary of Notifiable Diseases, United States, 2007",

  Citation CDC MMWR *56(53):1–94,* accessible at:
  https://www.cdc.gov/mmwr/PDF/wk/mm5653.pdf
  (hereafter "CDC Disease Notifications 2007")

  A true and correct copy of this report is attached hereto as **Exhibit 53**.

- "Summary of Notifiable Diseases, United States, 2008",

  Citation CDC MMWR 57(54);1-94, accessible at:
  https://www.cdc.gov/mmwr/pdf/wk/mm5754.pdf
  (hereafter "CDC Disease Notifications 2008")

  A true and correct copy of this report is attached hereto as **Exhibit 54**.

- "Summary of Notifiable Diseases, United States, 2009",

  Citation CDC MMWR 58(53);1-100, accessible at:
  https://www.cdc.gov/mmwr/pdf/wk/mm5853.pdf
  (hereafter "CDC Disease Notifications 2009")

  A true and correct copy of this report is attached hereto as **Exhibit 55**.

- "Summary of Notifiable Diseases, United States, 2010",

  Citation CDC MMWR 59(53);1-111, accessible at:
  https://www.cdc.gov/mmwr/pdf/wk/mm5953.pdf
  (hereafter "CDC Disease Notifications 2010")

  A true and correct copy of this report is attached hereto as **Exhibit 56**.

- "Summary of Notifiable Diseases, United States, 2011",

  Citation CDC MMWR 60(53);1-117, accessible at:
  https://www.cdc.gov/mmwr/pdf/wk/mm6053.pdf
  (hereafter "CDC Disease Notifications 2011")

  A true and correct copy of this report is attached hereto as **Exhibit 57**.

- "Summary of Notifiable Diseases, United States, 2012",

  Citation CDC MMWR 61(53);1-121, accessible at:
  https://www.cdc.gov/mmwr/pdf/wk/mm6153.pdf
  (hereafter "CDC Disease Notifications 2012")

A true and correct copy of this report is attached hereto as **Exhibit 58**.

- "Summary of Notifiable Diseases, United States, 2013",

  Citation CDC MMWR 62(53);1-119, accessible at:
  https://www.cdc.gov/mmwr/pdf/wk/mm6253.pdf
  (hereafter "CDC Disease Notifications 2013")

  A true and correct copy of this report is attached hereto as **Exhibit 59**.

- "Summary of Notifiable Diseases, United States, 2014",

  Citation CDC MMWR 63(54);1-152, accessible at:
  https://www.cdc.gov/mmwr/volumes/63/wr/pdfs/mm6354.pdf
  (hereafter "CDC Disease Notifications 2014")

  A true and correct copy of this report is attached hereto as **Exhibit 60**.

- "Summary of Notifiable Diseases, United States, 2015",

  Citation CDC MMWR 64(53);1–143, accessible at:
  https://www.cdc.gov/mmwr/volumes/64/wr/pdfs/mm6453.pdf
  (hereafter "CDC Disease Notifications 2015")

  A true and correct copy of this report is attached hereto as **Exhibit 61**.

(all nine reports last accessed June 8, 2020)

Each report states, for the relevant year:

> *"The Summary of Notifiable Diseases — United States… contains the official statistics, in tabular and graphic form, for the reported occurrence of nationally notifiable infectious diseases in the United States… These statistics are collected and compiled from reports sent by state health departments and territories to the National Notifiable Diseases Surveillance System (NNDSS), which is operated by CDC in collaboration with the Council of State and Territorial Epidemiologists (CSTE)."*

Based upon these excerpts, the CDC Disease Notifications contain the occurrences of nationally notifiable infectious diseases in the United States reported to the National Notifiable Diseases Surveillance System (NNDSS).

The CDC Disease Notifications do not state that the data is complete.

However, in the cases of:

- pertussis hospitalizations, a recently published reporting completeness estimate of 73% is available, which is assumed to apply to the relevant age range and accordingly is incorporated into the calculations of risk herein (in paragraph 7.3(d)i.e), and
- varicella disease, a published reporting completeness estimate of 65.7% is incorporated (in paragraph 7.6(a)ii).

With respect to other notifiable diseases, and these also to the extent that said reporting completeness percentages do not apply to the relevant age groups and years, the notifications data in the CDC Disease Notifications provide a starting basis for comparison.

(b) 2016 - 2018:

The Plaintiff hereby requests that the Court take judicial notice of the CDC Wonder tables entitled “Table 4 Reported cases of notifiable diseases and rates, by age group - United States”, for the years 2016 through 2018, all referenced under the title “Nationally Notifiable Infectious Diseases and Conditions, United States: Annual Tables”, accessible at:
https://wonder.cdc.gov/nndss/nndss_annual_tables_menu.asp

Individually, the titles and locations of the tables are respectively:

“TABLE 4. Reported cases of notifiable diseases and rates per 100,000, by age, excluding U.S. territories - - United States, 2016”, accessible at:
https://wonder.cdc.gov/nndss/static/2016/annual/2016-table4.html
(hereafter “CDC Disease Notifications 2016”)

A true and correct copy of this report is attached hereto as **Exhibit 62**.

- “TABLE 4. Reported cases of notifiable diseases and rates per 100,000, by age, excluding U.S. territories - - United States, 2017”, accessible at:
https://wonder.cdc.gov/nndss/static/2017/annual/2017-table4.html
(hereafter “CDC Disease Notifications 2017”)

  A true and correct copy of this report is attached hereto as **Exhibit 63**.

- “TABLE 4. Reported cases of notifiable diseases and rates per 100,000, by age, excluding U.S. territories - - United States, 2018”, accessible at:
https://wonder.cdc.gov/nndss/static/2018/annual/2018-table4.html
(hereafter “CDC Disease Notifications 2018”)

A true and correct copy of this report is attached hereto as **Exhibit 64**.

(all three reports last accessed June 8, 2020)

Hereafter this Notice may refer to all of the reports and tables combined for the years 2007 to 2018 (including relevant referenced Errata) (Exhibits 53 through 6417) as "CDC Disease Notifications".

CDC Disease Notifications 2016, CDC Disease Notifications 2017 and CDC Disease Notifications 2018 state the following:

> *"These are annual cases of selected infectious national notifiable diseases from the National Notifiable Diseases Surveillance System (NNDSS). NNDSS data reported by the 50 states, New York City, the District of Columbia, and the U.S. territories are collated and published."*

All calculations herein that are based upon the data provided in CDC Disease Notifications of disease incidence and deaths will also be based upon an assumption that the true numbers of cases and deaths from the diseases targeted by the subject vaccinations do not differ significantly from those published therein, except where the Notice states otherwise.

6.3 Vaccination effectiveness (VE)

(a) Assumptions in determination of vaccine-induced immunity

This Notice refers to medical research that has been conducted to measure effectiveness, including initial effectiveness and residual effectiveness after waning, and the calculations presented in the Notice are based upon assumptions of reliability of one or more of those methods. That is regardless of the amount of scientific evidence for or against the method's' reliability.

The "protection rate" is defined as the percentage of vaccine recipients judged to have become, and to have remained, protected against harm from the targeted infection, based upon one or more of those assumptions.

One potentially important assumption made in the numerical analysis of any benefit from any vaccination is that, with respect to the purpose of preventing a targeted infectious disease, any benefit gained by any success in doing so is not offset, or significantly offset, by any accompanying effect of increasing susceptibility to:

- related infections – other strains or serotypes of the same targeted virus or bacteria, such as the observation that pertussis *"vaccinated patients had*

significantly higher odds than unvaccinated patients of being infected with PRN-deficient strains", as discussed in paragraph 7.3(c)(1), and/or

- unrelated infections, by way of a weakening of any non-specific immune system defences, and/or
- the targeted infection in the longer term, such as by way of "linked-epitope suppression", as discussed in relation to pertussis also in paragraph 7.3(c)(1), or by loss of antibody transferred by the (vaccinated) mother to the fetus (increasing susceptibility to the infection during the more vulnerable age of infancy) or by another mechanism reducing the chance of development of natural immunity or reducing its duration, and/or
- immune system related disorders in the longer term by suppressing the development of natural immunity and as a result, suppressing any long term benefits that would otherwise be gained from the priming effect of going through that exercise on the immune system.

Another assumption is made where vaccination effectiveness estimates are based upon the results of studies that rely upon clinical diagnoses of the targeted infection for measuring the effectiveness. Such diagnoses are susceptible to:

- any parental and doctor observer bias, which is documented for example in relation to at least pertussis vaccination, as discussed in paragraph 7.3(c)(2), or
- any vaccination effect that results in an altered response to the infection and hence atypical symptoms, resulting in a reduction in the clinical recognizability of the infection but not necessarily reducing, indeed potentially increasing, the risk of a serious adverse effect arising from the infection, or
- any element of the case definition, upon which a diagnosis relies, which element artificially reduces the probability of diagnosis in a vaccinated person compared to an unvaccinated person.

Some other assumptions that are relevant and generally applicable to various subject vaccinations are listed below:

i. Seroprotection rate as measure of protection rate

In relation to the measured level of serum concentration of vaccine-induced neutralizing antibodies to the targeted antigen, said assumptions include, except where stated otherwise:

- that that concentration level is a reasonably reliable indicator of the level of protectiveness against any harm that would arise from infection of the individual, and
- that a threshold level that a referenced document states is an accepted indicator of existing protection is valid as such, resulting in all persons who have a concentration at least as high as that level, i.e. who are by definition “seroprotected”, being actually fully protected, or immune. Hence VE is assumed in these circumstances to be the seroprotection rate in the vaccinated population, and
- that essentially all of that level has come about as a result of prior vaccination, with an insignificant proportion of the population in the age group having instead developed the antibodies as a result of symptomatic or asymptomatic natural infection, and
- that the antigen-neutralizing power of those vaccine-induced antibodies that remain present does not significantly wane over time.

The making of any of the above assumptions, and especially all of them, has the potential to exaggerate the estimate of vaccine effectiveness.

ii. Exponential rate of decline in seroprotection rate

The Plaintiff hereby requests that the Court take judicial notice of the following document:

- a 20 page review by the World Health Organisation (WHO) entitled: “Diphtheria vaccine. Review of evidence on vaccine effectiveness and immunogenicity to assess the duration of protection ≥10 years after the last booster dose”, published April 2017, and accessible online at https://www.who.int/immunization/sage/meetings/2017/april/2_Review_Diphtheria_results_April2017_final_clean.pdf
  (hereafter “WHO Diphtheria Review”)

  A true and correct copy of the aforesaid report is attached hereto as **Exhibit 65**.

The WHO Diphtheria Review states (on page 12):

"Hammarlund et al 2016[52] performed a cross-sectional analysis of serum antibody titers in 546 adult subjects living in the United States. Based on analysis of antibody levels as a function of time after vaccination, diphtheria-specific immunity declined in the model with a 27-year half-life (95% CI: 18–51 years)."

According to this statement, the WHO believes that the decline in antibody level after vaccination occurs exponentially, meaning at a speed that varies according to the antibody level itself at any given time.

Except where otherwise specified, relevant interpolative calculations made in the Notice are accordingly based upon a simple model of decay occurring at an exponential rate following the initial phase of vaccine-induced production of the antibodies, which is assumed to be brief.

Hereafter the term "Waning Exponent" is defined as the approximate power (also called "exponent") to which the percentage of recipients who are so judged to be "protected", i.e. the "protection rate", is evidenced to exponentially wane over a year, or if specified, over a different time period. For example, if after a vaccination dose the protection rate is at some stage 90%, and the Waning Exponent is 2, then the protection rate a year later would be 81%.

(b) Calculation refinement where multiple protection rates within one age group

Vaccination coverage for a particular recommended vaccine dose may be lower than that for an earlier dose. Within a particular age group, based upon the above assumptions, those children given only the earlier dose may still hold some residual "protection" at the same time as others in the same age range hold "protection" from the more recent dose recommended to have been given to children around the beginning of the same age range. Therefore a determination of overall "protection" in that age range requires calculation of a weighted average of those two different average "protection" rates.

The weighted average VE is calculated according to the following formula, when VC1 is higher than VC2:

$$VE = (VC1 \times VE1 + (VC2 - VC1) \times VE2) / VC2$$

where VC1 = coverage rate for the more recent vaccine dose recommended to have been given to all children in that age group, and

VC2 = coverage rate applicable to the earlier dose, and

VE1 = average protection rate estimated for the more recent recommended dose, and

VE2 = average residual protection rate held by the remaining proportion (VC2 – VC1) of children given the earlier dose.

Therefore, in such circumstances as these,

- the Formula for Differential Disease Rate for Unvaccinated (defined in paragraph 6.1(a)) is refined to become:

  DRU = DRP / (1 – (VC2 x VE)), and

  Similarly, the Formula for Serious Outcome Rate in the Unvaccinated (defined in paragraph 6.1(a)) is refined to become:

  SRU = SRP x VE1 / (1 – (VC2 x VE)).

- the differential risk (associated with the vaccine-targeted disease(s)) for an unvaccinated child, DRIU, is defined herein as the level of risk above that for a child who is fully vaccinated according to CDC recommendations.

  Hence the Formula for Differential Disease Rate for Unvaccinated (defined in paragraph 6.1(b)) is refined to become:

  DRIU = DRU x VE1
  = DRP x VE1 / (1 – (VC2 x VE)).

  Similarly, the Formula for Differential Serious Outcome Rate for Unvaccinated (defined in paragraph 6.1(c)) is refined to become:

  SRIU = SRP x VE1 / (1 – (VC2 x VE)).

These calculations are applied herein in the case of the 11-19 year age group, for the booster vaccination doses against diphtheria, tetanus and pertussis.

6.4 Other factors affecting incidence of infection (DRP) and/or of SAE therefrom (SRD)

The Plaintiff hereby requests that the Court take judicial notice of the following documents:

- CDC-published report entitled “Annual Summary of Vital Statistics: Trends in the Health of Americans During the 20th Century.”

  Citation: Bernard Guyer, Mary Anne Freedman, Donna M. Strobino and Edward J. Sondik.. Pediatrics 2000;106;1307. DOI: 10.1542/peds.106.6.1307

https://www.factchecker.gr/wp-content/uploads/2017/10/PediatricsDec.2000-VOl-106No.6.pdf
(last accessed July 2, 2020)

(hereafter “Pediatrics Pre-Vaccination Mortality Decline Article”)

A true and correct copy of the aforesaid report is attached hereto as **Exhibit 66**.

- Chapter 1 “People and their environment” in report entitled “Australia’s food and nutrition 2012”

  Citation: Australian Institute of Health and Welfare 2012. Cat. no. PHE 163. Canberra: AIHW. https://doi.org/10.25816/5ec1da0b2547b
  (last accessed August 15, 2020)

  (hereafter “Australian Institute of Health and Welfare Report”)

  A true and correct copy of the aforesaid report is attached hereto as **Exhibit 67**.

- research article entitled: “Enhanced Human Neutrophil Vitamin C Status, Chemotaxis and Oxidant Generation Following Dietary Supplementation with Vitamin C-Rich *SunGold* Kiwifruit”

  Citation: Bozonet et.al 2015, Nutrients 2015, 7, 2574-2588; doi:10.3390/nu7042574. PMID:25912037
  https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4425162/pdf/nutrients-07-02574.pdf
  (last accessed October 10, 2020)

  (hereafter “Vitamin C-Rich Kiwifruit Benefit Article”)

  A true and correct copy of the aforesaid report is attached hereto as **Exhibit 68**.

- research article entitled: “Total vitamin C, ascorbic acid, and dehydroascorbic acid concentrations in plasma of critically ill patients”

  Citation: Schorah CJ et al. Am J Clin Nutr 1996 May;63(5):760-5. doi: 10.1093/ajcn/63.5.760. PMID:8615361 https://pubmed.ncbi.nlm.nih.gov/8615361/
  (last accessed October 10, 2020))

  (hereafter “Low Vitamin C in Critically ill Article”)

  A true and correct copy of the aforesaid report is attached hereto as **Exhibit 69**.

- research article entitled: “Vitamin C may affect lung infections”

  Citation: Hemila and Louhiala 2007. J R Soc Med; Nov; 100(11): 495–498. doi: 10.1258/jrsm.100.11.495
  (http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2099400/)
  (last accessed October 10, 2020)

  (hereafter “Vitamin C Protection Against Lung Infections Article”)

  A true and correct copy of the aforesaid report is attached hereto as **Exhibit 70**.

- research article entitled: “Vitamin C and infections”

  Citation: Hemilä H (2017). Nutrients. 9(4). pii:E339
  (https://www.ncbi.nlm.nih.gov/pubmed/28353648)
  (last accessed October 10, 2020)

  (hereafter “Vitamin C and Infections Review”)

  A true and correct copy of the aforesaid report is attached hereto as **Exhibit 71**.

- research article entitled: “Vitamin C: intravenous use by complementary and alternative medicine practitioners and adverse effects”

  Citation: Padayatty SJ, Sun AY, Chen Q, Espey MG, Drisko J, Levine M. *PLoS One*. 2010;5(7):e11414. Published 2010 Jul 7. doi:10.1371/journal.pone.0011414.
  (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2898816/)
  (last accessed October 10, 2020)

  (hereafter “Vitamin C Intravenous Use Article”)

  A true and correct copy of the aforesaid report is attached hereto as **Exhibit 72**.

The calculations presented herein of estimated risk of SAEs arising from non-vaccination are made on the basis of the risk approximating the estimated rate of such SAEs having occurred in the unvaccinated in recent years, primarily 2010-2018.

However that basis relies on an assumption that those SAEs were not otherwise avoidable by one or more alternative, safer (or risk-free) measures, which the precautionary principle obliges ought to be implemented first before resorting to risk-carrying measures. To whatever extent such measures could have been

implemented, as a result of relevant research and/or education and/or law and/or guidelines and/or programs, and hence those SAEs prevented, the estimated SAE risk arising from non-vaccination is overestimated.

i. **Disease declines in 20th century prior to targeting vaccinations**

The Pediatrics Pre-Vaccination Mortality Decline Article states:

"At the beginning of the 20th century, the leading causes of child mortality in the 1- to 19-year-old age group were infectious diseases, including diarrheal diseases, diphtheria, measles, pneumonia and influenza, scarlet fever, tuberculosis, typhoid and paratyphoid fevers, and whooping cough."

"Vaccines against diphtheria, tetanus, and pertussis became available during the late 1920s but only widely used in routine pediatric practice after World War II. Thus vaccination does not account for the impressive declines in mortality seen in the first half of the century."

"Between 1900 and 1998, the death rate from the major infectious diseases declined 99.7%, from 466 to 0.7 deaths per 100 000 (Fig 9). The percentage of child deaths attributable to infectious diseases declined from 61.6% to 2%... Once again, nearly 90% of the decline in infectious disease mortality among US children occurred before 1940, when few antibiotics or vaccines were available."

Based upon these statements, protective improvements in relation to factors other than vaccination have been responsible for virtually all of the "*impressive declines in mortality*" from vaccine-targeted and other infectious diseases in the 20th century, with "nearly 90%" of that decline having already occurred "*before 1940, when few antibiotics or vaccines were available*" and vaccines were not "*widely used in routine pediatric practice*".

which for infectious diseases for which the vaccination s

ii. **Post-vaccination declines in the unvaccinated without herd immunity**

The Pediatrics Pre-Vaccination Mortality also states:

"In the early 1920s, diphtheria accounted for about 175 000 cases annually and pertussis for nearly 150 000 cases; measles accounted for about half a million annual cases before the introduction of vaccine in the 1960s. Deaths from these diseases have been virtually eliminated, as have deaths from Haemophilus influenzae, tetanus, and poliomyelitis.[45]""

Importantly, the dramatic decline in morbidity and mortality rates have continued in the *unvaccinated* in spite of the fact that in the case of some of the applicable diseases, the nature of the disease or the design of the vaccine is such that vaccination does prevent transmission. This is covered in the case of diphtheria, tetanus and pertussis in paragraphs 7.1(f), 7.2(f) and 7.3(f) respectively. That means that the improvement cannot have arisen from vaccination, indirectly through herd immunity.

That then further undermines the validity of any assumption made that a reduction today in vaccination uptake would lead to a significant increase, or an increase at all, in morbidity in the case of other diseases, such as measles. As covered in paragraph 7.5(d)i.a. herein on measles, even in Britain in 1963, which was prior to vaccination, the case fatality rate had already declined to 1 in 10,000 in non-immunocompromised children.

It also follows, based upon the indicated protective power of such other factors, that a suboptimal status today in relation to one or more such other factors may make an important contribution to the risk that remains today from one or more vaccine-targeted diseases. This undermines:

- the validity of any assumption that is made that any disease-associated SAEs that occur today can be purely or predominantly attributed to inadequate vaccination coverage of the individual and/or community, and
- accordingly, the wisdom of diverting into vaccination programs resources that would otherwise be available for more completely investigating the importance of such other factors that are safer than vaccination and prioritizing, where possible, more complete implementation of them as preventative and/or treatment measures.

Only the SRP that remains after practically exhaustive implementation of improvements in relation to such other safer factors is the appropriate SAE rate to use to calculate the benefit of vaccination (SRIU) for comparison with the risk of vaccination (SRIV).

(a) Specific identification of important such factors

i. socioeconomic status, water, sewage, food safety, hygiene education, housing and crowding

The Pediatrics Pre-Vaccination Mortality Decline Article additionally refers to some of the factors believed to have caused of those "*impressive declines",* as follows:

> *"The major declines in child mortality that occurred in the first third of the 20th century have been attributable to a combination of improved socioeconomic conditions in this country and the public health strategies to protect the health of Americans. These public health measures included the establishment of local health departments in nearly all of the states. State and local health departments implemented these public health measures including water treatment, food safety, organized solid waste disposal, and public education about hygienic practices. …improvements in housing and decreased crowding in US cities are linked to the reductions in mortality from tuberculosis and other diseases attributable to person-to-person airborne transmission."*

Based upon those statements, such factors included socioeconomic conditions, water treatment, food safety, sewage systems, public hygiene education, housing and level of crowding.

ii. nutrition

Such other factors also include nutrition, according to the Australian Institute of Health and Welfare Report as follows:

> *"Good nutrition contributes to quality of life, helps maintain healthy body weight, protects against infections, and reduces the risk of chronic disease and premature death. Alternatively, poor dietary choices are associated with many chronic diseases that are a major cause of death and disability in Australia, and their prevalence is steadily increasing. The burden of disease due to poor diet is often associated with large intakes of energy-dense foods, with high saturated fat, sugar and/or salt content, and low intakes of nutrient-dense foods, such as vegetables, fruit and wholegrain cereals."*

a. **Example - vitamin C**

Based upon the document excerpts below, an important example of nutrition that is relevant today to the determination of the risk of vaccine-targeted infectious disease-associated SAEs is vitamin C.

The excerpts refer to vitamin C being used as a preventative and/or treatment to minimise the duration and severity of illness and to prevent complications and death.

The excerpts refer to vitamin C intakes by way of vitamin C-rich foods such as kiwifruit and/or by supplementation.

Minimum vitamin C level needed to avoid scurvy symptoms

The Vitamin C and Infections Review states:

"Clinical scurvy may appear when the plasma concentration falls below 11 µmol/L, which corresponds to an intake of less than 0.01 g/day [12–14]."

Low vitamin C uptake in the modern day

The Vitamin C and Infections Review states:

"Low vitamin C levels are not just of historical relevance. Cases of scurvy in hospitals have been described in several recent case reports [38,39]. Surveys have …shown that plasma vitamin C levels below 11 µmol/L were found for 14% of males and 10% of females in the USA"

"The mean vitamin C intake in adults in the USA has been about 0.10 g/day, but 10% of the population has had intake levels of less than 0.04 g/day [14]."

"Thus, if low intake levels of vitamin C have adverse effects on the incidence and severity of infections, this may be important also in population groups in western countries, and not just in developing countries."

and that indeed,

"Cases of scurvy in hospitals have been described in several recent case reports [38,39]. One survey estimated that about 10% of hospitalized elderly patients had scurvy [40]."

Low vitamin C predisposes to infections

The Vitamin C and Infections Review states:

> *'Alfred Hess (1920) …commented that in "a lack of the antiscorbutic factor (vitamin C) which leads to scurvy, at the same time predisposes to infections (particularly of the respiratory tract) ... Hess (1920) concluded… "Indeed one of the striking and important symptoms of scurvy is the marked susceptibility to infection" '*

and

> *"It seems plausible that less severe vitamin C deficiency, which may be called "marginal vitamin C deficiency", can also be associated with increased risk and severity of infections, although the effects may be less pronounced than those caused by scurvy."*

The body produces reactive oxygen species (ROS) to kill microbes

The Vitamin C and Infections Review states:

> *"Many infections lead to the activation of phagocytes, which release oxidizing agents referred to as reactive oxygen species (ROS)."*

The Vitamin C-Rich Kiwifruit Benefit Article states:

> *"Neutrophils are the body's primary defenders against invading pathogens. These cells migrate to loci of infection where they engulf micro-organisms and subject them to an array of reactive oxygen species and antimicrobial proteins to effect killing."*

However, ROS are also harmful to the host

The Vitamin C and Infections Review states:

> *"However, many of the ROS appear to be harmful to the host cells, and in some cases they seem to play a role in the pathogenesis of infections."*

Excessive ROS accordingly accompanies diseases

The Low Vitamin C in Critically ill Article states:

> *"The excessive generation of reactive oxygen species has been reported to occur as part of the metabolic process that accompanies both acute and chronic disease."*

Excess ROS need to be scavenged with sufficient antioxidants

The Low Vitamin C in Critically ill Article states:

"There is potential in critically ill patients for a massive increase in the generation of reactive oxygen species (3). If this increase exceeds the capacity of the antioxidant defense, these patients may be susceptible to further tissue damage, which could lead to complications such as adult respiratory distress syndrome (3)."

The Vitamin C and Infections Review states:

"Herpes zoster (reactivation of varicella zoster virus) can cause long lasting post-herpetic neuralgia (PHN). Chen (2009) found that patients with PHN had significantly lower plasma vitamin C plasma than healthy volunteers".

and

"Vitamin C is …a powerful antioxidant".

In the most critically ill, vitamin C levels are the lowest

The Low Vitamin C in Critically ill Article states:

"We …investigated plasma concentrations of ascorbic acid and total vitamin C (ascorbic acid and dehydroascorbic acid) in patients who are critically ill in an intensive care unit (ICU)"

and

"the lowest concentrations were associated with the most severe disease".

In infections, ROS deplete vitamin C, leading to oxidative damage

The Vitamin C and Infections Review states:

"There is evidence that plasma, leukocyte and urinary vitamin C levels decrease in the common cold and in other infections… Vitamin C levels are …decreased by pneumonia."

and

"Influenza A infection in mice resulted in a decrease in vitamin C concentration in bronchoalveolar lavage fluid, which was concomitant with an increase in dehydroascorbic acid, the oxidized form of vitamin C [20], and in vitamin C deficiency, influenza led to greater lung pathology [21]. Respiratory syncytial virus decreased the expression of antioxidant enzymes thereby increasing oxidative damage [22]. Bacterial toxins have also led to the loss of vitamin C from many tissues in animal studies".

The Low Vitamin C in Critically ill Article states:

"It is probable that the generation of free radicals during the inflammatory response, particularly by white cells (3, 5, 20), could have accounted for the excessive oxidation of ascorbate and its subsequent loss from plasma."

By implication, vitamin C administration might be important

The Vitamin C and Infections Review states:

"Decreases in vitamin C levels during various infections imply that vitamin C administration might have a treatment effect on many patients with infections.

How immune system uses vitamin C

– proposition

The Vitamin C and Infections Review states:

"Vitamin C is an efficient water-soluble antioxidant and may protect host cells against the actions of ROS released by phagocytes. Phagocytes have a specific transport system by which the oxidized form of vitamin C (dehydroascorbic acid) is imported into the cell where it is converted into the reduced form of vitamin C."

and

"Vitamin C levels in white blood cells are tens of times higher than in plasma, which may indicate functional roles of the vitamin in these immune system cells."

– proposition supported by laboratory evidence

The Vitamin C and Infections Review states:

"Vitamin C has been shown to affect the functions of phagocytes, production of interferon, replication of viruses, and maturation of T-lymphocytes, etc. in laboratory studies".

The Vitamin C-Rich Kiwifruit Benefit Article states:

"Overall, our study showed that supplementation with vitamin C-rich SunGold Kiwifruit is associated with a significant increase in neutrophil vitamin C status and the important anti-microbial functions of chemotaxis and oxidant production."

Benefit of vitamin C indicated by animal studies

The Vitamin C and Infections Review states:

'Table 2 summarizes the animal studies in which pure vitamin C was administered to the "vitamin C" group. Overall, 148 animal studies had been published by 2005…. Vitamin C was found to be beneficial against various groups of infectious agents including bacteria, viruses… It is apparent that vitamin C reduced mortality in all etiological groups.'

and

'The studies on guinea pigs are most interesting since that species is dependent on dietary vitamin C as are humans. Infections in guinea pigs against which vitamin C was significantly beneficial included Mycobacterium tuberculosis*, …diphtheria toxin'*

and

'From a large series of animal studies we may conclude that vitamin C plays a role in preventing, shortening, and alleviating diverse infections. It seems evident that vitamin C has similar effects in humans.'

Vitamin C beneficial to infections in humans

The Vitamin C and Infections Review states:

"Table 7 shows the findings of the three vitamin C and pneumonia trials. Each of them found a ≥80% lower incidence of pneumonia for their vitamin C group."

Vitamin C supplementation treats infections

The Vitamin C and Infections Review states:

> *"Two studies have reported on the therapeutic effect of vitamin C for pneumonia patients…. Hunt (1994) carried out a randomized, double-blind placebo controlled trial with elderly people in the UK (mean age 81 years), who were hospitalized because of acute bronchitis or pneumonia…. Vitamin C reduced the respiratory symptom score in the more ill patients… . There were also six deaths during the study… five in the placebo group, but only one in the vitamin C group."* Only *"0.2 g/day of vitamin C"* was given.

and

> *"In the early 1900s, Casimir Funk… noted that an epidemic of pneumonia in the Sudan disappeared when antiscorbutic (vitamin C-containing) treatment was given to the numerous cases of scurvy that appeared at about the same time."*

and

> *"Mochalkin (1970) examined the effect of vitamin C on pneumonia patients in the former Soviet Union…. In the low dose vitamin C group the hospital stay was 19% shorter and in the high dose vitamin C group it was 36% shorter. A benefit was also reported on the normalization of chest X-ray, temperature, and erythrocyte sedimentation rate."*

and

> *"Jahan (1984) studied the effect of 1 g/day of intravenous vitamin C on tetanus patients in Bangladesh [131]. In children aged one to 12 years, there were no deaths in the vitamin C group, whereas there were 23 deaths in the control group ($p = 10^{-9}$) [1] (p. 17). In tetanus patients aged 13 to 30 years, there were 10 deaths in the vitamin C group compared with 19 deaths in the control group (p = 0.03)."*

and

"The ...infections discussed above, … pneumonia, and tetanus, were selected on the basis that the effects of vitamin C have been evaluated in Cochrane reviews,…. However, the selection of these …infections does not imply that the effects of vitamin C are limited to them….

High dose vitamin C needed to treat infections effectively

The Vitamin C and Infections Review states:

"Hume and Weyers (1973) showed that supplementation at the level of 0.2 g/day was insufficient to normalize leukocyte vitamin C levels in common cold patients, but when 6 g/day of vitamin C was administered, the decline in leukocyte vitamin C induced by the common cold was essentially abolished."

Bias against vitamin C over past half century

The Vitamin C and Infections Review states:

"In the first half of the 20th century, a large number of papers were published in the medical literature on vitamin C and infections and several physicians were enthusiastic about vitamin C."

and

"The topic was not dismissed because of large-scale controlled trials showing that vitamin C was ineffective. Instead, many rather large trials found benefits of vitamin C. There seem to be four particular reasons why the interest in vitamin C and infections disappeared."

and

'First, antibiotics were introduced in the mid-20th century. They have specific and sometimes very dramatic effects on bacterial infections...

Secondly, vitamin C was identified as the explanation for scurvy, which was considered a disease of the connective tissues. Evidently it seemed irrational to consider that a substance that "only" participates in collagen metabolism might also have effects on infections. However, the biochemistry and actions of vitamin C are complex and not limited to collagen metabolism.

Thirdly, …three papers published in 1975 appeared to herald the loss of interest in vitamin C and the common cold (Figure 1) and it seems

likely that they increased the negative attitude towards vitamin C for other infections as well.'

and

- *'Karlowski, Chalmers, et al. (1975) …claimed that the observed benefit was not caused by the physiological effects of vitamin C, but by the placebo effect. However, the "placebo-effect explanation" was shown afterwards to be erroneous…*
- *In the same year (1975), Chalmers published a review of the vitamin C and common cold studies. He pooled the results of seven studies and calculated that vitamin C would shorten colds only by 0.11 (SE 0.24) days… However, …studies that used very low doses of vitamin C (down to 0.025 g/day) were included, and there were errors in the calculations…*

  …some case reports have proposed that vitamin C doses should be over 15 g/day for the best treatment of colds [88,89]. Thus, it is possible that the doses used in most of the therapeutic studies, up to just 6–8 g/day, have not been sufficiently high to properly test the effects of vitamin C that might be achievable….
- *The third paper was a review published in JAMA by Michael Dykes and Paul Meier (1975). They analyzed selected studies and concluded that there was no convincing evidence that vitamin C has effects on colds [73]. However, they did not calculate the estimates of the effect nor any p-values, and many comments in their analysis were misleading.'*

and

"Although the three papers have serious biases, they have been used …as references …in texts on infectious diseases… when the authors claimed that vitamin C had been shown to be ineffective for colds … These three papers are the most manifest explanation for the collapse in the interest in vitamin C and the common cold after 1975, despite the strong evidence that had emerged by that time that ≥2 g/day vitamin C shortens and alleviates colds [70]."

and

'*Fourthly, "if a treatment bypasses the medical establishment and is sold directly to the public ... the temptation in the medical community is to accept uncritically the first bad news that comes along*"'

and

"Goodwin and Tangum gave several examples to support the conclusion that there has been a systematic bias against the concept that vitamins may yield benefits in levels higher than the minimum needed to avoid the classic deficiency diseases."

and

"The use of vitamin C for preventing and treating colds falls into the category of alternative medicine under the classifications used by the National Institutes of Health in the USA and of the Cochrane collaboration. However, such categorization does not reflect the level of evidence for vitamin C, …and may further amplify the inertia and prejudices against vitamin C"

High dose intravenous vitamin C "remarkably safe"

The Vitamin C Protection Against Lung Infections Article states:

"Although there have been speculations of potential harms of large doses of vitamin C, they have been shown to be unfounded.2,7,18 Furthermore, it has been stated that patients with pneumonia can take up to 100 g/day of vitamin C without developing diarrhoea, possibly because of the changes in vitamin C metabolism caused by the severe infection.19 Finally, in a recent pharmacokinetic study, participants were administered up to 100 g of vitamin C intravenously within a few hours without any reported adverse effects, indicating the safety of such a high dose in healthy people.20 " "the appearance of diarrhoea… is a trivial adverse effect that disappears quickly".

The Vitamin C Intravenous Use Article states:

"Other than the known complications of IV vitamin C in those with renal impairment or glucose 6 phosphate dehydrogenase deficiency, high dose intravenous vitamin C appears to be remarkably safe. Physicians should inquire about IV vitamin C use in patients with …untreatable, or intractable conditions…."

The Vitamin C and Infections Review states:

> *"Vitamin C is safe and costs only pennies per gram, and therefore even modest effects may be worth exploiting"*

Summary regarding vitamin C

Based upon the above excerpts, vitamin C…

- **Effectiveness**

  …may be important as an effective measure for substantially reducing or even eliminating the SAE risk that remains today from multiple relevant vaccine-targeted diseases, and

- **Safety**

  … is "*remarkably safe*", and

- **Underutilization**

  … is at a substantially suboptimal level in a significant percentage of the population and especially hospital patients, and

- **Practicality of higher utilization**

  … is cheap, costing "*only pennies per gram*", so is available to state and/or federal governments for causing and/or encouraging vitamin C uptake in the community (e.g. government-funded educational programs and/or subsidies) and hospitals on a significantly wider scale than at present.

Hence, if or where it is scientifically demonstrated, or in the absence of adequate relevant scientific studies it is reasonably apparent *prima facie,* that vitamin C is safer than vaccination, then the precautionary principle obliges such administration to be given higher priority to attempting to prevent the morbidity and mortality by way of vaccination.

It would then follow that only after full nationwide implementation, wherever practical, of administration of demonstrably beneficial levels of vitamin C and other such safer preventative and treatment measures, is the then residual SRIU ethically relevant for a proper determination of the benefit of vaccination to compare with its risk.

On the above two bases, all estimates in this Notice of SRIU (serious risk attributable to non-vaccination) are expressed as approximate upper limits for those estimates, i.e. they are prefixed by "<" (less than).

(b) Other disease-risk factors that may bias VE calculations

i. Co-morbidity status link to vaccination coverage

The CDC Disease Notifications 2015 states that all three patients who died from pertussis in 2015 were *"adolescents and adults with co-morbidities*".

It does not state whether or not these patients were vaccinated. However,

- to the extent that the presence of chronic ill health contraindicates or discourages vaccination, it may be reasoned that any attempt to reliably measure vaccination effectiveness based upon a comparison of morbidity and/or mortality in vaccinated versus unvaccinated persons is invalidated by any lack of matching for such a potentially biasing factor, and
- based upon the above excerpts in this paragraph, it cannot be assumed that more complete implementation of one or more such other safer factors as those listed above would not have prevented those deaths, be that directly, and/or indirectly by enabling the co-morbidities to be overcome, and
- the average SRIU across a whole population that includes persons with predisposing conditions, will be greater than the SRIU for those individuals who do not suffer predisposing conditions.

The above form further bases upon which estimates in this Notice of SRIU (serious attributable to non-vaccination) are expressed as approximate upper limits of the true SRIU, i.e. are prefixed by "<" (less than).

ii. Insurance status link to vaccination coverage

According to the Vaccination Coverage in 19–35 month olds by Insurance Status Table 2017 and the Vaccination Coverage in 13-17 year olds by Insurance Status Table 2018, the vaccination coverage for those age groups in those years was substantially lower for those uninsured than those with private only insurance, and that applied especially to the vaccination coverage for the full number of doses recommended for children of those ages.

For example, according to the Vaccination Coverage in 19–35 month olds by Insurance Status Table 2017, the estimated vaccination coverage for 4 doses (at least) of DTaP vaccination in 19-35 month olds in 2017 was 28% lower in those uninsured (62.4%) compared to the coverage in those with private only insurance (86.9%).

Hence to whatever extent insurance status is associated with other factors such as those listed above, it may be reasoned that any attempt to reliably measure vaccination effectiveness based upon a comparison of morbidity and/or mortality in vaccinated versus unvaccinated persons is invalidated by any lack of matching for insurance status or any other factor(s) associated with it. That applies especially to measurements of effectiveness for the full number of multiple doses recommended for any subject age group.

7. Vaccine-targeted diseases

7.1 Diphtheria

The subject age range chosen for the risk analysis for diphtheria is 6 months to 19 years.

(The choice of that age range is based primarily upon the age grouping of hospitalization data published in the CDC Pertussis Surveillance Reports (paragraph 7.3(d), on page 204, given that vaccinations for diphtheria, tetanus and pertussis are combined).

(a) Diphtheria Disease notification Rate in the Population (DRP)

i. **Disease notification numbers**

The CDC Disease Notifications state that the number of diphtheria[2] cases reported in 2004-2018 for US residents have been as set out in the following table for the given age groups:

Diphtheria notifications 2010 – 2018

Age group (years) / Year	*< 1*	*1 - 4*	*5 - 14*	*15 - 24*	*> 24*
2004* - 2013	*0*	*0*	*0*	*0*	*1*
2014	*0*	*0*	*0*	*1*	*0*
2015 - 2017	*0*	*0*	*0*	*0*	*0*
2018	*0*	*0*	*1*	*0*	*0*

*** The basis for the lower end of this year range being stated in this table to be 2004 is that** CDC Disease Notifications 2012 (Exhibit 58) refers to the notification of "*probable"* case in 2012 in a "*man aged 28 years*" as "*the first since 2003*".

ii. **Refinement (assumption and exclusions) considering further details**

With respect to the single case reported to have occurred in each of the following periods:

[2] According to CDC Disease Notifications 2007, "*Cutaneous diphtheria ceased being notifiable nationally after 1979*." Based upon that statement, all references herein to incidence of "diphtheria" do not include incidence of cutaneous diphtheria.

a. 2014:

The case reported in 2014 will be excluded from the risk analysis hereafter because CDC Disease Notifications 2014 (Exhibit 60) states that the patient "*was fully vaccinated*":

"During 2014, a nonfatal case of diphtheria caused by nontoxigenic Corynebacterium diphtheriae was reported to CDC. The case occurred in a 17-year-old white female resident of Ohio. The patient was fully vaccinated*. No other family member or close contact was ill",* and

b. 2018:

CDC Disease Notifications 2018 does not provide the vaccination status, health status, vaccine eligibility, state/territory of residence or exact age for the single case reported in 2018, other than that it was in the 5 and 14 year age range.

CDC Disease Notifications 2018 also states that the data therein include:

"cases … reported by …the U.S. territories",

Hence, in that document, the CDC does not exclude the possibility that the case occurred not in any of the 50 US states or District of Columbia, but instead in a US territory, such as American Samoa, Guam, the Northern Mariana Islands, Puerto Rico, and the U.S. Virgin Islands.

However for the purpose of this analysis this case will be assumed to have occurred in a US state or the District of Columbia.

According to the Whole Population Table, whose "*population estimates"* include only the *"resident population*", not US territories, a total of 4,664,151,541 US resident person years transpired in the 15 year period of 2004 to 2018, based upon which the annual average incidence rate of confirmed diphtheria in that period was 1 in 4,664,151,541 in the whole US resident population.

This analysis, however, restricted to under 20 year olds in 2010 to 2018.

iii. **Summary for DRP**

Based upon the above information in this paragraph 7.1ii(a), the approximate annual average reported incidence (annual DRP) of confirmed diphtheria in the

period 2010 – 2018 was as set out in the table below for each subject age group:

Age group	1-6 yrs			7-10 yrs	11-19 yrs	Total
	6 – 11 mths	1 - 4 yrs	5 - 6 yrs			
Total notifications[3]	0	0	~ 0.19[3]	~ 0.38[3]	~ 0.43[3]	**1**
Person years transpired	234,950,184			147,713,332	340,722,902	**723,386,418**
DRP (annual average)	~ 1 / 1,239,883,641 [4]			~ 1 / 390,720,808	~ 1 / 788,472,120	**~ 1 / 723,386,418**

(b) Diphtheria Vaccination Coverage (VC)

Assumption for timing of vaccinations

According to the tables (or "*figure"*s) in all of the CDC Schedules, the routine schedule of CDC-recommended vaccinations targeting diphtheria, tetanus and pertussis has been as follows in the US for US residents aged under 20 years, since at least as early as 2006 to the present:

"Recommended … immunization schedule, by vaccine and age — United States"

Vaccine / Age	*Diphtheria, Tetanus, Pertussis*
2 months	*DTaP* (first dose)
4 months	*DTaP* (second dose)
6 months	*DTaP* (third dose)
15 months	*DTaP* (fourth dose)
18 months	
4–6 years	*DTaP* (fifth dose)
11–12 years	*Tdap* (sixth dose)

Except where stated otherwise, the analyses in this Notice are based on the assumption that in the case of each vaccination dose that is the subject of any

[3] CDC Disease Notifications do not state the exact age(s) of the notification(s) in the 5-14 age group. Therefore herein the number of notifications is apportioned across the various component age groups in accordance with their relative sizes, and adjusted so that that the calculated result for DRU (annual) will be the same for each of those smaller component age groups (5-6 years, 7-10 years and 11-14 years)

[4] This is a weighted average of the estimated rates for the component age groups.

coverage figure stated herein, all, or virtually all, of the "covered" children have received the dose approximately in accordance with the above schedule.

More narrowly, the fourth and fifth DTaP vaccine doses will respectively be assumed to be given when the ages of 15 months and 5 years are reached and the Tdap dose(s) when the age of 11 years is reached

i. Coverage in 6 month – 11 month olds (three doses)

According to the CDC Schedules, in 2009-2018 the CDC recommended three doses of diphtheria vaccination in the US in infancy, specifically at 2, 4 and 6 months of age.

The Vaccination Coverage in Infants report states that:

> *"For infants born in 2011 and 2012, first dose coverage at 3 months of age for DTaP was 86%.... At 7 months of age, coverage for …3 doses of DTaP was 73%... At 13 months of age, the coverage* (was) *…83%."*

It shall be hence assumed herein, that for the whole 2010-2018 period overall:

- approximately the same coverage levels as those quoted above applied. That assumption is based upon the (minimal) apparent degree of variation in estimated coverage during the period of 2006 through 2017 in the 19-35 month age group (as quoted in paragraph 5.2 herein), and
- the coverage for second dose at 6 and 7 months of age was approximately 86%, and
- the recommendations stated in the CDC Schedules, of vaccinating at 2, 4 and 6 months of age, were followed to the maximum extent within the upper boundaries of coverage determined as quoted or assumed above.

The approximate annual average diphtheria vaccination coverage in 2010-2018 in the 6 – 11 month age group is hence taken to be:

- 86% for at least two doses,
- 73% for three doses at 6 and 7 months, and
- 83% for three doses at 8 through 11 months.

ii. Coverage in 1 – 6 year olds (fourth and fifth doses)

a. Coverage **in 1 – 4 year olds (fourth dose)**

The CDC Daycare Coverage Reports provide estimated vaccination coverages overall (some averages, others medians) for diphtheria-containing vaccines in 19-35 month olds in the US as set out in the table below:

	Diphtheria Vaccine Coverage %			
	≥3 doses (average)		***≥4 doses (average)***	
Year	***%***	***(95% CI)***	***%***	***(95% CI)***
2008	*96.2*	*(±0.5)*	*84.6*	*(±1.0)*
2009	*95.0*	*(±0.6)*	*83.9*	*(±1.0)*
2010	*95.0*	*(±0.6)*	*84.4*	*(±1.0)*
2011	*95.5*	*(±0.5)*	*84.6*	*(±1.0)*
2012	*94.3*	*(±0.7)*	*82.5*	*(±1.2)*
2013	*94.1*	*(93.2–95.0)*	*83.1*	*(81.8–84.3)*
2014	*94.7*	*(94.0–95.4)*	*84.2*	*(83.0–85.4)*
2015	*95.0*	*(94.4–95.5)*	*84.6*	*(83.5–85.7)*
2016	*93.7*	*(92.8–94.5)*	*83.4*	*(82.1–84.6)*
2017	*94.0*	*(93.3–94.7)*	*83.2*	*(82.0–84.3)*
2018*	94.0		83.2	
2019*	94.0		83.2	

Based on the data in the above table, the average diphtheria vaccination coverage in 19-35 month olds over the period of 2008-2018 is estimated to have been 94.7% for receipt of at least three doses, and 83.8% for receipt of at least four doses.

According to the CDC Schedule throughout the period of 2010-2017, the fourth diphtheria-containing vaccination dose ("*DTaP*") was recommended to be given during the age range of "*15 months*" to "*18 months*". Based upon that stated recommendation, it will be assumed in the calculation set out in this Notice of DRU for diphtheria that virtually all of the 10.9% of 19-35 month old children in the population who were recorded at the time of the coverage surveys to be amongst the (approximately) 94.7% to have received the third dose but not the fourth, received that fourth dose soon after the relevant survey.

Based upon that assumption and given further that children aged 4 years in 2010 were aged 2 years in 2008, the maximum coverage for four doses in 1 – 4 year old children for 2010-2018 will be estimated to

be the coverage estimate given in the Vaccination Coverage Reports for "≥3 doses" in 19 to 35 month old children in 2008-2018.

Hence it will be estimated that the maximum coverage for four doses in 1 – 4 year old children in:

- 2010-2018 was 94.7%.

b. Coverage in 5 - 6 year olds (fifth dose)

The CDC Elementary School Coverage Reports provide estimated vaccination coverages overall (some averages, others medians) for diphtheria-containing vaccines in kindergarteners (and, up to the 2002-2003 school year inclusive, first graders[5]), in the US as follows:

School Year [5]	**Diphtheria Vaccine (DTaP / DTP / DT / Td) Coverage % (average/median)**	**≥# doses**
1997-1998	*96.7*	*3*
1998-1999	96.95 [6]	
1999-2000	*97.2*	*3*
2000-2001	96.63 [6]	
2001-2002	96.07 [6]	
2002-2003	*95.5*	*3, 4* (*19.6%, 76.5%* US states resp.)
2003-2004	*95.5*	*"up-to-date"*
2004-2005	95.50 [6]	
2005-2006	*95.5*	*"up-to-date" "four or more doses*"
2006-2007	*96.0*	*"up-to-date"*
2007-2008	95.77 [6]	
2008-2009	95.53 [6]	
2009-2010	*95.3*	*"up-to-date"*
2010-2011	95.25 [6]	
2011-2012	*95.2*	*3*, (mostly) *4*, or *5*
2012-2013	*95.1*	*3*, (mostly) *4*, or *5*
2013-2014	*95.0*	*3*, (mostly) *4*, or *5*
2014-2015	*94.2*	*3*, (mostly) *4*, or *5*
2015-2016	*94.2*	*5*
2016-2017	*94.5*	*5*
2017-2018	*95.1*	*5*
2018-2019	*94.9*	*5*
2019-2020	94.9 [6]	5 [6]

[5] The CDC Elementary School Coverage Reports state that, for the school years up to 2002-2003, the "*estimated vaccination coverage"* figures apply to a "*mix*" of "*children enrolled in kindergarten and first grade*", but that for all subsequent school years they apply to only "*children enrolled in kindergarten*".

[6] Coverage for this year has been estimated by interpolation based upon the figures available from the latest prior year and/or earliest subsequent year for which data is included in the CDC Elementary School Coverage Reports.

The CDC Elementary School Coverage Reports state that the term "*up-to-date*" means that the children had "*received all of the vaccine doses required for school entry in their state or area*". They state that most of the reporting states required four doses until 2013-2014, and that the vast majority after that year required five doses. (More details are quoted in paragraph 5.3 herein.)

Based upon the CDC Schedule tables for the years 2006 to 2018 showing a fifth DTaP vaccine dose scheduled at "*Age*" "*4-6 years*", an assumption shall be made in the relevant DRU calculation for diphtheria that the above estimates of average/median coverage rate applied to the fifth dose throughout all relevant years.

Based upon that assumption and upon the data in the above table, the average or median coverage in 2010-2018, for the fifth dose of diphtheria-containing vaccination approximated:

- 94.9% in 5-6 year olds, whose estimated coverage in kindergarten or first grade[5] was reported in the CDC Elementary School Coverage Reports for 2010-2011 through 2018-2019.

iii. Coverage in 7 – 10 year olds (fifth dose)

The CDC Schedule tables for the years 2006 through 2018 include no further diphtheria vaccination doses after the fifth dose scheduled at "*Age*" "*4-6 years*" prior to a dose stated to be scheduled at 11-12 years of age.

Based upon that fact and the information and assumption in the previous paragraph 7.1(b)ii.b headed "Coverage in 5 - 6 year olds", the average or median coverage in 2010-2018, for the fifth dose of diphtheria-containing vaccination approximated:

- 95.1% in 7-10 year olds, whose estimated coverage in kindergarten or first grade[5] was reported in the CDC Elementary School Coverage Reports for 2006-2007 through 2016-2017.

iv. Coverage in 11 – 19 year olds (sixth or fifth dose)

a. Coverage **for sixth dose**

The CDC Secondary School Coverage Reports provide estimated average vaccination coverages for diphtheria-containing vaccines in 13 to 17 year olds in the US in 2010-2018 as follows:

Diphtheria (and Tetanus) Vaccine Coverage (average) %			
		Age 13 – 17 yrs	
Vaccine [7]	***Year***	***%***	***(95% CI)***
≥1 dose Td or Tdap since age 10 years	*2010*	*81.2*	*(80.2–82.2)*
≥1 dose Td / Tdap on/after age 10 yrs	*2011*	*85.3*	*(±0.8)*
Tdap ≥1 dose on/at or after age 10 years / at age ≥10 years	*2012*	*84.6*	*(±0.9)*
	2013	*86.0*	*(±0.9)*
	2014	*87.6*	*(±0.9)*
	2015	*86.4*	*(±1.0)*
	2016	*88.0*	*(87.1–88.9)*
	2017	*88.7*	*(87.8–89.6)*
	2018	*88.9*	*(88.0–89.7)*
	Average	86.3	

According to the figures in the above table, the average coverage in 13-17 year olds in 2010-2018 for receipt of the booster Td or Tdap vaccination dose on or after age 10 years was 86.3%.

It shall be assumed herein that the overall rate for 11-19 year olds approximates that for 13-17 year olds, so is also approximately 86.3%.

b. Residual coverage for fifth dose

In addition to the approximate 86.3% of 11-19 year olds who received the sixth dose are those who did not receive it but in whom there may be residual antibody titers from the fifth dose scheduled about 7 years earlier.

Based upon the information in the previous paragraph 7.1(b)ii.b headed *"*Coverage in 5 - 6 year olds*",* the average or median coverage in 2010-2018 for the fifth dose of diphtheria-containing vaccination approximated:

- 95.9% in 11-19 year olds, whose coverage in kindergarten or first grade was reported in 1997-1998 to 2012-2013.

[7] Abbreviations: "*Td*" means tetanus and diphtheria toxoid or tetanus-unknown vaccine; "*Tdap*" means tetanus toxoid, reduced diphtheria toxoid and acellular pertussis vaccine, as quoted in paragraph **Error! Reference source not found.Error! Reference source not found.**5.4.

v. Summary for VC

Based upon the above information in this paragraph 7.1(b), the approximate annual average diphtheria vaccination coverage in 2010-2018 was as set out in the table below for each subject age group:

Age	1-6 yrs (DTaP)			7-10 yrs (DTaP)	11-19 yrs	
	6 – 11 mths	1-4 yrs	5-6 yrs		Td / Tdap	DTaP / DTP / DT / Td
VC	~86%	~94.6%	~94.9%	~95.1%	~86.3% ("VC1")	~95.9% ("VC2")

(c) Diphtheria Vaccination Efficacy (VE)

Determining efficacy - "seroprotection" approach and its limitations

The Plaintiff hereby requests that the Court take judicial notice of the following documents:

- the CDC web page headed "About Diphtheria, Tetanus, and Pertussis Vaccines", located at https://www.cdc.gov/vaccines/vpd/dtap-tdap-td/hcp/about-vaccine.html
  (hereafter "CDC Page About Diphtheria, Tetanus, and Pertussis Vaccines")

  A true and correct copy of the aforesaid report is attached hereto as **Exhibit 73**.

- the CDC "Pink Book" Diphtheria chapter, accessible at https://www.cdc.gov/vaccines/pubs/pinkbook/dip.html online or https://www.cdc.gov/vaccines/pubs/pinkbook/downloads/dip.pdf (pdf) (last accessed June 17, 2020)

  (hereafter "CDC Pink Book Diphtheria Chapter")
  A true and correct copy of the aforesaid report is attached hereto as **Exhibit 74**.

- a review entitled "2012 Antigen Review for the New Zealand National Immunisation Schedule: Diphtheria"

  Citation: Carter P, Taylor L, Poole T, Petousis-Harris H and Nowlan M. 2012 Antigen Review for the New Zealand National Immunisation Schedule: Diphtheria, published March 1, 2015, accessible via https://www.immune.org.nz/2012-antigen-review-new-zealand-national-immunisation-schedule-diphtheria and accessible at

https://www.immune.org.nz/sites/default/files/publications/Ebook%20Diphtheria%20antigen%20review%202012.pdf
(last accessed July 2, 2020)

(hereafter "NZ Diphtheria Review")

A true and correct copy of the aforesaid report is attached hereto as **Exhibit 75**.

- a measurement of seroprotective antibodies against diphtheria, including before the first vaccination dose in infancy:

  Citation: Van Der Meeren O, Kuriyakose S, Kolhe D, Hardt K. Immunogenicity of Infanrix™ hexa administered at 3, 5 and 11 months of age. *Vaccine*. 2012;30(17):2710-2714. doi:10.1016/j.vaccine.2012.02.024, accessible at http://www.academia.edu/download/47880476/j.vaccine.2012.02.02420160808-18219-1nxsa02.pdf
  (last accessed October 18, 2020)

  (hereafter "Diphtheria, Tetanus and Pertussis Infancy Immunity Study")

  A true and correct copy of the aforesaid report is attached hereto as **Exhibit 76**.

The CDC states on the "CDC Page About Diphtheria, Tetanus, and Pertussis Vaccines", under the subheading "Immunogenicity and Vaccine Efficacy":

> *"No one has ever studied the efficacy of tetanus toxoid and diphtheria toxoid in a vaccine trial. …experts infer efficacy from protective antitoxin levels."*

The WHO Diphtheria Review states:

> *"The WHO Immunological Basis Series for Diphtheria Immunization[21] confirm that there is no sharply defined level of antitoxin that gives complete protection from diphtheria. A certain range of variation must be accepted and the same concentration of antitoxin may give unequal protection in different persons. Other factors may influence vulnerability to diphtheria including the infecting dose and virulence of the diphtheria bacilli, and the general immune status of the person infected."*

Setting aside the lack of "*sharply defined level of antitoxin that gives complete protection from diphtheria*", the NZ Diphtheria Review states:

"Individuals with circulating antitoxin levels <0.01 IU/ml are generally considered susceptible, with less severe symptoms being associated with levels above this. The protective level is generally considered to be 0.1 IU/ml and an antitoxin level of >1.0 IU/ml is associated with long-term protection."

"Seroprotection rate" is accordingly defined in this paragraph 7.1 as the presence of circulating antitoxin levels of > 0.1 IU/ml.

i. **Seroprotection in 6 month – 11 month olds (three doses)**

The Diphtheria, Tetanus and Pertussis Infancy Immunity Study states:

> *"A pooled analysis …was undertaken to assess the immunogenicity of Infanrix™ hexa (DTPa-HBV-IPV/Hib…) when administered in a total of 702 healthy infants at 3, 5 and 11–12 months of age."*

It states in "*Table 2*" that the diphtheria seroprotection rate was found to be:

- "*98.0 [96.0; 99.1]*"% "*one month after dose 2*" ("*Post II*"), and
- "*100.0* [*99.4; 100.0*]"% "*after dose 3*" ("*Post III*").

The Diphtheria, Tetanus and Pertussis Infancy Immunity Study also reported that the seroprotection rate fell from 98% following dose 2 to:

- "*79.1 [75.4; 82.5]*"% over the 6 to 7 month period "*before dose 3*" at "*11–12 months of age*".

Based upon an initial seroprotection rate of 98% and its reported decline to 79.1% taken to have occurred over 7 months, a mathematical fit for the decline in seroprotection rate is for the Waning Exponent to be about 1.45 per month.

It shall be assumed herein that approximately the same initial seroprotection rates, 98% and 99.7% a month after the second and third doses respectively, and the Waning Exponent of a minimum of 1.45 per month, apply when the three doses are administered at 2, 4 and 6 months of age.

Based upon those assumptions and the estimated vaccination coverage for infants as set out in paragraph 7.1(b) herein, the average seroprotection rate over the age range of 6-11 months averaged approximately:

- 98.9% for the 73% and 83% of infants who are assumed herein to have been fully vaccinated by 6 and 8 months of age respectively (see

paragraph 7.1(b)i herein headed “Coverage in 6 month – 11 month olds (three doses**)**”), and

- 97.3% for the remaining 17% and 6% of infants respectively.

The weighted average of those seroprotection rates over the 6 – 11 month age range approximates 98.85%.

ii. **Seroprotection in 1 – 6 year olds (fourth and fifth doses**)

a. Seroprotection in 1 – 4 year olds (fourth dose)

Regarding diphtheria vaccination efficacy after four doses of DTaP:

- **Initial Seroprotection Rate**:

  The CDC Pink Book Diphtheria chapter states that:

  > *“After a primary series of three properly spaced diphtheria toxoid doses in adults or four doses in infants, a protective level of antitoxin (defined as greater than 0.1 IU of antitoxin/mL)”* is *“approximately 95%”* (text box on page 113).

- **Waning Exponent**

  The NZ Diphtheria Review states (on page 10):

  > *“Immunity to diphtheria …was analysed in 338 Austrian children aged four - eight years. Most …(323) had received …four doses of DTaP–HBV–IPV/Hib (according to the schedule of 2, 3, 4 months and a booster in the second year of life) …When measured between the ages of 4-8 years, 81% of children were seroprotected for diphtheria”.*

These estimates combined, of an initial efficacy of 95% at approximately 18 months of age and an average efficacy of 81% at 4 to 8 years (average of 4.5, 5.5, 6.5, 7.5 and 8.5 years), fit mathematically with the seroprotection rate declining exponentially such that after a starting rate of 95%, the Waning Exponent is 1.31.

Based upon that initial level and Waning Exponent, the annual average seroprotection rate after four doses in 1 to 4 year olds can be estimated by interpolation to be about 92.0%.

b. Seroprotection in 5 – 6 year olds (fifth dose)

The CDC Schedules state that in all material years, a fifth diphtheria vaccination dose was recommended to be given at "*Age*" "*4-6 years*", i.e. at around 5 years of age.

It shall be assumed herein that the initial seroprotection rate and Waning Exponent applicable after the fifth dose approximate those that apply after the sixth vaccination dose, which is scheduled in the US at 11-12 years of age, according to the CDC Schedules.

With respect to the sixth dose, the NZ Diphtheria Review states the following:

> *"In Finland, a follow-up study was conducted …post-vaccination with single dose of Tdap (dTap) vaccine at the age of 10-14 years"*

and refers to the results tabled on the following page (13) that the rates after 3, 5 and 10 years post-vaccination were "*93.5*", "*90.4*" and "*82.4*" respectively.

Those levels fit mathematically with an initial post-vaccination seroprotection rate of 96% and Waning Exponent of 1.17.

Based upon that initial rate and waning rate, the approximate average seroprotection rate is:

- 95.7% in 5 to 6 year olds, based upon averaging the hence approximated initial seroprotection rate and expected rate after 1 year.

iii. **Seroprotection in 7 – 10 year olds (fifth dose)**

Based upon the information in the previous paragraph 7.1(c)i.b, headed "Seroprotection in 5 **–** 6 year olds (fifth dose)", the average seroprotection rate for the fifth dose of diphtheria-containing vaccination approximates:

- 93.1% in 7-10 year olds.

iv. **Seroprotection in 11 – 19 year olds (sixth or fifth dose)**

a. Seroprotection after sixth dose

A sixth diphtheria vaccination dose is scheduled in the US at 11-12 years of age, according to the CDC Schedules.

Based upon what is presented in paragraph 7.1(c)i.b above, headed "Seroprotection in 5 – 6 year olds (fifth dose)", of an estimated initial post-vaccination seroprotection rate of 96% and Waning Exponent of 1.17, the average seroprotection rate approximates:

- 92.1% in those 11-19 year olds who have received the sixth dose of diphtheria-containing vaccination at 11 years of age.

b. Residual **seroprotection f**rom fifth dose

Based upon the estimation in paragraph 7.1(c)ii.b above, headed "Seroprotection in 5 – 6 year olds (fifth dose)", of an initial seroprotection rate of 96% and Waning Exponent of 1.17 after the fifth dose of diphtheria-containing vaccination at 5 years of age, the average residual diphtheria seroprotection rate approximates:

- 81.1% in 11-19 year olds who have received the fifth dose but not the sixth dose, which is scheduled in the US at 11-12 years of age.

v. **Summary for VE**

Based upon the above information in this paragraph 7.1(c), the approximate annual average diphtheria seroprotection rate is set out in the table below for each subject age group:

Age Group	1-6 yrs (DTaP)			7-10 yrs (DTaP)	11-19 yrs	
	6 – 11 mths	1-4 yrs	5-6 yrs		Td / Tdap	DTaP / DTP / DT / Td
VE	≤ 97.5%	≤ 92.0%	≤ 95.7%	≤ 93.1%	≤ 92.1% ("VE1")	≤ 81.1% ("VE2")

(d) Serious outcome Rate per Disease case (SRD)

In this Notice, a diphtheria disease-associated SAE is defined as any reported case of diphtheria. That results in the SRIU for any SAE being the same as the DRIU, in the case of diphtheria.

The CDC Pink Book Diphtheria Chapter states:

"The overall case-fatality rate for diphtheria is 5%-10%, with higher death rates (up to 20%) among persons younger than 5 and older than 40 years of age."

Based upon that statement, the maximum death rates for each of the subject age groups are set out in the table below:

Age	1-6 yrs			7-10 yrs	11-19 yrs
	6 – 11 mths	1-4 yrs	5-6 yrs		
SRD (Death) (Case fatality rate)	≤ 20%	≤ 20%	≤ 10%	≤ 10%	≤ 10%

(e) Differential Risk of unavoidable serious adverse effect (SRIU)

Based upon the calculated estimates presented in this paragraph 7.1, "Diphtheria" for

(a) the disease notification rate in the population (DRP), and

(b) the vaccination coverage (VC), and

(c) the vaccination effectiveness (VE), and

(d) the rate of serious adverse effects per disease case (SRD),

the approximate differential rates for disease (DRIU) and ultimately serious adverse effects (SRIU) can be calculated by applying the formulas set out in paragraphs 6.1 and 6.3 herein, with the results set out in the table below for each age group:

Diphtheria totals and averages in 2010-2018, approximated

Age range (targeting vaccine)	6 – 11 mths (DTaP)	1-6 yrs (DTaP)		7 – 10 yrs (DTaP)	11 – 19 yrs		Average / Total
					Td / Tdap	DTaP / DTP / DT / Td	
DRP (annual)	0	~ 1 / 1,144,507,977		~ 1 / 390,720,808	~ 1 / 788,472,120		1 / ~723,386,418
VC	≤ 86%	~ 94.7%	~ 94.9%	~ 95.1%	~ 86.3% ("VC1")	~ 95.9% ("VC2")	95.1% [4,8]
		~ 94.75%					
VE	≤ 97.5%	≤ 92.0%	≤ 95.7%	≤ 93.1%	≤ 92.1% ("VE1")	≤ 81.1% ("VE2")	92.3% [4,8]
		≤ 93.2% [4]			91.0%		
DRU (annual)	0	≤ 1 / 133,621,765 [4]		≤ 1 / 44,760,922	≤ 1 / 100,712,074		≤ 1 / 87,283,797 [4]
DRIU (annual)	0	≤ 1 / 143,336,109 [4]		≤ 1 / 48,089,859	≤ 1 / 109,361,401		≤ 1 / 94,051,498 [4]
SRIU (=DRIU) total over age range	0	≤ 1 / 23,889,351 [4]		≤ 1 / 12,022,465	≤ 1 / 12,151,267		**≤ 1 / 4,823,154** [4]
SRD: Case fatality rate	≤ 20%	≤ 16.7%		≤ 10%	≤ 10%		≤ 11.4%
SRIU (death): total over age range	0	≤ 1 / 143,336,109 [4]		≤ 1 / 120,224,649	≤ 1 / 121,512,667		**≤ 1 / 42,316,761** [4]

(f) Impact of vaccination on others' susceptibility

The Plaintiff hereby requests that the Court take judicial notice of the following documents:

- "MedlinePlus" webpage entitled "Vaccines (immunizations)", published by the National Institutes of Health, U.S. National Library of Medicine, accessible at https://medlineplus.gov/ency/article/002024.htm
  (last accessed October 18, 2020)

  (hereafter "MedlinePlus re Diphtheria Vaccine Design")

[8] This figure is included in the table for informatory purposes but is not used in the calculation of the average DRIU, which is a weighted average of the DRIU figures for the various age groups.

A true and correct copy of the aforesaid report is attached hereto as **Exhibit 77**.

- article entitled “Diphtheria immunization. Effect upon carriers and the control of outbreaks”

  Citation: Miller *et al*. (1972). *American Journal of Diseases of Children* 123(3):197-199, published by the National Institutes of Health, U.S. National Library of Medicine, accessible at https://doi.org/10.1001/archpedi.1972.02110090067004 (last accessed February 14, 2021)

  (hereafter “Diphtheria Vaccination and Herd Immunity Abstract”)

  A true and correct copy of the aforesaid report is attached hereto as **Exhibit 78.**

- the Communicable Disease Management Protocol, Manitoba Public Health Branch, Canada (Diphtheria), accessible at http://www.gov.mb.ca/health/publichealth/cdc/protocol/diphtheria.pdf (last accessed October 18, 2020)
  (hereafter “Manitoba Diphtheria Protocol”)

  A true and correct copy of the aforesaid report is attached hereto as **Exhibit 79**.

- Iowa Department of Public Health, Guide to Surveillance, Investigation, and Reporting – Diphtheria, accessible at https://wiki.idph.iowa.gov/Portals/3/userfiles/5/Files/Diphtheria%20Chapter.pdf (last accessed October 18, 2020)
  (hereafter “Iowa Diphtheria Guide”)

  A true and correct copy of the aforesaid report is attached hereto as **Exhibit 80**.

- Diphtheria Control Guideline, NSW Health, NSW, Australia, accessible at http://www.health.nsw.gov.au/Infectious/controlguideline/Pages/diphtheria.aspx (last accessed October 18, 2020)
  (hereafter “NSW Diphtheria Control Guideline”)

  A true and correct copy of the aforesaid report is attached hereto as **Exhibit 81**.

Many may assume that the reason for no cases being notified of diphtheria in any unvaccinated person in the entire US resident population over at least 14 years is that herd immunity is being provided to the unvaccinated by those who are vaccinated.

However it may be reasoned that for that to be able to be achieved with vaccination:

i. the vaccine needs to be designed to try to prevent transmission, and

ii. vaccination needs to be effective for preventing transmission, and

iii. the vaccination coverage needs to be sufficiently high to provide herd immunity.

A determination of whether or not these three criteria are met follows:

i. Are diphtheria vaccines designed to prevent transmission?

The WHO Diphtheria Review states (on page 1):

"Diphtheria toxoid is used for active immunization. Diphtheria vaccines are based on diphtheria toxoid, a modified bacterial toxin that induces protective antitoxin",

and MedlinePlus re Diphtheria Vaccine Design states:

"Toxoid vaccines contain a toxin or chemical made by the bacteria or virus. They make you immune to the harmful effects of the infection, instead of to the infection itself. Examples are the diphtheria and tetanus vaccines."

According to these statements, the vaccine contains only the *C. diphtheria* toxin that the bacterium produces (in a modified form), not any part of the bacterium itself, and hence is designed only to provide immunity to the "***harmful effects"* that** the toxin may cause to the recipient, rather than infection of the recipient or his/her contacts with *C. diphtheria* infection itself.

ii. Is vaccination preventing transmission?

ACIP and CDC: Vaccination does not prevent infection or transmission

The Manitoba Diphtheria Protocol states:

"Immunized individuals can …be infected by C. diphtheria"

and the WHO Diphtheria Review states (on page 2):

"The United States Immunization Practices Advisory Committee (ACIP) states, that immunization does not eliminate carriage of C. diphtheriae in the pharynx, nose or on the skin.[12]"

and the CDC Pink Book Diphtheria Chapter states:

"Although diphtheria disease is rare in the United States, it appears that toxigenic Corynebacterium diphtheriae continues to circulate in areas of the country with previously endemic diphtheria." (page 113)

and the Diphtheria Vaccination and Herd Immunity Abstract states:

"A diphtheria epidemic in a small central Texas community centered in the elementary school… There was no statistical difference in the risk of diphtheria infection among those with full, lapsed, inadequate, or no previous diphtheria immunizations… Diphtheria toxoid… does not prevent the carrier state nor stop the spread of infection."

According to these excerpts, diphtheria vaccination is not preventing infection or "*carriage or spread*" of *C. diphtheria*.

