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EUROPE & VACCINES

For effective vaccination policies in Europe

European Commission

PROTECTING HEALTH, SAVING LIVES

EU cooperation against vaccine-preventable diseases

Worldwide vaccines prevent every year

- 2.7 million **MEASLES**
- 2 million **NEONATAL TETANUS**
- 1 million **PERTUSSIS**

VACCINATION IN THE EU

Influenza vaccination coverage rates among people **aged 65+**

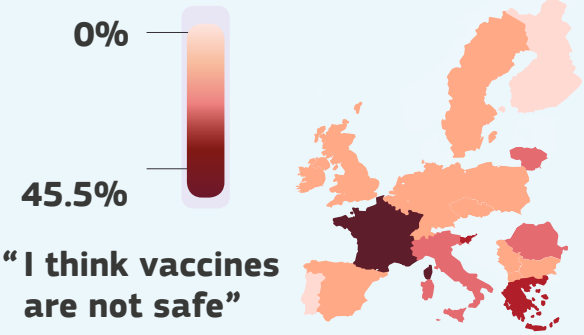
UK 71%
NL 67%
EU 34%
BG 2%
EE 2%

INFECTIOUS DISEASES ON THE RISE

More than **14 000 measles** & **696 rubella cases** in 2017

RO - 5 608 measles
IT - 5 098 measles
DE - 929 measles
GR - 967 measles

DISTRUST IN VACCINES



"I think vaccines are not safe"

EU ACTION

- Ensure **ACCESS** to vaccines for all
- Control all vaccines to ensure **HIGHEST SAFETY STANDARDS**
- Share **CLEAR**, **INDEPENDENT** and **TRANSPARENT** information
- More **RESEARCH** to develop new vaccines

Sources: ECDC; Eurostat; WHO; The Vaccine Confidence Project

European Commission: **ec.europa.eu/health/vaccination/overview_en**
European Centre for Disease Prevention and Control: **ecdc.europa.eu**
@EU_Health #EUvaccines

Health and Food Safety

EDITORIAL

EUROPE & VACCINES

Vaccination is the primary instrument for prevention in public health. Thanks to vaccination programmes, life expectancy in the world is one of humanity's greatest achievements. According to the WHO, vaccination can prevent between 2 and 3 million deaths per year worldwide.

Nowadays, several European and neighbouring countries are facing the return of some epidemics thought to be long forgotten, the resurgence of which is mainly due to a lack of vaccination coverage.

In an increasingly digitalized and introverted society, misinformation is on the rise, social media pose a new challenge when it comes to maintaining confidence in immunization. However, the use of digital tools would facilitate and improve vaccination programmes throughout Europe, using interoperability of systems, monitoring data, procurement and a real-time supply status, preventing waste, all as a way of fighting fire with fire.

Our policies and scientists must have a clear and unambiguous narrative about the need for vaccination and its coverage. The collective interest of vaccination should be more clearly highlighted. Providing reliable information to the general public and dispelling myths about vaccines and vaccination through the exchange of good practices is key to ensure effective public health.

For several years now, the sub-optimal vaccination coverage observed in Europe has led the European Commission to step up its vaccination efforts by working closely with Member States. In December 2018, the Council adopted a recommendation to strengthen EU cooperation against vaccine-preventable diseases. Subsequently, it established a roadmap to ensure better cooperation between Member States. A feasibility study on the development of a common EU vaccination map was launched this year. A draft common vaccination document, which could help EU citizens to continue their vaccination in the Member States, is expected to be completed in 2022.

Europe plays an important role in the production of these vaccines. Several European countries have experienced a shortage of vaccine production and supply which has hampered the implementation of their vaccination programmes. The Commission is considering the creation of a European virtual data warehouse on vaccine needs, which could facilitate the voluntary exchange of information on available supplies. This would ensure that the necessary measures are in place in the event of a pandemic.

Vaccination policies fall within the purview of national authorities. However, the EU must ensure fair access to vaccines for all EU citizens through free distribution in order to remove major financial barriers, combat disinformation and build confidence in vaccines, facilitating a vaccination pathway from an early age.

