Ref. Ares(2022)2416196 - 31/03/2022

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| **Grant Agreement No.:**<br><br>Start Date:<br>End Date: | 801495<br><br>01/08/2018<br>31/03/2022 |
| **Project title** | **European Joint Action on Vaccination — EU-JAV** |
| **WP number**<br>**Deliverable number**<br>**Title** | WP6<br>D6.2<br>Guidelines on procedures to estimate vaccine needs and procurement in EU |
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| **Nature**<br>R-report<br>O-other (describe) | R |
| **Dissemination Level**<br><br>**PU**-public<br>**CO**-only for consortium members | PU |
| **Delivery Month Planned** | M44 |
| **Actual Delivery Date**<br>(dd/mm/yyyy) | 31/03/2022 |

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## Acknowledgments

We would like to thank all survey participants for their time in completing the questionnaires, and all EU-JAV partners who contributed to the discussion We are also grateful to Vaccines Europe, in particular Dr. Sibilia Quilici, for useful discussions and for responding to our questionnaire. Finally, thank you to Olivier Epaulard, coordinator of the EU-JAV, for useful discussions throughout the project and comments to the final report.

# Acronyms

| | |
|---|---|
| **BCG** | **Bacillus Calmette–Guérin vaccine** |
| **COVID-19** | **COronaVIrus Disease-2019** |
| **DT** | **Diphtheria - Tetanus toxoid** |
| **EC** | **European Commission** |
| **ECDC** | **European Centre for Disease Prevention and Control** |
| **EEA** | **European Economic Agreement** |
| **EFPIA** | **European Federation of Pharmaceutical Industries and Associations** |
| **EU** | **European Union** |
| **EU-JAV** | **European Joint Action on Vaccination** |
| **HPV** | **Human Papillomavirus** |
| **IPV** | **Inactivated Polio vaccine** |
| **MCV** | **Measles-containing vaccine** |
| **MMR** | **Measles-Mumps-Rubella vaccine** |
| **MS** | **Member State** |
| **NIP** | **National immunization Programmes** |
| **NITAG** | **National Immunisation Technical Advisory Group** |
| **PPSV** | **Pneumococcal polysaccharide vaccine** |
| **SARS-CoV-2** | **Severe Acute Respiratory Syndrome CoronaVirus 2** |
| **Tdap** | **Tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis vaccine** |
| **UNICEF** | **United Nations Children's Fund** |
| **VE** | **Vaccines Europe** |
| **VPD** | **Vaccine-Preventable Diseases** |
| **WHO** | **World Health Organization** |
| **WP** | **Work Package** |

# Executive summary

Task 6.1 of Work Package 6 *Vaccine Supply and Preparedness*, of the EU Joint Action on Vaccinations (EU-JAV), had the following objectives:

- Review previous experiences about vaccine shortages and responses of EU countries (and non-EU consortium member countries);
- Analyse and evaluate local financing mechanisms for purchase and stock of vaccines;
- Develop guidelines on procedures to estimate vaccine needs and procurement in EU-MS in the short and long-term and actions recommended to prevent shortages.

This report is the third deliverable of Task 6.1 and refers to the objective "*Develop guidelines on procedures to estimate vaccine needs and procurement in EU-MS in the short and long-term*". The methodology used for the deliverable consisted in:

1) a survey on procedures to estimate vaccine needs in EU/EEA, conducted among persons in charge of national or subnational immunisation programme(s) or of vaccine supply/procurement;

2) a survey on introduction of new or improved vaccines and possible upcoming changes to recommendations for existing vaccines, conducted among National Immunization Technical Advisory Groups (NITAGs);

3) discussions with Vaccines Europe, one of the main stakeholders for this WP, including the collection of responses to a specific set of questions on vaccine procurement.

The literature shows that several methods, templates and tools have been previously developed by international organizations to facilitate vaccine forecasting. According to the World Health Organization (WHO), there are three forecasting methods, based respectively on the size of the target population for immunization, previous vaccine consumption data, and the size of the scheduled immunization sessions.

The method based on the size of the target population depends on reliable demographic data. If that data is available, it is an active and accurate planning method. The factors taken in account when using this method are, besides the target population of the area, the number of doses in the immunization schedule, the vaccination coverage target and the wastage multiplication factor. Once these data are known, it is possible to calculate the total number of doses needed for a particular vaccine. The accuracy of the estimation depends on the quality of data. The method based on previous vaccine consumption uses data on number of doses used during the previous reporting period (usually the previous year), with adjustments made if any increases in the population size have occurred since then. The equation considers remaining stock of vaccine at the beginning and end of a particular period, the vaccines received during that period, and the vaccines lost, destroyed or thrown away during the same period. Finally, the method based on size of the scheduled immunization sessions is mostly used in low-income countries and will not be considered in this report.

From November 2021 to January 2022, we conducted a survey among persons in charge of EU/EEA national or subnational immunisation programme(s) or of vaccine supply/procurement, to evaluate what procedures are used in the Member States to estimate vaccine needs. Results highlighted that overall, countries are satisfied with the forecasting methods used in their respective countries. Indeed, according to our survey on vaccine shortages and stockouts conducted in 2019, inaccurate forecasts had led to insufficient supplies of vaccine doses in only 4.3% of 115 shortage/stockout episodes, while the main reported causes of shortages/stockouts were actually production issues and global shortage. The survey on forecasting methods also revealed that most countries do not have written procedures for forecasting and that they use a combination of size of the target population and previous year consumption methods.

No countries reported to use mathematical modelling and very few countries reported to use other methods.
Despite countries' satisfaction with their forecasting methods, survey responses highlighted some critical aspects of the process, such as:

- *Estimating the size of risk groups.* Most EU/EEA countries include in their national immunization programs vaccination recommendations for persons at high risk of severe disease due to vaccine-preventable diseases; however, many countries report difficulties in estimating the numbers of individuals in risk groups, especially those with chronic medical conditions.
- *Estimating the number of women of childbearing age or who are pregnant.* Not all countries reported including the number of women of childbearing age / pregnant among the forecasting variables considered. Considering that for women of childbearing age vaccines for hepatitis B, measles, mumps, rubella and varicella are recommended and that two vaccines are routinely recommended in pregnancy (influenza vaccine and, in some countries, the combined tetanus, diphtheria, and acellular pertussis or Tdap vaccine and more recently the COVID-19 vaccine), an estimation of the size of these two groups is necessary for correctly forecasting vaccine demand for the above-mentioned vaccines.
- *Estimating the degree of vaccine hesitancy. The degree of* vaccine hesitancy (*hence refusal of vaccine doses)* is one of the most difficult factors to estimate when forecasting vaccine demand. Research carried out in the context of EU-JAV WP8 can help to understand underlying factors as perceived by the institutions responsible for the national immunisation programmes in the different countries, and disseminate the most efficient practices and lessons learnt that help overcoming it.
- *Wastage factor*. Only four countries reported to consider the possible wastage of vaccine doses as a variable to be included in the forecasting. Vaccine wastage is an important factor in forecasting vaccine needs and if not calculated correctly, the country concerned could be faced with an overestimation or underestimation of the number of vaccines needed.
- *Buffer/stockpile*. Only seven countries reported that they consider the state of stockpiles when forecasting vaccine needs. Buffer/stockpile is crucial for the continuity of the vaccine supply and provides the ability to immediately respond to epidemics, disease outbreaks, vaccine shortages or stock-outs at any level and should be contemplated when estimating vaccine need.
- *Long term forecasting*. Results from our previous surveys on vaccine shortages and financial mechanisms for vaccine procurement highlight that most EU countries use annual budget planning cycles (mostly centralised), while mid-term or long-term planning is seldom used. This is also confirmed in the present survey which shows that only five countries reported forecasting vaccine demand for a minimum of three to four years. Long-term demand forecasts offer visibility into future market needs to stakeholders, including industry partners.
- *Interaction with National Immunization Technical Advisory Groups (NITAGs).* Only three countries reported to interact with their country's NITAG during the forecasting process, prior to finalizing the number of vaccine doses needed per vaccine.
- *Limited use of available tools.* Four countries reported not using any templates nor electronic tools to forecast vaccine demand. The use of these tools, made available free of charge by international organizations, once the variables of interest have been correctly estimated, can facilitate and speed up the estimation of vaccine needs even in the long term.

The survey among NITAGS highlighted that "disease burden" and "availability of financial resources" are the most relevant criteria that inform vaccine recommendation development in their countries. For most

responding countries, NITAG recommendations are not "binding" for the government/health authority. NITAGs can endorse a recommendation for a vaccine, even though the vaccine may not be adopted, e.g., for economic reasons. Few countries specified which vaccine introduction and/or recommendations have been planned for the upcoming years. Belgium, Denmark and Italy reported new recommendations for seasonal influenza vaccination for healthy toddlers and younger children; some EU/EEA countries, including Finland, Latvia and United Kingdom, have already initiated influenza immunisation programmes for these younger age groups. The introduction of Herpes Zoster vaccination in adults or subjects with medical conditions is planned in Belgium, Croatia, Ireland and Italy, following recommendations in other nine EU countries.

Finally, discussions with Vaccines Europe highlighted, among others, the importance of an early and continuous dialogue between individual manufacturers and national competent health authorities, and the implementation of regulatory changes supporting the necessary flexibility to answer unpredicted evolutions in vaccine needs. Improved dialogue allows both sides to better anticipate the evolution of vaccine recommendations and more accurately forecast vaccine demand and would enable industry to plan manufacturing accordingly, taking into account the long vaccine lead times.

In conclusion, based on findings from all the activities carried out in the framework of WP6, we make some considerations and recommendations for preventing vaccine shortages and improving vaccine demand forecasting.

For preventing vaccine shortages:

- More research is needed on the causes of vaccine shortages and on how the different causes interplay with each other.
- There is a need for all countries to have an immunization supply chain improvement plan, defining strategies to assure a stable and adequate vaccine supply for the immunisation programme in order to prevent shortages, and a vaccine supply manager at national level.
- Procurement and tender mechanisms should take into consideration, among other things, multisource suppliers, other factors besides price, and the length of contract. Price should not be the only criterion considered in vaccine tenders.
- Sufficient stockpiles of vaccines at national level need to be in place including an emergency stockpile, as well as a comprehensive national overview of vaccine demand and stocks.
- Key mechanisms identified to better enable exchange of vaccines between EU countries are rapid exchange mechanisms on available vaccines between EU MS, harmonised labelling of vaccines in the EU, and liability protection for parties involved in making the vaccine available.
- Rarely used vaccines and immunoglobulins, vaccines to be used during epidemic outbreaks, and vaccines for emerging infectious diseases, should be the priority vaccines/products under focus for potential exchange mechanisms and a potential data repository.
- A continuous dialogue between public health authorities, NITAGs, manufacturers and regulatory agencies is needed.
- Joint procurement of vaccines during serious cross-border health threats caused by vaccine-preventable diseases, other forms of cross-border collaboration (such as sharing vaccine price and other market information), and lending of vaccines in case of vaccine shortages should be encouraged.

Regarding forecasting of vaccine needs:

- There is a need for innovative tools to identify persons with chronic illnesses with the aim of offering them the recommended vaccines. Immunization information systems (IIS) can be used for this purpose as they collect several types of data (e.g., vaccination coverage, morbidity data) which can then be linked by using a record linkage operation based on a unique code.

- An estimation of the number of women of childbearing age or pregnant is necessary for correctly forecasting vaccine demand for the vaccines recommended in these population groups.
- When forecasting vaccine needs, possible wastage and the state of buffer/stockpiles should be considered.
- Long-term demand forecasts are preferred, as they offer visibility into future market needs to stakeholders, including industry partners.
- Although for most countries NITAG recommendations are not "binding" on the government/health authority, it is very important that continuous two-way communication is established between NITAGs and policymakers. Interaction during the forecasting process, prior to finalizing the number of vaccine doses needed per vaccine, is also recommended.
- The use of templates or electronic tools to forecast vaccine demand, made available free of charge by international organizations, once the variables of interest have been correctly estimated, can facilitate and speed up the estimation of vaccine needs even in the long term.

