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# A White Paper To Understand The Market Structure Of Pediatric Pertussis Combination Vaccines

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## Glossary

### Antigen

Any substance that produces immune response in the body against a foreign substance.<sup>1</sup>

### Dosage Regimen

The number of hexavalent vaccines doses (2 or 3) recommended in each country in their national immunization schedule.<sup>2</sup>

### DTP Vaccine

A vaccine that produces immunity against three deadly diseases - namely diphtheria, tetanus, pertussis.<sup>3</sup>

### DTP<sub>3</sub> Immunization Rate

The percentage of one-year-olds who have received three doses of the combined diphtheria, tetanus toxoid and pertussis (DTP<sub>3</sub>) vaccine in a given year.<sup>4</sup>

### DTaP Vaccine

DTaP is a combined vaccine against diphtheria, tetanus, and pertussis, in which the pertussis component is acellular (contains purified components of *B. pertussis*).<sup>5</sup>

### DTwP Vaccine

DTwP is a combined vaccine against diphtheria, tetanus, and pertussis, in which the pertussis component is a whole-cell, which is an entire *B. pertussis* organism that has been inactivated.<sup>6</sup>

### GAVI

The Global Alliance for Vaccines and Immunizations (GAVI), is an international organization, bringing together public and private sectors with the shared goal of creating equal access to new and underused vaccines for children living in the world's poorest countries.<sup>7</sup>

### Hexavalent Vaccine

The hexavalent vaccine (DTaP-Hib-HepB-IPV) is a six-in-one vaccine recommended in three or four doses to protect babies against diphtheria (D), tetanus (T), pertussis (aP) (whooping cough), poliomyelitis (IPV), haemophilus influenza type B (Hib) and hepatitis B (Hep B). All hexavalent vaccines are intended for pediatric use.<sup>8</sup>

### Hexaxim®/Hexyon®/Hexacima®

Hexaxim® is a fully liquid, ready to use hexavalent vaccine, manufactured by Sanofi-Pasteur.<sup>9</sup>

### Infanrix Hexa®

Infanrix Hexa® is a hexavalent vaccine which needs to be reconstituted before the injection, manufactured by GlaxoSmithKline.<sup>10</sup>

### Public Markets (Hexavalent Vaccines)

Public markets include countries where hexavalent vaccines are included under national immunization schedules and supplied to the entire nation by the government or governmental agencies. These vaccines are generally procured through tenders, and distributed to healthcare practitioners (HCPs).<sup>11</sup>

### Private Markets (Hexavalent Vaccines)

Private markets include countries where hexavalent are given by private practitioners as they are not included in the national immunization schedule. The price for this vaccine may be partially or completely reimbursed by insurance companies, or entirely to be borne through out of pocket expenditure.<sup>12</sup>

### Pertussis vaccines (aP and wP)

Pertussis, also known as whooping cough, is a highly contagious respiratory disease caused by the bacterium *Bordetella pertussis*. Pertussis vaccine is available in two forms namely acellular pertussis (aP) or whole-cell pertussis (wP).<sup>13</sup>

### Surviving Infants

Surviving infants is the number of infants reaching their first birthday during a given year.<sup>14</sup> First three doses of hexavalent vaccines are administered to surviving infants under 12 months of age.<sup>15</sup>

### Statutory Insurance

Statutory health insurance is financed by funds, which are financially and organizationally independent, contributed by employees and employers through payroll taxes.<sup>16</sup>

### UNICEF

The United Nations International Children's Emergency Fund works in 190 countries and territories to protect the rights of every child.<sup>17</sup>

### WHO Vaccine Prequalification (Prequalified vaccine)

WHO prequalification ensures vaccines used in immunization programmes are safe and effective. It provides Member States and procurement agencies, such as GAVI and UNICEF, with the information required to purchase vaccines matching the specific needs of the programme.<sup>18</sup>

### Vaxelis®

Vaxelis® is a fully liquid hexavalent vaccine, manufactured by MCM Vaccine Company, a joint venture between Sanofi Pasteur and Merck.<sup>19</sup>

### V3P/MI4A Database

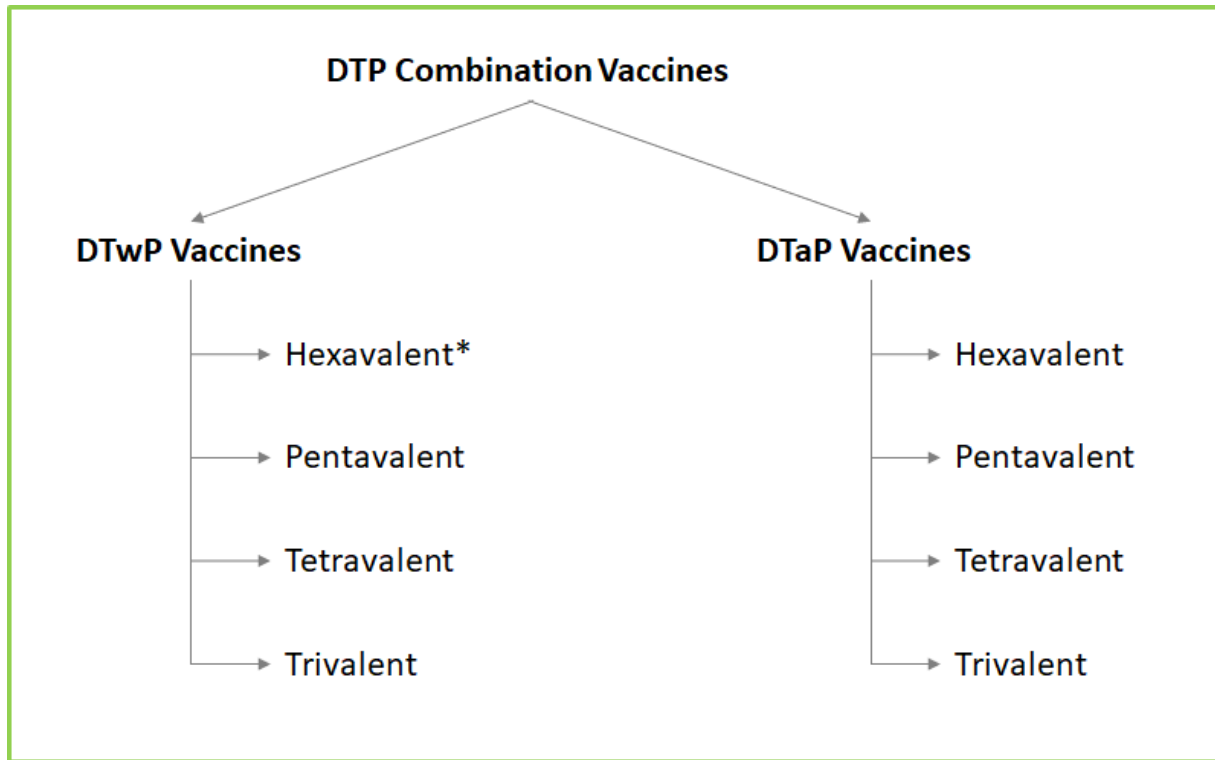
V3P/MI4A database contains information on vaccine prices, volumes, manufacturers, procurement modalities, contract length and more as reported by over 150 countries. This database is published by World Health Organization (WHO).<sup>20</sup>

### WHO

The World Health Organization is a specialized agency of the United Nations working in 194-member countries. This organization deals with issues related to public health.<sup>21</sup>

## Market Structure Of the DTP Combination Vaccines

The below schematic is to give a background understanding of the hexavalent vaccines market.



\*One wP hexavalent vaccine called easy six produced by panacea biotech but with registration and sales limited to India.

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## Abstract

The objective of the present study is to understand usage patterns for pediatric aP (acellular pertussis) hexavalent vaccines, and to identify the market structure (by volumes administered) among hexavalent aP vaccines. Hexavalent vaccines are (six-in-one ready to use) (or 5+1) combination vaccines recommended for administration in three or four doses to protect babies against diphtheria (D), tetanus (T), pertussis (P) (whooping cough), poliomyelitis (IPV), haemophilus influenza type B (Hib) and hepatitis B (Hep B). Hexavalent vaccines form a part of the DTaP based combination vaccines market (which also include pentavalent and tetravalent vaccine). DTaP vaccines together with DTwP based vaccines compose the DTP backbone combination vaccines market.