Vaccination is first and foremost about education for all of us. In this issue of The European Files, we capture the responses of our institutions and hope to encourage a public discussion faithful to the greater good.

Editor-in-Chief
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The benefits of digital tools for improving immunisation programmes

EU2019.FI

Krista KIURU

Finnish Minister for Family Affairs and Social Services

Immunisation programmes are one of the most cost-effective public health interventions, saving millions of lives every year. In addition to protecting individuals, vaccines can also protect the whole population against epidemics as well as significantly reduce healthcare and societal costs. A unique benefit of high vaccination coverage is herd immunity – population-level protection for individuals who cannot be vaccinated because they are too young or have pre-existing medical conditions.

While many new effective and safe vaccines have been introduced in national immunisation programmes in recent years, vaccines are still underused and vaccine hesitancy is posing a threat to the high vaccination coverage needed to stop the spread of communicable diseases in communities and internationally.

Council Recommendation (2018/C 466/01) on strengthened cooperation against vaccine-preventable diseases is a comprehensive and ambitious commitment from the Member States and the Commission to jointly ensure that European citizens have the full benefit of existing and new vaccines. The recommendation highlights eHealth and digital innovations as important new tools for improving immunisation programmes.

Comprehensive immunisation information systems are essential

Electronic vaccination registries or immunisation information systems (IIS) can show up-to-date vaccination coverage across all age groups and sub-populations, as well as in different geographic or healthcare-providing areas. Full interoperability of different electronic systems and registries is essential. For example, the IIS data can be analysed together with the disease-surveillance data to monitor the real-time impact of vaccines, both in terms of effectiveness and safety. The IIS data combined with vaccine procurement data can show the supply situation in real time and reduce vaccine wastage. The IIS can also provide new opportunities to inform those at risk that they should be vaccinated. This can be achieved through automated reminders via email, SMS alerts and dedicated health apps. When integrated with electronic healthcare records, the reminders can also target healthcare professionals, so that every time a patient visits any healthcare facility, the visit can be utilised as an opportunity to administer vaccine doses missed during previous visits.

All individuals should have easy access to the data on vaccines they have received. The IIS can generate individual electronic vaccination cards that can be accessed online — while respecting data protection and privacy requirements, naturally.

Some EU countries already have an operational IIS. However, more effort is still needed both at EU and Member State level to develop operational guidelines and remove infrastructural, legal and standardisation barriers in order to facilitate interoperability and electronic immunisation-data-sharing. The feasibility of developing a common EU vaccination card should also be explored as a matter of priority.

Internet and social media as tools to improve vaccination coverage

Never before has the creation, distribution, use and, unfortunately, manipulation of information been this easy. Ideally, the internet should provide fast and easy access to reliable information on vaccination to the public. However, the experience so far has been that misinformation from anti-vaccine groups may spread even faster than science-based information provided by healthcare professionals and public-health authorities. New digital information tools could correct the trend by using different context-based strategies to counter the spread of misinformation and create partnerships with civil society and other relevant stakeholders.

Modern website algorithms seek to determine which information a user would like to see, based on their previous internet activity. This might be harmful to both individuals and society if it leads to increasing hesitancy and mistrust concerning vaccines or information provided by health authorities. On the other hand, sophisticated search algorithms could also play an important role in addressing vaccine hesitancy. Health systems could be developed to individually tailor messages most likely to resonate with citizens. The real-time analysis of internet and social-media discussions and networks could also be utilised in vaccine confidence monitoring and to identify possible safety concerns.

Sustainable EU-level collaboration to improve vaccination programmes

Immunisation programmes are the responsibility of the Member States. However, it is clear that we should also enhance EU-level collaboration. Pursuant to Article 168 of the Treaty on the Functioning of the European Union (TFEU), a high level of human health protection is to be ensured in the definition and implementation of all Union policies and activities. Union action, which complements national policies, is to be directed towards improving public health, preventing physical and mental illness and disease, and obviating sources of danger to physical and mental health. The EU Joint Action on Vaccines and other initiatives provide important platforms for the creation of EU-level added value for immunisation programmes. In addition to initiatives and networks, we should also strengthen the role of the European Centre for Disease Prevention and Control (ECDC) as an EU agency responsible for providing scientific advice and support to Member States on the development and adaption of new tools to improve vaccination programmes.