# Background

Vaccines save millions of lives globally every year and are universally considered as one of the most successful and cost-effective public health interventions ever introduced. National immunisation programmes depend on an adequate supply of vaccines. Vaccine shortages represent a serious public health issue as they can lead to missed opportunities for vaccination and a greater risk of occurrence of deadly vaccine-preventable disease. Vaccine shortages have been reported globally and in the European Region in recent years (1, 2).

Work Package 6 (WP6) "*Vaccine supply and Preparedness*" aimed to improve vaccine supply and preparedness in EU/EEA. This aim was pursued through the following actions: a review of previous vaccine shortages experiences and assessment of responses at national and European level; a description of the local funding mechanisms used to purchase vaccines, and of Member State experiences and opinions on joint procurement of vaccines and other forms of cross-border collaboration; the development of guidelines on procedures for estimating short and long term vaccine needs and supplies; and exploration of the feasibility of developing a concept for an EU data warehouse for sharing data on vaccine supply and demand among stakeholders.

As highlighted in our first WP6 deliverable "*Report on previous experiences with vaccine shortages in EU countries (and non-EU consortium member countries), and responses at national and European levels*" (3), the causes of vaccine shortages are complex, multifaceted, may vary by vaccine and country, and include supply, demand and information factors. Prevention of vaccine shortages is a top priority globally and in the EU.

Vaccine supply and demand forecasting is of central importance to ensure vaccine security. Without the ability to forecast demand with reasonable certainty and some assurance of a viable market, manufacturers cannot scale production capacity, make commitments to suppliers of raw materials or justify a business case for investing in costly clinical trials to develop products (4). Accurate forecasting of vaccine demand is critical to prevent shortage/stock-outs as well as overstocks that can result in wastage due to expiry of vaccine. To improve the forecasting in vaccine requirements, good planning is critical. All potential factors, which could influence forecasting results should be taken into consideration, including the administration of booster doses and planned vaccination campaigns (5). Factors that can contribute to poor predictability of demand include variations in vaccine hesitancy and acceptance of vaccines (4). The latter topic has been addressed by Work Package 8 of the EU-JAV, in the report "*Vaccine hesitancy and uptake. From research and practices to implementation*" (6). Addressing different aspects related to vaccination, the EU-JAV sought to create synergies among the WPs with the aim of sharing concrete tools for improving national responses to vaccination challenges (7).

In 2018, the EU Commission in its Council Recommendation (8) on strengthened cooperation and coordination between EU countries, industry and other relevant stakeholders, against vaccine preventable diseases, included a reference to strengthening vaccine supply, procurement and stock management.

## Results of EU JAV surveys on vaccine shortages and on financial mechanisms for vaccine procurement

In 2019-2020, in the context of WP6, Task 6.1, two surveys were conducted, respectively for Tasks 6.1.1 and 6.1.3, the results of which will be briefly reported here, since they collected some information that is relevant to be included in the present guidelines (3, 9).

***Vaccine shortages and stockouts***

A first survey was conducted from February to May 2019 to collect information on vaccine shortages and stockouts in the years 2016-2019 and responses at the national and European level (task 6.1.1). The questionnaire was sent to persons in charge of the national or subnational immunisation programme(s) or of vaccine supply/procurement in EU/EEA and consortium (EU-JAV) Member States (MS). Twenty-one of 28 invited countries participated in the survey.

The survey enabled us to describe vaccine shortages and stock outs in Europe (including shortages and stock outs of other biological products), their impact and their main causes. Overall, 115 vaccine shortage and stock out episodes were reported in the three-year study period, 23 of which caused a disruption in immunization services. The most frequently involved vaccines were DT- and dT-containing combination vaccines, hepatitis B, hepatitis A, and BCG vaccines. The most frequently reported causes of shortages/stock outs were production issues and global shortage, which together accounted for approximately 65% of the events. In addition, the survey results provided some insights into the procurement and tendering mechanisms used in EU-JAV countries and other EU/EEA countries.

Most countries reported that they estimate vaccine needs at the national level, three countries do so at the subnational level, and one country in the private sector. Moreover, we asked participants to describe methods used to estimate vaccine needs in their respective countries. Responses received are shown in Table 1.

**Table 1. Methods used to estimate vaccines needs in EU-JAV and other EU/EEA countries.**

| Country | Vaccine needs estimation methods |
|---|---|
| Bosnia HG | Continuous follow up. At each procurement cycle (normally 4 years) Population calculations and historic review are used. |
| Bulgaria | Based on population registers, according to data from the National Statistical Institute; the expected birth rate; the expected morbidity from communicable diseases; the annual plans of GPs; the immunization coverage achieved during the previous year. |
| Croatia | Based on earlier consumption and size of birth cohort |
| Denmark | It is estimated from experience from previous years and taking new recommendations into consideration |
| Estonia | National database for birth cohorts and statistics of vaccination coverage, NITAG's approval for detailed procurement plan, including estimation of risks for vaccination coverage, monthly usage reports. |
| Finland | WHO methodology |
| France | NA |
| Greece | According to previous year's consumption |
| Hungary | Based on number of live births |
| Ireland | Target cohort figures are taken from the Central Statistics Office |
| Italy | For most vaccines, they are estimated at the regional level considering forecasts on the number of persons in the target cohorts and other population groups. For some vaccines (e.g., flu) the estimate is based on the number of doses administered in the previous year. |

| | |
|---|---|
| Latvia | Vaccine needs are estimated by the Centre for Disease Prevention and Control of Latvia, by taking into account in general foreseen size of immunized cohorts in case of routine vaccination or average number of vaccine doses used (for instance, Td for adults or rabies vaccine). Number of estimated doses is justified in relation to immunization coverage. |
| Lithuania | Centre for Communicable diseases prevention and control estimate vaccine needs according to Lithuanian immunization Schedule and number of children in different age cohorts. There are national guidelines for vaccine needs estimation. |
| Malta | Based on vaccination schedule and use in the NHS |
| Netherlands | Birth cohorts versus vaccine uptake |
| Norway | Based upon age cohort and vaccination coverage |
| Romania | Based on the request of the family doctors in correlation with epidemiological data |
| Serbia | Needs estimation is based upon: -Target population (birth-cohort)-Number of doses in the schedule-Target immunization coverage (95%)-Wastage factor (5%)-Buffer stock – 15% of total vaccine needs for the supply period |
| Slovenia | Estimated by the National Institute of Public Health |
| Spain | Vaccine needs are estimated at sub-national level according to the population of each region and coverage. |
| Sweden | Based on age cohort for vaccines within the NIP, for other vaccines according to earlier consumption. |

***Financial mechanisms used for* purchase and stock of vaccines*, and potential joint procurement of vaccines*.**

A second survey was conducted from August to October 2020, among persons in charge of the national or subnational immunisation programme(s) or of vaccine supply/procurement in EU/EEA and EU-JAV consortium Member States, to collect information on the financial mechanisms used for vaccine procurement, participation in joint procurement initiatives (and other forms of cross-border collaboration) and Member State opinions on joint procurement of vaccines (Task 6.1.3). Fourteen of 28 invited countries, all belonging to EU/EEA, participated in the survey.

Results highlighted that, in most EU/EEA countries, the vaccines included in national vaccination schedules are entirely funded by the national or subnational governments. Other reported sources of funding include health insurance contributions (either directly funded by the central government or with reimbursement of costs). Most countries allocate specific funds to vaccines and use annual budget planning, while midterm or long-term planning is seldom used by countries. Budget planning is centralised in most countries. Decision-making to finance introduction of a vaccine is based, among other things (epidemiology of the disease and cost-effectiveness evaluations), on NITAG recommendations.

Survey results suggested also that overall, the current financial mechanisms used for vaccine procurement seem to function well. Finally, the majority of participants reported being favourable to joint procurement of vaccines during serious cross-border health threats caused by vaccine preventable diseases. Other forms of cross-border collaboration (such as sharing vaccine price and other market information), and lending of vaccines in case of vaccine shortages have been used in EU, and should be encouraged.

## Objective of Task 6.1.2

The objective of Task 6.1.2 was to develop guidelines on procedures to estimate vaccine needs and procurement in EU-MS in the short and long-term. This report provides basic principles for vaccine demand planning and forecasting.

# Methodology

The methodology used to collect the necessary information for preparing guidelines on procedures to estimate vaccine needs and procurement in EU was the following:

1) a survey on procedures and methods used to estimate vaccine needs in EU/EEA countries and consortium Member States, conducted among persons in charge of the national or subnational immunisation programme(s) or of vaccine supply/procurement in these countries;
2) a survey on introduction of new or improved vaccines and possible upcoming changes to recommendations for existing vaccines conducted among NITAGs;
3) discussions with Vaccines Europe, one of the main stakeholders for this WP, including collection of responses to a set of questions on vaccine procurement.

We also used data from the literature and information collected in previous surveys.

## 1) Survey on procedures to estimate vaccine needs in EU/EEA

In order to understand how vaccine forecasting is carried out in EU/EEA countries, identify best practices, and verify the availability of projections for future vaccine demand, in November 2021, we sent a brief questionnaire in Word format, by email, to the 28 countries that had previously been invited to participate in the survey on vaccine shortages. The aim was to explore in better detail the methods and tools used to estimate vaccine needs. An information sheet was attached to the questionnaire, to inform participants of the objectives of the survey and the way any personal data would be handled. Reminders were sent to countries who had not responded by the deadline (30 November 2021). The last questionnaire was completed in January 2022.

The questionnaire (Appendix 1) consisted of 15 questions exploring:

- whether countries have written procedures/national guidelines for forecasting vaccine demand;
- the methods/procedures used to forecast vaccine demand, and the variables considered; (including use of templates and/or any forecasting tools, methods used to estimate high risk groups, and interactions with country NITAG);
- satisfaction with forecasting method used, critical aspects, accuracy of past projections (years 2019-2020), overall and for specific population groups;
- number of years for which vaccine doses are forecasted and vaccines at risk for shortages.

## 2) Survey on "Introduction of new or improved vaccines and possible upcoming changes to recommendations for existing vaccines"

The survey was conducted among NITAG representatives, or persons in charge of the national or subnational immunisation programme(s) in EU/EEA Member States. From December 2021 to January 2022, twenty-eight countries were invited to participate (all the 20 EU-JAV consortium partners and eight EU/EEA countries not participating in the EU-JAV), using the e-mail addresses provided during a mapping of NITAG representatives (WP4). Of note, this contact list was double-checked on each institution's website. A questionnaire was sent to collect information about upcoming plans to introduce new vaccine products (new vaccines or vaccine combinations) and/or new vaccine recommendations into the EU/EEA countries national immunization program during the upcoming three years.

Following a review of the literature and of documents from international and national agencies (10-16), a questionnaire was developed, made up of multiple-choice and open-ended questions. The questionnaire was piloted for comprehensibility and answerability with the help of four reviewers all familiar with NITAGs. It collected information regarding:

1. Key criteria to inform vaccine recommendation development in each country
2. New vaccine introduction and/or recommendations planned in the upcoming three years, by target age (infants and toddlers, children and adolescents, adults, elderly), medical condition, and other indications.

The questionnaire (Appendix 2) was created and administered via an online tool, Surveymonkey® (https://it.surveymonkey.com/r/9H9LYBP). Three reminders were sent to countries that had not responded by the given deadline. Participants could review and change their answers until closure of the survey which originally was on January 10, 2022. Because of the Covid-19 pandemic, the deadline was extended to January 21, 2022. The survey was followed by deeper phone discussions or email exchanges around points requiring clarification, when necessary.

Questionnaire responses were analyzed using MS Excel software. Variables were reported as absolute number and proportions. Results from open-ended questions were summarized.

