

Vaccines Europe priorities for vaccination policies in Europe

Executive Summary

The protection of European citizens at the highest possible levels against infectious diseases is a shared commitment and joint responsibility of the entire public health community, including industry.

Vaccination is one of the most cost-effective public health interventions ever implemented, significantly decreasing the worldwide incidence of numerous deadly diseases and associated mortality. As often noted, however, vaccination has become a victim of its own success. Today, the European region has the highest degree of vaccine hesitancy in the world¹. As a result, Europe is experiencing a decline in Vaccine Coverage Rates (VCR) causing outbreaks of Vaccine Preventable Diseases, unnecessary deaths and avoidable hospitalisations. The Joint Action on Vaccination is timely in seeking to address these issues.

Europe has a long history of vaccine discovery, development and manufacture. More than 80% of vaccine doses produced by the major research and development led companies are produced in Europe and 86% of these doses are exported for worldwide use. Keeping Europe's lead in such a key sector and ensuring European citizens benefit from the value of vaccination requires a concerted and coordinated effort by all stakeholders. It is the position of Vaccines Europe that the Joint Action on Vaccination should address the following key areas to ensure the sustainability and effectiveness of vaccination programmes in the EU^{2 3 4}:

1. To **strengthen European surveillance capabilities** to better assess infectious disease patterns, vaccines benefit/risks and the impact of vaccination across all ages. This will provide the data required to support the design and adaptation of the National Immunisation Strategies and Programmes. The European Centre for Disease Prevention and Control (ECDC) should play a more active role in providing guidelines to Member States to ensure consistent data collection and inform future national immunisation policies.
2. The causes underlying vaccine hesitancy are multifactorial and complex. The most effective role industry can play is to continue to develop and manufacture safe and effective vaccines of the highest quality and to increase awareness by enhancing fact-based information about vaccines and vaccination. Policies and programmes should be put in place to **address the vaccine hesitancy determinants** of confidence, complacency and convenience, including the better engagement of physicians, nurses and pharmacists in actively increasing vaccination coverage.
3. Vaccines are highly technical biological products with complex and lengthy manufacturing, control and release processes. Therefore, it is important to **establish sustainable supply and demand** through an early and continuous dialogue between manufacturers and public health authorities to better anticipate the evolution of vaccine recommendations, more accurately forecast vaccine demand and introduce procurement practices that would enable better manufacturing planning and reduce risks both to the purchaser and the manufacturer. This, together with streamlining diverse regulatory requirements in Europe and worldwide will improve the sustainability of vaccine supply.
4. Vaccines manufacturers are continuously investing in new and improved vaccines. In order to continue to do so in the future, especially considering increasing regulatory requirements and public health budget constraints, an open, multi-stakeholder collaboration is needed to more clearly **define vaccine research priorities** and **to implement policies that reward innovation and ensure vaccines are appropriately valued**. Furthermore, this reflection should also explore how to overcome barriers/blocking factors to the discovery and development of the next generation of vaccines capable of addressing unmet medical needs, including antimicrobial resistance and healthy ageing^{5 6}.

¹ Larson, Heidi J. et al. (2016). [The State of Vaccine Confidence 2016: Global Insights Through a 67-Country Survey](#). *EBioMedicine*. 2016; Volume 12, 295 - 301

² WHO Europe (2014). [European Vaccine Action Plan 2015–2020](#).

³ Council of the European Union (2009). [Council Recommendation on Seasonal Influenza Vaccination](#).

⁴ WHO Europe (2013). [Health 2020: a European policy framework supporting action across government and society for health and well-being](#).

⁵ WHO (2014). [WHO's first global report on antibiotic resistance reveals serious, worldwide threat to public health](#).

Introduction

Vaccines Europe welcomes the Commission initiative to launch a Joint Action on Vaccination. This EU Joint Action represents a unique opportunity to address common challenges faced by the EU Member States as highlighted in the Council Conclusions on vaccinations as an effective tool in public health⁷, in December 2014. This becomes even more relevant against a background of increasing vaccine preventable disease outbreaks leading to avoidable death and disability, the increase of antimicrobial resistance and the ageing of the population. Industry shares the commitment of the entire public health community to protect European citizens of all ages against infectious diseases.