To eliminate measles in Germany: The Measles Protection Act. Requirement for all children entering school or kindergarten to have both measles vaccinations

Jens SPAHN
Germany's Federal Health Minister

Measles are among the most contagious infectious diseases and – contrary to the widespread narrative – they are not a 'harmless children's disease'! In fact, globally, measles cases even doubled in 2018. In Germany, a large number of children, young people and adults are still not vaccinated against measles. This means that they can shed and spread the pathogen, causing repeated outbreaks. We cannot let this go unchallenged.

The best protection against measles is vaccination. Vaccines afford immunity for life. Therefore, I most strongly believe that not only do people who fail to have themselves or their children vaccinated put their own life and health at risk, but, as we live in an open society, they do the same to others. My goal is to protect all children in Germany, if at all possible, from measles infection – at day care facilities, at their day care mother's home and at school. This is why we seek to make measles vaccination mandatory in all of these settings. We want to do this by introducing the "Measles Protection Act". With the approval of the German *Bundestag*, it will become effective in spring of next year.

What specific regulations do we have in mind? Going forward, all children entering school or kindergarten will need to provide evidence of the two measles shots recommended by the German Standing Committee on Vaccinations (STIKO). This proof will also have to be furnished if the child is being looked after by a day care mother. Persons who work in these settings will also have to be vaccinated against this dangerous infectious disease. The same applies to staff working in healthcare facilities. Exempted from mandatory vaccinations are persons for whom the vaccine would not be safe on medical grounds and persons born before 1970. In the absence of this proof, the child can be barred from attending school or day care. Parents of school children will face a fine. After all, it is the same as in road traffic: if you put others at risk and get caught, you have to pay a fine.

Between August 2018 and late July 2019, more than 13,000 measles cases were reported across Europe. In Germany, as many as 485 cases were registered by early September of this year. In 2018, a total of 544 cases were reported nationally for the entire year. Measles commonly involve complications and lead to secondary conditions. One in 1,000 children who contract measles will develop a brain inflammation known as measles encephalitis. Children under five, and adults over 20 years of age, are at an increased risk of experiencing serious complications. This clearly debunks the argument put forward by many vaccine deniers that measles usually takes a mild course therefore rendering vaccination unnecessary.

However, according to current evaluations done by the Berlin-based Robert Koch Institute (RKI), despite all of the campaigns to educate the population, the measles vaccination gaps in Germany are still too large. While it is true that 97.1 per cent of all children starting school have had their first shot, there are large regional differences in the numbers of those getting the second, decisive shot. This means that, at Federal level, we still fall short of the target immunisation coverage of 95 per cent. Only this coverage rate can afford what is known as 'herd immunity'.

According to new data from the RKI, a good 93 per cent of children who started primary school in 2017 have had two measles shots. Here, it must be said that not all of the parents who failed to get the second shot for their child on schedule are out and out 'vaccine deniers'. This can be seen from the fact that the children already had their first shot. Apparently, there are those parents who just lose sight of the second shot and its importance for long-term immunity. It may be that the family is growing or that the demands of work, the children starting school and going about their hobbies sometimes make it hard to organise daily life. With all of that, the second shot is easily forgotten. We can therefore assume that our new regulation will provide a welcome reminder in these cases. And I trust that it will result in more children getting both measles vaccinations.

The case might be different for people who are against mandatory immunisation for other reasons. In such cases, reference is often made to the question of proportionality and the right to "free choice regarding vaccination". My counterargument is that any person who sits in a paediatrician's waiting room with their baby, who is still too young to be vaccinated, must be able to rely on the older children in the waiting room not having measles. That too is a precondition of freedom – and it applies particularly to those entrusted to our care who are children. And even more so to children who cannot be vaccinated for medical reasons. Naturally, it also becomes the State's business if unvaccinated children attend day care facilities and schools. This is especially the case if, as in Germany, school attendance is mandatory.