### 3) Questionnaire for Vaccines Europe.

In November 2021 we held a videoconference with representatives of Vaccines Europe (VE), one of the main stakeholder of WP6, in order to discuss their position on forecasting of vaccine demand in Europe. VE is a specialised vaccines group within the European Federation of Pharmaceutical Industries and Associations (EFPIA), the professional association of the pharmaceutical industry in Europe. Following the videoconference, we sent VE the following questions to explore some topics in further detail:

1. Has the manufacturing capacity been affected by the COVID-19 pandemic, and have you identified any vaccines at risk of shortages in the short to medium term?
2. Are there different actions to be undertaken (e.g. during forecasting) for different products depending on their level of risk for vaccine shortage/stockouts?"
3. How manufacturers estimate the number of vaccine doses/stockpiles to be produced? Which are the assumptions made and main variables considered?
4. What can be improved in the way vaccine forecasting is carried out by EU countries?
5. How can processes and mechanisms for manufacturers to engage with recommending bodies/payers on vaccination plans evolution and to obtain anticipated and accurate figures of future demand, be improved?
6. How can early warning systems from suppliers and manufacturers, for potential vaccine stockouts, be improved?
7. How is forecasting of rarely used vaccines, immunoglobulins, and antitoxins, different from others and how can shortages of these be avoided?

# Results

## Survey on procedures to estimate vaccine needs in EU/EEA and consortium Member States.

Between November 2021 and January 2022, 12 (Belgium, Denmark, Estonia, France, Ireland, Italy, Netherland, Norway, Portugal, Slovakia, Slovenia and Spain) of 28 invited countries completed the survey (response rate 43%). All twelve participating countries belong to the EU/EEA, and nine are part of EU-JAV consortium (Estonia, Ireland and Portugal are not members of the EU-JAV consortium). Nine of the 12 countries had also participated in the survey on vaccine shortages, while three countries (Portugal, Belgium and Slovakia) did not participate in the previous survey.

a) *Written procedures/national guidelines for forecasting vaccine demand*

Only three countries (Norway, Portugal and Slovenia) reported having written procedures for forecasting vaccine demand.

b) *Method used to forecast vaccine demand and variables considered*

Countries were asked to indicate whether they use a template (e.g. Excel sheet) to automatically calculate the number of doses needed, for each vaccine. They were also asked whether they use any of the electronic vaccine stock and supply management tools made available by WHO/Unicef or any other electronic Logistics Management Information System (eLMIS). Only three countries (Denmark, Norway and some of the Autonomous Regions of Spain) reported using a template. Three countries (Belgium, Norway and Slovenia) and some regions in Spain and Italy reported using an electronic tool. In detail:

- Belgium uses Vaccinnet (https://www.vaccinnet.be/Vaccinnet/welkom.do) a web-based ordering system for vaccines in Flanders, set up in 2004 and linked to an immunisation register;
- Norway uses a custom made tool by a Norwegian software provider;
- Slovenia also uses a national custom-made tool;
- One Italian region uses a web-based vaccine stock and supply management tool (http://valore.regione.puglia.it/VaLoRe/mainLogin.do) and the immunization registry kept by each vaccination centre.

In nine countries, vaccine demand for vaccines included in the national immunization plan (including childhood and life course immunizations) is estimated by using both size of target population and previous year consumption. One country (Ireland) estimates vaccine demand only by size of target population and one country (Norway) only by previous year consumption. Finally, in one country (France), vaccine needs are estimated by the private sector (pharmaceutical companies), which can rely on the advice of the Haute Autorité de Santé which assess the target population for each vaccine, but also on epidemiological data provided by the National Public Health institute. In addition, the companies can rely on the list of compulsory vaccines provided for in French regulations (National medicine and health products agency). Historically, before making vaccination compulsory, the Haute Autorité de Santé checked with the laboratories that the available vaccine quantities were sufficient (Table2).

**Table 2. Method used to estimate vaccine demand for vaccines included in the national immunization plan.**

| Country | Size of target population | Previous year consumption | Other methods |
|---|---|---|---|
| **Belgium** | X | X | - |
| **Denmark** | X | X | - |
| **Estonia** | X | X | YES, stocks and 2-3 years coverage trends |
| **France** | NA | NA | NA* |
| **Ireland** | X | - | - |
| **Italy**** | X | X | - |
| **Netherlands** | X | X | - |
| **Norway** | - | X | - |
| **Portugal** | X | X | - |
| **Slovakia** | X | X | - |
| **Slovenia** | X | X | - |
| **Spain***** | X | X | - |

***For France,** vaccine needs are estimated by the private sector in liaison with the Haute Autorité de Santé
****For Italy,** 3 regions, representing 17% of the Italian population completed the questionnaire
*****For Spain**, 7 regions, representing 39% of the total Spanish population completed the questionnaire

Countries using the size of the target population method consider several variables to estimate vaccine demand, including the number and size of high-risk groups for which certain vaccines may be indicated (11 countries), the number of women of childbearing age/pregnant (nine countries), the current vaccine coverage in the target groups (10 countries) and coverage targets (nine countries), and the needs in terms of catch-up vaccination (nine countries). Table 3 shows variables considered by each country.

**Table 3. Variables considered to estimate vaccine demand for vaccines included in the national immunization plan, by country.**

| Country | High risk groups | N. women of childbearing age/pregnant | Vaccine coverage in target groups | Coverage targets | Wastage of doses | Planned campaigns | Catch-up vaccinations | State of stockpiles | Buffer stock | Other |
|---|---|---|---|---|---|---|---|---|---|---|
| **Belgium** | Yes | Yes | Yes | Yes | No | Yes | Yes | No | Yes | Yes, not specified |
| **Denmark** | Yes | Yes | Yes | Yes | Yes | No | Yes | Yes | Yes | No |
| **Estonia** | Yes | No | Yes | Yes | Yes | Yes | Yes | Yes | Yes | No |
| **France** | NA | NA | NA | NA | NA | NA | NA | NA | NA | NA |
| **Ireland** | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | No |
| **Italy** | Yes | Yes/No* | Yes | Yes | No | Yes | Yes | Yes/No* | No - | No |
| **Netherlands** | Yes | Yes | Yes | No | Yes | Yes | Yes | Yes | Yes | Yes** |
| **Norway** | Yes | No | No | No | No | No- | Yes | Yes | Yes | No |
| **Portugal** | Yes | Yes | Yes | Yes | No | Yes | Yes | Yes | Yes | No |
| **Slovakia** | Yes | Yes | Yes | Yes | No | No | No | No | No | No |
| **Slovenia** | Yes | Yes | Yes | Yes | No | Yes | Yes | Yes | Yes | No |
| **Spain** | Yes | Yes | Yes | Yes | No | Yes | Yes | Yes | No | No |

*Yes in one Region
**Circumstances possibly changing the coverage (e.g. increasing flu vaccine uptake in recent years)

Participants where asked if they are able to estimate the size of "high-risk groups" (e.g. immunocompromised population, persons with cardiovascular diseases or that have diabetic or other

chronic diseases): five countries reported challenges in doing so. Among the six countries which are able to estimate the size of at risk groups:

- Denmark reported to have a national discharge register where all hospital contacts are registered. Diagnose codes and procedure codes registered as part of these hospital contacts are used to identify individuals with certain chronic/underlying diseases. Even though there is a register where prescribed medicine define certain underlying diseases (e.g. diabetes), only a few disease are identified through this register.
- Slovakia reported to use statistical data and Slovenia that the assessment is prepared by an expert group.
- Estonia reported that to estimate size of the risk groups, they use different available databases and sources, such as the internal treatment invoice data from hospitals, number of prescriptions in the national e-prescription system, other epidemiological data collected by the Health Board, and national statistics database (number of people in certain age groups, gender, etc.). The estimation of the coverage percentage in the risk group is discussed and decided in the NITAG for vaccines. There are no specific rules when estimating the coverage percentage but mostly either previous year data/ trends or experience of other neighbouring countries is the base line.
- Spain reported that *some of the regions use electronic medical records in primary care linked (or not) to hospital data as well as data from the Spanish National Statistics Institute (NIE)*, while - Norway reported to be able to estimate the size of risk groups but not to use it regularly for immunization programmes.

During the forecasting process, only three countries reported interacting with their country's NITAG, prior to finalizing the number of vaccine doses needed per vaccine.

c) *Opinions on effectiveness of method used for forecasting and critical aspects*

In the opinions of all but one respondent, the method used in their country to estimate vaccine needs was considered effective in accurately forecasting vaccine demand for all vaccines. Nevertheless, seven countries reported some critical aspects of the forecasting method used in their country (Table 4). In detail:

- Estonia reported difficulties in getting vaccine coverage and central warehouse numbers/trends and to analyse stock on a monthly basis;
- Ireland, reported that due to their relatively small population, it may require longer contracts to get a lower price;
- Italy mentioned lack of estimates of wasted doses;
- Netherlands reported that estimating the uptake for a new vaccine or a new target group is tricky;
- Slovakia, mentioned that critical aspects are linked to the manufacturer / distributor's ability to ensure sufficient vaccine stocks to meet the demand of the entire target population;
- Slovenia reported the difficulty to purchase vaccine in time when the vaccination program or the epidemiological situation changes;
- Spain reported the lack of workforce and the unpredictability of real consumption for high-risk groups or in regions with a high percentage of floating population.

**Table 4. Opinions and critical aspects regarding the effectiveness of method used for forecasting.**

| Country | Was method used to estimate vaccine needs effective in accurately forecasting vaccine demand? | Critical aspects |
|---|---|---|
| **Belgium** | Yes | None indicated |
| **Denmark** | Yes | None indicated |
| **Estonia** | Yes | Estimate coverage trends and central warehouse stocks |
| **France** | Yes | None indicated |
| **Ireland** | Yes | Longer contracts to get a lower price, because of small population |
| **Italy** | Yes | No estimation of possible wastage of doses.<br>One region indicated that it is very difficult to estimate the supply for flu vaccines |
| **Netherlands** | Yes | Estimate the uptake for a new vaccine or a new target group |
| **Norway** | Yes | None indicated |
| **Portugal** | Yes | None indicated |
| **Slovakia** | Yes | Manufacturer ability to ensure sufficient vaccine stocks to meet the demand |
| **Slovenia** | No | Timeliness in case of changes of program or epi situation |
| **Spain** | Yes | Lack of workforce, unpredictability of real consumption |

With reference to the vaccine doses forecasted in each country for the years 2019 and 2020, the projections made were correct for all population groups in six countries, while seven others reported that for some population groups, the actual demand was different (higher or lower) from the number of forecasted doses (Table 5).

**Table 5. Accuracy of vaccine demand forecasting for the years 2019-2020.**

| Country | Vaccines for which inaccurate forecasts occurred (2019-2020) | Possible reasons for inaccurate forecasting |
|---|---|---|
| **Belgium** | HPV and Tdap | Lockdown and postponement of vaccinations to the next school year. |
| **Denmark** | None reported | |
| **Estonia** | HPV vaccines | Number of HPV vaccines for catch-up programme among adolescents was over estimated because of an increase of the vaccination refusal in this target group. |
| **France** | None reported | |
| **Ireland** | Vaccines for primary immunization of the childhood and for Tdap vaccine | Decrease in the number of pregnancies (and consequently the decrease in the birth rate) and the delay in vaccinations due to the Covid-19 pandemic |
| **Italy** | 2020-2021 flu vaccination campaign: actual demand lower than forecasted | Initial overestimation of the target and delayed supply |
| **Netherlands** | Flu vaccine | In 2020 the demand for flu shots was much higher than in 2019 |
| **Norway** | None reported | |
| **Portugal** | None reported | |
| **Slovakia** | None reported | |
| **Slovenia** | Overestimation of travel vaccines and underestimation of flu vaccines | Reduction in travel and increased demand for Flu vaccines due to the pandemic. |
| **Spain** | Hexavalent, MMR, PCV, Men C were overestimated<br><br>Tdap, pneumococcal and flu vaccines were underestimated | Underused in infants/children because of decreased birth rate and reduced vaccine uptake due to pandemic<br><br>Demand increased among high risk groups and adults aged > 60 years because of the pandemic and increased mortality |

Only five countries forecast the number of vaccine doses needed in the long term (4-5 years). In the remaining seven countries the time period of estimation ranges from zero to three years (Table 6).