WHO and Manitoba Government: Vaccination hides infections

Further, The WHO Diphtheria Review also states (on page 2):

"Miller et al. 1970[4] suggests that diphtheria vaccination prevents symptomatic infections"

and the Manitoba Diphtheria Protocol states:

"Immunized individuals can …become asymptomatic carriers of toxin-producing strains."

According to these statements, vaccination prevents symptomatic infection and vaccine recipients can become asymptomatic carriers of the infection.

Hence, to the extent that the effectiveness of other infection control measures depends upon detection of the infection, it may be reasoned that vaccination may increase the chance of transmission by preventing the appearance of symptoms in cases of infection and hence hiding them.

The Manitoba Diphtheria Protocol states that indeed:

"Asymptomatic carriers, rather than persons with overt disease, are usually the major source of transmission during community outbreaks."

iii. Is vaccination coverage sufficiently high to provide herd immunity?

Notwithstanding what may be concluded from the statements quoted in paragraphs 7.1(f)i-ii above, CDC Disease Notifications 2015 states:

"Ensuring and sustaining high childhood vaccination coverage rates above 90% and high coverage with decennial booster doses in adolescents and adults are required for herd protection in the population."

Based upon this statement in combination with the CDC Secondary School Coverage Reports, which state that the vaccination coverage in 13-17 year olds ranged from "*60.1*"% in 2006 to "*88.9*"% in 2018 (increasing almost every year in between), vaccination coverage in adolescents has not reached a sufficient level for diphtheria vaccination to be able to provide herd protection, even if diphtheria vaccination was inherently able to prevent infection and/or transmission.

Based upon the above statements in paragraph 7.1(f), the protection that unvaccinated persons have enjoyed from diphtheria has not been dependent upon herd immunity arising from others in the community being vaccinated.

(g) Some other factors affecting susceptibility

Transmission requires prolonged, close contact

The Iowa Diphtheria Guide states:

"Close contacts are defined as those who sleep in the same house or who share food, drink, or eating/drinking utensils with the case, or otherwise share saliva with case such as child care contacts, and healthcare workers in contact with the case's oral or respiratory secretions. Those contacts that were in brief contact with the case, but do not meet the definition of a close contact, are not considered significant contacts."

and the NSW Diphtheria Control Guideline further states:

"The probability of spread depends on the closeness and duration of contact. Prolonged contact (eg sleeping in the same room as a case rather than casual contact) is usually required."

Based upon these statements, diphtheria requires prolonged, close contact to spread, whether or not infection is symptomatic. Not only does this naturally limit spread but also, when infection is detected, it provides an opportunity for active interruption of transmission by timely identification and separation of close contacts from the infected person.

The stated necessity for prolonged close contact may be reasoned to undermine the relevance to such risk of the particular vaccination coverage in the community as a whole, contact between virtually all members of which is merely casual. It especially undermines the plausibility of the theory that there is any particular critical threshold of community vaccination coverage that would achieve herd immunity to diphtheria.

Transmission additionally interruptible with antibiotic therapy

The CDC Pink Book further states (on page 112) that:

”Effective antibiotic therapy promptly terminates shedding”

Hence, the CDC states that on the occasions where infection is detected, spread of the infection is able to be controlled by “*effective antibiotic therapy*”.

7.2 Tetanus

The subject age range chosen for the risk analysis for diphtheria is 6 months to 19 years.

(The choice of that age range is based primarily upon the age grouping of hospitalization data published in the CDC Pertussis Surveillance Reports (paragraph 7.3(d), on page 204, given that vaccinations for diphtheria, tetanus and pertussis are combined).

(a) Tetanus Disease notification rate (DRP)

i. Disease notification numbers

The CDC Disease Notifications state that the number of tetanus cases reported in 2010-2018 have been as stated in the rows headed "*2010*" through "*2018*" in the following table, for the "*<1*", "*1-4*", "*5-14*" and "*15-24*" year age groups:

Tetanus notifications 2010 – 2018

Age group (years) / Year	*<1*	*1 - 4*	*5 - 14*	*15 - 24*
2010	*0*	*0*	*2*	*3*
2011	*1*	*0*	*0*	*2*
2012	*2*	*1*	*1*	*4*
2013	*0*	*0*	*2*	*1*
2014	*0*	*1*	*3*	*1*
2015	*0*	*0*	*2*	*1*
2016	*0*	*0*	*5*	*2*
2017	*0*	*0*	*3*	*0*
2018	*0*	*0*	*1*	*5*
Total	**3**	**2**	**19**	**19**

ii. Refinement (assumption and exclusion) considering further details

With respect to the cases reported to have occurred in 2016 – 2018,

a. No confirmation of occurrence in US residents

CDC Disease Notifications 2016, CDC Disease Notifications 2017 and CDC Disease Notifications 2018 state that the data therein include

"cases … reported by …the U.S. territories".

Hence, in those documents, the CDC does not exclude the possibility that one or more of the cases reported in those years occurred in a US territory, such as American Samoa, Guam, the Northern Mariana Islands, Puerto Rico, and the U.S. Virgin Islands, as opposed to all of them occurring in one of the 50 US states or District of Columbia.

However for the purpose of this risk analysis all of the cases reported therein will be assumed to have occurred in a US state or the District of Columbia.

b. Two of the reported cases in infants were of neonatal tetanus

The Plaintiff hereby requests that the Court take judicial notice of the following document:

- the CDC "Manual for the Surveillance of Vaccine-Preventable Diseases: Chapter 16: Tetanus", accessible at: https://www.cdc.gov/vaccines/pubs/surv-manual/chpt16-tetanus.html (html) or https://www.cdc.gov/vaccines/pubs/surv-manual/chpt16-tetanus.pdf (pdf)
  (last accessed October 18, 2020)
  (hereafter "CDC Surveillance Manual Tetanus Chapter")

  A true and correct copy of the aforesaid report is attached hereto as **Exhibit 82**.

The CDC Surveillance Manual Tetanus Chapter states:

> *"From 2009 through 2017, … (there were) 2 cases of neonatal tetanus)."*

Based upon that statement, only one of the three cases reported in the 2011-2012 period was in an infant who might have been in the 6 – 11 month age group. Therefore two of the reported cases in the <1 year age group will be excluded from the risk analysis hereafter.

CDC Disease Notifications do not provide the vaccination status, health status, vaccine eligibility, state/territory of residence or exact age for the remaining case in the <1 year age group reported in the 2011-2012 period, which was also the only case in that age group reported in the 2010-2018 period.

iii. Summary for DRP

Based upon the calculated totals, assumption and statement referenced above in this paragraph 7.2(a), the approximate annual average reported tetanus incidence (annual DRP) in the period 2010 – 2018 was as set out in the table below, for each subject age group:

Age group	6 – 11 mths	1-6 yrs		7-10 yrs	11-19 yrs	Total / Average
		1-4 yrs	5-6 yrs			
Tetanus notific-ations [3]	≤ 1	2	~ 3.7	~ 7.7	~ 17	**32**
Person years transpired	17,704,223	144,143,820	73,102,144	147,713,332	340,722,902	**723,386,418**
DRP (annual)	≤ 1 / 17,704,223	1 / 72,071,910	~ 1 / 19,836,172	~ 1 / 19,146,984	~ 1 / 19,925,316	**~ 1 / 23,053,732** [4]

(b) Tetanus Vaccination Coverage (VC)

Based upon the inclusion of a single row only for "*diphtheria*", "*tetanus*" and "*pertussis*" combined in each of the CDC Schedule "*Figure*"s, an assumption shall be made in this Notice that the statements in paragraph 7.1(b) herein, headed "Diphtheria Vaccination Coverage (VC)", apply equally to tetanus in all relevant years for all relevant age groups.

Based upon that assumption, the table below sets out the approximate annual average tetanus vaccination coverage for each subject age group in 2010-2018:

Age	6 – 11 mths	1-6 yrs (DTaP)		7-10 yrs (DTaP)	11-19 yrs	
		1-4 yrs	5-6 yrs		Td / Tdap	DTaP / DTP / DT / Td
VC	~86%	~94.6%	~94.9%	~95.1%	~86.3% ("VC1")	~95.9% ("VC2")

(c) Tetanus Vaccination Efficacy (VE)

The Plaintiff hereby requests that the Court take judicial notice of the following documents:

- a New Zealand Ministry of Health review of Tetanus vaccination, Citation: Petousis-Harris H, Batty K, Turner N and Nowlan M. 2012 Antigen Review for the New Zealand National Immunisation Schedule: Tetanus, February 1, 2015 (last updated: Sep 2018), accessible via

https://www.immune.org.nz/2012-antigen-review-new-zealand-national-immunisation-schedule-tetanus and accessible at https://www.immune.org.nz/sites/default/files/publications/Ebook%20Tetanus%202012.pdf
(last accessed October 18, 2020)
(hereafter "NZ Tetanus Review")

A true and correct copy of the aforesaid report is attached hereto as **Exhibit 83**.

- the following medical journal article, referenced by the NZ Tetanus Review (at reference number "*47*").
Citation: Livorsi DJ, Eaton M, Glass J. Generalized tetanus despite prior vaccination and a protective level of anti-tetanus antibodies. *Am J Med Sci*. 2010;339(2):200-1, accessible at https://pubmed.ncbi.nlm.nih.gov/20019579/
(last accessed October 18, 2020)
(hereafter "Livorsi Article")

  A true and correct copy of the aforesaid report is attached hereto as **Exhibit 84.**

- the CDC "Pink Book" Tetanus chapter, accessible at https://www.cdc.gov/vaccines/pubs/pinkbook/tetanus.html online or https://www.cdc.gov/vaccines/pubs/pinkbook/downloads/tetanus.pdf (pdf)
(last accessed October 18, 2020)
(hereafter "CDC Pink Book Tetanus Chapter")

  A true and correct copy of the aforesaid report is attached hereto as **Exhibit 85**.

i. **Determining efficacy - "seroprotection" approach and its limitations**

The CDC Pink Book Tetanus Chapter states that:

> *"efficacy of the toxoid has never been studied in a vaccine trial",* but is only *"inferred from protective antitoxin levels".*

However the NZ Tetanus Review also acknowledges that:

> *"a very small number of people with a protective antibody titre would still develop tetanus, if exposed (47, 48)."*

This may be considered significant in light of the result of the analysis herein indicating *also* that only a very small number of people *without* a protective antibody titre develop tetanus.

The Livorsi Article provides an example of a person with a “protective” antibody titre still developing tetanus. It states that a “*44-year-old man*” “*did give a history of tetanus vaccination*”, and his “*level of tetanus antibody was found to be 2.78 IU/mL*” but he “*was diagnosed with generalized tetanus*”. Accordingly the article states:

> *“Instead of an absolute protective level of antibody, the real level of protection is probably dependent on the immune status of the host and the quantity of tetanus toxin produced. Perhaps any given serum level of antibody could be overwhelmed by a sufficiently large quantity of toxin. Other authors have speculated that there may be some antigenic variability between the tetanus toxin and the tetanus toxoid.9 Such a phenomenon could also explain why clinical tetanus can still develop in vaccinated individuals. …the limitations of vaccination should be recognized. This case has illustrated that prior vaccination and protective antibody levels do not preclude tetanus. Physicians must instead rely on a patient’s clinical findings to confirm or refute the diagnosis.”*

The Livorsi Article also states:

> *“Clinicians in developed countries are unfamiliar with tetanus, which could delay a diagnosis. Furthermore, some physicians may falsely believe that tetanus does not occur in a patient who has been vaccinated.*
> *A history of prior immunization should not dissuade a physician from making a diagnosis of tetanus.…”*

Hence, in addition to the “*very small number of people*” in which tetanus cases are stated to be reported, the Livorsi Article indicates that there may be many more cases that go unreported due to physicians making an unfounded or false assumption that tetanus vaccination reliably prevents tetanus.

Hence the following presented analysis for estimation of average seroprotection rates is based upon the inference that they provide some indication of vaccination effectiveness. In view of the limitations of what they indicate, according to the statements quoted in this paragraph, they may be seen as inflated indicators of effectiveness but are calculated to as to

provide starting points for estimating upper limits of the true levels of effectiveness.

Specifically, the analysis of "seroprotection rates" herein will be based upon the statement in the NZ Tetanus Review that a "*generally accepted correlate of protection against tetanus is a tetanus toxoid antibody titre of ≥0.1 IU/mL (1)*".

ii. **Seroprotection in 6 – 11 month olds (three doses)**

The Diphtheria, Tetanus and Pertussis Infancy Immunity Study states:

> *"A pooled analysis …was undertaken to assess the immunogenicity of Infanrix™ hexa (DTPa-HBV-IPV/Hib…) when administered in a total of 702 healthy infants at 3, 5 and 11–12 months of age."*

It states in "*Table 2*" that the tetanus seroprotection rate was found to be:

- "*100.0 [99.1; 100.0]*"% "*one month after dose 2*" ("*Post II*"), and
- "*100.0 [99.4; 100.0]*"% "*after dose 3*" ("*Post III*").

The Diphtheria, Tetanus and Pertussis Infancy Immunity Study also reported that the seroprotection rate fell following dose 2 to:

- "*94.1 [91.7; 96.0]*"% over the 6 to 7 month period "*before dose 3*" ("*Pre III"*) at "*11–12 months of age*".

Based upon that decline, a mathematical fit for the decline in seroprotection rate is for the Waning Exponent to be about 1.6 per month.

It shall be assumed herein that approximately the same initial seroprotection rates, stated to approximate 99.7% after both second and third doses, and the Waning Exponent of a minimum of 1.6 per month, apply when the three doses are administered at 2, 4 and 6 months of age.

Based upon those assumptions and the estimated vaccination coverages for infants as set out herein regarding diphtheria vaccination coverage in paragraph 7.1(b)i headed "Coverage in 6 month – 11 month olds (three doses**)**" the average seroprotection rate over the age range of 6-11 months averaged approximately:

- 98.5% for the 73% and 83% of infants who are assumed herein to have been fully vaccinated by 6 and 8 months of age respectively (see paragraph 7.1(b)i herein), and

- 97% for the remaining 17% and 6% of infants respectively.

The weighted average of those seroprotection rates over the 6 – 11 month age range approximates 99.0%.

Evidence undermining assumption that "seroprotection" indicates protection.

Despite that almost 100% average seroprotection rate, the CDC Pink Book Tetanus Chapter states that:

- *"early doses of toxoid may not induce immunity, but only prime the immune system"* and
- *"If the child was younger than 12 months old when the first dose of DT was administered (as DTaP or DT), the child should receive a total of four primary DT doses".*

These statements may be seen to further undermine the reliability of the assumption that "seroprotection" is a good indicator of true protection.

iii. **Seroprotection in 1 – 6 year olds (fourth and fifth doses)**

a. Seroprotection in 1 – 4 year olds

The NZ Tetanus Review states:

> *"Tetanus antibody persistence was assessed in German children, aged four to six years (n=198) and seven to nine years (n=200), who had received three priming vaccinations followed by a booster vaccination between 12 – 18 months of age using DTaP-IPV-HepB/Hib (Infanrix®-hexa). All the children in the four - six years group and 51 children in the seven - nine years group had not received a fifth DTaP booster vaccination at five to six years of age. The mean time elapsed between the fourth DTaP-IPV-HepB/Hib booster vaccination and serology was 3.63 (SD 0.48) in the four-six years group and 6.4 (SD 0.5) in the seven-nine years group. In the four-six years group, 148/198 (74.7%) of participants continued to have seroprotective tetanus toxoid antibody titres ≥0.1 IU/mL. Of the children in the seven-nine years group, 33/51 (64.7%) of those who had only received four doses of DTaP-IPV-HepB/Hib continued to have seroprotective titres."* (pages 14-15)

The findings described in this statement fit mathematically with an initial seropositivity rate after the primary 3-dose course and booster between 12 – 18 months of age in the said German children of approximately 84%, and Waning Exponent of 1.155, resulting in the seroprotection levels of 74.7% and 64.7% after the elapsed years of 3.63 and 6.4 respectively (which are within the four-six years group and seven-nine year age groups respectively).

Based upon these results, , the annual average seroprotection rate after four doses in 1 to 4 year olds can be estimated by interpolation to be about 80.4%.

b. Seroprotection in 5 – 6 year old children

The CDC Schedules state that in all material years, a fifth tetanus vaccination dose was recommended to be given at “Age” “4-6 years”, i.e. at around 5 years of age.

It shall be assumed herein that the initial seroprotection rate and Waning Exponent applicable after the fifth dose approximate those that apply after the sixth vaccination dose, which is scheduled in the US at 11-12 years of age, according to the CDC Schedules.

With respect to the sixth dose, the NZ Tetanus Review states the following:

“A study assessed the immunogenicity of revaccination with Tdap (Adacel®), five years after a previous Tdap vaccination in 451 Canadian and US adolescents and adults (aged 15 – 69 years). Prior to revaccination after five years, 427/451 (96.0%) of participants had seroprotective titres of tetanus toxoid antibody ≥0.1 IU/mL.”

and

"Immunogenicity of revaccination with Tdap (Boostrix®) after vaccination with a Tdap vaccination given 10 years previously was assessed in 153 Australian adults aged 20 – 24 years. Prevaccination… Of the participants who had previously received Tdap vaccine, 94.8% (CI 95% 90.0 – 97.7) had titres ≥0.1 IU/mL.".

The findings described in this statement fit mathematically with an initial seroprotection rate of approximately 97% and Waning Exponent of

1.058, as those values result in the quoted seroprotection levels of 96% and 94.8% after the respective stated intervals of 5 and 10 years.

Based upon that initial rate and waning rate, the approximate average seroprotection rate is:

- 96.9% in 5 to 6 year olds, based upon averaging the hence approximated initial seroprotection rate and expected rate after 1 year.

iv. **Seroprotection in 7 – 10 year old children**

Based upon the information in the previous paragraph 7.2(c)iii.b above (headed ”Seroprotection in 5 **–** 6 year old children”), the average seroprotection rate for the fifth dose of tetanus-containing vaccination approximates:

- 96.4% in 7 – 10 year olds.

v. **Seroprotection in 11 - 19 year olds**

a. Seroprotection after sixth dose

A sixth tetanus vaccination dose is scheduled in the US at 11-12 years of age, according to the CDC Schedules.

Based upon what is presented in paragraph 7.2(c)iii.iii.b above, headed ”Seroprotection in 5 **–** 6 year old children”, of an estimated initial post-vaccination seroprotection rate of 97% and Waning Exponent of 1.058 as applicable to the sixth dose, the average seroprotection rate approximates:

- 96.2% in those 11 – 19 year olds who have received the sixth dose of tetanus-containing vaccination at 11 years of age.

b. Residual **seroprotection** from fifth dose

Based upon what is presented in paragraph 7.2(c)iii.iii.b above, headed ”Seroprotection in 5 **–** 6 year old children”, of an estimated initial post-vaccination seroprotection rate of 97% and Waning Exponent of 1.058 as applicable to the fifth dose, the average residual tetanus seroprotection rate approximates:

- 94.7% in 11-19 year olds who have received the fifth dose but not the sixth dose, which is scheduled in the US at 11-12 years of age.

vi. **Summary for VE**

Based upon the above information in this paragraph 7.1(c), the approximate annual average tetanus seroprotection rate is set out in the table below for each subject age group:

Age Group	1-6 yrs (DTaP)			7-10 yrs (DTaP)	11-19 yrs	
	6 – 11 mths	1-4 yrs	5-6 yrs		Td / Tdap	DTaP / DTP / DT / Td
VE	< 98.9%	< 80.4%	< 96.9%	< 96.4%	< 96.2% ("VE1")	< 94.7% ("VE2")

(d) Serious outcome Rate per Disease case (SRD)

In this Notice, a tetanus disease-associated SAE is defined as any reported case of tetanus. That results in the SRIU for any SAE being the same as the DRIU, in the case of tetanus.

The CDC Surveillance Manual Tetanus Chapter, under the heading "Background" states:

"From 2009 through 2017, a total of 264 cases and 19 deaths from tetanus were reported in the United States… 36 (13%) were in persons younger than 20 years … All tetanus-related deaths occurred among patients >55 years of age.[2]"

Based upon that statement, and the estimated VC and VE presented herein of approximately 95% and 93% respectively, and the Formula for Disease Rate in Unvaccinated, 15 of the said 36 cases "*in persons younger than 20 years"* could have been expected to have occurred in unvaccinated persons. None died, as all deaths were stated to have "*occurred among patients >55 years of age*".

Hence the death rate in unvaccinated persons under 20 years of age can be estimated to be less than 1 in 15, which is less than 7%.

Age	1-6 yrs			7-10 yrs	11-19 yrs
	6 – 11 mths	1-4 yrs	5-6 yrs		
SRD (Death) (Case fatality rate)	< 7%				

(e) Differential Risk of unavoidable serious adverse effect (SRIU)

Based upon the calculated estimates presented in this paragraph 7.2, “Tetanus” for

(a) the disease notification rate in the population (DRP), and

(b) the vaccination coverage (VC), and

(c) the vaccination effectiveness (VE), and

(d) the rate of serious adverse effects per disease case (SRD),

the approximate differential rates for disease (DRIU) and ultimately serious adverse effects (SRIU) can be calculated by applying the formulas set out in paragraphs 6.1 and 6.3, with the results set out in the table below for each age group:

Tetanus totals and averages in 2010-2018, approximated

<table>
<tr><th rowspan="2">Age range (targeting vaccine)</th><th rowspan="2">6 – 11 mths (DTaP)</th><th colspan="2">6 mths – 6 yrs (DTaP)</th><th rowspan="2">7 – 10 yrs (DTaP)</th><th colspan="2">11 – 19 yrs</th><th rowspan="2">Average / Total</th></tr>
<tr><th>1-4 yrs</th><th>5-6 yrs</th><th>Td / Tdap</th><th>DTaP / DTP / DT/ Td</th></tr>
<tr><td>DRP (annual)</td><td>≤ 1 / 17,704,223</td><td>1 / 72,071,910</td><td>~ 1 / 19,836,172</td><td>~ 1 / 19,146,984</td><td colspan="2">~ 1 / 19,925,316</td><td>~ 1 / 23,053,732 [4]</td></tr>
<tr><td>VC</td><td>≤ 86%</td><td>~ 94.7%</td><td>~ 94.9%</td><td>~ 95.1%</td><td>~ 86.3% (“VC1”)</td><td>~ 95.9% (“VC2”)</td><td>95.1% [4]</td></tr>
<tr><td rowspan="2">VE</td><td rowspan="2">< 98.9%</td><td rowspan="2">< 80.4%</td><td rowspan="2">< 96.9%</td><td rowspan="2">< 96.4%</td><td>< 96.2% (“VE1”)</td><td>< 94.7% (“VE2”)</td><td rowspan="2">92.3% [4]</td></tr>
<tr><td colspan="2">≤ 96.1%</td></tr>
<tr><td>DRU (annual)</td><td>< 1 / 2,653,606</td><td>< 1 / 17,233,417</td><td>< 1 / 1,597,302</td><td>< 1 / 1,597,302</td><td colspan="2">< 1 / 1,576,219</td><td>< 1 / 2,109,740[4]</td></tr>
<tr><td>DRIU (annual)</td><td>< 1 / 2,682,709</td><td>< 1 / 21,444,628</td><td>< 1 / 1,648,157</td><td>< 1 / 1,657,799</td><td colspan="2">≤ 1 / 1,638,176</td><td>< 1 / 2,054,116[4]</td></tr>
<tr><td rowspan="2">SRIU (= DRIU) total over age range</td><td rowspan="2">< 1 / 5,365,419</td><td>< 1 / 5,361,157</td><td>< 1 / 824,079</td><td rowspan="2">< 1 / 414,450</td><td colspan="2" rowspan="2">≤ 1 / 182,020</td><td rowspan="2">< 1 / 105,339 [4]</td></tr>
<tr><td colspan="2">< 1 / 714,284</td></tr>
<tr><td>SRD: Case fatality rate</td><td colspan="7">≤ 7%</td></tr>
<tr><td>SRIU (death): total over age range</td><td>< 1 / 76,648,841</td><td colspan="2">< 1 / 10,204,057</td><td>< 1 / 5,920,711</td><td colspan="2">< 1 / 2,600,279</td><td>< 1 / 1,504,847[4]</td></tr>
</table>

(f) Impact of vaccination on others' susceptibility

The CDC Pink Book Tetanus Chapter states under the heading "Communicability" that:

"Tetanus is not contagious from person to person."

Based upon that statement, tetanus vaccination cannot benefit any of the vaccine recipients' unvaccinated contact(s) by way of any form of herd immunity.

(g) Some other factors affecting susceptibility

In view of the unavailability to unvaccinated children of any herd immunity in the case of tetanus (as covered in the previous paragraph, 7.2(f)) all of the credit for the negligible tetanus incidence and death rate among unvaccinated children can only be attributed to factors and/or measures other than vaccination.

Based upon this statement by the Livorsi article:

"Instead of an absolute protective level of antibody, the real level of protection is probably dependent on the (general) immune status of the host"

and this statement in the CDC Surveillance Manual Tetanus Chapter, under the heading "Background":

"Diabetes, a history of immunosuppression, and intravenous drug use may be risk factors for tetanus.[10,11] From 2009 through 2017, persons with diabetes accounted for 12% of all reported tetanus cases, and 26% of all tetanus deaths. Intravenous drug users (IDUs) accounted for 8% of cases from 2009 through 2017;[2] a cluster of cases in IDUs was noted in California in the 1990s.[11]"

the key to protection against tetanus may be the general immune status of the host, rather than the vaccination status.

That may be seen to be supported by the information about tetanus in the CDC Surveillance Manual Tetanus Chapter, such as "Figure 1. Mortality and incidence rates of tetanus reported in the United States, 1900-2017", which evidences no acceleration in the already occurring decline in mortality when vaccination was introduced.

The CDC Surveillance Manual Tetanus Chapter does not include vitamin C or any other immune-boosting nutrition as either a prophylactic or treatment for

tetanus, to minimize any risk of harm. That is in spite of this statement in the Vitamin C and Infections Review:

> *"Jahan (1984) studied the effect of 1 g/day of intravenous vitamin C on tetanus patients in Bangladesh [131]. In children aged one to 12 years, there were no deaths in the vitamin C group, whereas there were 23 deaths in the control group ($p = 10^{-9}$) [1] (p. 17). In tetanus patients aged 13 to 30 years, there were 10 deaths in the vitamin C group compared with 19 deaths in the control group ($p = 0.03$)."*

Considering that excerpt and the observations also described in that same review article, as covered in paragraph 6.4(a)ii.a, about significant positive results being achieved with much higher vitamin C doses than 1 g/day, and other excerpts in paragraph 6.4(a), any SRIUs that remain today in some or all age groups may thus be able to be further reduced or eliminated.

7.3 Pertussis

The subject age range chosen for the risk analysis for diphtheria is 6 months to 19 years.

(The choice of that age range is based primarily upon the age grouping of hospitalization data published in the CDC Pertussis Surveillance Reports (paragraph 7.3(d), on page 204).

(a) Pertussis notification rates and vaccination failures

The Plaintiff hereby requests that the Court take judicial notice of the following documents:

- article entitled “Current Epidemiology of Pertussis In the United States”.

  Citation: Hutchins SS, Cochi SL, Brink EW, Patriarcha PA, Wassilak SGF, Rovira EZ and Hinman AR. Tokai J Exp Clin Med 1988. Vol 13; Suppl: 103-109, accessible at: https://pubmed.ncbi.nlm.nih.gov/2856218/
  (last accessed September 22, 2020)

  (hereafter “Hutchins Pertussis Article”)

  A true and correct copy of the aforesaid article is attached hereto as **Exhibit 86.**

- CDC web page headed “Pertussis Frequently Asked Questions”, accessible at https://www.cdc.gov/pertussis/about/faqs.html
  (hereafter “CDC Pertussis FAQ”)
  (last accessed October 18, 2020)

  A true and correct copy of the CDC Pertussis FAQs is attached hereto as **Exhibit 87**.

- CDC web page headed “Pertussis (Whooping Cough) (Bordetella pertussis) 2020 Case Definition”, accessible at https://wwwn.cdc.gov/nndss/conditions/pertussis/case-definition/2020/ (html)
  (last accessed November 3, 2020)

  (hereafter “CDC Pertussis Case Definition Web Page”)

  A true and correct copy of the CDC Pertussis Case Definition Web Page is attached hereto as **Exhibit 88**.

- article entitled “Asymptomatic transmission and the resurgence of *Bordetella pertussis”*

Citation: Althouse, B.M., Scarpino, S.V. *BMC Med* **13,** 146 (2015). https://doi.org/10.1186/s12916-015-0382-8, accessible at https://bmcmedicine.biomedcentral.com/articles/10.1186/s12916-015-0382-8 (html) or https://bmcmedicine.biomedcentral.com/track/pdf/10.1186/s12916-015-0382-8 (pdf)
(last accessed October 18, 2020)
(hereafter "Althouse Pertussis Article")

A true and correct copy of the Althouse Pertussis Article is attached hereto as **Exhibit 89**.

- article entitled "Asymptomatic transmission and the resurgence of *Bordetella pertussis"*

  Citation: Cherry JD. The 112-Year Odyssey of Pertussis and Pertussis Vaccines-Mistakes Made and Implications for the Future. J Pediatric Infect Dis Soc. 2019 Feb 22. pii: piz005. doi: 10.1093/jpids/piz005. [Epub ahead of print], accessible at https://academic.oup.com/jpids/article-pdf/8/4/334/30106988/piz005.pdf (pdf)
  (last accessed October 18, 2020)
  (hereafter "Cherry Pertussis LEP Article")

  A true and correct copy of the Cherry Pertussis LEP Article is attached hereto as **Exhibit 90**.

- article entitled "Antigen Review for the New Zealand National Immunisation Schedule: Pertussis"

  Citation: Turner N, Petousis-Harris H, Poole T and Nowlan M. September 2014. Prepared for: New Zealand Ministry of Health by a scientific team incorporating the Immunisation Advisory Centre, University of Auckland Institute of Environmental Science and Research Ltd, January 2013, accessible at https://www.immune.org.nz/sites/default/files/publications/Ebook%20Pertussis%20v2.pdf
  (last accessed October 18, 2020)
  (hereafter "NZ Pertussis Review")

  A true and correct copy of the NZ Pertussis Review is attached hereto as **Exhibit 91**.

i. Pertussis incidence history to recent years

a. Incidence in early 20th century

The Hutchins Pertussis Article states, in relation to the pertussis vaccine in use at the time of publication:

> *"in the United States …from 1922-1940, the average annual reported pertussis incidence of 150 cases per 100,000 population and mortality of 6 cases per 100;000 were orders of magnitude higher than in the present era (Figure 1)".*

b. Substantial decline in incidence up to year vaccination mandated

The Hutchins Pertussis Article states also that:

> since "*1922-1940"*, *"pertussis incidence declined markedly"* resulting *"in …the number of reported cases"* by *"the early 1970's"* falling to only *"1,000 to 4,000 cases per year".*

c. Vaccination mandated in 1978 to early 1980s

The Hutchins Pertussis Article then proceeds to state, in relation to the pertussis vaccine in use at the time:

> *"In 1978 a nationwide childhood immunization initiative was begun. Individual States passed legislation requiring proof of immunization for school entry at 5-6 years of age. By the early 1980's 42 of the 50 States plus the District of Columbia passed legislation requiring 3 doses of DTP for school entry. Since 1980 nationwide school entry coverage with 3 or more doses of DTP has exceeded 95 percent".*

d. Increased notifications starting from mandating of vaccination

The Hutchins Pertussis Article further states:

> *"During the period 1980-1986, a total of 17,396 cases of pertussis was reported to CDC by weekly telephone reports. The annual incidence of reported pertussis rose during this period from 0.5 cases per 100,000 population to 1.7/100,000. …The incidence rates for all age groups increased consistently between 1982 and 1986."*

e. Sustained increase in notifications to recent years

According to the CDC Pertussis FAQ, the increase in pertussis notifications continued:

"Since the early 1980s, there has been an overall trend of an increase in reported pertussis cases. Pertussis is naturally cyclic in nature, with peaks in disease every 3 to 5 years. But for the past few decades, peaks got higher and overall case counts went up."

The CDC Pertussis Case Definition Web Page similarly states:

"Bordetella pertussis is among the most poorly controlled bacterial vaccine-preventable diseases in the U.S. …the number of reported pertussis cases has increased steadily since the late 1980s, with a considerable resurgence observed over the last 10 years. The most notable peak was in 2012 when more than 48,000 cases and 18 deaths were reported, the largest number of cases in the U.S. since the mid-1950s. Significant numbers of cases were also reported in 2004, 2010 and 2014, ranging from 25,000–32,000 cases."

The Althouse Pertussis Article similarly states (on page 1-2):

"In the United States (US), 2012 saw more diagnosed B. pertussis cases than in any year since 1955… coverage has historically been high [1, 5], raising the likelihood that the resurgence is — at least in part — due to low vaccine effectiveness [6]."

f. Circulation now "in a manner similar to that in the prevaccine era"

The Cherry Pertussis LEP Article, published in 2019, states:

"In the prevaccine era, reported pertussis had cyclic peaks every 2 to 5 years [1, 2, 24–26]. …In the pertussis vaccine era (both whole-cell and acellular vaccines), the cyclic peaks of reported pertussis have been the same as those in the prevaccine era. Because the cycles of pertussis are the same today as they were in the prevaccine era, we know that B pertussis is circulating today in a manner similar to that in the prevaccine era [1, 2, 26–29].

ii. Failed "cocooning" strategy to prevent transmission to infants

The Plaintiff hereby requests that the Court take judicial notice of the following documents:

- Citation: Healy CM, Rench MA, Wootton SH, Castagnini LA. Evaluation of the impact of a pertussis cocooning program on infant pertussis infection. *Pediatr Infect Dis J*. 2015 Jan;34(1):22-6. doi:

10.1097/INF.0000000000000486, accessible at https://pubmed.ncbi.nlm.nih.gov/24992123/ (last accessed October 18, 2020) (hereafter "Healy Cocooning Article")

A true and correct copy of the Healy Cocooning Article is attached hereto as **Exhibit 92**.

- Citation: "Free whooping cough vaccine cut concerns experts", by Dr. Ananya Mandal, News Medical, May 9 2012, accessible at https://www.news-medical.net/news/20120509/Free-whooping-cough-vaccine-cut-concerns-experts.aspx (html) (last accessed October 18, 2020) (hereafter "Australian States End Cocooning Article")

  A true and correct copy of the Australian States End Cocooning Article is attached hereto as **Exhibit 93**.

a. Observation of high incidence in adults led to cocooning strategy

The NZ Pertussis Review states:

> *"Current strategies remain primarily focused on preventing severe disease in young infants."*

However, the Cherry Pertussis LEP Article states:

> *"Numerous studies since 2004 have noted that pertussis in adults is common and the major source for infections in infants [1, 2, 7, 30–40]".*

The Harnden Pertussis Article also notes:

> *a "20% incidence of* Bordetella pertussis *infection among adults with a persistent cough".*

Therefore, it was concluded in the Cherry Pertussis LEP Article that:

> *"We should increase our awareness of pertussis in adults, because they are the reservoir for the continued circulation of B pertussis and the source of infections in young infants."*

This resulted in the introduction of "cocooning", which the NZ Pertussis Review defines as follows:

"Immunising mothers and other family members in the postpartum period to protect the infants from pertussis exposure is called cocooning".

b. Cocooning effectiveness not established, at best

The NZ Pertussis Review states that:

"The effectiveness of cocooning strategies has not been established."

NZ Pertussis Review also similarly states:

"There is uncertainty regarding the degree of indirect protection provided by pertussis containing vaccines (71)"

and that in relation to the proposition that *"booster vaccination may generate herd immunity",* there is *"limited data"* that would support it.

c. Cocooning evidenced to be counterproductive

The Healy Cocooning Article states:

*"**Results:** One hundred ninety-six (49%) infants (≤6 months of age) with pertussis were born preintervention, 140 (35%) during maternal postpartum (PP) and 64 (16%) during cocooning (C) periods. Infants were similar in age at diagnosis (81.2 vs. 71.3 [PP] vs. 72.5 [C] days; P 0.07), sex (male 59% vs. 51% [PP] vs. 48% [C]; P 0.17), hospitalization (68% vs. 71% [PP] vs. 78% [C]; P 0.27) and outcome (2 deaths in the PP period; P 0.15), but more were admitted to intensive care units during cocooning (24% vs. 35% [PP] vs. 68% [C]; P < 0.001)…*

***Conclusions:** Postpartum immunization and cocooning did not reduce pertussis illness in infants ≤6 months of age."*

According to these statements, this study found that the rate of admission to intensive care was lowest in infants born when there had been *no* pre-intervention (24%), and found that, compared to those infants, the rate was almost three times higher (68%) in infants who were otherwise similar but born during cocooning periods.

d. Australia ends cocooning due to finding "no clinical effectiveness"

Australian States End Cocooning Article states:

"Despite more than 1600 whooping cough cases since January, Victorian Health Minister David Davis yesterday said he was cutting free vaccines for carers of infants from July because experts said it was not worth funding the program any more…

Mr Davis said he had taken the advice of the federal government's Pharmaceutical Benefits Advisory Committee (PBAC) and clinicians to end it. "The evidence that has come forward … is that the vaccination of parents is no longer worthy of support in the sense that it does not get the clinical result required," he said.

"The PBAC, which is totally independent and very expert, has determined that there is no clinical effectiveness of this strategy," Professor Brook said. He said this had made it clear the cocooning strategy should not be continued.

"So all jurisdictions who have been in this program will be effectively ceasing the cocooning strategy as of the end of June this year."

…asked by Labor MP Jill Hennessy if the government was "taking a massive gamble" withdrawing the free parental vaccine, given that whooping cough can kill babies, Mr Davis supported the decision to now withdraw it. "I make decisions of this type on the basis of the evidence that's put to me by the department and by clinical experts," Mr Davis said. "There has been a national committee meet to look at this and to make decisions on the basis of the best scientific evidence available ... the evidence is that the strategy has not been effective."

iii. Disease Notification Rates in Recent Years

The CDC Disease Notifications state that the number of pertussis cases reported in 2007-2018 have been as stated in *italics* in the following table for the given age groups, hereafter the Pertussis Notifications Table:

Pertussis notifications 2007 – 2018

Age group (years) / Year	<1	1 - 4	5 - 14	15 - 24	Total
2007	*1,720*	*1,026*	*2,650*	*1,694*	***7,090***
2008	*2,180*	*1,288*	*4,994*	*1,385*	***9,847***
2009	*3,089*	*2,100*	*6,545*	*1,437*	***13,171***
2010	*4,120*	*4,489*	*10,056*	*2,572*	***21,237***
2011	*2,772*	*2,642*	*7,176*	*1,502*	***14,092***
2012	*4,955*	*5,802*	*21,852*	*5,636*	***38,245***
2013	*4,000*	*3,853*	*11,281*	*3,818*	***22,952***
2014	*4,155*	*4,418*	*12,945*	*6,027*	***27,545***
2015	*2,672*	*2,806*	*6,870*	*4,193*	***16,541***
2016	*2,020*	*2,435*	*5,833*	*3,998*	***14,286***
2017	*2,237*	*2,779*	*6,015*	*4,204*	***15,235***
2018	*1,995*	*2,431*	*4,742*	*3,212*	***12,380***
Average 2007-2018	**2,993**	**3,006**	**8,413**	**3,307**	**17,718**

Based upon the figures in the Pertussis Notifications Table, the Five Year Age Group Population Table and the Selected Age Groups Population Table, the totals and average reported incidence for the under 25 years age groups over the 2007-2018 period can be calculated to be as set out in the following table:

Age group (years)	<1	1 - 4	5 - 14	15 – 24	Total < 25
Pertussis cases	35,915	36,069	100,959	39,678	**212,621**
Million person years	48	193	492	523	**1255**
Cases per 100,000	73.7	18.4	20.6	7.6	**17.3**
Case rate (approx.)	< 1 / 1,300	< 1 / 5,000	< 1 / 5,000	< 1 / 13,000	**< 1 / 6,000**

Based upon the figures in the above table, the overall annual average rate of pertussis notifications in under 25 year olds in 2007-2018 has been approximately 1 in 6,000, totaling approximately 1 in 230 over the 25 year age range.

With respect to the whole US resident population, the CDC Disease Notifications state that the total number of pertussis notifications for those same 12 years were respectively:

"*10,454"; "13,278"; "16,858; "27,550"; "18,719"; "48,277"; "28,639"; "32,971"; "20,762"; "17,972; "18,975*; and *"15,609"*.

Hence, ultimately, compared to the total number of pertussis cases in the US resident population having fallen in *"the early 1970's"*, according to Hutchins Pertussis Article, to only *"1,000 to 4,000 cases per year",* the total number that the CDC Disease Notifications state were reported in 2007-2018, after over three decades of mandatory vaccination, had grown to an average of 22,505 cases per year.

iv. History of hospitalization and mortality in relation to vaccination levels

a. Mortality "lowest ever" in the UK when uptake very low

The Plaintiff hereby requests that the Court take judicial notice of the following documents:

- article abstract entitled "Whooping cough and pertussis vaccine: a comparison of risks and benefits in Britain during the period 1968-83".

  Citation: Stewart GT. Dev Biol Stand. 1985;61:395-405, accessible at: https://www.ncbi.nlm.nih.gov/pubmed/3835080
  (last accessed July 11, 2020)
  (hereafter "Stewart DPT Risk Comparison Article Abstract")

  A true and correct copy of the aforesaid table is attached hereto as **Exhibit 94**.

The Stewart DTP Risk Comparison Article states, in relation to the pertussis vaccine in use at the time:

> *"Since 1975, acceptance of pertussis vaccine has fallen from over 70% to 50% or less in most parts of Britain… Hospital admissions show considerable variation between areas with relatively high rates in some areas of deprivation but very low rates in more affluent areas even where vaccine-acceptance is around 50%.... Deaths of infants with whooping cough have decreased steadily since 1900, the rate since 1975 being the lowest ever… outbreaks and severe cases requiring admission to hospital were concentrated consistently in a few areas of deprivation … Admissions to hospital decreased during the period 1970-83. There were no deaths attributable to proven or suspected infections with Bordetella pertussis during the*

period 1972-1983. No cases of encephalopathy, permanent brain damage or lung damage were detected in a follow up of all cases notified, surveyed or admitted to hospital between 1975 and 1982… Collectively, these national and local data provided estimates of the frequency of infection, complications of infection, admission to hospital and death in children with whooping cough for comparison with local, national and published estimates of the frequency and severity of adverse reactions, encephalopathy, permanent brain damage and death after injections of pertussis vaccine. It is concluded that, in children living in non-deprived circumstances in Britain, the risk of pertussis vaccine during the period 1970-83 exceeded those of whooping cough. In some deprived sectors, the risks from whooping cough might have been marginally higher but there was no evidence that this was associated with any increase in deaths or permanent disabilities."

Based upon this statement, the low pertussis vaccination coverage, including 50% or less, in most parts of Britain during the period of 1975 to 1982-3 did not lead to any increase in hospital admissions compared to when the *coverage* had previously been over 70%.

On the contrary, hospital admissions decreased, and there were no deaths, nor any cases of encephalopathy, permanent brain damage or lung damage attributable to pertussis.

b. Mortality rise in the US starting from when vaccination mandated

The Plaintiff hereby requests that the Court take judicial notice of the following documents:

- CDC web page headed "Appendix E: Reported Cases and Deaths from Vaccine Preventable Diseases, United States", accessible at https://www.cdc.gov/vaccines/pubs/pinkbook/appendix/appdx-e.html (html)
  (last accessed July 2, 2018)
  (hereafter "CDC Pink Book Historic Deaths Table")

  A true and correct copy of this document is attached hereto as **Exhibit 95**.

- article entitled “MMWR Summary of Notifiable Diseases – United States, 1993”,

  Citation CDC MMWR 42*(53):*1–73*,* accessible at: https://www.cdc.gov/mmwr/preview/mmwrhtml/00035381.htm (hereafter “CDC Pertussis Deaths 1982-1991”)

  A true and correct copy of this document is attached hereto as **Exhibit 96**.

- article entitled “Summary of Notifiable Diseases, United States, 2000”,

  Citation CDC MMWR 49(53);1-102*,* accessible at: https://www.cdc.gov/mmwr/preview/mmwrhtml/mm4953a1.htm (hereafter “CDC Pertussis Deaths 1989-1998”)

  A true and correct copy of this report is attached hereto as **Exhibit 97**.

- article entitled “Summary of Notifiable Diseases, United States, 2003”,

  Citation CDC MMWR 52(54);1-85*,* accessible at: https://www.cdc.gov/mmwr/preview/mmwrhtml/mm5254a1.htm

  (hereafter “CDC Pertussis Deaths 1996-2001”)

A true and correct copy of this report is attached hereto as **Exhibit 98**.

CDC Pink Book Historic Deaths Table and/or CDC Pertussis Deaths 1982-1991 state that the number of pertussis deaths reported in US residents in the years 1967 through 1986 was respectively:

> “*37*“,“*36*“,“*13*“,“*12*“,“*18*“,“*6*“,“*5*“,“*14*“,“*8*“,“*7*“,“*10*“,“*6*“,“*6*“,“*11*“,“*6*“, “*4*”, “*5*”, “*7*”, “*4*”, “*6*”.

CDC Pink Book Historic Deaths Table and/or CDC Pertussis Deaths 1982-1991 and/or CDC Pertussis Deaths 1989-1998 and/or CDC Pertussis Deaths 1996-2001 and/or CDC Disease Notifications 2009 state that the number of pertussis deaths reported in US residents in the years 1987 through 2005 was:

> “*1*”, “*4*”, “*12*”, “*12*”, “-”, ”*5*”, “*7*”, “*8*”, “*6*”, “*4*”, “*6*”, “*5*”, “*7*”, “*12*”, “*17*”, “*18*”, “*11*”, “*16*”, “*31*”

Based upon the above figures, the pertussis mortality overall (pertussis being stated CDC Pertussis FAQ to be "*naturally cyclic in nature*") fell until the 1980s which, according to the Hutchins Pertussis Article, was soon after a nationwide childhood immunization initiative was begun (in 1978) and vaccination mandated for school entry.

The numbers then began to rise and reached 31 in 2005.

The CDC Disease Notifications further state that the "*Cause-of-death code*", based upon which the pertussis deaths were published in the years 1982 through 2014, changed from "*ICD-9*" only to both "*ICD-9*" and "*ICD-10*" in the years 1996 through 1998, and was only "*ICD-10*" thereafter. In each of the three years 1996 through 1998, when the "*number of deaths based on the ICD-9 code*" was "*4*", "*6*" and "*5*" respectively, the "*number of deaths modified with the comparability ratio for IDC-10 code*" was zero. Hence, based upon these figures, the actual rise in mortality from 1998 to 2005 may have been much higher still than indicated by the published death numbers alone, with part of the rise potentially hidden by the change in "*Cause-of-death code"* that formed the basis for the reporting of death numbers.

v. Summary

Based upon the above quoted numbers in the Hutchins Pertussis Article, CDC Pertussis FAQ and CDC Disease Notifications, after decades of sustained decline in pertussis morbidity and mortality, the introduction of mandatory vaccination in the period of 1978 through the early 1980s was not followed by acceleration of the decline towards elimination of pertussis, but instead by an immediate halt of those declines, and then their reversal, with the mortality rate in recent years still higher than when mandatory vaccination was first introduced 40 years ago.

Hence this historical evidence, along with other contents within this paragraph 7.3 "Pertussis", gives no support to the proposition that mandatory pertussis vaccination provides protection to the community against pertussis, but only evidence to the contrary.

That evidence would only be countered if one or more other significant and relevant events occurred concomitantly with the mandating of vaccination and significantly and increasingly thereafter increased susceptibility to

disease and death from pertussis and/or notifications thereof. If any such other concomitant events occurred, they are not mentioned in the Hutchins Pertussis Article, in spite of their significance.

(b) Pertussis Vaccination Coverage (VC)

Based upon the inclusion of a single row only for "*diphtheria*", "*tetanus*" and "*pertussis*" combined in each of the CDC Schedule "*Figure*"s, an assumption shall be made in this Notice that the statements in the introductory section of paragraph 7.1(b) "Diphtheria Vaccination Coverage (VC)" prior to "i. Coverage in 6 month – 11 month olds (three doses**)**" apply equally to pertussis in all relevant years for all relevant age groups.

Based upon that assumption, the approximate annual average tetanus vaccination coverage in 2010-2018 was as set out in the table below for each subject age group:

Age	1-6 yrs (DTaP)			7-10 yrs (DTaP)	11-19 yrs	
	6 – 11 mths	1-4 yrs	5-6 yrs		Td / Tdap	DTaP / DTP / DT / Td
VC	~86%	~94.6%	~94.9%	~95.1%	~86.3% ("VC1")	~95.9% ("VC2")

The following are estimates of pertussis vaccination coverage in the US by age group during the material periods, based upon the Vaccination Coverage Reports.

i. **Coverage in 6 month – 11 month olds (three doses)**

According to the CDC Schedules, the CDC recommended pertussis vaccination in the US at 2, 4 and 6 months of age in 2008-2018.

The Vaccination Coverage in Infants report states that:

> *"For infants born in 2011 and 2012, first dose coverage at 3 months of age for DTaP was 86%.... At 7 months of age, coverage for …3 doses of DTaP was 73%... At 13 months of age, the coverage* (was) *…83%."*

Based upon the stated therein to be 86% for coverage of the first dose at 3 months, it shall be assumed herein, that for **the whole 2008-2019 period overall:**

- the coverage for 6 – 11 month olds was less than **approximately** 86%.

ii. **Coverage in 1 – 6 year olds (fourth and fifth doses)**

a. Coverage **in 1 – 4 year olds (fourth dose)**

The CDC Daycare Coverage Reports provide estimated vaccination coverages overall (some averages, others medians) for pertussis-containing vaccines in 19-35 month olds in the US as set out in the table below in *Italics*:

Pertussis Vaccine Coverage % (Daycare)

	≥3 doses (average)		***≥4 doses (average)***	
Year	***%***	***(95% CI)***	***%***	***(95% CI)***
2013	*94.1*	*(93.2–95.0)*	*83.1*	*(81.8–84.3)*
2014	*94.7*	*(94.0–95.4)*	*84.2*	*(83.0–85.4)*
2015	*95.0*	*(94.4–95.5)*	*84.6*	*(83.5–85.7)*
2016	*93.7*	*(92.8–94.5)*	*83.4*	*(82.1–84.6)*
2017	*94.0*	*(93.3–94.7)*	*83.2*	*(82.0–84.3)*
2018[9]	94.0	(93.3–94.7)	83.2	(82.0–84.3)
2019[9]	94.0	(93.3–94.7)	83.2	(82.0–84.3)
Average for 2012-2019	94.2		83.4	

Based on the data in the above table, the average pertussis vaccination coverages in 19-35 month olds over the period of:

- 2013-2019 and 2014-2019 approximated 94.2% for receipt of at least three doses, and 83.6% for receipt of at least four doses.

According to the CDC Schedule throughout the period of 2012-2019, the fourth pertussis-containing vaccination dose ("*DTaP*") was recommended to be given during the age range of "*15 months*" to "*18 months*". Based upon that stated recommendation, it will be assumed in the calculation set out in this Notice of SRIU for pertussis that virtually all of the 19-35 month old children in the population who were recorded at the time of the coverage surveys to have received the third dose but not the fourth (averaging approximately 10.6%), received that fourth dose soon after the relevant survey.

[9] Each coverage for this year is estimated herein to have been the same as that for the previous year.

Based upon that assumption and given further that children aged 4 years in 2013 or 2016 were aged 2 years in 2013 or 2014 respectively, the coverage for four doses in 1 – 4 year old children for 2013-2019 and 2016-2019 will be estimated to be the same as the coverage estimate given in the Vaccination Coverage Reports for "≥3 doses" in 19 to 35 month old children in 2013-2019 and 2014-2019 respectively.

Hence it will be taken that the coverage for four doses in 1 – 4 year old children approximated:

- 94.2% in both periods 2013-2019 and 2016-2019.

b. Coverage **in 5 – 6 year olds (fifth dose)**

Based upon the information and assumptions included in paragraph 7.1(b)ii.b headed "Coverage in 5 - 6 year olds (fifth dose)", and an assumption that virtually all children to whom the quoted "DTaP / DTP DT / Td" coverage figures applied had received the recommended number of doses of pertussis-containing vaccines (DTaP or DTP), the average or median coverage for the fifth dose of pertussis-containing vaccination in 5-6 year olds approximated:

- 94.7% in in both periods 2013-2019, and 2016-2019.

iii. **Coverage in 7 – 10 year olds (fifth dose)**

Based upon a combination of the information and assumptions included in paragraph 7.1(b)iii headed "Coverage in 7 – 10 year olds (fifth dose)" and the previous paragraph above, 7.3(b)ii.ii.b, the average or median coverage for the fifth dose of pertussis-containing vaccination in 7-10 year olds approximated:

- 94.9% in 2013-2019, and
- 94.8% in 2016-2019.

iv. **Coverage in 11 – 19 year olds (sixth or fifth dose)**

a. Coverage **for sixth dose**

The CDC Secondary School Coverage Reports provide estimated average vaccination coverages for pertussis-containing vaccines in 13 to 17 year olds in the US in 2010-2018 as follows (in *italics*):

Pertussis Vaccine Coverage % (Secondary School)

Vaccine [7]	*Year*	Age 13 – 17 yrs	
		%	*(95% CI)*
Tdap ≥1 dose on/at or after age 10 years / at age ≥10 years	*2013*	*86.0*	*(±0.9)*
	2014	*87.6*	*(±0.9)*
	2015	*86.4*	*(±1.0)*
	2016	*88.0*	*(87.1–88.9)*
	2017	*88.7*	*(87.8–89.6)*
	2018	*88.9* [9]	*(88.0–89.7)*
	2019	88.9 *	
Average for 2013-2019		87.8	
Average for 2016-2019		88.6	

* The coverage for 2019 is not published as at the date of filing this document and shall be assumed herein to be the approximately same as that for 2018.

It shall also be assumed herein that the overall rate for 11-19 year olds approximates that for 13-17 year olds.

Based on that assumption and the data in the above table, the average coverage for the sixth dose of pertussis-containing vaccination, Tdap, in 11-19 year olds approximated:

- 87.8% in 2013-2019, and
- 88.6% in 2016-2019.

b. Residual coverage for Fifth dose

Based upon the information and assumptions included in paragraph 7.3(b)iii above headed ”Coverage in 7 – 10 year olds (fifth dose)”, the average or median residual coverage for the fifth dose of pertussis-containing vaccination approximated:

- 95.7% for those aged 11-19 years in 2013-2019 (relevant elementary school entry years 1999-2000 through 2013-2014), and
- 95.4% for those aged 11-19 years in 2016-2019 (relevant elementary school entry years 2002-2003 through 2013-2014).

v. **Summary for VC**

Based upon the above information in this paragraph 7.1(b), the approximate annual average pertussis vaccination coverage in the respective material periods was as set out in the table below for each subject age group:

Age	Period	6 – 11 mths	1-6 yrs (DTaP)		7-10 yrs (DTaP)	11-19 yrs	
			1-4 yrs	5-6 yrs		Tdap	DTaP / DTP
VC	2013 - 2019	~86 %	~94.2%	~94.7%	~94.9 %	~ 87.8% ("VC1")	~95.7% ("VC2")
	2016 - 2019				~94.8 %	~ 88.6% ("VC1")	~95.4% ("VC2")

(c) Pertussis Vaccine Efficacy (VE)

The Plaintiff hereby requests that the Court take judicial notice of the following medical journal articles:

- Citation: Cherry JD, Heininger U, Stehhr K, Christenson P. The effect of investigator compliance (observer bias) on calculated efficacy in a pertussis vaccine trial. *Pediatrics* 1998 Oct;102(4 Pt 1):909-12, accessible at http://www.ncbi.nlm.nih.gov/pubmed/9755264
  (last accessed October 18, 2020)

  (hereafter "Cherry Pertussis Observer Bias Article")
  https://pediatrics.aappublications.org/content/102/4/909

  A true and correct copy of the Cherry Pertussis Observer Bias Article is attached hereto as **Exhibit 99**

- Citation: Cherry JD. Why do pertussis vaccines fail? Pediatrics. 2012 May;129(5):968-70. doi: 10.1542/peds.2011-2594. Epub 2012 Apr 23. PMID: 22529282, accessible at http://scepticsbook.com/wp-content/uploads/2012/05/Pediatrics-2012-Cherry-968-70.pdf
  (last accessed October 18, 2020)

  (hereafter "Cherry Pertussis Vaccine Failure Article")
  https://pediatrics.aappublications.org/content/102/4/909

  A true and correct copy of the Cherry Pertussis Vaccine Failure Article is attached hereto as **Exhibit 100**

- Citation: Cherry JD, Xing DX, Newland P, et al. Determination of serum antibody to Bordetella pertussis adenylate cyclase toxin in vaccinated and

unvaccinated children and in children and adults with pertussis. Clin Infect Dis 2004; 38:502–7, accessible at http://www.academia.edu/download/42424815/Cherry_202004.pdf (last accessed October 18, 2020) (hereafter "Cherry Pertussis ACT Article")

A true and correct copy of the Cherry Pertussis ACT Article is attached hereto as **Exhibit 101**

- Citation: Ozkal A, Sensoy G, Acuner C, Belet N, Guney AK. Seroprevalence of Bordetella pertussis immunoglobulin G antibodies among children in Samsun, Turkey. Turk J Pediatr. 2012;54(1):15-9, accessible at http://www.turkishjournalpediatrics.org/uploads/pdf_TJP_1011.pdf (last accessed October 19, 2020) (hereafter "Turkish Pertussis Study")

  A true and correct copy of the Turkish Pertussis Study is attached hereto as **Exhibit 102**.

(1) Vaccine design flaws – antigen differences between vaccines and circulating pertussis

Linked-epitope suppression of response to ACT toxin, not in vaccines

The Cherry Pertussis LEP Article states:

> *"numerous studies have shown the deficiencies of DTaP vaccines, including …the type of cellular immune response that they elicit. The type of cellular response…results in… linked-epitope suppression."*

The Cherry Pertussis ACT Article and the Cherry Pertussis LEP Article explain linked-epitope suppression:

- the Cherry Pertussis ACT Article provides this background:

  "B. pertussis has a number of virulence factors, including fimbriae, pertactin (PRN), pertussis toxin (PT), filamentous hemagglutinin (FHA), lipooligosaccharide, and adenylate cyclase toxin (ACT)… ACT is an important toxin that contributes to disease caused by B. pertussis" and

"ACT is an important virulence factor of B. Pertussis *which disrupts host cyclic 3',5'-adenosine monophosphate (cAMP) metabolism [1–4]. ACT enters a variety of mammalian cells and can inhibit the microbicidal cytotoxic function of neutrophils, monocytes, and natural killer cells. Its contribution to clinical pertussis may be through impairment of host defenses or through a direct effect on the respiratory mucosa",* but that

"at the present time, ACT has not been included as an antigen in any of the available DTaP products."

and reports a finding that:

"Primary infections with either B. pertussis *or* Bordetella parapertussis *stimulated a vigorous antibody response to ACT. In contrast, patients in whom DTP and DTaP vaccines failed had minimal ACT antibody responses."*

- the Cherry Pertussis LEP Article describes this phenomenon as "linked-epitope suppression" which it explains as:

  "similar to "original antigenic sin" in influenza. The concept of original antigenic sin in influenza was suggested more than 60 years ago. The immunologic memory of children is such that with a second influenza A infection, the major antibody response is directed at the strain with which they were infected originally and not to the new infecting strain", and

  'In "linked-epitope suppression," memory B cells out-compete naive B cells for access to the Bordetella epitopes because they are more numerous and their receptors exhibit a higher antigen affinity. Linked-epitope suppression applies as the immune response to novel epitopes is suppressed by the strong response to initial components if they are introduced together.'

The Cherry Pertussis ACT Article states as follows that upon natural exposure(s) to pertussis, and hence exposure to the important ACT pertussis toxin which is not "*in any of the available DTaP products*", the response of the vaccinated can be expected to be weaker, or "*less marked*", than that of the unvaccinated:

"With repeated exposure when older, the child responds preferentially to those epitopes shared with the original infecting agent or vaccine and can be expected to have responses to new epitopes of the infecting agent that are less marked than normal…. the patients who had been vaccinated …did not respond to the new antigen (i.e., ACT) associated with infection."

The Cherry Pertussis LEP Article states that the ACT antibody response is found to be lower in the DTaP-vaccinated than in the DTwP-vaccinated:

"the DTaP vaccination policy has created a cohort of people (the number of which is expanding yearly) who are more susceptible to repeated clinical illness with B pertussis *infection than are DTwP-vaccinated children"*

and

"Because of linked-epitope suppression, all children who were primed by DTaP vaccines will be more susceptible to pertussis throughout their lifetimes, and there is no easy way to decrease this increased lifetime susceptibility."

The Cherry Pertussis ACT Article adds, however, that the ACT antibody response is also suppressed after DTwP ("DTP") vaccination:

"In this investigation, … the postimmunization GMTs (geometric mean titers of antibody to ACT) of all vaccine groups (i.e., recipients of the DTP vaccine and the DTaP vaccine) were …low (table 1)."

Susceptibility to PRN-deficient strains is higher in the vaccinated

The Plaintiff hereby requests that the Court take judicial notice of the following document:

- Citation: Meeting of the Board of Scientific Counselors, Office of Infectious Diseases, Centers for Disease Control and Prevention, Tom Harkins Global Communication Center Atlanta, Georgia, December 11-12, 2013, accessible at

  https://www.cdc.gov/maso/facm/pdfs/BSCOID/2013121112_BSCOID_Minutes.pdf

  (last accessed October 19, 2020)

  (hereafter "CDC Meeting Report on Pertussis Resurgence")

  A true and correct copy of the Cherry Pertussis Article is attached hereto as **Exhibit 103**.

The CDC Meeting Report on Pertussis Resurgence states on page 6 regarding "*the recent resurgence in pertussis cases*":

> *"a recent study suggests another explanation….: an increase in* Bordetella pertussis *isolates that lack pertactin (PRN)--a key antigen component of the acellular pertussis vaccine. A study that screened* B. pertussis *strains isolated between 1935 and 2012 for gene insertions that prevent production of PRN found significant increases in PRN-deficient isolates throughout the United States.2 The earliest PRN-deficient strain was isolated in 1994; by 2012, the percentage of PRN-deficient isolates was more than 50%.*
>
> *…Findings indicated that 85% of the isolates were PRN-deficient and vaccinated patients had significantly higher odds than unvaccinated patients of being infected with PRN-deficient strains. Moreover, when patients with up-to-date DTaP vaccinations were compared to unvaccinated patients, the odds of being infected with PRN-deficient strains increased."*

Based upon this excerpt, the percentage in the population of circulating *Bordetella pertussis* strain isolates that do not contain the pertussis toxin PRN has increased to over 50% by 2012, with one assessment that year finding a percentage of 85%, and susceptibility to infection with those pertussis strains is higher for the DTaP-vaccinated than it is for the unvaccinated.

The same document suggests "*that PRN-bacteria may have a selective advantage in infecting DTaP-vaccinated persons*"

(2) Vaccine effectiveness measurement flaws

No "established correlates of protection"

The NZ Pertussis Review states on page iv:

> *"There are a number of challenges in measuring vaccine immunogenicity, efficacy and effectiveness due to there being* no established correlates of protection, limitations with case definitions…*"*

Hence, according to the authors of the NZ Pertussis Review, there is no reliable method of determining the protective effect of the vaccination. This means that there are no reliable serological markers, nor can there be reliance upon the rate of reporting of cases, which is based upon clinical case definitions which suffer "*limitations*".

Further details and possible reasons for the unreliability of those methods follow:

- **Unreliability of serological markers**

  Specifically with respect to serological markers, the NZ Pertussis Review states:

  "A Korean study …in 146 children aged three to 17 years with haematological malignancies" "found no significant correlation between levels of serum antibody titres *with the severity of the illness, treatment or age of the patient".*

  Serology method ignores important toxin ACT

  The NZ Pertussis Review states:

  "The immunogenicity of Tdap vaccines as a single dose in children aged four to eight years, adolescent, adults and the elderly have been assessed predominantly by measurement of serum levels of anti-PT, anti-PRN and anti-FIM."

  Hence, according to the NZ Pertussis Review authors, the method employed to assess the immunogenicity of Tdap vaccines does not include measurement of antibodies to ACT, despite ACT being "*an important toxin that contributes to disease caused by B. pertussis*", according to the Cherry Pertussis ACT Article.

  Serology method compromised by natural immunity effect

  The Turkish Pertussis Study states that in children who received "*DTaP"* only "*at the ages of 2, 4, 6 and 18-24 months*" plus a "*fifth dose… for 1st grade*",

  "The positivity rate of antibodies increased in the primary school children in grades 5 and 8, and the highest positivity was detected in grade 4 high school students (age 16-18 y). Furthermore, GMT (geometric mean titer) of antibodies was highest in the older children. These findings suggest natural immunization occurs after the age of 6-8 years."

  According to this excerpt, it is not only vaccination that can significantly contribute to seropositivity but also the development of natural immunity. This further undermines, or complicates, attempts to rely on seropositivity rates as a measure of protection provided by vaccination,

especially where there is a significant likelihood of asymptomatic natural infection in the population.

In relation to vaccine-targeted diseases to which natural immunity develops asymptomatically in a significant proportion of unvaccinated children, the effectiveness of the targeting vaccination is significantly less than the seroprotection rate. Where such a qualifying adjustment is evidenced to be appropriate to the "effectiveness" effect is referenced herein as the "Natural Immunity Effect". Numerically translated, if it is assumed that all of those who are seroprotected are actually protected, then the effectiveness % is:

VE% = 100% - (100% - SR%) / (100% - NIR%),

where SR% is the seroprotection rate % and
NIR% is the natural immunity rate %.

- **Unreliability of case definitions**

The Cherry Pertussis Vaccine Failure Article, dated 2012, states:

"our estimates of vaccine efficacy have been inflated because of case definition.3-11 At the time of the pediatric diphtheria and tetanus toxoids and acellular pertussis (DTaP) vaccine efficacy trials in the early 1990s, it was hoped that a universal case definition could be developed so that the results of the various trials could be compared. To this end, the World Health Organization (WHO) case definition was developed.' The primary case definition required laboratory confirmation and >21 days of paroxysmal cough. I was a member of the WHO committee and disagreed with the primary case definition because it was clear at that time that this definition would eliminate a substantial number of cases and therefore inflate reported efficacy values.4-11 Nevertheless, the Center for Biologics Evaluation and Research of the Food and Drug Administration accepted this definition, and package inserts of the US-licensed DTaP vaccines reflect this. For example, Infanrix (containing 25 p.g pertussis toxin [PTl. 25 p.g filamentous hemagglutinin [FHA], and 8 p.g pertactin [PRN]) and Daptacel (containing 10 p.g PT, 5 p.gFHA, 5 p.g fimbriae [FIMl-2/3, and 3 p.g PRN) have stated efficacies of 84% and 85% respectively. When less severe cough illness is included, however, the efficacies of these 2 vaccines decrease."

According to the Cherry Pertussis Vaccine Failure Article, studies that have relied upon such a case definition that requires the presence of a paroxysmal (or other) cough lasting a set minimum number of days, such as "*21 days*", have inflated reported efficacy values for their results.

This takes on further significance if natural immunity (meaning that following recovery from infection after natural exposure) is weaker and/or of shorter duration in the vaccinated than in the unvaccinated. Based upon the conclusion stated in the Cherry Pertussis ACT Article that vaccination results in linked-epitope suppression (paragraph 7.3(c)(1) above), that is a plausible scenario.

Missed infections in vaccinated

- **Missed asymptomatic infection in vaccinated**

The Althouse Pertussis Article states:

"Warfel et al. …found evidence that individuals vaccinated with current acellular B. pertussis vaccines (aP) can become asymptomatically infected, and can then transmit infection to susceptible individuals."

"the timing of changes in age-specific attack rates observed in the US and UK are consistent with asymptomatic transmission."

"We find that for realistic aP coverage rates (between 85% and 95%), the percentage of total cases expected to be observed is low (< 15 %), and is highly dependent on the probability of an infection becoming symptomatic (a parameter that is generally not known). These results are likely to be conservative given the low, but unknown, diagnosis rate of asymptomatic infections" (pages 6-7)

"The potential for this type of vaccine failure has been observed in humans where reanalyses of aP vaccine studies revealed that individuals vaccinated with components of the aP vaccine were protected against disease, but not bacterial colonization [10, 11]. This is in addition to the extant, but limited, evidence for natural asymptomatic infection [12–14]."

"These results demonstrate no changes in transmission due to vaccination." (Fig 6)

"Our results suggest that: 1) there is strong empirical support for asymptomatic transmission from both the epidemiological and genomic data; 2) the presence of asymptomatic transmitters will bias estimates of vaccine efficacy derived from observations of stochastic fadeouts across cities; and 3) asymptomatic transmission provides the most parsimonious explanation for many of the observed patterns associated with current B. pertussis dynamics in the US and UK (that is, the resurgence of cases…"

"Our results on the potential surveillance bias associated with B. pertussis incidence highlight a critical need for population-wide serological surveys to detect recent infection …more detailed studies of the incidence rate in unvaccinated individuals, and increased active surveillance of attenuated symptomatic B. pertussis infections"

"improvement in B. pertussis diagnostics… would not explain the bulk of the empirical evidence presented here."

"the total bacterial load in the nasopharynx of B. pertussis-infected non-human primates is similar between symptomatic and asymptomatic individuals (see Figure one, panel a in [9]). The same study suggested that the duration of higher bacterial loads may be longer in asymptomatic individuals, and that there may not be differences in routes of transmission between asymptomatic and symptomatic individuals. However, and perhaps more importantly, being asymptomatic suggests that individuals may not alter their behavior and thus contact more individuals than a symptomatic individual [58]. Therefore, it seems equally plausible to conclude that the R_0 (basic reproduction number) for aP vaccinated individuals is higher [47]. Future studies should make estimating the distribution of effective reproductive numbers for symptomatic and asymptomatic individuals a priority."

Hence, according to these articles,

- the vaccinated do not have a reduced chance of infection ("bacterial colonization") even if the chance of developing recognizable symptoms ("disease") is reduced, and
- vaccination does not lead to a reduction in the risk of transmission to vulnerable infants, but rather leads to "*the presence of vaccine-induced … asymptomatic individuals*" in whom "*the duration of higher bacterial*

loads may be longer" and who "*may not alter their behavior and thus contact more individuals than a symptomatic individual*".

- **Missed symptomatic infection in vaccinated due to observer bias**

Physicians' observer bias

The Plaintiff hereby requests that the Court take judicial notice of the following medical journal article:

- Citation: Harnden A. Whooping cough in school age children with persistent cough: prospective cohort study in primary care. *BMJ* 22 July *2006; 333:174,* accessible at https://www.bmj.com/content/bmj/333/7560/174.full.pdf (last accessed October 19, 2020) (hereafter "Harnden Pertussis Article")

  A true and correct copy of the Harnden Pertussis Article is attached hereto as **Exhibit 104**.

The Harnden Pertussis Article states:

> *"Studies in the United States report a 20% incidence of* Bordetella pertussis *infection among adults with a persistent cough.2 Despite data showing that neither infection nor immunisation results in lifelong immunity, whooping cough is seldom diagnosed in primary care because of the lack of specificity of clinical symptoms and signs. Whooping cough is perceived as a disease of very young children who have not been immunised and who have classic features such as whoop."*
>
> *"Our results show that a substantial proportion of school age children with persistent cough who present in primary care have evidence of a recent* Bordetella pertussis *infection. Despite this, general practitioners rarely diagnose and notify whooping cough in this age group. Most of the children in our study had received a full set of primary immunisations. Although immunisation failed to protect them against pertussis, it did result in attenuated clinical features. Few of the children had a classical whoop, although most children had coughing spasms followed by vomiting."*

The Harnden Pertussis Article noted the "*20% incidence of Bordetella pertussis infection among adults with a persistent cough*" and the Althouse

Pertussis Article referred to the "*known underreporting of symptomatic infections in adults*."