Being unvaccinated not only poses a considerable threat to the physical well-being of the affected person themselves but also constitutes a risk to other persons who, for example, because of their age or specific health limitations cannot be vaccinated. That is why mandatory vaccination must begin as early as possible and must begin in those places where people come into daily contact with one another.

Vaccination is one of humanity's greatest achievements. We have almost eradicated infectious diseases that in earlier generations took the life of many millions of people. I therefore have the utmost confidence that through this piece of legislation vaccination will become the norm and vaccination myths will be exposed. Mandatory vaccination for children should also cause parents to reflect and to ask themselves: why am I not vaccinated? In short, mandatory vaccination is health education!

In a free country, I must be able to bank on the fact that the person sitting opposite me does not pose a danger to me. That too is a precondition of freedom. We have an obligation to protect our children, so that they do not become infected and infect others. If parents do not do it, then the State must take action! No child in Germany should ever again become infected with measles or die as a consequence of this disease.

Place vaccination at the forefront of the public space

Agnès BUZYN

French Minister for Solidarity and Health,
Extract from the article in European immunisation week

As you know, vaccination is a topic dear to me. I am committed to it because vaccination is the great exponent of our history and a symbol of the progress in medicine and the fight against obscurantism.

Pasteur has blazed the trail that we are all walking on. Everyone can see that the fight against vaccination is never safe from opposing, still very dangerous, forces.

As soon as I took office, I made vaccination one of my top priorities. The choices and decisions I made were dictated by the context of vaccine hesitation and the resurgence of the epidemics we are facing.

It was also vital to place vaccination at the forefront of the public space and to have a clear, strong and responsible public narrative.

It is therefore with the greatest pleasure that I am here with you today for a new phase, the launch of European Immunisation Week 2019.

2018 and 2019 are two pivotal years in which many milestones have been set for vaccination.

Including vaccination as one of the priority issues of the Priority Prevention Plan presented in March 2018 by Edouard Philippe is a decisive support to this proactive policy.

Extending the immunisation obligations to infants or simplifying the vaccination process for seasonal influenza vaccination are all measures that redefine and revitalise the vaccination policy in France.

The European Immunisation Week was first launched back in 2005 at the behest of the World Health Organisation.

Many events, coordinated by Regional Health Agencies, such as the "vaccination info villages", take place in the regions during that Week every year.

These actions bring together a wide panel of field operators: health and education professionals, the civil society, health insurance funds, supplementary mutual insurances, scientific societies and professional associations, whom I sincerely thank for their work throughout the year towards improving the health of our fellow citizens.

I would like to start with a brief overview of the actions and steps taken since 2018.

I have proposed reforms that affect the daily lives of our fellow citizens in a spirit of collective and solidarity-based protection.

I am referring, of course, to the extension of the immunisation obligations to infants, which was implemented as early as 1 January 2018, alongside a whole series of support tools for the health professionals, parents and communities, including assistance in monitoring these obligations before children enter the community;

I am also thinking of simplifying the vaccination process for people eligible for seasonal flu vaccination since, from now on, anyone going for their first vaccination will have the choice to go to a nurse's or pharmacist's, in addition to a doctor's or midwife's practice;

By the upcoming 2019-2020 season, Influenza vaccination by pharmacists will have been generalized. As everyone knows, increasing vaccination opportunities by simplifying the process it is the best way to trigger this collective effort on the part of our fellow citizens.

Actions to inform and promote vaccination have been stepped up.

With the launch of the vaccination info service website for the general public and access of this vaccination info service website to professionals;

Also with, – and this is the key –, the commitment of all professionals. I should like to thank in particular the associations of health-care professionals that support the government vaccination policy. Their signing the charter last fall reflects their commitment to promoting the vaccination of these professionals.

We are right to wager on a proactive policy: our actions are starting to bear fruit.

As I had announced and as prescribed by law, I will present a review of the reform of the immunisation obligations at the end of 2019. Indeed, in order to take stock, we need to give children born after January 1 time to grow up a little and benefit from the vaccines.