**Table 6. Time period of estimation from 2022 onwards and countries that provided the number of doses forecasted per year.**

| | Time period of estimation from 2022 onwards | Countries that have provided the number of doses forecasted by year |
|---|---|---|
| **Belgium** | 4 years | yes |
| **Denmark** | 3-4 years | yes |
| **Estonia** | 1 year | no |
| **France** | NA | no |
| **Ireland** | 2-3 years | yes |
| **Italy** | 2 years | yes (for 1 Region) |
| **Netherlands** | 5 years | no |
| **Norway** | 4 years | no |
| **Portugal** | 0 | yes |
| **Slovakia** | 0 | no |
| **Slovenia** | 4 years | yes |
| **Spain** | 1-3 years | yes (for 6 Autonomous Regions) |

Five countries (Belgium, Estonia, France, Norway, and Spain) identified some vaccines as being at particular risk of shortages, as shown in Table 7.

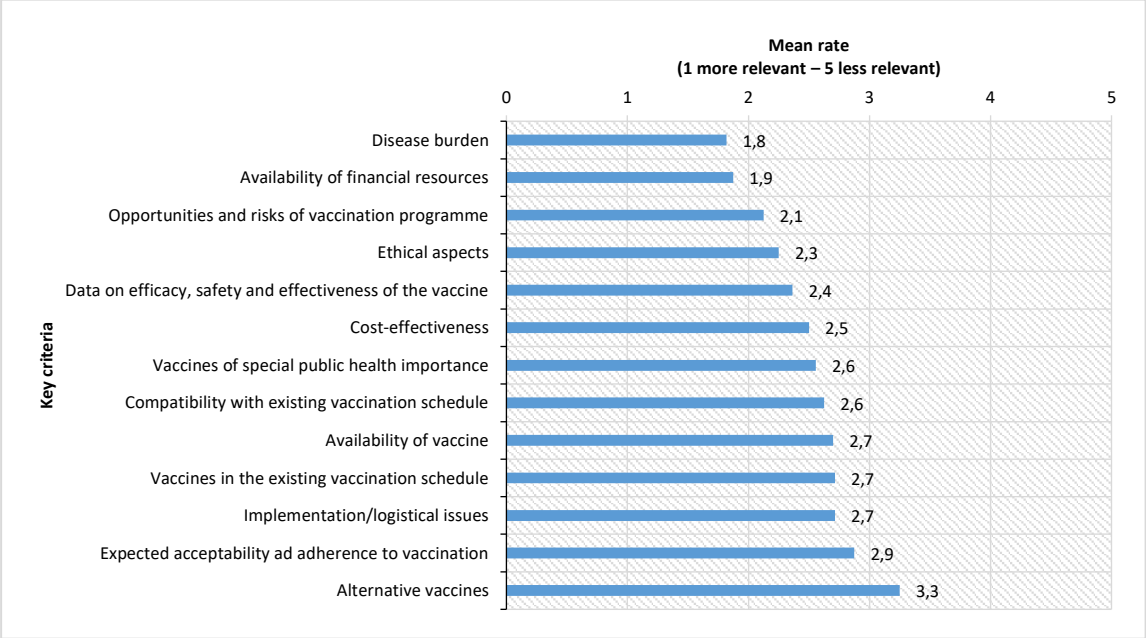
**Table 7. Vaccines identified as being at risk of shortages, by country.**

| | Vaccines at risk of shortages | Reasons for shortage |
|---|---|---|
| **Belgium** | HPV 9 and pneumococcal polysaccharide | Shortage of availability in Europe because of high demand internationally |
| **Estonia** | DT vaccine | Infants who cannot take hexavalent or pentavalent vaccine |
| **France** | Hexa- and pentavalent vaccines | Temporary packaging problems (normalization at the end of 2021) |
| **Italy** | Pneumococcal polysaccharide vaccine (PPSV). There is a stockout of cholera vaccine. | Cholera vaccine is no longer produced by the company |
| **Norway** | Seasonal influenza vaccine during the pandemic | Increased demand due to the pandemic |
| **Spain** | Adjuvanted Herpes Zoster<br>Pneumococcal polysaccharide<br>Hepatitis B and A<br>Rabies<br>IPV | Higher demand than production possibilities<br>Unknown reason<br>Previous experience on shortages<br>Change of supplier<br>There is still no national licence |

## Survey "Introduction of new or improved vaccines and possible upcoming changes to recommendations for existing vaccines"

Thirteen of 28 invited countries (response rate 39%) responded to the survey: Belgium, Bosnia-Herzegovina, Croatia, Denmark, Hungary, Ireland, Italy, Latvia, Norway, Portugal, Romania, Spain and Sweden. Respondents were representatives of NITAGs (for Ireland, Latvia and Portugal), NITAG Secretariats (Belgium Norway and Spain), representative of the Ministry of Health (Italy), experts of the National Public Health Institute (Bosnia-Herzegovina, Croatia, Denmark, Hungary Romania and Sweden). All participants ranked the key criteria that inform vaccine recommendation development in their countries. According to a previous NITAG survey [17], the five criteria ranked as more relevant were: "Disease burden", "Availability of financial resources", "Opportunities and risks of vaccination programme", "Ethical aspects", and "Data on efficacy, safety and effectiveness of the vaccine" (Figure 1).

**Figure 1. Ranking of relevant criteria that inform vaccine recommendation development in the 13 countries which responded to the survey.**




Only one country (Romania) specified that NITAG recommendations are "binding" for the government/health authority (i.e., must be implemented - e.g., a recommended new vaccine must be added to the immunization program schedule and the program implemented by the public authority) (Table 8). Findings from a previous NITAG survey showed that separate governmental or health insurance authorities can make the final decision of whether to adopt a new vaccine in the national immunization plan, or whether to reimburse the vaccine. Moreover, a NITAG can endorse a recommendation for a vaccine without the vaccine being adopted, e.g., for economic reasons. In some cases, additional committees or authorities are responsible for decision-making at subnational level [9].

**Table 8. Countries in which NITAG recommendations are "binding" for the government/health authority among the 13 countries which responded to the survey.**

| Country | Yes | No |
|---|---|---|
| Belgium | | X |
| Bosnia-Herzegovina | | X |
| Croatia | | X |
| Denmark | | X |
| Hungary | | X |
| Ireland | | X |
| Italy | | X |
| Latvia | | X |
| Norway | | X |
| Portugal | | X |
| Romania | X | |
| Spain | | X |
| Sweden | | X |
| **Total** | **1** | **12** |

Respondents for Belgium, Bosnia-Herzegovina, Croatia, Denmark, Ireland, Italy, Latvia, Norway, and Portugal reported that they are planning to introduce new vaccines and/or new vaccine recommendations into national immunization program over the next three years, as described in Tables 9 and 10.

**Table 9. Countries planning to introduce new vaccines and/or new vaccine recommendations over the next three years among the 13 countries which responded to the survey.**

| Country | Yes | No | Do not know |
|---|---|---|---|
| Belgium | X | | |
| Bosnia-Herzegovina | X | | |
| Croatia | X | | |
| Denmark | X | | |
| Hungary | | | X |
| Ireland | X | | |
| Italy | X | | |
| Latvia | X | | |
| Norway | X | | |
| Portugal | X | | |
| Romania | | | X |
| Spain | X | | |
| Sweden | X | | |
| **Total** | **11** | **0** | **2** |

**Table 10. Vaccine introduction / recommendations planned in the upcoming three years, by target age and medical condition or other indications in the 13 countries which responded to the survey.**

| Country | Infants and Toddlers (Birth – 23 months) | Children and Adolescents (2-18 years) | Adults 19-44 years | Adults 45-65 or older | Individuals with medical conditions or other indications |
|---|---|---|---|---|---|
| Belgium | X | X | | X | |
| Bosnia-Herzegovina | | | | | |
| Croatia | | | | | X |
| Denmark | | X | | | X |
| Hungary | | | | | |
| Ireland | X | X | | X | X |
| Italy | X | X | | X | X |
| Latvia | | X | X | | X |
| Norway | X | X | | X | |
| Portugal | | | | | |
| Romania | | | | | |
| Spain | X | X | | X | |
| Sweden | | | | X | |
| **Total** | **5** | **7** | **1** | **6** | **5** |

More specifically, **Belgium** reported new recommendations for:

- Meningococcus B vaccination in infants
- Use of Meningococcus ACWY conjugate vaccine in toddlers and adolescents (instead of MenC vaccine)
- Seasonal influenza quadrivalent vaccination in infants
- Herpes zoster recombinant, adjuvanted vaccination in adults ≥65 years.

**Croatia** reported a new recommendation for Herpes zoster vaccination in subjects with underlying medical conditions.

**Denmark** reported new recommendations for:

- Seasonal influenza live-attenuated, egg-based vaccine in children of 2-6 years of age
- Seasonal influenza inactivated, standard-dose, egg-based vaccine in health care personnel
- HPV nonavalent vaccination in men who have sex with men (introduced as a temporary programme).

**Ireland** stated the following:

- Review of the schedule for primary series in infants (Birth – 12 months of life)
- New recommendation for varicella vaccination in toddlers and children 2-10 years of age
- New recommendation for Herpes zoster recombinant, adjuvanted vaccination in adults 60-65 years or older and subjects with medical conditions.

**Italy** reported recommendations for:

- Meningococcus B reduced schedule of two primary doses plus a booster dose in infants
- Seasonal influenza quadrivalent vaccination in children
- Meningococcus ACWY conjugate vaccine in toddlers and adolescents (instead of MenC vaccine)
- PCV in adults ≥65 years
- Herpes zoster vaccination in adults ≥65 years and in subjects with medical conditions
- HPV nonavalent vaccination in women with CIN2+.

**Latvia** reported:

- Introduction of HPV gender neutral vaccination in adolescents
- Introduction of DTP vaccine in adolescents
- Introduction of pertussis vaccination in pregnant women.

**Norway** stated that:

- Varicella vaccination in children is being considered
- Meningococcal vaccine is considered for immunization program for adolescents
- Pneumococcal vaccine and Herpes zoster vaccine are considered for the elderly.

HTA and health economic evaluation are in progress before to give final advice to the MoH.

**Spain** reported:

- Introduction of rotavirus vaccination in infants
- Introduction of Meningococcus B and seasonal influenza vaccinations in paediatric population
- Introduction of HPV vaccination in male adolescents
- Introduction of new pneumococcal vaccines in adult population.

**Sweden** reported the introduction of pneumococcal vaccination in a national program for elderly.

Few countries specified which vaccine introductions and/or recommendations are planned. Belgium, Denmark, Italy and Spain have claimed new recommendations for seasonal flu vaccination for healthy children and younger children; some EU/EEA countries, including Finland, Latvia and the UK, have already reported to have initiated influenza immunization programs for these younger age groups [18]. The introduction of Herpes Zoster vaccination in adults or people with medical conditions is planned in Belgium, Croatia, Ireland, Italy, and Norway, following recommendations in nine other EU countries [19-27].

## Manufacturers' opinions on forecasting of vaccine demand in Europe

Below we report responses received by Vaccines Europe in the framework of EU-JAV, to the questionnaire aimed at exploring issues related to forecasting vaccine demand from the perspective of manufacturers. The responses are a synthesis of the responses collected by VE from the different manufacturers, members of VE.

***Q1.*** *Has the manufacturing capacity for any of the vaccines included in childhood and adult national immunisation programmes been affected by the COVID-19 pandemic, and have you identified any vaccines at risk of shortages in the short to medium term?*

R: Over the last two years in the context of the COVID-19 pandemic, EFPIA and VE run regular situational assessments on the "Impact of the COVID-19 outbreaks on the supply of medicines in the Union/EEA" to inform EU Institutions. Based on the collected feedback from the EFPIA & VE companies the following problems were reported: issues concerning raw materials, manufacturing equipment and materials for personal protection, primary packaging, single use devices for the production and batch release of some vaccines as well as transport restriction and problems with workforces. Despite the above issues, manufacturers have managed to avoid shortages thanks to the Business Continuity Plans in place in each company.