However, the Harnden Pertussis Article additionally stated the following with respect to children:

> *"general practitioners rarely diagnose and notify whooping cough" in "school age children", despite "a substantial proportion of school age children with persistent cough who present in primary care have evidence of a recent* Bordetella pertussis *infection".*

The reason that the Harnden Pertussis Article forwarded for the underreporting of pertussis was that:

> *"whooping cough is perceived as a disease of very young children who have not been immunised and who have classic features such as whoop",*

with the infected instead having been found to have had a

> *"lack of specificity of clinical symptoms and signs"* such that *"few of the children had a classical whoop, although most children had coughing spasms followed by vomiting".*

Thus, according to the Harnden Pertussis Article, physicians' observer bias is an important reason for the missing of pertussis cases in the vaccinated.

The Cherry Pertussis Observer Bias Article describes an analysis of the "*impact on calculated vaccine efficacy*" by the "*observer bias*" of "*physicians*". It states that:

> *"we analyzed study physician evaluation rates and rates of referral to the central investigators. Physician practices were separated into three compliance categories: high, intermediate, and low. We analyzed vaccine efficacy of an acellular pertussis component DTP vaccine (DTaP) and a whole cell pertussis component DTP vaccine (DTP) by compliance category.* Bordetella pertussis *infection was documented by culture of the organism in the study child or in a household contact or by a significant antibody response to pertussis toxin determined by enzyme-linked immunosorbent assay…*

Using a clinical case definition that included both mild and typical pertussis (cough illness ≥7 days duration) efficacy of DTaP vaccine was 40% (95% confidence interval [CI] = -3-65) in the high compliance category and 78% (95% CI = 65-86) and 75% (95% CI = 53-87) in the intermediate and low compliance groups, respectively…

Using a clinical case definition that required ≥21 days of cough with paroxysms, whoop, or vomiting (typical pertussis) the efficacy of DTaP vaccine was 69% (95% CI = 41–83) in the high compliance category and 86% (95% CI = 76–92) and 84% (95% CI = 64–93) in the intermediate and low compliance groups, respectively".

Hence, the article found physicians' observer bias against investigating clinical cases in vaccinated persons to be so substantial that after adjusting for that bias to some extent by analyzing the data only from the "high compliance" physicians, the combined result for typical and "mild" disease was that the efficacy at the lower limit of the 95% confidence interval was negative ("*-3*%").

The study concluded:

"Our data suggest that observer compliance (observer bias), can significantly inflate calculated vaccine efficacy. It is likely that all recently completed efficacy trials have been effected [sic] *by this type of observer bias and all vaccines have considerably less efficacy against mild disease than published data suggest."*

Parents' observer bias

The Cherry Pertussis Vaccine Failure Article also states:

"It is very likely that observer bias also occurred in the 2 double-blinded trials in Sweden and Italy,[10,11] because the study nurses called the families only every month (Italy) or every 6 to 8 weeks (Sweden). Therefore, in both studies the parents were the primary observers. Because …the parents "knew pertussis" (it was epidemic in both countries), they would be more likely to have their children evaluated if the illness was typical. This would inflate efficacy."

Based upon this excerpt, it may be concluded that to whatever extent vaccination leads to a variation from the typical, recognizable

symptomatology of pertussis, observer bias of not only physicians, but additionally parents, may inflate vaccine efficacy.

Based upon this excerpt and the Harnden Pertussis Article, it may be reasoned that in non-blinded studies also, vaccine efficacy can be expected to be inflated where this statement in the Harnden Pertussis Article (made in relation to physicians) applies to parents:

“whooping cough is perceived as a disease of very young children who have not been immunized ”,

especially where their children

‘have not had “classic features such as whoop”’,

because any of those perceptions may discourage parents who believe that they “know” that vaccination is effective and/or that they “know pertussis" from having their children evaluated.

(3) Calculation of upper limit of possible effectiveness

Caution needed for interpreting “protection” calculation results below

To permit the formation of a numerical basis as at least a starting point for a risk comparison, the numerical analyses presented in paragraphs 0(c)(3)i - iv below disregard all evidence that the effectiveness measurement methods are flawed and that pertussis vaccination may have zero to negative effectiveness. That includes the relevant evidence set out in the paragraphs 0(c)(1) and 0(c)(2) above.

The analyses are conducted instead in accordance with the assumption that the methods are reasonably indicative of the level of protection that pertussis vaccines used in the US provide against pertussis-associated long term harm. Those measurement methods include:

- serological markers, specifically the particular limited serological markers that have been used to date for determining effectiveness (see paragraph , and
- retrospective analysis of reported cases that are confirmed using culture or PCR testing, as described by the Misegades DTaP Fifth Dose Article and the Klein Tdap Article, which are respectively referenced in paragraph 7.3(c)(3)ii.b below headed “Protection in 5 - 6 year olds” and paragraph 7.3(c)(3)iv.a headed “Protection after sixth dose”.

Notably the original reporting of these studied cases is subject firstly to any parents' observer bias, and then to any physicians' observer bias as described in paragraph 7.3(c)(2)). Those two sources of bias have a compounding effect in their potential inflation of VE.

i. **Seroprotection in 6-11 month olds**

The Plaintiff hereby requests that the Court take judicial notice of the following document:

- the CDC "Pink Book" Pertussis chapter, accessible at https://www.cdc.gov/vaccines/pubs/pinkbook/pert.html#features online or https://www.cdc.gov/vaccines/pubs/pinkbook/downloads/pert.pdf (pdf) (hereafter "CDC Pink Book Pertussis Chapter")

  A true and correct copy of the aforesaid report is attached hereto as **Exhibit 105.**

The CDC Schedules state that three doses of pertussis vaccination are scheduled in infancy.

The level of seroprotection demonstrated to be provided by just the three doses may be taken to not be as high as after four doses, based upon the statement in the CDC Pink Book Pertussis Chapter that the "*Primary Series*" consists of "*four doses*", which are set out in a table that includes the following columns:

"Routine DTaP Primary Vaccination Schedule

Dose	***Age***
Primary 1	*6 weeks – 2 months*
Primary 2	*4 months*
Primary 3	*6 months*
Primary 4	*15-18 months"*

Nevertheless it shall be assumed herein that the seroprotection rate applicable to 6-11 month olds is as high as that in the six month period following the fourth vaccination dose referenced as "*Primary 4*" in said table, which has been scheduled in the US at "*15 months*" to "*18 months*", according to the CDC Schedules in all material years.

With respect to that dose, the NZ Pertussis Review states:

"A Turkish seroprevalence study was undertaken in 2008/2009 on 385 health [sic] *children, aged 18 months to eight years, all vaccinated against pertussis with a primary course and one booster."*

The Turkish Pertussis Study does not give the ages at which the children received the fourth dose. However, it shall be assumed herein that the fourth dose was received no earlier than 18 months of age, based upon this statement in the study:

"In 2008, DTP vaccine switched to …DTaP, …given …at the ages of 2, 4, 6 and 18-24 months."

To maximize the seroprotection result it shall be further assumed herein that the fourth dose was given at the lower end of the 18-24 month age range, which is 18 months.

With respect to which vaccine the children received, DTP or DTaP, the study states:

"Although there is a study that suggests a longer duration of protective immunity acquired by whole-cell pertussis vaccination than by acellular pertussis vaccination, other studies did not find a difference between these two vaccines".

The Turkish Pertussis Study states its findings to have been that:

"the seropositivity rate in 1.5-3-year-old children was" "52.7", which was *"lower than we expected, but a literature search revealed that other studies also support the rapid decrease in the anti-pertussis titers*[23,24]*"*

and

"The lowest positivity rate was determined in the 4-5 y age group (28.1%)"

These stated findings fit mathematically with an initial seropositivity rate after the 18 month dose having been approximately 69% and Waning Exponent approximately 1.31, resulting in the seroprotection levels matching 52.7% and 28.1% at the respective stated ages of "*1.5-3*" and "*four to five*" years respectively.

Based upon that initial seropositivity rate and Waning Exponent, the average seroprotection rate is interpolated to approximate:

- 67% in 6 – 11 month olds.

ii. **Protection in 1 – 6 year olds (fourth and fifth doses)**

a. Seroprotection in 1 - 4 year olds

Based upon the same initial and Waning Exponent approximations as stated in the previous paragraph 7.3(c)i headed "Seroprotection in 6-11 month olds", the annual average seroprotection rate can be interpolated to approximate:

- 56.7% in 1 to 4 year olds.

b. Protection in 5 - 6 year olds

The Plaintiff hereby requests that the Court take judicial notice of the following document:

- Citation: Misegades LK, Winter K, Harriman K, et al. Association of Childhood Pertussis With Receipt of 5 Doses of Pertussis Vaccine by Time Since Last Vaccine Dose, California, 2010 JAMA, November 28, 2012; Vol 308, No. 20, which is accessible at https://pubmed.ncbi.nlm.nih.gov/23188029/
  (last accessed October 20, 2020)
  (hereafter "Misegades 5-Dose DTaP Article")

A true and correct copy of the Misegades 5-Dose DTaP Article is attached hereto as **Exhibit 106.**

The Misegades 5-Dose DTaP Article describes an

> *"evaluation conducted in 15 California counties"* of "*children aged 4 to 10 years*" "*from January through December 14, 2010*" of *"the association between pertussis and receipt of 5 DTaP doses by time since fifth DTaP dose"*

and states:

> *"we conducted a secondary analysis using confirmed cases only",*

in relation to which

> *"A confirmed case was defined as cough plus isolation of Bordetella pertussis in culture or a clinical pertussis case with either a positive polymerase chain reaction (PCR) test result or epidemiologic link to a confirmed case."*

The document states that the "*Main Outcome Measures*" of the study described therein are of:

> *"(1) odds ratios (ORs) for the association between pertussis and receipt of the 5-dose DTaP series and (2) ORs for the association between pertussis and time since completion (<12, 12-23, 24-35, 36-47, 48-59, or ≥60 months) of the 5-dose DTaP series."*

The article includes a table headed "*Table 4. Odds Ratios for Pertussis Disease Associated With Receipt of 5 DTaP Doses and Estimated Vaccine Effectiveness for Each Year Following the Complete DTaP Series",* which contains the columns and rows in the following table, hereafter "Misegades 5-Dose DTaP VE Table":

Time since fifth dose, mo	*Secondary Analysis [b]*
	Estimated VE, %(95% IE)
< 12	*98.3 (97.8-98.9)*
12-23	*93.4 (91.1-96.0)*
24-35	*89.5 (85.7-93.7)*
36-47	*84.1 (80.1-90.4)*
48-59	*82.0 (75.8-88.4)*
≥ 60	*73.3 (65.1-83.0)*

Based upon an averaging of the estimated VE percentages stated therein for the periods of "*< 12*" and "*12-23*" months since the fifth dose, which were "98.3" and "93.4" respectively, the VE can be estimated to be approximately:

- 95.9% for 5 – 6 year olds.

The document additionally states:

> *"doses received less than 2 weeks prior to case illness onset or control enrollment were not included in the final dose count"*

Based upon this stated exclusion, it may be reasoned that the VE results were inflated if the vaccination caused or contributed to any pertussis cases within 2 weeks after vaccination.

The document further states:

> *"Participants were considered unvaccinated for pertussis if their medical record included …documentation of unvaccinated status"*

Based upon that statement, the study subjects in the "unvaccinated" comparison group were not limited to those who were officially "vaccine-eligible" and whose parents and doctors were comfortable that they were healthy enough to receive doses of pertussis vaccine. This mismatch with the vaccinated group was another potential cause of inflation of the VE results.

iii. **Protection in 7 - 10 year old children**

Based upon an averaging of the four "Estimated VE" percentages in the Misegades 5-Dose DTaP VE Table for the periods of "*24-35*" through "≥ *60*" months since the fifth dose, the VE can be estimated to be approximately:

- 82.2% in 7 – 10 year olds.

iv. **Protection in 11 – 19 year olds (sixth or fifth dose)**

a. Protection after sixth dose

The Plaintiff hereby requests that the Court take judicial notice of the following document:

- Citation: Klein NP, Bartlett J, Fireman B and Baxter R. Waning Tdap Effectiveness in Adolescents. Pediatrics March 2016, 137 (3) e20153326; DOI: https://doi.org/10.1542/peds.2015-3326, which is accessible at https://pediatrics.aappublications.org/content/137/3/e20153326 (last accessed October 20, 2020)
(hereafter "Klein Tdap Article")

  A true and correct copy of the Klein Tdap Article is attached hereto as **Exhibit 107.**

The Klein Tdap Article states that the researchers:

> *"investigated Tdap vaccine effectiveness (VE) and waning within Kaiser Permanente Northern California among adolescents exclusively vaccinated with DTaP vaccines",* during *"large pertussis outbreaks in 2010 and 2014"*

and

> *"defined a case as testing PCR positive for pertussis"*

and

"followed all KPNC members starting at age 10 years who had exclusively received DTaP vaccines in infancy and childhood. We limited the study population to individuals who were born in 1999 or later[13] or who were born in 1996–1998 and received 3 infant doses of DTaP at KPNC."

According to the last of the above excerpts, the control group in the study for the calculation of VE was not unvaccinated children but children who had received DTaP vaccines in infancy and childhood. Hence that VE will be referred to hereafter in this paragraph as the "relative Tdap VE".

Misegades 5-Dose DTaP Article states that the "*Age at fifth (DTaP) dose, y*" was "*4*" for "*68.7*"%, and "*5*" for "*30.8*"% of the children in that study.

Based upon that data, an assumption is incorporated into the calculation that is presented herein of the VE that results after all six pertussis vaccine doses (compared to zero doses), hereafter "absolute Tdap VE". That assumption is that the children in the study described by the Klein Tdap Article received a fifth DTaP dose at an average age of 4.5 years.

The results in the Misegades 5-Dose DTaP VE Table, following the estimated VE of "*89.5*"% as the stated VE estimate for "*12-23*" months after the fifth dose, fit mathematically with a decline in which the Waning Exponent was thereafter approximately 1.4.

The Klein Tdap Article includes a table entitled "*TABLE 1. Tdap Vaccination Rates and Follow-Up Time by Age, Gender, Birth Year, and Race/Ethnicity in the Study Population*" which contains the following selected rows and columns:

Age group, y	*Number Vaccinated With Tdap (%) Total = 175 094*
10	*20 423 (11.7)*
11	*117 019 (66.8)*
12	*33 162 (18.9)*

Based upon the figures in the above table, the age of 11.5 years shall be taken as the approximate age at which the Tdap vaccine was administered to the children in the study described by the Klein Tdap Article.

The Klein Tdap Article states that the results for (relative) "*Tdap VE*", were as follows:

> *"Tdap VE steadily decreased each additional year after vaccination, starting at 68.8% (95% CI 59.7% to 75.9%) during year 1, declining to 56.9% (95% CI 41.3% to 68.4%) during year 2, further declining to 25.2% (95% CI –4.3% to 46.4%) during year 3, and to 8.9% (95% CI –30.6% to 36.4%) during the 4+ years after vaccination".*

Based upon the above results and assumptions, the absolute Tdap VE can be calculated to be that in the last column in the table below, in the respective periods after administration of the Tdap:

Period after Tdap	Age (yrs)	Residual DTaP VE	Relative Tdap VE	Absolute Tdap VE
< 12 mths	11.5 - 12.5	55.1%	*68.8%*	86.0%
1 - 2 yrs	12.5 - 13.5	43.4%	*56.9%*	75.6%
2 - 3 yrs	13.5 - 14.5	31.1%	*25.2%*	48.4%
3 - 4 yrs	14.5 - 15.5	19.5%	*8.9%*	26.6%

The above calculation results of the VE in the 2 – 3 year period of 48.4% to the VE in the 3 – 4 year period of 26.6%, fit mathematically with a decline in which the Waning Exponent is approximately 1.825 following the 2 – 3 year period.

Based upon that Waning Exponent, and the absolute VE results in the above table for the first four years after Tdap vaccination, the average VE (relative to being unvaccinated) following a Tdap administered on the 11th birthday (after receipt of 5 DTaP doses in infancy and childhood) can be calculated to be approximately:

- 27.4% for 11 – 19 year olds.

Further to that:

- based upon the stated lower limits of the 95% confidence intervals (CIs) in the Klein Tdap Article, the possibility is within reasonable limits that the relative Tdap VEs are much lower than the stated calculated averages. That applies to the extent that the stated lower limit for the relative Tdap VE becomes negative during the third year after Tdap vaccination ("*–4.3%*") and the absolute Tdap VE becomes negative the following year (calculable to be approximately -5.2% during the 4+ years

after vaccination, based upon a residual DTaP effectiveness of 19.5% and stated CI lower limit VE of "*-30.6%*"), and

- the Klein Tdap Article states:

  "We limited the study population to individuals who… received 3 infant doses of DTaP…"

  According to this excerpt, the "unvaccinated group" had received at least 3 infant DTaP doses. However they may not have received the fourth and/or fifth doses. The assumption is made in this analysis that all "unvaccinated" children received all five DTaP doses. To the extent that that was not the case, it may be reasoned that the VE result was inflated.

- the Klein Tdap Article states:

  "Tdap vaccination status was specified as a set of time varying variables that indicated whether a person was unvaccinated, too-recently-vaccinated-to-benefit (within 1–7 days), or vaccinated in the previous 8 days to <1 year ("year 1"), 1 to <2 years ("year 2"), 2 to <3 years ("year 3"), or ≥3 years ("year 4+"). VE was assessed for each of the 4 ranges of vaccinated person-time beginning 8 days after receipt of Tdap."

  Based upon the exclusion described in this statement of subjects who had been vaccinated less than 8 days prior to disease onset, it may be reasoned that the VE results were inflated if the vaccination caused or contributed to any pertussis cases within 1 week after Tdap vaccination.

- the Klein Tdap Article states:

  "Adolescents were considered unvaccinated until they received Tdap…"

  Based upon that excerpt, in particular what is not included in that statement, the study subjects in the "unvaccinated" "control" group were not limited to those who were officially "vaccine-eligible" and whose parents and doctors were comfortable that they were healthy enough to receive doses of the Tdap vaccine. This mismatch with

the Tdap-vaccinated group was another potential cause of inflation of the VE results.

These points, in addition to other study deficiencies such as the potential VE inflating effect of observer bias as described in paragraph 7.3(c)(2)), can be reasoned to constitute a qualification to any conclusion drawn from this study about the VE of the Tdap vaccine dose.

b. Residual **protection** from fifth dose

Based upon the results in the Misegades 5-Dose DTaP VE Table, in particular the stated VE estimate of "*89.5*" for "*12-23*" months after the fifth dose and Waning Exponent of approximately 1.4 fitting the results thereafter, the average residual pertussis protection rate approximates:

- 25.5% in 11-19 year olds who have received the fifth dose but not the Tdap dose scheduled in the US at about 11 years of age.

v. **Summary for VE**

Based upon the calculated VE figures in this paragraph 7.3(c)(3) only, the approximate annual average pertussis seroprotection rate is set out in the table below for each subject age group:

Age Group	6 – 11 mths	1-6 yrs (DTaP)		7-10 yrs (DTaP)	11-19 yrs	
		1-4 yrs	5-6 yrs		Tdap	DTaP (residual)
VE	< 67%	< 56.7%	< 95.9%	< 82.2%	< 27.4% ("VE1")	< 25.5% ("VE2")

(d) Serious outcome Rate in the Population (SRP)

In this Notice, a pertussis disease-associated SAE is defined as a hospitalization or death.

The Plaintiff hereby requests that the Court take judicial notice of the following documents:

- the CDC's "2013 Final Pertussis Surveillance Report", "2014 Final Pertussis Surveillance Report", "2015 Final Pertussis Surveillance Report", "2016 Final Pertussis Surveillance Report", "2017 Final Pertussis Surveillance Report", "2018 Final Pertussis Surveillance Report" and "2019 Provisional Pertussis Surveillance Report", all of which are accessible via the CDC web page headed "Pertussis (Whooping Cough) Surveillance and Reporting" accessible here: https://www.cdc.gov/pertussis/surv-reporting.html#surv-reports

and which are respectively directly accessible at
https://www.cdc.gov/pertussis/downloads/pertuss-surv-report-2013.pdf ,
https://www.cdc.gov/pertussis/downloads/pertuss-surv-report-2014.pdf ,
https://www.cdc.gov/pertussis/downloads/pertuss-surv-report-2015.pdf ,
https://www.cdc.gov/pertussis/downloads/pertuss-surv-report-2016.pdf ,
https://www.cdc.gov/pertussis/downloads/pertuss-surv-report-2017.pdf , and
https://www.cdc.gov/pertussis/downloads/pertuss-surv-report-2018-508.pdf and
https://www.cdc.gov/pertussis/downloads/pertuss-surv-report-2019-508.pdf
(last accessed October 20, 2020)
(hereafter "CDC Pertussis Surveillance Reports")

A true and correct copy of each of the aforesaid reports is attached hereto as **Exhibit 108.**

The CDC Pink Book Pertussis Chapter states:

"In 2008 through 2011 a total of 72 deaths from pertussis were reported to CDC. Children 3 months of age or younger accounted for 60 (83%) of these deaths. During 2008-2011, the annual mean of pertussis cases in infants was 3,132 (range 2,230 – 4,298), the mean of hospitalizations was 1,158 (range 687-1,459) and the mean of deaths was 16 (range 11-25)."
(hereafter, the "CDC Pink Book Pertussis Chapter Statement*")*

All of the CDC Pertussis Surveillance Reports for the years 2013-2014 and 2017-2019 state:

"Deaths reported through NNDSS to CDC".

and the CDC Pertussis Surveillance Reports for the year 2019 states:

"Source: National Notifiable Disease Surveillance System".

Based in part upon this statement, it is assumed herein that the source of all of the figures in the CDC Pertussis Surveillance Reports is the NNDSS.

i. Hospitalization rates

a. 6—11 month olds

Infants 4—11 months old in 2008-2011:

According to the CDC Pink Book Pertussis Chapter Statement, the annual average number of hospitalizations in infants in 2008-2011 was "*1,158 (range 687-1,459)*".

Based proportionately upon the death numbers as set out in paragraph 7.3(d)ii.a below, 1/16th of those hospitalizations, i.e. an annual average of 72 (range 43-91), could be estimated to have occurred in infants 4 months of age or over.

Based upon the figures in the Selected Single Year Age Groups Population Table, the average population for "*0*" year olds in 2008-2011 was 4,012,711. Of that average it can be proportionally estimated that 2,675,141 were infants 4 months of age or over.

Hence the annualized average number of hospitalizations in infants over 3 months of age in 2008-2011 could be estimated to have been 72 (range 43-91) in 2,675,141 or **1 in 37,155** (range 1 in 62,213 to 1 in 29,397).

Infants 6—11 months old in 2016-2019:

The CDC Pertussis Surveillance Reports for 2016 through 2019 each include a table headed: "*Reported Pertussis Cases and Percent Hospitalization by Age Group*", containing columns headed: "*No. of Cases (% of total)*" and *"% Hospitalized by age***"* and a row headed "*6-11 mos*".

The figures stated therein for "*No. of Cases*" and *"% Hospitalized by age**"* are as set out (in *Italics*) in the respective columns in following table, which also includes in the right most column the resultant calculable result of the number ("No.") of cases hospitalized:

Year	*No. of Cases* (for "*Age*" "*6-11 mos*")	*% Hospitalized by age***	No. of Pertussis Cases Hospitalized (approx. - calculation result)
2016	*634*	*11.7*	74
2017	*731*	*37.1*	79
2018	*630*	*11.9*	75
2019	*638*	*9.8*	63

Based upon the hospitalization figures in the above table, the total number of hospitalizations in that age group over those 4 years was about 291.

Combining that total with the figures in the Five Year Age Group Population Table and Selected Single Year Age Groups Population Table, that was an annualized average hospitalization rate of **1 in 27,136** (range 1 / 32,505 in 2019 to 1 / 24,645 in 2017).

One might have expected the hospitalization rate in 6-11 month olds in 2016-2019 to be significantly lower than in 4-11 month olds in 2008-2011 in view of the higher average age of 6-11 month olds than that of 4-11 month olds, and other figures in this paragraph 7.3(d) "Serious outcome Rate in the Population (SRP)" that indicate a declining mortality and morbidity over the years since the 2008-2011 period. Instead, the hospitalization rate is higher in the older age group in the more recent period.

Notably however, another difference between the two age groups is that, based upon the CDC Schedules and information presented in paragraph 7.3(b)i headed "Coverage in 6 month – 11 month olds (three doses)", the average vaccination coverage was significantly higher in the 6-11 month old age group. Hence, the increased hospitalization rate in that older age group, with the higher vaccination coverage, might be seen to call into question whether DTaP vaccination decreases, or may increase, susceptibility to pertussis.

b. 1-6 year olds in 2016-2019

The CDC Pertussis Surveillance Reports for 2016 through 2019 each include a table headed: "*Reported Pertussis Cases and Percent Hospitalization by Age Group*", containing columns headed: "*No. of Cases (% of total)*" and *"% Hospitalized by age***"* and a row headed "*1-6 yrs*".

The figures stated therein for "*No. of Cases*" and *"% Hospitalized by age***"* are as set out (in *Italics*) in the following table, which also includes in the rightmost column the resultant calculable result of the number ("No.") of cases hospitalized and the calculable approximate total for those 4 years:

Year	*No. of Cases* (for "*Age*" "*1-6 yrs*")	*% Hospitalized by age***	No. of Pertussis Cases Hospitalized (approx. - calculation result)
2016	*3279*	*2.7*	89
2017	*3646*	*3.4*	124
2018	*3232*	*2.6*	84
2019	*3282*	*3.1*	102
		Total	399

Based upon the hospitalization figures in the above table, the total number of hospitalizations in the 1-6 year age group over those 4 years was about 399.

Combining that total with the figures in the Five Year Age Group Population Table and Selected Single Year Age Groups Population Table, that was an overall annual average hospitalization rate in that age group of about:

- **1 in 241,000** in the 1 – 6 year age group.

c. 7-10 year olds in 2016-2019

The CDC Pertussis Surveillance Reports for 2016 through 2019 each include a table headed: "*Reported Pertussis Cases and Percent Hospitalization by Age Group*", containing columns headed: "*No. of Cases (% of total)"* and "*% Hospitalized by age**"* and a row headed *"7-10 yrs".*

The figures stated therein for "*No. of Cases"* and "*% Hospitalized by age**"* are as set out (in *Italics*) in the respective columns in following table, which also includes in the right most column the resultant calculable result of the number ("No.") of cases hospitalized:

Year	*No. of Cases* (for age 7-10 yrs)	*% Hospitalized by age***	No. of Cases Hospitalized (approx. - calculation result)
2016	*2450*	*1.5*	37
2017	*2597*	*1.1*	29
2018	*1897*	*1.3*	25
2019	*1988*	*1.1*	22

Based on the hospitalization figures in the above table, the total number of hospitalizations in that age group over those 4 years was about 112 (which was an annual average of 7 hospitalizations per year group).

Combining that total with the figures in the Five Year Age Group Population Table and Selected Single Year Age Groups Population Table, that was an annual average hospitalization rate of **1 in 585,013.**

d. 11-19 year olds in 2016-2019

The CDC Pertussis Surveillance Reports for 2016 through 2018 each include a table headed: "*Reported Pertussis Cases and Percent Hospitalization by Age Group*", containing columns headed: "*No. of Cases*

(% of total)" and "*% Hospitalized by age***" and a row headed *"11-19 yrs".* The figures stated therein for "*No. of Cases"* and "*% Hospitalized by age***" are as set out (in *Italics*) in the respective columns in following table, which also includes in the right most column the resultant calculable result of the number ("No.") of cases hospitalized:

Year	*No. of Cases* (for age 7-10 yrs)	*% Hospitalized by age***	No. of Cases Hospitalized (approx. - calculation result)
2016	*6135*	*0.9*	55
2017	*6348*	*1.0*	63
2018	*4922*	*0.9*	44
2019	*4758*	*1.5*	71

Based on the hospitalization figures in the above table, the total number of hospitalizations in that age group over those 3 years was about 234 (which was an annual average of 7 hospitalizations per year group).

Combining that total with the figures in the Five Year Age Group Population Table and Selected Single Year Age Groups Population Table, that was an annual average hospitalization rate of about

- **1 in 645,017** in the 11-19 year age group.

e. Adjustment for underreporting

The Plaintiff hereby requests that the Court take judicial notice of the medical journal article entitled:

- Tracking Pertussis and Evaluating Control Measures through Enhanced Pertussis Surveillance, Emerging Infections Program, United States.

  Citation: Skoff TH, Baumbach J, Cieslak PR. Emerg Infect Dis. 2015;21(9):1568-1573. https://dx.doi.org/10.3201/eid2109.150023, accessible at https://wwwnc.cdc.gov/eid/article/21/9/pdfs/15-0023.pdf (last accessed February 5, 2021)

  (hereafter "Pertussis Reporting Completeness Article")

  A true and correct copy of the Cherry Pertussis Observer Bias Article is attached hereto as **Exhibit 109.**

The Pertussis Reporting Completeness Article includes a table entitled "Table. Completeness of pertussis surveillance data collected from the

NNDSS and EPS, United States, 2011–2012*", which contains the following selected columns, rows and note:

	Complete, %†
Characteristic	*NNDSS*
Hospitalized	*73*

†Unknown or missing responses were considered incomplete.

Based upon the information in the above table, and assuming that the finding of an overall reporting completeness of 73% in 2011-12 applied (approximately) throughout the relevant period of 2016-2019 and to the 6 month to 19 year age range, the hospitalization rates calculated in the above paragraphs 7.3(d)i.a-d are only approximately 73% complete, so must be divided by 73% to estimate the true hospitalization rates.

This adjustment is made simply to the overall SRP rate (for hospitalizations) based upon the conservative assumption that the underreporting applies to cases in the unvaccinated as much as it does to cases in the vaccinated. Given the observer bias documented in relation to pertussis, and level of concern expressed with vaccination uptake, that may well be a false assumption.

f. Summary of hospitalization rates for pertussis (SRP for hospitalization)

Based upon the information in this paragraph 7.3(d)i "Hospitalization rates", including adjusting for underreporting by dividing the results 7.3(d)i.a-d by 73%, the approximate annual average pertussis hospitalization rates in 2016-2019 were as set out in the table below for each subject age group:

Age	**1-6 yrs**			**7-10 yrs**	**11-19 yrs**
	6 – 11 mths	**1-4 yrs**	**5-6 yrs**		
SRP	1 / 19,809 (or < 1 in 27,123: 2008-2011 estimate, adjusted)	1 / 175,842		1 / 427,060	1 / 470,863

ii. Death rates

Based upon the CDC Pink Book Pertussis Chapter, the average annual number of deaths over all age groups for 2008-2011 was 18.

The CDC Pertussis Surveillance Reports for 2013 through 2018 each include a table headed: “Reported Pertussis Deaths”, containing columns headed: “Age” and “Deaths*†”.

In those tables, the total reported deaths for all age groups for 2013 through 2018 is stated to be “*13*”, “*13*”, “*6*”, “*7*”, “*13*” and “*5*“ respectively. Based on those numbers, the total annual average number of deaths in 2013-2018 in the US resident population was 9.5. That was almost half the annual average of 18 deaths (16 in infants) in 2008-2011.

a. infants under and over 3 or 4 months

2008-2011:

In 2008 through 2011, based upon the CDC Pink Book Pertussis Chapter Statement, the annual average number of deaths:

- in infants was “*16*”, and
- in infants aged 3 months or younger was 15, and
- in infants aged 4 months or older is calculable to have been 1.

Based upon the figures in the Single Year Age Group Population Table, the average population for “*0*” year olds in 2008-2011 was 4,012,711.

The 16 infant deaths in that period results in an overall risk of death for infants of 1 in 250,794.

Based upon 15 of those 16 infants having been ≤ 3 months of age, there was an average death rate of **1 in 2,675,141** infants aged 4 - 11 months of age.

2013-2014:

The tables headed “*Reported Pertussis Deaths*” in the CDC Pertussis Surveillance Reports include rows headed “*Infants, aged < 3 mos*”, “*Infants, aged 3-11 mos*” in the 2013 and 2014 reports.

The figures stated therein for infants are as set out (in italics) in the following table, which also includes, in the rightmost column, the resultant calculable total number of reported deaths in infants, which further total 45 for that 7 year period.

Year	*Age*	*Deaths*	**Total Infant Deaths** (calculation result)	
2013	*Infants, aged < 3 mos*	*12*	12	
	Infants, aged 3-11 mos	*0*		
2014	*Infants, aged < 3 mos*	*8*	9	
	Infants, aged 3-11 mos	*1*		
		Total for all infants	21	
		Annual average for all infants	10.5	
		Total person years 0 year olds	7,886,044	
		Annual average rate overall for infants	1 in 375,526	A
		Total aged 3-11 months	1	
		Total person years 3-11 mth olds (approx.)	5,914,533	
		Annual average rate 3-11 mth olds (approx.)	**1 in 5,914,533**	B

Based upon those figures, and the figures in the Single Year Age Group Population Table (for 0 year olds):

- in 2013-2014, all deaths except one of a total of 21 infant deaths (averaging 10.5 per year, down from 16 per year in 2008-2011) were in under 3 month olds.

  That remaining death was **1 in 5,914,533** approximately) infants aged 3-11 months in the total population in 2013 and 2014.

2015-2019:

The death rate in 6 – 11 month old infants after 2014 is not determinable from the CDC Pertussis Surveillance Reports, because all infant death numbers therein are grouped together under one total for infant deaths for each year.

The tables headed "*Reported Pertussis Deaths*" in the CDC Pertussis Surveillance Reports in the 2015 through 2019 reports include rows headed "*Infants, aged < 1 yr*".

The figures stated therein for infants are as set out (in italics) in the following table, which also includes, in the rightmost column, the resultant calculable total number of reported deaths in infants, which further total 45 for that 7 year period.

Year	*Age*	*Deaths*	
2015	*Infants, aged < 1 yr:*	*3*	
2016	*Cases, aged < 1 yr*	*6*	
2017	*Cases, aged < 1 yr*	*9*	
2018	*Cases, aged < 1 yr*	*3*	
2019	*Cases, aged < 1 yr*	*3*	
	Total for all infants	24	
	Annual average for all infants	4.8	
	Total person years in 0 year olds	19,776,924	
	Annual average rate overall for infants	1 in 824,039	C
	Annual average rate 3-11 mth olds (estimate)	= C x B ÷ A = **1 in 12,978,611**	

- in 2015-2019 the annual average number of deaths in infants was 4.8 (down from 16 in 2008-2011 and 10.5 in 2013-2014), which means that the overall death rate for infants fell by about 2.2 times from 1 in 375,526 to 1 in 824,039 in that later period (2015-2019).

Based upon the overall annual average rate in 2015-2019 of 1 in 824,039, combined with the figures for 2013-2014, it may be reasonably estimated by extrapolation that the rate in infants aged 3 months or older in 2015-2019 declined from 2013-2014 also by about (824.039 ÷ 375,526 =) 2.2 times. That results in a rate in 2015-2019 of about **1 in 12,978,611** for infants aged 3 months or older.

b. 1-4 year olds

The CDC Pertussis Surveillance Reports for 2013 and 2014 state that the number of "*Reported Pertussis Deaths*" in *"Children, aged 1-4 yrs*" were respectively "*1*" (in 2013) and "*2*" (in 2014).

Hence, based upon these reports, there were 3 deaths in 1 to 4 year olds. Combining that with the 2013 and 2014 data in the Single Year Age Group Population Table for "*0*" year olds, and in the column headed "*0 – 4"* in the Five Year Age Group Population Table, that was an annual average death rate of about **1 in 10,611,840**.

Based upon the approximate 2.2 times decline in infant death rate from 2013-2014 to 2015-2019 (as referenced in the previous paragraph 7.3(d)ii.a (under the heading "2015-2019"), it may be considered

reasonable to project that a similar rate of decline occurred in 1-4 year age group.

Based upon that projection, the annual average death rate in 2015-2019 in 1-4 year olds can be estimated to have been **1 in 28,479,737**.

c. over 5 year olds

2008-2011: Based upon the CDC Pink Book Pertussis Chapter Statement, the annual average number of deaths in persons over 1 year of age in 2008-2011 was 2 (as 16 out of an average of 18 deaths were in infants).

Based upon the Single Year Age Group Population Table (for under 1 year olds), and the Whole Population Table for over 3 month olds in 2008-2011, that was an annual average rate in over 1 year olds of **1 in 151,965,093.**

2013: The CDC Pertussis Surveillance Report for 2013 includes in its "*Reported Pertussis Deaths*" table no record of any death in any person over 5 years of age (the only other deaths being the "*12*" in under 3 month olds and the "*1*" in 1-4 year olds). Based upon that table, there were *no pertussis deaths* in the US that year in any person over 5 years of age.

2014: The CDC Pertussis Surveillance Report for 2014 states in the "*Reported Pertussis Deaths*" table that of all persons over 1 years of age, apart from the "*2*" in 1-4 year olds, there were only 2 other deaths, both of which were in "*Adults, aged 55+ yrs*". Based upon that table, there were *no pertussis deaths* in the US that year in any person between 5 and 54 years of age (inclusive).

2015: The CDC Pertussis Surveillance Reports for the years after 2014 group all deaths in infants together and group all deaths in older persons together - they do not make available the number of deaths specifically in 1 to 4 year olds or other older age groups.

The CDC Pertussis Surveillance Report for the year 2015 states that three deaths occurred in that year in "*Persons, aged > 1 yr*". Other than that, it does not give the ages or age groups.

However, in relation to those three deaths, the CDC Disease Notifications 2015 states that all three patients were *"adolescents and adults with co-morbidities*".

Based upon that statement, there were *no pertussis deaths* in the US in 2015 in any person between 1 and 10 years of age.

In the case of each of those three deaths, based upon their "*co-morbidities*" and without further information available to the contrary, it may be considered possible that the patient either had been vaccinated or, if not vaccinated, was medically contraindicated for vaccination, in which case the death rate in vaccine-eligible persons over the age of one was zero.

2016-2019: For the years 2016, 2017, 2018 and 2019, the CDC Pertussis Surveillance Reports provide a figure in "Deaths" column in the "*Reported Pertussis Deaths*" table row "*Cases, aged ≥ 1 yr*" as "*1*", "*4*", "*2*" and "*6*" respectively. Other than that, they do not state the age groups in which the deaths were reported to occur.

2013-2019 overall: Hence, based on the CDC Pertussis Surveillance Reports, in the 7 year period of 2013-2019 there were a total of 21 deaths in persons over 1 year of age, which was an average of 3 deaths per year.

Extrapolating the average of 1.5 deaths in 1-4 year olds in 2013-2014 to the rest of the 2013-2019 period, it may be estimated that subtracting that figure of 1.5 in 1-4 year olds from the annual average of 3 in over 1 year olds leaves 1.5 deaths on average in over 5 year olds in 2013-2019.

Based upon that result and the Whole Population Table and the Five Year Age Group Population Table for 2013-2019, the annual average death rate in persons over 5 years of age in 2013-2019, incorporating the 5-6, 7-10 and 11-19 year age groups, approximated 1 in 202,026,015.

d. Summary of death rates for pertussis (SRP for death)

Based upon the information in this paragraph 7.3(d)ii "Death rates", the approximate annual average pertussis vaccination coverage in 2010-2018 was as set out in the table below for each subject age group:

Age	1-6 yrs			7-10 yrs	11-19 yrs
	6 – 11 mths	1-4 yrs	5-6 yrs		
	(2015-2019 estimate)	(2013-2014 estimate)	2013-2019 estimate		
SRP	1 / 12,978,611	1 / 10,611,840	1 / 202,026,015		

(e) Differential Risk of SAE (SRIU)

Based upon the calculated estimates presented in this paragraph 7.3, “Pertussis” for: the vaccination coverage (VC), and the vaccination effectiveness (VE), and the rate of serious adverse effects (hospitalizations and death) per head of population (SRP), the approximate differential rates for disease incidence (DRIU) and ultimately serious adverse effects therefrom (SRIU) can be calculated by applying the formulas set out in paragraphs 6.1 and 6.3, with the results set out in the tables below for each age group.

Pertussis HOSPITALIZATIONS - totals and averages, approximated

<table>
<tr><th rowspan="2">Age range (targeting vaccine)</th><th colspan="3">6 mths – 6 yrs (DTaP)</th><th rowspan="2">7 – 10 yrs (DTaP)</th><th colspan="2">11 – 19 yrs</th><th rowspan="2">Average / Total</th></tr>
<tr><th>6 – 11 mths</th><th>1-4 yrs</th><th>5-6 yrs</th><th>Tdap</th><th>DTaP / DTP</th></tr>
<tr><td>SRP (annualized)</td><td rowspan="2">1 / 19,809 (or < 1 in 27,123</td><td colspan="2">1 / 175,842</td><td rowspan="2">~ 1 / 427,060[4]</td><td colspan="2" rowspan="2">~ 1 / 470,863</td><td rowspan="2">~ 1 / 221,988</td></tr>
<tr><td>1 / 125,364[10]</td><td>1 / 903,179[10]</td></tr>
<tr><td>VC</td><td>~ 86%</td><td>~ 94.2%</td><td>~ 94.7%</td><td>~ 94.8%</td><td>~ 88.6% (“VC1”)</td><td>~95.4% (“VC2”)</td><td>94.7% [4]</td></tr>
<tr><td>VE</td><td rowspan="2">< 67%</td><td rowspan="2">< 56.7%</td><td rowspan="2">< 95.9%</td><td rowspan="2">< 82.2%</td><td>< 27.4% (“VE1”)</td><td>< 25.5% (“VE2”)</td><td rowspan="2">52.6% [4]</td></tr>
<tr><td colspan="2">≤ 27.3%</td></tr>
<tr><td>SRU (annualized)</td><td>< 1 / 8,374</td><td>< 1 / 58,374</td><td>< 1 / 83,191</td><td>< 1 / 94,320</td><td colspan="2">< 1 / 348,241</td><td>< 1 / 88,424[4]</td></tr>
<tr><td>SRIU (annualized)</td><td>< 1 / 12,475</td><td>< 1 / 102,942</td><td>< 1 / 86,793</td><td>< 1 / 114,710</td><td colspan="2">< 1 / 1,269,805</td><td>< 1 / 135,473[4]</td></tr>
<tr><td>SRIU total over age range</td><td rowspan="2">< 1 / 24,949</td><td>< 1 / 25,736</td><td>< 1 / 43,396</td><td rowspan="2">< 1 / 28,677</td><td colspan="2" rowspan="2">< 1 / 193,273</td><td rowspan="2">< 1 / 6,947[4]</td></tr>
<tr><td colspan="2">< 1 / 16,155</td></tr>
</table>

[10] The SRP figures (of 1 / 125,364 and 1 / 903,179) are determined on the basis of allocating the hospitalizations in 1-6 year olds to the 1-4 and 5-6 age groups such that the two resultant SRU figures are in the same relative proportion as the two respective SRU figures below for Pertussis deaths

Pertussis DEATHS* - totals, averages and estimates

<table>
<tr><th rowspan="2">Age</th><th colspan="3">6 mths – 6 yrs (DTaP)</th><th rowspan="2">7 – 10 yrs (DTaP)</th><th colspan="2">11 – 19 yrs</th><th rowspan="2">Average / Total</th></tr>
<tr><th>6 – 11 mths (DTaP)</th><th>1-4 yrs</th><th>5-6 yrs</th><th>Tdap</th><th>DTaP / DTP</th></tr>
<tr><td>SRP (annual)</td><td>1 / 12,978,611</td><td>1 / 28,479,737</td><td colspan="4">~ 1 / 202,026,015</td><td>~ 1 / 77,007,064</td></tr>
<tr><td>VC</td><td>~86%</td><td>~94.2%</td><td>~94.7%</td><td>~ 94.9%</td><td>~ 87.8% (“VC1”)</td><td>~95.7% (“VC2”)</td><td>94.9% [4]</td></tr>
<tr><td>VE</td><td>< 67%</td><td>< 56.7%</td><td>< 95.9%</td><td>< 82.2%</td><td>< 27.4% (“VE1”)</td><td>< 25.5% (“VE2”)</td><td>52.6% [4]</td></tr>
<tr><td></td><td></td><td></td><td></td><td></td><td colspan="2">≤ 27.3%</td><td></td></tr>
<tr><td>SRU (annual)</td><td>< 1 / 5,486,315</td><td>< 1 / 13,264,364</td><td>< ~1 / 18,574,486</td><td>< ~ 1 / 44,318,357</td><td colspan="2">< ~ 1 / 149,322,761</td><td>< 1 / 29,958,589 [4]</td></tr>
<tr><td>SRIU (annual)</td><td>< 1 / 8,173,208</td><td>< 1 / 23,391,420</td><td>< ~ 1 / 19,378,703</td><td>< ~ 1 / 53,898,883</td><td colspan="2">< ~ 1 / 544,480,973</td><td>< 1 / 22,824,224 [4]</td></tr>
<tr><td>SRIU total over age range</td><td>< 1 / 16,346,415</td><td>< 1 / 5,847,855</td><td>< ~ 1 / 9,689,351</td><td>< ~ 1 / 13,474,721</td><td colspan="2">< ~ 1 / 60,497,886</td><td>< 1 / 2,346,718</td></tr>
<tr><td></td><td></td><td colspan="2">< 1 / 3,646,854</td><td></td><td colspan="2"></td><td></td></tr>
</table>

* Note that the adjustment based upon the reporting completeness estimate of 73% for pertussis hospitalizations has not been applied also to pertussis deaths, The same or similar rate may be applicable to deaths but the Pertussis Reporting Completeness Article does not include any reporting completeness estimate for deaths.

(f) Impact of vaccination on others’ susceptibility

The Plaintiff hereby requests that the Court take judicial notice of the following documents:

- the CDC “Manual for the Surveillance of Vaccine-Preventable Diseases: Chapter 10: Pertussis”, accessible at: https://www.cdc.gov/vaccines/pubs/surv-manual/chpt10-pertussis.html (html) or https://www.cdc.gov/vaccines/pubs/surv-manual/chpt10-pertussis.pdf (pdf) (last accessed November 1, 2020) (hereafter “CDC Surveillance Manual Pertussis Chapter”)

A true and correct copy of the CDC Surveillance Manual Pertussis Chapter is attached hereto as **Exhibit 110**.

- Citation: Wearing HJ, Rohani P. Estimating the Duration of Pertussis Immunity Using Epidemiological Signatures. *PLoS Pathog*. Oct 2009;5(10), accessible at https://journals.plos.org/plospathogens/article/file?id=10.1371/journal.ppat.1000647&type=printable
(last accessed October 20, 2020)
(hereafter "Wearing Natural Immunity Article")

  A true and correct copy of the Wearing Natural Immunity Article is attached hereto as **Exhibit 111**, and

- Citation: Crowcroft N, Stein C, Duclos P, Birmingham M. How best to estimate the global burden of pertussis? The Lancet Infectious Diseases. 2003; 3:413–418. [PubMed: 12837346, accessible at https://pubmed.ncbi.nlm.nih.gov/12837346/
(last accessed October 20, 2020)
(hereafter "Crowcroft Nutrition Protection Article")

  A true and correct copy of the Crowcroft Nutrition Protection Article is attached hereto as **Exhibit 112.**

Factors other than vaccination must be protecting the unvaccinated

Based upon the statement in the Althouse Pertussis Article that the results of the described study "*demonstrate no changes in transmission due to vaccination*", and upon the level of protection that the calculation results in paragraph 7.3(e) indicate is enjoyed by unvaccinated vaccine-eligible children against harm from pertussis, only factors other than vaccination remain to be considered as the true effective providers of that protection, some of which are discussed in paragraph 6.4 herein.

With respect to any SRIU that remains, the CDC Surveillance Manual Pertussis Chapter states:

- regarding prevention:

  "During outbreaks, prevention measures should focus on efforts to improve Tdap coverage during pregnancy to reduce severe illness and possible deaths in vulnerable infants." and

"CDC recommends administration of chemoprophylaxis to contacts at high risk and household members of a pertussis patient." and

- regarding treatment:

  "Treatment and chemoprophylaxis

  … Three macrolides (azithromycin, erythromycin, clarithromycin) are recommended for treatment of pertussis… If resistance to macrolides is suspected or if their use is contraindicated, it is recommended to treat with trimethoprim–sulfamethoxazole (TMP-SMZ)."

Based upon these excerpts and the rest of the CDC Surveillance Manual Pertussis Chapter, the CDC does not include vitamin C or any other immune-boosting nutrition as either a prophylactic or treatment for pertussis, to minimize any risk of harm.

Considering that in combination with the excerpts in paragraph 6.4(a) herein, especially paragraph 6.4(a)ii.a, the SRUs (and SRIUs) that remain today in some or all age groups, may thus be able to be further reduced or eliminated.

Protecting more vulnerable young infants

With respect to whatever extent the risk for young infants cannot thus be entirely eliminated, the Wearing Natural Immunity Article states:

"Our results support a period of natural immunity that is, on average, long-lasting (at least 30 years)…
a range of durations of naturally acquired immunity is consistent with the pre-vaccine and vaccine era data. 0(d)ii.aIf repeat infections are as infectious as primary infections with no immune-boosting then this range is 60–100 years, if they are half as infectious or 50% lead to immune-boosting infections, then this range is 30–80 years."

Based upon this excerpt in combination with all of the following:

- the evidence in paragraph 7.3(a)ii that the "cocooning" strategy has been found to be ineffective, and
- the evidence in paragraph 7.3(c) that vaccination suppresses immunity to the important ACT pertussis toxin and increases susceptibility to infection with PRN-deficient pertussis strains which are more common than others, and

- the statement in the Althouse Pertussis Article included in paragraph 7.3(c)(2) herein (under the heading “Missed asymptomatic infection in vaccinated”) that the results of the described study “*demonstrate no changes in transmission due to vaccination*”, and
- the evidence in paragraphs 7.3(d)i.a and 7.3(d)ii.a and the tables headed “Pertussis HOSPITALIZATIONS - totals and averages, approximated” and “Pertussis DEATHS - totals, averages and estimates” in paragraph 7.3(e), that pertussis SRUs in children over 1 year of age are minimal and substantially lower than in young infants, and
- the evidence in paragraph 7.3(c)(3) that whatever immunity is provided by pertussis vaccination is lost well within a significantly shorter period than 30 years,

it reasonably follows that the most effective and reliable way to protect young infants in the community from contracting pertussis is for individuals to be exposed to pertussis and develop natural immunity at a time in childhood when they are not in contact with young infants. After recovery from that infection they can expect to have decades-long protection which, when they become parents themselves, will protect their own young infants.

(g) Some other factors affecting susceptibility

Relevant to those other factors, the Crowcroft Nutrition Protection Article states:

> *“When coverage is high and a greater proportion of infections occur in older children with good nutritional status, many infections may be mild or subclinical.”*

Unless the authors of the Crowcroft Nutrition Protection Article considered that the nutritional status only makes a difference when in combination with vaccination, the statement may be judged to imply that good nutritional status is a significant factor for causing infections to be “*mild or subclinical*”.

The Hutchins Pertussis Article also cites related potential protective factors:

> *“Improvements in socioeconomic conditions, in supportive care, and the discovery and use of antimicrobials may have contributed to proportionately greater decreases in pertussis-related mortality as compared to morbidity.”*

Similarly, Stewart DPT Risk Comparison Article states, importantly,

> *“(pertussis) outbreaks and severe cases requiring admission to hospital were concentrated consistently in a few areas of deprivation”.*

(h) Summary of Pertussis

The following statements and calculation results are referenced herein, in relation to the expected outcome for unvaccinated vaccine-eligible children:

- the Cherry Pertussis ACT Article states that (unlike the vaccinated) those unvaccinated who were observed to contract either *Bordetella pertussis* or *Bordetella parapertussis* "*had a vigorous antibody response*" to the "*important*" toxin ACT, which is produced by *Bordetella pertussis (and Bordetella parapertussis),* and
- the CDC Meeting Report on Pertussis Resurgence states that the unvaccinated have a lower risk than the vaccinated of being infected with the PRN-deficient *Bordetella pertussis* strains, whose increased circulation is thought to be due to vaccine-driven selection, and
- the statement by Althouse Pertussis Article that vaccination does not prevent infection or transmission, and refers to good nutritional status as effective for protecting against severe disease, and
- the Wearing Pertussis Article statement that natural immunity "*is, on average, long-lasting (at least 30 years)*" and that it could last up to "*100 years*". These statements are perhaps of most significance when viewed in combination with the NZ Pertussis Review's statement that:

  > *"Current strategies remain primarily focused on preventing severe disease in young infants."*

  and the Cherry Pertussis LEP Article's statement that:

  > *"adults …are the reservoir for the continued circulation of B pertussis and the source of infections in young infants."*

The following statements and calculation results are referenced herein, in relation to the expected outcome for vaccinated children:

- the Cherry Pertussis ACT Article statement that unlike in the unvaccinated, the antibody response of (DTP and) DTaP-vaccinated infected persons to ACT is "blunted", and
- the CDC Meeting Report on Pertussis Resurgence states that the vaccinated have a higher risk than the unvaccinated of being infected with the PRN-deficient *Bordetella pertussis* strains, whose increased circulation is thought to be due to vaccine-driven selection, and

- the statement by CDC Pertussis Case Definition Web Page statement "*waning immunity from acellular pertussis vaccines*" is seen as potentially, in part, responsible for the "*resurgence*" of pertussis and the finding by the Turkish Pertussis Study of a "*rapid decrease in the anti-pertussis titers*" to reach only "*52.7*"% in "*1.5-3-year-old children*" and "*28.1%*" in "*the four to five year old age group*" "*all vaccinated against pertussis with a primary course and one booster*".

- the Althouse Pertussis Article statement that vaccination is likely to increase the risk of transmission due to:

  "the presence of vaccine-induced … asymptomatic individuals", in whom *"the duration of higher bacterial loads may be longer"* and who *"may not alter their behavior and thus contact more individuals than a symptomatic individual".*

Based upon the calculation results in paragraph 7.3(e), the maximum increased total risk (if there is an increase in risk) over the 6 month to 19 year age range that can be estimated to result from non-receipt of pertussis vaccination totals less than about **1 in 2,300,000** for death and less than about **1 in 10,000** for hospitalization over the entire period in which an average US resident is aged 6 months to 19 years.

In addition, there are concerns that pertussis vaccination may increase susceptibility to PRN-deficient *Bordetella pertussis* strains and/or interfere with the development of natural immunity to the ACT pertussis toxin, resulting in future increased susceptibility to pertussis. That includes in adults who are described as "*the reservoir for the continued circulation of B pertussis and the source of infections in young infants*."

7.4 Poliomyelitis ("Polio")

(a) Polio Disease notification rate (DRP)

The Plaintiff hereby requests that the Court take judicial notice of the following documents:

- the CDC "Pink Book" Polio chapter, accessible at https://www.cdc.gov/vaccines/pubs/pinkbook/polio.html online or https://www.cdc.gov/vaccines/pubs/pinkbook/downloads/polio.pdf (pdf) (hereafter "CDC Pink Book Polio Chapter")

  A true and correct copy of the aforesaid report is attached hereto as **Exhibit 113**.

- the CDC web page entitled "Our Progress Against Polio", accessible at https://www.cdc.gov/polio/progress/index.htm (hereafter "CDC Progress Against Polio Web Page")

  A true and correct copy of the aforesaid report is attached hereto as **Exhibit 114**.

- the following CDC report:

  Greene SA, Ahmed J, Datta SD, et al. Progress Toward Polio Eradication — Worldwide, January 2017–March 2019. MMWR 2019 (May 24);68:458–462. DOI: http://dx.doi.org/10.15585/mmwr.mm6820a3external icon , accessible at https://www.cdc.gov/mmwr/volumes/68/wr/mm6820a3.htm (html) or https://www.cdc.gov/mmwr/volumes/68/wr/pdfs/mm6820a3-H.pdf (pdf) (hereafter "CDC Progress Toward Polio Eradication Report")

  A true and correct copy of the aforesaid report is attached hereto as **Exhibit 115**.

- the CDC web page, entitled "World Polio Day 2019" (which states "*page last reviewed: October 24, 2019*"), accessible at https://www.cdc.gov/globalhealth/immunization/wpd/index.html (hereafter "CDC World Polio Day 2019 Web Page")

  A true and correct copy of the aforesaid report is attached hereto as **Exhibit 116**.

- the CDC web page, entitled "Global Certification of Eradication of Indigenous Wild Poliovirus Type 3" ("page last reviewed: October 24, 2019"), accessible

at https://www.cdc.gov/globalhealth/immunization/stories/global-certification-of-eradication-of-indigenous-wild-poliovirus-type-3.html
(hereafter "CDC Poliovirus Types 2 and 3 Eradication Web Page")
(last accessed July 22, 2020)

A true and correct copy of the aforesaid report is attached hereto as **Exhibit 117**.

i. In the US, no polio transmission reported since 1979

The CDC Pink Book Polio Chapter states:

> *"Transmission of wild poliovirus was interrupted in the United States in 1979 or possibly earlier."*

Based upon the Whole Population Table, during the years 1980 through 2018, 10,824,027,856 US resident person years have transpired, resulting in an annual incidence of polio of less than 1 in 10.8 billion.

Hence even if an average of only 5% of the entire population over the past 40 years, including adults, were unvaccinated, that would still be over 500 million unvaccinated person years having transpired since 1979, all without any transmission of polio.

That has also been in the face of all of the entries into the United States during the past 40 years by residents of foreign countries, still without leading to any reports of transmission of polio in the entire country.

ii. Globally, 99.9% fewer reported cases since 1988 and limited to 2 countries

Further, the CDC Progress Against Polio Page states:

> *"The number of worldwide polio cases has fallen from an estimated 350,000 in 1988 to 407 in 2013—a decline of more than 99% in reported cases."*

The CDC World Polio Day 2019 Web Page states:

> *"In 2019, we will celebrate …the 25th anniversary of the polio-free status of the Region of the Americas and the Global Certification Commission's certification of the eradication of type 3 wild poliovirus (WPV3)."*

The CDC Progress Toward Polio Eradication Report states:

"Since the Global Polio Eradication Initiative (GPEI) began in 1988, transmission of wild poliovirus (WPV) has been interrupted in all countries except Afghanistan, Nigeria, and Pakistan. WPV type 2 (WPV2) was declared eradicated in 2015; WPV type 3 has not been detected since 2012 (1). …Nigeria last reported WPV type 1 (WPV1) cases in 2016. …Afghanistan and Pakistan reported their lowest annual number of WPV cases (22) in 2017; …33 WPV1 cases were reported in 2018. During January–March 2019 (as of May 3), 12 WPV1 cases had been reported worldwide."

and

"the number of countries with endemic poliovirus transmission (has been) three since 2012 and the number of WPV cases …fewer than 100 every year since 2015".

The CDC World Polio Day 2019 Web Page states:

"Afghanistan and Pakistan …as of October 24, 2019" are *"the two-remaining polio-endemic countries".*

The CDC Poliovirus Types 2 and 3 Eradication Web Page states:

"…wild poliovirus type-3 (WPV3) has been eradicated worldwide… the genetic diversity of the wild poliovirus present in the world has dwindled to only one remaining type [wild polio virus type-1 (WPV 1)] and still circulates in only two countries (Afghanistan and Pakistan).

…Wild poliovirus type 2 (WPV2) was last detected in Aligarh, Northern India in 1999. … The last case of WPV3 was detected in Yobe, Nigeria on November 10, 2012."

Based upon these statements,

- by the time the Global Polio Eradication Initiative (GPEI) began in 1988, there were still as many as 350,000 polio cases worldwide, some of which cases occurred elsewhere in the Americas, and that was already 9 or more years after the last transmission of wild poliovirus in the United States.

  During those 9 years, according to the Whole Population Table, at least approximately 2 billion person years transpired, or more than 100 million

unvaccinated person years (if the vaccination coverage of the whole population was less than 95%).

Yet none of those cases elsewhere in the world led to a single reported case of polio transmission in any unvaccinated person in the United States during those 9 years, and

- since 1988, the global incidence of polio has fallen by 99.9% to less than 100 wild polio cases annually, with those few cases limited to only two distant countries, Afghanistan and Pakistan.

  Hence, to whatever extent in 1988 a risk could reasonably be said to have still remained that an importation from overseas could lead to polio transmission to an unvaccinated person in the United States, that risk has since declined to more than 1,000 times lower, and

- of the three wild polio virus types targeted by vaccination, i.e. type 1, type 2 and type 3, only type 1 has not been declared "*eradicated worldwide*", with the last case of type 2 having been detected 21 years ago, in "*1999*" in "*India*", and the last case of type-3 having been detected 8 years ago, in "*2012*" in "*Nigeria*".

(b) Polio Vaccination Coverage (VC)

Assumption for timing of vaccinations

According to the tables (or "*figure"*s) in all of the CDC Schedules, the routine schedule of CDC-recommended vaccinations targeting polio has been as follows in the US for US Residents aged under 20 years, since at least as early as 2006 to the present:

"Recommended … immunization schedule, by vaccine and age — United States"

Vaccine / *Age*	*Poliovirus*
2 months	*IPV* (first dose)
4 months	*IPV* (second dose)
6 months	*IPV (*third dose)
15 months	
18 months	
4–6 years	*IPV* (fourth dose)

Except where stated otherwise, the analyses in this Notice are based on the assumption that in the case of each vaccination dose that is the subject of any coverage figure stated herein, all, or virtually all, of the "covered" children have received the dose approximately in accordance with the above schedule.

More narrowly, the third and fourth polio vaccine doses will respectively be assumed to be given when the ages of 6 months and 5 years are reached.

i. Coverage in 6 month – 11 month olds (two doses)

According to the CDC Schedules, the CDC recommended administration of polio vaccination in the US at 2 and 4 months of age in 2007-2018.

It shall be assumed herein that the vaccination coverage for three polio vaccine doses in 6-11 month old infants in 2006-2018 has been approximately the same as the coverage for three DTaP vaccine doses, which is taken herein to be less than approximately 86% (see paragraph 7.1(b)i).

Hence it shall be assumed herein that for the whole 2007-2019 period overall:

- the coverage for two polio vaccine doses in 6 – 11 month olds was less than approximately 86%.

ii. Coverage in 1 – 6 year olds (third and fourth doses)

a. Coverage in 1 to 4 year olds (three doses)

According to the CDC Schedules, the CDC recommended a third polio vaccine dose in the US at 6 to 18 months of age in 2006-2018.

The CDC Daycare Coverage Reports provide estimated vaccination coverages overall (averages or medians) for polio-containing vaccines in 19-35 month olds in the US as set out in italics in the table below:

Polio Vaccine Coverage % (Daycare)

Year	≥3 doses (average)		Comment
	%	(95% CI)	
2006	*92.8*	*(±0.6)*	
2007	*92.6*	*(±0.7)*	
2008	*93.6*	*(±0.6)*	
2009	*92.8*	*(±0.7)*	
2010	*93.3*	*(±0.7)*	
2011	*93.9*	*(±0.6)*	
2012	*92.8*	*(±0.7)†*	
2013	*92.7*	*(91.6–93.6)*	
2014	*93.3*	*(92.5–94.1)*	
2015	*93.7*	*(93.0–94.3)*	
2016	*91.9*	*(90.9–92.9)*	
2017	*92.7*	*(91.9–93.5)*	
2018	92.7	(91.9–93.5)	Coverage in 2018 is assumed herein to approximate that in 2017
Average	93.0		

Based upon the figures in the table, the average vaccination coverage in 1 – 4 year olds in 2007-2018 was approximately 93.0%.

b. Coverage in 5 - 6 year olds (fourth dose)

The CDC Elementary School Coverage Reports provide estimated vaccination coverages overall (some averages, others medians) for polio-containing vaccines in US kindergarteners (and, up to the 2002-2003 school year inclusive, first graders[5]), which are listed (in italics) in the following table, hereafter “CDC Elementary School Polio Vaccination Coverage Table”:

Polio Vaccine Coverage % (Elementary School)

School Year [5]	Polio Vaccine (IPV) Coverage % (average/median)
1997-1998	*96.7*
1998-1999	97.0 [6]
1999-2000	*97.3*
2000-2001	96.93 [6]
2001-2002	96.57 [6]
2002-2003	*95.2*
2003-2004	*95.6*
2004-2005	95.7 [6]
2005-2006	*95.7*
2006-2007	*95.7*
2007-2008	95.7 [6]
2008-2009	95.7 [6]
2009-2010	*95.65*
2010-2011	95.78 [6]
2011-2012	*95.9*
2012-2013	95.9
2013-2014	95.9
2014-2015	95.9
2015-2016	95.9
2016-2017	95.9
2017-2018	95.9
2018-2019	95.9

After the 2011-2012 year, vaccination coverage survey data published by the CDC for school entry age children has not included figures for polio, but it will be assumed herein that the average coverage in 5 year olds remained at about the same as in the 2011-2012 year, which was reported to approximate 95.9%.

Based upon the CDC Schedule tables for the years 2006 to 2018 showing a fourth polio vaccine dose scheduled at "*Age*" "*4-6 years*", an assumption shall be made in the relevant DRU calculation for polio that the above estimates of average/median coverage rate applied to administration of a polio vaccination dose at about 5 years of age.

Based upon those assumptions and upon the data in the above table, the average or median coverage in 2007-2018, for a dose of polio-containing vaccination at about 5 years of age approximated:

- 95.8% in 5-6 year olds, whose estimated coverage in kindergarten or first grade[5] was reported in the CDC Elementary School Coverage Reports for 2006-2007 through 2018-2019.

Combining the above estimated coverage rate for 1-4 year olds (93%) with that for 5-6 year olds (95.8%), results in a weighted average rate of:

- 95.1% for 1 to 6 year olds.

iii. Coverage in 7 to 19 year olds (three doses)

Based upon the figures in the CDC Elementary School Polio Vaccination Coverage Table, the average polio vaccination coverage in 7 – 19 year olds in 2010-2018 (whose vaccination statuses had been surveyed for the CDC Elementary School Coverage Reports in 1997 through 2018) was approximately 96.1%.

Based upon that coverage level for 7-19 year olds in 2010-2018, it shall be assumed in the calculation herein of SRIU for polio that the average polio vaccination coverage for the entire US resident population in the 1980 to 2018 period was no higher than about 96.1%.

(c) Polio Vaccination Efficacy (VE)

The Plaintiff hereby requests that the Court take judicial notice of the following medical journal articles:

- the CDC web page, entitled “Polio Vaccine Effectiveness and Duration of Protection”, accessible at
  https://www.cdc.gov/vaccines/vpd/polio/hcp/effectiveness-duration-protection.html
  (last accessed October 21, 2020)
  (hereafter “CDC Polio Vaccine Effectiveness Duration Web Page”)

  A true and correct copy of the aforesaid report is attached hereto as **Exhibit 118**, and

- entitled “Persistence of antibodies at 5-6 years of age for children who had received a primary series vaccination with a pentavalent whole--cell pertussis

vaccine and a first booster with a pentavalent acellular pertussis vaccine: immunogenicity and tolerance of second booster with a tetravalent acellular vaccine at 5-6 years of age."
Citation: Langue J, Matisse N, Pacoret P, Undreiner F, Boisnard F, Soubeyrand B; Pentavac study group. Vaccine. 2004 Mar 29;22(11--12):1406--14, accessible at https://pubmed.ncbi.nlm.nih.gov/15063563/

(hereafter "Langue Study")

(last accessed September 15, 2020)

A true and correct copy of the aforesaid document is attached hereto as **Exhibit 119**, and

- entitled "Antibody persistence in five-year-old children who received a pentavalent combination vaccine in infancy."

  Citation: Carlsson R-M, Claesson BA, Fagerlund E, Knutsson N, Lundin C. The Pediatric Infectious Disease Journal: June 2002 - Volume 21 - Issue 6 - p 535-541, accessible at https://journals.lww.com/pidj/Abstract/2002/06000/Antibody_persistence_in_five_year_old_children_who.11.aspx

  (hereafter "Carlsson Study")

  (last accessed September 15, 2020)

  A true and correct copy of the aforesaid document is attached hereto as **Exhibit 120**.

Based upon the statements on the CDC Poliovirus Types 2 and 3 Eradication Web Page that polio virus types 2 and 3 have been "*eradicated*", it shall be taken that the relevant vaccine-induced immunity is to only polio virus type 1.

The CDC Polio Vaccine Effectiveness Duration Web Page states:

"It is not known how long people who received IPV will be immune to poliovirus".

The Langue Study states:

"The main objective of this study was to assess in 5–6-year-old French children (n = 162) the persistence of antibodies induced by a primary series vaccination (at 2–4 months of age) with a …combined vaccine (DTwcP-IPV-Hib; Pentacoq®) and a first booster (at 12–16 months of age) with a …combined vaccine (DTacP-IPV-Hib; Pentavac®)."

and

"Abbreviations: … IPV, inactivated polio vaccine"

and

"Antibodies against poliovirus types 1–3 were analysed …Results were expressed as reciprocal dilution (1/dil), with reference to a WHO standard, and a lower limit of detection of 5 (1/dil)."

and

"Table 1. Immune response to vaccine antigens after first booster (at 14–16 month of age) of Pentavac® and before/after second booster (at 5–6 years of age) of Tetravac® in children having received a 3-dose primary series with Pentacoq®"

and a table containing the following heading and selected row:

Vaccine antigens	*Criteria for evaluation*	*First booster 14–16 months DTacP-IPV-Hib Pentavac®*	*Second booster 5–6 years DTacP-IPV Tetravac®*	
		Post-booster vaccination	*Pre-booster vaccination*	*Post-booster vaccination*
Polio 1 (SN-1/dil)	*% ≥ 5*	*99*	*94*	*100*

Based upon these statements and table, the Langue study found the percentage of children who met the criteria of the lower limit of detection of 5 (1/dil) for seroprotection against polio after the third dose of inactivated polio vaccine 99% initially, and 94% about 4 to 5 years later.

Those findings fit mathematically with an initial seropositivity rate after the primary 3-dose course of approximately 98.6% at about 18 months of age, and Waning Exponent of 1.35, resulting in seroprotection rates of 95.4% and 93.9% at 5.5 and 6.5 years of age respectively prior to the booster at that age.

With respect to the trend in seroprotection rate after the fourth dose, the Carlsson Study states:

> *"We found …no clinically relevant differences in antibody concentrations demonstrated between children vaccinated according to a three dose or a four dose schedule in infancy."*

Based upon that statement in the Carlsson Study, it is inferred that the initial seroprotection rate and Waning Exponent are similar after the fourth polio vaccination dose recommended at 4-6 years of age to those after the third dose

recommended at 6 to 18 months of age, i.e. an initial seroprotection rate of 98.6% at about 5.5 years of age, and Waning Exponent of 1.35.

It is also assumed that the same seroprotection rate of about 98.6% applies, on average, to infants between about 6 and 11 months of age (inclusive).

Based upon that inference and assumption, the average vaccine-induced polio seroprotection rate is:

- about 98.6% between 6 and 11 months of age, and
- about 97.9% between 1 and 6 years of age ("VE-19"), and
- about 78.7% between 7 and 19 years of age ("VE-19"), and
- on average, less than 27% between 6 months and any age 65 years and above ("VE-life"), falling to 0.0% by about 30 years of age.