Europe has a long history of vaccine discovery, development and manufacture. More than 80% of vaccine doses produced by the major research and development led companies are produced in Europe and 86% of these doses are exported for worldwide use⁸. This makes Europe a leader in both vaccines and public health. However Europe also currently shows the highest level of vaccine scepticism. This already has consequences, for example, the decline in vaccine uptake in Europe has led to significant measles outbreaks and related deaths in several European countries and other parts of the world. Europe needs to address the decline in vaccination rates to ensure that EU citizens are optimally protected.

Vaccines Europe believes that the challenges affecting vaccines and vaccination can be overcome with a strategic and forward-looking approach. The EU Joint Action on Vaccination provides the needed political leadership to move forward the current status quo in the years to come (2018-2020), by enabling Member States to work together in identifying and developing the appropriate actions that can help them meet their public health objectives according to their National Immunisation Strategies and Programmes.

Vaccines Europe is committed to working with stakeholders to ensure a reliable supply of safe, effective and innovative vaccines in Europe and worldwide. Vaccines Europe has identified a number of key areas, which could significantly strengthen vaccination in Europe and facilitate the achievements of European Immunisation goals^{9 10}:

1. Strengthening European surveillance capabilities to support National Immunisation Strategies and Programmes

National Immunisation Strategies and Programmes need to evolve to meet the medical needs arising from changing infectious disease patterns in infants, children, adolescents, adults, older adults and those considered in an at-risk group. Surveillance networks and capabilities need to be strengthened to better assess (1) the burden of infectious disease (2) evolving and changing infectious disease epidemiology (3) vaccine safety (4) vaccine effectiveness and (5) vaccination coverage rates. When immunisation schedules change or incorporate new vaccines or target groups, these networks will allow tracking of the real-life impact of vaccines on diseases and will also flag trends in vaccine preventable disease evolution. Availability of these data is critical for continuous and reliable assessments to help to properly implement and/or adapt National Immunisation Strategies and Programmes.

Monitoring the benefits and risks of vaccines is complex but critical and involves multiple stakeholders. This can be particularly challenging where rapid action needs to be taken; e.g. for an urgent (updated) benefit/risk assessment.

Interaction exists between regulators and vaccine manufacturers, but in the case of vaccine manufacturers and national public health organizations/institutes, forums for dialogue are not well established, even when there is a common interest in a particular research area to generate real-life effectiveness and safety data.

⁶ European Commission (2016). [AMR: a major European and Global challenge](#).

⁷ Council of the European Union (2014). [Council Conclusions on vaccinations as an effective tool in public health](#).

⁸ Vaccines Europe Infographic (2016). [The EU Vaccines Industry In Figures](#).

⁹ WHO Europe (2014), [European Vaccine Action Plan 2015-2020](#)

¹⁰ Council of the European Union (2009). [Council Recommendation on Seasonal Influenza Vaccination](#).

The capability within the European Union for monitoring the benefits and risks of vaccines is limited and typically not integrated. Infectious disease surveillance is mostly organised by Public Health Institutes, whereas vaccination registries, when available, are managed by a variety of public organisations. Safety monitoring is mostly organised by Marketing Authorisation Holders and Regulatory Agencies. Regulatory Agencies, including the European Medicines Agency (EMA) may require vaccine manufacturers to conduct post-authorization effectiveness and safety studies. The European Centre for Disease Prevention and Control (ECDC) provides support and feedback to the Member States about vaccination programmes. In this fragmented landscape, there are recurrent challenges when there is a need to generate real-life effectiveness and safety data and combine information from different stakeholders. Ultimately most resources lie at a national level, and only the ECDC, EMA, the European Commission and vaccine manufacturers have supranational roles.