In order to meet the study objectives, we analyzed key indicators such as vaccine immunization schedules, recommended dosage regimens, vaccination coverage rate and population of surviving infants for all the 102 target countries, across the globe, in 2018. Qualitative and quantitative data gathered through application of these key parameters were used to estimate market volumes for hexavalent vaccines in each target country. We referred to UNICEF, WHO and other country-specific sources for data gathering.

Our results show that DTaP combination vaccines (acellular pertussis) have only a small presence in the DTP based combination vaccines market with a 17% share of the total 455 million doses in 2018. Hexavalent vaccines account for 40% of the DTaP market with approximately 35 million doses consumed in 2018. The study found that hexavalent vaccines are more often utilized in public markets. By region, hexavalent vaccines are consumed more in the European region (EUR). The three countries using the highest volumes of hexavalent vaccines are Iraq, South Africa and Mexico.

Based on our estimations, Hexaxim®, the hexavalent vaccine from Sanofi Pasteur, holds the leading position in the hexavalent vaccines market with 63% of the volumes consumed across the globe. Infanrix Hexa®, manufactured by GlaxoSmithKline (GSK) accounts for 33% of the hexavalent vaccines market, and Vaxelis®, manufactured by MCM accounts for 4% of the hexavalent vaccines market based on volumes administered in 2018. In public markets analyzed, Hexaxim® has 69.6% of market share and is the most used hexavalent vaccine.

**Key Words:** Hexavalent Vaccine, Immunization, Dosage, Hexaxim®, Infanrix Hexa®, Vaxelis®, Acellular Pertussis, Whole-cell Pertussis, Combination Vaccine

## 1. Introduction

Combination Vaccines are promoted to overcome the problems associated with multiple administration of monovalent vaccines. The use of combination vaccines, which include several antigens in a single administration, offer benefits such as reduced complications associated with multiple intramuscular injections, decreased costs of stocking and administering separate vaccines, and a lowering of the risk of delayed or missed vaccinations.<sup>22</sup> The combined diphtheria, tetanus and pertussis (DTP) vaccine, which includes a whole-cell pertussis component (DTwP) or two or more acellular pertussis components (DTaP) has already been incorporated into the national immunization schedules in most countries.<sup>23</sup> These DTP based vaccines serve as the backbone of several other combination vaccines such as tetravalent, pentavalent and hexavalent vaccines.

The traditional trivalent (DTP) and tetravalent (DTP-HepB) vaccines have been replaced with pentavalent vaccines (DTP-Hib, HepB) in most countries.<sup>24</sup> Pentavalent vaccines with a whole-cell pertussis component (wP) are used by most developing countries in accordance with WHO recommendations on pertussis vaccines,<sup>25</sup> whereas pentavalent & hexavalent vaccines with acellular pertussis component (aP) are increasingly used by developed countries.<sup>26</sup> Hexavalent vaccines have replaced pentavalent vaccines in most European countries, and are preferred vaccines in this region. Inclusion of hexavalent vaccines in the immunization schedule of a country is a potential approach to global inactivated polio vaccine (IPV) access, which supports the commitment of the World Health Organization (WHO) to eradicate the polio virus.<sup>27</sup>

Hexavalent vaccines are a way to increase the compliance with the full primary schedule and the coverage rate of these 6 antigens, assuring simplification of administration and a better control of vaccination program costs.<sup>28</sup>

The Hexavalent vaccine (DTaP Hib HepB IPV) is a six-in-one (all the antigen in the same container with no reconstitution) (or 5+1) vaccine recommended in three or

four doses schedule to help protect babies against diphtheria (D), tetanus (T), pertussis (aP)

(Whooping cough), poliomyelitis (IPV), *Haemophilus influenzae type B* (Hib) and hepatitis B (Hep B).<sup>29</sup> To date there is only one hexavalent vaccine with a whole-cell pertussis component available only in India.

There are three hexavalent vaccine preparations commercially available for administration to children; namely Hexaxim®/Hexyon®/Hexacima® (Sanofi Pasteur), Infanrix Hexa® (Glaxosmithkline, GSK) and Vaxelis® (manufactured by MCM). Hexaxim® and Vaxelis® are fully-liquid formulations available in ready to use syringes, while the Hib component in Infanrix Hexa® is supplied as a lyophilized white powder that has to be reconstituted with the components present in the pre-filled glass syringe.<sup>30</sup> These three vaccines have similar number of antigens with significant differences in the number of purified pertussis antigens available. Infanrix Hexa® has three purified antigens of *Bordetella pertussis* namely pertussis toxoid (PT), filamentous haemagglutinin (FHA), and pertactin (PRN), whereas Hexaxim® includes two purified antigens (PT, FHA), and Vaxelis® includes five purified antigens (PT, FHA, PRN, FIM (*Fimbriae*) type 2, 3)<sup>31</sup> (Table 6). Hexaxim® is the only hexavalent vaccine having World Health Organization (WHO) prequalification status and also the only one available in both pre-filled syringe or mono-dose vial presentation.

The primary goal of this white paper is to understand the utilization trends for hexavalent vaccines.

## 2. Methodology

The study is based on the worldwide demand estimates for the hexavalent vaccines. The potential size of the worldwide hexavalent vaccine market is determined by three factors — the annual worldwide birth cohort, the proportion of children receiving hexavalent vaccine, and the number of doses of vaccine a child receives as per the recommended dosage regimen. The stakeholders influencing the hexavalent vaccine demand include governments of industrialized and developing countries, and the private sector.<sup>32</sup>

## 2.1 Volumes of DTP vaccines by Type of Pertussis Antigens (wP and aP)

The global volumes for wP & aP DTP combination vaccines are taken from a global market study conducted by the WHO on diphtheria and tetanus containing vaccines.<sup>33</sup> The further split of aP vaccines into hexavalent, pentavalent, and others is based on inputs from the Vaccine Product, Price and Procurement (V3P) database.<sup>34</sup>

## 2.2 Public And Private markets For Hexavalent Vaccine

A total of 194 countries were selected from WHO Global Health Observatory (GHO) data and public and private markets for hexavalent vaccines are identified based on the inclusion or otherwise of the hexavalent vaccine in the government supply and in the national immunization schedule of the country. The countries having hexavalent vaccine in their national immunization schedule are designated public markets. Government bears a part or all of the expenditure for immunization in the public markets whereas vaccine expenditure in private markets is through out-of-pocket expenditure or reimbursement by private insurance payers.

All 194 countries selected from WHO are classified as high income, Upper middle income, Lower middle income, and low income countries based on World Bank classification,<sup>35</sup> which is adopted by WHO.<sup>36</sup> Low income countries are excluded in this analysis, based on the assumption that governments in low income countries cannot afford the supply of hexavalent aP vaccines and that the consumption of hexavalent vaccines are also limited among private markets in these countries.<sup>37</sup> Countries in which hexavalent brands are not registered, are also excluded in the study. Finally, 102 countries are considered for the current study which include 40 countries with public markets for hexavalent aP vaccines (Table 2) and 62 countries with hexavalent aP vaccines administered through private markets (Table 3)

For each of the countries in the public and private markets, data for the following indicators (surviving infants, immunization rate, and dosage regimen) are collected to estimate the volumes of hexavalent vaccines consumed in

a year. In this study, all the indicators and the volumes of the vaccines are estimated for 2018.

## 2.3 Indicators For calculating Hexavalent vaccine Volumes

**2.3.1 Surviving Infants:** The doses of hexavalent vaccines are administered to children less than 12 months of age.<sup>38</sup> Hence the surviving infant population below 12 months of age is the target population for this study. The data on the surviving children (birth cohort) is obtained from WHO, GAVI, UNICEF, UN population data, and national statistics from CIA Factbook (Table 2 & Table 3).

**2.3.2 Immunization Rate for Hexavalent vaccines:** The DTP3 vaccine immunization rate was considered for estimating the hexavalent vaccine immunization rate. For public markets with only hexavalent vaccine supplied through national schedule, the total immunization rate of DTP3 is considered as immunization rate of hexavalent vaccine (Table 2).

For public markets having hexavalent vaccines along with other multivalent vaccines, the immunization rate for hexavalent vaccines is estimated based on the consumption of hexavalent vaccines as a proportion of all the available multivalent vaccines (Table 2).