(d) Serious outcome Rate per Disease case (SRD)

In this Notice, polio disease-associated SAEs are defined as including flaccid paralysis and death.

i. **SRD (flaccid paralysis)**

If, in spite of all of the above countering factors, a case of polio transmission were to occur in an unvaccinated child, the CDC Pink Book Polio Chapter states:

"Up to 72% of all polio infections in children are asymptomatic."

and

"Approximately 24% of polio infections in children consist of a minor, nonspecific illness without clinical or laboratory evidence of central nervous system invasion. This clinical presentation …is characterized by complete recovery in less than a week."

and

"In 1%–5% of polio infections in children" "nonparalytic aseptic meningitis (symptoms of stiffness of the neck, back, and/or legs), usually following several days after a prodrome similar to that of minor illness, occurs." and *"Typically these symptoms will last from 2 to 10 days, followed by complete recovery."*

The CDC Pink Book Polio Chapter states:

"Fewer than 1% of all polio infections in children result in flaccid paralysis."

The CDC Pink Book Polio Chapter further states:

"Many persons with paralytic poliomyelitis recover completely and, in most, muscle function returns to some degree."

ii. **SRD (death)**

The CDC Pink Book Polio Chapter states:

"The death-to-case ratio for paralytic polio is generally 2%–5% among children".

(e) Differential Risk of unavoidable serious adverse effect (SRIU)

Based upon the calculated estimates presented in this paragraph 7.4, "Polio" for

(a) the disease notification rate in the population (DRP), and

(b) the vaccination coverage (VC), and

(c) the vaccination effectiveness (VE), and

(d) the rate of serious adverse effects per disease case (SRD),

the approximate differential rates for disease (DRIU) and ultimately serious adverse effects (SRIU) can be calculated by applying the formulas set out in paragraph 6.1, with the results set out in the table below for each age group.

Polio totals and averages (approx.)

Age Group	6 – 11 mths	1 - 6 yrs	7-10 yrs	11-19 yrs	> 20 yrs
DRP (annual) [11]	< 1 / 54,623, 333,444	< 1 / 120,763, 452,783	< 1 / 104,626,679,310		~ 1 / 8,415, 908,597
VC	~ 86%	~ 95.1%	< 96.1%		
VE (residual)	< 98.6%	< 97.9%	< 95.8%	< 71.1%	< 1.4%
DRU (annual) [8]	< 1 / 8,304,931,617				
DRIU (annual)	< 1 / 8,422, 851,538	< 1 / 8,481, 876,235	< 1 / 8,665, 582,442	< 1 / 11,687, 104,845	< 1 / 604,989, 415,150
DRIU total over age range	< 1 / 16,845, 703,077	< 1 / 1,413, 646,039	< 1 / 2,166, 395,610	< 1 / 1,298, 567,205	< 1 / 13,444, 209,226
SRIU total over age range (flaccid paralysis) (= DRIU x 1%)	< 1 / 1,684,570, 307,662	< 1 / 141,364, 603,917	< 1 / 216,639, 561,049	< 1 / 129,856, 720,502	< 1 / 1,344,420, 922,555
SRIU (death) total over age range (= SRIU (flaccid paralysis) x 5%)	< 1 / 33,691,406 ,153,245	< 1 / 2,827,292, 078,345	< 1 / 4,332,791, 220,988	< 1 / 2,597,134, 410,045	< 1 / 26,888,418, 451,106

(f) Impact of vaccination on others' susceptibility

The Plaintiff hereby requests that the Court take judicial notice of the following the following document:

- CDC page headed "Polio Disease and Poliovirus", accessible at https://www.cdc.gov/cpr/polioviruscontainment/diseaseandvirus.htm (hereafter "CDC Polio Containment Web Page")

  A true and correct copy of the aforesaid report is attached hereto as **Exhibit 121**.

According to the CDC Polio Containment Web Page,

[11] The DRP of < 1 in 10,824,027,856 overall for the US Resident population is apportioned to each age group such that, after VC and VE are taken into account, the estimated DRU is the same for each age group.

"IPV does not stop transmission of the virus."

Hence IPV vaccination coverage of the community is not what is protecting any unvaccinated individuals from contracting polio.

(g) Some other factors affecting susceptibility

The Plaintiff hereby requests that the Court take judicial notice of the following the following documents:

- article entitled "Notes from the Field: Outbreak of Poliomyelitis — Somalia and Kenya, May 2013".

  Citation: World Health Organization. National Center for Emerging and Zoonotic Infectious Diseases; National Center for Immunization and Respiratory Diseases; CDC. Corresponding contributors: Derek Ehrhardt, Nina Marano. CDC MMWR 2013 (June 14);62(23):484-484, accessible at https://www.cdc.gov/mmwr/preview/mmwrhtml/mm6223a7.htm (html) or https://www.cdc.gov/mmwr/pdf/wk/mm6223.pdf (pdf)
  (hereafter "CDC Report of Polio Outbreak in Somalia and Kenya")

  A true and correct copy of the aforesaid report is attached hereto as **Exhibit 122**.

- article entitled "Impact of Public Health Interventions on Drinking Water–Associated Outbreaks of Hepatitis A — United States, 1971–2017".

  Citation: Barrett CE, Pape BJ, Benedict KM, et al. CDC MMWR 2019;68:766–770, accessible at https://www.cdc.gov/mmwr/volumes/68/wr/mm6835a4.htm (html) or https://www.cdc.gov/mmwr/volumes/68/wr/pdfs/mm6835a4-H.pdf (pdf)
  (hereafter "CDC Drinking Water Regulations Improvement Report")

  A true and correct copy of the aforesaid report is attached hereto as **Exhibit 123**.

Personal hygiene and water treatment

If polio were to be transmitted to a person in the United States, then, in relation to the circumstances necessary for forward transmission, the CDC Report of Polio Outbreak in Somalia and Kenya states that rather than the virus being spread through the uncontrollable medium of the air,

"Poliovirus is spread person-to-person through fecal-oral contact and through contaminated water".

Hence forward transmission would require lack of personal hygiene or inadequate control by government of the drinking water.

If it could be reasonably judged that government drinking water regulations remained lacking in the period between 1979 to 1988, despite no polio transmission occurring during that time, the CDC Drinking Water Regulations Improvement Report refers to government drinking water regulation improvements that have since then been implemented, which it referenced as:

"[†] USEPA's 1989 Total Coliform Rule and Surface Water Treatment Rule, 2013 Revised Total Coliform Rule, and 2006 Ground Water Rule provide regulations for public ground water systems at risk for contamination."

7.5 Measles, Mumps and Rubella ("MMR")

The CDC Schedules state that the recommendation for measles-mumps-rubella vaccination in the US was in 2008-2018:

*" * 2-dose series at 12–15 months, 4–6 years"*

Based upon this stated schedule and availability of published notification rates, the lower limit of the age range that is the subject of the analyses for these vaccine-targeted diseases is 16 months. The upper limit is chosen to be 19 years, i.e. up to the time of reaching 20 years.

(a) MMR Disease notification rate (DRP)

i. Measles

The Plaintiff hereby requests that the Court take judicial notice of the following document:

- the CDC Morbidity and Mortality Weekly Report entitled "National Update on Measles Cases and Outbreaks — United States, January 1–October 1, 2019", located at https://www.cdc.gov/mmwr/volumes/68/wr/pdfs/mm6840e2-H.pdf (last accessed November 16, 2020) (hereafter "CDC Measles Cases to Oct 2019 Article")

  A true and correct copy of the aforesaid report is attached hereto as **Exhibit 124**, and

- the CDC web page headed "Measles Cases and Outbreaks", located at https://www.cdc.gov/measles/cases-outbreaks.html (last accessed November 16, 2020) (hereafter "CDC Measles Cases - 2019 Total Web Page")

  A true and correct copy of the aforesaid report is attached hereto as **Exhibit 125**.

The CDC Disease Notifications state that the number of indigenous measles cases reported in 2008-2018 for US residents have been as set out in *italics* in the following table for the given age groups:

Measles indigenous notifications 2008 – 2018

Age group (years) / Year	1 - 4	5 - 14	15 - 24
2008	*29*	*44*	*12*
2009	*18*	*12*	*7*
2010	*6*	*3*	*0*
2011	*36*	*22*	*19*
2012	*6*	*14*	*2*
2013	*34*	*37*	*27*
2014	*90*	*146*	*142*
2015	*19*	*23*	*29*
2016	*7*	*8*	*15*
2017	*55*	*18*	*7*
2018	*96*	*72*	*40*
Total for 2008 – 2018	396	399	300

The CDC Disease Notifications also states that the total number of measles cases reported in 2007 for the "1-4", "5-14" and "15-24" year age groups, which included both indigenous and imported cases, were: "*4*", "*3*" and "*13*" respectively. Because the CDC Disease Notifications does not provide any breakdown for the 2007 year as to which cases were imported and which were indigenous, the most generous assumption is made herein that all of those cases were indigenous.

The CDC Measles Cases to Oct 2019 Article includes a table headed "*TABLE. Number… of measles cases, by age group — United States, January 1–October 1, 2019*", which contains the following selected rows and columns:

Age group	***Measles cases no. (%)***
0–5 mos	*43 (3)*
6–11 mos	*116 (9)*
12–15 mos	*118 (9)*
16 mos–4 yrs	*274 (22)*
5–17 yrs	*339 (27)*
18–29 yrs	*144 (12)*
30–49 yrs	*160 (13)*
≥50 yrs	*55 (4)*
Overall	***1,249***

Based upon the 70% (274 out of 392) of the measles cases in 1-4 year olds stated in the above table to have been reported in the 16 month – 4 year age group, it shall be assumed that the same percentage of 70% applied also to 400 measles cases in 1-4 year olds notified to the NNDSS in the 2007-2018 years. That results in a total of approximately 280 cases in the 16 month – 4 year age group in those 12 years. Halving the 313 cases in the 15-24 year age group in 2007-2018 results in an estimate of 157 cases in 15-19 year olds. Hence the total number of cases in 16 month to 19 year olds in 2007-2018 can be estimated to have been (280 + 402 + 157 =) 839.

Based upon the 144 cases stated in the above table to have been reported in 18-29 year olds in the applicable period, and assuming that there was an approximately equal rate in each year group within that range, it is estimated that approximately 24 of those cases occurred in 18-19 year old subset. Adding that 24 to the (274+339 =) 613 total cases in 16 month to 17 year olds results in a total of 637 cases in 16 month to 19 year olds in the Jan 1 to Oct 1 2019 period.

The CDC Measles Cases to Oct 2019 Article further states:

> *"During January 1–October 1, 2019, a total of 1,249 measles cases were reported in 31 states and New York City,† including 1,211 (97%) among U.S. residents… 13% were infants aged <12 months (not routinely recommended to receive MMR vaccine), 31% were children aged 1–4 years, 27% were school-aged children aged 5–17 years…(Table)… Eighty-one cases were imported from other countries§ including 52 (64%) cases in U.S. residents returning from travel abroad."*

Based upon that excerpt, of the 1249 reported cases from Jan 1 to Oct 1 2019, 1211 were in US residents, and of those in US residents, 52 were in travelling residents. That leaves 1159, or 92.8%, that were non-imported cases US residents. Applying that same percentage of 92.8% to the 637 cases in 16 month to 19 year olds results in 591 indigenous cases in 16 month to 19 year old US residents from Jan 1 to Oct 1 2019.

The CDC Measles Cases - 2019 Total Web Page states:

> *"From January 1 to December 31, 2019, 1,282* individual cases of measles were confirmed in 31 states."*

Based upon that statement, an additional (1282 – 1249 =) 33 cases, which is 2.64% of 1249, occurred from October 1 to December 31, 2019.

Hence, it can be estimated that 2.64% of the 591 indigenous cases in 16 month to 19 year old US residents from Jan 1 to Oct 1 2019 can be added to that 591 figure to get the total for 2019 in 16 month to 19 year old US residents, which is (591 + 16 =) 607 cases.

Adding that estimated 607 cases in 2019 to the total of 839 for 2007-2018 results in a total of approximately 1446 total non-imported cases in 16 month to 19 year old US residents in 2007-2019.

That results in an average annual number of indigenous measles cases in 2007-2019 in 16 month to 19 year olds of approximately **111**.

In view of the fact that the CDC Measles Cases to Oct 2019 Article also states that of all cases only "*84%... were laboratory-confirmed*", the average number of confirmed cases in 16 month to 19 year olds in 2007-2020 might be estimated to be only about 80% of the above estimated average of 111, but the latter adjustment is not incorporated in the figures presented in this Notice.

a. Underreporting of measles cases

The Plaintiff hereby requests that the Court take judicial notice of the following documents:

- article entitled: "Completeness of Measles Case Reporting: Review of Estimates for the United States"

  Citation: Rafael Harpaz. The Journal of Infectious Diseases, Volume 189, Issue Supplement_1, May 2004, Pages S185–S190, https://doi.org/10.1086/378501, located at https://academic.oup.com/jid/article-pdf/189/Supplement_1/S185/28479148/189-supplement_1-s185.pdf (last accessed February 13, 2021)
  (hereafter "Measles Reporting Completeness Article")

  A true and correct copy of the aforesaid report is attached hereto as **Exhibit 126**

- the CDC web page headed "Measles / Rubeola 2013 Case Definition", located at

https://wwwn.cdc.gov/nndss/conditions/measles/case-definition/2013/
(last accessed February 13, 2021)
(hereafter "Measles Case Definition Web Page")

A true and correct copy of the aforesaid report is attached hereto as **Exhibit 127**.

- article abstract entitled: "Mild measles and secondary vaccine failure during a sustained outbreak in a highly vaccinated population"

  Citation: Edmonson MB, Addiss DG, McPherson JT, Berg JL, Circo SR, Davis JP. JAMA. 1990 May 9;263(18):2467-71. PMID: 2278542., located at https://pubmed.ncbi.nlm.nih.gov/2278542/
  (last accessed February 13, 2020)
  (hereafter "Measles Underreporting in the Vaccinated Abstract")

  A true and correct copy of the aforesaid report is attached hereto as **Exhibit 128.**

The Measles Reporting Completeness Article states:

> *"The portion of total (incident) measles cases that is reported to health departments is termed "completeness of reporting." Few studies describe this measure of the quality of surveillance in the United States; these studies use different methods, but they are all limited because the actual number of measles cases needed to derive completeness of reporting could not be determined. Estimates of completeness of reporting from the 1980s and 1990s vary widely, from 3% to 58%. One study suggests that 85% of patients with measles sought health care, the proportion of compatible illnesses for which measles was considered varied from 13% to 75%, and the proportion of suspected cases that were reported varied from 22% to 67%. Few cases were laboratory-confirmed, but all were reported. Surveillance in the United States is responsive, and its sensitivity likely increases when measles is circulating. Continued efforts to reinforce the clinical recognition and reporting of measles cases are warranted."*

Based upon this excerpt, the reporting completeness for measles cases is unknown, but estimates 1980s and 1990s have varied from 3% to 58%.

Disproportionate underreporting in the vaccinated

Specifically in relation to vaccinated persons,

- the Measles Case Definition Web Page states:

  “Confirmed

  An acute febrile rash illness with:

  - *Isolation of measles virus‡ from a clinical specimen; or*
  - *Detection of measles-virus specific nucleic acid‡ from a clinical specimen using polymerase chain reaction; or*
  - *IgG seroconversion‡ or a significant rise in measles immunoglobulin G antibody‡ using any evaluated and validated method; or*
  - *A positive serologic test for measles immunoglobulin M antibody‡§; or*
  - *Direct epidemiologic linkage to a case confirmed by one of the methods above.*

  ‡ Not explained by MMR vaccination during the previous 6-45 days."

  Based upon this excerpt, any measles infection that develops within 6-45 days following vaccination, whether the infection arises from vaccination or is merely coincident with vaccination, is not confirmed as measles, because the symptoms would be judged as able to be "explained by MMR vaccination during the previous 6-45 days".

  This may lead to underreporting of measles in vaccinated persons, and also indirectly their contacts because the latter would be less likely to have a “Direct epidemiologic linkage to a case confirmed by one of the methods above”.

- the Measles Underreporting in the Vaccinated Abstract states:

“A prolonged school-based outbreak of measles provided an opportunity to study "vaccine-modified" mild measles and secondary vaccine failure. Thirty-six (97%) of 37 unvaccinated patients had rash illnesses that met the Centers for Disease Control clinical case definition of measles, but 29 (15%) of 198 vaccinated patients did not, primarily because of low-grade or absent fever. Of 122 patients with seroconfirmed measles, 10 patients (all previously vaccinated) had no detectable measles-specific IgM and significantly milder illness than either vaccinated or unvaccinated patients with IgM-positive serum. Of 108 vaccinated patients with seroconfirmed measles, 17 patients (16%) had IgM-negative serology or rash illnesses that failed to meet the clinical case definition; their mean age (13 years), age at the time of vaccination, and time since vaccination did not differ from those of other vaccinated patients. The occurrence of secondary vaccine failure and vaccine-modified measles does not appear to be a major impediment to measles control in the United States but may lead to underreporting of measles cases and result in overestimation of vaccine efficacy in highly vaccinated populations.”

Based upon this excerpt, 15% of vaccinated patients in a measles outbreak did not meet the CDC clinical case definition of measles, primarily because they failed to mount, or at least did not mount, all of the recognizable immune system defences to measles infection, in particular fever. Hence the vaccine-induced alteration of symptoms is another reason that underreporting of measles in vaccinated persons may occur. It may also result in overestimations of vaccine effectiveness.

Based upon the excerpts from these two articles, plus a likelihood of observer bias given that has been observed in relation to pertussis (see paragraph 7.3(c)(2)) the underreporting of measles may be occurring disproportionately in the vaccinated compared to the unvaccinated, and may be leading to overestimations of vaccine effectiveness.

There is a reasonable possibility that the same principle applies additionally to other vaccine-targeted infectious diseases.

ii. Mumps

The CDC Disease Notifications state that the number of mumps cases reported in 2007-2018 for US residents have been as set out in the following table for the given age groups:

Mumps notifications 2007 – 2018

Age group (years) / Year	1 - 4	5 - 14	15 - 24
2007	4	3	13
2008	29	44	12
2009	18	12	7
2010	6	3	0
2011	36	22	19
2012	6	14	2
2013	34	37	27
2014	90	146	142
2015	19	23	29
2016	7	8	15
2018	55	18	7

Based upon the 69.9% (274 out of 392) of the measles cases in 1-4 year olds stated by CDC Measles Cases Jan 1 - Oct 1, 2019 to have occurred in the 16 month – 4 year age group, it shall be assumed that the same percentage of 69.9% applied also to mumps cases in 1-4 year olds in 2007-2018.

Based upon all of the above quoted mumps figures and assumption, the average annual number of mumps cases in 2007-2018 in 16 month to 19 year olds can be estimated to be **906**.

iii. **Rubella**

The Plaintiff hereby requests that the Court take judicial notice of the following documents:

- the CDC “Manual for the Surveillance of Vaccine-Preventable Diseases: Chapter 15: Congenital Rubella Syndrome”, accessible at: https://www.cdc.gov/vaccines/pubs/surv-manual/chpt15-crs.html online or https://www.cdc.gov/vaccines/pubs/surv-manual/chpt15-crs.pdf (pdf) (last accessed February 7, 2021) (hereafter “CDC Surveillance Manual CRS Chapter”)

A true and correct copy of the CDC Surveillance Manual CRS Chapter is attached hereto as **Exhibit 129**.

Rubella Notifications

The CDC Disease Notifications state that the number of rubella cases reported in 2007-2018 for US residents have been as set out in the following table for the given age groups:

Rubella notifications 2007 – 2018

Age group (years) / Year	1 - 4	5 - 14	15 - 24
2007	1	0	5
2008	2	1	---
2009	---	0	---
2010	—	1	2
2011	—	0	1
2012	—	1	1
2013	1	1	1
2014	—	0	3
2015	—	0	2
2016	—	—	—
2018	1	—	2

Based upon the 69.9% (274 out of 392) of the measles cases in 1-4 year olds stated by CDC Measles Cases Jan 1 - Oct 1, 2019 to have occurred in the 16 month – 4 year age group, it shall be assumed that the same percentage of about 70% applied also to rubella cases in 1-4 year olds in the 2007-2018 years.

Based upon all of the above quoted rubella figures and assumption, the average annual number of rubella cases in 2007-2019 in 16 month to 19 year olds can be estimated to have been **1.3**.

Rubella and Congenital Rubella Syndrome are eliminated in the US

The Surveillance Manual CRS Chapter states:

"Congenital rubella syndrome (CRS) is an illness in infants that results from maternal infection with rubella virus during pregnancy. When rubella infection occurs during early pregnancy, serious consequences— such as miscarriages, stillbirths, and a constellation of severe birth defects in infants can result. The risk of congenital infection and defects is highest during the first 12 weeks of gestation and decreases thereafter; defects are rare after infection in the 20th week (or later) of gestation.[1–3]"

and

"In 2004, an independent panel of internationally recognized experts ... unanimously agreed that rubella elimination (i.e., the absence of year-round endemic transmission) had been achieved in the United States.[6] … The United States elimination of rubella and CRS was reconfirmed in 2011 and maintenance of elimination was reported in 2014.[9, 11] … The United States has established and achieved the goal of eliminating CRS and the indigenous transmission of rubella."

and

"During 2005–2017, the number of reported CRS cases in the United States declined dramatically to <1 case per year …Among the 15 CRS cases that occurred during this time, all but one were known importations"

Based upon the above excerpts, the probability of an indigenous transmission in the US of the disease of rubella, and especially of the chance of congenital rubella syndrome resulting, is zero to negligible.

iv. **Summary for DRP**

Based upon the above information in this paragraph 7.5(a) and the Population Tables, the approximate annual average reported incidence (annual DRP) of confirmed measles, mumps and rubella cases in the period 2007 – 2018/2019 was as set out in the table below for the 16 mo - 19 years age group:

Disease	**Measles**	**Mumps**	**Rubella**
DRP (annual)	~ 1 / 650,000	~ 1 / 83,200	~ 1 / 56,700,000

(b) MMR Vaccination Coverage (VC)

According to the CDC Schedules, in 2006-2018 the CDC recommended one dose of measles-mumps-rubella vaccination at 12-15 months of age and a second dose at 4 – 6 years.

i. Coverage in 1 – 4 year olds (first doses)

The CDC Daycare Coverage Reports provide estimated vaccination coverages overall (some averages, others medians) for measles-containing vaccines in 19-35 month olds in the US as set out in the table below:

Year	Measles-mumps-rubella Vaccine Coverage % *(average) - first dose*
2006	***92.3***
2007	***92.3***
2008	***92.1***
2009	***90.0***
2010	***91.5***
2011	***91.6***
2012	***90.8***
2013	***91.9***
2014	***91.5***
2015	***91.9***
2016	***91.1***
2017	***91.5***
2018*	***91.5***
2019*	***91.5***

Based on the data in the above table, the average coverage for the first measles-mumps-rubella vaccination dose over the period of 2007-2018/2019 is estimated to have been:

- 91.7%.in 16 month - 4 year olds.

ii. Coverage in 5 to 19 year olds (second dose)

The CDC Elementary School Coverage Reports provide estimated vaccination coverages overall (some averages, others medians) for measles-mumps-rubella-containing vaccines in kindergarteners (and, up to the 2002-2003 school year inclusive, first graders[5]), in the US as follows:

School Year [5]	Measles/mumps/rubella Vaccine Coverage % (average/median)	≥# doses
1997-1998	*96.0 / 96.5 / 96.5*	*1*
1998-1999	96.55 / 96.95 / 96.95 [6]	
1999-2000	*97.1 / 97.4 / 97.4*	*1*
2000-2001	96.63 / 96.97 / 96.97 [6]	
2001-2002	96.17 / 96.53 / 96.53 [6]	
2002-2003	*95.7 / 96.1 / 96.1*	*1*
2003-2004	*95.4 / 96.0 / 95.9*	*"up-to-date"*
2004-2005	95.4 / 95.95 / 95.9 [6]	
2005-2006	*95.4 / 95.9 / 95.9*	*"up-to-date"*
2006-2007	*95.6*	*"up-to-date"*
2007-2008	95.3 [6]	
2008-2009	95.0 [6]	
2009-2010	*94.75*	*"up-to-date"*
2010-2011	94.8 [6]	
2011-2012	*94.8*	*2*
2012-2013	*94.5*	*2*
2013-2014	*94.7*	*2*
2014-2015	*94.0*	*2*
2015-2016	*94.6*	*2*
2016-2017	*94.0*	*2*
2017-2018	*95.3*	*2*
2018-2019	*94.7*	*2*
2019-2020	94.7 [6]	2 [6]

The CDC Elementary School Coverage Reports state that the term "*up-to-date*" means that the children had "*received all of the vaccine doses required for school entry in their state or area*".

Based upon the CDC Schedule tables for the years 2006 to 2018 showing a second MMR-containing vaccine dose scheduled at "*Age*" "*4-6 years*", an assumption shall be made in the relevant DRU calculation for measles-mumps-rubella that the above estimates of average/median coverage rate applied to two doses throughout all relevant years.

A further assumption will be made that the coverages for the years 1996-1997, 1995-1996, 1994-1995 and 1993-1994 were approximately the same as those for 1997-1998.

Based upon those assumptions and the data in the above table, the average or median coverage in 2007-2018 for the second dose of measles-mumps-rubella-containing vaccination approximated:

- 94.4% / 95.5% / 95.5% for measles / mumps / rubella in 5-19 year olds.

iii. Summary for VC

Based upon the above information in this paragraph 7.5(b), the approximate annual average vaccination coverage in 2010-2018 was as set out in the table below for each subject age group:

Disease	**Measles**	**Mumps**	**Rubella**
VC (16 mos to 4 years)	91.7%		
VC (5 to 19 years)	95.4%		
VC (16 mos to 19 years)	94.7%		

(c) MMR Vaccination Efficacy (VE)

i. Measles

The Plaintiff hereby requests that the Court take judicial notice of the following documents:

- the CDC "Pink Book" Measles chapter, accessible at https://www.cdc.gov/vaccines/pubs/pinkbook/meas.html online or https://www.cdc.gov/vaccines/pubs/pinkbook/downloads/meas.pdf (pdf) (last accessed November 17, 2020)
  (hereafter "CDC Pink Book Measles Chapter")
  A true and correct copy of the aforesaid report is attached hereto as **Exhibit 130**.

- the CDC web page headed: "Measles, Mumps, and Rubella (MMR) Vaccination: What Everyone Should Know", accessible at https://www.cdc.gov/vaccines/vpd/mmr/public/index.html
  (last accessed November 17, 2020)
  (hereafter "CDC Measles Vaccine Effectiveness Web Page")
  A true and correct copy of the aforesaid report is attached hereto as **Exhibit 131**.

- article entitled "Persistence of Measles Antibodies After 2 Doses of Measles Vaccine in a Postelimination Environment",

Citation: LeBaron CW, Beeler J, Sullivan BJ, et al. Arch Pediatr Adolesc Med. 2007;161(3):294–301. doi:10.1001/archpedi.161.3.294 located at https://jamanetwork.com/journals/jamapediatrics/fullarticle/569784 (last accessed November 17, 2020)
(hereafter "Rapid Post-MMR2 Measles Titer Decline Article")
A true and correct copy of the aforesaid report is attached hereto as **Exhibit 132**.

- article entitled "Measles Antibody: Reevaluation of Protective Titers", Citation: Chen RT, Markowitz LE, Albrecht P, Stewart JA, Mofenson LM, Preblud SR, Orenstein WA. J Infect Dis. 1990 Nov;162(5):1036-42. doi: 10.1093/infdis/162.5.1036. PMID: 2230231, located at https://www.researchgate.net/profile/Lynne_Mofenson/publication/20926293_Measles_Antibody_Reevaluation_of_Protective_Titers/links/54bd88dd0cf27c8f2814ba83/Measles-Antibody-Reevaluation-of-Protective-Titers.pdf
(last accessed November 17, 2020)
(hereafter "Chen Secondary Measles Vaccine Failure Article")
A true and correct copy of the aforesaid report is attached hereto as **Exhibit 133**.

- article entitled "The Role of Secondary Vaccine Failures in Measles Outbreaks",
Citation: Mathias RG, Meekison WG, Arcand TA, Schechter MT. The role of secondary vaccine failures in measles outbreaks. Am J Public Health. 1989;79(4):475-478. doi:10.2105/ajph.79.4.475, located at https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1349980/pdf/amjph00230-0075.pdf
(last accessed November 17, 2020)
(hereafter "Matthias Secondary Vaccine Failure Article")
A true and correct copy of the aforesaid report is attached hereto as **Exhibit 134**.

The CDC Pink Book Measles Chapter states:

"Measles antibodies develop in approximately 95% of children vaccinated at 12 months of age and 98% of children vaccinated at 15 months of age. Seroconversion rates are similar for single-antigen measles vaccine, MMR, and MMRV. Approximately 2%–5% of children who receive only one dose of MMR vaccine fail to respond to it (i.e., primary vaccine failure)."

The CDC Measles Vaccine Effectiveness Web Page states:

"One dose of MMR vaccine is 93% effective against measles, 78% effective against mumps, and 97% effective against rubella.

Two doses of MMR vaccine are 97% effective against measles and 88% effective against mumps."

The Rapid Post-MMR2 Measles Titer Decline Article states:

"One month after MMR2, titers significantly increased for each study group, but beyond 6 months titers were not significantly different from pre-MMR2 levels."

The Chen Secondary Measles Vaccine Failure Article states:

"In one recent outbreak… a 5% attack rate among persons who had seroconverted after vaccination 10 years earlier was reported [23]"

The Mathias Secondary Measles Vaccine Failure Article states:

"The preexisting antibody titer results on our cohort confirm that secondary vaccine failure was important in our study population."

and

"If a significant role is established for secondary vaccine failure, this must be taken into account in the predictions of measles control programs. The assumption that measles immunity as induced by vaccine is as high as the seroconversion rate appears to be an overestimate of the true situation."

Based upon these excerpts and, for simplicity of calculation deeming the first dose to be given at 12 months of age (slightly earlier than the scheduled age rate of 15 to 18 months), the initial and waning seroprotection and protection rates from measles vaccination can be estimated to be as follows:

- initial seroprotection rate after first dose: 96%
- percentage of population who fail to respond to first dose but response to second dose ("second responders"): 3.5%

- resultant seroprotection rate after second dose (after waning seroprotection to 95.7% in first responders plus the extra 3.5% from the second responders): 99.2%
- average Waning Exponent after first dose and in second responders after second dose: > 1.02
- average Waning Exponent after second dose in first responders: > 1.1
- percentage of "seroprotected" who are protected (which may be perceived to be a measure of the avidity of the antibody-antigen binding strength): 97.35%, which is assumed herein not to significantly decline over the material period.

Based upon those parameter values, measles vaccination effectiveness can be calculated to average approximately:

- 93.34% in 1-4 year olds (or 16 month to 4 year olds)
- < 92.28% in 5-17 year olds
- < 85.47% in 18-19 year olds.

ii. Mumps

The Plaintiff hereby requests that the Court take judicial notice of the following documents:

the CDC "Pink Book" Mumps chapter, accessible at https://www.cdc.gov/vaccines/pubs/pinkbook/mumps.html online or https://www.cdc.gov/vaccines/pubs/pinkbook/downloads/mumps.pdf (pdf) (last accessed November 17, 2020)
(hereafter "CDC Pink Book Mumps Chapter")
A true and correct copy of the aforesaid report is attached hereto as **Exhibit 135**.

- article entitled "Waning immunity against mumps in vaccinated young adults, France 2013",
Citation Vygen S, Fischer A, Meurice L, Mounchetrou Njoya I, Gregoris M, Ndiaye B, Ghenassia A, Poujol I, Stahl JP, Antona D, Le Strat Y, Levy-Bruhl D, Rolland P. Euro Surveill. 2016;21(10):30156. doi: 10.2807/1560-7917.ES.2016.21.10.30156. PMID: 26987576, located at https://www.eurosurveillance.org/docserver/fulltext/eurosurveillance/21/10/eurosurv-21-30156-3.pdf

(last accessed November 17, 2020)
(hereafter “Vygen Secondary Mumps Vaccine Failure Article”)
A true and correct copy of the aforesaid report is attached hereto as **Exhibit 136**.

- article entitled “Persistence of mumps antibodies after 2 doses of measles-mumps-rubella vaccine”,
Citation: Arch Pediatr Adolesc Med. 2007;161:294-301
located at https://academic.oup.com/jid/article/199/4/552/2192152
(last accessed November 17, 2020)
(hereafter “Post-MMR2 Mumps Titer Decline Article”)
A true and correct copy of the aforesaid report is attached hereto as **Exhibit 137**.

The CDC Pink Book Mumps Chapter states:

> *“Postlicensure studies determined that one dose of mumps or MMR vaccine was 78% (49% to 92%) effective. Two dose mumps vaccine effectiveness is 88% (66% to 95%).”*

The Vygen Secondary Mumps Vaccine Failure Article states:

> *“The odds of mumps increased for twice-vaccinated individuals by 10% for every year that had passed since the second dose (aOR 1.10; 95% confidence interval (CI): 1.02-1.19; p = 0.02). Adjusting for age, sex, and cluster unit, the odds of mumps increased by 10% for every year increase in time since the second dose (aOR 1.10; 95% CI: 1.02–1.19). This odds increased by 162% (aOR 2.62; 95%CI 1.9–5.8) for 10 years since the second dose.”*

The Post-MMR2 Mumps Titer Decline Article states:

> *“The mumps antibody response to MMR2 was vigorous, but over a 12-year period titers declined to levels similar to pre-MMR2 titers.”*

Based upon these excerpts and, for simplicity of calculation deeming the first dose to be given at 12 months of age (slightly earlier than the scheduled age rate of 15 to 18 months), the initial and waning seroprotection and protection rates from mumps vaccination can be estimated to be as follows:

- initial seroprotection rate after first dose: 78%
- seroprotection rate after second dose: 88%

- average Waning Exponent after first dose: > 1.175
- average Waning Exponent after second dose: > 1.115

Based upon those parameter values, and disregarding any avidity-related deficiency, mumps vaccination effectiveness can be calculated to average approximately:

- 72.62% in 1-4 year olds (or 16 month to 4 year olds)
- < 79.42% in 5-14 year olds
- < 60.49% in 15-19 year olds.

iii. Rubella

The Plaintiff hereby requests that the Court take judicial notice of the following documents:

- the CDC "Pink Book" Rubella chapter, accessible at https://www.cdc.gov/vaccines/pubs/pinkbook/rubella.html online or https://www.cdc.gov/vaccines/pubs/pinkbook/downloads/rubella.pdf (pdf) (last accessed November 17, 2020)
  (hereafter "CDC Pink Book Rubella Chapter")
  A true and correct copy of the aforesaid report is attached hereto as **Exhibit 138**.

The CDC Pink Book Rubella Chapter states:

> *"In clinical trials, 95% or more of vaccinees aged 12 months and older developed serologic evidence of rubella immunity after a single dose. More than 90% of vaccinated persons have protection against both clinical rubella and viremia for at least 15 years."*

Based upon this excerpt, the effectiveness of the rubella vaccination over the age range of 16 months to 19 years is less than 95%.

v. **Summary for VE**

Based upon the information in this paragraph 7.5(c), the approximate annual average seroprotection rates are set out in the table below for each subject age group:

Disease	**Measles**	**Mumps**	**Rubella**
VE (16 mos to 4 years)	93.3%	72.6%	**< 95%**
VE (5 to 19 years)	91.4%	73.1%	
VE (16 mos to 19 years)	**91.8%**	**73.0%**	

(d) Serious outcome Rate per Disease case (SRD)

i. Measles

The Plaintiff hereby requests that the Court take judicial notice of the following documents:

- article entitled “Frequency of Complications of Measles, 1963”,

  Citation: Miller D. L. Br Med J 1964; 2 :75, accessible at https://www.bmj.com/content/bmj/2/5401/75.full.pdf
  (last accessed November 17, 2020)
  (hereafter “Miller Measles Article”)
  A true and correct copy of the aforesaid report is attached hereto as **Exhibit 139**.

- article entitled “Vitamin A levels and severity of measles. New York City”,

  Citation: Frieden TR, Sowell AL, Henning KJ, Huff DL, Gunn RA. Am J Dis Child. 1992 Feb;146(2):182-6. doi: 10.1001/archpedi.1992.02160140048019. PMID:1285727, accessible at https://pubmed.ncbi.nlm.nih.gov/1285727/
  (last accessed November 18, 2020)
  (hereafter “Vitamin A Halves Measles Risk Article”)
  A true and correct copy of the aforesaid report is attached hereto as **Exhibit 140**.

a. Raw SRD rate in unvaccinated

The Miller Measles Article, published in Britain in 1964, describes the complications and their frequencies from measles prior to the availability of vaccination, stating:

> *“Recent advances in the development of measles vaccines give reason to expect that an acceptable, safe, and effective means of immunization will soon become available. But "the need or desire" for large-scale vaccination in this country is subject to debate (British Medical Journal, 1963b).”*

and including a table headed “TABLE I - Composition of Sample Studied”, which states that the studied cases of measles were:

> *“notified in England and Wales from week ending 5 January to week ending 27 April (1963), inclusive”*

- **Hospitalizations**

The Miller Measles Article also includes tables headed “TABLE III.- Age and Sex Frequency of All Complications” and “TABLE V.- Age and Sex Distribution of Cases Admitted to Hospital”, which include the following selected rows and columns in *italics*:

Age	***Total No. of Cases***	***Admitted to Hospital, Reason for Admission: Complications***
1 year	*6,052*	*92*
2 years	*7,559*	*84*
3-4 years	*14,915*	*101*
5-9 “	*20,911*	*136*
10-14 “	*795*	*5*
15-19 “	*189*	*0*
Total	**50,421**	**418**

Based on the figures in the above table, the hospitalization rate per case was (418 ÷ 50,421 =) 0.83%, or approximately **1 / 120**.

- **Serious complications**

The Miller Measles Article also states:

> *“the number of cases studied in this inquiry was just over 50,000. Thus, if the results of this inquiry are generally applicable, to obtain an estimate of the number of complications occurring in the whole country during an epidemic the figures should be multiplied tenfold. This would mean that about 35,000 patients might be expected to have serious complications, and over 6,000 be admitted to hospital.”*

Based on this excerpt, and the rate of serious complications is approximately (35,000 ÷ 6,000 =) 5.83 times as frequent as hospitalizations, so based upon a hospitalization rate of 0.83%, the rate is approximately (5.83 x 0.83% =) 4.8%, or **1 / 21**.

The Miller Measles Article does not give a definition for “serious complication”, and may merely mean a severe complication that does not necessarily fit the narrower definition herein of a SAE, as stated in paragraph 2.1 herein. However it is reasonable to treat the rate of occurrence of “serious complications” as an upper limit, likely a generous one, for the value of SRD.

SSPE

The CDC Pink Book Measles Chapter states:

> *"Subacute sclerosing panencephalitis (SSPE) is a rare degenerative central nervous system disease believed to be due to persistent measles virus infection of the brain. Onset occurs… in five to ten cases per million reported measles cases…. SSPE has been extremely rare since the early 1980s."*

Based upon this excerpt, the risk of SSPE per reported measles case is less than 0.001%, or 1 in 100,000.

- **Death**

The Miller Measles Article states that:

> *"Deaths (from measles) have… declined rapidly in recent years to about 2 per 10,000 notifications, and a recent study has shown that about half the deaths occur in persons with serious chronic disease or disability."*

Based upon this excerpt ("Miller Measles Mortality Statement"), and an assumption that the proportion of the British population at that time who suffered a serious chronic disease or disability was relatively insignificant ("Serious Chronic Disease or Disability Assumption"), the risk of death from measles in an unvaccinated person not so afflicted had already fallen to only about **1 in 10,000**.

It is also notable that the article states that case fatality rate had *"declined rapidly in recent years"*. Hence it is reasonable to extrapolate that the case fatality would have continued to decline, likely also rapidly, without the introduction of vaccination, in which case it would likely, without vaccination, be zero to negligible by now, almost 60 years later.

b. Adjustment to SRD rate for healthy, well nourished children

Based upon the Miller Measles Mortality Statement and Serious Chronic Disease or Disability Assumption, it may be estimated more broadly that the average measles-associated SAE risk for those who are free of a

serious chronic disease or disability is approximately half of the average risk across the US resident population.

Further, the CDC Pink Book Measles Chapter states:

"Measles is more severe in malnourished children, particularly those with vitamin A deficiency."

and the Vitamin A Halves Measles Risk Article states:

"We… measured vitamin A levels in 89 children with measles younger than 2 years and in a reference group in New York City, NY. Vitamin A levels in children with measles ranged from 0.42 to 3.0 mumol/L; 20 (22%) were low. Children with low levels were more likely to have fever at a temperature of 40 degrees C or higher (68% vs 44%), to have fever for 7 days or more (54% vs 23%), and to be hospitalized (55% vs 30%). Children with low vitamin A levels had lower measles-specific antibody levels… seem to have lower measles-specific antibody levels and increased morbidity… Additional studies of vitamin A in measles and other infectious diseases… should be done."

Based upon these excerpts, the risk of a SAE from measles is further approximately halved for a child who does not have low Vitamin A status.

c. Resultant SRD rates for healthy, adequately nourished

Based upon all of the tables and excerpts in paragraphs 7.5(d)i a and b above, the SRD for measles for children/adolescents who suffer neither a serious chronic disease or disability nor low vitamin A status can be estimated to be as follows, incorporating for each of those two factors a reduction by 50%, the combination of which results in a reduction by 75%:

SRD		
Any SAE	**Hospitalization**	**Death**
< 1 in 83	< 1 in 482	1 in 20,000

ii. Mumps

The Plaintiff hereby requests that the Court take judicial notice of the following document:

- article entitled "Recommendations of the Immunization Practices Advisory Committee Mumps Prevention",

Citation: CDC MMWR, June 9 1989, 38(22);388-392,397-400, accessible at https://www.cdc.gov/mmwr/preview/mmwrhtml/00001404.htm (last accessed November 17, 2020) (hereafter "CDC Mumps Complication Rate Article") A true and correct copy of the aforesaid report is attached hereto as **Exhibit 141**.

- CDC web page headed "For Healthcare Providers", accessible at https://www.cdc.gov/mmwr/preview/mmwrhtml/00001404.htm (last accessed November 17, 2020) (hereafter "CDC Mumps For Healthcare Providers Web Page") A true and correct copy of the aforesaid report is attached hereto as **Exhibit 142**.

Serious complications

The CDC Mumps Complication Rate Article states:

> *"Sensorineural deafness is one of the most serious of the rare complications involving the central nervous system (CNS). It occurs with an estimated frequency of 0.5-5.0 per 100,000 reported mumps cases."*

The CDC Pink Book Mumps Chapter states:

> *"The incidence of mumps encephalitis is reported to range from 1 in 6,000 mumps cases (0.02%) to 1 in 300 mumps cases (0.3%)."*

Neither the CDC Mumps Complication Rate Article nor the CDC Pink Book Mumps Chapter state the proportion of these complications that are SAEs. However it is reasonable to treat the total rate of their occurrence as an upper limit for the total value of SRD.

Death

The CDC Mumps Complication Rate Article states:

> *"Permanent sequelae are rare, but the reported encephalitis case-fatality rate has averaged 1.4%."*

The CDC Mumps For Healthcare Providers Web Page states:

"Death from mumps is exceedingly rare. There have been no mumps-related deaths reported in the United States during recent mumps outbreaks."

Summary

Based upon those excerpts, the SRD rates for mumps are estimated to be less than:

- 1 in 20,000 (sensorineural deafness) + 1 in 300 (mumps encephalitis) = less than 1 in 296 for any SAE, and
- 1 in 300 (mumps encephalitis) x 1.4% (mumps encephalitis case-fatality rate) = less than 1 in 21,429 for death.

iii. Rubella

The only rubella complication relevant to children for which CDC Pink Book Rubella Chapter cites the frequency is:

"Hemorrhagic manifestations occur in approximately one per 3,000 cases"

This will be accordingly taken herein as the SRD for rubella.

Based upon the lack of statements in the CDC Pink Book Rubella Chapter to the contrary, the rate of hospitalization or death from rubella in the 16 month to 19 year age group is no more than negligible.

iv. Summary for SRD

Based upon the above information in this paragraph 7.5(d), the approximate annual average measles seroprotection rate is set out in the table below for each subject age group:

Disease	Measles	Mumps	Rubella
SRD - (any SAE)	< 1 in 83	< 1 in 296	< 1 in 3,000
- (hospitalization)	< 1 in 482	< 1 in 296	negligible
- (death) (case fatality rate)	< 1 in 20,000	< 1 in 21,549	negligible

(e) Differential Risk of unavoidable serious adverse effect (SRIU)

Based upon the calculated estimates presented in this paragraph 7.5, "Measles, Mumps and Rubella" for

(a) the disease notification rate in the population (DRP), and

(b) the vaccination coverage (VC), and

(c) the vaccination effectiveness (VE), and

(d) the rate of serious adverse effects per disease case (SRD),

the approximate differential rates for disease (DRIU) and ultimately serious adverse effects (SRIU) can be calculated by applying the formulas set out in paragraph 6.1, with the results set out in the table below for each age group.:

Measles, mumps, rubella totals in 2007-2018/2019, approximated

Disease	**Measles**	**Mumps**	**Rubella**	**TOTAL**
DRP (annual), age 16 mo - 19 years	~ 1 / 650,000	~ 1 / 83,200	~ 1 / 56,700,000	
VC	94.7%	94.7%	94.7%	
VE	91.8%	73.0%	95%	
DRU (annual)	~1 / 90,000	1 / 25,677	1 / 5,700,000	
DRIU (annual)	~1 / 100,000	1 / 35,168	1 / 6,000,000	
DRIU (total over age range)	~1 / 5,300	< 1 / 1,884	1 / 320,000	
SRD - (any SAE)	< 1 in 83	< 1 / 296	< 1 / 3,000	
- (hospitalization)	< 1 in 482	< 1 / 296	zero to negligible	
- (death) (case fatality rate)	< 1 / 20,000 *	< 1 / 21,549	zero to negligible	
SRIU - (any SAE)	< 1 / 440,478	< 1 / 553,375	< 1 / 965,653,132	**< 1 / 245,195**
- (hospitalization)	< 1 / 2,569,455	< 1 / 553,375	zero to negligible	**< 1 / 455,101**
- (death)	< 1 / 106,506,429	< 1 / 40,371,594	zero to negligible	**< 1 / 28,413,478**

* Estimate is for those who are not immunocompromised nor deficient in Vitamin A.

(f) Broader impacts of vaccination and other factors on susceptibility

i. How necessary is vaccination for preventing transmission?

The CDC Pink Book Measles Chapter states:

> *"The first measles vaccines were licensed in 1963. In that year, both an inactivated ("killed") and a live attenuated vaccine (Edmonston B strain) were licensed for use in the United States. The inactivated vaccine was withdrawn in 1967 because it did not protect against measles virus infection… The original Edmonston B vaccine was withdrawn in 1975… Another live, further attenuated strain vaccine (Edmonston-Enders strain) was licensed in 1968."*

Hence it can be reasoned that measles vaccination had begun by the end of the 1960s. Those recipients have now reached 50 years of age and over.

Based upon the initial seroprotection rate and Waning Exponents presented in paragraph 7.5(c) herein, the vaccine-induced seroprotection rates against measles and mumps can be estimated to have fallen to <40% and 0% respectively by 40 years of age, and that against measles fallen to 13% by the age of 50 years.

Even by the year 2002, the vaccine-induced seroprotection rate against measles can be estimated to have fallen to <52% in 35 year olds who had vaccinated in 1968 (born in 1967).

Yet the CDC Pink Book Measles Chapter states:

> *"Measles elimination from the Americas was achieved in 2002 and has been sustained since then".*

Hence, even when waning antibody avidity rates are not additionally taken into account, it is not reasonable to assume that the burden of immunity in the entire population is dependent upon the vaccination rates amongst a limited subset of the population - children who attend childcare and school, being maintained at virtually 100%.

Clearly there are other factors that are preventing illness (“disease”) arising from these infections. Many or all those factors may be the same alternative factors that are protecting those who are not vaccinated against diseases that by their nature, and/or vaccine design, are not preventable in the unvaccinated by the vaccination of others, such as tetanus which is not contagious.

Hence the circumstances again point back to the factors such as those listed in paragraph 6.4 herein.

ii. Adverse impact upon susceptibility of offspring

The CDC Pink Book Measles Chapter states:

> *“In addition, measles susceptibility of infants younger than 1 year of age may have increased. During the 1989–1991 measles resurgence, incidence rates for infants were more than twice as high as those in any other age group. The mothers of many infants who developed measles were young, and their measles immunity was most often due to vaccination rather than infection with wild virus. As a result, a smaller amount of antibody was transferred across the placenta to the fetus, compared with antibody transfer from mothers who had higher antibody titers resulting from wild-virus infection. The lower quantity of antibody resulted in immunity that waned more rapidly, making infants susceptible at a younger age than in the past.”*

According to the CDC in this excerpt, girls for whom vaccination is not medically contraindicated) who are vaccinated during the childhood age range will increase the susceptibility of their offspring to measles during infancy.

Individual couples, reasonably, may prefer to expose their healthy daughters to measles at an age at which the evidence herein indicates that measles infection almost certainly would not be harmful (especially if well nourished, according to other research quoted herein), in order to increase protection to future offspring (future grandchildren) during the latters’ infancy, as well as to avoid for their daughters vaccination risks and permit them to develop lifelong natural immunity, fully protecting them during adulthood.

iii. Decline in vaccine-induced antibody avidity

The Plaintiff hereby requests that the Court take judicial notice of the following documents:

- article entitled “Waning Antibody Levels and Avidity: Implications for MMR Vaccine-Induced Protection”,

  Citation: Mia Kontio, Sari Jokinen, Mikko Paunio, Heikki Peltola, Irja Davidkin. The Journal of Infectious Diseases, Volume 206, Issue 10, 15 November 2012, Pages 1542–1548, https://doi.org/10.1093/infdis/jis568, accessible at https://academic.oup.com/jid/article-pdf/206/10/1542/2553487/jis568.pdf (last accessed February 11, 2021)
  (hereafter “Kontio Measles Vaccine Avidity Article”)
  A true and correct copy of the aforesaid report is attached hereto as **Exhibit 143**.

The Kontio Measles Vaccine Avidity Article states:

> *“Twenty years after a second MMR vaccination, antibody levels for all 3 viruses waned. Also, the mean avidity index decreased by 8% for measles, 24% for mumps ….*
> *Waning of both the concentration as well as the avidity of antibodies might contribute to measles and mumps infections in twice-MMR–vaccinated individuals.”*

Based upon this excerpt, not only does a decline occur over time in the presumed “protective” levels of antibodies – by 8% for measles and 24% for mumps over 20 years - but so also does a decline occur in the avidity of those still present antibodies. This provides further evidence that any prevention of infection effected to adults by past vaccinations becomes increasingly low as they age.

To the extent that adults remain protected from infection-induced illness by alternative factors that is not a problem, but those that have not gone through these infections naturally lack the benefit of lifelong natural immunity.

iv. Adverse effect of vaccination upon long term protection

It may be reasoned that any effective method of preventing natural infection with measles, mumps or rubella in childhood results in the preventing the recipient from developing natural immunity in childhood.

To the extent that natural immunity provides longer lasting protection than vaccine-induced immunity, vaccination increases the chance of the person being susceptible to the targeted disease at an older age.

The CDC Mumps Complication Rate Article states:

"Although overall mortality is low, death due to mumps infection is much more likely to occur in adults; about half of mumps-associated deaths have been in persons greater than or equal to 20 years old (2)."

and

"Orchitis (usually unilateral) has been reported as a complication in 20%-30% of clinical mumps cases in postpubertal males (3)."

The CDC Pink Book Rubella Chapter states:

"Arthralgia or arthritis may occur in up to 70% of adult women who contract rubella, but it is rare in children"

According to these excerpts, these disease risks are higher in adulthood than in childhood.

Individual parents may prefer to expose their healthy children to childhood infections in order to provide the benefits that going through the infection brings to children, including lifelong immunity, protecting against such conditions in later life, at more vulnerable ages.

7.6 Varicella (Chickenpox)

The CDC Schedules state that the recommendation for varicella vaccination in the US was in 2016-2018:

*" * 2-dose series at 12–15 months, 4–6 years"*

Based upon this stated schedule and availability of published notification rates, the lower limit of the age range that is the subject of the analyses for this vaccine-targeted disease is 16 months. The upper limit is chosen to be 19 years, i.e. up to the time of reaching 20 years.

(a) Varicella notification rate (DRP)

The Plaintiff hereby requests that the Court take judicial notice of the following document:

- article entitled "The Incidence and Clinical Characteristics of Herpes Zoster Among Children and Adolescents After Implementation of Varicella Vaccination",

  Citation: Civen R, Chaves SS, Jumaan A, Wu H, Mascola L, Gargiullo P, Seward JF (2009) The incidence and clinical characteristics of herpes zoster among children and adolescents after implementation of varicella vaccination. Pediatr Infect Dis J. 2009, 28(11):954-959. doi: 10.1097/INF.0b013e3181a90b16, accessible at https://journals.lww.com/pidj/fulltext/2009/11000/The_Incidence_and_Clinical_Characteristics_of.4.aspx
  (last accessed January 22, 2020)
  (hereafter "Herpes Zoster Rate Article")

  A true and correct copy of the aforesaid report is attached hereto as **Exhibit 144**.

i. Varicella notification rate to NNDSS

The CDC Disease Notifications state that the varicella notification rates "*per 100,000*" for the years 2016 to 2018 were those in *italics* in the following table:

Age group (yrs) / ***Year***	***1 – 4***	***5 – 14***	***15 – 24***
2016	*14.95*	*9.75*	*2.60*
2017	*14.31*	*9.02*	*2.45*
2018	*13.69*	*8.13*	*2.18*
Average rate per 100,000:	**14.32**	**8.97**	**2.41**

ii. Adjustment for underreporting

The Herpes Zoster Rate Article states that the reporting completeness for children aged under 10 years in the case of the surveillance that is described in the article was estimated to be 65.7% to 75.8%, as follows:

"Antelope Valley (Los Angeles County), California, population ~350,000, is 1 of 2 US surveillance project sites (the other being West Philadelphia, PA) that have collected community based active surveillance data for varicella in residents of all ages since 1995[25] and for herpes zoster in residents <20 years of age since 2000. Details of the populations and methods for this surveillance have been described.[25] Every 2 weeks, preschools, schools, hospitals, and public and private healthcare providers report on cases of varicella and herpes zoster, even when no cases are identified."

and

"To account for under reported varicella cases, we used capture-recapture methodology,[26] which compares 2 surveillance sources, childcare/ preschools/ schools, and medical providers."

and

"We estimated that between 1995 and 2006, the completeness of annual reporting for varicella cases among 2- to 18-year-old children ranged from 65.7% to 75.8%. Thus, we increased the denominator of children aged <10 years with varicella disease for each surveillance year (1995–2006) by the number estimated to be under-reported (1-completeness for each year; range: 24.2%–34.3%)."

Based upon the said reporting completeness estimate of "*65.7% to 75.8%*", the lower limit of that range, 65.7% is taken herein to approximate the reporting completeness for varicella notifications in 16 month to 19 year olds to NNDSS.

iii. Summary for DRP

Based upon the above information in this paragraph 7.6(b), the approximate average varicella incidence in 2016 to 2018 was as set out in the table below for each subject age group:

Age	**16 mths - 4 yrs**	**5 - 14 yrs**	**15 - 19 yrs**
DRP (annual)	~ 1 / 4,589	~ 1 / 7,327	~ 1 / 27,261

(b) Varicella Vaccination Coverage (VC)

i. Coverage in 1 – 4 year olds

The CDC Daycare Coverage Reports provide estimated coverages overall (averages or medians) for at least one dose of varicella-containing vaccines in 19-35 month olds in the US as set out in the table below:

Year	Varicella Vaccine Coverage % (average)
2013	*91.2*
2014	*91.0*
2015	*91.8*
2016	*90.6*
2017	*91.0*
2018	*91.0*
Average	**91.1**

Based on the data in the above table, the average coverage for at least one doses of varicella vaccination over the period of 2016-2018 is estimated to have been:

- 91.1% in 1 - 4 year olds.

An assumption shall be incorporated into the calculations for the analysis of the level of benefit for this vaccination that in all of relevant year cohorts, the second dose was not given until around the time of turning 5 years of age.

ii. Coverage in 5 – 14 year olds

The CDC Elementary School Coverage Reports provide estimated vaccination coverages overall (some averages, others medians) for 3 doses of varicella-containing vaccines in Kindergarteners in the US as follows:

School Year	Varicella Vaccine Coverage % (average/median)	
	1 dose	*2 doses*
2002-2003	93.3 [6]	
2003-2004	*93.3*	
2004-2005	94.65 [6]	
2005-2006	*96.0*	
2006-2007	*96.5*	
2007-2008	96.8 [6]	
2008-2009	97.1 [6]	
2009-2010	*97.4*	*90.3*
2010-2011	96.4 [6]	91.8 [6]
2011-2012	*95.4*	*93.2*
2012-2013	*96.5*	*93.8*
2013-2014	*96.6*	*93.3*
2014-2015	96.4 [6]	*93.6*
2015-2016	96.1	*94.3*
2016-2017	96.5	*93.8*
2017-2018	96.2	*93.8*
2018-2019	96.2 [6]	*94.8*
Average 2007-2019	**96.5**	
Average 2002-2009	**96.2**	

* The CDC Elementary School Coverage Report for

* 2011-2012 states:

"13 grantees required 1 dose and 37 grantees required 2 doses of varicella vaccine… Median coverage with 2 doses of varicella vaccine among 33 grantees reporting was 93.2%"

* 2012-2013 states:

"Median 2-dose varicella vaccination coverage among the 36 states and DC requiring and reporting 2 doses was 93.8% (range: 84.6% in Colorado to ≥99.9% in Mississippi)"

* 2013-2014 states:

"For varicella vaccine, 13 required 1 dose, 36 required 2 doses, and 1 did not require varicella vaccination… Median 2-dose varicella vaccination coverage among the 36 states and DC requiring and reporting 2 doses was 93.3%."

* 2014-2015 states:

"In most jurisdictions, kindergartners with a history of varicella disease are considered to be vaccinated against varicella, whereas in some jurisdictions they may be given a medical exemption."

* 2015-2016 and 2016-2017 states:

"Kindergartners with a history of varicella disease were reported as either vaccinated against varicella or medically exempt, varying by program"

* 2018-2019 states:

"Reporting of varicella vaccination status for kindergartners with a history of varicella disease varied within and among states; some were reported as vaccinated against varicella and others as medically exempt"

The following two assumptions shall be incorporated into the calculations for the analysis of the level of benefit for this vaccination, and both assumptions will inflate the calculated result:

(1) Based upon the above excerpts from the CDC Elementary School Coverage Reports and similar ones for most of the other relevant years, the vaccination coverage is lower than may be suggested by the figures in the table because an unvaccinated child who has a history of varicella is counted as vaccinated. However, the assumption shall be made that the coverage for the second dose was the same as that for the first, and

(2) Although the coverage for the second varicella vaccine dose is reported to have been lower than for the first dose in each relevant year, an assumption shall be made that the coverage for the second dose was the same as for the first.

Based upon the figures in the above table for the years 2007-2008 to 2018-2019 and the above two assumptions, the average coverage for two doses of varicella-containing vaccines approximated:

- 96.5% in children aged 5-14 year olds in 2016 to 2018.

iii. Coverage in 15 – 19 year olds

The CDC Secondary School Coverage Reports does not provide estimated average vaccination coverages for varicella-containing vaccines separately from the adolescent's "*history of varicella disease*" status.

The vaccination coverage of this age group may alternatively be estimated on the basis of the "coverage" of the same cohort in the year of entry into elementary school. Even though in the CDC Elementary School Coverage Reports unvaccinated children with a history of varicella were counted as vaccinated, the probability of a history of varicella can be reasoned to be significantly lower at the age of about 5 years than by the time the person reaches 15-17 years of age.

Based upon averaging the figures for the years 2002-3 to 2008-9 in the table in the previous paragraph 7.6(b)ii, and the same assumptions stated in that paragraph, the average coverage for two doses of varicella-containing vaccines approximated:

- 95.4% in children aged 15-19 year olds in 2016 to 2018.

iv. Summary for VC

Based upon the above information in this paragraph 7.6(b), the approximate average vaccination coverage for 1 dose of varicella-containing vaccine in 2016-2018 was as set out in the table below for each subject age group:

Age	16 mths-4 yrs	5-14 yrs	15-19 yrs
VC	91.1%	96.5%	96.4%

(c) **Varicella Vaccination Effectiveness (VE)**

The Plaintiff hereby requests that the Court take judicial notice of the following documents:

- the CDC web page headed "About the Varicella Vaccines", accessible at https://www.cdc.gov/vaccines/vpd/varicella/hcp/about-vaccine.html (last accessed November 29, 2020)
  (hereafter "CDC Page About the Varicella Vaccine")
  A true and correct copy of the aforesaid report is attached hereto as **Exhibit 145**.

- an article entitled "Effectiveness Over Time of Varicella Vaccine",
  Citation: Vázquez M, LaRussa PS, Gershon AA, Niccolai LM, Muehlenbein CE, Steinberg SP, Shapiro ED. JAMA. 2004 Feb 18;291(7):851-5 accessible at https://www.immunize.ca/sites/default/files/resources/134e.pdf (pdf)
  (last accessed November 29, 2020)
  (hereafter "Vázquez Varicella Vaccine Duration Article")

A true and correct copy of the aforesaid report is attached hereto as **Exhibit 146**.

- the CDC's Vaccine Information Statement for the varicella vaccine, headed "Vaccine Information Statement" with subheading "Varicella (Varicella) Vaccine ", accessible at https://www.cdc.gov/vaccines/hcp/vis/vis-statements/varicella.html (html) or https://www.cdc.gov/vaccines/hcp/vis/vis-statements/varicella.pdf (pdf) (last accessed November 29, 2020) (hereafter "CDC Varicella VIS") A true and correct copy of the aforesaid report is attached hereto as **Exhibit 147**.

- an article entitled "Live-attenuated varicella vaccine", Citation: Gershon AA. Infect Dis Clin North Am. 2001 Mar;15(1):65-81, viii. doi: 10.1016/s0891-5520(05)70268-3. PMID: 11301823 accessible at https://www.sciencedirect.com/science/article/abs/pii/S0891552005702683 (pdf) (last accessed January 19, 2020) (hereafter "Gershon Varicella Vaccine Article") A true and correct copy of the aforesaid article is attached hereto as **Exhibit 148**.

i. Effectiveness for 1 – 4 year olds (first dose only)

The CDC Page About the Varicella Vaccine states:

> *"Duration of Protection*
>
> *It is not known how long a vaccinated person is protected against varicella…*
>
> - *A case-control study conducted from 1997 to 2003 showed that 1 dose of varicella vaccine was 97% effective in the first year after vaccination and 86% effective in the second year. From the second to eighth year after vaccination, the vaccine effectiveness remained stable at 81 to 86%...1…*

- *A meta-analysis that included 1-dose vaccine effectiveness reported through 2015 found a pooled estimate of 82% within the first decade.… Four studies reported decline in VE with time since vaccination; however, the differences did not reach statistical significance.3…*

[1] *Vázquez M, LaRussa PS, Gershon AA, Niccolai LM, Muehlenbein CE, Steinberg SP, Shapiro ED. Effectiveness over time of varicella vaccine. JAMA. 2004 Feb 18;291(7):851-5*"

The Vázquez Varicella Vaccine Duration Article states:

"Case subjects, identified by active surveillance of all practices, consisted of 339 eligible children 13 months or older who were clinically diagnosed as having chickenpox and who also had a polymerase chain reaction (PCR) test result that was positive for varicella-zoster virus DNA. For each case subject, 2 controls were selected, matched by both age and pediatric practice."

and under the heading "Results" includes the following table:

*"Table 3. Effectiveness of the Varicella Vaccine by Time Since Vaccination**

Years Since Vaccination	No. Vaccinated		Effectiveness, % (95% CI)	P Value
	Cases	Controls		
1†	4	84	97 (91-99)	<.001
2	22	108	86 (76-92)	<.001
3	26	92	83 (69-90)	<.001
4	24	68	81 (62-90)	<.001
5	24	65	84 (67-93)	<.001
6	13	33	82 (54-93)	<.001
7-8	9	20	81 (40-94)	0.005
2-8	118	386	84 (76-89)	<.001

Abbreviation: CI, confidence interval.

** Results are adjusted for sex, race, attendance at group day care, asthma, use of steroids, and receipt of varicella vaccine within 28 days after receiving the measles-mumps-rubella vaccine. The P values in the table refer to whether the adjusted estimates of the vaccine's effectiveness are statistically significantly different than 0%.*

†Difference in overall effectiveness in year 1 vs years 2 to 8 (97% vs 84%; P = .003)."

The CDC Page About the Varicella Vaccine references the Vázquez Varicella Vaccine Duration Article in relation to the statement "*From the second to eighth year after vaccination, the vaccine effectiveness remained stable at 81 to 86%."* However, taking into consideration the size of the confidence intervals (Cis) in the above table, and the lower and upper limits of the CIs, the results therein accord with a waning of the effectiveness from approximately 86% in the second year to approximately 81% in the eighth year.

Based upon the above statements in these excerpts, it may be concluded that the first varicella vaccine dose has a brief initial effectiveness in the first year averaging 97% but that it rapidly falls so that the average effectiveness in the second year is about 86% and the Waning Exponent thereafter until the second dose can be estimated to be approximately 1.06.

Based upon the above estimated initial and waning rates, the approximate average effectiveness of the varicella vaccine is:

- 88.2% in 16 month to 4 year olds.

Deficiencies in study measuring effectiveness

The Vázquez Varicella Vaccine Duration Article states:

"For each case subject, 2 controls were selected, matched by both age and pediatric practice."

and

"potential cases and potential controls who had received the vaccine in the preceding 4 weeks were excluded from the study… Antecedent vaccination was defined as written documentation that varicella vaccine had been received at least 4 weeks before focal time",

and

according to *"Table 1", "99""%"* of each of the *"Children With Chickenpox"* and *"Controls" "received the MMR vaccine",*

and

"Because this is a nonexperimental study, bias may have affected the results"

Based upon the above excerpts from the article, several features of the study described in the Vázquez Varicella Vaccine Duration Article potentially inflated the effectiveness results, so the average effectiveness is likely to be lower than that cited above. For example:

- all were excluded who contracted varicella within 4 weeks after vaccination, whether directly from the vaccination or as a result of the vaccination increasing susceptibility to infection, and
- there was also a failure to match the controls to the test subjects in relation to other factors that may impact upon susceptibility to varicella, such as socioeconomic status and medical history, such as an adverse effect of past vaccination(s) medically contraindicating, or discouraging the parents from consenting to, varicella vaccination, and
- virtually all of the test and control groups received the MMR vaccine, so the study only attempted to measure the relative effectiveness of the varicella vaccination amongst MMR recipients, without regard to the varicella incidence in vaccine-free children, and
- for the same reason as has been discussed in relation to pertussis in this Notice (in paragraph 7.3(c)(2)), there was also the potential for the effectiveness results to be inflated by doctor and/or parents' observer bias.

ii. Effectiveness for 5 – 19 year olds (second dose)

The CDC Page About the Varicella Vaccine also states:

"Two doses of varicella vaccine add improved protection, pooled estimate of 92% (assessed ~5 years after vaccination)."

The CDC Varicella VIS states:

"Most people who are vaccinated with 2 doses of varicella vaccine will be protected for life."

.

According to these statements, it may be estimated that the second varicella vaccine dose, when given at the age of about turning 5 years, has an initial effectiveness (possibly after a brief phase of higher effectiveness) of 93% and the Waning Exponent thereafter can be estimated to be approximately 1.03.

Based upon the above estimated initial and waning rates, the approximate average effectiveness of the varicella vaccine is less than:

- 91.9% in 5 to 14 year olds, and
- 90.0% in 15 to 19 year olds.

iii. Above estimates of effectiveness appear to be inflated

The Gershon Varicella Vaccine Article states:

> *"The true efficacy of the currently licensed varicella vaccine has not been established entirely. Studies of vaccine efficacy comparing the occurrence of varicella after vaccination to natural rates of chickenpox for children of various ages have indicated an overall 90% efficacy against varicella.*[49,86] *In an analysis of household exposures to varicella, however, the most stringent assessment of protection, 53/267 (20%) of exposed children developed varicella."*

Based upon this excerpt (though disregarding the article's omission of time interval from vaccination to the exposure), the maximum level of effectiveness the vaccination could have against the development of infection is 80% and that level itself would apply only if it were the case that without vaccination, 100% of those exposed would become infected. Nevertheless, the higher effectiveness figures in paragraphs 7.6(c)i and ii above will be used in the calculation presented in this Notice of the risk from non-vaccination.

iv. Summary for VE

Based upon the above information in this paragraph 7.6(c), the approximate maximum average vaccination effectiveness for varicella-containing vaccine is as set out in the table below for each subject age group:

Age	16 mth-4 yrs	5-14 yrs	15-19 yrs
VE	< 88.2%	< 91.9%	< 90.0%

(d) **Serious outcome Rate per Disease case (SRD)**

The Plaintiff hereby requests that the Court take judicial notice of the following documents:

- table entitled "Table 1. Clinical presentation of herpes zoster by age at rash onset and history of exposure to varicella zoster virus, N=372", referenced by the previous article in the list (Herpes Zoster Rate Article) as

  "Table, Supplemental Digital Content 1", accessible via a link at the end of the Herpes Zoster Rate Article located online at https://journals.lww.com/pidj/fulltext/2009/11000/The_Incidence_and_Clinical_Characteristics_of.4.aspx

  (last accessed February 15, 2021)
  (hereafter "Herpes Zoster Rate Article Supplemental Table")
  A true and correct copy of the aforesaid report is attached hereto as **Exhibit 149**.

- the CDC "Pink Book" "Varicella" chapter, accessible at https://www.cdc.gov/vaccines/pubs/pinkbook/varicella.html online or https://www.cdc.gov/vaccines/pubs/pinkbook/downloads/varicella.pdf (pdf)
  (last accessed November 29, 2020)
  (hereafter "CDC Pink Book Varicella Chapter")
  A true and correct copy of the aforesaid report is attached hereto as **Exhibit 150**.

- article entitled "Children hospitalized for varicella: A prevaccine review",

  Citation: Peterson et al. The Journal of Pediatrics 1996 Vol 129, Issue 4: 529–536, accessible at.
  http://www.sciencedirect.com/science/article/pii/S0022347696701178

  (last accessed February 10, 2021)
  (hereafter "Varicella Prevaccine Fatalities Article")
  A true and correct copy of the aforesaid report is attached hereto as **Exhibit 151**.

i. HRD (Herpes zoster risk per case)

Herpes zoster (HZ) after varicella does not necessarily fall within the definition of SAE but a calculation of the increased chance of HZ for an unvaccinated child is presented herein for the purpose of comparison of the

outcomes of non-vaccination versus vaccination, since HZ is also stated to be an adverse outcome that may occur after vaccination.

"HRD" is hereby defined as varicella disease-associated Herpes zoster Rate per Disease case in an unvaccinated, vaccine-eligible person.

The Herpes Zoster Rate Article includes a table that is entitled "TABLE 2. Estimated RR of Herpes Zoster in Residents Aged <10 Years With a History of Varicella Vaccination Versus Those With a History of Varicella Disease", which contains the following selected rows and columns:

Yr	*Disease History*	
	No. Cases§	*Population‖*
2000–2006	*84*	*35,213*

and is accompanied by the following notes:

> *"§ Herpes zoster cases with a varicella disease history include those with disease history only (n = 81) and those with disease history and unknown vaccine history (n = 3).*
>
> *‖ Population with a history of varicella disease corrected by annual completeness of case reporting."*

The Herpes Zoster Rate Article also states:

> *"Of the 459 herpes zoster cases, 372 (81%) had complete clinical and vaccination information (Table, Supplemental Digital Content 1, http://links.lww.com/A1165)."*

The Herpes Zoster Rate Article Supplemental Table, to which the above paragraph refers, includes the following selected rows and columns in relation to the 81 cases for which complete clinical and vaccination information is available, out of the aforesaid 372 HZ cases:

Table 1. Clinical presentation of herpes zoster by age at rash onset and history of exposure to varicella zoster virus, N=372. [a]	
Clinical Characteristic	***No. (%) by Age Group and History <10 years Disease History (n = 81)***
Pre-existing condition	
No medical conditions	*69 (85)*
Hospitalization	
No	*81 (100)*

Based upon this excerpt, approximately 85% of the 84 aforesaid cases of HZ occurred in children who had no pre-existing medical conditions, which was about 72 children, from a population of at most 35,213 – 12 = 352,201.