During the first year of Covid-19 pandemic, an increase of demand for pneumococcal and influenza vaccines have also been observed and reported to EU Institutions. Manufacturers did their best to address these increases of demand but were not able to fully address them due to the long lead times of production (18-24 months for most of the vaccines and for some specific beyond 36 months) and the complexity of the global regulatory lifecycle management of vaccines. At the beginning of the COVID-19 pandemic, EFPIA/VE reports (on vaccine availability) have been submitted first weekly, then biweekly and at the end of 2021 and in 2022, on a monthly basis.

***Q2****. Are there different actions to be undertaken (e.g. during forecasting) for different products depending on their level of risk for vaccine shortage/stockouts?"*

R: All VE members have established a Business Continuity Plan, which is relevant for their vaccines portfolio and is confidential. The general rules are included in the "Vaccines Europe Position of forecasting of vaccines demand in Europe".

***Q3**. Can you explain how manufacturers estimate the number of vaccine doses/stockpiles to be produced? Which are the assumptions made and main variables considered? Are possible wastage, production failures, and stocks also considered?*

- Companies have their own processes/tools reflecting production processes and the normal market demand, which is influenced by recommendation status & engagement with relevant authorities on their needs. Data analytic tool cannot be described further as it is industrial private know-how.
- Example of assumptions:
    - For established programs:
        - if reimbursed market: share evolution, future evolution of recommendations (new cohorts, change in regimen [3+1 to 2+1 injections for example], etc.),
        - if tender market: probability of being awarded, stable versus increased quantities, schedule of delivery, etc.
    - For future programs:
        - estimation of date of implementation, target population, number of cohorts of implementation, catch-up cohort, etc.
- Ability to make short-term changes can also depend upon finished product or component shelf life and availability of individual vaccines & manufacturing complexity or inherent variability.
- Allowance is made for certain thresholds of wastage in every production process. Vaccines as biological products are also often subject to varying yields, which are often estimated on the basis of historical production data.

***Q4**. What do you think can be improved in the way vaccine forecasting is carried out by EU countries?*
**Q5**. *In your position paper on vaccine forecasting (28), it is stated that "Today, processes and mechanisms for manufacturers to engage with recommending bodies/payers on vaccination plans evolution and to obtain anticipated and accurate figures of future demand are limited. As a consequence, manufacturers mainly make their own assumptions on future medical needs at a global level several years in advance" How can these processes and mechanisms be improved?*

<u>VE combined response to Q4 and Q5</u>

Planning/anticipation:

Today there is no consistent mechanism in place to allow dialogue between industry and national competent health authorities for vaccination programme implementation. Such dialogue would enable industry to plan manufacturing accordingly, taking into account the vaccine lead times which can be beyond 36 months for some vaccines to manufacture and the fact that between 5 and 10 years are needed to build and license a new production facility. A short-term response to unexpected changes of demand may be difficult. Such dialog should also be established with purchasing body. This is in place in some countries but not in all EU countries.

Proposal:

- Instigate an early and continuous dialogue between individual manufacturers and public health authorities that allows both sides to better anticipate the evolution of vaccine recommendations and more accurately forecast vaccine demand.

- Expand dialog between purchasing bodies and vaccines manufacturers in each and every EU country. More information are available in the Vaccines Europe priorities for vaccination policies in Europe paper (29).
- Implement regulatory changes supporting the necessary flexibility to answer unpredicted evolutions in vaccine needs, for example: simplification of regulatory variation (post approval changes), regulation allowing accelerated change implementation, common EU packaging and e-leaflet replacing paper leaflet allowing immediate reallocation of available inventories (30).

**Q6.** *Currently, manufacturers in Europe are obliged to communicate vaccine shortages at least two months before they occur to EMA and/or to National Agencies of Medicines. Timely communication of anticipated shortages from manufacturers to regulatory agencies and to public health authorities is essential so that reactive measures can be implemented. How can early warning systems from suppliers and manufacturers, for potential vaccine stockouts, be improved?*

R: Vaccine Europe fully recognises the importance of a timely communication of shortages to authorities so that appropriate mitigation actions can be taken to minimise the impact of supply disruption.

Unfortunately, there is today no common definition of shortage and no harmonised requirements for shortage reporting across EU/EEA Member States. The criteria and thresholds may be different from country to country and are not always clearly set in local legislations. For example, in some countries, a shortage as short as of 1 day for one presentation has to be reported, while in other countries, only shortages of 2 weeks for all presentations must be reported. In some countries, risks of shortages have to be notified while in others, authorities are expecting notification of confirmed shortages only.

A harmonised and standardised definition would provide a stronger evidence-based understanding of the root causes of shortages and therefore inform on the appropriateness of actions to be carried out to prevent and mitigate shortages. The definition of shortages should be workable and meaningful from a public health perspective. For instance, if MAHs have to report anticipated shortages with a duration of few days, the vast majority will have absolutely no public health impact given the availability of stocks at the level of distributors or pharmacies. Ultimately, immediate reallocation of available inventories globally can happen, but depends on the ability of the National Competent Authorities (NCA) to grant permission to import specific batches planned for another country. The common EU packaging and replacement paper leaflet by e-leaflet would speed up immediate reallocation of available inventories. VE is aligned with EFPIA's recommendation to define a shortage of a medicinal product for human use as arising in the situation when *supply does not meet patient need at a national level for a period of more than two weeks*.

A balance between early and meaningful communication is needed. An early communication of potential shortages will in many cases never result in actual shortages as manufacturers are doing their best to mitigate the impact of manufacturing issues. Reinforced obligations of earlier communication of potential shortages would result in many false signals and extra administrative burden for manufacturers and authorities without an added value in terms of public health. Notification obligations should also take into account that disruption of supply may happen in the very late stages of production (up to the release by OMCLs) and that early notification is not always possible.

**Q7.** *In a recent EU JAV report, rarely used vaccines, immunoglobulins (e.g., rabies IGs), and antitoxins (e.g., diphtheria antitoxin), were listed by countries as most important focus areas. How is forecasting of rarely used vaccines IGs and antitoxins different from others and how can shortages of these be avoided?*

R: The question could only be answered by very limited number of VE members companies. For Rabies Immunoglobulins, the forecasting process is similar to other products when it comes to private markets. As for public market, companies try to monitor closely the needs especially with the Army, but they could face unexpected demand decrease triggered by local countries budget re-allocation. A safety stock packaged using only one language in one presentation is ensured in case of urgent need for such a critical product.
For such rarely used immunoglobulins, a drastic limitation of the SKUs (Stock Keeping Unit), using the same box for all markets is the best way to limit the risk of shortages by re-routing doses when needed.

## Guidelines for vaccine forecasting

Several methods, templates and tools (e.g. WHO Stock management tool (SMT), web–based vaccine stock and Supply management tool (wVSSM), WHO vaccine wastage rates calculator, electronic logistic management information system (eLMIS)) have been developed by international organizations to facilitate vaccine forecasting (31-35).

In particular, WHO has developed "EPI Logistic forecasting tool", a tool designed to guide the process of forecasting the needs for vaccines, safe injection equipment, cold chain and storage capacity for national immunization programmes. The tool has been developed using Microsoft Excel and it consists of 11 worksheets (data entry, planning, output, and data source sheets). It facilitates decision making in support for the purchase of supplies for the immunization programs and supports the planning of the processes and structures required to achieve efficient logistical operations (36).

According to WHO (12) there are three forecasting methods, respectively based on:

- size of the target population for immunization;
- previous vaccine consumption data;
- size of the scheduled immunization sessions (for low-income countries).

The first two methods are commonly used (often in combination) in EU countries, while the size of the scheduled immunization sessions is mostly used in low-income countries and is appropriate when the rates of vaccine wastage cannot be determined, or vaccine stock management is not good.

According to WHO, the target population method remains the most suitable method for vaccine forecasts at higher levels (provincial, national, and global). It depends on reliable demographic data. If that data is available, it is an active and accurate planning method. To use this method is important to know the target population of the area, the number of doses in the immunization schedule, the vaccination coverage target and the wastage multiplication factor. Once this information is known, it is possible to calculate the total number of doses needed for a particular vaccine. The accuracy of the estimation depends on the quality of data. Estimating vaccine needs based on previous vaccine consumption is used when no reliable demographic data are available but there are reliable stock data and there is a relatively stable demand.

The target population method is recommended also by Vaccines Europe, in a recent paper "Position on forecasting of vaccine demand in Europe" (28). Vaccines Europe encourages authorities from all MSs to use a common and systematic approach for forecasting based on the same parameters suggested by WHO to obtain a more accurate estimation of the vaccine demand in EEA. In particular, for vaccines with no anticipated change of recommendation:

- size of the recommended target population (e.g. age cohorts, risk groups), including changes of target population (e.g. extension of target population to include pregnant women);
- vaccination schedule, including changes in vaccination schedule (e.g. from 3+1 to 2+1, introduction of booster);
- vaccination coverage and compliance (schedule completion) rates expected in the target population.

Furthermore, with respect to the WHO, Vaccines Europe suggests considering two additional parameters (which, however, are not easily estimated):

- anticipated knock-on effects on private vaccination (e.g. parents' decision to vaccinate older siblings outside of the recommended target group);
- vaccine hesitancy.

For new vaccines or introduction of new combination vaccines, Vaccines Europe recommends to consider:

- size of the target population;
- vaccination schedule;
- catch up strategy (e.g. no catch-up, catch up until a certain age limit, catch up cohorts step-by-step over years or in one big catch-up program);
- targeted vaccination coverage and compliance rates;
- date of introduction and planned duration of the program.

Finally, an additional method for forecasting vaccine demand, described in the literature consists in the use of mathematical models for building a decision support system for forecasting the annual vaccine demand of a specific vaccine (37-39).

The target population and previous consumption methods are briefly described below.

## Estimation of vaccine needs: Target populations method

The formula for estimating demand is:

$$\left(P_{\text{target}} \times \text{V}_{\text{coverage}} \times No._{doses} \times F_{\text{wastage}}\right) + \text{Buffer}$$

where: $P_{target}$ = Target Population, $V_{Coverage}$ = Vaccination Coverage, $No._{doses}$ = Number of doses required per target and $F_{wastage}$ = Wastage Factor

1. *Target Population ($P_{target}$)*

Target population is the number of people who are eligible for vaccination with a particular vaccine.
For routine vaccination, target population may include e.g., total births, surviving infants, pregnant women, adolescent girls. For supplementary immunization activities target population may include specific age groups of population, e.g.: < 5years, <15years, women of childbearing age.

2. *Vaccination coverage ($V_{coverage}$)*

Vaccination coverage is the estimated percentage of people who have received specific vaccines. The estimate is derived by dividing the total number of vaccinations given by the number of people in the

target population, often based on census projections. Planned coverage should be realistic and based on the national disease control priorities.

3. *Number of doses (No. $_{doses}$ )*

For routine immunization the number of doses needed for each primary vaccination series should be considered.

E.g.: Routine:

- BCG = 1 dose
- MCV = 1-2 doses
- Polio = 3-4 doses
- Pneumo = 3 doses
- Rotavirus = 2-3 doses

For SIAs: • No. of doses per target and No. of rounds, must be considered.

4. *Wastage factor ($F_{wastage}$)*

Wastage factor is the factor (number) that you multiply your estimated vaccine needs by, in order to allow for some doses being wasted.

$$\mathrm{F_{wastage}} = \frac{100}{100 - \text{ Wastage rate}}$$

E.g.

| Wastage rate = | 5 | 20 | 50 | 80 |
|---|---|---|---|---|
| Wastage factor = | 1.05 | 1.25 | 2.0 | 5 |

5. *Buffer Stock*

Buffer stock is the provision made to cover unforeseen circumstances (e.g. increased demand due to an outbreak). Buffer stock is calculated as follows: annual demand x duration of buffer stock / 12months. For multiyear forecasts, buffer should be rolled out and incremented.