For private markets, the immunization rate for hexavalent vaccines is estimated, based on data collected from secondary sources such as WHO,<sup>39</sup> and the Center of Disease Control and Prevention (CDC).<sup>40</sup> Parameters such as the income status of a country, sourced from WHO is also considered for estimating private hexavalent vaccine market volumes for some of the countries. (Table 3)

**2.3.3 Dosage Regimen:** The number of doses of hexavalent vaccines suggested under each country's immunization schedule is obtained from the WHO. (Table 2) For countries under private markets, the standard number of doses suggested by recognized authorities and European Union is considered (Table 3).



## 2.4 Calculation Of Volumes Of Hexavalent Vaccine:

The hexavalent market volumes are calculated using these parameters— surviving infants' population, hexavalent vaccine immunization rate, and dosage regimen. The objective is to find the utilization of hexavalent vaccine by region, by country and by individual brand.

## 2.5 Brand Analysis of Hexavalent Vaccines

Brand preference among the hexavalent brands is estimated for the top 25 countries having high sales volumes for the hexavalent vaccines.

Our criterion for identifying the top 25 countries is that these countries account for more than 84% of the hexavalent vaccines market by volume. On average, the brand of vaccine that is consumed more in these 25 countries will be a market leader in the overall hexavalent vaccine market. (Table 4)

The consumption patterns for each brand of vaccines across the target countries is obtained through information gathered by various sources as below-

1. National and Regional Tenders
2. Ministry Of Health (MOH) and National Health Authorities
3. Primary Interviews with Pediatricians and Vaccine Manufacturers

The method by which vaccines are purchased and financed in each country influences the proportion of individual brands of vaccine consumed. In hexavalent public markets, the government finances and procures vaccines in large quantities through tenders. In hexavalent private markets, where individual consumers pay for the vaccine through out-of-pocket or private insurance, hexavalent vaccines are procured by either GP/ pediatricians offices or by pharmacies, directly from the manufacturer and/or through wholesalers.

### National and Regional Tenders

Governmental vaccine procurement departments under the country's Ministry of Health generally procure vaccines through national or regional tenders. For instance,

hexavalent vaccines are procured by national tenders in Iraq, Mexico, Australia, Romania and the Netherlands. Italy and Spain procure vaccines through regional tenders. In Saudi Arabia, vaccines are procured through Gulf Cooperation Council (GCC) unified tenders coordinated by Gulf Health Council. Tendering information details and their outcomes in terms of brands purchased are as below-

- In Iraq, The State Co. For Marketing Drugs and Medical Appliances (KIMADIA), under Ministry of Health procures vaccines through annual tenders. The latest tender for hexavalent vaccines of three million doses (for the consumption in 2018), is awarded to Sanofi's 'Hexaxim®'.<sup>41</sup>
- In Saudi Arabia, the Gulf Health council procures vaccines, through annual GCC tenders. In 2018, tender for hexavalent vaccines is awarded to Sanofi's Hexaxim®.<sup>42</sup> More than 90% of hexavalent vaccine administered in Saudi Arabia is through national immunization schedule and is of 'Hexaxim®' brand.
- In Mexico, Ministry of Health (MOH) procures tenders for the hexavalent vaccines. Only Hexaxim® is procured by the MOH in 2018.<sup>43</sup> Around 96% of hexavalent vaccines administered in Mexico are of Hexaxim®.
- In Australia, Infanrix hexa® is the only brand of hexavalent vaccine procured by the Department of Health through national tenders. Around one million doses of Infanrix hexa® vaccine are procured in 2018.<sup>44</sup>
- Romania Ministry of Health procured both Infanrix hexa® and Hexaxim® brands of hexavalent vaccines in 2018<sup>45</sup>. Around 60% of the hexavalent vaccine doses procured are of Hexaxim®<sup>46</sup> and the remaining market constitute Infanrix Hexa®.
- In Chile, The National Health Service System (CENABAST), under the Ministry of Health procures vaccines, and it procured 'Hexaxim®' vaccine for public immunization in 2018.<sup>47</sup>
- In Netherlands, vaccines are procured through national tenders in the country<sup>48</sup>. Infanrix hexa® and Vaxelis® are administered in equal volumes in Netherlands in 2018.<sup>49</sup>
- In Italy and Spain, vaccines are procured through regional tenders. In 2018, Hexaxim®,<sup>50</sup> and Infanrix

hexa<sup>®</sup>,<sup>51</sup> are procured by regional tenders in both the countries.

### Ministry Of Health (MOH) and National Health Authorities

The information on brands of hexavalent vaccine administered in national immunization schedules in the different countries is gathered through authentic secondary sources such as Ministry of Health (MOH) sites, publications by government health authorities among others. For instance, the Swedish public health authority publishes information on the hexavalent brands and the volumes consumed in the country. This along with the information from the regional tenders awarded for 2018 in the country are used to assess the hexavalent vaccines brand utilization in the country.<sup>52</sup>

In UK, Switzerland, Canada, Belgium and Libya, only one brand of vaccine is administered or available in the public markets, and so the entire public market consists of these brands of vaccine. For instance, in the UK<sup>53</sup>, Switzerland<sup>54</sup>, and Canada<sup>55</sup>, Infanrix hexa<sup>®</sup> is the only brand of vaccine available and administered to all the target children. In Libya<sup>56</sup> and Belgium<sup>57</sup> 'Hexaxim<sup>®</sup>' is the brand of hexavalent vaccine available and administered to the target children. The National Center for Disease Control (NCDC) provides medical supplies and vaccines in Libya.

According to United Nations Industrial Development Organization (UNIDO), South Africa, has allocated around 40% of its vaccine supplies budget for the procurement of hexavalent vaccine from Sanofi (Hexaxim<sup>®</sup> brand).<sup>58</sup> The vaccinator's manual published by the National Department of Health, recommends only Hexaxim<sup>®</sup> under hexavalent vaccines, to be administered to children.<sup>59</sup>

### Primary Interviews

In some of the countries, especially in countries with hexavalent private markets, data on vaccine procurement by pharmacies or clinics, and or wholesaler sales data is not publicly accessible. Primary interviews with physicians, nurses and vaccine manufacturers were conducted for such countries to know the brand utilization.

Insights on the brand split of vaccines in Germany, the Czech Republic, France, Thailand, Indonesia, India, and Poland were obtained through primary interviews. (Table 5)

## 3. Findings & Discussion

### 3.1 DTP Combination Vaccines by Type of Pertussis Antigens (wP and aP)

In China, USA, and Japan no hexavalent vaccines were commercialized at the time of the study. In China only pentavalent aP vaccine is available from Sanofi Pasteur, whereas in USA the DTaP vaccine market is shared between Sanofi Pasteur and GSK. The global DTP-based combination vaccine market in this study excludes DTP vaccines produced and sold only in China.

In 2018, the global demand for DTP-based combination vaccines was 455 million doses.<sup>60</sup> DTP combination vaccines with a whole-cell pertussis component (DTwP) had an 83% share of the total DTP combination vaccines market in 2018, which accounts to 380 million doses. DTaP combination vaccines (acellular pertussis) had only a 17% share of the DTP combination vaccines market, which accounts to 75 million doses.

DTaP based combination vaccines are more expensive than DTwP vaccines. Pooled procurement agencies such as UNICEF and GAVI procure pentavalent vaccine with a whole-cell pertussis (wP) component for supply to low- and middle-income countries. Also developing countries that procure by self-financing methods procure wP based DTP combination vaccines for the supply in their countries.<sup>61</sup> Acellular component (aP) based DTP vaccines are supplied to the public by governments of high-income countries or consumed in private markets in some high- and middle-income countries through out-of-pocket expenditures.<sup>62</sup>

The above reasons explain the consumption of higher volumes of DTwP vaccines than DTaP vaccines.