Based upon that result, the rate of HRD in an under 10 year old healthy unvaccinated child is approximately (85% x 84 ÷ 35,201 =):

- **0.2%** (about 1 in 500), which is assumed herein to apply approximately to each of the age groups 16 mths-4 years, 5-14 and 15-19 years.

Notably, according to the above table, none of the HZ cases in unvaccinated children, including those with pre-existing medical conditions, required hospitalization.

ii. SRD for hospitalization

The CDC Pink Book Varicella Chapter states:

"In the prevaccine era… Hospitalization rates were approximately 1 to 2 per 1,000 cases among healthy children and 14 per 1,000 cases among adults"

Based upon this statement, including the significantly higher SRD cited for adults than children, it is estimated that the SRD is approximately:

- **0.1%** (1 in 1000) for each of the age groups 16 mths-4 years and 5-14 years, and
- **0.2%** (2 in 1000) for the age group 15-19 years.

iii. SRD for death

The CDC Pink Book Varicella Chapter states:

"In the prevaccine era… The fatality rate for varicella was approximately 1 per 100,000 cases among children age 1 through 14 years, 6 per 100,000 cases among persons age 15 through 19 years"

Based upon this statement, the prevaccine varicella fatality rate was approximately 1 per 100,000 and 6 per 100,000 among children aged 1 through 14 and 15 through 19 years respectively.

The Varicella Prevaccine Fatalities Article states:

"A retrospective record review of children hospitalized for varicella between January 1, 1990, and March 31, 1994, was conducted in nine large acute care hospitals in Los Angeles County, California."

and

"There were seven deaths: one caused by streptococcal TSS in a previously well child and six in immunocompromised children"

Based upon this statement, only approximately 1 in 7 prevaccine varicella fatalities occurred in non-immunocompromised children. Hence the SRD for non-immunocompromised children can be estimated to be $1/7^{th}$ the above respective rates.

Based upon this statement, the SRD for death from varicella is approximately:

- 0.00014% (about 1 per 700,000) for each of the age groups 16 mths-4 years and 5-14 years, and
- 0.00086% (about 1 per 120,000) for the age group 15-19 years.

(e) **Differential Risk of unavoidable serious adverse effect (SRIU)**

Based upon the calculated estimates presented in this paragraph 7.6, "Varicella" for

(a) the disease notification rate in the population (DRP), and

(b) the vaccination coverage (VC), and

(c) the vaccination effectiveness (VE), and

(d) the rate of serious adverse effects per disease case (SRD),

the approximate differential rates for disease (DRIU) and ultimately serious adverse effects (SRIU) can be calculated by applying the formulas set out in paragraph 6.1, with the results set out in the table below for each age group.

Varicella totals and averages for 2016-2018 (approx.)

Age group (yrs)	16 mths – 4	5 – 14	15 – 19	TOTAL
DRP (annual)	1 / 4,589	1 / 7,327	1 / 27,261	
VC	< 91.1%	< 96.5%	< 96.4%	
VE	< 88.2%	< 91.9%	< 90.0%	
DRU (annual)	1 / 900	< 1 / 832	< 1 / 3,855	
DRIU (annual)	1 / 1,020	< 1 / 905	< 1 / 4,282	
DRIU (total over age range)	1 / 278	< 1 / 90	< 1 / 856	< 1 / 63
SRD - (hospitalization)	≤ 0.1%		≤ 0.2%	
- (death) (case fatality rate)	0.00014%		0.00086%	
SRIU - (hospitalization)	**< 1 / 278,219**	**< 1 / 90,498**	**< 1 / 428,189**	**< 1 / 58,894**
- (death)	**< 1 / 194,753,405**	**< 1 / 63,348,781**	**< 1 / 99,910,858**	**< 1 / 32,331,860**

Differential risk of Herpes zoster for Unvaccinated

Following the same principle as that for calculating the differential rate/risk of an SAE occurring due to non-vaccination, the formula for calculating the differential rate/risk of varicella disease-related herpes zoster (HZ) due to non-vaccination can be seen to be:

HRIU = DRIU x HRD

where HRIU = Differential (increased) varicella disease-associated HZ Rate for an unvaccinated person above that for a vaccinated person.

The estimates that result from that calculation are presented in the table below:

Age group (yrs)	16 mths – 4	5 – 14	15 – 19	TOTAL
DRIU (total over age range)	1 / 278	< 1 / 90	< 1 / 856	
HRD - (herpes zoster)	0.20%			
HRIU - (herpes zoster)	**< 1 / 137,000**	**< 1 / 44,617**	**< 1 / 422,204**	**< 1 / 31,180**

7.7 Hepatitis A

The CDC Schedules state that the recommendation in the US for "*Hepatitis A vaccination*" is a "*2-dose series (minimum interval: 6 months) beginning at age 12 months*".

Based upon that recommendation, the lower limit of the subject age range for the risk analysis herein for hepatitis A vaccination is set at 1 year. The upper limit is set at the approximate age of leaving secondary school, which is 17 years (inclusive).

(a) Hepatitis A notification rate (DRP)

i. Hepatitis A Notification Rates in 1 to 5 year olds

The CDC Disease Notifications state that the acute hepatitis A notifications for the years 2012 to 2018 were those in *italics* in the following table for 1 to 4 year olds:

Age group (yrs) / *Year*	*1 – 4*
2012	32
2013	22
2014	13
2015	16
2016	18
2017	19
2018	26
Average	**20.9**

Based upon that excerpt and the Population Tables, the average annual hepatitis A notification rate in 1 to 4 year olds in 2012-2018 was approximately:

- **1 in 765,386.**

ii. Hepatitis A Notification Rates in 5 to 17 year olds

The Plaintiff hereby requests that the Court take judicial notice of the following document:

- the CDC "Pink Book" "Hepatitis A" chapter, accessible at https://www.cdc.gov/vaccines/pubs/pinkbook/hepa.html online or https://www.cdc.gov/vaccines/pubs/pinkbook/downloads/hepa.pdf (pdf) (last accessed November 17, 2020)
  (hereafter "CDC Pink Book Hepatitis A Chapter")
  A true and correct copy of the aforesaid report is attached hereto as **Exhibit 152**.

The objective of the analysis presented in this paragraph 7.7 includes the determination of hepatitis A-related risk in the 5-17 year age group as well as the 1-4 year age group. However notification data for those aged 1-4 years only is used for the analysis. The reasons for not using the notification data for those aged over 5 years for the analysis are mainly:

- the estimates of vaccination coverage stated in neither the CDC Elementary School Coverage Reports, nor the CDC Secondary School Coverage Reports, include estimates for coverage of the hepatitis A vaccine, and
- the CDC Disease Notifications includes notification data for the entire 15-24 age group combined, so it does not reveal the notification rate in 15-17 adolescents still studying at school, to whom the mandate relates, as distinct from the rate amongst those up to the age of 24 years who may, in some cases by their own choice, be leading very different lifestyles which may carry a significantly higher risk for hepatitis A than what is not reasonably avoidable and is relevant to the vast majority of the population in the age group.

  The CDC Pink Book Hepatitis A Chapter states:

  > *"Schools are not common sites for HAV transmission"*

  but that

  > *"Groups at increased risk for hepatitis A or its complications include international travelers (particularly high-risk itineraries like travel to rural areas in high-risk countries), contacts of recent international adoptees from HAV endemic countries, men who have sex with men, and users of illegal drugs. Outbreaks of hepatitis A have also been reported among persons working with hepatitis A-infected primates. This is the only occupational group known to be at increased risk for hepatitis A… outbreaks have been observed in neonatal intensive care units and in association with adult fecal incontinence…*

In 2010, 75% of hepatitis A cases (who responded to any question about risk behaviors and exposures) indicated no risk factors for their infection. Of cases indicating at least one risk factor 2-6 weeks prior to the onset of illness, the most frequently reported source of infection was personal contact (sexual or household) with an infected person (7.3%). Employment or attendance at a nursery, day-care center, or preschool involved 3.1% of cases; 4% involved contact with a child or employee in child care; 14.1% occurred among persons reporting recent international travel… Injection-drug use was a reported risk factor in 2% of cases; men who have sex with men represented 4.9% of cases.

Of the … case reports of acute hepatitis A received by CDC during 2011,… of…827 case reports… 78%... indicated no risk behaviors/exposures for acute hepatitis A… during the 2-6 weeks prior to onset of illness."

The resultant levels of risk for hepatitis A for those to which these higher risk circumstances apply cannot reasonably be assumed to be the same as that for the average student in elementary or secondary school.

It is assumed herein that the *unavoidable* hepatitis A risk for those who are aged 5-17 years is similar to the risk for 1-4 year olds. The risk may indeed be less than that for 1-4 year olds, based upon the CDC's statement that "*Employment or attendance at a nursery, day-care center, or preschool involved 3.1% of cases; 4% involved contact with a child or employee in child care*".

(b) Hepatitis A Vaccination Coverage (VC)

i. Coverage in 1 – 4 year olds

The CDC Daycare Coverage Reports provide estimated coverages overall (averages or medians) for ≥1 and ≥2 doses of hepatitis A-containing vaccine in 19-35 month olds in the US as set out in the table below:

Year	Hepatitis A Vaccine Coverage % (average)	
	One dose	Two doses
2010	*78.3*	49.7
2011	*81.2*	52.2
2012	*81.5*	53.0
2013	*83.1*	54.7
2014	*85.1*	57.5
2015	*85.8*	59.6
2016	*86.1*	60.6
2017	*86.0*	59.7
2018	*86.0* [6]	59.7 [6]
Average	83.7	56.3

Based on the data in the above table, the average coverage for one dose of hepatitis A vaccination over the period of 2012 to 2018 is estimated to have been:

- 83.7% in 1 - 4 year olds.

Although the coverage for the second dose was on average 27% less than that for the first dose, those lower coverage figures will be disregarded and the assumption is made in the calculations herein that the average coverage for 2 doses in 1-4 year olds approximated that for 1 dose.

ii. Coverage in 5 – 17 year olds

The estimates of vaccination coverage stated in neither the CDC Elementary School Coverage Reports, nor the CDC Secondary School Coverage Reports, include estimates for coverage of the hepatitis A vaccine in that age range.

However, given that the coverage estimates gradually increased throughout the 2010-2018 period, it is reasonable to estimate that the average coverage for 5-17 year olds in 2012-2018 was less than that for 1-4 year olds, i.e. that the average coverage was

- < 83.7% in 5-17 year olds in 2012-2018.

The calculation of DRU presented herein for hepatitis A incorporates an assumption that the DRU (incidence rate in the unvaccinated) in 2012-2018 in 5-17 year olds approximated that in 1-4 year olds.

iii. Summary for VC

Based upon the above information and assumption in this paragraph 7.7(b), the approximate annual average vaccination coverage for 2 doses of hepatitis A-containing vaccines in the 7 year period of 2012 to 2018 is taken as being as set out in the table below for the single relevant subject age group:

Age	1-4 yrs
VC	83.7%

(c) Hepatitis A Vaccination Effectiveness (VE)

The Plaintiff hereby requests that the Court take judicial notice of the following documents:

- article entitled "Persistence of antibody to hepatitis A virus 20 years after receipt of hepatitis A vaccine in Alaska",

  Citation: Plumb ID, Bulkow LR, Bruce MG, et al. J Viral Hepat. 2017 Jul;24(7):608–12. doi: 10.1111/jvh.12676. Epub 2017 Feb 2. https://pubmed.ncbi.nlm.nih.gov/28092416/
  (last accessed November 17, 2020)
  (hereafter "Plumb Hepatitis A Vaccine Duration Article")
  A true and correct copy of the aforesaid report is attached hereto as **Exhibit 153**.

- article entitled "Hepatitis A vaccine immune response 22 years after vaccination",

  Citation: Mosites E, Gounder P, Snowball M, et al. J Med Virol. 2018 Aug;90(8):1418–22. doi: 10.1002/jmv.25197. Epub 2018 May 1. https://dl.uswr.ac.ir/bitstream/Hannan/66361/1/2018%20JoMV%20Volume%2090%20Issue%208%20August%20%2815%29.pdf

  (last accessed November 17, 2020)
  (hereafter "Mosites Hepatitis A Vaccine Duration Article")
  A true and correct copy of the aforesaid report is attached hereto as **Exhibit 154**.

The Plumb Hepatitis A Vaccine Duration Article states:

"Hepatitis A vaccine is recommended for children ≥1 year old to prevent hepatitis A virus (HAV) infection. However, the duration of vaccine-induced immunity is unknown. We evaluated a cohort of Alaska Native persons 20 years after HAV vaccination. Children aged 3-6 years had been previously randomized to receive three doses of HAV vaccine (360 ELISA units/dose) at: (i) 0,1,2 months; (ii) 0,1,6 months; and (iii) 0,1,12 months. We measured anti-HAV antibody concentrations… Overall, 46 (88.5%) of 52 available participants had anti-HAV antibody concentrations ≥20 mIU mL-1 , and overall GMC was 107 mIU mL-1."

The Plumb Hepatitis A Vaccine Duration Article states:

"…the duration of immunogenicity for the hepatitis A vaccine is not known… "We report on the 22 year follow-up time point of a cohort of Alaska children who were randomized to three different vaccine schedules: A) 0, 1, and 2 months; B) 0, 1, and 6 months; and C) 0, 1, and 12 months."

and

"143 Alaska Native children aged 3-6 years who were seronegative for anti-HAV antibody were recruited… Eligible children were randomized to receive injections… in one of three vaccination schedules with three-doses of the inactivated HepA vaccine HAVRIX® (360 Elisa Units, GlaxoSmithKline Biologicals, Lot# VHA-046A4 IND NR 3200, Rixenart, Belgium)."

and

"Among 46 participant available for follow-up, 40 (87%) maintained protective levels of anti-hepatitis A antibody."

Based upon the statements in these excerpts, the initial seroprotection rate after three hepatitis A vaccination doses can be estimated to be about 95.3% soon after the last dose, followed by a decline with a Waning Exponent of approximately 1.048.

The reliance herein upon the results of that study are likely to inflate the effectiveness of the vaccination due to, but not limited to, one or both of the following:

i. the CDC Pink Book Hepatitis A Chapter states:

"Children generally have asymptomatic or unrecognized illnesses".

Based upon that statement, natural infection is likely to be the cause of "*protective levels of anti-hepatitis A antibody*" found in a substantial

proportion of the vaccine recipients, but in whom the protection is falsely attributed to vaccination, and

ii. the study measures the seroprotection rate of recipients of three doses of hepatitis A vaccine. However, only two, not three, "*Hepatitis A vaccination*" doses are recommended in the US. Further, the vaccination coverage figure used in the calculation of DRU is based upon the coverages reported for "at least one dose", whereas the coverage in the primary subject population of children for this analysis (1-4 year olds in 2012-2018) was only 56%. Therefore to whatever extent the seroprotection rate is indicative of actual protection, and is boosted by a second and third dose, the effectiveness of the received doses, can reasonably be expected to be less than what these results would indicate.

Based upon the above rates and statements, the approximate average seroprotection rate is less than:

- 94.8% in 1 to 4 year olds, and
- 92.3% in 5 to 17 year olds.

(d) Serious outcome Rate (SRP or SRD)

i. SRP (not SRD) for hospitalization

The Plaintiff hereby requests that the Court take judicial notice of the following document:

- article entitled: "Hepatitis A Hospitalizations in the United States, 2002-2011"

  Citation: Melissa G. Collier, Xin Tong, Fujie Xu. Hepatology 2014. (First published 29 September), pages 481-485, accessible at https://aasldpubs.onlinelibrary.wiley.com/doi/epdf/10.1002/hep.27537 (last accessed February 16, 2021)
  (hereafter "Hepatitis A Hospitalizations Article")
  A true and correct copy of the aforesaid report is attached hereto as **Exhibit 155**.

The Hepatitis A Hospitalizations Article states:

> *"A retrospective descriptive study of the epidemiological characteristics of patients admitted to the hospital for hepatitis A was conducted using data from the National Inpatient Sample (NIS),[15] the largest population-based hospital inpatient care database available in the U.S."*

and includes a table entitled "Table 1. Characteristics of Patients Hospitalized With Hepatitis A as Principal Diagnosis, NIS 2002-2011", which contains the following selected rows and columns:

	Weighted %
Characteristics	***2010-2011***
Weighted N	*1792*
Age (years)	
<18	*8.8*

Based upon the above table, 1792 hospitalizations were recorded in the National Inpatient Sample (NIS) in 2010-2011, which was an annual average of 896, and of those, 8.8% were in under 18 year olds.

The article further states:

> *"NIS is a stratified, cross-sectional sample that includes ~20% of all community (nonfederal) hospital discharges in the U.S"*

Based upon that excerpt, the 896 annual average hospitalizations represented only about 20% of hospitalizations across the US.

Hence the approximate number of hospitalizations in 2010-2011was (896 ÷ 20% =) 4480, of which 8.8%, i.e. about 394, were in under 18 year olds. Based upon that annual average of 394 hospitalizations in 2010-2011, the SRP (hospitalization rate per head of population) was about:

- **1 in 185,749** for under 18 year olds in 2010-2011.

The article also states:

> *"Rates of hospitalization for hepatitis A as a principal diagnosis decreased from 0.72/100,000 to 0.29/100,000 (P < 0.0001) and mean age of those hospitalized increased from 37.6 years to 45.5 years (P < 0.0001) during 2002-2011",* and

Table 1 states that the number of hospitalizations was "*4185", '3776","2598"* and *"2059"* in "*2002-2003*", "*2004-2005*", "*2006-2007*" and "*2008-2009*" respectively

and that the percentage of hospitalizations in <18 year olds in 2002-2003 had been almost twice as high, at *"16.0"* than the 8.8% in 2010-2011.

Based upon these excerpts, the hospitalization rate per case, especially in the <18 year olds, was on the decline. So the average hospitalization rate over the subsequent years 2012-2018 was probably lower still, and likely significantly lower.

ii. SRD for death

The CDC Pink Book Hepatitis A Chapter states:

"recent case-fatality estimates range from 0.3%-0.6% for all ages."

Based upon this statement, to arrive at an estimate of SRIU for death from hepatitis A, the SRD rate applied to (i.e. multiply by) the DRIU for hepatitis A is 0.6%.

(e) Differential Risk of unavoidable serious adverse effect (SRIU)

Based upon the calculated estimates presented in this paragraph 7.7, "Hepatitis A" for (a) the disease notification rate in the population (DRP), (b) the vaccination coverage (VC), with an assumption of one dose of hepatitis A vaccination given soon after 12 months of age and a second dose 6 months later), (c) the vaccination effectiveness (VE), and (d) the rates of serious adverse effects (SRP and SRD), the approximate differential rates for disease (DRIU) and ultimately serious adverse effects (SRIU), the results of applying the formulas set out in paragraph 6.1 are set out in the table below:

Hepatitis A totals and averages for 2012-2018, approximated

Age Group	1 - 4 yrs	5-17 yrs	Average / Total 1 – 17 years
DRP (annual)	1 / 765,386		
SRP (annual) (hospitalization)	~ 1 / 185,749		
VC	83.7%	< 83.7%	
VE (residual)	< 94.8%	< 92.3%	
DRU (annual) [8]	< 1 / 157,978	< 1 / 157,978 *	
DRIU (annual) [8]	< 1 / 166,574	< 1 / 171,146	
DRIU total over age range	< 1 / 41,643	< 1 / 13,165	**< 1 / 10,003**
SRIU (hospitalization)	< 1 / 44,235		**< 1 / 44,235**
SRD (death)	< 0.6%		
SRIU (death)	<1 / 6,940,583	< 1 / 2,194,178	**< 1 / 1,667,135**

* See paragraph 7.7(a)ii headed "Hepatitis A Notification Rates in 5 to 17 year olds".

(f) Impact of vaccination on others' susceptibility

The CDC Pink Book Hepatitis A Chapter states:

> *"HAV infection is acquired primarily by the fecal-oral route by either person-to-person contact or ingestion of contaminated food or water. Since the virus is present in blood during the illness prodrome, HAV has been transmitted on rare occasions by transfusion. Although HAV may be present in saliva, transmission by saliva has not been demonstrated. Waterborne outbreaks are infrequent and are usually associated with sewage-contaminated or inadequately treated water."*

Based upon this excerpt, the virus is not spread through the uncontrollable medium of the air. The primary mode of transmission is instead "by the fecal-oral route by either person-to-person contact or ingestion of contaminated food or water". Hence forward transmission would require lack of personal hygiene or inadequate control by government of the drinking water, which are respectively able to be controlled by individuals or the government, without the need for vaccination of contacts.

Hence vaccination of childcare and school children is not necessary to reduce the risk of others becoming infected.

7.8 Hepatitis B

The CDC Schedules state that the recommendation in the US for "*Hepatitis B vaccination*" is a "*3-dose series at 0, 1–2, 6–18 months*".

Based upon the last dose being recommended at 6–18 months, of which the average age is 12 months, the lower limit of the subject age range for the risk analysis herein for hepatitis B vaccination is set at 1 year. The upper limit is set at the approximate age of completing tertiary education, which is 22 years (inclusive).

(a) Hepatitis B (HBV) notification rate (DRP)

The analysis presented herein of risk for hepatitis B is limited to the incidence of chronic hepatitis B. One reason for that is that the CDC Disease Notifications state that all of the notification "*rates per 100,000*" in age groups "*1-4 yrs*" and "*5-14 yrs*" in the period of 2012 to 2018 period were only "*0*" or "*0.01*" "*per 100,000*" as a population average including amongst those at higher risk, the notification rate of acute hepatitis B in 1-14 year olds in the US is negligible.

i. Notification Rates in under 15 year olds

The Plaintiff hereby requests that the Court take judicial notice of the following documents:

- CDC article entitled "Prevention of Hepatitis B Virus Infection in the United States: Recommendations of the Advisory Committee on Immunization Practices", accessible at https://www.cdc.gov/mmwr/volumes/67/rr/pdfs/rr6701-H.PDF (last accessed November 22, 2020) (hereafter "ACIP Hepatitis B Recommendations") A true and correct copy of the aforesaid report is attached hereto as **Exhibit 156**.

- CDC web page headed "People Born Outside of the United States and Viral Hepatitis", accessible at:

  https://www.cdc.gov/hepatitis/populations/Born-Outside-United-States.htm (last accessed November 24, 2020) (hereafter "CDC HBV in US-born Web Page") A true and correct copy of the aforesaid report is attached hereto as **Exhibit 157**.

The CDC Disease Notifications state that the chronic hepatitis B notification rates "*per 100,000*" for the years 2014 to 2015 were those in *italics* in the following table:

Age group (yrs) / *Year*	*< 1*	*1 – 4*	*5 – 14*	Average for 1 - 14 yr olds
2014	*0.41*	*0.22*	*0.24*	0.234
2015	*0.21*	*0.14*[12]	*0.29*	0.247

- **Adjustments to determine rate in non-high risk US residents**

  An assumption will be made in the calculation of DRU for hepatitis B that all of the reported cases were unique and confirmed.

[12] The CDC Disease Notifications states that this rate was "13.99". However that is assumed to be the result of an erroneous multiplication by 100 of the true notification rate. The basis of that assumption is that the stated number of notified cases in 2015 was only "17".

However, this may result in a significant exaggeration of the true rate because the CDC Disease Notifications include the following footnote to those figures:

"Reported cases of chronic hepatitis B… past or present might not reflect unique case reports and might include both confirmed and probable case reports."

Adjustment for where no HBV risk indicated in prior 6 months

The ACIP Hepatitis B Recommendations states:

"In 2015, CDC received 3,370 surveillance case-reports of acute HBV infection. Of 2,207 case-reports with risk information, 1,151 (52.2%) indicated no risk for HBV during the 6 weeks to 6 months prior to illness onset."

It is assumed herein that approximately the same rate as that quoted of "52.2%" applied to chronic hepatitis B infection, for children whose lifestyle showed no risk for hepatitis B infection in the previous 6 weeks to 6 months prior to illness onset.

Adjustment for where "Non-U.S.-born"

The CDC HBV in US-born Web Page states that only about 30% of cases of chronic hepatitis b infections are in people born in the US, as follows:

"Non-U.S.-born people account for 70% of all chronic hepatitis B infections in the United States."

Based upon the above assumption and statement, combined with the above notification rate figures and footnote in the CDC Disease Notifications, the average rates in 2014-15 can be estimated to have been as set out in the following table for children who were born in the US and whose lifestyle showed no risk for hepatitis B infection in the previous 6 weeks to 6 months prior to illness onset:

Age group (yrs) / Year	< 1	1 – 4	5 – 14
Rate	< 1 / 2,067,825	< 1 / 3,562, 243	< ~ 1 / 2,418,965

ii. Notification Rates in under 1 year olds and 15-22 year olds

The objective of the analysis presented in this paragraph 7.8 includes the determination of hepatitis B-related risk in the 15-22 year age group.

However notification data for those aged 1-14 years only is used for the analysis. The reasons for selecting those lower and upper age range limits for analysis are mainly:

- in relation to those aged under 1 year, the contribution of unvaccinated vaccine-eligible infants to the risk during childhood/adolescence is judged to be:
  - difficult to accurately determine, due to limited data of vaccination coverage data and ages in months of cases, but
  - nevertheless relatively low due the limited number of months between the third dose scheduled at 6 months of age and the attainment of one year of age, and
  - limited notification rate in under 1 year olds, and
- in relation to those in the 15-24 year age group, the inflating impact of lifestyle choices of a proportion of that group upon the average of the notification rates for the entire population in that age group. The ACIP Hepatitis B Recommendations states:

  > *"Among adults, HBV is transmitted primarily by percutaneous exposure to blood (e.g., by injection-drug use) and sexual contact. HBV is transmitted efficiently by sexual contact both among heterosexuals and among men who have sex with men (MSM). Risk factors for sexual transmission among heterosexuals include having unprotected sex with an infected partner, having unprotected sex with more than one partner, and a history of another sexually transmitted infection (STI). Risk factors associated with sexual transmission among MSM include having multiple sex partners, history of another STI, and anal intercourse."*

  The resultant hepatitis B-related risks for those who engage in such high risk activities are essentially irrelevant to those who make different, hepatitis B-risk-free lifestyle choices.

  It is assumed herein that the unavoidable risk for those who are aged 15-22 years, and are able to choose to avoid the vast majority of high risk situations, and do choose to avoid them, is similar to or less than the risk for 5-14 year olds. The risk may be less because some 5-14 year olds may be forced by their younger age, as minors, to live or spend time in environments in which they are exposed to risk.

(b) Hepatitis B Vaccination Coverage (VC)

i. Coverage in 1 – 4 year olds

The CDC Daycare Coverage Reports provide estimated coverages overall (averages or medians) for 3 doses of hepatitis B-containing vaccines in 19-35 month olds in the US as set out in the table below:

Year	Hepatitis B Vaccine Coverage % (average)
2011	*91.0*
2012	*89.7*
2013	*90.8*
2014	*91.6*
2015	*92.6*
Average	91.7

Based on the data in the above table, the average coverage for doses of hepatitis B vaccination over the period of 2014-2015 is estimated to have been:

- 91.7% in 1 - 4 year olds.

ii. Coverage in 5 – 14 year olds

The CDC Elementary School Coverage Reports provide estimated vaccination coverages overall (some averages, others medians) for 3 doses of hepatitis b-containing vaccines in Kindergarteners in the US as follows:

School Year	Hepatitis B Vaccine Coverage % (average/median)
2005-2006	*96.0*
2006-2007	*96.8*
2007-2008	96.7 [6]
2008-2009	96.8 [6]
2009-2010	*97.0*
2010-2011	96.8 [6]
2011-2012	*96.6*
2012-2013	96.6 [6]
2013-2014	96.6 [6]
2014-2015	96.6 [6]
2015-2016	96.6 [6]
Average	**96.6**

The CDC Secondary School Coverage Reports provide estimated average vaccination coverages for hepatitis B-containing vaccines in 13 to 14 year olds in the US in 2014-2015 as follows (in *italics*):

Hepatitis B Vaccine Coverage % (Secondary School)

Year	Age 13 yrs		Age 14 yrs	
	%	*(95% CI)*	*%*	*(95% CI)*
2014	*91.3*	*(±1.8)*	*91.7*	*(±1.5)*
2015	*91.0*	*(±1.9)*	*91.8*	*(±1.7)*

Based upon averaging the figures in the above two tables, the average coverage for 3 doses of hepatitis b-containing vaccines over the 2 year period of 2014 to 2015 approximated:

- 94.0% in children aged 5-14 years.

iii. Summary for VC

Based upon the above information in this paragraph 7.8(b), the approximate annual average vaccination coverage for 3 doses of hepatitis b-containing vaccines in the 2 year period of 2014 to 2015 was as set out in the table below for each subject age group:

Age	1-4 yrs	5-14 yrs
VC	91.7%	94.0%

(c) Hepatitis B Vaccination Effectiveness (VE)

The Plaintiff hereby requests that the Court take judicial notice of the following document:

- manufacturer product information named “Engerix-B thiomersal-free vaccine”, made available by the Australian Therapeutic Goods Administration (TGA), accessible via https://www.ebs.tga.gov.au/ebs/picmi/picmirepository.nsf/pdf?OpenAgent&id=CP-2010-PI-06573-3

  (last accessed November 22, 2020)
  (hereafter “Engerix-B Package Insert”)
  A true and correct copy of the aforesaid report is attached hereto as **Exhibit 158**.

The ACIP Hepatitis B Recommendations states:

“The 3-dose HepB vaccine series produces a protective antibody response (anti-HBs ≥10 mIU/mL) in approximately 95% of healthy infants overall (response is lower for infants with lower birth weights)”

and

“*Approximately 16% of persons vaccinated at age <1 year have antibody levels of ≥10 mIU/mL 18 years following vaccination”*

The Engerix-B Package Insert states:

“The seroprotection rates (SP) obtained with the two different dosages and schedules recommended in participants from 11 years up to and including 15 years of age were evaluated up to 66 months after the first dose of the primary vaccination and are presented in Table 2.”

and

in *“Table 2”,* in the row headed *“ENGERIX-B 10 µg (0, 1, 6 months schedule)”,* the following SPs, including in parentheses “*95% confidence interval, (lower limit – upper limit)*“ (CI) for *“specific humoral antibodies (anti-HBs)”* at various stated elapsed months *“after the first dose of the primary vaccination” (*with *“Month 7”* in “*Table 2”* hence being one month after the third dose given at 6 months)*:*

Months	*7*	*30*	*42*	*54*	*66*
SP %	*98.2*	*96.9*	*92.5*	*94.7*	*91.4*
C I	*93.8 - 99.8*	*89.2-99.6*	*84.4 - 97.2*	*87.1 - 98.5*	*82.3 -96.8*

Based upon the statements in these excerpts, the initial and waning seroprotection rates in the case of infants, the seroprotection rate after the three hepatitis B vaccination doses scheduled in the first six months can be estimated to be about 94.5% at 12 months, followed by a decline with a Waning Exponent of approximately 1.226.

Based upon those rates, the approximate average seroprotection rates are:

- 91.6% in 1 to 4 year olds, and
- 67.3% in 5 to 14 year olds.

(d) Serious outcome Rate per Disease case (SRD)

The ACIP Hepatitis B Recommendations states:

"Approximately 25% of persons who become chronically infected during childhood and 15% of those who become chronically infected after childhood will die prematurely from cirrhosis or liver cancer."

Based upon this statement, the SRD for hepatitis B is estimated to be:

- 25% for 1-4 year olds, and
- 20% for 5-14 year olds (half of which age range is in childhood), and
- 15% for 15-22 year olds.

Given that "after childhood" includes much older age groups, and that no adjustment is made in any of these age ranges for how healthy or unhealthy the lifestyles are of those chronically infected, these estimates may be significantly inflated when applied to those who, by choice available to them (or their parents), have or adopt healthier lifestyles than those of others chronically infected.

(e) Differential Risk of unavoidable serious adverse effect (SRIU)

Based upon the calculated estimates presented in this paragraph 7.8, "Hepatitis B" for

(a) the disease notification rate in the population (DRP), and

(b) the vaccination coverage (VC), and

(c) the vaccination effectiveness (VE), and

(d) the rate of serious adverse effects per disease case (SRD),

the approximate differential rates for disease (DRIU) and ultimately serious adverse effects (SRIU) can be calculated by applying the formulas set out in paragraph 6.1, with the results set out in the table below for each age group:

Hepatitis B totals and averages for 2014-2015, approximated

Age Group (yrs)	1 - 4	5-14	15-22	Average / Total
DRP (annual)	< ~ 1 / 3,562,243	< ~ 1 / 2,418,965		
VC	91.7%	94.0%		
VE (residual)	91.6%	67.3%	15.0%	
DRU (annual) [8]	< ~ 1 / 588,784	< ~ 1 / 887,899	< ~ 1 / 887,899*	
DRIU (annual) [8]	< ~ 1 / 642,875	< ~ 1 / 1,319,281	< ~ 1 / 5,934,590	
DRIU total over age range	< ~ 1 / 160,719	< ~ 1 / 131,928	< ~1 / 741,824	**< ~1 / 66,007**
SRD	25%	20%	15%	
SRIU (premature death in long term) associated with infection over age range	< ~ 1 / 642,875	< ~ 1 / 659,641	< ~ 1 / 4,945,492	**< ~ 1 / 305,465**

* See paragraph 7.8(a)ii herein headed “Notification Rates in under 1 year olds and 15-22 year olds”.

(f) Impact of vaccination on others’ susceptibility

The Plaintiff hereby requests that the Court take judicial notice of the following document:

- the CDC “Pink Book” hepatitis B chapter, accessible at https://www.cdc.gov/vaccines/pubs/pinkbook/hepb.html online or https://www.cdc.gov/vaccines/pubs/pinkbook/downloads/hepb.pdf (pdf) (last accessed February 10, 2021)
  (hereafter “CDC Pink Book Hepatitis B Chapter”)
  A true and correct copy of the aforesaid report is attached hereto as **Exhibit 159**.

The CDC Pink Book Hepatitis B Chapter states:

"HBV is transmitted by parenteral or mucosal exposure to HBsAg-positive body fluids from persons who have acute or chronic HBV infection. The highest concentrations of virus are in blood and serous fluids; lower titers are found in other fluids, such as saliva, tears, urine, and semen. Semen is a vehicle for sexual transmission and saliva can be a vehicle of transmission through bites; other types of exposure (e.g., to saliva through kissing) are unlikely modes of transmission. HBsAg is also found in other body fluids (e.g., breast milk, bile, feces, nasopharyngeal washings, and sweat). However, most body fluids are not efficient vehicles of transmission (unless they contain blood) because they contain low quantities of infectious HBV.

In the United States, the most important routes of transmission are injection-drug use, perinatal, and sexual contact with an infected person. Fecal-oral transmission does not appear to occur. However, transmission occurs among men who have sex with men (MSM), possibly via contamination from asymptomatic rectal mucosal lesions. In the 2000s and 2010s, outbreaks of hepatitis B occurred in long-term care facilities (e.g., assisted living facilities and nursing homes) as the result of inadequate infection control practices related to blood glucose monitoring. Transmission occurs in households from persons who have immigrated from endemic areas and who have chronic HBV infection."

Based upon the modes of transmission as described in this excerpt, the vaccination status of childcare and school children is not reasonably likely to have any significant impact upon the risk of others becoming infected, especially beyond the risk of transmission that is avoidable anyway by other means.

7.9 Haemophilus Influenzae type b (Hib) (invasive)

The CDC Schedules state:

"Previously unvaccinated children age 60 months or older who are not considered high risk do not require catch-up vaccination."

On that basis of the stated absence of routine recommendation for Hib vaccination for those aged ≥5 years, the risk analysis herein for Hib vaccination does not include persons over 5 years of age.

(a) Hib notification rate (DRP)

The Plaintiff hereby requests that the Court take judicial notice of the following document:

- the CDC “Pink Book” “Hib” chapter,
  accessible at https://www.cdc.gov/vaccines/pubs/pinkbook/hib.html online or https://www.cdc.gov/vaccines/pubs/pinkbook/downloads/hib.pdf (pdf)
  (last accessed November 17, 2020)
  (hereafter “CDC Pink Book Hib Chapter”)
  A true and correct copy of the aforesaid report is attached hereto as **Exhibit 160**.

The CDC Disease Notifications state that the Hib notifications for the years 2007 to 2018 were as stated in *italics* in the following table:

Age group (yrs) / ***Year***	***< 1***	***1 – 4***	
2007	*14*	*8*	
2008	*18*	*12*	
2009	*24*	*14*	
2010	*11*	*12*	
2011	*8*	*6*	
2012	*16*	*14*	
2013	*19*	*12*	
2014	*25*	*15*	
2015	*21*	*8*	
2016	*19*	*11*	
2017	*17*	*16*	
2018	*27*	*11*	
Total for 2007-2018	**219**	**139**	**358**

The CDC Pink Book Hib Chapter states:

> *“During 2010-2011, 33% of children younger than 5 years of age with confirmed invasive Hib disease were younger than 6 months of age and too young to have completed a three-dose primary vaccination series.”*

Based upon the reported vaccination coverage in 2010-2011 in 1-4 year olds having approximated the average for 2007-2018 (see paragraph 7.9(b) below), and an assumption that it also did for 6-11 month olds, the above stated finding from 2010-2011 of 33% of confirmed invasive Hib cases occurring in children younger than 6 months of age is extrapolated in the analysis presented herein to be estimated to apply to 2007-2018.

Based upon that fact and assumption, it is estimated herein that the average number of notifications of Hib in under 6 month olds in 2007-2018 was approximately 358 x 33% = 118, and hence that that the number of notifications of Hib in 6 – 11 month olds was 219 – 118 = 101.

The estimated notification rates in 6-11 month olds and 1-4 year olds are hence as stated in the table below:

Based upon the above figures and the Population Tables, the average annual invasive Hib notification rate (DRP) in 6 month to 4 year olds in 2007-2018 was approximately:

Age group (yrs)	***6 – 11 mos***	***1 – 4 yrs***	**Average for *6 mos* - 4 yr olds**
DRP	1 / 236,431	1 / 1,384,900	< 1 / 900,000

(b) Hib Vaccination Coverage (VC)

According to the CDC Schedules, the CDC recommendation for full series of Hib vaccination in the US in 2006-2018 was for either:

- a 4-dose series at "*2 months*", "*4 months*" and "*6 months*" ("primary course") and at "*>12*" or "*12–15" "months*" of age, or
- a 3-dose series at "*2 months*" and "*4 months*" ("primary course") and at "*>12*" or "*12–15" "months*" of age.

i. Coverage in 6 month – 11 month olds (two doses)

It shall be assumed herein that the vaccination coverage for the primary course of Hib vaccination in 6-11 month old infants in 2006-2018 has been approximately the same as the coverage for three DTaP vaccine doses, which is taken herein to be less than approximately 86% (see paragraph 7.1(b)i).

Hence it shall be assumed herein that for the 2007-2018 period overall:

- the coverage for the primary course of Hib vaccination in 6 – 11 month olds was less than approximately 86%.

ii. Coverage in 1 – 4 year olds

The Plaintiff hereby requests that the Court take judicial notice of the following document:

- CDC web page headed "Figure Depicting Coverage with Individual Vaccines from the Inception of NIS, 1994 Through 2012".

accessible at: https://www.cdc.gov/vaccines/imz-managers/coverage/nis/child/figures/2012-map.html
(last accessed November 30, 2020)
(hereafter "CDC Vaccination Coverage 1994-2012 Web Page")

A true and correct copy of the aforesaid article is attached hereto as **Exhibit 161**.

The CDC Daycare Coverage Reports and CDC Vaccination Coverage 1994-2012 Web Page provide estimated coverages overall (averages or medians) for the primary course and final dose of Hib-containing vaccines in 19-35 month olds in the US as set out in the table below:

Year	Hib Vaccine Coverage (average) %	
	Primary Course	Full course
2005	*93.9*	*54.8*
2006	*93.3*	*54.8*
2007	*92.7*	*54.8*
2008	*90.9*	*54.8*
2009	*92.1*	*54.8*
2010	*92.2*	*66.8*
2011	*94.2*	*80.4*
2012	*94.3*	*80.9*
2013	*93.7*	*82.0*
2014	*93.3*	*82.0*
2015	*94.3*	*82.7*
2016	*92.8*	*81.8*
2017	*92.8*	*80.7*
2018	*92.8* [6]	*80.7* [6]
Average	**93.1**	**70.9**

Based on the data in the above table, the average coverage for Hib vaccination over the period of 2007-2018 is estimated to have been approximately:

- 93.1% in 1 - 4 year olds for the primary course, and
- 70.9% in 1 - 4 year olds for the full course.

iii. **Summary for VC**

Based upon the above information in this paragraph 7.9(b), the approximate average vaccination coverage for Hib-containing vaccines in 2016-2018 was as set out in the table below for each subject age group:

Age	6-11 months (Primary course)	1-4 yrs	
		Primary Course	Full Course
VC	< 86%	93.1%	70.9%

(c) Hib Vaccination Effectiveness (VE)

The Plaintiff hereby requests that the Court take judicial notice of the following documents:

- article entitled "Antigen Review for the New Zealand National Immunisation Schedule: Haemophilus influenza [sic] type b"

  Citation: Carter P, Turner N, Poole T, Petousis-Harris H and Nowlan M. Prepared for: New Zealand Ministry of Health by a scientific team incorporating the Immunisation Advisory Centre, University of Auckland Institute of Environmental Science and Research Ltd, March 1, 2015, accessible at https://www.immune.org.nz/sites/default/files/publications/Ebook%20Hib%20antigen%20review%202012.pdf
  via https://www.immune.org.nz/2012-antigen-review-new-zealand-national-immunisation-schedule-haemophilus-influenzae-type-b
  (last accessed 30 November 2020)
  (hereafter "NZ Hib Review")

  A true and correct copy of the NZ Hib Review is attached hereto as **Exhibit 162**.

  The NZ Hib Review states:

  > *"Vaccines against H. influenzae serogroup b (Hib) have been developed using the polyribosylribitol (PRP) capsule polysaccharide as the immunogen":*

i. Effectiveness in 6 – 11 month olds (after primary course only)

The NZ Hib Review states:

"A systematic review of studies examining Hib conjugate vaccines estimated effectiveness of 95% after three doses of vaccine. Antibody levels against PRP are known to decline between the primary series of vaccinations and the booster dose"

and

"Recent publications have shown that the percentage of infants aged 12 – 15 months with protective levels of antibody prior to a booster is between 65% and 82%".

Based upon these excerpts, the initial effectiveness of the primary course is 95%, and the Waning Exponent is between 1.7 and 2.3 per month.

Hence, assuming that the average effectiveness over the 6-11 age range is approximately the same or equivalent to that resulting from an initial effectiveness of 95% at approximately 6 months of age with a subsequent Waning Exponent of between 1.7 and 2.3 per month, it may be estimated that the approximate average effectiveness of the Hib vaccine is:

- 86.7% to 91.0% in 6 to 11 month olds.

ii. Effectiveness in 1 – 4 year olds (after final dose)

a. Seroprotection rate

The NZ Hib Review states:

"Measurement of anti-PRP antibody levels, two years following a booster dose of HibMenC-TT, showed nearly all participants (98.7%) maintained protective levels of anti-PRP antibody.
Long term persistence of anti-PRP antibodies was measured in infants who have received a booster dose of HibMenC-TT vaccine. All participants who received the booster vaccine had protective levels of antibody at five years of age (22).
A similar study measuring the antibody levels following a booster dose of HibMenC-TT at 12 – 15 months of age showed 98% of participants had protective antibody levels two years following the booster dose (59)."

Based upon this excerpt, the seroprotection rate of the final dose of Hib vaccine, which applies at around 6 months of age, is 95%, and the Waning Exponent is between 1.7 and 2.3 quarterly.

Hence it may be estimated that the approximate average effectiveness of the booster Hib vaccine is no higher than:

- 98.7% in 1 to 4 year olds.

For those who did not receive the booster dose, the residual effectiveness from the primary course in infancy can be estimated, based upon the estimate of initial and waning rate stated in the previous paragraph 7.9(c)i to have been:

- 9.3% to 18.9% in 1 – 4 year olds.

Combining these estimates for the booster and residual effectiveness results in an overall vaccination effectiveness of

- < 79.6% in 1 - 4 year olds.

b. Effectiveness

The CDC Pink Book Hib Chapter states:

"In the prevaccine era, most children acquired immunity by age 5 or 6 years through asymptomatic nasopharyngeal carriage of Hib bacteria"

and similarly

"Children 60 months of age and older account for less than 10% of invasive disease. The presumed reason for this age distribution is the acquisition of immunity to Hib with increasing age."

Based upon the stated development of natural immunity asymptomatically in most unvaccinated children, effectiveness of vaccination is less than the seroprotection rate. Numerically translated, if it is assumed that all of those who are seroprotected are actually protected, then the effectiveness % is:

(d) Serious outcome Rate per Disease case (SRD)

i. SRD for hospitalization

The CDC Pink Book Hib Chapter states:

"Invasive Hib disease generally requires hospitalization."

Based upon this statement, the SRD hospitalization rate per case is close to, or approximately, 100%.

ii. **SRD for death**

The Plaintiff hereby requests that the Court take judicial notice of the following document:

- article entitled "Worldwide Haemophilus influenzae Type b Disease at the Beginning of the 21st Century: Global Analysis of the Disease Burden 25 Years after the Use of the Polysaccharide Vaccine and a Decade after the Advent of Conjugates".

  Citation: Peltola H. Clin Microbiol Rev. 2000;13(2):302-317. doi:10.1128/cmr.13.2.302-317.2000, accessible at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC100154/pdf/cm000302.pdf (last accessed November 30, 2020)

  (hereafter "Peltola Hib SRD Article")

  A true and correct copy of the aforesaid article is attached hereto as **Exhibit 163**.

The Peltola Hib SRD Article states:

"Prior to the introduction of Hib vaccination, the fatality rates for Hib were approximately 1 per 100,000 cases among children 1-14 years of age, 2.7 per 100,000 cases among persons 15-19 years of age."

and includes a table headed:

"TABLE 3

*Estimated worldwide yearly toll of invasive Hib infections before the conjugate vaccine era ***"***

which contains the selected columns and rows below:

Disease	***Developed regions***
	0–4-yr-old children
No. of cases including pneumonia	*53,000*
No. of deaths including pneumonia	*2,000*

Based upon the estimates quoted in the above table, the case fatality rate (SRD for death) in 0 to 4 year olds is approximately 2000 ÷ 53,000 = 3.77%

(e) Differential Risk of unavoidable serious adverse effect (SRIU)

Based upon the calculated estimates presented in this paragraph 7.9 "Hib", for

(a) the disease notification rate in the population (DRP), and

(b) the vaccination coverage (VC), and

(c) the vaccination effectiveness (VE), and

(d) the rate of serious adverse effects per disease case (SRD),

the approximate differential rates for disease (DRIU) and ultimately serious adverse effects (SRIU) can be calculated by applying the formulas set out in paragraphs 6.1 and 6.3, with the results set out in the table below for each age group.

Hib (invasive) totals and averages for 2014-2018 (approx.)

Age	6 – 11 mos	1 – 4 yrs		Average / Total
		Booster	Residual from primary	
DRP (annual)	1 / 236,431	1 / 1,384,900 (average)		< 1 / 900,000
VC	~ 86%	70.9% ("VC1")	93.1% ("VC2")	
VE	< 91.0%	≤ 98.7% ("VE1")	< 18.9% ("VE2")	
		< 79.6%		
DRU (annual)	< 1 / 51,487	< 1 / 358,104		
DRIU (annual)	< 1 / 56,605	< 1 / 449,635		
DRIU (=SRIU) total over age range	< 1 / 113,211	< 1 / 112,409		**< 1 / 56,400**
SRD - (hospitalization)	100%			
SRIU - (hospitalization)	< 1 / 113,211	< 1 / 112,409		**< 1 / 56,400**
SRD - (death) (case fatality rate)	3.77%			
SRIU - (death)	**< 1 / 3,000,000**	**< 1 / 3,000,000**		**< 1 / 1,500,000**

7.10 Pneumococcal disease (invasive) (IPD)

The Plaintiff hereby requests that the Court take judicial notice of the following document:

- the CDC "Pink Book" "IPD" chapter, accessible at https://www.cdc.gov/vaccines/pubs/pinkbook/pneumo.html (html) or https://www.cdc.gov/vaccines/pubs/pinkbook/downloads/pneumo.pdf (pdf) (last accessed November 17, 2020) (hereafter "CDC Pink Book IPD Chapter")

A true and correct copy of the aforesaid report is attached hereto as **Exhibit 164**.

The risk analysis presented herein for IPD is restricted to IPD caused by any of the 13 serotypes targeted by the pneumococcal conjugate vaccine called “PCV13”. Hereafter, IPD caused by any of those serotypes will be referred to as “IPD13”.

The CDC Pink Book IPD Chapter states:

“Routine use of PCV13 is not recommended for healthy children 5 years of age or older.”

On that basis of the stated absence of routine recommendation for IPD vaccination for those aged 5 years or older, the risk analysis herein for IPD also excludes those persons.

(a) IPD notification rate (DRP) in 6 month to 4 year olds

The Plaintiff hereby requests that the Court take judicial notice of the following document:

- the CDC web page headed “Pneumococcal Disease” “Surveillance and Reporting”, subheaded “Trends”, accessible at https://www.cdc.gov/pneumococcal/surveillance.html
  (last accessed December 6, 2020)
  (hereafter “CDC IPD Surveillance and Reporting Web Page”)
  A true and correct copy of the aforesaid report is attached hereto as **Exhibit 165**

- article entitled “Global review of the distribution of pneumococcal disease by age and region”, accessible at https://www.who.int/immunization/sage/6_Russel_review_age_specific_epidemiology_PCV_schedules_session_nov11.pdf

  Citation: F Russell, C Sanderson, B Temple, K Mulholland. World Health Organization, Geneva (2011)
  (last accessed December 6, 2020)
  (hereafter “WHO Review of IPD Age Distribution”)
  A true and correct copy of the aforesaid report is attached hereto as **Exhibit 166**.

i. Notification rates for IPD caused by all serotypes

The CDC Disease Notifications state that the IPD notification rates "*per 100,000*" for the years 2014 to 2018 were as stated in *italics* in the following table:

Age group (yrs) / ***Year***	***< 1***	***1 – 4***
2014	*12.78*	*5.75*
2015	*12.34*	*5.73*
2016	*12.86*	*5.75*
2017	*14.39*	*6.09*
2018	*12.83*	*5.64*

Based upon the figures in the above table and the Population Tables, the average number of IPD cases in 2014-2018 can be estimated to have been:

- 512 in < 1 olds, and
- 924 in 1-4 year olds,

Totaling these numbers results in an annual average of 1,436 cases in under 5 year olds.

ii. Percentage of IPD cases in over 6 month olds

The WHO Review of IPD Age Distribution states:

"A case of IPD was defined as: a child with pneumococcus isolated from a normally sterile site, such as blood, cerebrospinal fluid (CSF), or pleural fluid."

and

"The aims are to:

• Determine whether the distribution of IPD in children in the first 5 years of life varies significantly between regions"

and

"IPD and pneumococcal meningitis data were collated from the following sources:… A comprehensive global IPD burden of disease review… published in 2009 which included data obtained between 1980 and 2005 from 164 sources (6)… For data published from January 2006 to June 2011, surveillance sites supported by the pneumoADIP… or other known research sites… Cases and deaths in the control group from the phase 3 PCV randomized controlled trials from… the US Kaiser Permanente studies".

and

"A model was constructed to estimate the proportional risk by month for the period 0-59m of age for regions and selected countries".

Under the heading "*Results*:", the WHO Review of IPD Age Distribution states:

"Of all the cases of IPD in children aged 0-59m, about 20% of cases occur in infants aged <6m."

and

"There is not convincing evidence of major differences between or within regions with respect to the age distribution of cases of IPD."

Based upon these excerpts, the number of IPD cases in under 6 month olds, which will be excluded from the risk analysis presented herein, is estimated to be about 20% of all IPD cases in under 5 year olds in 2014-2018.

Applying that adjustment (subtraction of 20%) to the results stated in paragraph 7.10(a)i above, the IPD notification number and rate applicable to 6-11 month olds can be estimated by subtracting 20% of the 1,436 average cases in under 5 year olds (=287) from the number of IPD cases in under 1 year olds (512), which results in an annual average over the years 2014-2018 of approximately:

- (512 – 287 =) 225 IPD cases in 6-11 month olds.

iii. Percentage of IPD that is IPD13

The CDC IPD Surveillance and Reporting Web Page states:

"Following the introduction of the pneumococcal conjugate vaccines in the United States (PCV7 in 2000 and PCV13 in 2010)… among children less than 5 years old… Overall, invasive pneumococcal disease decreased… to 9 cases per 100,000 in 2015. Invasive pneumococcal disease caused by the 13 serotypes covered by PCV13 decreased…to 2 cases per 100,000 people in 2015."

Based upon this statement, in 2015, among children less than 5 years old, the percentage of IPD cases caused by the 13 serotypes covered by the pneumococcal conjugate vaccine called "PCV13" was 2 ÷ 9 = 22%.

It is assumed in the analysis presented herein that approximately the same percentage of 22% in 2015 applied overall to under 5 year olds for the whole period of 2014-2018.

This assumption receives support from "*Figure 1*" on the CDC IPD Surveillance and Reporting Web Page, which states that the "*Cases per 100,000*" for "*children aged <5 years old*" numbered "*9*" for "*All IPD*" for each of the years "*2012*", "*2014*", "*2015*" and "*2016"* (and *"10" for "2013"),* and numbered "*2*" for "*PCV13 type*" for each of the years "*2012*" through "*2016"*.

Applying that adjustment (multiplication by 22%) to the results stated in paragraph 7.10(a)ii above for 6-11 month olds and paragraph 7.10(a)i above for 1-4 year olds, the IPD13 notifications can be estimated by multiplying the 225 and 924 average cases in 6-11 month and 1-4 year olds respectively each by 22%, which results in an annual average over the years 2014-2018 of approximately:

- (225 x 22% =) 50 IPD13 cases in 6-11 month olds, and
- (924 x 22% =) 205 IPD13 cases in 1-4 year olds.

iv. Resultant DRP in 6 month to 4 year olds

Based upon the above figures in this paragraph 7.10(a) and the Population Tables, the average annual IPD13 notification rate (DRP) in 6 month to 4 year olds in 2014-2018 was approximately:

Age group (yrs)	6 – 11 mos	1 – 4 yrs	Average for *6 mos* - 4 yr olds
DRP	1 / 39,304	1 / 77,682	1 in 70,078

(b) PCV13 Vaccination Coverage (VC)

According to the CDC Schedules, the CDC recommendation for full series of PCV13 vaccination in the US in 2012-2018 was for:

- a 4-dose series at "*2 months*", "*4 months*" and "*6 months*" ("primary course") and at "*12 months"* to *"15 months*" of age.

i. Coverage in 6 month – 11 month olds (two doses)

It shall be assumed herein that the vaccination coverage for the primary course of PCV13 vaccination in 6-11 month old infants in 2014-2018 was approximately the same as the coverage for three DTaP vaccine doses, which is taken herein to be less than approximately 86% (see paragraph 7.1(b)i).

Hence it shall be assumed herein that for the 2014-2018 period overall:

- the coverage for the primary course of PCV13 vaccination in 6 – 11 month olds was less than approximately 86%.

ii. Coverage in 1 – 4 year olds

The CDC Daycare Coverage Reports and CDC Vaccination Coverage 1994-2012 Web Page provide estimated coverages overall (averages or medians) for the primary course and final dose of PCV13 vaccine in 19-35 month olds in the US as set out in *italics* in the table below:

	PCV13 Vaccine Coverage (average) %	
Year	Primary Course	Full course
2012	*92.3 (±0.8)†*	*81.9 (±1.1)†*
2013	*92.4 (91.4–93.3)*	*82.0 (80.6–83.3)*
2014	*92.6 (91.8–93.4)*	*82.9 (81.6–84.2)*
2015	*93.3 (92.5–94.0)*	*84.1 (83.0–85.2)*
2016	*91.8 (90.8–92.7)§*	*81.8 (80.4–83.1)§*
2017	*91.9 (90.9–92.8)*	*82.4 (81.1–83.6)*
2018	91.9 [6]	82.4 [6]
Average	**92.3**	**82.5**

Based on the data in the above table, the average coverage for IPD vaccination over the period of 2007-2018 is estimated to have been approximately:

- 92.3% in 1 - 4 year olds for the primary course, and
- 82.5% in 1 - 4 year olds for the full course.

iii. Summary for VC

Based upon the above information in this paragraph, the approximate average vaccination coverage for PCV13 vaccine in 2014-2018 was as set out in the table below for each subject age group:

Age	**6-11 months (Primary course)**	**1-4 yrs**	
		Primary Course	**Full Course**
VC	< 86%	92.3%	82.5%

(c) PCV13 Vaccination Effectiveness (VE)

The Plaintiff hereby requests that the Court take judicial notice of the following documents:

- section entitled “Executive Summary” in “The Evidence Base for Pneumococcal Conjugate Vaccines (PCVs): Data for decision-making around PCV use in childhood”,

  Citation: Prepared by International Vaccine Access Center, Johns Hopkins University Bloomberg School of Public Health. January 2017, accessible at https://www.jhsph.edu/ivac/wp-content/uploads/2018/05/PCVEvidenceBase-Jan2017.pdf
  (last accessed December 8, 2020)
  (hereafter “IVAC PCV Article”)

  A true and correct copy of the IVAC PCV Analysis is attached hereto as **Exhibit 167**.

- article entitled “Effectiveness of 13-valent pneumococcal conjugate vaccine for prevention of invasive pneumococcal disease in children in the USA: a matched case-control study”

  Citation: Moore MR, Link-Gelles R, Schaffner W, Lynfield R, Holtzman C, Harrison LH, Zansky SM, Rosen JB, Reingold A, Scherzinger K, Thomas A, Guevara RE, Motala T, Eason J, Barnes M, Petit S, Farley MM, McGee L, Jorgensen JH, Whitney CG. Lancet Respir Med. 2016 May;4(5):399-406. doi: 10.1016/S2213-2600(16)00052-7. Epub 2016 Mar 14. PMID: 26987984, accessible at https://pubmed.ncbi.nlm.nih.gov/26987984/
  (last accessed December 12, 2020)
  (hereafter “Moore IPD Effectiveness Study”)
  A true and correct copy of the aforesaid report is attached hereto as **Exhibit 168**.

The IVAC PCV Article states under the heading “Executive Summary”:

> *“There are limited data on the duration of protection following PCV administration. The natural history of pneumococcus, with declining NP colonization prevalence after the first few years of life, and the role of natural immune system boosting following exposure to circulating serotypes complicate the interpretation of long-term follow up studies comparing immunized and unimmunized children.”*

Based upon this statement, there is limited data regarding the effectiveness of PCV13 vaccination over the material age range and hence the following

estimates of effectiveness, and the consequent results of level of benefit of the vaccination, must be interpreted with caution.

i. Maximum Effectiveness

The Plaintiff hereby requests that the Court take judicial notice of the following document:

- article entitled "Efficacy, Safety, and Immunogenicity of Heptavalent Pneumococcal Conjugate Vaccine in Children"

  Citation: Black S, Shinefield H, Fireman B, et al. Northern California Kaiser Permanente Vaccine Study Center Group. Pediatr Infect Dis J. 2000;19:187–195, accessible at http://ajmc.s3.amazonaws.com/_media/_pdf/AMSub10_2000jlBlackS536_49.pdf
  (last accessed December 8, 2020)
  (hereafter "Black PCV7 Clinical Trial Article")

  A true and correct copy of the Black PCV7 Clinical Trial Article is attached hereto as **Exhibit 169**.

The Black PCV7 Clinical Trial Article states:

"The Wyeth Lederle heptavalent CRM197 PCV was given to infants at 2, 4, 6 and 12 to 15 months of age in a double-blind trial; 37,868 children were randomly assigned 1:1 to receive either the pneumococcal conjugate vaccine, or meningococcus type C CRM197 conjugate... We report the results of the Kaiser Permanente trial evaluating the efficacy, safety, and immunogenicity of the heptavalent pneumococcal conjugate vaccine (Wyeth; PNCRM7) conducted in Northern California between October 1995 and August 1998 and the posttrial blinded efficacy follow-up through April 20, 1999"

and:

"A child younger than 16 months of age was considered fully vaccinated if the child had received 3 or more doses of vaccine, and a child 16 months of age or older was considered fully vaccinated after receipt of a fourth dose of vaccine."

and:

"18,927 received 1 or more doses of pneumococcal conjugate… Of the children who received at least 1 dose of pneumococcal conjugate vaccine, 17,174 received at least 2 doses, …15,565 received at least 3 doses, and 10,940 received at least 4 doses."

and

"there were 40 fully vaccinated cases of invasive disease caused by vaccine serotypes, of which 39 had occurred in controls, for an efficacy of 97.4% (95% confidence interval, 82.7% to 99.9%; P < 0.001)"

The CDC Pink Book IPD Chapter states:

"In a large clinical trial, PCV7 was shown to reduce invasive disease caused by vaccine serotypes by 97%.... PCV13 was licensed in the United States based upon studies that compared the serologic response of children who received PCV13 to those who received PCV7. These studies showed that PCV13 induced levels of antibodies that were comparable to those induced by PCV7 and shown to be protective against invasive disease."

It is assumed that the "*large clinical trial*" that the CDC Pink Book IPD Chapter describes in stating that "*PCV7 was shown to reduce invasive disease caused by vaccine serotypes by 97%*" is the Black PCV7 Clinical Trial.

The Moore IPD Effectiveness Study states:

"We did an individually matched case-control study of PCV13 effectiveness against invasive pneumococcal disease… Cases in children aged 2–59 months were identified through active surveillance… Among children receiving the full four-dose schedule recommended by the Advisory Committee on Immunization Practices (ACIP), only four discordant pairs were identified, leading to estimated vaccine effectiveness of 90·4% (95% CI 7·6 to 99)."

Based upon the above statements in the Black PCV7 Clinical Trial Article, the CDC Pink Book IPD Chapter and the Moore IPD Effectiveness Study, it is estimated that for the PCV13-targeted serotypes, the initial protection rate of PCV13 is approximately 99.3% and Waning Exponent 1.65 half-yearly.

Based upon these figures, the estimated average effectiveness against the targeted serotypes is:

- 99.1% over the 6-11 month age range, and
- 90.4% over the 1-4 year age range.

ii. **Overall protectiveness may be significantly lower**

a. Flaws in selection of control and test groups

Based upon the first of the above excerpts from the Black PCV7 Clinical Trial Article, the "control group" in the study that it describes did not receive an inert injection, simulating the real world in which an unvaccinated child receives no vaccination in place of the test vaccine. Instead, the "control group" received a "meningococcus type C CRM197 conjugate" vaccine ("MnCC"), which the article did not state had been licenced or been demonstrated to not increase susceptibility to other bacterial infections such as pneumococcal.

Hence the "effectiveness" result was only a relative effectiveness compared to the effect of an apparently experimental vaccine on the risk of IPD. To any extent that MnCC did have the non-specific effect of provoking or increasing susceptibility to invasive bacterial infections such as IPD, the effectiveness of MnCC was negative and hence the relative effectiveness result for PCV7 was inflated.

The Moore IPD Effectiveness Study also stated:

> *"Any dose of PCV7 or PCV13 given… at least 2 weeks before the culture date of the case was considered valid"*

Based upon this excerpt, any case of pneumococcal disease that developed within 2 weeks after vaccination was excluded. So this was another study design feature that potentially inflated the effectiveness results.

(d) Serious outcome Rate per Disease case (SRD)

i. SRD for any SAE

Based upon the level of seriousness of IPD (the disease being "invasive"), the value of SRD for IPD is taken herein to be the same as the DRP, and hence the SRIU the same as the DRIU.

ii. SRD for hospitalization

The Plaintiff hereby requests that the Court take judicial notice of the following document:

- article entitled “Invasive Pneumococcal Disease in Young Children Before Licensure of 13-Valent Pneumococcal Conjugate Vaccine --- United States, 2007”.

  Citation: CDC MMWR 2010 (March 12);59(09):253-257, accessible at: https://www.cdc.gov/mmwr/pdf/wk/mm5909.pdf
  (last accessed December 14, 2020)
  (hereafter “CDC IPD SRD Article”)

  A true and correct copy of the aforesaid article is attached hereto as **Exhibit 170**.

The CDC IPD SRD Article states:

“In 2007,… information on hospitalization and clinical outcome was available for 99% of serotyped IPD cases. Among 272 children with IPD caused by serotypes covered by PCV13 for whom hospitalization status, clinical presentation, and outcome were known, 168 (62%) were hospitalized.”

Based upon this statement, the SRD hospitalization rate per IPD case is approximately 61.76%.

iii. **SRD for death**

The CDC Pink Book IPD Chapter states:

“Before routine use of pneumococcal conjugate vaccine… among children younger than 5 years of age… An estimated 17,000 cases of invasive disease occurred each year… An estimated 200 children died every year as a result of invasive pneumococcal disease.”

Based upon this excerpt, the IPD case fatality rate in unvaccinated children is approximately 200 ÷ 17000 = 1.176%.

(e) Differential Risk of unavoidable serious adverse effect (SRIU)

Based upon the calculated estimates presented in this paragraph 7.10 “IPD”, for

(a) the disease notification rate in the population (DRP), and

(b) the vaccination coverage (VC), and

(c) the vaccination effectiveness (VE), and

(d) the rate of serious adverse effects per disease case (SRD),

the approximate differential rates for serious adverse effects SRIU can be calculated by applying the formulas set out in paragraphs 6.1 and 6.3, with the results set out in the table below for each age group.

Invasive Pneumococcal Disease totals and averages for 2014-2018 (approx.)

Age	6 – 11 mos	1 – 4 yrs		Average / Total
		After 4th dose	Residual from 3 doses	
DRP (annual)	1 / 39,304	1 / 77,682 (average)		< 1 / 70,000
VC	~ 86%	82.5% ("VC1")	9.8% ("VC2")	
VE	< 99.1%	≤ 90.4% ("VE1")	< 85.3% ("VE2")	
		< 89.9%		
DRU (annual)	< 1 / 5,816	< 1 / 13,245		
DRIU (annual)	< 1 / 5,870	< 1 / 14,649		
DRIU (=SRIU) total over age range	< 1 / 11,740	< 1 / 3,662		**< 1 / 2,800**
SRD - (hospitalization)	< 62%			
SRIU - (hospitalization)	< 1 / 18,935	< 1 / 5,907		**< 1 / 4,500**
SRD - (death) (case fatality rate)	1.18%			
SRIU - (death)	**< 1 / 1,000,000**	**< 1 / 310,000**		**< 1 / 236,500**

7.11 Meningococcal disease (invasive) ("IMD") (serogroups A, C, W and Y)

The Plaintiff hereby requests that the Court take judicial notice of the following document:

- the CDC "Pink Book" "IMD" chapter, accessible at https://www.cdc.gov/vaccines/pubs/pinkbook/mening.html (html) or https://www.cdc.gov/vaccines/pubs/pinkbook/downloads/mening.pdf (pdf)
  (last accessed December 26, 2020)
  (hereafter "CDC Pink Book IMD Chapter")
  A true and correct copy of the aforesaid report is attached hereto as **Exhibit 171**.

Any reference herein to "IMD" means IMD caused by any of the four serogroups A, C, W and Y, unless stated otherwise. Meningococcal vaccines that were available in the US for the relevant age groups in the period under analysis, which is selected herein to be 2012-2015, are collectively referred to as "MenACWY".

The CDC Schedule 2020 states the following:

> *"Meningococcal serogroup A,C,W,Y vaccination*
> *(…[MenACWY-CRM, Menveo], …[MenACWY-D, Menactra])*
>
> *Routine vaccination*
>
> - *2-dose series at 11–12 years, 16 years*
>
> *Catch-up vaccination*
>
> - *Age 13–15 years: 1 dose now and booster at age 16–18 years (minimum interval: 8 weeks)*
> - *Age 16–18 years: 1 dose…*
>
> *First-year college students who live in residential housing (if not previously vaccinated at age 16 years or older) or military recruits:*
>
> - *1 dose Menveo or Menactra"*

and the CDC Pink Book IMD Chapter states:

> *"Antibody persistence studies indicate that circulating antibody declines 3 to 5 years after a single dose of Menactra or Menveo (MenACWY). In addition, results from a vaccine effectiveness study demonstrate waning effectiveness, and many adolescents are not protected 5 years after vaccination."*

Based upon the above excerpts from the CDC Schedule 2020 and the CDC Pink Book IMD Chapter, the IMD and MenACWY analysis herein is restricted to the age range of 11-20 years inclusive, in particular the age groups of 11-15 years, 16-17 years and 18-20 years.

(a) IMD notification rates (DRP)

The Plaintiff hereby requests that the Court take judicial notice of the following document:

- article entitled "Current Epidemiology and Trends in Meningococcal Disease—United States, 1996–2015", accessible at https://academic.oup.com/cid/article-pdf/66/8/1276/25084908/cix993.pdf

  Citation: Jessica R MacNeil, Amy E Blain, Xin Wang, Amanda C Cohn, *Clinical Infectious Diseases*, Volume 66, Issue 8, 15 April 2018, Pages 1276–1281, https://doi.org/10.1093/cid/cix993
  (last accessed January 1, 2021)
  (hereafter "Meningococcal Notification Article")
  A true and correct copy of the aforesaid report is attached hereto as **Exhibit 172**.

i. IMD Notification rates in 11 to 15 year olds

The Meningococcal Notification Article includes a table headed:

"Table 2.

Meningococcal Disease Cases, Incidence, and Percentage Change by Age Group and Serogroup, National Notifiable Diseases Surveillance System, United States, 2006–2015"

hereafter the "Meningococcal Notification Table",
which contains the following selected columns and rows:

Age, y	*2012–2013*		*2014–2015*	
	No. of Cases	*(Incidence)*	*No. of Cases*	*(Incidence)*
11–15	*6*	*(0.01)*	*3*	*(0.01)*

Based upon the figures in the above table and the Population Tables the notification rate of IMD in 2012-15 was approximately

- 1 in 9,215,892 in the 11-15 year age group.

ii. IMD Notification rates in 16 to 17 year olds

The Meningococcal Notification Table also contains the following selected columns and rows:

Age, y	*2012–2013*		*2014–2015*	
	No. of Cases	*(Incidence)*	*No. of Cases*	*(Incidence)*
16–20	*34*	*(0.08)*	*11*	*(0.03)*

Based upon the figures in the above table and the Population Tables, and an assumption that the notification rate in 16-17 year olds is similar to that in 18-20 year olds, the notification rate of IMD in 2012-15 was approximately:

- 1 in 1,905,453 in the 16-17 year age group.

iii. IMD Notification rates in 18 to 20 year olds

Based upon the same figures and assumption stated in the previous paragraph 0(a)ii, the notification rate of IMD in 2012-15 was approximately:

- 1 in 1,905,453 in the 18-20 year age group.

iv. Summary for DRP

Summarising the above figures in this paragraph 0(a), the average annual IMD notification rates (DRP) in 11-20 year old US residents in 2012-2015 were approximately as stated in the table below:

Age group (yrs)	**11 – 15 yrs**	**16 – 17 yrs**	**18 – 20 yrs**
DRP	1 in 9,215,892	1 in 1,905,453	1 in 1,905,453

(b) IMD Vaccination Coverage (VC)

The Plaintiff hereby requests that the Court take judicial notice of the following document:

- article entitled “Meningococcal Vaccination: Recommendations of the Advisory Committee on Immunization Practices, United States, 2020”

  Citation: Mbaeyi SA, Bozio CH, Duffy J, et al. CDC MMWR Recomm Rep 2020;69(No. RR-9):1–41. DOI: http://dx.doi.org/10.15585/mmwr.rr6909a1, accessible at https://www.cdc.gov/mmwr/volumes/69/rr/pdfs/rr6909a1-H.pdf (last accessed December 25, 2020)
  (hereafter “ACIP Current MenACWY Recommendations Article”)

  A true and correct copy of the ACIP Current MenACWY Recommendations Article is attached hereto as **Exhibit 173.**

A reference to “general population” within this paragraph 0(b) excludes college students vaccinated because of college enrolment requirements.