There have been some attempts to create collaborative projects between public and academic stakeholders, such as VENICE¹¹, I-MOVE¹², VAESCO¹³. However, each addressed only a single component of respectively programme evaluation, benefit or risk. In ADVANCE¹⁴, a project under the Innovative Medicines Initiative (IMI)¹⁵, substantial progress has been made in integrating benefit-risk assessment and developing the necessary public-private framework, including governance. A consortium of Public Health Institutes (PHI), regulators, academia and industry participate in this project. However, despite these advancements, the concern of public perception regarding public private partnership remains and is thus far, limiting participation of PHI in some IMI projects. Their partial successes are unlikely, today, to be made sustainable without wider support. There is, therefore, still a need for common approaches in vaccine outcome data collection, improved and harmonised communication and collaboration at EU level across Member States.

Proposals:

- 1.1. Strengthen Member States' infrastructure for data collection to track infectious disease patterns and the real-life impact of vaccines to support the delivery of immunisation programmes across an individual's life span. Data collection at Member State level could additionally be coordinated by the ECDC who should play a more active role in providing guidelines to Member States to ensure consistent data collection and inform future national immunisation policies;
- 1.2. Address fragmentation and barriers by increasing the communication channels and aligning on ways of working between the national / supranational levels and between stakeholders, including industry. Effective collaboration will ensure expanded and more effective and sustainable post-marketing surveillance of vaccines;
- 1.3. Establish/Strengthen vaccine registries that can be used both as a management tool to deliver Member States' immunisation programmes and for surveillance purposes to monitor national immunisation programmes. Data from such system can guide public health action to improve vaccination rates and reduce vaccine-preventable diseases. This would also enable national authorities, for example, to enhance communication efforts with the public if data show relatively low vaccine coverage and uptake¹⁶;
- 1.4. Establish a transparent framework for regular interactions between the ECDC and the vaccine manufacturers to enable data sharing and horizon scanning of future vaccination needs.

2. Tackling vaccine hesitancy and improving confidence in vaccination

Between 2008-2015 there were 215,000 cases of Vaccine Preventable Diseases (VPDs) in Europe, according to the *Council on Foreign Relations, Vaccine-Preventable Outbreak Maps 2015*¹⁷. These data exclude influenza which each year infects approximately ten to thirty per cent of Europe's population, and causes hundreds of thousands of hospitalisations¹⁸.

¹¹ [Vaccine European New Integrated Collaboration Effort](#)

¹² [Influenza - Monitoring Vaccine Effectiveness](#)

¹³ [Vaccine Adverse Event and Surveillance](#)

¹⁴ [Accelerated Development of Vaccines Benefit Risk Collaboration in Europe](#)

¹⁵ [Innovative Medicines Initiative \(IMI\)](#)

¹⁶ ECDC (2017). [Immunisation information systems in the EU and EEA](#).

¹⁷ Council on Foreign Relations (2015). [Vaccine-Preventable Outbreak Maps 2015](#).

¹⁸ ECDC (2017). [Seasonal influenza](#).

Suboptimal uptake of available effective vaccines is a major factor in the continued vaccine preventable diseases outbreaks in the EU. The reasons for these outbreaks are multiple but increased hesitancy towards vaccination has been identified as a leading cause. A large worldwide survey undertaken by the Vaccine Confidence Project showed that the European region has the highest negative responses in terms of perception of the importance of vaccines and their safety and effectiveness, leading to the highest degree of vaccine hesitancy in the population¹⁹.

There is not a single solution to this concern and therefore, a discussion at EU and national level should take place on how to effectively tackle the drivers of hesitant behaviour, which put both general public and the Healthcare Professionals (HCPs), at risk of vaccine preventable infectious diseases outbreaks.

The most effective role industry can play is to continue to develop and manufacture safe and effective vaccines of the highest quality and to support initiatives that enhance fact-based information about vaccines and vaccination. But the vaccine industry would like to propose a number of potential actions to address vaccine hesitancy.