The results are already noticeable, and the first immunisation coverage data for children born between January and May 2018, at the age of 7 months, is proceeding as expected.

For hexavalent vaccination, which, may I remind you, includes vaccinations against DTP, whooping cough and Heamophilus influenzae type B infections and hepatitis B, we have gone from 93.1% (compared with the same period in 2017) to 98.6%.

Vaccination coverage against meningococcal C infections with one dose is now estimated at 75.7%, compared with only 39.3% over the same period in 2017. We have clearly made significant progress here, too.

Vaccination coverage for the MMR vaccine for children born in 2018 is not yet available because this vaccination begins at the child's first birthday. But the vaccination rate also progressed in 2018, from 85 to 87.2% for the first dose, which was hoped for in the face of the tragedies caused by the epidemic we experienced then and are still seeing with the 2019 outbreaks.

The movement brought about by the reform of the immunisation obligations benefits vaccination in the broadest sense.

The rate for the first dose of HPV vaccine among 15-year-old girls, albeit still far too low, has improved, rising from 26.2% for girls born in 2002 to 29.4% for girls born in 2003.

In terms of parents' participation, Santé publique France has also carried out surveys among parents of children under two years of age.

Parents' opinions about the importance of vaccination for children's health is increasing by +5 points (compared with June 2018). The perception of collective vaccination protection is making progress in the same direction.

A slightly less positive figure: 47% of the parents admit to being unfamiliar with the immunisation obligations for infants. We, institutions and health professionals alike, must therefore keep up our collective efforts, in terms of communication with and information to the parents.

Finally, the Collège de la médecine générale, in partnership with Santé publique France, interviewed a number of general practitioners.

99% say they are in favour of vaccination in general, and 75% of them perceive the extension of the immunisation obligations as a positive step. I do not know whether the latter figure will increase, or whether it reflects the bitterness of having to exercise pressure in order to increase the immunisation coverage.

We are well on our way to achieve the collective protection of the new generations, and I cannot help but think that every point gained in vaccination coverage means fewer tragedies.

I know that there are still parents out there who fear the adverse effects of vaccination, but the risks of not vaccinating a child are infinitely higher.

As I was committed to this for the sake of transparency, to which I am very much attached, I will also present a pharmacovigilance report at the end of the year.

The National Agency for the Safety of Medicines and Health Products (ANSM) is working with stakeholders and will present in June 2019 a first progress report on the safety of mandatory vaccines for children under 2 years of age vaccinated during the years 2012-2017 (i.e. before the implementation of the reform).

With this new approach, a reference framework for pharmacovigilance is a necessary prerequisite. This inventory will be accompanied by data on the first 6 months of the implementation of the reform of the extension of immunisation obligations from January to June 2018.

While our first actions are already taking shape, and in a positive way, many challenges still await us and we must restore confidence and keep being vigilant.

We face recurring clustered cases of measles; and the latest outbreak has attracted the interest of the media. These situations, which mark the return to times and epidemics we believed were over, are due to the inadequacy of measles vaccination coverage, particularly among young adults.

That is why the current measles epidemic, although less intense than in 2018 but still worrying, needs to raise our awareness about the potential seriousness of this disease: it was responsible for one death early in 2019, and I would like to remind you that in 2018 three deaths were linked to this disease.

This epidemic must also make us aware of the need to protect ourselves against measles in order to protect the most vulnerable.

Similarly, despite our efforts, the rate of seasonal influenza vaccination among the target population is 50%, a figure that remains well below the WHO target of 75%.

I am also thinking of the vaccination against HPV. Initial activity data show an increase, but we are still a long way from achieving our goal. Preventing cervical cancer is yet a major challenge.

We must therefore build upon this dynamic and consolidate our foundations:

I have asked the Haute Autorité de Santé (HAS or High Authority for Health) to propose changes for even simpler vaccine pathways, and expanding the vaccination skills of the health professionals will do just that;

I also asked the HAS to extend the HPV vaccination programme to young boys;

Experiments will also be conducted between 2019 and 2020 to identify new means for action to promote vaccination.