The ACIP Current MenACWY Recommendations Article states:

“BOX 2. Timeline of meningococcal vaccine licensure and recommendations, United States, 2005—2020

2005

… ACIP recommended routine vaccination of adolescents with a single MenACWY-D dose at age 11–12 years…

2007

… ACIP recommended vaccination for all adolescents aged 11–18 years….

2010

… ACIP added a MenACWY booster dose at age 16 years…

Abbreviations: ACIP = Advisory Committee on Immunization Practices; … MenACWY-D = meningococcal groups A, C, W, and Y polysaccharide diphtheria toxoid conjugate vaccine (Menactra).”

According to the Vaccination Coverage Reports, the coverage estimates (omitting the confidence intervals) for:

- at least one dose of MenACWY vaccination in 13-17 year olds was the following for the years 2006-2015:

Year	Age at interview (yrs) 13	14	15	16	17
2006	*11.3*	*12.5*			
2007	*32.6*	*31.6*	*33.9*		
2008	*42.0*	*43.0*	*46.4*	*40.5*	
2009	*53.8*	*56.1*	*54.6*	*54.4*	*48.8*
2010	*63.8*	*66.6*	*64.0*	*61.8*	*57.1*
2011	*71.4*	*72.0*	*71.1*	*69.5*	*68.5*
2012	*72.5*	*73.4*	*75.3*	*74.6*	*74.2*
2013	*76.1*	*78.2*	*80.0*	*77.8*	*76.7*
2014	*78.0*	*81.0*	*79.2*	*79.4*	*78.8*
2015	*79.2*	*81.9*	*81.3*	*81.4*	*82.5*

(hereafter "MenACWY First Dose Coverage Table")

For the purposes of estimating the coverages:

- in 11 and 12 year olds in each of the years 2006 through 2015, it shall be assumed that in the case of each of those two year groups, the same number of persons were vaccinated as 13 year olds between the relevant year and the following year (when the latter group progressed to become 14 year olds), and
- in 11-13 year olds in 2005 when it is stated that routine MenACWY vaccination was first recommended, it shall be assumed that the coverage in each year group was about half of that in the progressed age group in 2006.

- two doses of MenACWY vaccination in 17 year olds for the years 2014-2016 were as stated in the relevant rows below:

Year	Age at interview (yrs) 17
2009	0
2010	28.5 [6]
2011	28.5 [6]
2012	28.5 [6]
2013	28.5 [6]
2014	*28.5*
2015	*33.3*
2016	*39.1*

(hereafter “MenACWY Second Dose Coverage Table”)

Based upon the earlier excerpt in the ACIP Current MenACWY Recommendations Article stating that the MenACWY recommendation since “*2010*” was of a “*booster dose at age 16 years*”, it is assumed herein that virtually all of the vaccinated 17 year olds in the years 2011 through 2015 had received the second vaccination dose soon after turning 16 years of age, and that in 2010, which was the year the booster dose was introduced, the percentage of 16, 17 and 18 year olds in the general population who were vaccinated was the same as that for 17 year olds in 2014, i.e. 28.5%.

iv. Coverage in 11-15 year olds (first dose)

Based upon the figures in the MenACWY First Dose Coverage Table and above assumptions stated within this paragraph 0(b), the average vaccination coverage for the first MenACWY dose was approximately:

- 76.0% in 11-15 year olds in 2012-2015, with 2 years as the average period elapsed since vaccination.

v. Coverage in 16 – 17 year olds

Based upon the figures in the MenACWY Second Dose Coverage Table and above assumptions stated within this paragraph 0(b), the average vaccination coverage was approximately:

- 31.0% in 16-17 year olds in 2012-2015 for the second MenACWY dose (“VC1”) with about 1 year as the average period elapsed since vaccination.

Based upon the figures in the MenACWY First Dose Coverage Table and above assumptions stated within this paragraph 0(b), the average vaccination coverage was approximately 78.2% for at least one MenACWY dose, and hence was approximately (78.2% - 31.0% =):

- 47.2% in 16-17 year olds in 2012-2015 for only one MenACWY dose (“VC2”), with 4.5 years as the average period elapsed since vaccination.

vi. Coverage in 18 – 20 year olds

All references to “college” herein, except within quoted excerpts, include university and other post-secondary educational institution.

a. Percentage of 18-20 year olds attending college

The Plaintiff hereby requests that the Court take judicial notice of the following document:

- article entitled "Meningococcal Disease Among College-Aged Young Adults: 2014–2016"

  Citation: Sarah A. Mbaeyi, Sandeep J. Joseph, Amy Blain, Xin Wang, Susan Hariri and Jessica R. MacNeil. Pediatrics January 2019, 143 (1) e20182130; DOI: https://doi.org/10.1542/peds.2018-2130, accessible at:
  https://pediatrics.aappublications.org/content/pediatrics/143/1/e20182130.full-text.pdf
  (last accessed December 23, 2020)
  (hereafter "Percentage of Population in College Article")

  A true and correct copy of the aforesaid article is attached hereto as **Exhibit 174**.

- National Conference of State Legislatures web page headed "50 State Summary of Meningitis Legislation and State Laws", last updated "October 2012", accessible at:
  https://www.ncsl.org/research/health/meningitis-state-legislation-and-laws.aspx
  (last accessed December 29, 2020)
  (hereafter "State MenACWY Laws Page")

  A true and correct copy of the aforesaid article is attached hereto as **Exhibit 175**.

The Percentage of Population in College Article states:

"The number of college students aged 18 to 24 years overall in the 50 US states and District of Columbia was obtained from the 2015 National Center for Education Statistics Integrated Postsecondary Education Data System Fall Enrollment Survey and classified by age group (18- to 19-year-olds, 20- to 21-year-olds, and 22- to 24-year-olds).[14]… The proportion of college students was calculated overall (38.3%) and for each age group: 18- to 19-year-olds (52.1%), 20- to 21-year-olds (47.0%), and 22- to 24-year-olds (24.4%)."

Based upon the above excerpt, the proportion of the US 2015 population who were college students was 52.1% in the case of 18- to 19-year-olds, and 47.0% in the case of 20- to 21-year-olds.

Hence the proportion of 18-20 year old US residents in 2012-2015 who were college students is estimated herein to have been approximately **52%**.

The State MenACWY Laws Page states:

"Thirty-nine states have one or more laws related to meningitis… State laws address this issue by requiring the distribution of meningitis information, receipt of a vaccine or waiver, or adding the meningitis vaccine to the state's established requirements and exemptions. The two target groups captured in these laws are college students (usually first year students residing on campus) and young adolescents (usually 6th graders)."

and

"Four states—Connecticut, New Jersey, Texas and Vermont—require certain post-secondary students (e.g. those living in dorms) to receive the vaccine allowing only for state established immunization exemptions. Fifteen states—Alaska, California, Colorado, Delaware, Florida, Georgia, Kansas, Louisiana, Maryland, Massachusetts, Missouri, New York, Oklahoma, Pennsylvania, and Virginia—and the District of Columbia require this same population of students to receive the vaccine or sign a waiver."

b. Coverage of 18-20 year old college and non-college attendees

A reference to "general population" within this paragraph 0 excludes college students vaccinated because of college enrolment requirements.

Based upon the figures in the MenACWY First Dose Coverage Table, and assuming that for each year, or on average, in the period of 2012-2015 the same number of 18 year olds in the general population had been vaccinated over the past 12 months as 17 year olds, the percentage of 18-20 year olds in 2012-2015 in the general population who had received at least one dose was approximately 72.1%.

Based upon the figures in the MenACWY Second Dose Coverage Table, and assuming that the coverage figure therein for the year 2014 applied also to all earlier relevant years (i.e. back to 2009 when 20 year olds in 2012 had been 17 years of age), 28.5% of 18-20 year olds had received a second MenACWY dose at around age 16 years in 2012-2015.

Subtracting that 28.5% from the 72.1% vaccinated, the remaining 43.6% of 18-20 year olds had received only the first dose, between 11 and 18 years inclusive.

Based upon the above excerpt from the State MenACWY Laws Page, which states that some US states in 2012 required meningococcal vaccination for “certain post-secondary students (e.g. those living in dorms)”, it will be assumed in the calculation of DRU herein that all 18-20 year old US residents who were college freshman at around age 18 years were vaccinated prior to enrolment in college. That is disregarding the availability of exemptions and/or waivers, and the absence of MenACWY requirement in many states for non-live-in students, and in other states for any students at all.

That percentage of college students can be estimated to be 100% less the 72.1% already vaccinated between 11 and 18 years inclusive, i.e. 27.9%.

Hence, based upon the earlier stated estimate that 52% of the population of 18-20 year olds were enrolled in college, approximately (52% x 27.9% =) 14.5% of 18-20 year old US residents can be estimated to have been vaccinated around the time of enrolment in college.

Hence in summary, based upon the above figures and assumptions, of 18-20 year olds in 2012-2015, approximately:

- 14.5% received a first MenACWY at around the time of enrolment in college.
- 28.5% had received a second MenACWY dose at about age 16, and
- 43.6% had received a first MenACWY dose in the age range 11-18 years.

vii. Summary for VC

Based upon the above information in this paragraph 0(b), the approximate annual average MenACWY vaccination coverage in the relevant age groups in 2012-2015 was as set out in the table below:

11-15 yrs	16-17 yrs		18-20 yrs Age in years last vaccinated (dose)		
	2nd dose	1st dose	~ 18 for college (1st)	~ 16 (2nd)	~ 11-18 (1st)
~76.0%	~31.0% ("VC1")	~47.2% ("VC2")	14.5% ("VC1")	28.5% ("VC2")	43.6% ("VC3")

(c) IMD Vaccination Effectiveness (VE)

The Plaintiff hereby requests that the Court take judicial notice of the following document:

- article entitled "Persistence of bactericidal antibodies 4 years after a booster dose of quadrivalent meningococcal diphtheria toxoid conjugate vaccine (MenACWY-D)"

  Citation: Robertson, C.A.; Hedrick, J.; Bassily, E.; Greenberg, D.P. Vaccine 2019, 37, 1016–1020, accessible at https://www.sciencedirect.com/science/article/pii/S0264410X19300398 (last accessed December 25, 2020)
  (hereafter "Meningococcal Vaccine Second Dose Duration Article")

  A true and correct copy of the Meningococcal Vaccine Second Dose Duration Article is attached hereto as **Exhibit 176**

- CDC report entitled "Active Bacterial Core Surveillance (ABCs) Report, Emerging Infections Program Network, *Neisseria meningitidis*, 2004", Dec 2005 File – 05 Jan 2005, accessible at https://www.cdc.gov/abcs/reports-findings/survreports/mening04.pdf (last accessed December 25, 2020)
  (hereafter "CDC ABCs Report for IMD in 2004")

  A true and correct copy of the CDC ABCs Report for IMD in 2004 is attached hereto as **Exhibit 177**

- CDC report entitled "Active Bacterial Core Surveillance (ABCs) Report, Emerging Infections Program Network, *Neisseria meningitidis*, 2006", Nov 2007 File – 15 Jan 2008, accessible at https://www.cdc.gov/abcs/reports-

findings/survreports/mening06.pdf
(last accessed December 25, 2020)
(hereafter "CDC ABCs Report for IMD in 2006")

A true and correct copy of the CDC ABCs Report for IMD in 2006 is attached hereto as **Exhibit 178**.

i. Initial Seroprotection rates and Waning Exponents after first and second doses

The CDC Pink Book IMD Chapter states:

"the presence of detectable circulating antibody appears to be important for protection against N. meningitidis*."*

Based upon that statement, the seroprotection rate represents the upper limit of the potential protective effect of MenACWY vaccination.

The ACIP Current MenACWY Recommendations Article states:

"MenACWY-D was first licensed in the United States in 2005…
2010 FDA licensed a second vaccine, MenACWY-CRM, for persons aged 11–55 years."

Based upon the above excerpt, the only MenACWY vaccine licenced during the period of 2005-2010 was MenACWY-D, so the calculation of MenACWY effectiveness will be based upon seroprotection rates after administration of MenACWY-D.

The ACIP Current MenACWY Recommendations Article also states:

"An …rSBA titer ≥1:8 and/or a fourfold rise in rSBA or hSBA titers have been used to infer vaccine-mediated immunologic protection against meningococcal disease (73)….

MenACWY-D (Menactra)

Among adolescents and adults aged 10–55 years, 64%–71% achieved an hSBA titer ≥1:8 against serogroup A, 72%–99% against serogroup C, 64%–90% against serogroup W, and 39%–82% against serogroup Y at 1 month after vaccination with a single dose (81,87,89,99). In studies assessing immunogenicity using rSBA, ≥80% and ≥88% achieved seroprotection across serogroups when the thresholds of ≥1:128 and ≥1:8 were used, respectively (85,90,92,102,104). …
Persistence studies conducted among adolescents and adults demonstrated antibody waning after primary vaccination; however, serogroup-specific degree

of waning varied between the studies. In one study, antibody waning was observed for all serogroups… by 22 months postvaccination and titers remained stable thereafter at 3 and 5 years postvaccination; 21%–34% of recipients achieved an hSBA titer ≥1:8 for serogroup A, 58%–62% for serogroup C, 71%–74% for serogroup W, and 53%–54% for serogroup Y between 22 months and 5 years postvaccination (83,84,86). In another study, antibody waning was observed by 4–6 years postvaccination… for serogroups C and Y (44% and 39% achieved an hSBA titer ≥1:8, respectively)… although antibody waning after primary vaccination of adolescents and adults was observed across studies, time points assessed and patterns of waning by serogroup were not consistent. In a study of adolescents who received a booster dose of MenACWY-D, ≥99% achieved hSBA titers ≥1:8 against all serogroups at 1 month postvaccination; this proportion remained ≥90% 4 years later (105,106)."

and the Meningococcal Vaccine Second Dose Duration Article states:

""Our study, which examined antibody persistence 4 years after MenACWY-D booster vaccination, revealed… at least 94.5% of participants maintained titers 1:8 for serogroups A, W, and Y, while 81.7% of participants maintained such titers for serogroup C"

Based upon the above excerpt, the approximate seroprotection rate is:

(1) after the first MenACWY vaccination dose, for serogroup:

- C, 89.8% soon after vaccination, followed by a decline with a Waning Exponent of 1.225 half-yearly, and

- Y, 79.5% soon after vaccination, followed by a decline with a Waning Exponent of 1.15 half-yearly, and

(2) after the second MenACWY vaccination dose, for serogroup:

- C, 95% soon after vaccination, followed by a decline with a Waning Exponent of 1.18 half-yearly, and

- Y, 98% soon after vaccination, followed by a decline with a Waning Exponent of 1.13 half-yearly.

The CDC ABCs Report for IMD in 2004 contains a table which includes the following selected columns and rows containing the number of reported "*cases*"

of "*Invasive meningococcal disease: isolation of* Neisseria meningitidis *from normally sterile site in a resident of a surveillance area in 2004*":

	Serogroups		
Age (years)	C No.	Y No.	Other‡ No.
5-17	6	4	3

"‡ Other includes serogroup W-135 and non-groupables"

Based upon the figures in the above table, the ratio of reported cases of IMD serogroup C to serogroup Y in the year prior to 2005, when the ACIP Current Recommendations Article states that routine vaccination with MenACWY-D was introduced for 11-12 year olds, was approximately 6:4.

The CDC ABCs Report for IMD in 2006 contains a table which includes the following selected columns and rows containing the number of reported "*cases*" of "*Invasive meningococcal disease: isolation of* Neisseria meningitidis *from normally sterile site in a resident of a surveillance area in 2006*":

	Serogroups		
Age (years)	C No.	Y No.	Other‡ No.
18-34	11	7	0

"‡ Other includes serogroup W-135 and non-groupables"

Based upon the figures in the above table, the ratio of reported cases of IMD serogroup C to serogroup Y in the year prior to 2007, when the ACIP Current Recommendations Article states that routine MenACWY vaccination became recommended for adolescents aged 13–18 years, was approximately 11:7, which is approximately the same as the ratio 6:4 stated above as found for 2004 for the 11-17 age group.

Hence, for all age groups in the age range of 11-20 years, and for both the first and second doses recommended, the approximate overall seroprotection rate and duration of MenACWY shall be calculated herein as a 6:4 weighted average of the seroprotection rate and duration figures for serogroups C and Y. That method of calculation is supported additionally by the statement in the CDC Pink Book IMD Chapter that "*serogroup A… is rarely isolated in the United States*".

ii. Seroprotection rate in 11 – 15 year olds (after first dose)

Based upon the 2 year average period elapsed since vaccination, the above figures result in an overall average seroprotection rate of approximately:

- 74.0% in 11-15 year olds

iii. Seroprotection rate in 16 – 17 year olds

a. Seroprotection rate after second dose

Based upon the 1 year average period elapsed since the second MenACWY vaccination dose, the above figures result in an average seroprotection rate of approximately:

- 94.8% in 16-17 year olds after the second dose.

b. Residual seroprotection rate after first dose

Based upon the 4.5 year average period elapsed since the first MenACWY vaccination dose, the above figures result in an overall average residual seroprotection rate of approximately:

- 48.6% in 16-17 year olds after the first dose.

iv. Seroprotection rate in 18 – 20 year olds

Based upon the figures in paragraphs 0(c)ii and iii above, the overall seroprotection rate and duration of MenACWY vaccination for 18-20 year olds in relation to the first and second doses can be estimated to be a weighted average of the seroprotection rate and duration figures in paragraphs 0(c)i (1) and (2) above respectively, in each case weighted more heavily towards those for serogroup C compared to Y by the ratio 6:4.

a. In those vaccinated at around college enrolment

Based upon the 0 to less than 3 year period elapsed since the first MenACWY vaccination dose at around 18 years of age, the above figures result in an overall average seroprotection rate of approximately:

- 76.6% in 18-20 year olds who received a first MenACWY vaccination dose at age 18 years.

b. Residual seroprotection rate after second dose at ~16 years

Based upon the approximately 3.2 year average period elapsed since the second MenACWY vaccination dose, the above figures result in an overall average seroprotection rate of approximately:

- < 90.6% in 18-20 year olds who had received a second MenACWY vaccination dose at age 16 years.

c. Residual seroprotection rate after first dose to general population at 11-18 years

Based upon the approximately 5.6 year average period elapsed since the first MenACWY vaccination dose, the above figures result in an overall average seroprotection rate of approximately:

- < 35.8% in 18-20 year olds who received a first MenACWY vaccination dose at age 11-18 years.

v. Summary for VE

The resultant approximate annual average MenACWY vaccination seroprotection rate in the relevant age groups in 2012-2015 are summarized in the table below for each subject age group:

	16-17 yrs		18-20 yrs		
			Age in years last vaccinated (dose)		
11-15 yrs	2nd dose	1st dose	~ 18 for college (1st)	~ 16 (2nd)	~ 11-18 (1st)
~73.9%	~94.8%	~48.6%	76.6% ("VE1")	< 90.6% ("VE2")	35.8% ("VE3")

(d) Serious outcome Rate per Disease case (SRD)

i. SRD for any SAE

Based upon the self-evident level of seriousness of IMD (the disease being "invasive"), the value of SRD for IMD is taken herein to be the same as the DRP, and hence the SRIU the same as the DRIU.

ii. SRD for hospitalization

The SRD hospitalization rate per IMD case is assumed herein to be 100%.

iii. SRD for death

The CDC Pink Book IMD Chapter states:

"The case-fatality ratio of meningococcal disease is 10% to 15%"

Based upon that statement, the SRD (death) is estimated to be ≤ 15% for each of the age groups within the age range of 11-20 years.

(e) Differential Risk of unavoidable serious adverse effect (SRIU)

The Plaintiff hereby requests that the Court take judicial notice of the following documents:

- article entitled "Risk Factors for Meningococcal Disease in College Students"

  Citation: Bruce MG, Rosenstein NE, Capparella JM, Shutt KA, Perkins BA, Collins M. JAMA. 2001;286(6):688–693. doi:10.1001/jama.286.6.688, accessible at:
  https://www.researchgate.net/profile/Michael_Bruce2/publication/11848421_Risk_Factors_for_Meningococcal_Disease_in_College_Students/links/09e415093eee5c7a51000000/Risk-Factors-for-Meningococcal-Disease-in-College-Students.pdf
  (last accessed December 30, 2020)
  (hereafter "College IMD Risk Factors Article")

  A true and correct copy of the aforesaid article is attached hereto as **Exhibit 179**.

  Dormitory Resident Risk Factor

  The College IMD Risk Factors Article includes a table headed:

  "Table 1. Rates of Meningococcal Disease in College Students, September 1998 to August 1999"*

  hereafter the "IMD Rates Table",
  which contains the following selected columns and rows:

Characteristic	*No. of Cases*	*Population†*	*Rates per 100 000 (95% Confidence Interval)*
Demographic groups			
All 18-23 y	*304*	*22 070 535*	*1.4 (1.2-1.5)*
18-23 y, nonstudents	*211*	*14 579 322*	*1.4 (1.3-1.7)*
All college students	*96*	*14 897 268*	*0.6 (0.5-0.8)*
Undergraduates	*93*	*12 771 228*	*0.7 (0.6-0.9)*
Freshmen	*44*	*2 285 001*	*1.9 (1.4-2.6)*
Nonfreshmen	*52*	*12 612 267*	*0.4 (0.3-0.5)*
Dormitory resident	*48*	*2 085 618*	*2.3 (1.7-3.1)*
Freshmen in dormitories	*30*	*591 587*	*5.1 (3.4-7.2)*

Based upon the figures in the above table, the notification rate of IMD in September 1998 to August 1999, which was prior to the introduction of routine MenACWY vaccination, was higher in college dormitory residents than that in the general population of 18-23 year olds by a factor of approximately (2.3 ÷ 1.4 =) 1.64 (hereafter “Dormitory Resident Risk Factor” or “DRRF”).

The DRU for a person who attends college and resides in a dormitory is hereafter “DRU (Dorm)” and estimated to be DRU for 18-20 year olds multiplied by the DRRF of 1.64.

Estimation of SRIUs

Based upon the calculated estimates presented in this paragraph 7.11 “IMD”, for

(a) the disease notification rate in the population (DRP), and

(b) the vaccination coverage (VC), and

(c) the vaccination effectiveness (VE), and

(d) the rate of serious adverse effects per disease case (SRD),

(e) the Dormitory Resident Risk Factor (DRRF),

the approximate differential rates for serious adverse effects (SRIU) can be calculated by applying the formulas set out in paragraphs 6.1 and 6.3, with the results set out in the table below for each age group:

Invasive Meningococcal Disease totals and averages for 2012-2015 (approx.)

Age	11-15 yrs	16-17 yrs		18-20 yrs			Avg / Total
				Age in years last vaccinated (dose)			
		2nd dose	2nd dose	~ 18 for college (1st)	~ 16 (2nd)	~ 11-18 (1st)	
DRP (annual)	< 1 / 9,215,892	< 1 / 1,905,453		< 1 / 1,905,453			**< 1 / 863,463**
VC	~ 76.0%	31.0% ("VC1")	47.2% ("VC2")	14.5% ("VC1")	28.5% ("VC2")	43.6% ("VC3")	
		~ 78.2%		86.6%			
VE	< 73.9%	≤94.8% ("VE1")	≤48.6% ("VE2")	< 76.6% ("VE1")	<90.6% ("VE2")	< 35.8% ("VE2")	
		< 67.0%		< 60.7%			
DRU (annual)	< 1 / 4,044,010	< 1 / 908,112		< 1 / 908,112			
DRRF	N/A	N/A		~1.64			
DRU (annual)	< 1 / 4,044,010	< 1 / 908,112		< 1 / 550,416			
DRIU (annual)	< 1 / 5,474,484	< 1 / 957,464		< 1 / 587,215			
DRIU (=SRIU) total over age range	< 1 / 1,094,897	< 1 / 478,732		< 1 / 195,738			**< 1 / 123,289**
SRD - (hospitalization)	100%						
SRIU - (hospitalization)	< 1 / 1,094,897	< 1 / 189,973		< 1 / 321,570			**< 1 / 123,289**
SRD - (death) - (case fatality rate)	≤ 15%						
SRIU - (death)	**< 1 / 7,300,000**	**< 1 / 3,200,000**		**< 1 / 1,300,000**			**< 1 / 820,000**

7.12 Influenza-associated Pediatric Mortality ("IPM")

(a) Influenza Pediatric Death notification rate (DRP)

i. Influenza mortality history to recent years

The Plaintiff hereby requests that the Court take judicial notice of the following documents:

- article entitled "Estimates of Deaths Associated with Seasonal Influenza — United States, 1976–2007",

  Citation: MG Thompson, PhD, DK Shay, MD, H Zhou, MSc, MPH, CB Bridges, MD, PY Cheng, PhD, E Burns, MA, JS Bresee, MD, NJ Cox, PhD, Influenza Div, National Center for Immunization and Respiratory Diseases, CDC. August 27, 2010 / 59(33);1057-1062, accessible at https://www.cdc.gov/mmwr/preview/mmwrhtml/mm5933a1.htm (html) or https://www.cdc.gov/mmwr/pdf/wk/mm5933.pdf (pdf)
  (last accessed November 20, 2020)
  (hereafter "Influenza Deaths 1976-2007 Article")
  A true and correct copy of the aforesaid report is attached hereto as **Exhibit 180**.

- article entitled "Influenza-associated deaths among children in the United States, 2003-2004",

  Citation: Bhat N, Wright JG, Broder KR, et al. N Engl J Med. 2005;353:2559–67. https://doi.org/10.1056/NEJMoa051721, accessible at https://www.nejm.org/doi/full/10.1056/nejmoa051721
  (last accessed November 19, 2020)
  (hereafter "Influenza Deaths 2003-2004 Article")
  A true and correct copy of the aforesaid report is attached hereto as **Exhibit 181**.

- CDC web page entitled "Influenza-associated Pediatric Mortality 2004 Case Definition", accessible at https://wwwn.cdc.gov/nndss/conditions/influenza-associated-pediatric-mortality/case-definition/2004/
  (last accessed February 15, 2020)
  (hereafter "CDC Influenza Pediatric Mortality Case Definition")

A true and correct copy of the aforesaid report is attached hereto as **Exhibit 182**.

The Influenza Deaths 1976-2007 Article states that the estimated number of influenza-associated deaths with underlying pneumonia and influenza causes in under 19 year olds in the US in 1978-2007 were as stated in *italics* in the table below:

Season	***<19 yrs***	
	No.	***(95% CI§)***
1978--79	*128*	*(86--343)*
1979--80	*100*	*(65--280)*
1980--81	*115*	*(78--284)*
1981--82	*41*	*(18--155)*
1982--83	*114*	*(78--222)*
1983--84	*123*	*(78--241)*
1984--85	*130*	*(100--217)*
1985--86	*88*	*(52--172)*
1986--87	*70*	*(47--167)*
1987--88	*75*	*(44--144)*
1988--89	*120*	*(71--212)*
1989--90	*91*	*(65--158)*
1990--91	*56*	*(35--123)*
1991--92	*82*	*(53--158)*
1992--93	*88*	*(57--164)*
1993--94	*77*	*(63--142)*
1994--95	*71*	*(47--128)*
1995--96	*76*	*(38--144)*
1996--97	*97*	*(71--153)*
1997--98	*78*	*(66--141)*
1998--99	*85*	*(65--146)*
1999--00	*85*	*(67--159)*
2000--01	*67*	*(43--136)*
2001--02	*107*	*(80--176)*
2002--03	*82*	*(40--148)*
2003--04	*103*	*(87--184)*
2004--05	*115*	*(83--192)*
2005--06	*101*	*(64--193)*
2006--07	*67*	*(20--212)*
Average	**91**	

Based upon those figures,

- the annual average number of such deaths in the period of 1978-2007 was 91, and
- the annual average of such deaths over the last few listed seasons of 2004-05 through 2006-2007, i.e. 94, was not lower than that for the prior seasons of 1978-79 through 2003-04, i.e. 90.

ii. **Influenza mortality history since influenza vaccination recommended**

The Influenza Deaths 2003-2004 Article states:

"In the 2002–2003 and 2003–2004 seasons, influenza vaccination of all children 6 to 23 months of age was encouraged when feasible.1 Beginning with the 2004–2005 season, the ACIP formally recommended annual influenza vaccination for all children in this age group."

Based upon that excerpt, influenza vaccination was not formally recommended for all U.S. resident children aged 6 to 23 months until the 2004-2005 season.

The CDC Schedule 2007 states:

"The changes to the previous childhood and adolescent immunization schedule, published January 2006 (1), are as follows..:
The influenza vaccine is now recommended for all children aged 6–59 months (3)."

Based upon that excerpt, influenza vaccination was not formally recommended for all U.S. resident children aged 24-59 months until January 2006.

The CDC Schedule 2009 states:

"Changes to the previous schedule (1) are as follows:
Routine annual influenza vaccination is recommended • for all children aged 6 months through 18 years."

Based upon that excerpt, influenza vaccination was not formally recommended for all U.S. resident children aged over 5 years until 2008-2009.

The CDC Disease Notifications provide the following figures for influenza-associated pediatric deaths for the years 2007 to 2018 (excluding the H1N1 pandemic year 2009).

Age group (yrs) / Year	< 1	1 – 4	5 – 14	"15 – 24" (15 – 17*)	Total estimable for < 19 yr olds
2007	18	16	35	8	77
2008	10	12	27	12	90
2010	10	12	27	12	61
2011	25	30	49	14	118
2012	10	9	28	5	52
2013	24	40	73	23	160
2014	33	31	61	16	141
2015	25	37	56	12	130
2016	8	26	39	9	82
2017	16	31	64	15	126
2018	20	48	74	17	159
				Average	**109**

The CDC Influenza Pediatric Mortality Case Definition states:

"Influenza-associated Pediatric Mortality

2004 Case Definition

Clinical Description

An influenza-associated death is defined for surveillance purposes as a death resulting from a clinically compatible illness that was confirmed to be influenza by an appropriate laboratory or rapid diagnostic test. There should be no period of complete recovery between the illness and death. Influenza-associated deaths in all persons aged <18 years should be reported.

A death should not be reported if:…

3. The death occurs in a person 18 years or older…."

Based upon that definition of "Influenza-associated Pediatric Mortality", the notification figures in the column with the heading "15 – 24" as the age group apply only to 15 to 17 year olds.

Based upon the figures in the above table,

- the annual average number of influenza-associated pediatric deaths in the period of 2007 through 2018 was 109, and

- the overall annual average of such deaths over the period of 2007 through 2018 did not decrease, but increased from 80 in 2007-2012 (excluding the H1N1 pandemic year 2009) to 133 (67% higher) 2013-2018.

  An overall increase the annual average of such deaths occurred during 2007-2018 in all pediatric age groups except for under 1 year olds, for whom vaccination was recommended only for those over 6 months of age. In that age group, the overall average remained about the same throughout the 2007-2018 period.

Although the figures in the above two tables may not be directly comparable, especially between the tables, the trends of the figures within each of the tables indicate that the beginning in 2004-2005 and expansions in 2006 and 2008-2009 of the formal recommendation of influenza vaccination does not appear to have led to a decline in influenza-associated pediatric mortality in the US to date. The recommendations have been followed only by increases in influenza-associated mortality in the relevant age groups.

Unless these increases can be shown to be caused by one or more other factors, such as a substantial increase in testing for influenza and/or change(s) in death coding coinciding with expansion of vaccination recommendations, the childhood influenza vaccination recommendations have not demonstrably reduced the risk of influenza-associated mortality, and may have increased it.

iii. **Detailed death figures for non-high risk 6 month – 17 year olds in 2007-2012**

The Plaintiff hereby requests that the Court take judicial notice of the following documents:

- article entitled “Influenza Vaccine Effectiveness Against Pediatric Deaths: 2010–2014”,

  Citation: Flannery B, Reynolds S B et al. Pediatrics Apr 2017, e20164244; DOI: 10.1542/peds.2016-4244, accessible at https://pediatrics.aappublications.org/content/pediatrics/early/2017/03/30/peds.2016-4244.full.pdf
  (last accessed November 19, 2020)
  (hereafter “Influenza Vaccine Effectiveness Article”)

  A true and correct copy of the aforesaid report is attached hereto as **Exhibit 183**.

The CDC Disease Notifications state that the number of influenza-associated deaths in US residents aged 6 to 59 months reported in 2007-2012 (except 2009) have been as follows:

> *"In 2007 ...10 (13%) were aged 6–23 months; 10 (13%) were aged 24–59 months; and 44 (57%) were aged >5 years. ... (43%) children had one or more underlying or chronic conditions"*
>
> *"2008 ...14 (16%) were aged 6–23 months; 19 (21%) were aged 24–59 months; and 47 (52%) were aged >5 years… (57%) children had one or more underlying or chronic medical conditions, placing them at increased risk for influenza-associated complications."*
>
> *"2010: ...8 (13%) were aged 6–23 months; 7 (11%) were aged 24–59 months; 15 (26%) were aged 5–8 years; 8 (13%) were aged 9–12 years; and the remaining 16 (26%) were aged 13–17 years … (63%) children had one or more underlying or chronic medical conditions placing them at increased risk for influenza-associated complications"*
>
> *"2011: 18 (15%) were aged 6–23 months; 21 (18%) were aged 24–59 months; 17 (14%) were aged 5–8 years; 17 (14%) were aged 9–12 years; and the remaining 29 (25%) were aged 13–17 years.… (51%) children had one or more underlying or chronic medical conditions, placing them at increased risk for influenza-associated complications"*
>
> *"2012: 12 (23%) were aged 6–59 months, and 33 (63%) were aged 5‑17 years … (55%) children had one or more underlying or chronic medical conditions placing them at increased risk for influenza-associated complications"*

According to the above excerpts, the number of influenza-associated pediatric deaths and the percentages of those that occurred in children with increased risk for influenza-associated complications in 2007-2012 (excluding 2009) were as set out in the following table:

Year	Age group				% in increased risk children (approx.)
	6 – 23 mos	2 – 4 yrs	5-12 yrs	13-17 yrs	
2007	*10*	*10*	*44*		*43%*
2008	*14*	*19*	*47*		*57%*
2010	*8*	*7*	*23*	*16*	*63%*
2011	*18*	*21*	*34*	*29*	*51%*
2012	*12*		*33*		*55%*

Based upon the figures in the above table, the number of influenza-associated pediatric death notifications and percentages in children without increased risk for influenza-associated complications in 2007-2012 (excluding 2009) were as set out in the following table:

Year	Age group						
	6 – 23 mos	2 – 4 yrs	Total 6 mos – 4 yrs	5-12 yrs	13-17 yrs	Total 5-17 yrs	Total 6 mos - 17 yrs
2007	6	6	12	25		25	37
2008	6	8	14	20		20	34
2010	3	3	6	8	6	14	20
2011	9	10	19	17	14	31	50
2012	5		5	15		15	20
Annual average			**11**			**21**	**32**

The Influenza Deaths 2003-2004 Article states:

> *"At least one ACIP-defined high-risk condition was present in 33 percent of the children, as compared with an estimated prevalence of 7 percent among U.S. residents younger than 18 years of age."*

Based upon that excerpt and the Population Tables, the average annual number of 6 month to 17 year olds without any high-risk condition in 2007-2012 was approximately 93% of the total average annual population.

That results in approximate annual average influenza-associated pediatric mortality rates in non-increased-risk 6 month to 17 year olds that are set out in the following table, for the years 2007-2012 (excluding 2009):

Age group	6-59 months	5-17 years
DRP	< 1 / 1,532,372	< 1 / 2,384,036

(b) Influenza Vaccination Coverage (VC)

The Plaintiff hereby requests that the Court take judicial notice of the following document:

- CDC article entitled "Prevention and Control of Influenza. Recommendations of the Advisory Committee on Immunization Practices (ACIP)", accessible at https://www.cdc.gov/mmwr/preview/mmwrhtml/rr5510a1.htm

  (last accessed November 20, 2020)
  (hereafter "ACIP 2006 Influenza Vaccine Recommendations")
  A true and correct copy of the aforesaid report is attached hereto as **Exhibit 184**.

The Plaintiff hereby requests that the Court take judicial notice of the following documents, the group of which may hereafter be referenced as "CDC Influenza Vaccination Coverage Reports":

- CDC article entitled "Influenza Vaccination Coverage Among Children Aged 6--23 Months --- United States, 2006--07 Influenza Season", accessible at https://www.cdc.gov/mmwr/preview/mmwrhtml/mm5738a2.htm

  (last accessed November 20, 2020)
  (hereafter "CDC Influenza Vaccination Coverage 2006--07")
  A true and correct copy of the aforesaid report is attached hereto as **Exhibit 185**.

- CDC article entitled "Influenza Vaccination Coverage Among Children Aged 6--23 Months --- United States, 2007--08 Influenza Season", accessible at https://www.cdc.gov/mmwr/preview/mmwrhtml/mm5838a2.htm

  (last accessed November 20, 2020)
  (hereafter "CDC Influenza Vaccination Coverage 2007--08")
  A true and correct copy of the aforesaid report is attached hereto as **Exhibit 186**.

- CDC web page headed "Final estimates for 2009–10 Seasonal Influenza and Influenza A (H1N1) 2009 Monovalent Vaccination Coverage – United States, August 2009 through May, 2010", accessible at https://www.cdc.gov/flu/fluvaxview/coverage_0910estimates.htm
  (last accessed November 19, 2020)
  (hereafter "CDC Influenza Vaccination Coverage 2009--10")

A true and correct copy of the aforesaid report is attached hereto as **Exhibit 187**.

- CDC web page headed “Final state-level influenza vaccination coverage estimates for the 2010–11 season–United States, National Immunization Survey and Behavioral Risk Factor Surveillance System, August 2010 through May 2011”, accessible at https://www.cdc.gov/flu/fluvaxview/coverage_1011estimates.htm (last accessed November 19, 2020)
  (hereafter “CDC Influenza Vaccination Coverage 2010--11”)
  A true and correct copy of the aforesaid report is attached hereto as **Exhibit 188**.

- CDC report entitled “Flu Vaccination Coverage, United States, 2011-12 Influenza Season”, accessible at https://www.cdc.gov/flu/pdf/fluvaxview/vax-coverage-1112estimates.pdf (last accessed November 19, 2020)
  (hereafter “CDC Influenza Vaccination Coverage 2011--12”)
  A true and correct copy of the aforesaid report is attached hereto as **Exhibit 189**.

According to the ACIP 2006 Influenza Vaccine Recommendations and CDC Schedules, in the seasons 2006-2007 through 2011-2012 the CDC recommended an annual dose of influenza vaccination for all 6 to 59 month olds (inclusive) with an extra dose also included in the first year of administration.

The CDC Influenza Vaccination Coverage 2006--07 states:

> *“Children aged <5 years have more influenza-related medical-care visits compared with older children, and those aged <2 years are at the greatest risk for influenza-related hospitalizations (1). In 2002, the Advisory Committee on Immunization Practices (ACIP) encouraged annual influenza vaccination of children aged 6--23 months and then, in 2004, recommended vaccination for this group (2). Two doses, spaced at least 4 weeks apart, are recommended to fully vaccinate children aged <9 years who are receiving influenza vaccination for the first time.”*

and

"Beginning with the 2008--09 influenza season, ACIP has expanded its recommendation for universal influenza vaccination to include all children aged 5--18 years, in addition to those aged 6--59 months, for whom vaccination was recommended previously (1)."

The CDC Influenza Vaccination Coverage 2009—10 states:

"For the 2009–10 season, trivalent influenza vaccination was recommended by the ACIP for all children aged 6 months—18 years"

The CDC Influenza Vaccination Coverage 2010—11 states:

"This is the first season under the Advisory Committee on Immunization Practices (ACIP) recommendation for annual influenza vaccination for all persons ≥6 months and the second season under the ACIP recommendation for annual influenza vaccination for children 6 month–18 years (4)."

The CDC Influenza Vaccination Coverage 2011—12 states:

"the Advisory Committee on Immunization Practices (ACIP) recommends flu vaccination for everyone 6 months and older."

According to the CDC Influenza Vaccination Coverage Reports, the influenza vaccination coverages for the years 2006-2007 through 2011-2012 (excluding 2008-2009) were the following (in *italics*) for *"≥1 or more doses*": for the specified age groups:

Age group / Year	6 – 23 mos	2 – 4 yrs	Average (6 mos – 4 yrs)	5 – 12 yrs	13 – 17 yrs
2006-2007	*31.8%*	< 31.8%	< 31.8%		
2007-2008	*40.7%*	< 40.7%	< 40.7%		
2009-2010	*43.7%*				
2010-2011	*68.2%*	*60.6%*	*63.1%*	*54.7%*	*34.5%*
2011-2012	*74.6%*	*63.3%*	*67.1%*	*54.2%*	*33.7%*

The figures in the above table that are not in italics are estimates based upon the timing of later initial recommendation by the CDC of vaccination for successively older age groups.

Based upon the above excerpts that state when the formal recommendations were first made by the Advisory Committee on Immunization Practices (ACIP), in particular from 2002 for children aged 6--23 months and from 2004 for children aged 2 – 4 years, it is assumed herein, as reflected in the above table, that the

coverage for 2-17 olds in 2006-2007 and 2007-2008 was lower than the coverage stated for the 6-23 months age group.

Hence, based upon those figures in the table, the annual average vaccination coverage in the seasons of 2006-2012 (excluding the 2008-2009 season) was approximately as set out in the table below for each subject age group:

Age	**6 mos – 4 yrs**	**5 – 17 yrs**
VC	**< 49.3%**	**< 46.9%**

(c) Influenza Vaccination Effectiveness (VE)

The Influenza Vaccine Effectiveness Article includes a table which is entitled: "TABLE 2 Percentage Vaccinated Among Influenza-Associated Pediatric Deaths Compared With NIS-Flu Cohorts, With VE Estimates by Season and Age Group", and includes the following columns:

Stratum	*VE*	
	%	*95% CI*
Age		
6 mo–4 y	*61*	*40 to 76*
5–12 y	*76*	*63 to 85*
13–17 y	*40*	*0 to 67*

It will be assumed in the calculation of the benefit of the vaccination that its maximum effectiveness is as high as stated in the above table in the face of:

- the analysis presented in paragraph 7.12(a) herein concluding that the true effectiveness appears to be negative to zero based upon the trend in mortality rates before and after vaccination became recommended by the CDC in these age groups, and
- all of the deficiencies in the study described by the Influenza Vaccine Effectiveness Article, such as lack of a proper control group and observer bias, as discussed in paragraph 7.3(c) herein in relation to pertussis.

Hence, based upon those figures in the table, the annual average vaccination coverage in the seasons of 2006-2012 (excluding the 2008-2009 season) was approximately as set out in the table below for each subject age group:

Age	**6 mos – 4 yrs**	**5 – 17 yrs**
VC	**61%**	**62%**

(d) Differential Risk of unavoidable serious adverse effect (SRIU)

Based upon the calculated estimates presented in this paragraph 7.12 "Influenza-associated Pediatric Mortality" ("IPM"), for

(a) the IPM notification rate in the population (SRP), and

(b) the vaccination coverage (VC), and

(c) the vaccination effectiveness (VE),

the approximate differential rates for IPM ("SRIU (death)") can be calculated by applying the relevant formulas set out in paragraphs 6.1, with the results set out in the table below for each age group:

Influenza mortality totals and averages for 2007-2012, approximated

Age group	**6 mos – 4 yrs**	**5 – 17 yrs**	**Total**
SRP (annual)	1 / 1,532,372	1 / 2,384,036	1 / 2,384,036
VC	**< 49.3%**	**< 46.9%**	**< 47.5%**
VE	61.0%	62.2%	65%
SRU (annual)	< 1 / 1,071,729	< 1 / 1,689,086	< 1 / 1,471,170
SRIU (annual)	< 1 / 1,756,933	< 1 / 2,717,588	< 1 / 2,378,335
SRIU (death) (total over age range)	< 1 / 390,429	< 1 / 209,045	< 1 / 135,905

8. Summary of non-vaccination risks

The following tables summarise the results of the calculations presented in Part 2 herein of the approximate risk for the various relevant age groups of a serious adverse outcome (SAE) arising from non-vaccination against:

(a) diphtheria, tetanus, pertussis and polio,.and

(b) measles, mumps, rubella, varicella, hepatitis b, hepatitis a, Hib, pneumococcal, meningococcal and (for deaths only) influenza,

based upon what is stated in the documents exhibited in Part 2 of the Notice

8.1 Diphtheria (D), Tetanus (T), Pertussis (P) and Polio

RISK FROM NON-VACCINATION (SRIU)

SRIU - Any SAE

Age	6-11 mths	1-6 yrs	7-10 yrs	11-19 yrs	Total
D	0 (or negligible)	< 1 / 23,889,351	< 1 / 12,022,465	< 1 / 12,151,267	**< 1 / 4,823,154**
T	< 1 / 5,365,419	< 1 / 714,284	< 1 / 414,450	< 1 / 182,020	**< 1 / 105,339**
P	1 / 24,949	1 / 16,155	1 / 28,677	1 / 141,089	< 1 / 6,947
D+T+P	**< 1 / 24,834**	**< 1 / 15,787**	**< 1 / 26,762**	**< 1 / 78,965**	**< 1 / 6,509**
Polio	<1 / 1,685 billion	< 1 / 141 billion	< 1 / 217 billion	< 1 / 130 billion	**< 1 / 50 billion**
Total	**< 1 / 24,834**	**< 1 / 15,787**	**< 1 / 26,762**	**< 1 / 78,965**	**< 1 / 6,509**

SRIU - Death

Age	6-11 mths	1-6 yrs	7-10 yrs	11-19 yrs	Total
D	0 (or negligible)	<1 / 143,336,109	< 1 / 120,224,649	<1 / 121,512,667	**<1 / 42,509,839**
T	< 1 / 76,648,841	< 1 / 10,204,057	< 1 / 5,920,711	< 1 / 2,604,275	**< 1 / 1,506,184**
P	< 1 / 16,346,415	< 1 / 3,646,854	< 1 / 13,474,721	< 1 / 60,497,886	**< 1 / 2,346,718**
D+T+P	**< 1 / 13,473,094**	**< 1 / 2,637,230**	**< 1 / 3,977,259**	**< 1 / 2,442,997**	**< 1 / 897,529**
Polio	< 1 / 34 trillion	< 1 / 2.8 trillion	< 1 / 4.3 trillion	< 1 / 2.6 trillion	**< 1 / 1 trillion**
Total	**< 1 / 13,473,088**	**< 1 / 2,637,227**	**< 1 / 3,977,255**	**< 1 / 2,442,995**	**< 1 / 897,528**

CUMULATIVE RISK FROM NON-VACCINATION (SRIU)

SRIU - Any SAE

Age	6-11 mths	6 mths to 6 yrs	6 mths - 10 yrs	6 mths - 19 yrs
Diphtheria (D)	0 (or negligible)	< 1 / 23,889,351	< 1 / 7,997,615	**< 1 / 4,823,154**
Tetanus (T)	< 1 / 5,365,419	< 1 / 630,365	< 1 / 250,049	**< 1 / 105,339**
Pertussis (P)	< 1 / 24,949	< 1 / 9,806	< 1 / 7,307	< 1 / 6,947
Total D+T+P	**< 1 / 24,834**	**< 1 / 9,652**	**< 1 / 7,093**	**< 1 / 6,509**
Polio	< 1 / 1,685 billion	< 1 / 130 billion	< 1 / 81 billion	**< 1 / 50 billion**
Total	**< 1 / 24,834**	**< 1 / 9,652**	**< 1 / 7,093**	**< 1 / 6,509**

SRIU - Death

Age	6-11 mths	6 mths to 6 yrs	6 mths - 10 yrs	6 mths - 19 yrs
Diphtheria (D)	0 (or negligible)	< 1 / 143,336,109	< 1 / 65,383,532	**< 1 / 42,509,839**
Tetanus (T)	< 1 / 76,648,841	< 1 / 9,005,216	< 1 / 3,572,125	**< 1 / 1,506,184**
Pertussis (P)	< 1 / 16,346,415	< 1 / 2,981,653	< 1 / 2,441,421	**< 1 / 2,346,718**
Total D+T+P	**< 1 / 13,473,094**	**< 1 / 2,202,520**	**< 1 / 1,418,767**	**< 1 / 897,529**
Polio	< 1 / 34 trillion	< 1 / 2.6 trillion	< 1 / 1.6 trillion	**< 1 / 1 trillion**
Total	**< 1 / 13,473,088**	**< 1 / 2,202,938**	**< 1 / 1,417,698**	**< 1 / 897,528**

8.2 Measles, mumps, rubella, varicella, hepatitis b, hepatitis a, Hib, pneumococcal, meningococcal and influenza

RISK FROM NON-VACCINATION (SRIU)

Disease	Age range	SRIU	SRIU (hosp)	SRIU (death)
Measles (Me)	16 mos -19 yrs	< 1 / 440,478	< 1 / 2,569,455	< 1/ 106,506,429
Mumps (Mu)		< 1 / 553.375	< 1 / 553.375	< 1 / 40.371.594
Rubella (Ru)		< 1 / 965,653,132	zero to negligible	zero to negligible
	Total Me+Mu+Ru	**< 1 / 245,195**	**< 1 / 455,101**	**< 1 / 28,413,478**
Varicella	16 mos-19 yrs	< 1 / 58,894	< 1 / 58,894	< 1 / 32,331,860
Hepatitis A	1 - 17 yrs	< 1 / 10,000	< 1 / 44,235	< 1 / 1,667,135
Hepatitis B	1 - 22 yrs	< 1 / 66,000	< 1 / 66,000	< 1 / 305,465
Hib	6 mos - 4 yrs	< 1 / 56,400	< 1 / 56,400	< 1 / 1,494,710
Pneumococcal	6 mos - 4 yrs	< 1 / 2,790	< 1 / 4,500	< 1 / 236,562
Meningococcal	11 - 20 yrs	< 1 / 123,290	< 1 / 123,290	< 1 / 821,925
Influenza (deaths)	16 mos-17 yrs			< 1 / 135,905
	Total	**< 1 / 1,922**	**< 1 / 3,280**	**< 1 / 57,400**

Additionally, HRIU (differential risk of varicella disease-related herpes zoster) is estimated to be 1 in < 1 / 31,180.

8.3 Summary totals of non-vaccination risks for all targeted infectious diseases

Totalling the above risks for all of the above infectious diseases results in the following estimated totals for SRIU:

Disease	SRIU (total)	SRIU (hosp)	SRIU (death)
Total for diphtheria, tetanus, pertussis and polio	< 1 / 6,500	< 1 / 6,500	< 1 / 900,000
Total for measles, mumps, rubella, varicella, hepatitis B, hepatitis A, Hib, pneumococcal, meningococcal and influenza	< 1 / 1,922	< 1 / 3,280	< 1 / 57,400
Total	**< 1 / 1,480**	**< 1 / 2,180**	**< 1 / 54,000**

PART 3 – RISK FROM VACCINATION

9. Vaccination Risk (SRIV) – generally applicable information and background notes

The Plaintiff hereby requests that the Court take judicial notice of the following documents:

- entitled “Surveillance for Safety After Immunization: Vaccine Adverse Event Reporting System (VAERS) --- United States, 1991--2001”.

  Citation: MMWR Surveillance Summaries, Jan 24, 2003 / 52(ss01);1-24, accessible at https://www.cdc.gov/mmwr/preview/mmwrhtml/ss5201a1.htm
  (Erratum at https://www.cdc.gov/mmwr/preview/mmwrhtml/mm5206a7.htm)
  (last accessed July 11, 2020)

  (hereafter “CDC VAERS Surveillance 1991-2001 Report”)

  A true and correct copy of the aforesaid report is attached hereto as **Exhibit 190.**

9.1 Surveillance methods and their limitations

Types of vaccine safety surveillance – active and passive, and their limitations

Surveillance of adverse events (AEs) that arise after a vaccination, in particular serious AEs that are potentially causally related, may be done actively or passively.

Active surveillance

In active surveillance, the entity conducting the surveillance requests reports from individual subjects as to whether or not AEs have occurred. Hence it is more labor-intensive and easier to conduct when there is a more limited population of subjects.

Such circumstances provides more easily for the conduct of SAE causality assessments directly of individual reported SAEs, which, when combined with the known exact number of vaccine recipients and controls implemented in relation to the receipt of other vaccinations, enables a more direct estimate of the risk of that occurring.

Limitations of active surveillance

However, the number of monitored subjects, types of subject and monitoring period in active surveillance is limited by the practicalities of resources available for follow-up of each individual subject.

It follows that, as CDC VAERS Surveillance 1991-2001 Report states:

"Some adverse events are unlikely to be detected in prelicensure clinical trials because of their low frequency, the limited numbers of enrolled subjects, and other study limitations."

It can be reasoned that some serious adverse effects which do not become apparent soon enough and/or occur frequently enough to be likely to be picked up in clinical trials may, individually or as a group, nevertheless occur at a higher rate after vaccination than the rate of serious adverse effects from non-vaccination.

Even in the case of uncommon serious adverse effects that are picked up in active surveillance, the number of subjects may still be too limited to enable an estimate with an acceptable level of precision to be made of the overall frequency of such SAEs.

Resultant stated need for passive surveillance

CDC VAERS Surveillance 1991-2001 Report proceeds to state that to fully assess the level of risk after vaccination, it is "*essential*" to analyze data collected from postmarketing monitoring of spontaneously reported adverse events, i.e. passive surveillance, as follows:

"Therefore, postmarketing monitoring of adverse events after vaccinations is essential. The cornerstone of monitoring safety is review and analysis of spontaneously reported adverse events."

Accordingly, the CDC VAERS Surveillance 1991-2001 Report subsequently states:

"VAERS is a passive surveillance system: reports of events are voluntarily submitted by those who experience them, their caregivers, or others."

In passive surveillance, recipients of the vaccination are not individually contacted with requests for reports as to whether or not AEs have occurred, but a public health agency, in this case the CDC with VAERS, merely provides a collection point for such reports to be made spontaneously from a/the wider population, though the agency may issue broadly to the population and/or to interested groups within it, general encouragement to submit such reports.

Limitations of passive surveillance

However, the CDC VAERS Surveillance 1991-2001 Report states that passive surveillance also suffers from limitations:

"Passive surveillance systems (e.g., VAERS) are subject to multiple limitations, including underreporting, reporting of temporal associations or unconfirmed diagnoses, and lack of denominator data and unbiased comparison groups."

A further limitation of either surveillance – option to withdraw

A further limitation occurs due to the choice available to subjects of active or passive surveillance to withdraw from following the recommended vaccination schedule after experiencing an adverse event, even if the event is not an acknowledged medical contraindication. An example is the active surveillance of pneumococcal vaccination, as described in paragraph 11.6(a) herein.

There is a reasonable possibility that withdrawal of such subjects may artificially deflate SAE rates for the remaining recommended doses of the subject vaccination and/or other vaccinations. The result is that the surveillance is not of the safety of vaccinations as recommended but of the safety of those that are optionally taken.

Resultant requirement for other studies

CDC VAERS Surveillance 1991-2001 Report states:

"Vaccine safety concerns identified through adverse event monitoring nearly always require confirmation using an epidemiologic or other (e.g., laboratory) study".

However, application of the precautionary principle leads to emphasis on the converse – that any *low level* or *absence* of vaccine safety concerns identified through adverse event monitoring nearly always requires confirmation using an epidemiologic or other (e.g., laboratory) studies. Further, that requirement is all the more important where the risk posed in the community by the targeted disease is minimal to low.

Limitations of causality assessments, especially in the absence of such studies

In addition to the limitations listed above of active and passive surveillance, the determination of the rate of causally-associated SAEs without a properly conducted, large and rigorous enough non-vaccination versus vaccination comparison study is critically reliant upon the assessment of causality by causality assessors.

Such assessors are limited by their level of objectivity, accountability, training, knowledge and/or expertise. The level of scientific knowledge available to them is especially limited where such proper comparison studies have not already been conducted. An example of the potential effect of such limitations is that in the

absence of such studies that enable comparison with those unvaccinated, a comparison of SAE rate may be made instead with the "background rate" of the SAE type in a large population, in spite of that population being virtually entirely vaccinated. Hence a causal relationship may be unjustifiably rejected when the SAE is observed in any vaccine safety surveillance at a similar rate to the background rate.

Nevertheless, in this Part, quantitative analyses are presented of vaccination SAE risk that are based upon active surveillance in some cases, and passive surveillance in others. Hence they are all subject to the above limitations of active and/or passive surveillance.

9.2 Passive surveillance sources

(a) VAERS-related sources

The Plaintiff hereby requests that the Court take judicial notice of the following documents:

- the VAERS web page headed "About VAERS", located at
  https://vaers.hhs.gov/about.html
  (last accessed October 22, 2020)

  (hereafter "VAERS Page About VAERS")

  A true and correct copy of the aforesaid web page is attached hereto as **Exhibit 191**

- entitled "Introducing MEDWatch – A New Approach to Reporting Medication and Device"

  Citation: JAMA, June 2, 1993-Vol 269, No. 21, accessible at
  http://www.fda.gov/downloads/Safety/MedWatch/UCM201419.pdf
  (last accessed July 9, 2020)
  (hereafter "FDA SAE Underreporting Article")

  A true and correct copy of the aforesaid report is attached hereto as **Exhibit 192**

- entitled "Electronic Support for Public Health–Vaccine Adverse Event Reporting System (ESP:VAERS)"

  Citation: Grant ID: R18 HS017045, Inclusive dates: 12/01/07 - 09/30/10
  Principal Investigator: Lazarus, Ross, MBBS, MPH, MMed, GDCompSci;
  Team members: Michael Klompas, MD, MPH; Performing Organization:

Harvard Pilgrim Health Care, Inc.; Project Officer: Steve Bernstein; Submitted to: The Agency for Healthcare Research and Quality (AHRQ), U.S. Department of Health and Human Services, accessible at https://healthit.ahrq.gov/sites/default/files/docs/publication/r18hs017045-lazarus-final-report-2011.pdf
(last accessed July 9, 2020)
(hereafter "Lazarus Report")

A true and correct copy of the aforesaid report is attached hereto as **Exhibit 193**

- entitled "Electronic Support for Public Health - Vaccine Adverse Event Reporting System (ESP:VAERS) (Massachusetts), Summary"

  Citation: Grant Number: R18 HS017045, Funding Mechanism: Ambulatory Safety and Quality Program: Enabling Quality Measurement through Health IT (R18), Principal Investigator: Lazarus, Ross, Organization: Harvard Pilgrim Health Care, Inc., Location: Boston, Massachusetts. Project Dates: 12/7/2007 to 9/29/2010, accessible at https://digital.ahrq.gov/ahrq-funded-projects/electronic-support-public-health-vaccine-adverse-event-reporting-system
  (last accessed July 9, 2020)
  (hereafter "Lazarus Summary")

  A true and correct copy of the aforesaid report is attached hereto as **Exhibit 194**.

(b) Source for estimation of causality rate applicable to passive surveillance

The Plaintiff hereby requests that the Court take judicial notice of the following document:

- entitled "Surveillance of adverse events following immunisation: Australia, 2000–2002"

  Citation: Glenda Lawrence, Robert Menzies, Margaret Burgess, Peter McIntyre, Nicholas Wood, Ian Boyd, Patrick Purcell, David Isaacs, Commun Dis Intell 2003;27(3), located at https://www1.health.gov.au/internet/main/publishing.nsf/Content/cda-cdi2703-pdf-cnt.htm/$FILE/cdi2703a.pdf
  (last accessed July 8, 2020)

(hereafter “Report with AE Causality Rating Definitions”)

A true and correct copy of the aforesaid report is attached hereto as **Exhibit 195**.

The Plaintiff hereby requests that the Court take judicial notice of the following three documents, hereafter “AEFI Reports”:

- entitled “Annual Report on Surveillance of Adverse Events Following Immunisation In Australia, 2006”

  Citation: Glenda L Lawrence, Padmasiri E Aratchige, Ian Boyd, Peter B McIntyre, Michael S Gold. Commun Dis Intell 2007;31(3), located at https://www1.health.gov.au/internet/main/publishing.nsf/Content/cda-cdi3103-pdf-cnt.htm/$FILE/cdi3103b.pdf
  (last accessed July 8, 2020)
  (hereafter “AEFI Report 2006”)

  A true and correct copy of the aforesaid report is attached hereto as **Exhibit 196**.

- entitled “Annual Report on Surveillance of Adverse Events Following Immunisation In Australia, 2007”

  Citation: Glenda Lawrence, Michael S Gold, Richard Hill, Shelley Deeks, Amy Glasswell, Peter B McIntyre. Commun Dis Intell 2008;32(4), located at https://www1.health.gov.au/internet/main/publishing.nsf/Content/cda-cdi3204-pdf-cnt.htm/$FILE/cdi3204a.pdf
  (last accessed July 8, 2020)
  (hereafter “AEFI Report 2007”)

  A true and correct copy of the aforesaid report is attached hereto as **Exhibit 197**.

- entitled “Annual Report on Surveillance of Adverse Events Following Immunisation In Australia, 2008”

  Citation: Rob Menzies, Deepika Mahajan, Michael S Gold, Ilnaz, Roomiani, Peter McIntyre, Glenda Lawrence. Commun Dis Intell 2009;33(4), located at https://www1.health.gov.au/internet/main/publishing.nsf/Content/cda-cdi3304-pdf-cnt.htm/$FILE/cdi3304a.pdf
  (last accessed July 8, 2020)
  (hereafter “AEFI Report 2008”)

A true and correct copy of the aforesaid report is attached hereto as **Exhibit 198**.

Hereafter, the Notice may refer to the combined group of the above four documents: “Report with AE Causality Rating Definitions”, “AEFI Report 2006”, “AEFI Report 2007” and “AEFI Report 2008”, as “Australian Post-licensure Surveillance Reports”.

Adverse Event in Australian Surveillance (“AEFI”): The Australian Post-licensure Surveillance Reports provide the definition of an ‘adverse event following immunisation’ (hereafter “AEFI”) as follows:

“An ‘adverse event following immunisation’ is defined as any serious or unexpected adverse event that occurs after a vaccine has been given that may be related to the vaccine itself or to its handling or administration.”

Data contained in the AEFI Reports includes the following:

i. SAEFI

The AEFI Reports define an AEFI as “serious” (hereafter a “SAEFI”) as follows:

“In this report, an AEFI is defined as ‘serious’ if the record indicated that the person had recovered with sequelae; been admitted to a hospital or hospitalisation was prolonged; experienced a life-threatening event; or died.”

This definition of a serious adverse event accords with the VAERS SAE Definition (in paragraph 2.1 herein).

ii. SAEFI_ALL_CR

The Report with AE Causality Rating Definitions states:

“A causality rating is assigned to each AEFI using the criteria described in the Box, which describes the level of certainty that suspected vaccines or drugs caused the reported AEFI.”

and

“The data have been assessed using protocols consistent with international practice allowing comparison with AEFI surveillance data from other countries particularly the USA.”

and includes the following box under the title:

“Box. Criteria used to determine the causality rating of a notified adverse event”:*

The basic criteria used by the Adverse Drug Reactions Advisory Committee in determining causality ratings are consistent with international World Health Organization criteria and are as follows:

Certain
A reaction in association with a single drug/vaccine which is confirmed by re-challenge; or
reaction in association with a single drug/vaccine which is confirmed by laboratory data specifically implicating that drug/vaccine; or
reaction whose onset is immediately following the administration of a single drug/vaccine (within five minutes if injection was the method of administration); or
reaction with a precise spatial correlation with the administration of a single drug/vaccine (e.g. at the exact site of injection).

Probable
A reaction with a close temporal or spatial (e.g. skin) correlation with the administration of a single drug/vaccine; or
reaction is in reasonable temporal association with a single drug/vaccine and recovery on withdrawal of the drug/vaccine if no other drug/vaccine is withdrawn and no therapy given; or
an uncommon clinical phenomenon associated with the administration of a single drug/vaccine and the reasonable exclusion of other factors.

Possible
An alternative explanation exists; or
more than one drug/vaccine is suspected; in association with the adverse event; or
data are incomplete; or
recovery follows withdrawal of more than one drug/vaccine; or
the time relationship is not clear; or
the outcome of the reaction is not recorded; or
recovery follows therapy in addition to withdrawal of the drug/vaccine.

SAEFI_ALL_CR is the overall percentage of serious adverse events for all vaccine types covered in the report that have been given the causality categorization of ‘*certain*’ or ‘*probable*’.

Each year's AEFI Report provides the figure for SAEFI_ALL_CR for that year in "*Table 2*", in the column that is headed "*'Certain' or 'probable' causality rating*" and subheaded "*%*", and in the row that is headed "*Serious*".

The value of SAEFI_ALL_CR is stated in Row "B" in Table AU below.

For the purposes of this analysis it shall be assumed, despite the lack of certainty indicated by the "*probable*" and "*possible*" causality categories for SAEFIs, that approximately:

- all SAEFIs given a "*'Certain' or 'probable' causality rating*" are certainly caused by the administered vaccination(s), and that
- no other SAEs are caused by the administered vaccination(s), even though some that are categorized as "*possibly*" caused (or that are just "*suspected*" to be caused) may indeed be caused by the vaccination.

Hence, SAEFI_ALL_CR shall be taken as the approximate proportion of SAEFIs that are caused by the administered vaccination.

Parameters whose values are derived from SAEFI and SAEFI_ALL_CR include:

iii. SAEFI_C

SAEFI_C is, for each year's AEFI Report, the number of subject vaccination SAEFIs that will be estimated herein to have been caused by the administered vaccination, based upon SAEFI_ALL_CR and SAEFI. The formula applied herein for calculating SAEFI_C is:

SAEFI_C = SAEFI_ALL_CR x SAEFI,

and

vi. SAEFI_CR

SAEFI_CR is, as a single total for all AEFI Reports, the overall percentage of all subject vaccine SAEFIs that will be estimated herein to have been caused by the administered vaccination. The formula applied for calculating SAEFI_CR is:

SAEFI_CR = Total of SAEFI_Cs for all years 2006-2008

÷ Total of SAEFIs for all years 2006-2008.

9.3 Terms and parameters in vaccination risk analyses – definitions and derivations

(a) Terms

Where vaccinations being assessed include different doses that are scheduled to be administered prior to elementary school and secondary school, any risk analysis presented in this Part based upon passive surveillance may be divided into different analyses for respective applicable age ranges applicable to those doses:

a. in relation to vaccinations recommended and/or required to be administered prior to elementary school entry at around 5 years of age, hereafter the "Elementary Analysis", and

b. in relation to vaccinations scheduled recommended and/or required to be administered at 11-17 years of age, hereafter the "Secondary Analysis".

This Notice may refer to "Elementary Analysis" and "Secondary Analysis" together as the "Elementary and Secondary Analyses" or "Analyses" or to any one of the analyses as "Elementary or Secondary Analysis" or "Analysis".

With respect to an analysis based on passive or active surveillance:

i. **subject disease(s)**: the disease(s) targeted by the vaccination(s) that are the subject of the analysis will be referred to as the "subject disease(s)"

ii. **subject disease subgroup**: See paragraph 9.3(b)xiv (headed "PCENT_SUBGRP_SUBJ")

iii. **subject vaccine(s)/vaccination(s):** the vaccine(s)/vaccination(s) that are the subject of the analysis will be referred to as the "subject vaccine(s)/vaccination(s)".

iv. **Surveillance Period**: any passive or active analysis presented herein is limited to a period of time called the "Surveillance Period",

v. **subject children**: the children (or adolescents) who received the subject vaccination(s) dose(s) during the Surveillance Period are the "subject children".

vi. **subject vaccine(s)/vaccination(s) dose(s):** the vaccine(s)/vaccination dose(s) to which the analysis relates will be referred to as the "subject vaccine(s)/vaccination(s) dose(s)". All subject vaccine(s)/vaccination(s) doses are administered during the Surveillance Period.

vii. **subject vaccine type**: “subject vaccine type” is a vaccine product that may be recorded in a relevant surveillance report as having been administered against one or more of the subject diseases

viii. **concomitant**: the word “concomitant” is used to refer to a non-subject vaccine that is reported to have been administered at the same time as a subject vaccine.

ix. **VAERS Extraction Reports**: the primary risk data upon which analyses of passive surveillance relates is sourced from reports extracted from the Vaccine Adverse Event Reporting System (VAERS) database, using the online query facility provided by the CDC to the public. Those reports that relate to the “Elementary Analysis” are referred to as “Elementary Reports”. Those relating to the “Secondary Analysis” are referred to as “Secondary Reports”. A report that may be either a Elementary Report or Secondary Report is referred to as a “VAERS Extraction Report”.

x. **Population (“P”)**: relevant for passive surveillance analysis of VAERS, “Population” (“P”) is the relevant target population to which vaccination coverage estimates apply, when calculating the approximate number of vaccination doses administered to the subject children during the Surveillance Period.

(b) Parameters

The following parameters will form the basis of each Analysis herein:

i. SAE_REP

“SAE_REP” means the number of SAEs Reported to the active or passive surveillance data base that is the source of data for any vaccine risk analysis presented herein.

ii. SAE_DEATH

“SAE_DEATH” means the number of SAE_REPs that are either recorded for the SP in the “*Event Category*” “*Death*”, or estimated on average for a surveillance period of the same length, proportionately based upon the number recorded in the same database over a longer surveillance period, to enable a statistically more precise estimation of the overall frequency of reported deaths after the vaccination.

iii. SAE_HOSP

"SAE_HOSP" means the number of SAE_REPs that are recorded for the SP in the "*Event Category*" "*Hospitalized*" or "*Existing Hospitalization Prolonged"*.

iv. NR

The CDC VAERS Surveillance 1991-2001 Report states:

> *"VAERS is subject to the limitations inherent in any passive surveillance system (54). Among those, …only a fraction of the total number of potentially reportable events occurring after vaccination are reported".*

Of all post-vaccination serious adverse events that occur in the US and are at least possibly causally related, the maximum percentage that is reported in passive surveillance is the Notification (or reporting) completeness Rate, hereafter "NR".

NR is estimated herein to be 1%, based upon the following statements:

- in the FDA SAE Underreporting Article:

  > *"Only about 1% of serious events are reported to the FDA, according to one study"*

- in the Lazarus Report, under the heading "*Results*":

  > *"Although 25% of ambulatory patients experience an adverse drug event, less than 0.3% of all adverse drug events and 1-13% of serious events are reported to the Food and Drug Administration (FDA). Likewise, fewer than 1% of vaccine adverse events are reported."*

- in the Lazarus Summary:

  > *"Adverse events from vaccines are common but underreported, with less than one percent reported to the Food and Drug Administration (FDA). Low reporting rates preclude or delay the identification of "problem" vaccines, potentially endangering the health of the public. New surveillance methods for drug and vaccine adverse effects are needed."*

It shall be assumed herein that the NR of 1% applies specifically to hospitalizations (including extended hospitalizations) and deaths as well as to the overall number of SAEs.

v. SAE_ACTUAL

"SAE_ACTUAL" is the known or the estimated minimum actual number of serious adverse events that occurred during the Surveillance Period following the subject vaccination(s) with or without concomitant vaccination(s) within the query age group of the Population.