## Estimating vaccine needs based on previous consumption

This method is based on the consumption of vaccines during the previous reporting period (usually the previous year). Some adjustment may be necessary if any increase in the population size since the previous vaccine consumption was recorded.

For the calculation of the annual vaccine needs from previous consumption, the equation is based on the remaining stock of vaccine at the beginning and end of a particular period, the vaccines received (purchased) during that period, and the vaccines lost, destroyed or thrown away during that period.

The equation is:

$$\text{Annual vaccine needs (in doses)} = (\mathrm{i} + \mathrm{r}) - (f + l)$$

where:
(i) initial vaccine stock at the beginning of the period; (r) vaccines received during the period;
(f) stock remaining at the end of the period; (l) lost, destroyed or expired doses.

## Discussion

Our survey on forecasting methods to estimate vaccine demand highlighted that overall, countries are satisfied with their forecasting methods. Indeed, according to our first survey (3), inaccurate forecasts led to insufficient supplies of vaccine doses in 4.3% (n=5) of shortage episodes while approximately 65% of shortages were due to production issues or global shortages. Most countries do not have written procedures for forecasting. They use a combination of size of the target population and previous year consumption methods. No countries reported using mathematical modelling and very few countries reported to use other methods. Despite countries' satisfaction with their forecasts, survey responses highlighted some critical aspects in the forecasting process that deserve to be considered. In detail:

*1. Variables considered for forecasting*

When a new vaccine is introduced, making clear decisions about who is eligible to be vaccinated and effectively communicating that information to health workers and the community is important. Decisions on eligibility for vaccination need to be incorporated into the planning and forecasting of supply needs.
For vaccines given in early infancy, the estimated number of births should be used as the target population, while vaccines given to older infants and children (e.g., MMR, DTP boosters) should be based on the number of surviving infants or children (especially in developing countries that may have high infant mortality rates), taking infant and child mortality rates into account.

a) *Estimating the size of risk groups.*

Most EU/EEA countries include in their national immunization programs vaccination recommendations for persons at high risk of severe disease due to vaccine-preventable diseases; however, many countries report difficulties in estimating the numbers of individuals in risk groups, especially those with chronic medical conditions. The responses to our survey highlighted the need for innovative tools to identify persons with chronic illnesses with the aim of offering them the recommended vaccines. Immunization information systems (IIS) can be used for this purpose as they collect several types of data (e.g., vaccination coverage, morbidity data) which can then be linked by using a record linkage operation based on a unique code (21,40).

To this end, the research carried out under WP5, Task 5.2, aimed at strengthening the interaction of IISs in Europe through common methodological guidelines, data structure and criteria for standardised assessment of vaccination coverage, is of paramount importance and should be adopted.
There is a need to ensure proper interaction of immunisation information systems to document uptake of vaccines and to increase vaccine surveillance capabilities as well as a better understanding of best practices and interventions to improve confidence in vaccines.

*b) Estimating the number of women of childbearing age/pregnant*

Not all countries reported including the number of women of childbearing age/pregnant among the forecasting variables considered. Considering that, in most countries, for women of childbearing age vaccines for hepatitis B, measles, mumps, rubella and varicella are recommended and that two vaccines are routinely recommended in pregnancy (influenza vaccine and the combined Tdap vaccine), an estimation of the size of these two groups is necessary for correctly forecasting vaccine demand for these vaccines.

*c) Estimating degree of vaccine hesitancy*

The current degree of vaccine hesitancy (hence potential refusal of vaccine doses) is one of the most difficult factors to estimate when forecasting vaccine demand. However, research carried out in the context of EU-JAV WP8 can help to understand its underlying factors as perceived by the institutions

responsible for the National Immunisation Programmes in the different countries, and disseminate the most efficient practices and lessons learnt that help overcome it.

*d) Wastage factor.*

Only four countries reported to consider the possible wastage of vaccine doses as a variable to be included in the forecasting. Vaccine wastage is an important factor in forecasting vaccine needs and if not calculated correctly, the country concerned could be faced with an overestimation or underestimation of the amount of vaccines needed. Therefore, wastage should be considered when forecasting vaccine need.

*e) Buffer/stockpile*

Only seven countries reported that they consider the state of stockpiles when forecasting vaccine needs. Buffer/stockpile is crucial for the continuity of the vaccine supply and provides the ability to immediately respond to epidemics, disease outbreaks, vaccine shortages or stock-outs at any level and should be contemplated when estimating vaccine need.

*2. Long term forecasting.*

Long-term demand forecasts offer visibility into future market needs to stakeholders including industry partners. GAVI points out that improvements in demand forecasting would reduce risks to inventory and potentially increase capacity and supply. In fact, accurate demand forecasting of new vaccines can reduce the risk to manufacturers and positively impact supply thereby reducing the negative impacts of demand uncertainty on price.

Results from our surveys on vaccine shortages and financial mechanism for vaccine procurement, confirmed also by the present survey (where only 5 countries reported a vaccine demand forecasting lasting at least 3-4 years), highlight that most EU countries use annual budget planning cycles (mostly centralised), while mid-term or long-term planning is seldom used.

Longer-term planning, in spite of some limitations highlighted by Vaccines Europe in a recent paper on Position on forecasting of vaccine demand in Europe (estimated vaccine needs may evolve over time; longer-term forecasts (≥ 5 years) and forecasts for products in development are inevitably less accurate; for any vaccine, unforeseeable short- to mid-term supply disruptions may occur such as temporary shutdown of facilities for maintenance, fluctuations in antigen production, batch failure or delivery delays, etc.), is strongly recommended because it allows a more comprehensive view of future vaccine demand. Indeed, visibility on vaccine demand for the upcoming 5 years would inform manufacturers' decisions related to minor to medium size investments (e.g. installation and validation of a new packaging line), and horizon scanning in the timeframe of 5 to 10 years would guide manufacturers in their decisions for major investments (e.g. new facilities for antigen production).

*3. Interaction with NITAGs*

Only three countries reported to interact with their national NITAG during the forecasting process, prior to finalizing the number of vaccine doses needed per vaccine. Our survey among NITAGs, despite the low response rate that made the trends observed in the sample non-generalizable, provided an interesting snapshot. Although for most countries NITAGs recommendations are not "binding" on the government/health authority, it is very important that frequent two –way communication is established between NITAGs and policymakers, so as to enable policymakers to make informed immunization policy and programme decisions, and consider any possible upcoming changes to vaccine recommendations in forecasting vaccine needs.

*4. Limited use of available tools*

Four countries reported not using a template nor any electronic tool to forecast vaccine demand.
The use of these tools, made available free of charge by international organizations, can facilitate and speed up the estimation of vaccine needs even in the long term, once the variables of interest have been correctly estimated

## Final considerations and recommendations

The following considerations and recommendations for preventing vaccine shortages and improving vaccine demand forecasting stem from the work carried out in the various tasks of WP6.

- More research is needed on the causes of vaccine shortages (including analysis of the economic and market–related causes) and on how the different causes interplay with each other.

- There is a need for all countries to have an immunization supply chain improvement plan, defining strategies to assure a stable and adequate vaccine supply for the immunisation programme in order to prevent shortages, and a vaccine supply manager at national level.

- Procurement and tender mechanisms, although considered effective by countries surveyed, should be improved and take into consideration, among others, multisource suppliers, other factors besides price, and the length of contract. Most countries, in fact, reported using price criteria which may be a disincentive for manufacturers to participate in tenders and invest in R&D. One of the requirements of a healthy market is that a range of suppliers be available; in order to achieve this requirement, price should not be the only criterion considered in vaccine tenders (9).

- The majority of countries reported being favourable to joint procurement of vaccines during serious cross border health threats caused by vaccine preventable diseases. Other forms of cross border collaboration (such as sharing vaccine price and other market information) and lending of vaccines in case of vaccine shortages have been used in EU and should be encouraged.

- Although it emerged from our survey on vaccine shortages, that an EU platform for exchanging information on vaccine shortages and actions taken across countries would be useful, one of the main findings in the report of EU-JAV WP 6 – Task 6.2 is that there seems to be uncertainty among countries about the need and options for an EU virtual data repository (41). Only four countries believed establishing a virtual data repository would prevent shortages in the EU, while eight countries said they were unsure and four said no. In this regard, Vaccines Europe has underlined that any initiative to increase the accuracy of vaccine demand forecasts, such as an EU data warehouse for European vaccine demand and supply data under evaluation by the EU-JAV, must ensure that vaccine manufacturers are not infringing EU competition rules and data confidentiality. Clear governance and communication rules should be established to guarantee that the EU data warehouse meets its objectives.

- The WP6 – Task 6.2 report highlights that some MSs have national stockpiles to protect against potential disease outbreaks (41). However, a global overview of size of these stockpiles and how they are forecasted in each MS is still lacking. Sufficient stockpiles of vaccines at national level need to be in place including an emergency stockpile, as well as a comprehensive national overview of vaccine demand and stocks.

- Exchange of vaccines among EU countries has been suggested as a useful mechanism to temporarily overcome shortages of vaccines in a country. Countries identified rapid exchange mechanisms on available vaccines between EU MS, harmonised labelling of vaccines in the EU, and liability protection for parties involved in making the vaccine available, as key mechanisms to better enable exchange of vaccines between EU countries.

- According to several MS, rarely used vaccines and immunoglobulins, vaccines to be used during epidemic outbreaks, and vaccines for emerging infectious diseases, should be the priority vaccines/products under focus for potential exchange mechanisms and a potential data repository (41).

- Improved communication between public health authorities, manufacturers and regulatory agencies is needed. Mechanisms for an early and continuous dialogue between manufacturers, NITAGs and health authorities should be established to better anticipate the evolution of vaccine recommendations and more accurately forecast vaccine demand. In case of vaccine shortages, communication by competent authorities to the public should not trigger undue concerns regarding the quality of vaccines.

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Co-funded by
the Health Programme
of the European Union

# APPENDIX 1

## Work Package 6 "Vaccine Supply and Preparedness". Survey on procedures to estimate vaccine needs in Europe.

### Please provide your country, name, affiliation, and contact details

| | |
|---|---|
| Country: | |
| Name of Respondent: | |
| Affiliation: | |
| Qualification and Role: | |
| E-mail: | |
| Office Telephone N.: | |
| Mobile N.: | |

### May we contact you if we need clarifications on the responses given or any further information?

□Yes
□ No

In our previous survey on vaccine shortages we asked participants to describe methods used to estimate vaccine needs in their respective countries. Considering the heterogeneity of the responses received, we would like to ask you some additional more specific questions in order to have a complete picture of forecasting methods used and draw some recommendations for the planned guidelines.
Responses received in the previous survey are shown in the Table below. Please refer to this table and the specific responses given for your country to respond to the questions below and integrate the information already given.
The complete report is available at the following link: https://eu-jav.com/wp-content/uploads/2019/09/Report-on-Vaccine-shortages-WP6-Task-6.1-.pdf