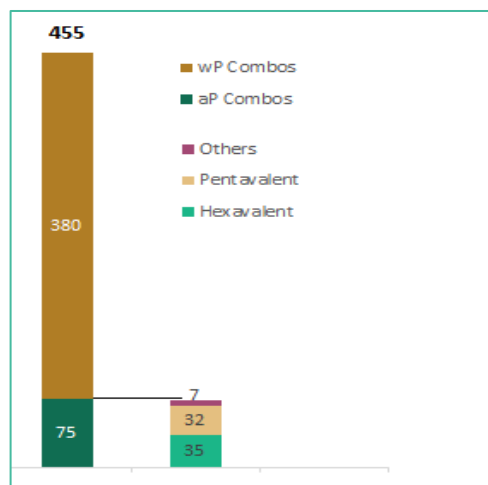


Fig 1: aP and wP Vaccine split; (Others Include tetravalent)  
Global DTP combination market volumes excluding China

The total DTaP combination vaccine market (as shown in Figure-1) is split into hexavalent, pentavalent, and other vaccines. Based on our assumptions, in 2018 the global hexavalent vaccine demand was 35 million doses, which is 47% of the total DTaP market. The demand for pentavalent vaccines and other vaccines were 32 million doses and 7 million doses respectively. The high share of hexavalent vaccines among DTaP based vaccines can be attributed to a shift to hexavalent vaccines by high income countries, particularly among the European countries.

### 3.2 Public & Private Markets For Hexavalent Vaccines

Based on government supply and inclusion of hexavalent vaccine in the immunization schedule, the countries are split into public and private markets.

Out of 102 countries considered for the study, 40 countries are public markets for hexavalent vaccines and the remaining 62 countries are private markets, as shown in Figure 2.

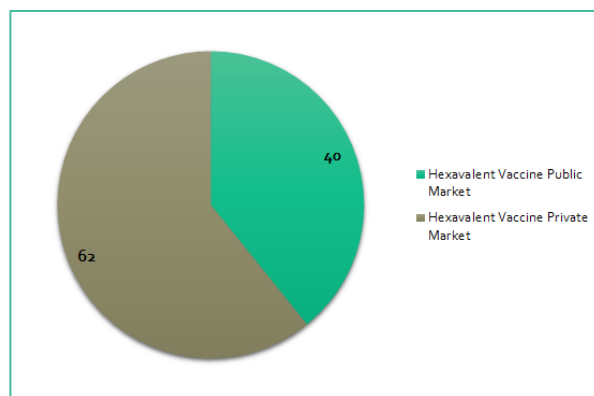


Fig 2: Hexavalent public & private markets  
(refer to Table 2 & Table 3 in appendix)

The hexavalent vaccines are used in 40 countries for public programs which includes 30 high income countries, 9 upper middle-income countries, and one lower middle-income country. The high proportion of high-income countries among these public markets is due to the affordability of the hexavalent vaccines by the governments of high-income countries.

Hexavalent vaccines are provided by private services in 62 countries, of which 17 are high income, 24 are upper middle income, 20 are lower middle-income countries, and only one country is from the low-income group.<sup>63</sup>

### 3.3 Analysis Of Indicators For Calculating Hexavalent Vaccine Volumes In Public And Private Markets

Three indicators that are used for the estimation of the hexavalent vaccine market in each target country are the annual worldwide birth cohort (surviving infants), the proportion of children receiving hexavalent vaccine (vaccine coverage rate), and the dosage regimen.

#### 3.3.1 Surviving Infants

The countries with high surviving infant's population demand for more volume of hexavalent vaccine doses. Some hexavalent public markets, namely those of Mexico, Iraq, and South Africa, have high levels of surviving infant population. In 2018, Mexico had a surviving infant population of around two million, whereas Iraq and South Africa each had around one million. The consumption of hexavalent vaccines is high in these public market countries, due to the supply of free or subsidized

hexavalent vaccines by government agencies to the target population (Table 2).

In private markets, countries such as India, Nigeria, Pakistan, and Indonesia have a high surviving infant population. In 2018, India and Nigeria had surviving infant populations of 24 million and seven million respectively, whereas Pakistan and Indonesia each had five million. (Table 3). But only a tiny fraction of population in these countries have access to private vaccination.

### 3.3.2 Dosage Interval

Most of the countries with hexavalent public markets have implemented the three-dose hexavalent vaccine schedule. Only seven countries have recommended two doses of hexavalent vaccine in their immunization schedule. In these seven countries a dose of pentavalent vaccine is administered instead of a third dose of hexavalent vaccine (Table 2).

For countries with hexavalent private markets, three doses of hexavalent vaccine are considered as suggested by recognized authorities and/or the European Union (Table 3).

### 3.3.3 Immunization Rate by Hexavalent Vaccine Among Public And Private Markets

Globally, hexavalent vaccines are consumed more in public markets than private markets.

For public markets where hexavalent is the only vaccine supplied through the national schedule, the rate of immunization is high, ranging from 90% to 99% in most of the countries. For public markets where both hexavalent and other multivalent vaccines are used, the immunization rate for hexavalent vaccines varies by country depending on specific factors such as geographical distribution and availability of vaccines within the country, or particular conditions under which hexavalent vaccines are administered. The immunization rate for hexavalent vaccines ranges from 70%-90% in most of these countries. However, Argentina and Canada have hexavalent vaccine immunization rates of 8% and 30% respectively (Table 2). Even though the overall immunization rate is high in

Argentina and Canada the coverage rate for hexavalent vaccine is low due to local conditions. In Argentina hexavalent vaccines are only administered to children weighing less than 1500 grams (or pre-term born infants) thus in Argentina Public market Hexaxim® was in 2018 the only Hexavalent vaccine used for pre-term born infants, which is about 8% of the total infant population. In Canada, hexavalent vaccines are available only in four provinces out of the ten provinces. These reasons explain the low immunization rates of hexavalent vaccine in both the countries.

The immunization rate for hexavalent vaccines is low in private markets and ranges from 1-50%, excluding France and Germany which have 95% immunization rates (thanks to public funding or reimbursement). In private markets most of the high-income countries have hexavalent vaccine immunization rates ranging from 10-20%, whereas upper middle-income countries and lower middle-income countries have hexavalent vaccine immunization rates ranging from 2-5% and 1-2% respectively. The high immunization rates in France and Germany are due to the administration of more than 90% of all the vaccines in the private sector. Also, in these countries there is no central government financing for immunizations, rather statutory (funds from payroll taxes) and private health insurance policies pay for all recommended vaccines making them free of charge to the public.<sup>64</sup> (Table 3).

### 3.4 Volumes Of Hexavalent Vaccines:

In 2018, 25 million doses (71.8%) of hexavalent vaccine were administered in public markets through national immunization programs (NIPs), and 9.8 million doses (28.2%) were administered to infants in private markets (see Figure 3).

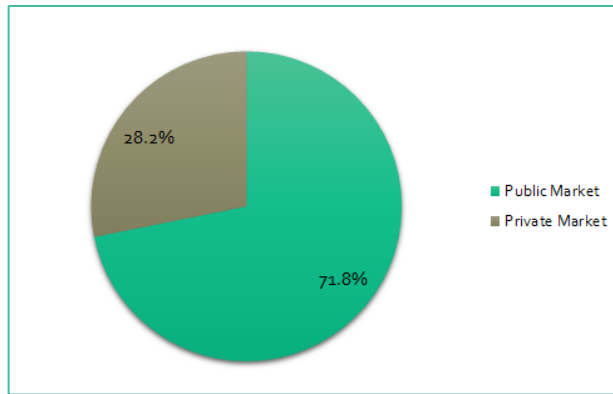


Fig 3: Public and Private Hexavalent Market Share

Hexavalent vaccines were included in the national immunization schedules of many high-income and upper middle-income countries, due to the strong public immunization financing in these countries. The higher cost of hexavalent vaccine is a hindrance to the supply of these vaccines in the low- and middle-income countries.

#### 3.4.1 Hexavalent Vaccines Volume Analysis, By Region

As shown in Figure 4, in 2018 Europe accounted for the major share of the hexavalent vaccines market by volume at 44%, followed by Eastern Mediterranean Region (EMR) with 21% and American Region (AMR) with 14%. African Region (AFR) and Western Pacific Region (WPR) regions accounted for 11% and 6% respectively, followed by South East Asian Region (SEAR) with the lowest share at 4% of the hexavalent vaccine market.