Proposals:

- 2.1. Engage EU and national HCP organisations to increase awareness and education of HCP on the benefits of vaccination across the life-span with the support of the ECDC, including securing reinforced minimum vaccines training course during “Health Care Provider curricula”;
- 2.2. Organise pan-EU vaccination campaigns targeted to different groups (e.g. healthcare professionals, adolescents, parents, older adults), involving local institutions such as schools and universities, health insurance companies and civil society;
- 2.3. Reinforce alignment and streamline communications activities around European Immunisation Week in partnership with WHO Europe and consider setting up targeted initiatives around vaccination, such as a European Influenza Day to launch seasonal vaccination every year;
- 2.4. Extend access to vaccines by considering other channels e.g., vaccination by pharmacists, onsite vaccination in hospitals ward, etc., that will overcome barriers for adequate uptake;
- 2.5. Share Member States’ best practices, such as reminder systems, Government programmes to encourage HCPs to vaccinate, recommended population coverage targets, measures to ensure HCPs are vaccinated etc.;
- 2.6. Expand EU tools enabling a detailed and stratified monitoring of acceptance attitudes, baseline levels of risk awareness, as well as sentiment towards specific vaccines and vaccination programmes²⁰. These tools should be used to inform the development of evidence based communications strategies on immunisation to be implemented at the appropriate level in Member States.

3. Establishing predictable vaccine supply and demand

Supply and demand sides need to be in balance to ensure a healthy vaccine ecosystem. This should (1) recognise the strategic value of the EU vaccine industry in providing prevention against communicable diseases; (2) ensure the long-term funding of vaccination programmes; (3) measure the public health outcomes resulting from vaccination programmes; and (4) foster sustainable supply.

Today, the vaccines sector faces unique challenges that raise fundamental sustainability questions. Shortages of medicines, including vaccines are of increasing concern in the EU and globally. The causes are multiple. Finding solutions requires a concerted effort by all key stakeholders.

The manufacturing of biological medicines is highly complex and can be unpredictable. Vaccine manufacturers strive to anticipate and respond to production issues and to continuously improve production processes in order to meet demand. There are several opportunities that could help mitigate supply issues where manufacturers are trying to improve/manage the situation; these would require the support of the authorities to have the desired impact and can be summarised below:

¹⁹ Larson, Heidi J. et al. (2016). [The State of Vaccine Confidence 2016: Global Insights Through a 67-Country Survey](#). *EBioMedicine*. 2016; Volume 12, 295 – 301.

²⁰ Innovation Partnership for a Roadmap on Vaccines in Europe (IPROVE) (2016). [A strategic European Roadmap for the Vaccines of Tomorrow: A Joint Stakeholder Reflection \(2016\)](#).

3.1. Regulatory and quality issues: Vaccines are highly technical biological products with complex and lengthy manufacturing, control and release processes. Cycle times can average up to two years or more, with quality control tests representing 70 per cent of that time²¹. Unlike the vast majority of the pharmaceutical industry, control testing of each batch of a vaccine may still rely on in-vivo methods (animal testing) with their inherent variability and related risks, compounded by the dual (or multiple) batch release testing performed by health authorities. The increasing and diverse regulatory requirements worldwide, notably for post approval changes, lead to significant challenges in planning and production. This together with the diversity of country specific product and packaging and labelling requirements creates inefficiencies. Vaccines Europe member companies propose options to streamline vaccine manufacturing and to optimize existing capacity²².

Proposals:

- 3.1.1. Reduce the number of specific national/regional product and packaging and labelling requirements. This will streamline vaccine manufacturing thereby increasing supply and at the same time it will facilitate the transfer of vaccines between EU countries in case of shortages;
- 3.1.2. Reduce duplicate testing and work towards the elimination of animal testing by facilitating faster regulatory adaptation and better scientific collaboration to enable the modernization of control techniques by health authorities in line with Directive 2010/63/EU revising Directive 86/609/EEC on the protection of animals used for scientific purposes adopted on 22 September 2010;
- 3.1.3. Harmonise regulatory requirements across countries and regions and, in particular, focus on reducing the lead time for post-approval changes based on science and a risk based approach, since this currently is a major supply chain bottleneck.

3.2. Planning/anticipation: Today there is no 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 up to 24 months to manufacture and the fact that between 5 and 10 years are needed to build and license a new facility²³. A short-term response to unexpected changes of demand may be difficult as a result.