- A project is underway to make vaccines available in doctors' and midwives' practices,
- An experiment is being conducted to bring the professionals closer to the young with the aim of promoting and improving the HPV vaccination coverage.

Finally, this year, Santé publique France will conduct a nationwide survey in a number of health facilities and EHPADs (residential establishments for dependant elderly people) to assess the vaccination coverage of the health professionals, and identify the obstacles to their vaccination against influenza. On this basis, we will launch in 2020 trial cooperation actions between professionals to promote the vaccination of health professionals.

And I will conclude with a more comprehensive objective, to which the European Immunisation Week is contributing: restoring confidence.

Restoring confidence by talking about vaccination, restoring confidence by having a clear, strong and responsible narrative.

Restoring confidence also by being there where the French citizens get their information and by combatting misinformation or disinformation. Fake news is a scourge, as rampant and dangerous as ever.

Health-wise, the European Union is also a major field of action. Health is our common good, and Europe has a role to play.

Since September 2018, France has been coordinating a joint European action on vaccination. This action, which is planned over 3 years, will strengthen cooperation and communication between all Member States in order to have common tools at their disposal and to fight, for example, against vaccine hesitation or fake news.

Coming back to the European Immunisation Week, I would like to stress that this event of general mobilisation extends beyond our boundaries and gets the same message across everywhere to rally around the same objective.

Our common objective of promoting vaccination will have a new and very concrete translation this year.

Dedicated supra-structural vaccination organizations: the driver of a successful vaccination schemes

Maggie DE BLOCK

Belgian Minister of Social Affairs and Public Health and Asylum Policy and Migration

Success and high participation in vaccination schemes by the population is a multi-layered issue. A solid reimbursement regulation and the mere availability of vaccines will not guarantee that there will be a high uptake or vaccination coverage. Two other equally important drivers to success are the supra-structural organization responsible for vaccination and the legal framework regarding vaccination.

First lets highlight how supra-structural organizations for vaccination can contribute to a high coverage. By this we mean all facilities that assure the successful functioning of a vaccination program. In Belgium, the government guarantees access to vaccination for all children. Three supra-structural organizations oversee the administering of vaccines: Kind & Gezin in Flanders, ONE in Wallonia and Kaleido DG in Ostbelgien. Working in close collaboration with the maternity department in the hospitals, these organizations assure basic vaccination and the follow-up according to the vaccination scheme for young children set by the government. The presence on the field of this supra-structural organizations leads to a vaccination coverage among newborn babies of over 93% in both Flanders and Wallonia for the most essential recommended vaccination.

In Wallonia nearly 55% of these vaccines are given to children by the ONE, 35% by private pediatricians, 5% by general practitioners, 5% by hospital services. (Groupe de réflexion scientifique Vaccinations, 2016) In Flanders a totality of 85.4% of the children were vaccinated by Kind & Gezin, 9.5% by the pediatrician, 4.4% by the general practitioner and 0.7% by other authorities, for example vaccination programs overseas. (Vandermeulen C, e.a., 2017)

In Flanders, Wallonia and Ostbelgien a supra-structure of medical supervision works in schools themselves (CLB, PSE and Kaleido-DG). Every two or three years each pupil visits this medical service. The visit of school children to these facilities gives a unique access to vaccination. Flanders started with HPV vaccination for girls through this medical school supervision supra-structure in 2010, which led to a vaccination coverage of 90%. In Wallonia this supra-structure was not offering this possibility. Only approximately 35% of the eligible female target population is vaccinated. Luckily since 2019 with new HPV-vaccines on the market, both in Flanders and Wallonia this supra-structure will now offer HPV-vaccination to all boys and girls. The coverage of vaccination against measles, is different in the two parts of our country: in Wallonia and Brussels, 75% of the adolescents are vaccinated, while in Flanders 93% is vaccinated. A recent rapport (Devos C, 2019) on the Belgian health system, showed however the necessity that not only actions are needed to attain a high level of vaccination in children, but also for the detection and vaccination of non-vaccinated adults in order to prevent outbreaks.