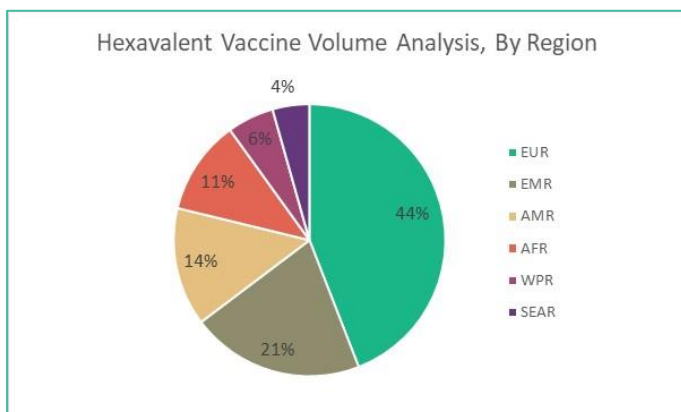


Fig 4: Hexavalent vaccine volume analysis by region

The high share for EUR is due to early approval and adoption of hexavalent vaccines by most European countries. In 2018, the major European countries such as

Germany, UK, France, Italy, and Spain each consumed more than one million doses of hexavalent vaccine. In France the use of hexavalent vaccines is mandatory for children born from January 1<sup>st</sup> 2018, while in the UK these vaccines have been used in their national immunization schedule from August 2017. Some EU countries, such as Italy, France and Romania, adopted strategies like policy changes and enforcing mandatory vaccination to protect the community when vaccination coverage levels were not satisfactory.

In the EMR Iraq and Saudi Arabia, are the top countries in hexavalent vaccine consumption. In 2018, more than 3.5 million doses of hexavalent vaccines were used in Iraq, while 1.5 million doses of hexavalent vaccines were used in Saudi Arabia.

In AMR, only four countries, namely Argentina, Canada, Chile, and Panama have included hexavalent vaccines in their national immunization schedules. The low consumption of hexavalent vaccines in the AMR region compared to the EUR region can be attributed to the use of hexavalent vaccines only in special situations. In Argentina hexavalent vaccines are used only in preterm newborns weighing less than 1500 grams at birth and aged less than 6 months.<sup>65</sup> In Canada, only 4 out of 10 provinces use hexavalent vaccines. Recently hexavalent vaccine has been approved in the USA (December, 2018); this may launch by 2020.<sup>66</sup>

In AFR, South Africa was the first country to introduce hexavalent vaccine in its immunization schedule replacing the pentavalent and HepB Vaccines.<sup>67</sup> More than 70% of hexavalent vaccine volumes consumed in Africa are in South Africa.

In the WPR region only two countries, namely Australia, New Zealand, have hexavalent vaccines in their immunization schedule.

In SEAR hexavalent vaccine is available only through private markets and is not included in the countries' immunization schedules.<sup>68</sup>

### 3.4.2 Hexavalent Vaccine Volume Analysis, By Country

In 2018, the top 25 countries consumed 30 million doses of hexavalent vaccines which is 86% of the hexavalent vaccine global consumption (see Table 1).

| Country Name   | Type of Market | Hexavalent Vaccine (Volume, mn) | (% Share among top 25 markets) |
|----------------|----------------|---------------------------------|--------------------------------|
| Iraq           | Public         | 3.53                            | 10.2%                          |
| South Africa   | Public         | 3.18                            | 9.1%                           |
| Mexico         | Public         | 3.03                            | 8.7%                           |
| Germany        | Private        | 2.78                            | 8.0%                           |
| UK             | Public         | 2.27                            | 6.5%                           |
| France         | Private        | 2.25                            | 6.4%                           |
| Saudi Arabia   | Public         | 1.69                            | 4.9%                           |
| Italy          | Public         | 1.33                            | 3.8%                           |
| Spain          | Public         | 1.18                            | 3.4%                           |
| Australia      | Public         | 0.90                            | 2.6%                           |
| India          | Private        | 0.86                            | 2.5%                           |
| Libya          | Public         | 0.81                            | 2.3%                           |
| Vietnam        | Private        | 0.76                            | 2.2%                           |
| Romania        | Public         | 0.66                            | 1.9%                           |
| Kazakhstan     | Public         | 0.65                            | 1.9%                           |
| Poland         | Private        | 0.61                            | 1.8%                           |
| Chile          | Public         | 0.52                            | 1.5%                           |
| Belgium        | Public         | 0.51                            | 1.5%                           |
| Netherlands    | Public         | 0.51                            | 1.5%                           |
| Canada         | Public         | 0.47                            | 1.3%                           |
| Sweden         | Public         | 0.36                            | 1.0%                           |
| Czech Republic | Private        | 0.35                            | 1.0%                           |
| Thailand       | Private        | 0.32                            | 0.9%                           |
| Indonesia      | Private        | 0.32                            | 0.9%                           |
| Switzerland    | Public         | 0.25                            | 0.7%                           |

Table 1: Hexavalent vaccine volumes for top 25 countries

Of these 25 countries, 17 have public hexavalent markets, and 8 have private hexavalent markets. In 2018, Iraq had the highest consumption of hexavalent vaccines at 3.5 million doses which is 10.2% of the total volume of hexavalent vaccines consumed, while Switzerland had the lowest consumption of 0.2 million doses which is 0.7% of global hexavalent vaccines consumed.

In public markets, the top three countries with high volumes of hexavalent vaccine include Iraq, South Africa and Mexico.

In private markets the top three countries with high volumes of hexavalent vaccine consumption include Germany, France, and India. Germany and France although having high immunization rates are included in the private market category as most of the immunization in these countries are financed by private insurers.

### 3.5 Brand Analysis of Hexavalent Vaccines

In 2018, Hexaxim® has the highest share of the hexavalent vaccines market by volume with 63%, followed by Infanrix Hexa® with 33%, and Vaxelis® with 4% (see Figure 5). In 2018, around 19 million doses of Hexaxim® were consumed, followed by Infanrix Hexa® with 10 million doses, and Vaxelis® with one million doses.

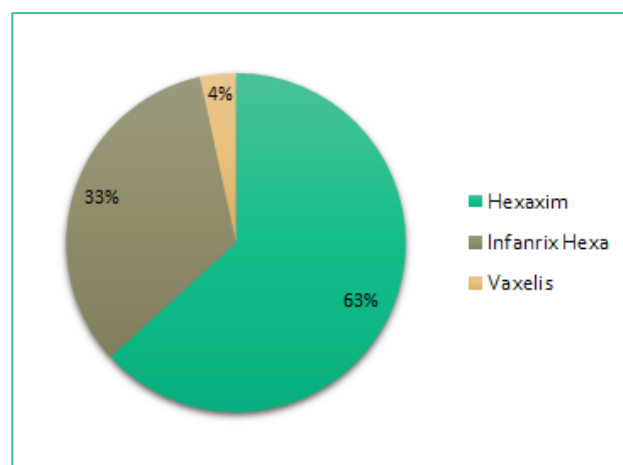


Fig 5: Share of different hexavalent vaccine brands in top 25 countries

## Brand Analysis In Public Markets

There are 17 public markets among top 25 countries for hexavalent vaccines. These 17 public markets account for 87% share of total hexavalent vaccine public market.

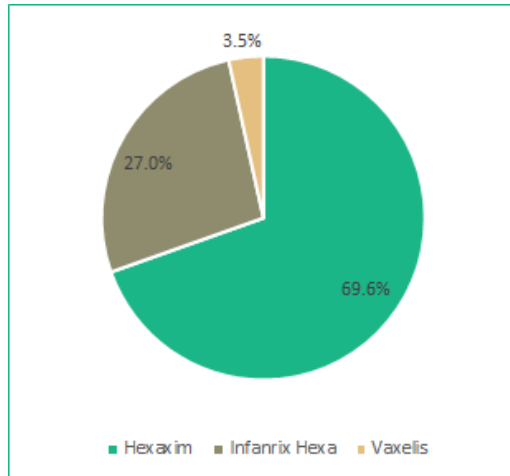


Fig 6: Share of different hexavalent vaccine brands in top 25 countries in public markets

In public markets Hexaxim® is the most used hexavalent vaccine with 69.6% of market share, followed by Infanrix hexa® with 27%, and Vaxelis® with 3.5% of market share.