**Methods used to estimate vaccines needs in EU-JAV and other EU/EEA countries.**

| COUNTRY | Vaccine need estimation methods |
|---|---|
| Bosnia HG | Continuous follow up. At each procurement cycle (normally 4 years) Population calculations and historic review are used. |
| Bulgaria | Based on population registers, according to data from the National Statistical Institute; the expected birth rate; the expected morbidity from communicable diseases; the annual plans of GPs; the immunization coverage achieved during the previous year. |
| Croatia | Based on earlier consumption and size of birth cohort |
| Denmark | It is estimated from experience from previous years and taking new recommendations into consideration |
| Estonia | National database for birth cohorts and statistics of vaccination coverage, NITAG's approval for detailed procurement plan, including estimation of risks for vaccination coverage, monthly usage reports. |
| Finland | WHO methodology |
| France | NA |
| Greece | According to previous year's consumption |
| Hungary | Based on number of live births |
| Ireland | Target cohort figures are taken from the Central Statistics Office |
| Italy | For most vaccines, they are estimated at the regional level considering forecasts on the number of persons in the target cohorts and other population groups. For some vaccines (e.g. flu) the estimate is based on the number of doses administered in the previous year. |
| Latvia | Vaccine needs are estimated by the Centre for Disease Prevention and Control of Latvia, by taking into account in general foreseen size of immunized cohorts in case of routine vaccination or average number of vaccine doses used (for instance, Td for adults or rabies vaccine). Number of estimated doses is justified in relation to immunization coverage. |
| Lithuania | Centre for Communicable diseases prevention and control estimate vaccine needs according to Lithuanian immunization Schedule and number of children in different age cohorts. There are national guidelines for vaccine needs estimation. |
| Malta | Based on vaccination schedule and use in the NHS |
| Netherlands | Birth cohorts versus vaccine uptake |
| Norway | Based upon age cohort and vaccination coverage |
| Romania | Based on the request of the family doctors in correlation with epidemiological data |
| Serbia | Needs estimation is based upon:-Target population (birth-cohort)-Number of doses in the schedule-Target immunization coverage (95%)-Wastage factor (5%)-Buffer stock – 15% of total vaccine needs for the supply period |
| Slovenia | Estimated by the National Institute of Public Health |
| Spain | Vaccine needs are estimated at sub-national level according to the population of each region and coverage. |
| Sweden | Based on age cohort for vaccines within the NIP, for other vaccines according to earlier consumption. |

**1) Do you have written procedures/national guidelines for forecasting vaccine demand?**

□ Yes
□ No

*If Yes*, can you please share the procedures with us? (add link here _____ or send via email to antonietta.filia@iss.it)

**2) Do you have a template (e.g. Excel sheet) to complete and which automatically calculates the number of doses needed by vaccine?**

□ Yes
□ No

*If Yes* can you please share the template with us? (add link here _____ or send via email to antonietta.filia@iss.it)

**3) For vaccines included in the national immunization plan (including childhood and life course immunizations), could you please check all the variables listed below that are considered in your country when estimating vaccine demand.**

□ Size of target population:
- Newborns/infants/children
- Adolescents
- Adults (18-59)
- Older adults (≥60 y)
- Women of childbearing age/Pregnant women
- High risk groups (i.e. for which certain vaccines may be specifically indicated)

□ Previous year consumption
□ Current vaccine coverage in the target groups
□ Coverage targets
□ N. of doses included in the vaccination series, including boosters
□ Possible wastage of doses (indicate % or range _____)
□ Any planned supplementary immunization campaigns
□ Catch-up vaccinations
□ State of stockpile
□ Buffer stock (indicate % or range _____)
□ Other (please specify:
_____
_____)

**4) If you are able to estimate the size of "high risk groups" (e.g. immunocompromised population, persons with cardiovascular or diabetes or other chronic diseases), please specify the method used:**

_____
_____
_____
_____
_____

**5) For countries who indicated, in the Table above, forecasting methods not included in Question 3. (e.g., monthly usage reports, WHO methodology, annual plans of GPs, etc.) could you please give us more details regarding these items?**

_____
_____
_____
_____
_____
_____

6) **During the forecasting process, do any interactions take place with your country's NITAG, prior to finalizing the number of vaccine doses needed per vaccine?**

□ Yes
□ No

If yes, please specify the objectives, type and frequency of interactions with NITAGs.

_____
_____
_____

7) **In your opinion, is the method used in your country to estimate vaccine needs effective in accurately forecasting vaccine demand for all vaccines?**

□ Yes
□ No, please specify:

8) **What are some critical aspects, if any, of the forecasting method used in your country?**

_____
_____
_____
_____
_____

9) **With reference to the vaccine doses forecasted for your country for the years 2019 and 2020, were the projections made correct for all population groups and if not, for which of the following groups was actual demand different (higher or lower) from the number of forecasted doses and what are possible reasons for this?**

| **Population group** | **Vaccines for which inaccurate forecasts occurred (2019-2020)** | **Possible reasons for inaccurate forecasting** |
|---|---|---|
| Newborns/infants/children | | |
| Adolescents | | |
| Adults (18-59) | | |
| Older adults(≥60 y) | | |
| Women of childbearing age/Pregnant women | | |
| High risk groups | | |
| Other, specify: | | |

10) **Have forecasts been made in your country for vaccine doses needed in the next few years?**

□ Yes
□ No

**If Yes, could you please indicate the estimated n. of doses needed for each of the following vaccines for the years forecasts are available?**

| Vaccine | Doses forecasted | | | | | Total doses forecasted |
|---|---|---|---|---|---|---|
| | 2021 | 2022 | 2023 | 2024 | 2025 | |
| Pneumococcal (any type) | | | | | | |
| Hexavalent Vaccine (Hexa) | | | | | | |
| Pentavalent (DTP-Hib-HepB) | | | | | | |
| Measles-Mumps-Rubella (MMR) | | | | | | |
| Measles-Mumps-Rubella-Varicella (MMR-V) | | | | | | |
| Varicella | | | | | | |
| Meningococcal (any type) | | | | | | |
| HPV | | | | | | |
| Influenza | | | | | | |
| Hepatitis B | | | | | | |
| Hepatitis A | | | | | | |
| Hepatitis A-B | | | | | | |
| Herpes zoster | | | | | | |
| BCG | | | | | | |
| Rotavirus | | | | | | |

**11) Have any vaccines been identified in your country as being at particular risk of shortages?**

_____

_____

_____

*If Yes,* can you please list them and explain the reason.

_____

_____

_____

**12) Additional Comments. Please feel free to add here any additional comments you may have on procedures to estimate vaccine needs.**

_____

_____

_____

***Thank you for completing the questionnaire.***

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# APPENDIX 2.

## Questionnaire: EU-JAV: NITAG online survey on "Introduction of new or improved vaccines and possible upcoming changes to recommendations for existing vaccines"

*Dear NITAG representative:*

*We would be grateful for your participation in this short online survey "Introduction of new or improved vaccines and possible upcoming changes to recommendations for existing vaccines", a task of the ongoing EU Joint Action on Vaccination (EU-JAV).*

*The aim of the survey is to collect information about upcoming plans to introduce new vaccine products (new vaccines or vaccine combinations) and/or new vaccine recommendations into the EU/EEA countries national immunization program during the next three years. You will be asked to complete the survey to gather in information regarding*:

- *Your contact details, in case we need any further clarification or information*
- *Key criteria that inform vaccine recommendation development in your country.*
- *The new vaccine introduction and/or recommendations planned in the upcoming three years, by target age (infants and toddlers, children and adolescents, adults, elderly), by medical condition and other indications.*

*Your participation in this study is your decision and you will not be adversely affected in any way if you choose not to participate. Once you have submitted the questionnaire, the data cannot be retracted. Your survey responses will be kept confidential and will not be linked to your name or contact information. Your name and contact information will be stored on a secure server and will not be shared or published.*

*Results from the survey will be summarised into a report that will be sent to you for your revision. Should you have any questions regarding the survey, please do not hesitate to contact us at any time at: domenico.martinelli@unifg.it, elisa.dimaggio@unifg.it.*

*Link to the questionnaire: https://it.surveymonkey.com/r/9H9LYBP*

*Thank you very much in advance for participating in this survey.*

*Kind regards,*

*EU-JAV WP6 Team - Italy*

# NITAG online survey on "Introduction of new or improved vaccines and possible upcoming changes to recommendations for existing vaccines"

*Please provide your country, name, affiliation and contact details*

| | |
|---|---|
| Country: | *Drop down menu* |
| Name of Respondent: | |
| Affiliation: | |
| Qualification and Role: | |
| E-mail: | |
| Telephone N: | |

*Q.1 - What is your current role in immunization in your country? (Please check all that apply)*

[ ] National Immunization Technical Advisory Group (NITAG) representative

[ ] NITAG Secretariat

[ ] Ministry of Health

[ ] National Public Health Institute/equivalent

[ ] Other, specify _____

*Q.2 – Which key criteria inform vaccine recommendation development in your country? Please rank in a scale from 1 to 5 the five most relevant items (1 more relevant – 5 less relevant)*

[ ] Disease burden

[ ] Availability of vaccine

[ ] Data on efficacy, safety and effectiveness of the vaccine

[ ] Alternative vaccines

[ ] Vaccines of special public health importance

[ ] Cost-effectiveness

[ ] Opportunities and risks of vaccination programme

[ ] Expected acceptability ad adherence to vaccination

[ ] Compatibility with existing vaccination schedule

[ ] Vaccines in the existing vaccination schedule

[ ] Availability of financial resources

[ ] Implementation/logistical issues

[ ] Ethical aspects

[ ] Other, specify _____

*Q.3 - In your country, are NITAG recommendations "binding" for the government/health authority (i.e., must be implemented - e.g. a recommended new vaccine must be added to the immunization program schedule and the program implemented by the public authority)?*

[ ] Yes

[ ] No

[ ] Do not know

*Q.4 - Over the next three years, are you planning to introduce new vaccines and/or new vaccine recommendations into your national immunization program?*

[ ] Yes

[ ] No

[ ] Do not know

*If **yes**: Please check all that apply*

## Vaccine introduction / recommendations planned in the upcoming three years, by target age

### *Infants and toddlers*

| Antigen | | Birth | Months | | | | | | | | | | | | | | | | | | | | | | Considerations | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 | 21 | 22 | 23 | Introduced | Recommended |
| BCG | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Hepatitis B | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Polio | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| DTP-containing vaccine | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| *Haemophilus influenzae* type b | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Pneumococcal | Conjugate | | | | | | | | | | | | | | | | | | | | | | | | | | |
| | Polysaccharide | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Rotavirus | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Meningococcal | MenA conjugate | | | | | | | | | | | | | | | | | | | | | | | | | | |
| | MenC conjugate | | | | | | | | | | | | | | | | | | | | | | | | | | |
| | MenACWY conjugate | | | | | | | | | | | | | | | | | | | | | | | | | | |
| | MenB | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Measles, Mumps, Rubella | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Measles, Mumps, Rubella, Varicella | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Varicella | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Hepatitis A | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| HPV | Nonavalent | | | | | | | | | | | | | | | | | | | | | | | | | | |
| | Quadrivalent | | | | | | | | | | | | | | | | | | | | | | | | | | |
| | Bivalent | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Seasonal Influenza | Quadrivalent | | | | | | | | | | | | | | | | | | | | | | | | | | |
| | Trivalent | | | | | | | | | | | | | | | | | | | | | | | | | | |
| | Inactivated, standard-dose, egg-based | | | | | | | | | | | | | | | | | | | | | | | | | | |
| | Inactivated, standard-dose, cell culture-based | | | | | | | | | | | | | | | | | | | | | | | | | | |
| | Live attenuated, egg-based | | | | | | | | | | | | | | | | | | | | | | | | | | |
| | Inactivated, high-dose, egg-based | | | | | | | | | | | | | | | | | | | | | | | | | | |
| | Inactivated, standard-dose, egg-based with MF59 adjuvant | | | | | | | | | | | | | | | | | | | | | | | | | | |
| | Recombinant HA | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Herpes zoster | Live, attenuated | | | | | | | | | | | | | | | | | | | | | | | | | | |
| | Recombinant, adjuvanted | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Japanese Encephalitis | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Yellow Fever | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Tick-borne Encephalitis | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Typhoid | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Cholera | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Rabies | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Dengue (CYD-TDV) | | | | | | | | | | | | | | | | | | | | | | | | | | | |