In the case of passive surveillance, the SAE_ACTUAL is calculated based upon SAE_REP and the Notification completeness Rate, by applying the following formula:

SAE_ACTUAL = SAE_REP ÷ NR

vi. SAE_CR

Based upon the statement in the VAERS Page About VAERS that AEs are only "*possible side effects …after a person has received a vaccination*", a proportion of AEs may not be caused by the administered vaccination.

"SAE_CR" is the known or estimated proportion or percentage of SAE_ACTUALs that were caused by the administered vaccination(s).

In the case of sets of SAEs where no causality assessment has been recorded, the value of SAE_CR is assumed to approximate SAEFI_CR, which is derived from the AEFI Reports (see paragraph (b)(b)(b) herein).

vii. SAE_C

Based upon SAE_CR, "SAE_C" is the subset of SAE_ACTUALs assessed or estimated to have been caused by the administered vaccination(s), including the subject vaccinations and, where any, concomitant non-subject vaccinations.

Accordingly, where SAE_C is not determined by direct assessment but an estimate is available for SAE_CR, the formula for calculating SAE_C is:

SAE_C = SAE_ACTUAL x SAE_CR

viii. SAE_SUBJ_ONLY

"SAE_SUBJ_ONLY" is the number of SAE_REPs where only the subject vaccination(s) were administered, i.e. where no non-subject vaccinations were concomitantly administered.

ix. PCENT_SUBJ_ONLY

"PCENT_SUBJ_ONLY" is the percentage of SAE_REPs where only the subject vaccination(s) were administered, i.e. where no non-subject vaccinations were concomitantly administered.

Accordingly, the formula applied for calculating PCENT_SUBJ_ONLY will be:

PCENT_SUBJ_ONLY = SAE_SUBJ_ONLY ÷ SAE x 100%

x. V_SP_SUBJ_COM

For the set of SAE_REPs, "V_SP_SUBJ_COM" is the number of subject vaccine doses that were concomitantly administered with non-subject vaccine doses.

xi. V_SP_ALL_COM

For the set of SAE_REPs, the total number of concomitantly administered subject and non-subject vaccine doses is "V_SP_ALL_COM".

xii. PCENT_SUBJ_COM

For the set of SAE_REPs where subject and non-subject vaccine doses were concomitantly administered, the percentage of those doses that were of the subject vaccine(s) is "PCENT_SUBJ_COM".

Accordingly, the formula for calculating PCENT_SUBJ_COM is:

PCENT_SUBJ_COM = V_SP_SUBJ_COM ÷ V_SP_ALL_COM x 100%.

xiii. SAE_C_SUBJ

"SAE_C_SUBJ" is the number of SAE_Cs estimated to be attributable to one or more of the subject vaccines, excluding those attributable to concomitantly administered vaccines.

In sets of SAEs where the assessment of which SAEs or SAE_C are SAE_C_SUBJs is not recorded, it is derived by adding:

- in relation to those SAE_Cs where only the subject vaccine(s) were administered (PCENT_SUBJ_ONLY),
  PCENT_SUBJ_ONLY multiplied by SAE_C,

plus

- in relation to the remaining percentage (100% minus PCENT_SUBJ_ONLY) of SAE_Cs, i.e. where other vaccinations were

concomitantly administered, the estimated proportional contribution made by the subject vaccines, based upon the proportional number of administered doses that were subject vaccine doses, i.e. (100% minus PCENT_SUBJ_ONLY) multiplied by PCENT_SUBJ_COM multiplied by SAE_C.

In estimating the proportional contribution made by the subject vaccines as PCENT_SUBJ_COM, an assumption is made that the average proportional contribution made by each subject vaccine injection to the causation of the SAE_Cs approximated the average proportional contribution made by each non-subject vaccine injection.

Accordingly, the formula for estimating SAE_C_SUBJ is:

SAE_C_SUBJ = SAE_C x (PCENT_SUBJ_ONLY + (100% - PCENT_SUBJ_ONLY) x PCENT_SUBJ_COM).

xiv. PCENT_SUBGRP_SUBJ

In the case of any analysis, there may be two or more subgroups of subject vaccinations, each targeting its own “subject disease subgroup” (which may be alternatively referred to by just the one word “subgroup”). The subgroups may be in the earlier part of the analysis be analysed together as a group, before it is broken down for separate analysis of each subgroup.

That applies in the case of DTaP-IPV vaccinations. One subject disease subgroup includes diphtheria, tetanus and pertussis only. The other subject disease subgroup includes only poliomyelitis. The causality of the associated SAEs can accordingly be further apportioned, approximately, to the different vaccinations associated with each of those different two subgroups.

In relation to DTaP-IPV, the method presented herein for that apportionment is to first take the subset of VAERS IDs associated only with SAE_SUBJ_ONLYs. After excluding those VAERS IDs where a combined vaccination which targets multiple subject disease subgroups, all the remaining VAERS IDs are where only vaccines targeting any of the individual subgroups was administered. Of the total number of vaccine doses associated with those remaining VAERS IDs, the percentage of doses administered to each subject disease subgroup is “PCENT_SUBGRP_SUBJ” for that subject disease subgroup.

Where there is only one group, or subgroup, of subject vaccinations, PCENT_SUBGRP_SUBJ is 100%.

xv. SAE_C_SUBGRP

Based upon PCENT_SUBGRP_SUBJ for a particular subject disease subgroup, an estimate is made of the number of SAE_C_SUBJs attributable to the vaccinations for that subject disease subgroup, and that number is “SAE_C_SUBGRP”.

Accordingly, the formula applied for estimating SAE_C_SUBGRP for each subject disease subgroup will be:

SAE_C_SUBGRP = SAE_C_SUBJ x PCENT_SUBGRP_SUBJ.

That formula incorporates an assumption that each subject vaccine injection made, on average, an approximately equal contribution to the causation of the associated serious adverse events.

xvi. V_SP

In order to estimate the rate at which SAEs occurred per vaccine dose against the subject disease, disease group or subgroup in the Surveillance Period, an estimate is made of the number of respective subject disease subgroup vaccine doses that were administered during the Surveillance Period, which number is “V_SP”.

Where V_SP is not directly available, it can be estimated by multiplying, for the relevant age range, the US resident population (“P”), by the vaccination coverage (VC) for the subject disease subgroup during the Surveillance Period.

Accordingly, in relation to a particular subject disease subgroup, the applicable formula is:

V_SP = P x VC

where “V_SP” is the total number of vaccination doses, targeting that subject disease subgroup, that were administered during the Surveillance Period to the Population.

xvii. SRI

"SRI" is the estimated minimum rate of occurrence per dose of serious adverse effects attributable to the particular vaccination(s) that target(s) the subject disease subgroup.

Accordingly, the formula applicable for calculating SRI, where the value of SAE_C_SUBGRP is known, is for any subject disease subgroup,

SRI = SAE_C_SUBGRP ÷ V_SP

for the subject disease subgroup.

xviii. V_SCH

In relation to a subject disease subgroup, "V_SCH" is the number of vaccination doses that are, as at the date of filing of this Notice, recommended by the CDC to be administered prior to a particular age range for protection against the targeted disease(s) during that age range.

V_SCH is determined based upon the text in relation to the subject disease(s) under the heading "*Notes*" in CDC Schedule 2020, where the text indicates the youngest age at which each dose is recommended.

If any dose is intended to protect over multiple age ranges, or only a portion of an age range, that is/are chosen for the analysis, the value of V_SCH is apportioned to each age range based upon the number of years within the age range. (See paragraph 10.1(f) herein where V_SCH is calculated for diphtheria-tetanus-pertussis and polio.)

xix. SRIV

"SRIV" for a subject disease subgroup for a given age range is the estimated minimum total rate, or risk, of occurrence of SAEs attributable to the full number of vaccination doses that, according to the CDC schedules, the CDC recommends be administered, on average, to an individual against that subject disease subgroup for disease protection primarily over that age range.

An estimate of SRIV is calculated for the purpose of comparison with the total rate of occurrence of serious disease-associated adverse effects sought to be prevented by that vaccination dose(s) or set of doses over the same age range.

An assumption will be made herein that the SRI for each vaccination dose is the same regardless of the age at which the vaccination dose is administered or other circumstances that may differ from one administration to the next.

Based upon that assumption, SRIV for any period is directly proportional to the number of vaccination doses administered in relation to that period.

Accordingly, the formula that will be applied for calculating SRIV in this Notice will be:

SRIV = SRI x V_SCH

SRIV may alternatively be expressed as follows in terms of all of the above source variables, if all of their values are known:

SRIV = (SAE_REP / NR x SAE_CR x (PCENT_SUBJ_ONLY +
(1 - PCENT_SUBJ_ONLY) x PCENT_SUBJ_COM)) x
PCENT_SUBGRP_SUBJ / V_SP x V_SCH

xx. SRIV_HOSP

"SRIV_HOSP" is the same as SRIV except that it is limited to SAEs that are in the Event Categories of "Hospitalization" and "Extended Hospitalization".

SRIV_HOSP is estimated based upon the proportion of SAE_HOSP to SAE recorded in the VAERS Extraction Reports.

Hence SRIV_HOSP is estimated by the calculation:

SRIV_HOSP = SRIV x SAE_HOSP ÷ SAE

xxi. SRIV_DEATH

"SRIV_DEATH" is the same as SRIV except that it is limited to SAEs that are in the Event Category of "Death".

SRIV_DEATH is estimated based upon the proportion of SAE_DEATH to SAE recorded in the VAERS Extraction Reports.

Hence SRIV_DEATH is estimated by the calculation:

SRIV_DEATH = SRIV x SAE_DEATH ÷ SAE.

10. Risk from diphtheria, tetanus, pertussis and polio vaccinations

The analysis presented herein of risk from diphtheria, tetanus, pertussis and polio vaccinations is based upon records collected from passive surveillance and relevant reports.

10.1 Parameter values not sourced from VAERS Extraction Reports

(a) Subject diseases and subject vaccine(s)/vaccination(s)

In the case of:

- the Elementary Analysis, the subject diseases are diphtheria, tetanus, pertussis and/or poliomyelitis, and the subject vaccine(s)/vaccination(s) are the combined vaccine(s)/vaccination(s) that target diphtheria-tetanus-pertussis in under 10 year olds (DTaP) and the single vaccine that targets poliomyelitis (IPV) and the combined vaccine(s)/vaccination(s) that target diphtheria-tetanus-pertussis-poliomyelitis (DTaP-IPV), and
- the Secondary Analysis, the subject diseases are diphtheria, tetanus and pertussis, and the subject vaccine(s)/vaccination is the combined vaccine(s)/vaccination(s) that targets diphtheria-tetanus-pertussis in over 10 year olds (Tdap).

(b) Query age range/group

In relation to analysis of the VAERS passive surveillance data base, a “query age range” is selected amongst the criteria applied for the query of the VAERS database (the “Query Criteria”) for the purpose of the analysis. The choice of query age range is restricted to the limited set of query age ranges that the CDC provides in the publicly available VAERS query facility.

In the case of:

- the Elementary Analysis, the query age range is 3-5 years.
- the Secondary Analysis, the query age range is 6-17 years.
- the subject children selected in the query are residents of a US State or the District of Columbia.

(c) Surveillance Period

The Surveillance Period (“SP”) chosen for the

- Elementary Analysis is the 3 year period of June 1 2006 to May 31 2009, and

- Secondary Analysis is the 4 year period of January 1 2006 to December 31 2009.

In each VAERS Extraction Report the Surveillance Period accordingly appears amongst the criteria applied in the query of the VAERS database (the "Query Criteria").

(d) SAE_CR

Each year's AEFI Report provides the **SAEFI** figure for the "DTPa-IPV" [13] vaccine type in "Table 3", in the column headed "'Serious' outcome" and subheaded "n".

SAEFI_ALL_CR respectively. Rows "C" and "D" contain the results of calculations that are based upon those values, based upon the stated formulas:

Row	Description	Abbreviation	Source (S) / Formula	Report year			Total
				2006	2007	2008	
A	'Serious' outcome from DTaP-IPV vaccine	SAEFI	S: AEFI reports	*28*	*24*	*18*	70
B	% all SAEFIs with causality rating 'certain' or 'probable'	SAEFI_ALL_CR	S: AEFI reports	*29%*	*20%*	*12%*	
C	DTaP-IPV SAEFIs with causality rating 'certain' or 'probable' (estimate)	SAEFI_C	Formula: A x B	8	5	2	15
D	% all DTaP-IPV SAEFIs with causality rating 'certain' or 'probable' (estimate)	SAEFI_CR	Formula: Total C ÷ Total B				**21.4%**

Based upon these calculations therein, the value of SAE_CR for DTPa-IPV is 21.4%. It is assumed herein that the same value of SAE_CR is approximately equally applicable to individual DTaP, IPV and Tdap vaccinations.

[13] The AEFI Reports provides the following definition of the "DTPa-IPV " abbreviation used therein: "*combined diphtheria-tetanus-pertussis (acellular) and inactivated poliovirus (quadrivalent)*". Based upon that definition, the abbreviation "*DTPa-IPV*" in the AEFI Reports is taken to mean the same as the abbreviation "DTaP-IPV" used in this Notice.

(e) V_SP

i. Elementary V_SP

a. Population

The CDC Schedule tables for the years 2006 to 2009 show, after the fourth DTaP vaccine dose scheduled at "*Age*" "*15 months*" and "*18 months*", the next DTaP vaccine dose, the fifth, is not scheduled until "*Age*" "*4-6 years*". However, the query age range is the 3-5 year age range.

Based upon these facts and the intersection of the 4-6 year and 3-5 year age ranges, the Population for the Elementary Analysis is taken to approximate the US resident population in the 4-5 year age range during the Surveillance Period.

The Selected Single Year Age Groups Population Table includes the midyear US resident population data for the years 2006 to 2009 for ages 4 and 5 years.

That data is quoted in the column headed "*Midyear Population*" in the table below, along with the calculated average of those populations over the Surveillance Period.

Year	*Age*	Mid-year Population	Average 4-5 year old mid-year Population	Average 4-5 year old end-of-year Population
2006	*4*	*3,970,880*	4,010,731	4,003,303
	5	*4,050,582*		
2007	*4*	*3,998,260*	3,995,875	4,014,304
	5	*3,993,489*		
2008	*4*	*4,041,170*	4,032,734	
	5	*4,024,297*		
2009	*4*	*4,033,457*	4,051,861	4,042,297
	5	*4,070,265*		
Estimated Population during Surveillance Period:				**12,039,339**

Based upon the data in the above table, the Population for the 3 year Surveillance Period during the Elementary Analysis shall be estimated to be **12,039,339**.

b. Vaccination Coverage

According to the two relevant CDC Elementary School Coverage Reports that are available, i.e. for 2006-2007 and 2009-2010, the "*up-to-*

date" vaccination coverages in the US for the subject vaccine "*doses required for school entry"* in the years 2006-2007 and 2009-2010 "*among children in kindergarten*" in the respective years were as set out for the respective two periods 2006-2007 and 2009-2010 in the table below:

Year	***DTP / DTaP / DT*** [14]	***Polio***
2006-2007	*96.0%*	*96.3%*
2009-2010	*95.3%*	*95.65 %*
Estimated Average for Surveillance Period	**95.7%**	**96.0%**

In relation to the calculation presented herein of an estimate of the number of subject disease subgroup vaccine doses administered during the Surveillance Period, an assumption is made that the said "*up-to-date*" vaccination coverage estimates apply reasonably closely to coverage of one dose in the query age range of 3-5 years.

That assumption is made in spite of:

- the fact that the two reports respectively state:

  "the vaccinations required …vary substantially among states"

  and

  "All reporting grantees require 3 or 4 doses of poliovirus vaccine… School entry requirements for other vaccinations vary by state/area: 44 grantees require 4 or 5 doses of DTP/DTaP/DT".

  Based upon those statements, potentially many of those "covered" children did not receive any subject vaccine dose while in the query age range of 3-5 years.

- any possibility, on the other hand, that a significant number of subject children received more than one subject vaccine dose while in the query age range of 3-5 years during the Surveillance Period.

[14] Given that the CDC Schedules did not include the option of DPT or DT in the recommendations for children in the relevant age range, it is assumed herein that an insignificant number of children, if any, received either of those vaccinations instead of DTaP.

c. Combining Population and Vaccination Coverage estimates

Based upon the above assumption and the estimated population and coverage figures in the two tables above, the following approximations can be made for the two subject disease subgroups:

- for diphtheria, tetanus and pertussis,

  V_SP ≈ < 12,039,339 x 95.7%,

  ≈ < 11,535,298, and

- for polio,

  V_SP ≈ < 12,039,339 x 96.0%,

  ≈ < 11,574,493.

ii. Secondary V_SP

The CDC Schedule 2006 is dated "*January 6, 2006*" and states:

"A new tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis vaccine recommended by ACIP for adolescents (Tdap adolescent preparation) was approved by the Food and Drug Administration (FDA) on May 5, 2005, for use in the United States. Tdap is recommended for adolescents aged 11–12 years who have completed the recommended childhood diphtheria and tetanus toxoids and pertussis/diphtheria and tetanus toxoids and acellular pertussis (DTP/DTaP) vaccination series and have not received a tetanus and diphtheria toxoids (Td) booster dose. Adolescents aged 13–18 years who missed the age 11–12-year Td/Tdap booster dose should also receive a single dose of Tdap if they have completed the recommended childhood DTP/DTaP vaccination series."

Based upon that date and those statements in CDC Schedule 2006, approximately one year elapsed from when the Tdap vaccination was first approved by the FDA (May 5, 2006) to the beginning of the Surveillance Period (June 1, 2006) and a single dose of the Tdap vaccine was recommended from at least as early as January 6, 2006.

Nevertheless, in the calculation of V_SP (=P x VC) in the analysis, an assumption will be made that all Tdap vaccines administered to the subject children were administered during the Surveillance Period.

- In the case of the Secondary Analysis, the CDC Schedules state that the Tdap vaccine dose was recommended to be administered no more than once during the 6-17 age range (from the age of 11 years of age).

The table below contains columns “A” to “D” whose values are sourced or calculated as follows:

a. Column A, headed “Population”

This column contains the midyear US resident population data for the years 2006 – 2009 for each age 11 through 17 years, sourced from the Single Year Age Group Data.

b. Column B, headed “Estimated Coverage”

This column contains in *italics* the published Tdap vaccination coverage estimates published in the CDC Secondary School Coverage Reports. The other figures in that column (not in italics) are coverage estimates for children 11-12 years of age, which are derived from backward extrapolation from the decline in coverage from 13 to 14 year olds, except for the estimate for 12 year olds in 2006 (18.7%), which is based upon the decline from 14 to 15 year olds.

As each cohort ages by a year, more children/adolescents in the cohort are vaccinated, so the coverage is thus accumulative. For example, the coverage for 14 year olds in 2007 is 37.3%, which grows to 41.5% in 2008 for a group who are assumed to be virtually the same individuals, by then aged 15.

c. Column C, headed “Estimated doses by year end”

This figure is the estimated number of Tdap doses received by that year based upon the Population in Column A and vaccination coverage in Column B.

d. Column D, headed “Incremental doses during SP”

This figure is the incremental number of doses estimated to have been received by that cohort of children/adolescents since the previous year or, in the case of 2006, since the beginning of the Surveillance Period (“**SP**”) and prior to its end, based upon the assumption that all Tdap vaccines administered to the subject children were administered during

the Surveillance Period, even though some may have been administered in 2005.

For 12 through 17 year olds in 2007 and 2009, the figure in Column D is derived by subtracting from that row's figure in Column C, the figure in Column C for the one year lower age group in the previous year. For example, for 15 year olds in 2008, the figure of 203,583 in Column D is derived by subtracting from 1,792,378 in Column C the figure of 1,588,795 in Column C for 14 year olds in 2007.

It is assumed herein that, in accordance with the CDC recommendation stated in the CDC Schedules, virtually no Tdap vaccine doses are administered to children under 11 years of age.

Column:		A	B	C = A x B	D
Year	***Age***	***Population (mid-year)***	**Estimated Coverage by year end**	**Estimated doses by year end**	**Incremental doses during SP**
2006	*11*	*4,141,970*	24.7%	1,023,067	1,023,067
	12	*4,196,880*	18.7%	784,817	784,817
	13	*4,264,733*	*12.7%*	541,621	541,621
	14	*4,308,450*	*15.4%*	663,501	663,501
	15	*4,406,515*	*12.1%*	533,188	533,188
	16	*4,502,997*	*8.0%*	360,240	360,240
	17	*4,331,493*	*5.1%*	220,906	220,906
2007	*11*	*4,106,492*	55.0%	2,258,571	2,258,571
	12	*4,192,002*	49.1%	2,058,273	1,035,206
	13	*4,207,326*	*43.2%*	1,817,565	1,032,748
	14	*4,259,504*	*37.3%*	1,588,795	1,047,174
	15	*4,364,495*	*28.3%*	1,235,152	571,651
	16	*4,452,250*	*24.9%*	1,108,610	575,422
	17	*4,521,045*	*19.0%*	858,999	498,759
2008	*11*	*4,055,388*	61.1%	2,477,842	2,477,842
	12	*4,159,477*	56.5%	2,350,105	91,534
	13	*4,200,016*	*51.9%*	2,179,808	121,535
	14	*4,198,094*	*47.3%*	1,985,698	168,134
	15	*4,318,982*	*41.5%*	1,792,378	203,583
	16	*4,411,176*	*35.1%*	1,548,323	313,171
	17	*4,467,060*	*28.7%*	1,282,046	173,436
2009	*11*	*4,066,605*	68.6%	2,789,691	2,789,691
	12	*4,110,576*	66.9%	2,749,975	2,749,975
	13	*4,164,413*	*65.2%*	2,715,197	2,715,197
	14	*4,185,880*	*63.5%*	2,658,034	2,658,034
	15	*4,259,907*	*58.3%*	2,483,526	2,483,526
	16	*4,365,338*	*46.8%*	2,042,978	2,042,978
	17	*4,421,341*	*43.6%*	1,927,705	1,927,705
Estimated total doses in Surveillance Period					**19,729,057**

(f) V_SCH

The "*Notes*" in CDC Schedule 2020 state:

> *"Diphtheria, tetanus, and pertussis (DTaP) vaccination …*
>
> *Routine vaccination*
>
> • *5-dose series at 2, 4, 6, 15–18 months, 4–6 years*
>
> *- Prospectively: Dose 4 may be administered as early as age 12 months if at least 6 months have elapsed since dose 3"*

and

"Poliovirus vaccination …

Routine vaccination

- *4-dose series at ages 2, 4, 6–18 months, 4–6 years; administer the final dose at or after age 4 years and at least 6 months after the previous dose."*

According to those notes, the following numbers of doses are recommended with approximate apportionment by the number of years in respective age ranges that follow their recommended administration:

- 6 months – 11 months, 3 doses of DTaP and 2 doses of IPV,
- 1 – 4 years, 1 dose of DTaP and 1 dose of IPV,
- 5 – 6 years, 1/3 dose of DTaP and 2/15 dose of IPV
- 7 – 10 years, 2/3 dose of DTaP and 4/15 dose of IPV
- 11 – 19 years, 1 dose of Tdap and 9/15 doses of IPV.

Based upon those recommendations, for the age ranges of 6 to 11 months, 1 – 6 years, 7 to 10 years and 11 – 10 years,

- V_SCH is 3, $1^{1}/_{3}$, $^{2}/_{3}$ and 1 respectively for the diphtheria-tetanus-pertussis subgroup, and
- V_SCH is 2, $1^{2}/_{15}$, $^{4}/_{15}$ and $^{9}/_{15}$ for the polio subgroup.

10.2 VAERS Extraction Reports sources for parameter values

The Plaintiff hereby requests that the Court take judicial notice of the following documents, all of which are entitled "The Vaccine Adverse Event Reporting System (VAERS) Results", and available from:

Vaccine Adverse Event Reporting System (VAERS),
CDC WONDER Online Database,
United States Department of Health and Human Services (DHHS) Public Health Service (PHS),
Centers for Disease Control (CDC) / Food and Drug Administration (FDA),
accessible from http://wonder.cdc.gov/vaers.html

and subtitled (by the Plaintiff):

(a) VAERS Extraction Reports for Elementary Analysis

i. **"SAEs totaled**

- Elementary (DTaP-IPV, DTaP, IPV), June 2006 – May 2009 (141 VAERS IDs,253 SAEs)",

to which a submitted search request is located at
https://wonder.cdc.gov/controller/saved/D8/D95F373[15]
(last accessed Nov 7, 2020)
(hereafter "Elementary DTaP & IPV – Reported SAEs Totaled")

A true and correct copy of the aforesaid report is attached hereto as **Exhibit 199**

ii. "VAERS IDs

- Elementary (DTaP-IPV, DTaP, IPV), Jun 2006 – May 2009 (141 VAERS IDs 253 SAEs)",

to which a submitted search request is located at
https://wonder.cdc.gov/controller/saved/D8/D95F369[14]
(last accessed Nov 7, 2020)
(hereafter "Elementary DTaP & IPV – VAERS IDs")

A true and correct copy of the aforesaid report is attached hereto as **Exhibit 200**

iii. "**All Vaccine Types for VAERS-IDs**

- Elementary (DTaP-IPV, DTaP, IPV), Jun2006-May2009 (141 VAERS IDs,253 SAEs)",

to which a submitted search request is located at
https://wonder.cdc.gov/controller/saved/D8/D95F325[14]
(last accessed Nov 7, 2020)
(hereafter "Elementary DTaP & IPV – All Vaccine Types for VAERS-IDs")

A true and correct copy of the aforesaid report is attached hereto as **Exhibit 201**

iv. "SAEs Where No Concomitant Vaccinations

- Elementary(DTaP-IPV,DTaP,IPV), Jun2006 – May2009 (21 VAERS IDs, 36 SAEs)",

[15] On the online "Request Form" to which this web page links, the query date ranges in sections 7, 8, 10 and 11 may need to be reset to their default values (by clicking on blue counter-clockwise swoop image to the right of the date range fields) for the full results to appear in the report.

to which a submitted search request is located at
https://wonder.cdc.gov/controller/saved/D8/D95F326[14]
(last accessed Nov 7, 2020)
(hereafter "Elementary DTaP & IPV – SAEs Where No Concomitant Vaccinations")

A true and correct copy of the aforesaid report is attached hereto as **Exhibit 202**

v. "**Vaccine Types and Doses Where Concomitants**

- Elementary (DTaP-IPV, DTaP, IPV), Jun2006 – May2009 (120 VAERS IDs, 217 SAEs, 407 doses)"

to which a submitted search request is located at
https://wonder.cdc.gov/controller/saved/D8/D95F587[14]
(last accessed Nov 10, 2020)
(hereafter
"Elementary DTaP & IPV – Vaccine Types and Doses Where Concomitants")

A true and correct copy of the aforesaid report is attached hereto as **Exhibit 203.**

vi. "**All Subject Vaccine Doses Where No Concomitants**

- Elementary (DTaP-IPV,DTaP,IPV), Jun 2006 – May 2009 (21 VAERS IDs, 36 SAEs, 32 doses)"

to which a submitted search request is located at
https://wonder.cdc.gov/controller/saved/D8/D95F329[14]
(last accessed Nov 7, 2020)
(hereafter "Elementary DTaP & IPV –All Subject Vaccine Doses Where No Concomitants")

A true and correct copy of the aforesaid report is attached hereto as **Exhibit 204.**

The above five documents may be referenced as a group herein as the "Elementary Reports".

vii. "**SAEs (death) over 9 years**

- Elementary (DTaP-IPV,DTaP,IPV), June 2008 – May 2017 (9 deaths)

to which a submitted search request is located at
https://wonder.cdc.gov/controller/saved/D8/D96F617[14]
(last accessed Nov 26, 2020)
(hereafter "Elementary DTaP & IPV – Total Deaths over 9 Year Period")

A true and correct copy of the aforesaid report is attached hereto as **Exhibit 205.**

The above seven documents may be referenced as a group herein as the "Elementary Reports".

(b) VAERS Extraction Reports for Secondary Analysis

i. "**SAEs totaled**

- Secondary (Tdap), 2006 - 2009 (198 VAERS IDs, 388 SAEs)"

to which a submitted search request is located at
https://wonder.cdc.gov/controller/saved/D8/D95F375[14]
(last accessed November 7, 2020)
(hereafter "Secondary Tdap – Reported SAEs Totaled")

A true and correct copy of the aforesaid report is attached hereto as **Exhibit 206**

ii. "**VAERS IDs**

- Secondary (Tdap), 2006 – 2009 (198 VAERS IDs, 388 SAEs)",

to which a submitted search request is located at
https://wonder.cdc.gov/controller/saved/D8/D95F376[14]
(last accessed November 7, 2020)
(hereafter "Secondary Tdap – VAERS IDs")

A true and correct copy of the aforesaid report is attached hereto as **Exhibit 207**

iii. "All Vaccine Types for VAERS-IDs

- Secondary (Tdap), 2006 - 2009 (198 VAERS IDs, 388 SAEs)",

to which a submitted search request is located at
https://wonder.cdc.gov/controller/saved/D8/D95F378[14]
(last accessed November 7, 2020)
(hereafter "Secondary Tdap – All Vaccine Types for VAERS-IDs")

A true and correct copy of the aforesaid report is attached hereto as **Exhibit 208**

iv. "SAEs Where No Concomitant Vaccinations

- Secondary (Tdap), 2006 - 2009 (30 VAERS IDs, 67 SAEs)",

to which a submitted search request is located at
https://wonder.cdc.gov/controller/saved/D8/D95F380[14]
(last accessed November 7, 2020)
(hereafter
"Secondary Tdap – SAEs Where No Concomitant Vaccinations")

A true and correct copy of the aforesaid report is attached hereto as **Exhibit 209**

v. "Vaccine Types and Doses Where Concomitants

- Secondary (Tdap), 2006 - 2009 (168 VAERS IDs, 321 SAEs, 493 doses)",

to which a submitted search request is located at
https://wonder.cdc.gov/controller/saved/D8/D95F588[14]
(last accessed November 7, 2020)
(hereafter
"Secondary Tdap – Vaccine Types and Doses Where Concomitants")

A true and correct copy of the aforesaid report is attached hereto as **Exhibit 210**.

10.3 Parameter values sourced or derived from VAERS Extraction Reports

(a) For Elementary Analysis

Within this paragraph 10(a):

- each referenced Elementary Report states the following in the section headed "*Query Criteria*" within that report:

  "Age: 3-5 years

  Serious: Yes

  State / Territory: Alabama; Alaska; Arizona; Arkansas; California; Colorado; Connecticut; Delaware; District of Columbia; Florida; Georgia; Hawaii; Idaho; Illinois; Indiana; Iowa; Kansas; Kentucky; Louisiana; Maine; Maryland; Massachusetts; Michigan; Minnesota; Mississippi; Missouri; Montana; Nebraska; Nevada; New Hampshire; New Jersey; New Mexico; New York; North Carolina; North Dakota; Ohio; Oklahoma; Oregon; Pennsylvania; Rhode Island; South Carolina; South Dakota; Tennessee; Texas; Utah; Vermont; Virginia; Washington; West Virginia; Wisconsin; Wyoming"

- each referenced Elementary Report except for Elementary DTaP & IPV – Total Deaths over 9 Year Period also states the following in the section headed "*Query Criteria*" within that report:

  Date Vaccinated: *Jun., 2006 to May, 2009*

i. **Elementary SAE_REP, SAE_HOSP, SAE_ACTUAL, SAE_C**

The document "Elementary DTaP & IPV – Reported SAEs Totaled" includes in the section headed "*Query Criteria*", under the heading "*Vaccine Products*", the following list:

"DIPHTHERIA AND TETANUS TOXOIDS AND ACELLULAR PERTUSSIS VACCINE (DTAP); DIPHTHERIA AND TETANUS TOXOIDS AND ACELLULAR PERTUSSIS VACCINE + INACTIVATED POLIOVIRUS VACCINE (DTAPIPV); DIPHTHERIA AND TETANUS TOXOIDS AND PERTUSSIS VACCINE (DTP); DIPHTHERIA AND TETANUS TOXOIDS, PEDIATRIC (DT); DIPHTHERIA/PERTUSSIS/INACTIVATED POLIO VIRUS (DPIPV); DIPHTHERIA/PERTUSSIS/POLIO (ORAL [LIVE] OR INACTIVATED NOT NOTED) (DPP); DT-IPV COMBINED DT AND IPV VACCINE (DTIPV); DTP-IPV COMBINED DTP AND IPV VACCINE (DTPIPV); POLIOVIRUS VACCINE INACTIVATED (IPV)"

(hereafter "Elementary Subject Vaccine Types List")

and under the heading *"Group By*", "*Event Category*".

The document states that the query result, under the title and subtitle, is the following table, hereafter "Elementary DTaP & IPV - Reported SAEs Totaled Table":

Event Category	***Events Reported***	***Percent (of 141)***
Death	1	0.71%
Life Threatening	*31*	*21.99%*
Permanent Disability	*13*	*9.22%*
Hospitalized	*115*	*81.56%*
Existing Hospitalization Prolonged	*6*	*4.26%*
*Emergency Room / Office Visit ***	*85*	*60.28%*
*Emergency Room **	*1*	*0.71%*
*Office Visit **	*1*	*0.71%*
	253	*179.43%*

Based upon the Elementary DTaP & IPV - SAEs Totaled Table, the following parameter values can be derived for the subject vaccinations in the Surveillance Period:

- SAE_REP = 253 and
- SAE_HOSP = 121, and
- SAE_ACTUAL = SAE_REP ÷ NR
  = 253 ÷ 1%
  = 25,300, and
- SAE_C = SAE_ACTUAL x SAE_CR
  = 25,300 x 21.54%
  = 5,450.

ii. **Elementary VAERS IDs**

The document "Elementary DTaP & IPV - VAERS IDs" includes, in the section headed "*Query Criteria*", under the heading "*Vaccine Products*", the Elementary Subject Vaccine Types List and under the heading "*Group By*:" "*VAERS ID*".

The document lists, as the query result, under the title and subtitle, the following 141 VAERS IDs, which list is hereafter "Elementary VAERS IDs list":

Elementary DTaP & IPV - VAERS IDs					
258091-1	*266252-1*	*279459-1*	*308695-1*	*324686-1*	*341796-1*
258455-1	*266672-1*	*282920-1*	*309006-1*	*324718-1*	*342102-1*
259121-1	*267741-1*	*285686-1*	*309430-1*	*325141-1*	*342796-1*
259493-1	*268292-1*	*286767-1*	*310083-1*	*325205-1*	*343049-1*
259494-1	*269758-1*	*288160-1*	*311296-1*	*326394-1*	*343626-1*
260839-1	*271095-1*	*288302-1*	*311350-1*	*329438-1*	*344797-1*
260845-1	*271197-1*	*289347-1*	*312014-1*	*329972-1*	*344818-1*
260898-1	*271804-1*	*290589-1*	*313770-1*	*332131-1*	*345422-1*
262198-1	*271809-1*	*291704-1*	*313870-1*	*332443-1*	*346096-1*
262240-1	*272086-1*	*292905-1*	*316307-1*	*333134-1*	*346345-1*
262247-1	*274446-1*	*294162-1*	*316388-1*	*334998-1*	*353922-1*
262756-1	*274831-1*	*294660-1*	*316550-1*	*335227-1*	*356046-1*
262757-1	*275191-1*	*296546-1*	*316682-1*	*335573-1*	*383688-1*
262770-1	*275419-1*	*297180-1*	*318045-1*	*336322-1*	*387064-1*

263130-1	*276612-1*	*297567-1*	*319471-1*	*337672-1*	*392791-1*
263524-1	*276618-1*	*297934-1*	*319930-1*	*337735-1*	*400371-1*
263731-1	*277868-1*	*298328-1*	*320714-1*	*338476-1*	*413007-1*
263910-1	*278191-1*	*301952-1*	*320842-1*	*339027-1*	*446271-1*
263997-1	*278585-1*	*302608-1*	*321515-1*	*339176-1*	*489034-1*
264026-1	*278606-1*	*305357-1*	*321915-1*	*340254-1*	*621125-1*
264171-1	*278793-1*	*305602-1*	*323207-1*	*340428-1*	*796697-1*
264191-1	*278989-1*	*306956-1*	*323799-1*	*340432-1*	
264963-1	*279097-1*	*307066-1*	*324030-1*	*341640-1*	
265214-1	*279279-1*	*307704-1*	*324161-1*	*341753-1*	

iii. **Elementary Vaccine Types for VAERS IDs**

The document "Elementary DTaP & IPV - All Vaccine Types for VAERS-IDs" includes in the section headed "*Query Criteria*" under the heading "***VAERS IDs***", the Elementary VAERS IDs list, and under the heading **"*Group By***" "*Vaccine Type; VAERS ID*".

This document states that the query result, under the title and subtitle, is a table of 141 VAERS IDs grouped by vaccine type, in which:

- the 21 VAERS IDs in the following list are listed in the document only in association with the vaccine types in the Elementary Subject Vaccine Types List, hereafter "Elementary Non-Concomitant VAERS IDs List":

Elementary DTaP & IPV - VAERS IDs where only subject vaccines given					
(21 VAERS IDs)					
258091-1	*263130-1*	*266672-1*	*316307-1*	*332443-1*	*346345-1*
260839-1	*263524-1*	*276618-1*	*319471-1*	*333134-1*	*353922-1*
262756-1	*263731-1*	*301952-1*	*320714-1*	*335227-1*	*387064-1*
262757-1	*263997-1*	*308695-1*			

and

- the 120 VAERS IDs in the following table are the remaining VAERS IDs, listed in the document both in association with one or more of the vaccine types in the Elementary Subject Vaccine Types List and one or more other vaccine type(s) given concomitantly:

Elementary DTaP & IPV - VAERS IDs where concomitant vaccines					
(120 VAERS IDs)					
258455-1	*271095-1*	*285686-1*	*307704-1*	*324161-1*	*341640-1*
259121-1	*271197-1*	*286767-1*	*309006-1*	*324686-1*	*341753-1*
259493-1	*271804-1*	*288160-1*	*309430-1*	*324718-1*	*341796-1*
259494-1	*271809-1*	*288302-1*	*310083-1*	*325141-1*	*342102-1*
260845-1	*272086-1*	*289347-1*	*311296-1*	*325205-1*	*342796-1*

260898-1	*274446-1*	*290589-1*	*311350-1*	*326394-1*	*343049-1*
262198-1	*274831-1*	*291704-1*	*312014-1*	*329438-1*	*343626-1*
262240-1	*275191-1*	*292905-1*	*313770-1*	*329972-1*	*344797-1*
262247-1	*275419-1*	*294162-1*	*313870-1*	*332131-1*	*344818-1*
262770-1	*276612-1*	*294660-1*	*316388-1*	*334998-1*	*345422-1*
263910-1	*277868-1*	*296546-1*	*316550-1*	*335573-1*	*346096-1*
264026-1	*278191-1*	*297180-1*	*316682-1*	*336322-1*	*356046-1*
264171-1	*278585-1*	*297567-1*	*318045-1*	*337672-1*	*383688-1*
264191-1	*278606-1*	*297934-1*	*319930-1*	*337735-1*	*392791-1*
264963-1	*278793-1*	*298328-1*	*320842-1*	*338476-1*	*400371-1*
265214-1	*278989-1*	*302608-1*	*321515-1*	*339027-1*	*413007-1*
266252-1	*279097-1*	*305357-1*	*321915-1*	*339176-1*	*446271-1*
267741-1	*279279-1*	*305602-1*	*323207-1*	*340254-1*	*489034-1*
268292-1	*279459-1*	*306956-1*	*323799-1*	*340428-1*	*621125-1*
269758-1	*282920-1*	*307066-1*	*324030-1*	*340432-1*	*796697-1*

iv. Elementary **PCENT_SUBJ-ONLY**

The document “Elementary DTaP & IPV - Reported SAEs Where No Concomitant Vaccinations” includes in the section headed “*Query Criteria*” under the heading “*VAERS IDs*“, the 21 VAERS IDs in the Elementary Non-Concomitant VAERS IDs List, and under the heading “*Group By*” “*Event Category*”, and as the query result, under the title and subtitle, the following table, hereafter

“Elementary DTaP & IPV - Reported SAEs Where No Concomitant Vaccinations Table”:

Event Category	***Events Reported***	***Percent (of 21)***
Life Threatening	*3*	*14.29%*
Permanent Disability	*4*	*19.05%*
Hospitalized	*19*	*90.48%*
Existing Hospitalization Prolonged	*1*	*4.76%*
*Emergency Room / Office Visit **	*9*	*42.86%*
Total	***36***	***171.43%***

Based upon the Elementary DTaP & IPV - Reported SAEs Where No Concomitant Vaccinations Table, the number of Reported SAEs where the only vaccine(s) administered was/or one or more of the subject vaccine(s), i.e. SAE_SUBJ_ONLY, was 36.

Hence, PCENT_SUBJ_ONLY can be calculated to be:

PCENT_SUBJ_ONLY = SAE_SUBJ_ONLY ÷ SAE x 100%

= 36 ÷ 253 x 100%

= 14.23%.

v. **Elementary V_SP_SUBJ_COM, V_SP_ALL_COM, PCENT_SUBJ_COM, SAE_C_SUBJ**

The document "Elementary DTaP & IPV – Vaccine Types and Doses Where Concomitants" includes in the section headed "*Query Criteria*" under the heading "*VAERS IDs*", the 120 VAERS IDs in the Elementary Concomitant VAERS IDs List, and under the heading "*Group By*" "*Vaccine Type*", and as the query result, under the title and subtitle, the first three columns in the following table, hereafter "Elementary DTaP & IPV – Vaccine Types and Doses Where Concomitants Table":

Elementary DTaP & IPV – Vaccine Types and Doses Where Concomitants Table

Vaccine Type**	***Events Reported****	***Percent (of 120)***	**Total doses**
Subject vaccine types			
DIPHTHERIA AND TETANUS TOXOIDS AND ACELLULAR PERTUSSIS VACCINE (DTAP)	*100*	*77.24%*	
*DIPHTHERIA AND TETANUS TOXOIDS AND PERTUSSIS VACCINE (DTP)****	*3*	*2.07%*	
*DIPHTHERIA/PERTUSSIS/POLIO (ORAL [LIVE] OR INACTIVATED NOT NOTED) (DPP)****	*1*	*0.69%*	
*DIPHTHERIA AND TETANUS TOXOIDS, PEDIATRIC (DT)****	*1*	*0.69%*	**105**
POLIOVIRUS VACCINE INACTIVATED (IPV)	*96*	*74.48%*	**96**
DIPHTHERIA AND TETANUS TOXOIDS AND ACELLULAR PERTUSSIS VACCINE + INACTIVATED POLIOVIRUS VACCINE (DTAPIPV)	*9*	*13.79%*	**9**

Total subject vaccinations where concomitants			**210**
Non-subject vaccine types			
HAEMOPHILUS B CONJUGATE VACCINE (HIBV)	*3*	*2.76%*	
HEPATITIS A (HEPA)	*13*	*9.66%*	
HEPATITIS B VACCINE (HEP)	*1*	*1.38%*	
INFLUENZA VIRUS VACCINE, NO BRAND NAME (FLUX(SEASONAL))	*1*	*0.69%*	
INFLUENZA VIRUS VACCINE, TRIVALENT (INJECTED) (FLU3(SEASONAL))	*8*	*8.97%*	
INFLUENZA VIRUS VACCINE, TRIVALENT (INTRANASAL SPRAY) (FLUN3(SEASONAL))	*3*	*4.83%*	
MEASLES, MUMPS AND RUBELLA VIRUS VACCINE, LIVE (MMR)	*81*	*69.66%*	
MEASLES, MUMPS, RUBELLA, AND VARICELLA VACCINE (PROQUAD) (MMRV)	*21*	*15.17%*	
PNEUMOCOCCAL VACCINE, POLYVALENT (PPV)	*4*	*2.76%*	
PNEUMOCOCCAL, 7-VALENT VACCINE (PREVNAR) (PNC)	*4*	*2.76%*	
VARIVAX-VARICELLA VIRUS LIVE (VARCEL)	*56*	*53.10%*	**195**
Total vaccinations where concomitants			**405**

Notes to table:

** Records of a “TETANUS TOXOID” and “TDAP” vaccinations are also included in the query results but are excluded from this analysis.

*** The DTP, DPP and DT vaccine type names are interpreted herein to mean DTaP vaccine type and assumed to be erroneously recorded.

Based upon the Elementary DTaP & IPV – Vaccine Types and Doses Where Concomitants Table,

- the total number of subject vaccine doses concomitantly administered with non-subject vaccine doses in the Surveillance Period, i.e. V_SP_SUBJ_COM, was 210, and
- the total number of all vaccine doses administered where subject and non-subject vaccine doses were administered concomitantly in the Surveillance Period, i.e. V_SP_ALL_COM, was 405.

Hence the total number of subject vaccine doses administered as a percentage of total number of all vaccine doses administered, i.e. PCENT_SUBJ_COM, can be calculated to be:

PCENT_SUBJ_COM = V_SP_SUBJ_COM ÷ V_SP_ALL_COM

= 210 ÷ 405

= 51.9%.

Hence SAE_C_SUBJ can be calculated to be:

SAE_C_SUBJ = SAE_C x (PCENT_SUBJ_ONLY + (100% - PCENT_SUBJ_ONLY) x PCENT_SUBJ_COM)

= 1,817 x (14.23% + (100% - 14.23%) x 51.9%)

= 1,066.

vi. **Elementary PCENT_SUBGRP_SUBJ, SAE_C_SUBGRP**

The document “Elementary DTaP & IPV - All Subject Vaccine Doses Where No Concomitants” includes in the section headed “*Query Criteria*” under the heading “*VAERS IDs*“ the 21 VAERS IDs in the Elementary Non-Concomitant VAERS IDs List, and under the heading “*Group By*” “*Vaccine Type*”

The document includes in the query result, under the title and subtitle, the data in the first two columns in the table below, hereafter “PCENT_SUBGRP_SUBJ Table”:

Vaccine Type	*Events Reported **	Total
DIPHTHERIA AND TETANUS TOXOIDS AND ACELLULAR PERTUSSIS VACCINE + INACTIVATED POLIOVIRUS VACCINE (DTAPIPV)	*1*	N/A
DIPHTHERIA AND TETANUS TOXOIDS AND ACELLULAR PERTUSSIS VACCINE (DTAP)	*20*	31
POLIOVIRUS VACCINE INACTIVATED	*11*	

Based upon the data in the PCENT_SUBGRP_SUBJ Table, of the 39 VAERS IDs associated with vaccines targeting only one of the two subject disease subgroups, i.e. the diphtheria, tetanus and pertussis subgroup OR the poliomyelitis subgroup, but not both subgroups (i.e. excluding the DTaP-IPV vaccines),

- those VAERS IDs that were associated with only diphtheria-tetanus-pertussis vaccination (DTaP) numbered 20, and hence
  for that subgroup,
  PCENT_SUBGRP_SUBJ can be estimated to be 20 ÷ 31 = 64.5%, and
- those VAERS IDs that were associated with only the poliomyelitis vaccination (IPV) numbered 11, and hence
  for that subgroup,
  PCENT_SUBGRP_SUBJ can be estimated to be 11 ÷ 31 = 35.5%.

Accordingly, SAE_C_SUBGRP for each subject disease subgroup can be calculated to be:

- for diphtheria-tetanus-pertussis vaccination (DTaP),

  SAE_C_SUBGRP = SAE_C_SUBJ x PCENT_SUBGRP_SUBJ

  = 1,066 x 64.5%

  = 688, and
- for polio vaccination (IPV),

  SAE_C_SUBGRP = SAE_C_SUBJ x PCENT_SUBGRP_SUBJ

  = 1,066 x 35.5%

  = 378.

vii. **Elementary SAE_DEATH**

The document "Elementary DTaP & IPV – Total Deaths over 9 Year Period" includes in the section headed "*Query Criteria*" under the heading "*Date Vaccinated*" "*Jun, 2008 to May, 2017*", under the heading "*Vaccine Products*" the Elementary Subject Vaccine Types List, and under the heading "*Group By*" "*Event Category*".

The document includes in the query result, under the title and subtitle, the data in the table below:

Event Category	***Events Reported***
DEATH	*9*

Based upon the data in the above table, nine deaths were reported where all of the criteria for Elementary DTaP & IPV – Reported SAEs Totaled were met other than the Event Category being limited to deaths and the "*Date Vaccinated*" set to "*Jun, 2008 to May, 2017*"

(b) For Secondary Analysis

Within this paragraph 10(b):

- each referenced Secondary Report states the following in the section headed "*Query Criteria*" within that report:

  "Age: 6-17 years

  Date Vaccinated: Jan., 2006 to Dec., 2009

  Serious: Yes

  State / Territory: Alabama; Alaska; Arizona; Arkansas; California; Colorado; Connecticut; Delaware; District of Columbia; Florida; Georgia; Hawaii; Idaho; Illinois; Indiana; Iowa; Kansas; Kentucky; Louisiana; Maine; Maryland; Massachusetts; Michigan; Minnesota; Mississippi; Missouri; Montana; Nebraska; Nevada; New Hampshire; New Jersey; New Mexico; New York; North Carolina; North Dakota; Ohio; Oklahoma; Oregon; Pennsylvania; Rhode Island; South Carolina; South Dakota; Tennessee; Texas; Utah; Vermont; Virginia; Washington; West Virginia; Wisconsin; Wyoming"

i. Secondary SAE_REP, SAE_DEATH, SAE_HOSP, SAE_ACTUAL, SAE_C

The document "Secondary Tdap - Reported SAEs Totaled" includes in the section headed "*Query Criteria*", under the heading "*Vaccine Products*", the following list:

"TETANUS AND DIPHTHERIA TOXOIDS AND ACELLULAR PERTUSSIS VACCINE (BOOSTRIX/ADACEL) (TDAP)"

and under the heading **"***Group By*", "*Event Category*".

The document states that the query result, under the title and subtitle, is the following table, hereafter "Secondary Tdap - Reported SAEs Totaled Table":

Event Category	***Events Reported***	***Percent (of 198)***
Death	*5*	*2.53%*
Life Threatening	*51*	*25.76%*
Permanent Disability	*39*	*19.70%*
Hospitalized	*161*	*81.31%*
Existing Hospitalization Prolonged	*18*	*9.09%*
Emergency Room / Office Visit **	*113*	*57.07%*
Office Visit *	*1*	*0.51%*
Total	***388***	*195.96%*

Based upon the Secondary Tdap - Reported SAEs Totaled Table, the following parameter values can be derived for the subject vaccinations in the Surveillance Period:

- SAE_REP was **388**
- SAE_HOSP was (161 + 18 =) **179**
- SAE_DEATH was **5**
- SAE_ACTUAL = SAE_REP ÷ NR

  = 388 ÷ 1%

  = 38,800
- SAE_C = SAE_ACTUAL x SAE_CR

  = 38,800 x 21.54%

  = 8,358.

ii. Secondary VAERS IDs

The document “Secondary Tdap - VAERS IDs” includes, in the section headed “*Query Criteria*”, under the heading “*Vaccine Products*”, the Secondary Subject Vaccine Types List, and under the heading “*Group By*:”, “*VAERS ID*”.

The document lists, as the query result, under the title and subtitle, the following 198 VAERS IDs, which list is hereafter “Secondary VAERS IDs list”:

Secondary Tdap - VAERS IDs (198)					
252216-1	*276435-1*	*293289-1*	*319854-1*	*343601-1*	*364301-1*
253342-1	*276797-1*	*295191-1*	*320331-1*	*343764-1*	*365292-1*
254224-1	*277388-1*	*295526-1*	*320607-1*	*343965-1*	*366668-1*
255491-1	*277494-1*	*295528-1*	*320905-1*	*344094-1*	*367336-1*
256024-1	*278884-1*	*297720-1*	*322431-1*	*344160-1*	*370316-1*
256758-1	*279460-1*	*298468-1*	*322641-1*	*346145-1*	*373189-1*
256959-1	*280436-1*	*298767-1*	*323210-1*	*346155-1*	*381778-1*
257357-1	*281660-1*	*299066-1*	*323435-1*	*348475-1*	*381918-1*
258197-1	*281973-1*	*303199-1*	*323976-1*	*349018-1*	*382746-1*
258573-1	*282385-1*	*308770-1*	*324450-1*	*349407-1*	*383350-1*
258880-1	*283628-1*	*308875-1*	*324863-1*	*350465-1*	*387752-1*
259855-1	*283833-1*	*303612-1*	*325601-1*	*350574-1*	*402038-1*
261264-1	*284663-1*	*304030-1*	*326520-1*	*350704-1*	*405787-1*
261649-1	*286052-1*	*304148-1*	*327552-1*	*350817-1*	*408255-1*
261667-1	*286284-1*	*306198-1*	*328753-1*	*351067-1*	*413712-1*
262592-1	*286378-1*	*306734-1*	*329242-1*	*351428-1*	*414486-1*
263015-1	*286488-1*	*308900-1*	*329296-1*	*351893-1*	*414550-1*
264146-1	*287352-1*	*309048-1*	*331290-1*	*352153-1*	*419106-1*
264745-1	*287376-1*	*311070-1*	*334604-1*	*352668-1*	*420174-1*
264983-1	*288215-1*	*311352-1*	*334952-1*	*354471-1*	*420819-1*
265275-1	*288464-1*	*312134-1*	*335849-1*	*354520-1*	*423105-1*
265954-1	*288695-1*	*312938-1*	*335993-1*	*354959-1*	*428365-1*
266164-1	*288762-1*	*314770-1*	*338467-1*	*355048-1*	*428399-1*
266655-1	*289040-1*	*315581-1*	*339718-1*	*355137-1*	*482432-1*
266889-1	*289952-1*	*316085-1*	*340119-1*	*355489-1*	*487741-1*
268291-1	*290113-1*	*316429-1*	*340675-1*	*356183-1*	*488943-1*
268894-1	*290328-1*	*317411-1*	*340781-1*	*356265-1*	*508966-1*
269773-1	*290355-1*	*317629-1*	*340835-1*	*356756-1*	*538517-1*
271868-1	*290559-1*	*317935-1*	*341073-1*	*356939-1*	*540405-1*
272807-1	*290711-1*	*318598-1*	*341618-1*	*357932-1*	*567058-1*
273099-1	*290787-1*	*318611-1*	*341639-1*	*358429-1*	*586270-1*
275936-1	*291064-1*	*318993-1*	*342045-1*	*360996-1*	*662875-1*
276047-1	*291585-1*	*319725-1*	*342334-1*	*363160-1*	*810759-1*

iii. Secondary Vaccine Types for VAERS IDs

The document "Secondary Tdap - All Vaccine Types for VAERS-IDs" includes in the section headed "*Query Criteria*" under the heading "*VAERS IDs*", the Secondary VAERS IDs list, and under the heading "*Group By*", "*VAERS ID; Vaccine Type*".

The document states that the query result, under the title and subtitle, is a table of vaccine types grouped by VAERS IDs, in which:

- the 30 VAERS IDs in the following table are listed only in association with the vaccine types in the Secondary Subject Vaccine Types List, hereafter the "Secondary Non-Concomitant VAERS IDs List":

Secondary Tdap - VAERS IDs where only subject vaccines given					
256959-1	*266655-1*	*289952-1*	*311352-1*	*338467-1*	*373189-1*
258573-1	*271868-1*	*290113-1*	*315581-1*	*341618-1*	*381918-1*
261264-1	*272807-1*	*290787-1*	*318611-1*	*343965-1*	*428399-1*
264146-1	*276047-1*	*291064-1*	*318993-1*	*350465-1*	*586270-1*
266164-1	*278884-1*	*311070-1*	*323976-1*	*364301-1*	*810759-1*

and

- the 68 VAERS IDs in the following table are the remaining 168 VAERS IDs, listed both in association with one or more of the vaccine types in the Secondary Subject Vaccine Types List and one or more other vaccine type(s) given concomitantly, hereafter the "Secondary Concomitant VAERS IDs List":

Secondary Tdap - VAERS IDs where concomitant vaccines					
252216-1	*279460-1*	*297720-1*	*322431-1*	*344094-1*	*363160-1*
253342-1	*280436-1*	*298468-1*	*322641-1*	*344160-1*	*365292-1*
254224-1	*281660-1*	*298767-1*	*323210-1*	*346145-1*	*366668-1*
255491-1	*281973-1*	*299066-1*	*323435-1*	*346155-1*	*367336-1*
256024-1	*282385-1*	*303199-1*	*324450-1*	*348475-1*	*370316-1*
256758-1	*283628-1*	*303612-1*	*324863-1*	*349018-1*	*381778-1*
257357-1	*283833-1*	*304030-1*	*325601-1*	*349407-1*	*382746-1*
258197-1	*284663-1*	*304148-1*	*326520-1*	*350574-1*	*383350-1*
258880-1	*286052-1*	*306198-1*	*327552-1*	*350704-1*	*387752-1*
259855-1	*286284-1*	*306734-1*	*328753-1*	*350817-1*	*402038-1*
261649-1	*286378-1*	*308770-1*	*329242-1*	*351067-1*	*405787-1*
261667-1	*286488-1*	*308875-1*	*329296-1*	*351428-1*	*408255-1*
262592-1	*287352-1*	*308900-1*	*331290-1*	*351893-1*	*413712-1*
263015-1	*287376-1*	*309048-1*	*334604-1*	*352153-1*	*414486-1*
264745-1	*288215-1*	*312134-1*	*334952-1*	*352668-1*	*414550-1*
264983-1	*288464-1*	*312938-1*	*335849-1*	*354471-1*	*419106-1*
265275-1	*288695-1*	*314770-1*	*335993-1*	*354520-1*	*420174-1*
265954-1	*288762-1*	*316085-1*	*339718-1*	*354959-1*	*420819-1*

266889-1	*289040-1*	*316429-1*	*340119-1*	*355048-1*	*423105-1*
268291-1	*290328-1*	*317411-1*	*340675-1*	*355137-1*	*428365-1*
268894-1	*290355-1*	*317629-1*	*340781-1*	*355489-1*	*482432-1*
269773-1	*290559-1*	*317935-1*	*340835-1*	*356183-1*	*487741-1*
273099-1	*290711-1*	*318598-1*	*341073-1*	*356265-1*	*488943-1*
275936-1	*291585-1*	*319725-1*	*341639-1*	*356756-1*	*508966-1*
276435-1	*293289-1*	*319854-1*	*342045-1*	*356939-1*	*538517-1*
276797-1	*295191-1*	*320331-1*	*342334-1*	*357932-1*	*540405-1*
277388-1	*295526-1*	*320607-1*	*343601-1*	*358429-1*	*567058-1*
277494-1	*295528-1*	*320905-1*	*343764-1*	*360996-1*	*662875-1*

iv. Secondary PCENT_SUBJ-ONLY

The document “Secondary Tdap - Reported SAEs Where No Concomitant Vaccinations” includes in the section headed “*Query Criteria*” under the heading “*VAERS IDs*“, the 30 VAERS IDs in the Secondary Non-Concomitant VAERS IDs List, and under the heading “*Group By*” “*Event Category*”, and as the query result, under the title and subtitle, the following table, hereafter

“Secondary Tdap - Reported SAEs Where No Concomitant Vaccinations Table”:

Event Category	***Events Reported***	***Percent (of 28)***
Death	*1*	*3.70%*
Life Threatening	*9*	*33.33%*
Permanent Disability	*9*	*33.33%*
Hospitalized	*25*	*81.48%*
Existing Hospitalization Prolonged	*4*	*11.11%*
*Emergency Room / Office Visit **	*18*	*55.56%*
*Office Visit **	*1*	*3.70%*
Total	***67***	*222.22%*

Based upon the Secondary Tdap - Reported SAEs Where No Concomitant Vaccinations Table, the number of Reported SAEs where the only vaccine(s) administered was/or one or more of the subject vaccine(s), i.e. SAE_SUBJ_ONLY, was 67.

Hence, PCENT_SUBJ_ONLY can be calculated to be:

$$\text{PCENT\_SUBJ\_ONLY} = \text{SAE\_SUBJ\_ONLY} \div \text{SAE} \times 100\%$$

$$= 67 \div 388 \times 100\%$$

$$= 17.27\%.$$

v. Secondary V_SP_SUBJ_COM, V_SP_ALL_COM, PCENT_SUBJ_COM, SAE_C_SUBJ

The document "Secondary Tdap – All Vaccine Doses Where Concomitants" includes in the section headed "***Query Criteria***" under the heading "*VAERS IDs*", the 168 VAERS IDs in the Secondary Concomitant VAERS IDs List, and under the heading: "*Group By*", "*Vaccine Type*", and as the query result, under the title and subtitle, the first three columns in the following table, hereafter "Secondary Tdap – Vaccine Types and Doses Where Concomitants Table":

Secondary Tdap – Vaccine Types and Doses Where Concomitants Table

*Vaccine Type**	*Events Reported*	*Percent (of 129)*	Total doses
Subject vaccine type			
TETANUS AND DIPHTHERIA TOXOIDS AND ACELLULAR PERTUSSIS VACCINE (BOOSTRIX/ADACEL) (TDAP)	*168*	*100%*	**168**
Non-subject vaccine types			
HAEMOPHILUS B CONJUGATE VACCINE (HIBV)	*1*	*0.60%*	
HEPATITIS A (HEPA)	*49*	*29.17%*	
HEPATITIS A AND HEPATITIS B VACCINE (HEPAB)	*1*	*0.60%*	
HEPATITIS B VACCINE (HEPB)	*12*	*7.14%*	
HUMAN PAPILLOMAVIRUS (TYPES 6, 11, 16, 18) RECOMBINANT VACCINE (HPV4)	*61*	*36.31%*	
HUMAN PAPILLOMAVIRUS VACCINE (HPVX)	*2*	*1.19%*	
INFLUENZA (H1N1) MONOVALENT, (INJECTED) (FLU(H1N1))	*2*	*1.19%*	
INFLUENZA (H1N1) MONOVALENT, (INTRANASAL SPRAY) (FLUN(H1N1))	*2*	*1.19%*	
INFLUENZA VIRUS VACCINE, TRIVALENT (INJECTED) (FLU3(SEASONAL))	*10*	*5.95%*	
INFLUENZA VIRUS VACCINE, TRIVALENT (INTRANASAL) SPRAY) (FLUN3(SEASONAL))	*3*	*1.79%*	
MEASLES, MUMPS AND RUBELLA VIRUS VACCINE, LIVE (MMR)	*6*	*3.57%*	
MENINGOCOCCAL POLYSACCHARIDE VACCINE (MEN	*7*	*4.17%*	
MENINGOCOCCAL VACCINE (MENACTRA) (MNQ)	*116*	*69.05%*	
PNEUMOCOCCAL VACCINE, POLYVALENT (PPV)	*4*	*2.38%*	
TYPHOID VACCINE (TYP)	*1*	*0.60%*	
VARIVAX-VARICELLA VIRUS LIVE (VARCEL)	*45*	*26.79%*	**322**
Total vaccinations included in this analysis			**490**

Notes to table:

* There are also three (3) "*POLIOVIRUS VACCINE INACTIVATED (IPV)*" vaccinations included in the query results but excluded from this analysis.

Based upon the Secondary Tdap – Vaccine Types and Doses Where Concomitants Table,

- the total number of subject vaccine doses concomitantly administered with non-subject vaccine doses in the Surveillance Period, i.e. V_SP_SUBJ_COM, was 168, and
- the total number of all vaccine doses administered where subject and non-subject vaccine doses were administered concomitantly in the Surveillance Period, i.e. V_SP_ALL_COM, was 490

Hence the total number of subject vaccine doses administered as a percentage of total number of all vaccine doses administered, i.e. PCENT_SUBJ_COM, can be calculated to be:

PCENT_SUBJ_COM = V_SP_SUBJ_COM ÷ V_SP_ALL_COM
= 168 ÷ 490
= 34.3%.

Hence SAE_C_SUBJ can be calculated to be:

SAE_C_SUBJ = SAE_C x (PCENT_SUBJ_ONLY +
(100% - PCENT_SUBJ_ONLY) x
PCENT_SUBJ_COM)
= 2089 x (17.27% + (100% - 17.27%) x 34.3%)
= 954.

SAE_C_SUBGRP = SAE_C_SUBJ x PCENT_SUBGRP_SUBJ
= 954 x 100%
= 954.

10.4 Final analyses for Diphtheria, Tetanus, Pertussis and Polio - estimation of SRIV

The following table includes, for the Elementary and Secondary Analyses, the results of combining the extracted, set and estimated values of the various parameters referenced in this paragraph 10 above:

Analyses results - Diphtheria, Tetanus, Pertussis and Polio vaccination risks

Description	Polio (IPV)	Diphtheria, Tetanus, Pertussis		Totals
		DTaP	Tdap	
# VAERS records	141		198	
# SAEs reported during SP (SAE_REP)	253		388	
# Hospitalizations / Extended Hospitalizations in SP (SAE_REP_HOSP)	121		179	
# Deaths during SP (SAE_REP_DEATH)	3		5	
Notification completeness Rate (NR)	< 1%			
# Estimated actual number of SAEs during SP (SAE_ACTUAL)	> 25,300		> 38,800	
% SAEs estimated to be vaccine-caused (SAE_CR)	21.54%			
# Estimated vaccine-caused SAE_ACTUALs (SAE_C)	> 5,450		> 8,358	
% SAE_REPs where no concomitant vaccination(s) (PCENT_SUBJ_ONLY)	14.2%		17.3%	
Where concomitant vaccinations, % of all doses that were of the subject vaccine(s) (PCENT_SUBJ_COM)	51.9%		34.3%	
# Estimated SAE_Cs caused by subject vaccines, based on above two %'s (SAE_C_SUBJ)	> 3,199		> 3,814	
% SAE_REP-associated doses that targeted this disease subgroup (PCENT_SUBGRP_SUBJ)	35.5%	64.5%	100%	
# Estimated SAE_Cs attributable to subgroup vaccine doses (SAE_C_SUBGRP)	> 1,135	> 2,064	> 3,814	
# Vaccine doses administered to relevant Population during SP for that subgroup (V_SP)	11,574,493	11,535,298	19,729,057	
Estimated rate of SAE_C_SUBGRP per subgroup vaccine dose (SRI)	> 1 / 10,196	> 1 / 5,589	> 1 / 5,173	
# Doses scheduled (V_SCH) - 6-11 mths	2	3		
- 1-6 years	1.13	1.33		
- 7-10 years	0.27	0.67		
- 11-19 years	0.6		1	

RISK FROM VACCINATION – Diphtheria, Tetanus, Pertussis and Polio (continued)

Description (cont)	Polio (IPV) (cont)	Diphtheria, Tetanus, Pertussis (cont)		Totals (cont)
		DTaP	Tdap	
SRIV - 6-11 months	> 1 / 5,098	> 1 / 1,863		**> 1 / 1,364**
- 1-6 years	> 1 / 8,997	> 1 / 4,192		**> 1 / 2,859**
- 7-10 years	> 1 / 38,236	> 1 / 8,384		**> 1 / 6,876**
- 11-19 years	> 1 / 16,994		> 1 / 5,173	**> 1 / 3,966**
SRIV Total - 6 months-19 years	**> 1 / 2,549**	**> 1 / 919**		**> 1 / 676**
SRIV_HOSP - 6-11 months	> 1 / 10,660	> 1 / 3,895		**> 1 / 2,853**
- 1-6 years	> 1 / 18,811	> 1 / 8,765		**> 1 / 5,979**
- 7-10 years	> 1 / 79,949	> 1 / 17,529		**> 1 / 14,377**
- 11-19 years	> 1 / 35,533[9]		> 1 / 11,213	**> 1 / 8,523**
SRIV_HOSP Total - 6 months-19 yrs	**> 1 / 5,330**	**> 1 / 1,934**		**> 1 / 1,419**
SRIV_DEATH - 6-11 months	> 1 / 429,946	> 1 / 157,113		**> 1 / 115,065**
- 1-6 years	> 1 / 758,728	> 1 / 353,504		**> 1 / 241,149**
- 7-10 years	> 1 / 3,224,595[9]	> 1 / 707,009		**> 1 / 579,869**
- 11-19 years	> 1 / 1,433,153[9]		> 1 / 401,429	**> 1 / 313,592**
SRIV_DEATH Total - 6 months-19 yrs	**> 1 / 214,973**	**> 1 / 76,341**		**> 1 / 56,335**

CUMULATIVE RISK FROM VACCINATION – Diphtheria, Tetanus, Pertussis and Polio

Description	Polio (IPV)	Diphtheria, Tetanus, Pertussis (DTaP / Tdap)	Totals
Cumulative SRIV - 6-11 months	> 1 / 5,098	> 1 / 1,863	**> 1 / 1,364**
- 6 mths - 6 years	> 1 / 3,254	> 1 / 1,290	**> 1 / 924**
- 6 mths -10 years	> 1 / 2,999	> 1 / 1,118	**> 1 / 814**
- 6 mths -19 years	**> 1 / 2,549**	**> 1 / 919**	**> 1 / 676**
Cumulative SRIV_HOSP - 6-11 mths	> 1 / 10,660	> 1 / 3,895	**< 1 / 2,853**
SRIV_HOSP - 6 mths - 6 yrs	> 1 / 6,804	> 1 / 2,697	**< 1 / 1,931**
SRIV_HOSP - 6 mths - 10 yrs	> 1 / 6,270	> 1 / 2,337	**< 1 / 1,703**
SRIV_HOSP - 6 mths - 9 yrs	**> 1 / 5,330[9]**	**> 1 / 1,934**	**< 1 / 1,419**
Cumulative SRIV_DEATH - 6-11 mths	< 1 / 429,946	> 1 / 157,113	**> 1 / 345,196**
SRIV_DEATH - 6 mths -6 yrs	< 1 / 274,434	> 1 / 108,771	**> 1 / 233,690**
SRIV_DEATH - 6 mths-10 yrs	> 1 / 252,909[9]	> 1 / 94,268	**> 1 / 206,015**
SRIV_DEATH - 6 mths-19 yrs	> 1 / **214,973**[9]	**> 1 / 76,341**	**> 1 / 131,966**

Summarizing the main results for the risk from diphtheria, tetanus, pertussis and polio vaccination, the risk of a vaccination-caused SAE in any event category, totalled for all vaccination doses over the age range of 6 months to 19 years, is estimated to be greater than:

- 1 in 919 for diphtheria-tetanus-pertussis vaccination, and
- 1 in 2,549 for polio vaccination

totaling greater than 1 in 676 for diphtheria-tetanus-pertussis-polio vaccination.

11. Risk from other vaccinations - Measles, mumps, rubella, varicella, hepatitis B, hepatitis A, Hib, pneumococcal, meningococcal and influenza

11.1 Measles, mumps and rubella

(a) Cited SAE_C_SUBJ rates

The Plaintiff hereby requests that the Court take judicial notice of the following documents:

- CDC publication entitled Understanding MMR Vaccine Safety",

  "Last updated February 2013", accessible at https://www.cdc.gov/vaccines/hcp/patient-ed/conversations/downloads/vacsafe-mmr-color-office.pdf
  (last accessed January 17, 2021)
  (hereafter "Understanding MMR Vaccine Safety Publication")
  A true and correct copy of the aforesaid report is attached hereto as **Exhibit 211**.

- article entitled "Risk of Serious Neurologic Disease After Immunization of Young Children in Britain and Ireland",

  Citation: Katherine N. Ward, Naomi J. Bryant, Nick J. Andrews, Jennifer S. Bowley, Anu Ohrling, Christopher M. Verity, Euan M. Ross and Elizabeth Miller. DOI: 10.1542/peds.2006-3743. Pediatrics 2007;120;314, accessible at https://media.ellinikahoaxes.gr/uploads/2020/04/ward2007.pdf
  (last accessed January 17, 2021)
  (hereafter "MMR Serious Neurologic Disease Risk Article")
  A true and correct copy of the aforesaid report is attached hereto as **Exhibit 212**.