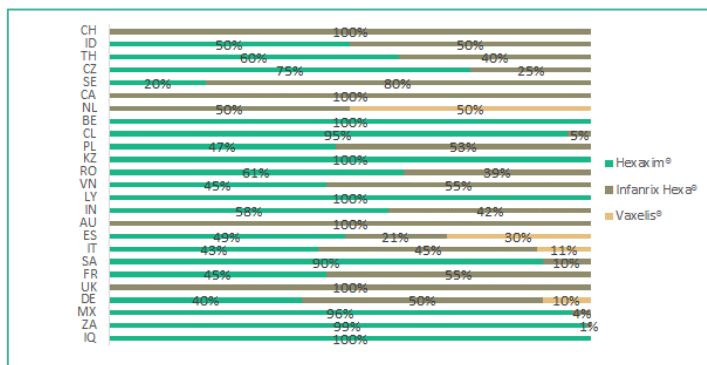


Fig 7: Volume share of hexavalent vaccines by brand, detailed description is given in Table 4 in the Appendix

In eight public markets, namely those of Iraq, Mexico, South Africa, Saudi Arabia, Libya, Kazakhstan, Belgium, and Chile, Hexaxim® is the only brand used in their national immunization schedule. The market for Hexaxim® in these countries is more than 90% of total hexavalent vaccines consumed in those countries. Preterm births (babies born alive before 37 weeks of pregnancy are completed) among

these eight countries account to an average of 9% of the surviving infants (Iraq 10%, South Africa 12%, Mexico 7%, Saudi Arabia 4%, Libya 13%, Kazakhstan 5%, Chile 8%, and Belgium 10%).<sup>69</sup> It is estimated that a total of 0.5 million preterm babies in these eight countries were administered with Hexaxim® vaccine, in 2018.<sup>70</sup>

In five public markets, namely those of the UK, Australia, Canada, Sweden, and Switzerland Infanrix Hexa® is the only brand used in their national immunization schedule. More than 80% of hexavalent vaccines consumed in these countries are of Infanrix Hexa®.

Vaxelis® is recently approved in Europe, and is present in only four European countries, namely those of Germany, Italy, Spain, and Netherlands. Of the total hexavalent vaccine doses consumed, Vaxelis® consumption is 50% in Netherlands, 30% in Spain, and 10% each in Germany and Italy.

#### 4. Value Of the Study

The current study evaluates the volumes of hexavalent vaccines administered across the globe. The proportion of hexavalent vaccines administered among the other DTP based multivalent vaccines is also analyzed. Information on utilization of hexavalent vaccines by region, by country and by individual brand is also analyzed as one of the major objectives of the study (not all countries were included also missing USA, China and Japan, but that are country where no hexavalent were available at the time of the study).

Major indicators that drive the demand for hexavalent vaccines such as immunization rate, surviving infants' population and dosage regimen are studied and the correlation between these indicators and the vaccine volumes are described. These indicators directly affect the volumes of hexavalent vaccines consumed.

Different factors drive the demand for hexavalent vaccines among the public and private markets. Government financing and inclusion of the hexavalent vaccine in the immunization schedule drive the vaccine consumption in public markets whereas availability and affordability of the vaccines drive the vaccine consumption in private markets.

#### 5. Conclusions

In 2018, DTaP combination vaccines account for 17% share of the DTP combination vaccines market for primary vaccination (excluding China), with 75 million doses of the 455 million DTP vaccine doses consumed.

Most public markets occur in high and upper middle-income countries and most private markets in lower middle- and low-income countries. The study summarizes that hexavalent vaccines were consumed more in public markets than in private markets in 2018.

Europe accounts for the major share of the hexavalent vaccines market by volume at 44%, followed by EMR at 21% and AMR at 14%. In 2018, the top 25 countries consumed 30 million doses of hexavalent vaccines which is 86% of global consumption.

Among the commercially available brands of vaccines, Hexaxim® is most administered followed by Infanrix Hexa® and Vaxelis®. In 2018, Hexaxim® has the highest market share in volumes with 63%, followed by Infanrix Hexa® with 33%, and Vaxelis® with 4% of the hexavalent vaccine market by volumes. In public markets analyzed, Hexaxim® has 69.6% of market share and is the most used hexavalent vaccine.

Hexaxim® is the market leader among the hexavalent vaccines based on the volumes administered in 2018 across the globe.



## Conflict of Interest

The research study reported in this whitepaper was sponsored by Sanofi Pasteur. The author of the study serves as an employee of the entity ReportLinker, which conducted the research for Sanofi in return for a consultancy fee. As the consultancy conducted the research through an independent study and the consultancy fee for the research was not affected by the results of the research, a conflict of interest was not found to exist.

## Limitations Of The Study

The methodology is very robust to size public market dynamics which represents 71.8% of the total hexavalent vaccine volumes. The methodology followed for private markets is less strong due to the constraints of limited secondary information, but this only represents 28.2% of total hexavalent vaccine volumes. The brand analysis of vaccines in some of the hexavalent private markets is not precise as the information on the exact volumes of the brands administered is not publicly available. The number of primary interviews conducted for the analysis of brand proportion in the target countries are limited. (Not all countries were included also missing USA, China and Japan, but that are country where no hexavalent were available at the time of the study)

## Appendix

Table 2-Hexavalent Vaccine Public Markets

The table below shows the parameters considered for hexavalent vaccine volume estimation in public market

| S.No  | Country Name         | Income Status <sup>1</sup> | Region | # Vaccines <sup>2</sup> | Hexavalent Vaccine Immunization Rate <sup>3</sup> | Surviving Infants Population <sup>4</sup> | Dosage Interval |
|-------|----------------------|----------------------------|--------|-------------------------|---|---|-----------------|
| 1     | Panama               | High income                | AMR    | 1                       | 86%   | 78252                                     | 3               |
| 2     | Andorra              | High income                | EUR    | 1                       | 99%   | 1000                                      | 3               |
| 3     | Austria              | High income                | EUR    | 1                       | 91%   | 84767                                     | 3               |
| 4     | Belgium <sup>1</sup> | High income                | EUR    | 1                       | 98%   | 130761                                    | 4               |
| 5     | Croatia              | High income                | EUR    | 1                       | 92%   | 37285                                     | 4               |
| 6     | Czech Republic       | High income                | EUR    | 1                       | 96%   | 120000                                    | 3               |
| 7     | Ireland              | High income                | EUR    | 1                       | 96%   | 63581                                     | 3               |
| 8     | Netherlands          | High income                | EUR    | 1                       | 94%   | 186948                                    | 4               |
| 9     | San Marino           | High income                | EUR    | 1                       | 85%   | 280                                       | 3               |
| 10    | United Kingdom of    | High income                | EUR    | 1                       | 94%   | 805003                                    | 3               |
| 11    | Australia            | High income                | WPR    | 1                       | 95%   | 314775                                    | 3               |
| 12    | New Zealand          | High income                | WPR    | 1                       | 94%   | 62000                                     | 3               |
| 13    | Mexico               | Upper middle income        | AMR    | 1                       | 45%   | 2254598                                   | 3               |
| 14    | Slovakia             | Upper middle income        | EUR    | 1                       | 96%   | 55753                                     | 3               |
| 15    | Romania              | Upper middle income        | EUR    | 1                       | 81%   | 184815                                    | 3               |
| 16    | Georgia              | Lower middle income        | EUR    | 1                       | 92%   | 47190                                     | 3               |
| 17    | Iraq                 | Upper middle income        | EMR    | 1                       | 95%   | 1240052                                   | 3               |
| 18    | South Africa         | Upper middle income        | AFR    | 1                       | 70%   | 1134000                                   | 4               |
| 19-19 | Argentina            | High income                | AMR    | 2                       | 8%  | 741501                                    | 3               |
| 20    | Chile                | High income                | AMR    | 2                       | 75%   | 235256                                    | 3               |
| 21    | Canada               | High income                | AMR    | 2                       | 30%   | 388007                                    | 4               |
| 22    | Latvia               | High income                | EUR    | 2                       | 99%   | 18531                                     | 4               |
| 23    | Luxembourg           | High income                | EUR    | 2                       | 99%   | 7275                                      | 3               |
| 24    | Norway               | High income                | EUR    | 2                       | 96%   | 63773                                     | 3               |
| 25    | Portugal             | High income                | EUR    | 2                       | 98%   | 91886                                     | 2               |
| 26    | Spain                | High income                | EUR    | 2                       | 98%   | 400000                                    | 3               |
| 27    | Sweden               | High income                | EUR    | 2                       | 97%   | 122283                                    | 3               |
| 28    | Switzerland          | High income                | EUR    | 2                       | 70%   | 89029                                     | 4               |
| 29    | Denmark              | High income                | EUR    | 2                       | 99%   | 60253                                     | 3               |
| 30    | Estonia              | High income                | EUR    | 3                       | 93%   | 14000                                     | 3               |

|    |                            |                     |     |   |     |        |   |
|----|----------------------------|---------------------|-----|---|-----|--------|---|
| 31 | Italy                      | High income         | EUR | 8 | 95% | 477944 | 3 |
| 32 | Kazakhstan                 | Upper middle income | EUR | 2 | 99% | 328020 | 2 |
| 33 | Bulgaria                   | Upper middle income | EUR | 2 | 75% | 65000  | 3 |
| 34 | Macedonia                  | Upper middle income | EUR | 2 | 90% | 22000  | 2 |
| 35 | Oman                       | High income         | EMR | 2 | 99% | 80768  | 2 |
| 36 | Qatar                      | High income         | EMR | 2 | 97% | 26809  | 2 |
| 37 | Saudi Arabia               | High income         | EMR | 2 | 90% | 626293 | 3 |
| 38 | United Arab Emirates (the) | High income         | EMR | 2 | 80% | 95073  | 2 |
| 39 | Bahrain                    | High income         | EMR | 3 | 89% | 22257  | 2 |
| 40 | Libya                      | Upper middle income | EMR | 2 | 96% | 280000 | 3 |