Reaching the elderly is a challenge. How can we establish a dedicated supra-structure to reach the elderly population easily in terms of pro-active vaccination? In contrary to the maternity wards and the schools where the eligible target population flocks together, the major part of the elderly population is scattered all over the geographical area, except for elderly homes. An interesting option to study is whether a dedicated team in a home nursing service could take up this role similar to the supra-structural organizations to ensure pro-active vaccination in this population.

A second driver for vaccination might be to make it compulsory by law. In 1966 the Belgium government made poliomyelitis vaccination obligatory for each newborn child. Today, with a coverage of 97,2% Belgium is at the point of eradication. An obvious question is: why not make all vaccinations obligatory?

An advice on the matter by the Belgian Advisory Committee on Bioethics expresses a pragmatic and valuable approach regarding this question: "It is ethically unacceptable for a parent to deny his / her child a vaccine that is effective against a serious and preventable disease such as poliomyelitis or tetanus. On the other hand, it is ethically acceptable to refuse the vaccination of his / her child if the balance of vaccination / disease risks is not scientifically decisive. Parents must always make their decisions in the best interest of the child, and it is legally and ethically unacceptable for them to make decisions that are manifestly to the detriment of their child." (Belgian Advisory Committee on Bioethics, 2015) This conclusion undoubtfully will be used as a benchmark in the debate should the anti-vax movement keep growing.

Summing up, making vaccination complementary by law, should be a last resort. However, when the public health is at stake, such drastic measures need to be considered. The priority is to invest in common sense of the citizens and to ensure supra-structural organizations that can facilitate and contribute to pro-actively vaccinate the population. Especially in adult and older populations, there is a gap to fill.

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Promote vaccination, particularly the childhood immunisation programme and the HPV vaccine for both girls and boys

Simon HARRIS
Irish Minister for Health

"Misinformation about vaccines is as contagious and dangerous as the diseases it helps to spread." Dr Tedros Adhanom, Director-General of the World Health Organisation, September 2019

Global life expectancy gains resulting from universal immunisation programmes represent one of the greatest achievements of humanity. The irony is that this success can lead to complacency as we forget the morbidity and mortality caused by diseases such as smallpox and polio in the past. In recent years in Ireland we have had to face new challenges to vaccination confidence. Much work has gone into restoring that confidence but undoubtedly this work is not over.

HPV Vaccine Uptake Under Threat

Chronic infection with Human Papilloma Virus (HPV) infection causes cervical cancer, along with other cancers of the vulva, vagina, penis, anus, and oropharynx. A school-based programme of HPV vaccination for teenage girls began in Ireland in 2010. It was initially well received with an 87% uptake in the 2014-15 academic year. However, following a coordinated anti-vaccination campaign this plummeted to an estimated 50% in 2016-17. Anti-vaccine campaigners managed to utilise both traditional media and social media to spread misinformation about the HPV vaccine with devastating effect.

The response to the drop in HPV vaccination uptake required a co-ordinated effort from a wide range of stakeholders. This included the formation of an HPV Vaccination Alliance (www.hpvalliance.ie), led by the Irish Cancer Society, to promote the vaccine and regain parental trust.

The role of patient advocates in the Alliance was vital in connecting with the public. I would particularly like to remember the contribution of one such advocate, Laura Brennan, who sadly passed away at the age of 26 in March this year as a result of cervical cancer. Her legacy will be the lives saved through her inspirational efforts to encourage girls to get vaccinated. Her work and the work of everyone involved in the HPV Vaccination Alliance has seen uptake rates dramatically improve to over 70%. In addition, from this academic year, boys in secondary school are now able to avail of HPV vaccination which will further reduce HPV related cancer deaths in years to come.

The Vaccine Alliance

Regrettably, Ireland has experienced a drop in the uptake of many of our other routine childhood vaccinations over the past five years. This has been associated with recent national outbreaks of vaccine preventable diseases such as measles and pertussis and has highlighted the need for on-going vigilance regarding our childhood immunisation programmes.

In September this year I launched the Vaccine Alliance which includes members from a wide range of health and civil society organisations. The alliance will look to replicate and build on the good work done by the HPV Vaccination Alliance. Their vison is to ensure all children in Ireland are protected from vaccine preventable diseases and I will support them in whatever way I can to achieve this goal.