Proposal:

- 3.2.1 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.

3.3. Purchasing models: Some aspects of procurement are inconsistent with ensuring reliable supply. In general, tenders across the EU may not recognise the long lead times required for proper planning and the end-to-end manufacture and release of vaccines, as well as supply fluctuations inherent in biological processes. Tenders often seek supply for short periods of time, incorporate rigid supply requirements that cannot always be fulfilled and require significant resources to prepare. These issues become more relevant in periods of supply constraint and may contribute to exacerbate vaccine shortages.

Proposal:

- 3.3.1. Advise Member States to introduce procurement practices which would enable manufacturers to better manage risk and optimise vaccine supply e.g., longer lead times for the production and delivery of products and longer contract duration to enable better manufacturing planning and reduce risks both to the purchaser and the manufacturer.

3.4. Vaccination recommendations: When supply is constrained, there may be a need to review vaccine recommendations to ensure the continuity of the vaccination programme.

²¹ IFPMA (2013), [Vaccine Research & Development](#) – Infographic; and IFPMA (2014), [Maintaining the Vaccines Innovation Edge](#) - Infographic

²² Vaccines Europe Position (2016). [From vaccines shortages to sustainable vaccine supply.](#)

²³ Vaccines Europe Position (2016). [From vaccines shortages to sustainable vaccine supply.](#)

Proposal:

- 3.4.1. Recommend that ECDC should continue to provide, during periods of constrained supply, rapid risk assessment reports to Member States, in order to support decision-making on priority groups to receive vaccines. This could, for example, lead to delaying booster doses and to deferring vaccination of other target groups.

4. Setting up a R&D framework to develop vaccines for the future

Currently close to 30 infectious diseases are vaccine preventable but there remain many unmet needs, for example:

- Infections that have an important medical impact and for which vaccines remain elusive (e.g. cytomegalovirus, *Chlamydia trachomatis*, *Clostridium difficile*, *Staphylococcus aureus*, *Escherichia coli*);
- Infectious diseases (e.g. seasonal influenza, tuberculosis, herpes zoster) for which vaccines are already available and where efficacy could potentially be further improved through novel technologies;
- Specific populations that could be better protected (e.g. chronic disease patients, the elderly and immunocompromised patients).

Moreover in most countries across the European Union, Antimicrobial Resistance (AMR), which represents a serious threat to public health, is increasing. While existing vaccines reduce the use of antibiotics by preventing infection in the first place and by avoiding the inappropriate prescription of antibiotics for viral infections (e.g. influenza vaccines) new vaccines could play a critical role in preventing infection with multi-drug resistant bacteria, such as *S. aureus* and extra-intestinal pathogenic *E. coli*²⁴.

Through the Horizon 2020 initiative²⁵ the Commission demonstrates its commitment to European R&D. The Innovative Medicines Initiative (IMI) represents a way forward to put together all stakeholders to collaborate on different research projects. Over the last years there have been an increased number of vaccine research projects being launched under IMI and these collaborative efforts should continue. In the future the need to adapt current Commission funding rules, in particular for public-private partnerships to take into account challenges resulting from the limited number of companies involved in vaccines R&D, should be considered. Furthermore, research grants should ensure the added value of the research in order to drive research into the most beneficial areas for public health and healthcare systems. Priority should be given to efforts in discovery, pre-clinical research and early stage clinical development of novel vaccine candidates. This would align incentives for innovators with social objectives and lead to the best possible allocation of vaccine research investment. Given the impact of vaccine hesitancy and shift in public attitudes to vaccines, more funding should also be allocated to social research proposals and projects to explore the reasons behind this phenomenon.

In addition, there is a risk that innovative vaccines for which there is a medical need will not be developed nor made available to EU citizens and indeed citizens of the rest of the world if the EU fails to maintain its global leadership in the development of vaccines. This is due to increasing regulatory requirements and pressure on healthcare spending. Member States currently devote an average of 2.7% of healthcare expenditure on primary prevention and less than 0.5% is spent on vaccines²⁶. These ever-increasing quality standards and budget constraints are making it increasingly difficult for vaccine manufacturers to make additional long-term investments needed to develop and manufacture new vaccines.