1. Income Status: Data for type of country income classification, such as High Income, Upper middle income, Lower middle income & Low-income country were collected from World Bank (WHO follows World Bank classification).

2. #Vaccines: Number of DTP vaccine within national immunization schedule followed in each country

3. The immunization rates for countries 1-18 are taken from WHO (having only hexavalent in immunization schedule). From countries 19-40 the immunization rates are taken from sources such as WHO, country specific MOH sites, News articles, and other secondary sources. For instance, in Argentina, children weighing <1500 grams should be administered hexavalent vaccine, these children are around 8% of total surviving infant population. Hence hexavalent immunization rate is considered 8% for Argentina. In Canada hexavalent vaccines are used only in 4 provinces out of 10 provinces. In Latvia infants who receive hepB mono vaccine due to hepB risk exposure from mothers will use pentavalent vaccine, all others are given Hexavalent vaccines. According to Bulgarian MOH, the hexavalent vaccines are used around 75% and pentavalent 25%. According to infectious diseases department of Italy's Higher Health Institute (ISS) the immunization rate for 6 in 1 vaccine has reached 95%.

4. WHO vaccine-preventable diseases: monitoring system (Global summary 2018), GAVI-Country Hub, The World Factbook 2018, UNICEF child survival and sustainable development goals (SGD), United Nations (UN) Population data.

Table 3-Hexavalent Vaccine Private Markets

The table below shows the parameters considered for hexavalent vaccine volume estimation in private market

| S.No | Country Name        | Income Status <sup>1</sup> | Region | # Vaccines | Hexavalent Vaccine Private Share in the market <sup>2</sup> | Surviving Infants Population <sup>3</sup> | Dosage Interval |
|------|---------------------|----------------------------|--------|------------|---|---|-----------------|
| 1    | Trinidad and Tobago | High income                | AMR    | 1          | 15.0%   | 17,758                                    | 3               |
| 2    | Greece              | High income                | EUR    | 1          | 50.0%   | 98,500                                    | 3               |
| 3    | Cyprus              | High income                | EUR    | 1          | 40.0%   | 13,000                                    | 3               |
| 4    | Finland             | High income                | EUR    | 1          | 0.5%  | 60,253                                    | 3               |
| 5    | Hungary             | High income                | EUR    | 1          | 1.0%  | 86,507                                    | 3               |
| 6    | Iceland             | High income                | EUR    | 1          | 10.0%   | 3,783                                     | 3               |
| 7    | Lithuania           | High income                | EUR    | 1          | 10.0%   | 31,000                                    | 3               |
| 8    | Malta               | High income                | EUR    | 1          | 10.0%   | 4,000                                     | 3               |
| 9    | France              | High income                | EUR    | 1          | 95.9%   | 780,000                                   | 3               |
| 10   | Poland              | High income                | EUR    | 3          | 60.0%   | 340,655                                   | 3               |
| 11   | Germany             | High income                | EUR    | 3          | 95.0%   | 730,437                                   | 4               |
| 12   | Russia              | High income                | EUR    | 4          | 1.0%  | 1,782,681                                 | 4               |
| 13   | Israel              | High income                | EMR    | 3          | 6.0%  | 165,000                                   | 3               |
| 14   | Jordan              | High income                | EMR    | 2          | 1.0%  | 246,363                                   | 3               |
| 15   | Singapore           | High income                | WPR    | 1          | 7.0%  | 50,253                                    | 3               |
| 16   | South Korea         | High income                | WPR    | 3          | 7.0%  | 451,006                                   | 3               |
| 17   | Indonesia           | High income                | SEAR   | 1          | 2.2%  | 4,776,945                                 | 3               |
| 18   | Guatemala           | Upper middle income        | AMR    | 1          | 1.0%  | 414,797                                   | 3               |
| 19   | Ecuador             | Upper middle income        | AMR    | 1          | 1.0%  | 324,250                                   | 3               |
| 20   | Costa Rica          | Upper middle income        | AMR    | 1          | 3.0%  | 67,509                                    | 3               |
| 21   | Paraguay            | Upper middle income        | AMR    | 1          | 0.8%  | 137,251                                   | 3               |
| 22   | Brazil              | Upper middle income        | AMR    | 1          | 2.4%  | 2,851,412                                 | 3               |
| 23   | Colombia            | Upper middle income        | AMR    | 1          | 2.4%  | 714,643                                   | 3               |
| 24   | Peru                | Upper middle income        | AMR    | 1          | 2.4%  | 597,017                                   | 3               |
| 25   | Guyana              | Upper middle income        | AMR    | 1          | 2.4%  | 15,000                                    | 3               |
| 26   | Dominican Republic  | Upper middle income        | AMR    | 2          | 2.0%  | 208,012                                   | 3               |
| 27   | Jamaica             | Upper middle income        | AMR    | 2          | 2.4%  | 46,753                                    | 3               |
| 28   | Belarus             | Upper middle income        | EUR    | 1          | 9.0%  | 111,013                                   | 3               |
| 29   | Turkey              | Upper middle income        | EUR    | 1          | 0.3%  | 1,267,771                                 | 3               |
| 30   | Albania             | Upper middle income        | EUR    | 1          | 7.0%  | 34,000                                    | 3               |

|    |                    |                     |      |   |       |            |   |
|----|--------------------|---------------------|------|---|-------|------------|---|
| 31 | Azerbaijan         | Upper middle income | EUR  | 1 | 4.0%  | 162,059    | 3 |
| 32 | Serbia             | Upper middle income | EUR  | 1 | 0.5%  | 91,507     | 3 |
| 33 | Armenia            | Upper middle income | EUR  | 1 | 20.0% | 37,285     | 3 |
| 34 | Montenegro         | Upper middle income | EUR  | 1 | 2.0%  | 7,000      | 3 |
| 35 | Bosnia-Herzegovina | Upper middle income | EUR  | 1 | 0.2%  | 31,755     | 3 |
| 36 | Lebanon            | Upper middle income | EMR  | 1 | 10.0% | 93,579     | 3 |
| 37 | Iran               | Upper middle income | EMR  | 1 | 3.0%  | 1,251,298  | 3 |
| 38 | Mauritius          | Upper middle income | AFR  | 1 | 10.0% | 12,761     | 3 |
| 39 | Namibia            | Upper middle income | AFR  | 1 | 2.0%  | 70,771     | 3 |
| 40 | Malaysia           | Upper middle income | WPR  | 1 | 7.0%  | 541,507    | 3 |
| 41 | Thailand           | Upper middle income | SEAR | 1 | 16.0% | 676,443    | 3 |
| 42 | Nicaragua          | Lower middle income | AMR  | 1 | 10.0% | 116,021    | 3 |
| 43 | Bolivia            | Lower middle income | AMR  | 1 | 0.8%  | 245,756    | 3 |
| 44 | El Salvador        | Lower middle income | AMR  | 1 | 1.5%  | 115,751    | 3 |
| 45 | Honduras           | Lower middle income | AMR  | 1 | 5.0%  | 194,251    | 3 |
| 46 | Uzbekistan         | Lower middle income | EUR  | 1 | 0.3%  | 633,016    | 3 |
| 47 | Ukraine            | Lower middle income | EUR  | 2 | 5.0%  | 457,658    | 3 |
| 48 | Pakistan           | Lower middle income | EMR  | 1 | 0.5%  | 5,129,593  | 3 |
| 49 | Morocco            | Lower middle income | EMR  | 1 | 2.0%  | 677,033    | 3 |
| 50 | Tunisia            | Lower middle income | EMR  | 1 | 10.0% | 201,257    | 3 |
| 51 | Egypt              | Lower middle income | EMR  | 1 | 5.0%  | 2,454,755  | 3 |
| 52 | Nigeria            | Lower middle income | AFR  | 1 | 0.0%  | 6,980,622  | 3 |
| 53 | Cameroon           | Lower middle income | AFR  | 1 | 2.0%  | 821,122    | 3 |
| 54 | Ivory Coast        | Lower middle income | AFR  | 1 | 3.0%  | 854,642    | 3 |
| 55 | Kenya              | Lower middle income | AFR  | 1 | 10.0% | 1,499,182  | 3 |
| 56 | Cambodia           | Lower middle income | WPR  | 1 | 0.6%  | 358,250    | 3 |
| 57 | Philippines        | Lower middle income | WPR  | 1 | 2.5%  | 2,377,953  | 3 |
| 58 | India              | Lower middle income | SEAR | 1 | 1.2%  | 24,234,960 | 3 |
| 59 | Bangladesh         | Lower middle income | SEAR | 1 | 0.2%  | 2,965,995  | 3 |