- abstract of article entitled "Vaccines for measles, mumps and rubella in children (Review)",

  Citation: Demicheli V, Rivetti A, Debalini MG, Di Pietrantonj C. Cochrane Database of Systematic Reviews 2012, Issue 2. Art. No.: CD004407.DOI: 10.1002/14651858.CD004407.pub3., accessible at https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6458016/pdf/CD004407.pdf
  (last accessed January 17, 2021)
  (hereafter "Cochrane MMR Review Abstract")

A true and correct copy of the aforesaid abstract is attached hereto as **Exhibit 213**.

The CDC Pink Book Measles Chapter states:

"The experts determined that evidence supports a causal relation between MMR vaccination and anaphylaxis, febrile seizures, thrombocytopenic purpura, transient arthralgia, and measles inclusion body encephalitis in persons with demonstrated immunodeficiencies."

and

"Immediate, anaphylactic reactions to MMR vaccine occur in 1.8 to 14.4 cases per million doses."

and

"MMR vaccine may cause thrombocytopenia within two months after vaccination."

The Understanding MMR Vaccine Safety Publication states:

"What are the known side effects of MMR vaccine?
…Moderate problems include seizure caused by fever (about 1 out of 3,000 doses), and temporary low platelet count, which rarely can cause a bleeding disorder (about 1 out of 30,000 doses)".

The MMR Serious Neurologic Disease Risk Article states:

"we can estimate the vaccine-attributable risk of serious neurologic disease after the first dose of MMR vaccine as 1 in 365 000 doses (95% CI: 1 in 1460 000 to 1 in 140 000)."

Based upon these excerpts the approximate average acknowledged risks of SAEs caused by one dose of MMR vaccination (SRI), include, at the minimum, the SAE types, listed in the following table along with their above cited frequencies:

SAE_C_SUBJ type	**Level of risk (SRI)**		
Anaphylactic reactions	<= 1 in 70,000		0.00144%
Thrombocytopenic purpura	1 in 30,000	=	0.0033%
Febrile seizures	1 in 3,000		0.0333%
Serious neurologic disease	1 in 365,000		0.0003%
Total	**~1 in 2,600**	=	**0.0384%**

(b) SRI

Based upon the excerpts above, the risk of one dose of MMR vaccine in the US causing a serious adverse event is at least approximately:

- **1 in 2650**, in 12 to 23 month olds.

(c) Potential for additional SAE_C_SUBJs

The above list of SAE_C_SUBJ types does not include any reported SAE within an additional SAE_C_SUBJ type in relation to which:

- the Institute of Medicine has found that the available scientific literature is insufficient to conclude whether or not the SAE type is caused or contributed to by MMR vaccination.

Hence the total SRI for one dose of MMR vaccination may be significantly higher than about 1 in 2,650 but how much higher has not been determined. With respect to that uncertainty, the Cochrane MMR Review Abstract states in the conclusion:

> *"The design and reporting of safety outcomes in MMR vaccine studies, both pre- and post-marketing, are largely inadequate."*

11.2 Varicella

The Plaintiff hereby requests that the Court take judicial notice of the following document:

- article entitled "Varicella Virus Vaccine Live: A 22-Year Review of Postmarketing Safety Data",

  Citation: Woodward M, Marko A, Galea S, Eagel B, Straus W. Open Forum Infect Dis. 2019 Aug 1;6(8):ofz295. doi: 10.1093/ofid/ofz295. PMID: 31392326; PMCID: PMC6685817, accessible at https://academic.oup.com/ofid/article-pdf/6/8/ofz295/33575326/ofz295.pdf
  (last accessed January 22, 2021)
  (hereafter "Varicella Vaccine 22-Year Review")
  A true and correct copy of the aforesaid document is attached hereto as **Exhibit 214**

(a) HRI - Herpes Zoster rate attributable to varicella vaccination

"HRI" is hereby defined, by the same essential principle as SRI, as the rate of occurrence per dose of herpes zoster attributable to varicella vaccination.

The Herpes Zoster Rate Article states:

> *"In the United States, a 1-dose childhood varicella vaccination program was initiated in 1995,[7] and a 2-dose schedule was recommended in 2006.[8]"*

and

> *"From 2000 through 2006, 579 cases of herpes zoster among persons aged <20 years were reported. Of these, 120 were excluded from the study… The remaining 459 cases of herpes zoster, had case investigations and medical records review completed…. Of the 459 herpes zoster cases, 154 (34%) were <10 years old."*

Based upon this excerpt and the fact that there is no mention in the article of any of the research subjects receiving a second dose, it is assumed herein the number of children stated in the article in each of the years 2000 through 2005 to have been vaccinated had received only one dose of the vaccine. (That may apply to the cases reported in 2006 also, completely or almost completely, but that is not assumed to be the case.)

The Herpes Zoster Rate Article states:

> *"Of the 459 herpes zoster cases,… Nine (2%) herpes zoster cases had underlying immunocompromised conditions; all had a history of varicella disease and none were vaccinated."*

Based upon this excerpt, none of the vaccinated children whom the study reports to have developed herpes zoster were immunocompromised. So if immunocompromise had been a contraindication to vaccination in the material period of 2000-2005, it would have made no difference to the rate at which children developed HZ after vaccination.

The Herpes Zoster Rate Article includes a table that is entitled "TABLE 2. Estimated RR of Herpes Zoster in Residents Aged <10 Years With a History of Varicella Vaccination Versus Those With a History of Varicella Disease", which contains the following selected rows and columns:

Yr	*Vaccination History*	
	*No. Cases**	*Population*
2000	*4*	*23,752*

2001	*5*	*30,512*
2002	*7*	*35,722*
2003	*9*	*39,924*
2004	*8*	*43,046*
2005	*8*	*45,694*
Total	**41**	**218,650**
2006	*10*	*47,266*
2000–2006	51	265,916

and is accompanied by the following note:

> *"§*Herpes zoster cases with a varicella vaccination include those with vaccine history only (n = 40), vaccine and unknown disease history (n = 3), and vaccine and disease history (n = 8)."*

Based upon the above accompanying note, 40 (78%) of the 51 cases stated in the table to have been reported in 2000-2006 had a vaccine history but definitely no disease history.

Applying that 78% to the 41 cases in 2000-2005 (and subtracting the remaining 22%, i.e. 9, cases from the population) results in approximately 32 cases of HZ out of the 218,641 doses in that period, which is an HRI rate of:

- **1 in 6,800 doses.**

If all of the cases in the vaccinated that were excluded from that rate calculation on the basis of their unknown or definite disease history, were instead included given that they may nevertheless have acquired HZ as a result of the vaccination, the HZ rate would increase to 1 in 5,333 doses.

(b) SAE_C_SUBJ from passive surveillance

The Plaintiff hereby requests that the Court take judicial notice of the following document:

- article entitled "European Medicines Agency. ICH Topic E2A. Clinical safety data management: definitions and standards for expedited reporting: step 5", dated 1995, accessible at: https://www.ema.europa.eu/en/documents/scientific-guideline/international-conference-harmonisation-technical-requirements-registration-pharmaceuticals-human-use_en-15.pdf

(last accessed January 26, 2021)
(hereafter “AE and SAE Definitions in VVVL Passive Surveillance”)
A true and correct copy of the aforesaid document is attached hereto as **Exhibit 215.**

The Varicella Vaccine 22-Year Review refers to:

“varicella zoster virus (VZV)”

and

“varicella virus vaccine live (VVVL [VARIVAX])

and

“wild-type VZV (WTV)”

and

“shingles (herpes zoster [HZ])”

and states:

“This comprehensive review of the VVVL safety profile is based on 22 years of postmarketing adverse event (AE) data received through spontaneous and noninterventional study reports submitted by health care providers and on a review of the published literature (cumulatively from March 17, 1995, through March 16, 2017, during which period >212 million doses were distributed globally).”

and

“This report reviews 22 years of postmarketing safety data received by Merck, Sharp & Dohme (MSD).”

Based upon these excerpts, the subject of the Varicella Vaccine 22-Year Review is passive surveillance (by Merck, Sharp & Dohme) of AEs reported after vaccination with Varivax for which the Surveillance Period was the 22-year period of March 17, 1995, through March 16, 2017.

The Varicella Vaccine 22-Year Review states:

“Serious AEs (SAEs) were defined per the International Conference on Harmonisation guidelines [13, 14]…
14. European Medicines Agency. ICH Topic E2A. Clinical safety data management: definitions and standards for expedited reporting: step 5. 1995. Available at: https://www.ema.europa.eu/documents/scientific-guideline/international-conferenceharmonisation-technical-requirements-registration-pharmaceuticals-humanuse_en-15.pdf Accessed 8 July 2018..”

The AE and SAE Definitions in VVVL Passive Surveillance states:

"1. Adverse Event (or Adverse Experience)

Any untoward medical occurrence in a patient or clinical investigation subject administered a pharmaceutical product and which does not necessarily have to have a causal relationship with this treatment. An adverse event (AE) can therefore be any unfavourable and unintended sign (including an abnormal laboratory finding, for example), symptom, or disease temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product."

and

"A serious adverse event (experience) or reaction is any untoward medical occurrence that at any dose:

- *results in death,*
- *is life-threatening,*

NOTE: The term "life-threatening" in the definition of "serious" refers to an event in which the patient was at risk of death at the time of the event; it does not refer to an event which hypothetically might have caused death if it were more severe.

- *requires inpatient hospitalisation or prolongation of existing hospitalisation,*
- *results in persistent or significant disability/incapacity, or*
- *is a congenital anomaly/birth defect."*

Based upon these excerpts, the SAE definition used in the Varicella Vaccine 22-Year Review accords in all respects with the definition of the term "serious adverse event" (SAE) in this Notice, as defined in paragraph 2.1, apart from its additional inclusion of "significant disability/incapacity", which might not necessarily be technically permanent. It will be assumed herein that the proportion of adverse events that fall into the latter category is relatively insignificant.

The Varicella Vaccine 22-Year Review also states:

"Based on European Medicines Agency (EMA) guidelines [15], potentially immunocompromised patients were identified based on medical histories, concurrent conditions, and concomitant therapies. Samples were analyzed using polymerase chain reaction (PCR) methodology to confirm the presence and type (vaccine strain or wild-type virus [WTV]) of VZV [16]."

and

"Reports of AEs of interest, with PCR analysis from all laboratories, are presented in Table 1"

and includes a table that is entitled "Table 1. PCR Results From All Laboratories by AE of Interest [a] ", which contains the following selected rows and columns that are in *italics*:

AE, No.	*Oka/Merck Vaccine Strain VZV*	*Wild-Type VZV*	*VZV-Negative*	Total typed	Vaccine Strain as % of typed ("SAE_CR_VVVL")
Varicella	*67*	*97*	*12*	176	38%
Herpes zoster	*117*	*57*	*27*	201	58%
Rash events	*25*	*39*	*33*	97	26%
Secondary transmission	*8*	*38*	*14*	60	13%
CNS events	*17*	*7*	*40*	64	27%
Other AEs	*17*	*2*	*13*	32	53%
Total No. of samples	*251*	*240*	*139*	778	32%

hereafter "SAE_CR_VVVL Percentages Table",

and is accompanied by the following notes:

"Abbreviations: AE, adverse event; CNS, central nervous system; CSF, cerebrospinal fluid; PCR, polymerase chain reaction; VZV, varicella zoster virus.

a The table includes all PCR samples received by MSD from all laboratories through March 16, 2017; 1 individual may have had more than 1 type of sample (ie, rash/lesion sample and sputum sample).

The Varicella Vaccine 22-Year Review states the following with respect to some of the AEs and AEs reported:

*"**Varicella After Vaccination***

There were 10 677 reports of 11 095 varicella events (10 751 AEs, 344 SAEs)… Most fatal outcomes occurred in immunocompromised patients, in whom VVVL is contraindicated (see below). Lesion samples (n = 204; more than 1 sample may have been submitted per patient) submitted for PCR testing included 49 from immunocompromised patients (32 vaccine strain VZV, 9 WTV, 4 untypable/no strain identified, and 4 inadequate samples).”

and

“Herpes Zoster

Over the evaluation period, 1602 reports of 1803 HZ events were submitted (1646 AEs, 157 SAEs)… There were 260 reports with 261 rash/lesion samples submitted for PCR analysis, including 26 from immunocompromised patients (17 vaccine strain VZV, 4 WTV, 2 VZV-negative, 1 untypable/no strain identified, and inadequate samples).”

and

“Rash (Nonvaricella, Non-HZ)

There were 6153 reports (6887 AEs, 345 SAEs) of a rash related AE.… There were 127 reports with 128 rash/lesion samples submitted for PCR analysis, including 4 from immunocompromised patients (2 vaccine strain VZV, 1 WTV, and 1 inadequate sample).”

and

“CNS Events

... SAEs comprised 73% (571/781) of CNS event reports... Seventy-three cases with 78 samples (samples for PCR analysis included cerebrospinal fluid and brain tissue) submitted for PCR analysis were reported, including 9 from immunocompromised patients (7 vaccine strain VZV, 1 VZV negative, and 1 untypable/no strain identified).”

and

“Disseminated Vaccine-Strain VZV

Disseminated disease caused by the Oka/Merck vaccine strain VZV, with or without visceral involvement, was confirmed by PCR analysis in 39 cases. Eleven cases occurred in immunocompetent individuals, and 28 involved patients who had underlying immunosuppressive conditions and/or who reported concomitant use of immunosuppressant therapies (Tables 2 and 3).”

The last (rightmost) column in the above table is headed “SAE_CR_VVVL” which means, in relation to any SAE type covered in the Varicella Vaccine 22-Year

Review, the percentage of successfully typed SAE_REPs for which the VZV strains present were the Oka/Merck vaccine strain. Hence, that percentage represents the estimated minimum percentage of SAE_REPs that were caused by vaccination with VVVL.

SAE_CRV_VVVL is described as a minimum because the calculation of this percentage excludes all of those SAEs that were caused by the VVVL but where the vaccine strain itself was not involved, i.e. where the SAE was caused by the injection of one or more other ingredients in the vaccine.

Based upon these excerpts and assumptions stated below, the following table can be constructed of approximate SAE numbers and rates after VVVL vaccination, with the figures in *italics* taken directly from these excerpts:

SAE type	Varicella	Herpes Zoster	Rash (Non-varicella, Non-HZ)	CNS Events	Vaccine strain disseminated disease	**Total**
# doses	> 212,000,000					
SAE_REP	*344*	*157*	*345*	*571*	*39*	***1456***
SAE_REP in IC[1]	*49*	*26*	*4*	*9*	*28*	***116***
SAE_REP in non-IC	295	131	341	562	11	**1340**
NR%[2]	< 1%					
SAE_ACTUAL[3]	> 29500	> 13100	> 34100	> 56200	> 1100	**> 134,000**
% SAE_CR_VVVL[3]	38%	58%	26%	27%	100%	**33%**
SAE_C_SUBJ[3]	> 11200	> 7600	> 8800	> 14900	> 1100	**> 43,700**
SRI (SAE_C_SUBJ per dose) [3]	> 1 / 18,878	> 1 / 27,802	> 1 / 24,122	> 1 / 14,201	> 1 / 192,727	**> 1 / 4,854**

* Notes: 1. Abbreviation “IC” means immunocompromised vaccine recipients. It is assumed herein that for all of those vaccine recipients, the AE was recorded in the relevant database as a SAE.

2. The Notification Rate (“NR”) applicable to reporting to MSD is assumed to be the same as the rate applicable to reporting to VAERS.

3. These do not include AEs that were reported in IC individuals.

(c) SRI

Based upon the excerpts above, the risk of one dose of varicella vaccine in the US causing a serious adverse event is at least approximately:

- **1 / 4,854**.

11.3 Hepatitis A

The Plaintiff hereby requests that the Court take judicial notice of the following document:

- manufacturer product information named "VAQTA® (Hepatitis A Vaccine, Inactivated)", accessible via https://www.fda.gov/media/74519/download (last accessed January 19, 2021)
  (hereafter "Vaqta Package Insert")
  A true and correct copy of the aforesaid document is attached hereto as **Exhibit 216**.

(a) SAE_ACTUAL rate derived from passive surveillance

The Vaqta Package Insert states:

> *"Across the five studies conducted in subjects 12-23 months of age, 0.7% (32/4374) of subjects reported a serious adverse event following any dose of VAQTA….The serious adverse events were collected over the period defined in each protocol (14, 28, or 42 days)"*

Based upon this excerpt, the manufacturer found the SAE_ACTUAL rate to be approximately 32 in 4374, which is approximately:

- 1 in 137 in 12 to 23 month olds within 14, 28 or 42 days after vaccination.

(b) SAE_C_SUBJ rate derived from passive surveillance

The above statement in the Vaqta Package Insert is immediately followed by:

> *".. and 0.1% (5/4374) of subjects reported a serious adverse event judged to be vaccine related by the study investigator."*

(c) SRI

Based upon the raw SAE_ACTUAL rate and SAE_C_SUBJ above, the risk of one dose of the hepatitis A vaccine in the US causing a serious adverse event is approximately (5 ÷ 4374 =):

- **1 in 875**, in 12 to 23 month olds within 14, 28 or 42 days after vaccination.

11.4 Hepatitis B

The Plaintiff hereby requests that the Court take judicial notice of the following document:

- article entitled “Immunogenicity and safety of an investigational hepatitis B vaccine with a Toll-like receptor 9 agonist adjuvant (HBsAg-1018) compared to a licensed hepatitis B vaccine in healthy adults 40–70 years of age”,

  Citation: W.L. Heyward, M. Kyle, J. Blumenau, M. Davis, K. Reisinger, M.L. Kabongo, et al. Vaccine. 2013 Nov 4;31(46):5300-5. doi: 10.1016/j.vaccine.2013.05.068. Epub 2013 May 30. PMID: 23727002, accessible at https://academic.oup.com/ofid/article-pdf/6/8/ofz295/33575326/ofz295.pdf
  (last accessed January 29, 2021)
  (hereafter “Heyward Hepatitis B Vaccine Risk Article”)
  A true and correct copy of the aforesaid document is attached hereto as **Exhibit 217**

- article entitled “Prospective clinical trial of hepatitis B vaccination in adults with and without type-2 diabetes mellitus”,

  Citation: Van Der Meeren O, Peterson JT, Dionne M, Beasley R, Ebeling PR, Ferguson M, Nissen MD, Rheault P, Simpson RW, De Ridder M, Crasta PD, Miller JM, Trofa AF. Hum Vaccin Immunother. 2016 Aug 2;12(8):2197-2203. doi: 10.1080/21645515.2016.1164362. Epub 2016 Apr 28. PMID: 27123743; PMCID: PMC4994745, accessible at https://academic.oup.com/ofid/article-pdf/6/8/ofz295/33575326/ofz295.pdf
  (last accessed January 29, 2021)
  (hereafter “Van Der Meeren Hepatitis B Vaccine Risk Article”)
  A true and correct copy of the aforesaid document is attached hereto as **Exhibit 218**

(a) SAE_C_SUBJ rates from active surveillance

The Heyward Hepatitis B Vaccine Risk Article states:

> *“A Phase 3, multicenter, randomized, subject- and observer-blinded, active-controlled trial was conducted among healthy subjects… comparing the … safety of… HBsAg-1018… to three doses of licensed hepatitis B vaccine… Engerix-B®, referred to as HBsAg-Eng…*

Eligible subjects were healthy adults 40 through 70 years of age with no clinically significant illness who were seronegative for HBsAg, anti-HBs, antibody against hepatitis B core antigen (anti-HBc), and human immunodeficiency virus… Subjects in the HBsAg-Eng group received injections of HBsAg-Eng at weeks 0, 4, and 24.

Subjects were randomly assigned to receive… HBsAg-1018 or HBsAg-Eng… Randomization was stratified by age (40–49, 50–59, and ≥60 years) and by site….

The reporting period for SAEs and autoimmune events began at the time of first injection and extended through week 52….

The safety population was comprised of 2449 subjects (HBsAg-1018: n = 1968 subjects; HBsAg-Eng: n = 481)…. one related SAE of reactive airway disease occurred in the HBsAg-Eng group"

The Heyward Hepatitis B Vaccine Risk Article also includes a table entitled "Table 3. Summary of treatment-emergent adverse events (safety population)" containing the following selected columns and rows:.

Event	*HBsAg-Eng (N = 481)*
Any related AE	*29 (6.0%)*
Any severe AE (grade 3 and above)	*95 (4.8%)*
Any AE Within 28 days after active injection	*250 (52.0%)*
Any SAE	*23 (4.8%)*
Any related SAE	*1 (0.2%)*
Any AE leading to discontinuation of study treatment	*2 (0.4%)*
Death	*1 (0.2%)*

a HBsAg-1018 safety population (4 lots HBsAg-1018).
b Includes adverse events with onset between the first dose and 4 weeks following the last dose. Percentages are based on the number of subjects (n) for each category. A subject with multiple occurrences of the same category of event is counted only once.

The Van Der Meeren Hepatitis B Vaccine Risk Article states:

"Four hundred and sixteen participants with Type-2 diabetes and 258 controls matched for age and body mass index (BMI) (2:1 ratio) received 3-doses of HBV vaccine (Engerix-B™, GSK Vaccines, Belgium) according to a 0, 1, 6 months schedule… 674 were vaccinated (Fig. S1)…

Serious adverse events (SAEs)… were captured from the first vaccination until one month after the third dose.

SAEs were reported by 3.8% (95% CI 2.2; 6.2) of participants with diabetes and 1.6% (95% CI 0.4; 3.9) of controls, none of which were considered to be related to vaccination."

Based upon these excerpts, among a total of (481+416+258 =) 1,155 subjects, the SAEs were observed to occur at the rate of 4.8%, 3.8% and 1.6% in the subjects in the three Engerix-B groups in the two trials – that in the first trial, the diabetic group in the second trial and the non-diabetic group in the second trial respectively, totalling 43 SAEs, which was an overall rate of 3.7%. Of those 43 SAEs in 1155 subjects after three doses, one SAE was assessed to be vaccine-related.

(b) SRI

Hence, in the absence of more precise and relevant data, it is estimated that SRIV approximates 1 in 1,155 and assumed that approximately the same rate applies to infants, which per dose (of the three doses) is 1 in (1155 x 3 =) 3,465.

Based upon that result, SRI for hepatitis b vaccination in infants is approximately:

- 1 in 3,465 (i.e. per dose), within 30 days after the last of the three doses.

The Van Der Meeren Hepatitis B Vaccine Risk Article also states:

"There was one death during the study: a 45-y old man in the diabetes group was diagnosed with glioblastoma multiforme and died 334 d post-dose 2… The event was considered unrelated to vaccination."

This rule out of causality was made in the face of the fact that all subjects were healthy enough when enrolled in the study (apart from the diabetes in the diabetes group) and the fact that the Engerix-B Package Insert states under the headings "*Genotoxicity*" and "*Carcinogenicity*", "*No data available*".

11.5 *Haemophilus Influenzae* type b (Hib)

The Plaintiff hereby requests that the Court take judicial notice of the following document:

- article entitled "Lot-to-lot consistency, safety and immunogenicity of 3 lots of Haemophilus influenzae type b conjugate vaccine: results from a phase III randomized, multicenter study in infants",

Citation: Klein, N. P., Abu-Elyazeed, R., Cornish, M., Leonardi, M. L., Weiner, L. B., Silas, P. E., Grogg, S. E., Varman, M., Frenck, R. W., Cheuvart, B., Baine, Y., Miller, J. M., Leyssen, M., Mesaros, N., & Roy-Ghanta, S. (2017). Vaccine, 35(28), 3564-3574. https://doi.org/10.1016/j.vaccine.2017.05.018, accessible at https://www.sciencedirect.com/science/article/pii/S0264410X17306266 (last accessed January 28, 2021)
(hereafter "Hib Vaccine Risk Article")
A true and correct copy of the aforesaid report is attached hereto as **Exhibit 219**.

(a) SAE_C_SUBJ rates from active surveillance

The CDC Schedule 2020 states the following:

"Hib vaccination (minimum age: 6 weeks [PCV13]…

Routine vaccination with PCV13

- *4-dose series at 2, 4, 6, 12–15 months"*

The Hib Vaccine Risk Article states:

"This phase III, randomized, multi-centered study (NCT01000974) evaluated the safety and immunogenicity of a monovalent tetanus toxoid-conjugate Hib vaccine (Hib-TT) compared to a monovalent (Hib-TT control) and a combination Hib-TT vaccine.

The study enrolled eligible healthy infants aged 6–12 weeks at any of the study centers, who were born at a gestational age of ≥36 weeks,

Study participants received one of the following Hib-containing vaccines, according to a 3 + 1 vaccination schedule: Hib-TT vaccine (Hiberix, GSK), Hib-TT control vaccine (ActHIB, Sanofi Pasteur), or a combination vaccine containing diphtheria-tetanus-acellular pertussis (DTaP), inactivated poliovirus (IPV) and Hib-TT components (DTaP-IPV/Hib-TT; Pentacel, Sanofi Pasteur).

We recorded adverse events (AEs) for 4 (solicited) and 31 days (unsolicited) postvaccination and serious AEs (SAEs) throughout the study…

The primary phase of the study was conducted between June 18, 2010 (first visit for the first enrolled participant) and May 4, 2012 (last visit), with a 6-month follow-up period completed on August 3, 2012.

For the booster vaccination phase, the first visit occurred on July 12, 2011 and the last contact for the 6-month follow-up was on July 17, 2013.

…We recorded serious AEs (SAEs) and AEs of specific interest (AESIs) from study start up to 6 months after the final vaccination. We defined an SAE as any untoward medical occurrence that resulted in death, was life-threatening, required hospitalization or prolonged existing hospitalization, or resulted in disability or incapacity.

Of the 4009 infants enrolled in the study, 4003 were vaccinated, and 3665 completed the primary vaccination phase; 3172 toddlers received a booster dose and 3086 completed the booster phase.

..... Post-primary vaccination, 107/2963 (3.6%) infants receiving Hib-TT, 24/520 (4.6%) receiving Hib-TT control, and 21/520(4.0%) receiving DTaP-IPV/Hib-TT (Table S5) experienced a total of 233 SAEs. We assessed 6 SAEs as being causally related to vaccination…

..... Postbooster vaccination, we recorded 35 SAEs in 29/2337 (1.2%) toddlers in the Hib-TT group, 4/435 (0.9%) in the Hib-TT control and 2/400 (0.5%) in the DTaP-IPV/Hib-TT group (Table S5). We assessed 1 SAE in the Hib-TT group as being related to vaccination."

The following table (including directly quoted figures *in italics)* summarizes the above information:

Vaccine phase	**Primary**	**Booster**	**Average/Total**
# Subjects	Between 3665 and 4003*	3172	
# SAE_C_SUBJ	6	1	
# vaccine doses administered in trials	3 (max)	1	
SRI	1 in 2,002 to 1 in 1,833	1 in 3,172	**1 in 2,205** to **1 in 2,049**
# doses recommended	3	1	4
SRIV	1 in 667 to 1 in 611	1 in 3,172	1 in 551 to 1 in 512

* Note: The article states that although "*4003 were vaccinated*" with at least one vaccine, only "*3665 completed the primary vaccination phase*", so the number of those in receipt of three doses was between 3665 and 4003.

(b) SRI

Based conservatively upon the lower limit of the above range for SRI, the average SRI for Hib vaccination is approximately:

- **> 1 in 2,205**, in infants and toddlers, up to 6 months after the booster dose.

11.6 Pneumococcal

The Plaintiff hereby requests that the Court take judicial notice of the following document:

- article entitled "Safety of 13-valent pneumococcal conjugate vaccine in infants and children: Meta-analysis of 13 clinical trials in 9 countries",

  Citation: Thompson A, Gurtman A, Patterson S, Juergens C, Laudat F, Emini EA, Gruber WC, Scott DA. Vaccine. 2013 Oct 25;31(45):5289-95. doi: 10.1016/j.vaccine.2013.08.025. Epub 2013 Aug 20. PMID: 23973321, accessible at https://www.sciencedirect.com/science/article/pii/S0264410X1301116X (last accessed January 29, 2021)
  (hereafter "Pneumococcal Vaccine Risk Article")
  A true and correct copy of the aforesaid document is attached hereto as **Exhibit 220**

(a) SAE_C_SUBJ rates from active surveillance

The CDC Schedule 2020 states the following**:**

"Pneumococcal vaccination (minimum age: 6 weeks [PCV13]…

Routine vaccination with PCV13

- *4-dose series at 2, 4, 6, 12–15 months"*

The Pneumococcal Vaccine Risk Article states:

"A meta-analysis was performed of integrated safety data from 13 infant studies (PCV13n = 4729 and PCV7 n = 2760) conducted in 9 North American, European, and Asian countries. Local reactions at the vaccine injection site and systemic events were collected for 4–7 days after each dose into electronic diaries. Adverse events (AEs) were collected after each vaccination…

This meta-analysis comprised all data available from phase 2 and 3 infant studies in the PCV13 clinical development program as of November, 18, 2008.… Choice of concomitant vaccines, described in Table 1, was based upon national recommendations. Ten studies used PCV7, which was equivalent to the marketed Prevnar® vaccine (Pfizer Inc., Collegeville, PA), as a single active comparator; and 3 studies compared different formulations or lots of PCV13. All data utilized in this analysis were contained within the Pfizer PCV13 Oracle Clinical database.

Serious AEs (SAEs) were reported from study enrollment to final visit.

SAEs that the investigator considered related to study vac-cine were reported for 11 subjects. Related SAEs in the PCV7 group included febrile convulsion (n = 2), infantile spasms (n = 1), nephroblastoma (n = 1), and pyrexia (n = 1). Related SAEs in thePCV13 group included febrile convulsion and pyrexia (n = 1), pyrexia (n = 1), bronchitis (n = 1), inconsolable crying (n = 1), allergyto vaccine (n = 1), and bronchiolitis (n = 1). Among the 7489 vac-cinated infants, 3 (0.063%) vaccinated with PCV13 and 1 (0.036%) vaccinated with PCV7 died as a result of Sudden Infant Death Syn-drome (SIDS) considered unrelated to study vaccine."

The article also states that:

"withdrawals due to AEs occurred (Table 2); 23 subjects (15 PCV13 (0.3%) subjects and 8 PCV7 (0.3%) subjects) during the infant series, 16 subjects (7 PCV13 (0.3%) subjects and 9 PCV7 (0.5%) subjects) between the infant series and toddler dose, and no subjects following the toddler dose. Types of AEs most frequently resulting in withdrawal were nervous system disorders and infections and infestations (Table 2)."

and includes the following table referenced therein, entitled: "Table 2. Withdrawals due to adverse events (AEs) by System Organ Class [a] and pneumococcal conjugate vaccine group (includes events which are not related to vaccination as well as those that are possibly related)"

N	*PCV13*	*PCV7*
	n = 4723 infant series; n = 2569 between infant and toddler dose [b,c]; n = 2499 [d]	*n = 2754 infant series; n = 1800 between infant and toddler dose [b,c]; n = 1482 [d]*
Any AE	***22***	***17***

Nervous system disorders	*8*	*9*
Infections and infestations	*5*	*3*
Skin and subcutaneous tissue disorders	*2*	*3*
Psychiatric disorders	*2*	*2*
Blood and lymphatic system disorders	*3*	*0*
General disorders/administration site disorders	*2*	*1*

Based upon the above paragraph and figures in this table, 4723 and 2754 subjects received at least one dose of PCV13 and PCV7 respectively, but there were withdrawals during the infant series, so a minimum of only 2569 and 1800 respectively received all three doses in the infant series.

In the following table,

- the first four rows (including the header) summarize the above information, and
- in the last two rows are the results that can be derived therefrom, for the number of doses that were administered and the resultant SRI:

Vaccine	**PCV13**	**PCV7**	**Total**
SAE_C_SUBJ	6	5	11
Infant series (3 doses) – Min # subjects:	2569	1800	4369
– Max # subjects	4723	2754	7477
Toddler (4th dose) – # subjects	2499	1482	3981
Total # doses – Minimum	10206	6882	17088
– Maximum	16668	9744	26412
SRI – Maximum	>1 in 1,701	> 1 in 1,376	>1 in 1,553
– Minimum	>1 in 2,778	> 1 in 1,949	**>1 in 2,401**

(b) SRI

Based upon the above figures, and assuming that the differences between the SRIs for PCV13 and PCV7 were due to the limited sample sizes as opposed to statistically significant differences in safety, the combined total for PCV13 and PCV7 is taken herein to be the approximate SRI for Prevnar13.
That is, the resultant SRI is taken to be approximately:

- **> 1 in 2,401**, in infants and toddlers, up to 6 months after the booster dose.

The article also states:

"Polysorbate 80 (P80) is a nonionic detergent that is widely used in both oral and injectable medications to solubilize proteins. Most studies included in the analysis used PCV13 without P80 [7–11,13–15,18,19]. However, following a decision to produce a commercial formulation of PCV13 containing P80, later studies utilized a PCV13 formulation containing P80 [12,16,17]."

Based upon this excerpt, not all of the studied vaccine doses included polysorbate 80. To any extent that the vaccination risk is increased by the inclusion of polysorbate 80 in PCV13, the SRI result could be expected to be greater than the above stated figure.

11.7 Meningococcal

The calculation of SRI for meningococcal vaccination, referred to herein as "MenACWY", is based upon passive surveillance of MenACWY, with reports made to VAERS, during the surveillance period of January 2006 – December 2009, which is the same as that used for Tdap in the analysis thereof, which is presented in paragraph 10.3 herein.

(a) **V_SP**

The CDC Secondary School Coverage Reports for 2006-2009 provide the figures in *italics* in the following table for Tdap and MenACWY vaccination coverages in 13-17 year olds, based upon which the non-italicized averages in the same table are calculated:

Vaccination Coverage %

	Age (yrs)					
Year, Vaccine	***13***	***14***	***15***	***16***	***17***	**Average %**
2006						
≥1 dose Tdap	*12.7*	*15.4*	*12.1*	*8.0*	*5.1*	**10.7**
MCV4 ≥1 dose	*11.3*	*12.5*	*13.9*	*13.2*	*7.1*	**11.6**
2007						
≥1 dose Tdap	*43.2*	*37.3*	*28.3*	*24.9*	*19.0*	**30.5**
MCV4 ≥1 dose	*32.6*	*31.6*	*33.9*	*31.0*	*33.0*	**32.4**
2008						
≥1 dose Tdap	*51.9*	*47.3*	*41.5*	*35.1*	*28.7*	**40.9**
MCV4 ≤ [sic] 1 dose	*42.0*	*43.0*	*46.4*	*40.5*	*36.7*	**41.7**
2009						
≥1 dose Tdap	*65.2*	*63.5*	*58.3*	*46.8*	*43.6*	**55.5**
MenACWY ≥1 dose	*53.8*	*56.1*	*54.6*	*54.4*	*48.8*	**53.5**

2006-2009 average						
≥1 dose Tdap	43.3	40.9	35.1	28.7	24.1	**34.4**
MenACWY ≥1 dose	34.9	35.8	37.2	34.8	31.4	**34.8**

In view of the fact that, according to the CDC Schedules in the material years,

- only one dose of Tdap was recommended for adolescents, and
- according to the ACIP Current MenACWY Recommendations Article,

it was not until "*2010*" that "*ACIP added a MenACWY booster dose at age 16 years*",

it is reasoned that the above coverages apply to a single dose of the respective vaccinations, and that the coverage for two doses is negligible.

Based upon the above vaccination coverage figures, which average 34-35% in the case of each vaccination, and the above reasoning, it can be estimated that the number of doses of MenACWY administered to the relevant age group during the Surveillance Period of January 2006 through December 2009 approximated the number of doses administered of Tdap during the same period.

(b) SAE_REP from passive surveillance

The Plaintiff hereby requests that the Court take judicial notice of the following document

- entitled "The Vaccine Adverse Event Reporting System (VAERS) Results", and available from:

  Vaccine Adverse Event Reporting System (VAERS),
  CDC WONDER Online Database,
  United States Department of Health and Human Services (DHHS) Public Health Service (PHS),
  Centers for Disease Control (CDC) / Food and Drug Administration (FDA),
  accessible from http://wonder.cdc.gov/vaers.html

and subtitled (by the Plaintiff)
"SAEs totaled - Secondary MenACWY, 2006 - 2009 (313 VAERS IDs, 613 SAEs),

to which a submitted search request is located at
https://wonder.cdc.gov/controller/saved/D8/D109F766[14]
(last accessed January 30, 2020)
(hereafter "Secondary MenACWY – Reported SAEs Totaled")

A true and correct copy of the aforesaid report is attached hereto as **Exhibit 221.**

The document “Secondary MenACWY - Reported SAEs Totaled” includes in the section headed “*Query Criteria*”:

“Age: 6-17 years

Date Vaccinated: Jan., 2006 to Dec., 2009

Serious: Yes

State / Territory: Alabama; Alaska; Arizona; Arkansas; California; Colorado; Connecticut; Delaware; District of Columbia; Florida; Georgia; Hawaii; Idaho; Illinois; Indiana; Iowa; Kansas; Kentucky; Louisiana; Maine; Maryland; Massachusetts; Michigan; Minnesota; Mississippi; Missouri; Montana; Nebraska; Nevada; New Hampshire; New Jersey; New Mexico; New York; North Carolina; North Dakota; Ohio; Oklahoma; Oregon; Pennsylvania; Rhode Island; South Carolina; South Dakota; Tennessee; Texas; Utah; Vermont; Virginia; Washington; West Virginia; Wisconsin; Wyoming”

Vaccine Products: MENINGOCOCCAL CONJUGATE VACCINE (MNC); MENINGOCOCCAL POLYSACCHARIDE VACCINE (MEN); MENINGOCOCCAL VACCINE (MENACTRA) (MNQ)”

Group By: Vaccine Dose; Event Category”.

The document states that the query result, under the title and subtitle, is the following table, hereafter “Secondary Tdap - Reported SAEs Totaled Table”:

Vaccine Dose	*Event Category*	*Events Reported*	*Percent (of 313)*
1 Dose	*Death*	*7*	*2.24%*
	Life Threatening	*56*	*17.89%*
	Permanent Disability	*44*	*14.06%*
	Hospitalized	*186*	*59.42%*
	Existing Hospitalization Prolonged	*26*	*8.31%*
	*Emergency Room / Office Visit ** *	*136*	*43.45%*
	*Office Visit * *	*1*	*0.32%*
	Total	***456***	***145.69%***
2 Doses	*Life Threatening*	*2*	*0.64%*
	Permanent Disability	*2*	*0.64%*
	Hospitalized	*4*	*1.28%*
	*Emergency Room / Office Visit ** *	*5*	*1.60%*
	Total	***13***	***4.15%***
4 Doses	*Hospitalized*	*1*	*0.32%*
	Total	***1***	***0.32%***
7 or more Doses	*Hospitalized*	*1*	*0.32%*
	Total	***1***	***0.32%***
Unknown	*Death*	*3*	*0.96%*
	Life Threatening	*17*	*5.43%*
	Permanent Disability	*17*	*5.43%*
	Hospitalized	*60*	*19.17%*
	Existing Hospitalization Prolonged	*6*	*1.92%*
	*Emergency Room / Office Visit ** *	*39*	*12.46%*
	Total	***142***	*45.37%*
Total		***613***	***195.85%***

The figures in the above table can be summarized as follows:

Event Category	**Events Reported**	**Percent (of 198)**
Death	10	3.19%
Life Threatening	75	23.96%
Permanent Disability	63	20.13%
Hospitalized	252	80.51%
Existing Hospitalization Prolonged	32	10.22%
Emergency Room / Office Visit **	180	57.51%
Office Visit *	1	0.32%
Total	**613**	195.85%

Based upon the above figures, the following parameter values can be derived for the subject vaccination, MenACWY, in the Surveillance Period:

- SAE_REP was 613
- SAE_HOSP was (252 + 32 =) 284

On the basis of:

- the probability, as explained in the previous paragraph 11.7(a), that virtually every subject MenACWY vaccine recipient received only one dose, and
- the fact that 456, i.e. 96.8%, of the 471 SAE_REPs where the "Vaccine Dose" was reported to be known, were reported to have been after "1 Dose",

it is estimated by extrapolation that 96.8% also of the 142 SAE_REPs where the "Vaccine Dose" was reported to be "Unknown", occurred also after the first dose. That results in a total number of (456 + 137 =) 593 SAE_REPs in the SP.

Applying the same extrapolation to hospitalizations (including prolongation of existing hospitalizations) results in a total number of (212 + 64 =) 276 SAE_HOSPs in the SP

All of the above listed figures can be seen to be more than 1.5 times the respective figures for Tdap, of 388, 179 and stated in paragraph 10.3(b)i herein.

(c) SRI

Hence, the calculation of SRI is based upon SAE_REP and SAE_HOSP being taken to be 593 and 276 respectively, both of which are 1.5 times greater than the respective values in the case of Tdap, which are 388 and 179.

Notably, the same factor of 1.18 applies also to the differences in SAE_HOSP, i.e. (186 + 26 =) 212 for MenACWY compared to 179 for Tdap.

Conservatively, the same factor of 2 that applies to the difference between the two respective figures for SAE_DEATH (i.e. 10 vs 5) shall be disregarded, and be taken to also be only 1.5 also.

Proportionately based upon that conservative factor of 1.5 times, the SRI estimate for MenACWY can accordingly be estimated to be 1.5 times the SRI estimate for Tdap of 1 / 5,173.

That results in an approximate SRI for MenACWY of:

- **1 / 4,400.**

11.8 Influenza

The Plaintiff hereby requests that the Court take judicial notice of the following documents:

- article entitled “Immunogenicity and safety of an inactivated quadrivalent influenza vaccine candidate: a phase III randomized controlled trial in children”.

  Citation: : Langley JM, Carmona Martinez A, Chatterjee A, et al. [published correction appears in J Infect Dis. 2014 May 1;209(9):1494]. J Infect Dis. 2013;208(4):544-553. doi:10.1093/infdis/jit263, accessible at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3719910/pdf/jit263.pdf (last accessed January 26, 2021)

  (hereafter “Fluarix Clinical Trial NCT01198756 Article”)

  A true and correct copy of the aforesaid article is attached hereto as **Exhibit 222**.

- manufacturer product information named “FluLaval Quadrivalent”, accessible via https://www.fda.gov/media/115785/download (last accessed January 26, 2021)
  (hereafter “FluLaval Package Insert”)
  A true and correct copy of the aforesaid document is attached hereto as **Exhibit 223**.

- manufacturer product information named “Fluarix Quadrivalen”, accessible via https://www.fda.gov/media/79278/download

  (last accessed January 26, 2021)
  (hereafter “Fluarix Package Insert”)
  A true and correct copy of the aforesaid document is attached hereto as **Exhibit 224**.

- U.S. National Library of Medicine web page entitled: “An Efficacy Study of GlaxoSmithKline (GSK) Biologicals' Candidate Influenza Vaccine GSK2321138A in Children”, accessible via https://clinicaltrials.gov/ct2/show/results/NCT01439360 (last accessed January 26, 2021)
  (hereafter “Fluarix Clinical Trial NCT01439360 Results”)

  A true and correct copy of the aforesaid document is attached hereto as **Exhibit 225**

- WHO document entitled “NEWS UPDATE – 12-17 April 2013”, accessible at https://www.who.int/influenza_vaccines_plan/news/news_update_16_2013.pdf (last accessed February 1, 2020)

(hereafter “WHO Fluarix Tetra Name Document”)

A true and correct copy of the aforesaid report is attached hereto as **Exhibit 226**

- article entitled “A Randomized Trial of Candidate Inactivated Quadrivalent Influenza Vaccine versus Trivalent Influenza Vaccines in Children Aged 3–17 Years”.

  Citation: Domachowske JB, Pankow-Culot H, Bautista M, et al. J Infect Dis. 2013;207(12):1878-1887. doi:10.1093/infdis/jit091, accessible at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3654742/pdf/jit091.pdf
  (last accessed January 26, 2021)
  (hereafter “Fluarix Clinical Trial NCT01196988 Article”)

  A true and correct copy of the aforesaid article is attached hereto as **Exhibit 227**.

(a) SAE_C_SUBJs as assessed in clinical trials

The Fluarix Clinical Trial NCT01198756 Article states:

> *“In a randomized controlled trial, immunogenicity and safety of an inactivated quadrivalent influenza vaccine candidate (QIV) versus trivalent inactivated influenza vaccine (TIV)-Victoria(Vic) and TIV-Yamagata(Yam) in children 3–17 years of age was evaluated. In an open-label study arm, QIV only was assessed in children 6–35 months of age…A total of 3094 children (932 QIV, 929 TIV-Vic, 932 TIV-Yam, and 301 QIV only) were vaccinated”*

and

> *“Among children age 3–17 years, 3 (0.3%) children from the QIV group, 6 (0.6%) children from the TIV-Vic group, and 5 (0.5%) children from the TIV-Yam group reported 4, 12, and 9 SAEs, respectively, over the 6-month follow-up.*
> *Among children age 6–35 months in the QIV-only arm, 7 children (2.3%) reported a total of 10 SAEs.*
>
> *Four SAEs in 3 children were considered by the investigator to be related to the study vaccines: 2 SAEs… were reported for a 12-year-old boy… A 1-year-old… and a 2-year-old.”*

The FluLaval Package Insert states:

"Trial 4 (NCT02242643) was a randomized, observer-blind, active-controlled immunogenicity and safety trial. The trial included subjects aged 6 through 35 months who received FLULAVAL QUADRIVALENT (n = 1,207) or FLUZONE QUADRIVALENT, a U.S.-licensed inactivated influenza vaccine (n = 1,217) used as comparator, manufactured by Sanofi Pasteur Inc. Children with no history of influenza vaccination received 2 doses of FLULAVAL QUADRIVALENT or the comparator vaccine approximately 28 days apart. Children with a history of influenza vaccination received one dose of FLULAVAL QUADRIVALENT or the comparator vaccine… The mean age of subjects was 20 months. Subjects were followed for safety for 6 months"

and

"Serious adverse events occurring during the study period (approximately 6 months) were reported in 2% of subjects who received FLULAVAL QUADRIVALENT and in 2% of subjects who received the comparator vaccine."

The Fluarix Package Insert states:

"Trial 7 (NCT01439360) was a randomized, observer-blind, non-influenza vaccine-controlled trial evaluating the efficacy of FLUARIX QUADRIVALENT. In this trial, subjects aged 6 through 35 months received FLUARIX QUADRIVALENT (n = 6,006) or a control vaccine (n = 6,012).
The comparator was pneumococcal 13-valent conjugate vaccine [Diphtheria CRM197 Protein] (Wyeth Pharmaceuticals, Inc.) in children younger than 12 months, HAVRIX (Hepatitis A Vaccine) in children 12 months and older with a history of influenza vaccination, or HAVRIX (Dose 1) and a varicella vaccine (U.S. Licensed Manufactured by Merck & Co., Inc. or Non-U.S. Licensed Manufactured by GlaxoSmithKline Biologicals) (Dose 2) in those with no history of influenza vaccination.

Subjects were aged 6 through 35 months, and one child aged 43 months (mean age: 22 months);… Children aged 12 months and older with no history of influenza vaccination and children younger than 12 months received 2 doses of FLUARIX QUADRIVALENT or the control vaccine approximately 28 days apart. Children aged 12 months and older with a history of influenza vaccination received one dose."

and

"Serious adverse events (SAEs) occurring during the study period (6 to 8 months) were reported in 3.6% of subjects who received FLUARIX QUADRIVALENT and in 3.3% of subjects who received the comparator vaccine.."

The Fluarix Clinical Trial NCT01439360 Results lists as the first item under the heading "*Interventions*", "*Biological: Quadrivalent seasonal influenza vaccine (Flu D-QIV) GSK2321138A*"

and includes the following under the heading

"*22. Secondary Outcome*"

Title	*Number of Subjects Reporting Any and Related Serious Adverse Events (SAEs).*	
Description	*SAEs assessed include medical occurrences that results in death, are life threatening, require hospitalization or prolongation of hospitalization, results in disability/incapacity or are a congenital anomaly/birth defect in the offspring of a study subjects. Related = symptom assessed by the investigator as causally related to the study vaccination.*	
Time Frame	*During the entire study period (approximately 6- 8 months per subject).*	
Analysis Population Description		
The Total Vaccinated cohort included all subjects with at least one vaccine administration documented.		
Arm/Group Title	*D-QIV*	
Arm/Group Description:	*Subjects received 1 or 2 doses of candidate influenza Influsplit™ Tetra vaccine (GSK2321138A).*	
Overall Number of Participants Analyzed	*6006*	
Any SAEs	*217*	*3.6%*
Related SAEs	*6*	*0.1%*

The vaccine name "*Influsplit™ Tetra*" in the above table refers to Fluarix Tetra according to the following statement in the WHO Fluarix Tetra Name Document:

"GlaxoSmithKline (GSK) recently announced the receipt of marketing authorization for its four-strain seasonal influenza vaccine in Germany and the UK. The vaccine will be marketed as Influsplit Tetra in Germany and Fluarix Tetra in the UK."

The Fluarix Clinical Trial NCT01196988 Article states:

"We assessed a candidate inactivated quadrivalent influenza vaccine (QIV) containing both B lineages vs TIV in healthy children aged 3–17 years… Children were randomized 1:1:1 to receive QIV or 1 of 2 TIVs (either B/Victoria or B/Yamagata lineage; N = 2738)."

and

"Over the 6-month follow-up, in the QIV, TIV-Vic, and TIV-Yam groups, 271 (29.6%), 278 (30.5%), and 303 (33.3%) children, respectively, experienced an MAE,… Twenty-one children experienced 27 SAEs, including 8 (0.9%) children in the QIV group, and 6 (0.7%) and 7 (0.8%) children in the TIV groups. None of the SAEs were considered to be vaccine-related by the investigator."

The following table summarizes the information in the above excerpts, with the monitoring period 6 months in the case of each trial except for NCT01439360 which it was stated to be 6 – 8 months:

Age group	Trial	# subjects	SAE_REP	SAE_C_SUBJ	Avg SAE_C_SUBJ per subject
6-35 mth olds	NCT01198756	301	7	2	
	NCT02242643	1217	24	0	
	NCT02242643	1207	24	0	
	NCT01439360	6006	217	6	
	Total	**8,731**	**272**	**8**	**1 in 1,091**
3-17 yr olds	NCT01196988	2738	21	0	
	NCT01198756	2793	25	2	
	Total	**5,531**	**46**	**2**	**1 in 2,766**

(b) SRI

i. SRI in 6 - 35 month olds and 3 – 17 year olds

The Fluarix Clinical Trial NCT01196988 Article also states:

"Children who were considered "primed" received 1 dose of candidate or control vaccine, and those considered "unprimed" received 2 doses of candidate or control vaccine given 28 days apart"

and includes a table entitled: "Table 1. Demographic Characteristics in Children Aged 3–17 Years and Aged 6–35 Months in the Total Vaccinated Cohort" which contains the following selected columns and rows that are in *italics*:

Age group	***3–17 y***	***6 - 35 mths***	**3–17 y**

Vaccine administered	*QIV (N = 915)*	*TIV-Vic (N = 912)*	*TIV-Yam (N = 911)*	*QIV (N = 277)*	**Total**
Age strata, n					
3–8 y	*598*	*596*	*597*	–	1791
9–17 y	*317*	*316*	*313*	–	946
Priming status in children aged ≤8 y, n					
Primed	*89*	*89*	*88*	*15*	266
Unprimed	*509*	*507*	*509*	*262*	1525
Average # doses administered in NCT01196988 trial	1.56	1.55	1.55	**1.95**	**1.56**

Assuming that the average number of doses administered to each subject in the NCT01196988 trial applied approximately, on average, to the other influenza vaccine trials described in this paragraph 11.8, the average value of SRI (average SAE-C rate per dose) in these trials was:

- (1 in 1,091 subjects ÷ 1.95 doses =) **1 in 2,124** doses in 6 - 35 month olds, and
- (1 in 2,766 subjects ÷ 1.56 doses =) **1 in 4,305** doses in 3 – 17 year olds.

ii. SRI overall in 6 month – 17 year olds

The CDC Schedule 2020 states:

"Routine vaccination

* *Use any influenza vaccine appropriate for age and health status annually:*

- *2 doses, separated by at least 4 weeks, for children age 6 months–8 years who have received fewer than 2 influenza vaccine doses before July 1, 2019, or whose influenza vaccination history is unknown (administer dose 2 even if the child turns 9 between receipt of dose 1 and dose 2)*
- *1 dose for children age 6 months–8 years who have received at least 2 influenza vaccine doses before July 1, 2019*
- *1 dose for all persons age 9 years and older"*

Based upon that statement, a child following the CDC schedule from birth (or 6 months) will be given:

- 4 influenza vaccine doses in the age range of 6 - 35 months, and

- 15 influenza vaccine doses in the age range of 3 - 17 years.

Combining that with the SRI calculated above for each of those two age ranges results in an overall of average SRI of approximately:

- **1 in 2,090** doses for a child aged 6 months to 17 years:

12. Summary of vaccination risks

The following table summarizes the results of the calculations of the estimated risks of vaccinations that are presented herein, in:

- paragraph 10.4 in the case of diphtheria, tetanus, pertussis and polio vaccinations, and
- paragraph 11, in the case of measles, mumps, rubella, varicella, hepatitis b, hepatitis a, Hib, pneumococcal, meningococcal and influenza vaccinations:

RISK FROM VACCINATION – measles, mumps, rubella, varicella, hepatitis b, hepatitis a, Hib, pneumococcal, meningococcal and influenza

Vaccination	SRI (avg)	# doses in CDC schedule	SRIs monitored post-vacc to…	SRIV (total SRI for all doses)	SRIV (hosp)	SRIV (death)
D+P+T+Polio	>1 / 4,053	6	no limit	>1 / 676	>1 / 1,419	> 1 / 56,335
Me+Mu+Ru	>1 / 2,606	2	not stated	>1 / 1,303	>1 / 2,737	>1 / 108,666
Varicella	>1 / 4,854	2	not stated	>1 / 2,427	>1 / 5,099	>1 / 202,398
Hepatitis A	>1 / 1,750	2	14/28/42 dys	>1 / 875	>1 / 1,838	>1 / 72,948
Hepatitis B	>1 / 3,465	3	30 days*	>1 / 1,155	>1 / 2,426	>1 / 96,314
Hib	>1 / 2,205	4	6 months*	>1 / 551	>1 / 1,158	>1 / 45,966
Pneumococcal	>1 / 2,401	4	6 months*	>1 / 600	>1 / 1,261	>1 / 50,056
Meningococcal	>1 / 3,385	2	not stated	>1 / 1,692	>1 / 3,555	>1 / 141,124
Influenza pediatric deaths	>1 / 3,578	19	6 months	> 1 / 188	> 1 / 396	> 1 / 15,702
Total				**> 1 / 71**	**> 1 / 150**	**> 1 / 5,900**

* post last dose

The SRIV estimates for hospitalization (“SRIV (hosp)”) and death (“SRIV (death)”) in the above table for measles, mumps, rubella, varicella, hepatitis b, hepatitis a, Hib, pneumococcal, meningococcal and influenza vaccinations are derived by applying the same ratios of SRIV (hosp) and SRIV (death) respectively to SRIV (total) that were the results of the combined analyses (including all doses) for diphtheria-tetanus-pertussis and polio vaccinations.

Differential risk of Herpes zoster from varicella vaccination

Following the same principle as that for calculating SRIV, the formula for calculating the risk of herpes zoster (HZ) caused by varicella vaccination, “HRIV”, is:

HRIV = HRI x V_SCH

Since the minimum value of HRI is estimated to be 1 in 6,800 (paragraph 11.2(a) herein), and 2 varicella vaccination doses are recommended, the estimated value of HRIV is **≥ 1 in 3,400**.

PART 4 – COMPARISON OF RISK FROM NON-VACCINATION VS VACCINATION

13. Risk Comparison Results

"Relative risk" herein means the ratio of the probability of causally-related SAE occurring as a result of vaccination to the probability of an SAE occurring as a result of non-vaccination, i.e. SRIV ÷ SRIU.

The following are the relative risk estimates, including two significant figures, resulting from comparing the causally-related SAE risk estimates calculated and presented in Part 2 (non-vaccination) and Part 3 (vaccination), based upon what is stated in the documents exhibited in the Notice, for:

i. diphtheria, tetanus, pertussis and polio, and

ii. measles, mumps, rubella, varicella, hepatitis B, hepatitis A, Hib, pneumococcal, meningococcal and pediatric deaths from influenza.

13.1 Diphtheria, Tetanus, Pertussis and Polio

(a) Relative risks from vaccination per age group within total age range

SRIU and SRIV types	Age	Total D+T+P	Polio	Total
SRIU: Any SAE ÷ SRIV: Any SAE	6-11 mths	> 13	> 330,000,000	> 18
	1-6 yrs	> 3.8	> 16,000,000	> 5.5
	7-10 yrs	> 3.2	> 5,700,000	> 3.9
	11-19 yrs	> 15	> 7,600,000	> 20
	Total	**> 7.1**	**> 20,000,000**	**> 9.6**
SRIU: Any SAE ÷ SRIV: Hospitalization (incl. Extended Hospitalization)	6-11 mths	> 6.4	> 160,000,000	> 8.7
	1-6 yrs	> 1.8	> 7,500,000	> 2.6
	7-10 yrs	> 1.5	> 2,700,000	> 1.9
	11-19 yrs	> 7.0	> 3,700,000	> 9.3
	Total	**> 3.4**	**> 9,400,000**	**> 4.6**
SRIU: Death ÷ SRIV: Death	6-11 mths	> 86	> 78,000,000	> 120
	1-6 yrs	> 7.5	> 3,700,000	> 11
	7-10 yrs	> 5.6	> 1,300,000	> 6.9
	11-19 yrs	> 6.1	> 1,800,000	> 7.8
	Total	**> 12**	**> 4,700,000**	**> 16**

The calculated approximate relative risks presented in the above table are all greater than 1, and in the case of the comparison results represented in the first and last rows - of any SAE or of death respectively, all relative risks are greater than 3.

The calculated estimates, which are *minimum* differences, vary within the following ranges:

- for diphtheria-tetanus-pertussis, the lowest estimated minimum relative risk is 1.5, which is for just hospitalizations only (including extended hospitalization) from vaccination compared to the risk for any SAE (hospitalizations and other SAEs) from non-vaccination, in 7-10 year olds, and the highest is 86, which is the estimated relative risk of death to 6 to 11 month olds from vaccination compared to non-vaccination, and
- for polio, the lowest estimated minimum relative risk is about 1,800,000, which is for death in 11-19 year olds, and the highest is about 300 million, which is for any SAE in 6 to 11 month olds.

(b) Cumulative relative risks as the subject prospective recipients age

SRIU and SRIV types	Age	Total D+T+P	Polio	Total
SRIU: Any SAE ÷ SRIV: Any SAE	6-11 mths	> 13	> 330,000,000	> 18
	6 mths to 6 yrs	> 7.5	> 40,000,000	> 10
	6 mths - 10 yrs	> 6.3	> 27,000,000	> 8.7
	6 mths - 19 yrs	**> 7.1**	**> 20,000,000**	**> 9.6**
SRIU: Any SAE ÷ SRIV: Hospitalization (incl. Extended Hospitalization)	6-11 mths	> 6.4	> 160,000,000	> 8.7
	6 mths to 6 yrs	> 3.6	> 19,000,000	> 5.0
	6 mths - 10 yrs	> 3.0	> 13,000,000	> 4.2
	6 mths - 19 yrs	**> 3.4**	**> 9,400,000**	**> 4.6**
SRIU: Death ÷ SRIV: Death	6-11 mths	> 86	> 78,000,000	> 120
	6 mths to 6 yrs	> 20	> 9,500,000	> 28
	6 mths - 10 yrs	> 15	> 6,400,000	> 21
	6 mths - 19 yrs	**> 12**	**> 4,700,000**	**> 16**

The calculated approximate relative risks presented in the above table are all greater than 1, and in the case of the comparison results represented in the first and last rows - of any SAE or of death respectively, all relative risks are greater than 5.

Cumulated over the entire age range, the estimates of relative risks of vaccination compared to non-vaccination vary within the following ranges:

- for diphtheria-tetanus-pertussis, the lowest is about 3.4 which is for hospitalizations only (including extended hospitalization) from vaccination compared to the risk for any SAE (hospitalizations and other SAEs) from non-vaccination, and the highest is about 12, which is for death, and
- for polio, the lowest is about 4,700,000 (which is for death), and the highest is about 20 million (for any SAE).

13.2 Measles, mumps, rubella, varicella, hepatitis B, hepatitis A, Hib, pneumococcal, meningococcal and influenza

Relative risks from vaccination within stated age range

Disease / Vaccination	Age range	# doses in CDC schedule	SRIs monitored post-vacc to…	SRIV ÷ SRIU (any)	SRIV ÷ SRIU (hosp)	SRIV ÷ SRIU (death)
Me+Mu+Ru	16 mos-19 yrs	2	not stated	> 190	> 170	> 260
Varicella	16 mos-19 yrs	2	not stated	> 24	> 12	> 160
Hepatitis A	1 - 17 yrs	2	14/28/42 days	> 11	> 24	> 23
Hepatitis B	1 - 22 yrs	3	30 days*	> 57	> 27	> 3.2
Hib	6 mos - 4 yrs	4	6 months*	> 100	> 49	> 33
Pneumococcal	6 mos - 4 yrs	4	6 months*	> 4.7	> 3.6	> 4.7
Meningococcal	11 - 20 yrs	2	not stated	> 73	> 35	> 5.8
Influenza deaths	16 mos-17 yrs	19	6 months			> 8.7
			Total for Me+Mu+Ru, Varicella, etc	**> 24**	**> 20**	**> 8.7**

Additionally, in the case of herpes zoster, the approximate minimum relative risk of vaccination, HRIV ÷ HRIU, is 1 / 3,400 ÷ 1 / 31,180 = 9.2. HRIV includes only cases caused by the vaccine strain, not any involving the wild strain but vaccine-induced.

Based upon the results presented in the above table, the total benefit of vaccination over the period of the stated age ranges does not outweigh the respective vaccination risk in the case of any of the vaccinations analyzed therein. The reverse is the case.

The calculated estimates of relative risks vary within the following ranges:

- the lowest relative risk is about 3.3, which applies to the relative risk of death from vaccination for hepatitis B. However, this figure is especially unreliable for multiple reasons. One is that “reported cases of chronic hepatitis B… might not

reflect unique case reports and might include both confirmed and probable case reports." (see paragraph 7.8(a)i), which would lead to an underestimation of the relative risk. Another is that the total study sample size for hepatitis b vaccination risk was only 1,155 (see paragraph 11.4(b), all of whom were adults. Therefore the rate at which "serious adverse effects" (as defined in this Notice, in paragraph 2.2) arise from vaccination could be significantly be different.

- the highest relative risk is about 270, which applies to the relative risk of death from vaccination for measles. As discussed in paragraph 7.5(a)i.a, measles is believed to be underreported, and hence so also may be mumps (and maybe even congenital rubella syndrome). Disease underreporting could artificially inflate this figure. However, such an inflation may be mitigated in view of the evidence that the underreporting may be significantly disproportionately in the vaccinated and hence that vaccination may be less effective than generally believed. Ultimately, although the figure of 270 may be an overestimate, the lower end in the range of reporting completeness estimates from the 1980s and 1990s is still as high as 3%. So even after making an adjustment for that reporting completeness, the relative risk of MMR vaccination compared to non-vaccination would still be greater than 1.

  There is a reasonable possibility that the same principles as these apply to other of the diseases whose relative risks of vaccination are analyzed herein.

  Additionally, in the case of all of the figures in the "death" column, the low frequency of reports of death SAEs, especially given the small sample population sizes for SAEs after vaccination, prevents calculation of precise risk and relative risk figures.

13.3 Summary total relative risks of vaccination compared to non-vaccination

Although a reasonable allowance must be made for imprecision, all of the relative risks are high enough to reasonably justify a conclusion that the total benefit of the CDC-recommended vaccination doses to a healthy individual child or adolescent is outweighed by the total risk, in the case of all of the vaccinations included in the analyses presented herein, over the respective stated age ranges.

At the minimum, the results strongly indicate that it cannot reasonably be concluded that the benefit outweighs the risk. Yet the precautionary principle requires the ability to make that conclusion for vaccination to be ethically justified.

The overall relative risks found in the analyses presented herein, for all of the vaccinations combined, are set out in the following table:

OVERALL RELATIVE RISKS FROM VACCINATION (TOTAL SRIV ÷ TOTAL SRIU)

Disease / Vaccination	SRIV / SRIU (any)	SRIV / SRIU (hosp)	SRIV / SRIU (death)
Total overall for diphtheria, tetanus, pertussis, polio, measles, mumps, rubella, varicella, hepatitis B, hepatitis A, Hib, pneumococcal, meningococcal and influenza	**> 21**	**> 15**	**> 9**

Relative risks may be higher still

With respect to any or all of the diseases, the relative risks may be found to be higher still than those above after adjustments are made as a result of such measures as:

- in relation to the diseases, more application of risk-free preventative measures, such as those discussed in paragraph 6.4, and
- in relation to the vaccines, addressing the multiple active surveillance limitations which suppress detection of serious risks, a more accurate measurement of passive surveillance reporting completeness than a mere establishment of about 1% or less, and further proper, scientifically conducted investigations (and/or acknowledgment of existing evidence) into the causal links, or possible causal links, between vaccines and temporally associated serious conditions, especially those that have become existent or much more frequent since the introduction or intensification of widespread vaccination, and
- in relation to both, bringing about a greater availability of data that can be substituted for the assumptions made in these analyses, most of which favour vaccination.

14. Supportive evidence in published risk comparisons

The Plaintiff hereby requests that the Court take judicial notice of the following documents:

- article entitled "The Introduction of Diphtheria-Tetanus-Pertussis and Oral Polio Vaccine Among Young Infants in an Urban African Community: A Natural Experiment".

  Citation: Mogensen, Søren Wengel et al. EBioMedicine 2017;17:192-198. http://dx.doi.org/10.1016/j.ebiom.2017.01.041, accessible at: https://www.thelancet.com/action/showPdf?pii=S2352-3964%2817%2930046-4 (last accessed July 11, 2020)
  with supplementary data to this article accessible at http://dx.doi.org/10.1016/j.ebiom.2017.01.041 (last accessed October 22, 2020)

  (hereafter "Mogensen DPT Risk Comparison Article")

  A true and correct copy of the aforesaid article is attached hereto as **Exhibit 228**.

14.1 Mogensen DPT non-vaccination versus vaccination risk comparison

The Mogensen DTP Risk Comparison Article, about a study of "y*oung Infants in an urban African community*", states:

> *"We examined the introduction of diphtheria-tetanus-pertussis (DTP) and oral polio vaccine (OPV) in an urban community in Guinea-Bissau in the early 1980s"*

and

> *"Bandim Health Project (BHP) has followed an urban community with a demographic surveillance system since December 1978, and took part in the introduction of vaccines well before a full-fledged national program was implemented with UNICEF support in 1986 (Aaby et al., 1984, 2004a)."*

and

> *"In June 1981, BHP started to provide vaccinations at the quarterly weighing sessions. A health center nurse accompanied the weighing team and vaccinated eligible children. DTP and OPV were provided from 3 months and MV from 9 months of age. OPV-at-birth was not given then. The three DTP and OPV doses could be given with an interval of one month but since we only arranged weighing every three months, most children had longer intervals between doses."*

and

"Results: Among 3–5-month-old children, having received DTP (±OPV) was associated with a mortality hazard ratio (HR) of 5.00 (95% CI 1.53–16.3) compared with not-yet-DTP-vaccinated children. Differences in background factors did not explain the effect. The negative effect was particularly strong for children who had received DTP only and no OPV (HR = 10.0 (2.61–38.6)). All-cause infant mortality after 3 months of age increased after the introduction of these vaccines (HR = 2.12 (1.07–4.19))"

and

"The present analysis assessed DTP and child survival in a "natural experiment" in which the children were allocated by the timing of their birth and community weighing sessions and the group allocation was therefore not influenced by the usual selection biases to the same extent as most other studies of DTP (Aaby et al., 2016). To assure that the censoring from the main analysis of children who were not vaccinated had not produced the unexpected strong result we made an intention-to-treat analysis but this did not change the result. If anything the unvaccinated children had slightly worse nutritional status before 3 months of age than the children who were subsequently DTP vaccinated (p = 0.09) (Table 2); the unvaccinated children travelled more than the DTP vaccinated children. These biases would tend to favor rather than increase mortality in the DTP group and the estimates from the natural experiment may therefore still be conservative"

and

"There is only one other study of the introduction of DTP. …All studies that documented vaccination status and followed children prospectively indicate that DTP has negative effects; a meta-analysis of the eight studies found 2-fold higher mortality for DTP-vaccinated compared with DTP-unvaccinated, mostly BCG-vaccinated controls (Aaby et al., 2016) (Appendix A).

The negative effect of DTP was much worse in this natural experiment than has been reported in previous studies of DTP. This is presumably due to the "unvaccinated" control children in previous studies having been a frail subgroup too frail to get vaccinated. Previous studies have not been able to compare DTP-vaccinated children with "normal" controls. Hence, most previous studies have probably underestimated the negative effect of DTP

… It should be of concern that the effect of routine vaccinations on all-cause mortality was not tested in randomized trials. All currently available evidence suggests that DTP vaccine may kill more children from other causes than it saves from diphtheria, tetanus or pertussis."

and

"a vaccine may have non-specific effects (NSEs) on susceptibility to other infections… DTP may increase susceptibility to unrelated infections."

Based upon the above statements, the researchers in this study found a *10-fold increase in mortality in the DTP-vaccinated (without OPV) infants compared to non-DTP-vaccinated infants*.

The researchers also raised a point of substantial relevance to all vaccinations – the potential or plausibility for any vaccination to have a non-specific effect of increasing susceptibility to "unrelated infections". This potential SAE arising from a vaccination cannot be assumed to be one that would be likely to be detected and reported in passive surveillance, if the potential reporters are not aware for the potential of vaccines to non-specifically affect risks in relation to unrelated infections.

This is also important in relation to vaccine effectiveness studies where the "control" group is not administered an injection containing inert substances, but instead receives another vaccination which, without foundation, is assumed to not increase susceptibility to the infectious disease that is the subject of the trial.

14.2 CDC Risk Comparison of DPT versus DTaP

The CDC VAERS Surveillance 1991-2001 Report states:

"Two major vaccine substitutions occurred during the 11-year period: diphtheria and tetanus toxoids and acellular pertussis (DTaP) replaced diphtheria and tetanus toxoids and pertussis vaccine (DTP)"

and

"The overall reporting rate has decreased …after vaccination with DTaP (12.5 reports per 100,000 net doses distributed), compared with that for DTP (26.2)… VAERS reports …documented that the overall vaccine-specific reporting rates of both serious and nonserious reports for DTaP had decreased to less than one half of that for DTP among children aged <7 years (Table 10)."

Based upon the above statements, the SAE reporting rate from DTaP is about half of that from DTP.

14.3 Combining Mogensen DTP-vs-non-DTP and CDC DPT-vs-DTaP Results

By combining:

- the statements in the Mogensen DTP Risk Comparison Article of a finding of a *10-fold increase in mortality in the DTP-vaccinated (without OPV) compared non-DTP-vaccinated infants*

and

- the statements in the CDC VAERS Surveillance 1991-2001 Report of a finding of the SAE reporting rate from DTaP being about half of that from DTP,

it may be concluded that for infants in the "*urban community in Guinea-Bissau in the early 1980s*", the DTaP vaccination doses administered in infancy would have increased their risk of death by more than five (5) times (i.e. 10 times halved).

Hence these comparisons, combined, support the proposition that the benefit of vaccination does not outweigh its risks at the least, and further that the benefits are likely significantly outweighed by the risks. Although these comparisons are of direct relevance only to DTaP vaccination, they add further weight to the probability that the same overall effect applies to other vaccinations also.

178
179
180
181
182
183
184
185
186
187
188
189
190
191
192
193
194
195
196
197
198
199
200
201
202
203
204
205
206
207
208
209
210
211
212
213
214
215
216
217
218
219
220
221
222
223
224
225
226
227
228