Vaccine developers should have opportunities to interact with all relevant stakeholders from the earliest stages of development onwards. Such a dialogue will ensure that manufacturers understand EU and Member States' public health priorities and do not spend resources on development activities for vaccines for which approval, recommendation and use are unlikely. In the absence of

²⁴ The review on Antimicrobial Resistance (Chaired by Jim O'Neill) (February 2016). "[Vaccines and alternative approaches: reducing our dependence on antimicrobials](#)".

²⁵ Horizon 2020. [The EU Framework Programme for Research and Innovation](#).

²⁶ Ethgen, Olivier; Baron-Papillon, Florence; Cornier, Murielle (2016); [How much money is spent on vaccines across Western European Countries](#). Human Vaccines & Immunotherapeutics, Vol. 12, Iss. 8, 2016.

such systematic early and continuous open dialogue, vaccine companies pursue their investment and R&D effort to develop safe and effective vaccines of which some may ultimately never be included in the national/regional immunisation programmes and strategies.

Considerable efforts are being made at the EU level to foster early dialogue with regulators (RA) and health-technology-assessment (HTA) bodies. For vaccines multidisciplinary groups of national experts (National Immunisation Technical Advisory Groups [NITAGs]) are responsible for providing independent, evidence informed advice to health authorities on policy issues related to immunization and vaccines. The roles of NITAGs and HTA bodies in the decision making process varies from country to country. Now that parallel RA²⁷/HTA scientific advices has demonstrated its added value for drug developers we would encourage exploring the possibility of involving NITAGS in seeking parallel RA/HTA/NITAGs scientific advice for prophylactic vaccines.

In this discussion, we should also consider the recently launched strategic European roadmap for the vaccines of tomorrow (IPROVE). This roadmap is the result of an open and extensive stakeholder consultation process funded by the European Union's Seventh Framework Programme for R&D²⁸. The roadmap's ultimate goal is to avoid fragmentation in funding across Europe, to fill technological gaps and to remove the bottlenecks that interfere with translation of breakthrough research into innovative vaccines.

Finally, despite the development of initiatives to support vaccines research for Global Health Threats, experience in previous years shows that in practice it is difficult for large companies to be selected for funding, even for high impact projects (e.g. EDCTP2²⁹, H2020: TB project³⁰, HIV, malaria).

Proposals:

- 4.1. A discussion should take place on how to adapt the existing EU funding instruments to take into account: (1) the challenges resulting from the limited number of companies involved in vaccines R&D; (2) a reflection on how to increase and improve the involvement of large R&D vaccine companies in different EU vaccine projects targeting global health threats (e.g. EDCTP2, H2020: TB project, HIV, malaria), and new high priority initiatives (e.g. biopreparedness and AMR); and (3) how research grants could be better focused on the added value to support prioritisation in discovery, pre-clinical and early stage clinical development of novel vaccine candidates;
- 4.2. The IPROVE roadmap should be the basis for further discussion of selecting priority areas for funding future EU research projects and the funding model to be used;
- 4.3. Launch a multi-stakeholder reflection beyond fundamental research to more clearly define vaccine research priorities of the future given the advance of new technologies and to understand the factors blocking the development of innovative vaccines to address unmet medical needs. This reflection should also seek to understand the opportunities and barriers to whether an early and continuous dialogue throughout development could be established with all relevant stakeholders (in particular EMA, NITAGs and HTA bodies).

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²⁷ Regulatory authorities

²⁸ Innovation Partnership for a Roadmap on Vaccines in Europe (IPROVE) (2016). [A strategic European Roadmap for the Vaccines of Tomorrow: A Joint Stakeholder Reflection \(2016\)](#).

²⁹ [The European & Developing Countries Clinical Trials Partnership \(EDCTP\)](#).

³⁰ [Tuberculosis Vaccine Initiative](#).