|    |                 |                     |      |   |      |         |   |
|----|-----------------|---------------------|------|---|------|---------|---|
| 60 | Sri Lanka       | Lower middle income | SEAR | 1 | 0.3% | 305,961 | 3 |
| 61 | Myanmar (Burma) | Lower middle income | SEAR | 1 | 1.0% | 897,779 | 3 |
| 62 | Haiti           | Low income          | AMR  | 1 | 1.0% | 249,502 | 3 |

1. Income Status: Data for type of country income classification, such as High Income, Upper middle income, Lower middle income & Low-income country were collected from World Bank (WHO follows World Bank classification).

2. Hexavalent Vaccine Private Market Share: The share of hexavalent vaccine in these countries of total DTP immunization rate. Data taken from WHO private vaccine shares.

3. WHO vaccine-preventable diseases: monitoring system (Global summary 2018), GAVI-Country Hub, The World Factbook 2018, UNICEF child survival and sustainable development goals (SGD), United Nations (UN) Population data.

**Table 4-Hexavalent Vaccines Brand Consumption in Top 25 Countries**

The table below shows the volumes of hexavalent vaccines consumed in top 25 countries by brand

| S.No | Country Name                | Country Code | Type of Market | Volumes (Million doses) | Hexaxim®  | Infanrix Hexa® | Vaxelis® |
|------|-----------------------------|--------------|----------------|-------------------------|-----------|----------------|----------|
| 1    | Iraq <sup>1</sup>           | IQ           | Public         | 3.53                    | 3,534,147 | NA             | NA       |
| 2    | South Africa <sup>2</sup>   | ZA           | Public         | 3.18                    | 3,143,448 | 31,752         | NA       |
| 3    | Mexico <sup>3</sup>         | MX           | Public         | 3.03                    | 2,906,573 | 122,720        | NA       |
| 4    | Germany <sup>P</sup>        | DE           | Private        | 2.78                    | 1,110,265 | 1,387,831      | 277,566  |
| 5    | United Kingdom <sup>4</sup> | UK           | Public         | 2.27                    | NA        | 2,274,444      | NA       |
| 6    | France <sup>5</sup>         | FR           | Private        | 2.25                    | 1,010,264 | 1,234,767      | NA       |
| 7    | Saudi Arabia <sup>6</sup>   | SA           | Public         | 1.69                    | 1,521,892 | 169,099        | NA       |
| 8    | Italy <sup>7</sup>          | IT           | Public         | 1.33                    | 577,815   | 604,690        | 147,813  |
| 9    | Spain <sup>8</sup>          | ES           | Public         | 1.18                    | 576,240   | 246,960        | 352,800  |
| 10   | Australia <sup>9</sup>      | AU           | Public         | 0.90                    | NA        | 899,966        | NA       |
| 11   | India <sup>10,P</sup>       | IN           | Private        | 0.86                    | 460,000   | 400,000        | NA       |
| 12   | Libya <sup>11</sup>         | LY           | Public         | 0.81                    | 807,399   | NA             | NA       |
| 13   | Viet Nam                    | VN           | Private        | 0.76                    | 342,000   | 418,000        | NA       |
| 14   | Romania <sup>12</sup>       | RO           | Public         | 0.66                    | 399,672   | 255,528        | NA       |
| 15   | Kazakhstan <sup>13</sup>    | KZ           | Public         | 0.65                    | 649,480   | NA             | NA       |
| 16   | Poland                      | PL           | Private        | 0.61                    | 288,194   | 324,984        | NA       |
| 17   | Chile <sup>14</sup>         | CL           | Public         | 0.52                    | 470,000   | 25,000         | NA       |
| 18   | Belgium <sup>15</sup>       | BE           | Public         | 0.51                    | 513,521   | NA             | NA       |
| 19   | Netherlands <sup>P</sup>    | NL           | Public         | 0.51                    | NA        | 254,398        | 254,398  |
| 20   | Canada <sup>16</sup>        | CA           | Public         | 0.47                    | NA        | 465,608        | NA       |
| 21   | Sweden <sup>17</sup>        | SE           | Public         | 0.36                    | 71,065    | 284,259        | NA       |
| 24   | Czech Republic <sup>P</sup> | CZ           | Private        | 0.35                    | 258,886   | 86,295         | NA       |
| 22   | Thailand <sup>P</sup>       | TH           | Private        | 0.32                    | 194,816   | 129,877        | NA       |
| 23   | Indonesia <sup>P</sup>      | ID           | Private        | 0.32                    | 157,639   | 157,639        | NA       |
| 25   | Switzerland <sup>18</sup>   | CH           | Public         | 0.25                    | NA        | 249,282        | NA       |

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- P. Primary Inputs



**Table 5-Primary Inputs**

The table below shows the primary respondents' information

| S.No | Designation                                  | Company/University               | Country                               |
|------|--|----------------------------------|---------------------------------------|
| 1    | Pediatrician                                 | Universitair ziekenhuis brussel  | Belgium                               |
| 2    | Senior Product Manager for Pediatric Vaccine | Vaccine Manufacturing Company    | Indonesia                             |
| 3    | Marketing Manager                            | Vaccine Manufacturing Company    | Czech Republic                        |
| 4    | Professor                                    | Leiden University Medical Center | Netherlands                           |
| 5    | Registered Nurse                             | Samitivej Hospital               | Thailand                              |
| 6    | Brand Manager                                | Vaccine Manufacturing Company    | Germany, India, France Poland, Mexico |

**Table 6-Characteristics of Hexavalent Vaccine Brands**

The table below shows the characteristics of different hexavalent brands

| Vaccine Characteristics | Infanrix Hexa®                      | Hexaxim®                            | Vaxelis®                                 |
|-------------------------|-------------------------------------|-------------------------------------|--|
| Diphtheria toxoid       | Not less than 30 UI                 | Not less than 20 UI                 | Not less than 20 UI                      |
| Tetanus toxoid          | Not less than 40 UI                 | Not less than 40 UI                 | Not less than 40 UI                      |
| Pertussis               | PT 25 µg                            | PT 25 µg                            | PT 20 µg                                 |
|                         | FHA 25 µg                           | FHA 25 µg                           | FHA 20 µg;                               |
|                         | PRN 8 µg                            | -                                   | PRN 3 µg                                 |
|                         | -                                   | -                                   | FIM type 2,3: 5 µg                       |
| Hepatitis B - HBsAg     | Saccharomyces cerevisiae            | Hansenula polymorpha                | Saccharomyces cerevisiae                 |
| Hib -PRP                | 10 µg Conjugated to Tetanus toxoid  | 12 µg Conjugated to Tetanus toxoid  | 3 µg Conjugated to Meningococcal protein |
| IPV Polio               | Poliovirus inactivated type 1, 2, 3 | Poliovirus inactivated type 1, 2, 3 | Poliovirus inactivated type 1, 2, 3      |

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