***Children and Adolescents***

| | | Years | | | | | | | | | | | | | | | | Considerations | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Antigen** | | **2** | **3** | **4** | **5** | **6** | **7** | **8** | **9** | **10** | **11** | **12** | **13** | **14** | **15** | **16** | **17** | **18** | **Introduced** | **Recommended** |
| BCG | | | | | | | | | | | | | | | | | | | | |
| Hepatitis B | | | | | | | | | | | | | | | | | | | | |
| Polio | | | | | | | | | | | | | | | | | | | | |
| DTP-containing vaccine | | | | | | | | | | | | | | | | | | | | |
| *Haemophilus influenzae* type b | | | | | | | | | | | | | | | | | | | | |
| Pneumococcal | Conjugate | | | | | | | | | | | | | | | | | | | |
| | Polysaccharide | | | | | | | | | | | | | | | | | | | |
| Rotavirus | | | | | | | | | | | | | | | | | | | | |
| Meningococcal | MenA conjugate | | | | | | | | | | | | | | | | | | | |
| | MenC conjugate | | | | | | | | | | | | | | | | | | | |
| | MenACWY conjugate | | | | | | | | | | | | | | | | | | | |
| | MenB | | | | | | | | | | | | | | | | | | | |
| Measles, Mumps, Rubella | | | | | | | | | | | | | | | | | | | | |
| Measles, Mumps, Rubella, Varicella | | | | | | | | | | | | | | | | | | | | |
| Varicella | | | | | | | | | | | | | | | | | | | | |
| Hepatitis A | | | | | | | | | | | | | | | | | | | | |
| HPV | Nonavalent | | | | | | | | | | | | | | | | | | | |
| | Quadrivalent | | | | | | | | | | | | | | | | | | | |
| | Bivalent | | | | | | | | | | | | | | | | | | | |
| Seasonal Influenza | Quadrivalent | | | | | | | | | | | | | | | | | | | |
| | Trivalent | | | | | | | | | | | | | | | | | | | |
| | Inactivated, standard-dose, egg-based | | | | | | | | | | | | | | | | | | | |
| | Inactivated, standard-dose, cell culture-based | | | | | | | | | | | | | | | | | | | |
| | Live attenuated, egg-based | | | | | | | | | | | | | | | | | | | |
| | Inactivated, high-dose, egg-based | | | | | | | | | | | | | | | | | | | |
| | Inactivated, standard-dose, egg-based with MF59 adjuvant | | | | | | | | | | | | | | | | | | | |
| | Recombinant HA | | | | | | | | | | | | | | | | | | | |
| Herpes zoster | Live, attenuated | | | | | | | | | | | | | | | | | | | |
| | Recombinant, adjuvanted | | | | | | | | | | | | | | | | | | | |
| Japanese Encephalitis | | | | | | | | | | | | | | | | | | | | |
| Yellow Fever | | | | | | | | | | | | | | | | | | | | |
| Tick-borne Encephalitis | | | | | | | | | | | | | | | | | | | | |
| Typhoid | | | | | | | | | | | | | | | | | | | | |
| Cholera | | | | | | | | | | | | | | | | | | | | |
| Rabies | | | | | | | | | | | | | | | | | | | | |
| Dengue (CYD-TDV) | | | | | | | | | | | | | | | | | | | | |

***Adults 19-44***

| | | Years | | | | | | | | | | | | | | | | | | | | | | | | | Considerations | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Antigen** | | **19** | **20** | **21** | **22** | **23** | **24** | **25** | **26** | **27** | **28** | **29** | **30** | **31** | **32** | **33** | **34** | **35** | **36** | **37** | **38** | **39** | **40** | **41** | **42** | **43** | **44** | **Introduced** | **Recommended** |
| BCG | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Hepatitis B | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Polio | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| DTP-containing vaccine | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| *Haemophilus influenzae* type b | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Pneumococcal | Conjugate | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| | Polysaccharide | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Rotavirus | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Meningococcal | MenA conjugate | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| | MenC conjugate | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| | MenACWY conjugate | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| | MenB | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Measles, Mumps, Rubella | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Measles, Mumps, Rubella, Varicella | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Varicella | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Hepatitis A | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| HPV | Nonavalent | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| | Quadrivalent | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| | Bivalent | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Seasonal Influenza | Quadrivalent | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| | Trivalent | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| | Inactivated, standard-dose, egg-based | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| | Inactivated, standard-dose, cell culture-based | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| | Live attenuated, egg-based | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| | Inactivated, high-dose, egg-based | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| | Inactivated, standard-dose, egg-based with MF59 adjuvant | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| | Recombinant HA | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Herpes zoster | Live, attenuated | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| | Recombinant, adjuvanted | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Japanese Encephalitis | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Yellow Fever | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Tick-borne Encephalitis | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Typhoid | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Cholera | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Rabies | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Dengue (CYD-TDV) | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |

***Adults 45-65 or older***

| | | Years | | | | | | | | | | | | | | | | | | | | | | Considerations | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Antigen** | | **45** | **46** | **47** | **48** | **49** | **50** | **51** | **52** | **53** | **54** | **55** | **55** | **56** | **57** | **58** | **59** | **60** | **61** | **62** | **63** | **64** | **65** | **>65** | **Introduced** | **Recommended** |
| BCG | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Hepatitis B | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Polio | | | | | | | | | | | | | | | | | | | | | | | | | | |
| DTP-containing vaccine | | | | | | | | | | | | | | | | | | | | | | | | | | |
| *Haemophilus influenzae* type b | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Pneumococcal | Conjugate | | | | | | | | | | | | | | | | | | | | | | | | | |
| | Polysaccharide | | | | | | | | | | | | | | | | | | | | | | | | | |
| Rotavirus | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Meningococcal | MenA conjugate | | | | | | | | | | | | | | | | | | | | | | | | | |
| | MenC conjugate | | | | | | | | | | | | | | | | | | | | | | | | | |
| | MenACWYconjugate | | | | | | | | | | | | | | | | | | | | | | | | | |
| | MenB | | | | | | | | | | | | | | | | | | | | | | | | | |
| Measles, Mumps, Rubella | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Measles, Mumps, Rubella, Varicella | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Varicella | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Hepatitis A | | | | | | | | | | | | | | | | | | | | | | | | | | |
| HPV | Nonavalent | | | | | | | | | | | | | | | | | | | | | | | | | |
| | Quadrivalent | | | | | | | | | | | | | | | | | | | | | | | | | |
| | Bivalent | | | | | | | | | | | | | | | | | | | | | | | | | |
| Seasonal Influenza | Quadrivalent | | | | | | | | | | | | | | | | | | | | | | | | | |
| | Trivalent | | | | | | | | | | | | | | | | | | | | | | | | | |
| | Inactivated, standard-dose, egg-based | | | | | | | | | | | | | | | | | | | | | | | | | |
| | Inactivated, standard-dose, cell culture-based | | | | | | | | | | | | | | | | | | | | | | | | | |
| | Live attenuated, egg-based | | | | | | | | | | | | | | | | | | | | | | | | | |
| | Inactivated, high-dose, egg-based | | | | | | | | | | | | | | | | | | | | | | | | | |
| | Inactivated, standard-dose, egg-based with MF59 adjuvant | | | | | | | | | | | | | | | | | | | | | | | | | |
| | Recombinant HA | | | | | | | | | | | | | | | | | | | | | | | | | |
| Herpes zoster | Live, attenuated | | | | | | | | | | | | | | | | | | | | | | | | | |
| | Recombinant, adjuvanted | | | | | | | | | | | | | | | | | | | | | | | | | |
| Japanese Encephalitis | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Yellow Fever | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Tick-borne Encephalitis | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Typhoid | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Cholera | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Rabies | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Dengue (CYD-TDV) | | | | | | | | | | | | | | | | | | | | | | | | | | |

Co-funded by
the Health Programme
of the European Union

## Vaccine introduction / recommendations planned in the upcoming three years, by medical condition and other indications

| Antigen | | Immuno-compromised (excluding HIV infection) | HIV infection CD4 count | | Kidney failure, end-stage renal disease, or on hemodialysis | Heart disease | Chronic lung disease | Alcoholism | CSF leak or cochlear implant | Asplenia or persistent complement component deficiencies | Chronic liver disease | Diabetes | Considerations | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | <200/mm³ | ≥200/mm³ | | | | | | | | | Introduced | Recommended |
| BCG | | | | | | | | | | | | | | |
| Hepatitis B | | | | | | | | | | | | | | |
| Polio | | | | | | | | | | | | | | |
| DTP-containing vaccine | | | | | | | | | | | | | | |
| *Haemophilus influenzae* type b | | | | | | | | | | | | | | |
| Pneumococcal | Conjugate | | | | | | | | | | | | | |
| | Polysaccharide | | | | | | | | | | | | | |
| Rotavirus | | | | | | | | | | | | | | |
| Meningococcal | MenA conjugate | | | | | | | | | | | | | |
| | MenC conjugate | | | | | | | | | | | | | |
| | MenACWY conjugate | | | | | | | | | | | | | |
| | MenB | | | | | | | | | | | | | |
| Measles, Mumps, Rubella | | | | | | | | | | | | | | |
| Measles, Mumps, Rubella, Varicella | | | | | | | | | | | | | | |
| Varicella | | | | | | | | | | | | | | |
| Hepatitis A | | | | | | | | | | | | | | |
| HPV | Nonavalent | | | | | | | | | | | | | |
| | Quadrivalent | | | | | | | | | | | | | |
| | Bivalent | | | | | | | | | | | | | |
| Seasonal Influenza | Quadrivalent | | | | | | | | | | | | | |
| | Trivalent | | | | | | | | | | | | | |
| | Inactivated, standard-dose, egg-based | | | | | | | | | | | | | |
| | Inactivated, standard-dose, cell culture-based | | | | | | | | | | | | | |
| | Live attenuated, egg-based | | | | | | | | | | | | | |
| | Inactivated, high-dose, egg-based | | | | | | | | | | | | | |
| | Inactivated, standard-dose, egg-based with MF59 adjuvant | | | | | | | | | | | | | |
| | Recombinant HA | | | | | | | | | | | | | |
| Herpes zoster | Live, attenuated | | | | | | | | | | | | | |
| | Recombinant, adjuvanted | | | | | | | | | | | | | |
| Japanese Encephalitis | | | | | | | | | | | | | | |
| Yellow Fever | | | | | | | | | | | | | | |
| Tick-borne Encephalitis | | | | | | | | | | | | | | |
| Typhoid | | | | | | | | | | | | | | |
| Cholera | | | | | | | | | | | | | | |
| Rabies | | | | | | | | | | | | | | |
| Dengue (CYD-TDV) | | | | | | | | | | | | | | |

| **Antigen** | | **Pregnancy** | **Health care personnel** | **Men who have sex with men** | **Other indications/ Special situations** | |
|---|---|---|---|---|---|---|
| | | | | | | ***Considerations*** |
| BCG | | | | | | |
| Hepatitis B | | | | | | |
| Polio | | | | | | |
| DTP-containing vaccine | | | | | | |
| *Haemophilus influenzae* type b | | | | | | |
| Pneumococcal | Conjugate | | | | | |
| | Polysaccharide | | | | | |
| Rotavirus | | | | | | |
| Meningoccocal | MenA conjugate | | | | | |
| | MenC conjugate | | | | | |
| | MenACWY conjugate | | | | | |
| | MenB | | | | | |
| Measles, Mumps, Rubella | | | | | | |
| Measles, Mumps, Rubella, Varicella | | | | | | |
| Varicella | | | | | | |
| Hepatitis A | | | | | | |
| HPV | Nonavalent | | | | | |
| | Quadrivalent | | | | | |
| | Bivalent | | | | | |
| Seasonal Influenza | Quadrivalent | | | | | |
| | Trivalent | | | | | |
| | Inactivated, standard-dose, egg-based | | | | | |
| | Inactivated, standard-dose, cell culture-based | | | | | |
| | Live attenuated, egg-based | | | | | |
| | Inactivated, high-dose, egg-based | | | | | |
| | Inactivated, standard-dose, egg-based with MF59 adjuvant | | | | | |
| | Recombinant HA | | | | | |
| Herpes zoster | Live, attenuated | | | | | |
| | Recombinant, adjuvanted | | | | | |
| Japanese Encephalitis | | | | | | |
| Yellow Fever | | | | | | |
| Tick-borne Encephalitis | | | | | | |
| Typhoid | | | | | | |
| Cholera | | | | | | |
| Rabies | | | | | | |
| Dengue (CYD-TDV) | | | | | | |