Social Media

Although the absolute effect on vaccine uptake is difficult to measure, I have no doubt that social media has played a role in undermining confidence in vaccination. The dynamic nature of social media presents a new challenge for maintaining confidence in immunisation programmes worldwide. Misinformation on social media has the potential to spread and amplify in manner not seen before. However, it also provides an opportunity to disseminate information regarding the benefits of vaccines to a wide audience especially younger generations who are less inclined to use traditional media.

It has been heartening to see that social media companies have begun to recognise the important role they can play in preventing the spread of vaccine misinformation on their platforms. Information about vaccines on social media can be misleading. I welcome efforts to direct parents to trusted sources of information with the appropriate scientific advice which can enable them to make the right choice to vaccinate their children. From an Irish perspective, I look forward to engaging with social media companies in the coming weeks and months to discuss what further measures can be put in place to combat vaccine misinformation.

The Role of the European Union

Cooperation between member states plays an important role in protecting the health of all Europeans as infectious diseases do not respect national boundaries. We have seen evidence of this with the rise in outbreaks of measles across Europe in over the past couple of years.

Within the European Union I would like to especially commend the ongoing collaborative research on Vaccine Hesitancy. "The State of Vaccine Confidence in the EU 2018" report highlights the need to maintain high levels of confidence in vaccination programmes to achieve herd immunity but also underlines the complexities involved, including both individual and environment factors that can influence confidence.

At an international level I think it is important to recognise the role that transnational agencies play in protecting us all. The work of the GAVI Alliance has seen huge strides being made in countries that would otherwise not be able to financially support and organise national immunisation programmes. Similarly, the work of the WHO and of representative member states in reacting to Public Health Emergencies of International Concern and preparing for future pandemics is vital and I hope this work continues and strengthens into the future.

Vaccinations save lives

Vaccinations have saved millions of lives since they were first introduced towards the end of the 18th century, and we continue to improve and strengthen our vaccination programmes with the introduction of more vaccines, like those against HPV and rotavirus, as they become available. It would be a travesty to see this progress stall or regress, however there are worrying signs both in Ireland and in Europe. I therefore call on all member states to redouble their efforts in maintaining robust childhood immunisation programmes to protect the futures of all children in Europe.

European Commission roadmap on vaccination

Anne BUCHER

Director-General DG SANTE, European Commission

Last September, during the Global Vaccination Summit in Brussels - co-organized with the World Health Organization (WHO), I was particularly moved by the presentations of two of our participants: Ethan Lindenberger, at the age of 18, went against his mother's anti-vaccine stance and inoculated himself; and Kevin Brennan, whose sister Laura Brennan died of cervical cancer this year aged 26 after dedicating her last two years of life to advocate for the HPV vaccine - which she had not received[1] . What struck me most about both of these cases, was that they could – and should - have been unnecessary.

Yet, these testimonies are crucial. According to a 2018 WHO/UNICEF report, vaccine hesitancy has been reported in more than 90% of countries worldwide, while according to a recent Eurobarometer, 38% of Europeans believe that vaccines could cause the illnesses from which they protect[2].

Let us be clear - vaccines work. In 1980, the World Health Organization declared smallpox, which once killed 400,000 in Europe each year, to be eradicated. This was as a direct result of extensive vaccination campaigns. These campaigns save lives. In 2019 three EU Member States lost their measles-free status. There is still work to be done.

Vaccination is a safe and cost-effective way to protect people – especially infants and young children – from certain infectious diseases. Despite this, many children in Europe go unvaccinated and remain vulnerable to potentially life-threatening diseases. The key to preventing serious consequences as a result is to ensure that every community is not only prepared but also well informed that vaccinations protect the individual and those around them.

At the EU level, our role is to assist countries in coordinating their policies and programmes. The European Commission has stepped up its action on vaccination, working closely with EU Member States and key partners in the global community. In December 2018, the Council adopted a Recommendation to strengthen EU cooperation on vaccine-preventable diseases. Moving forward, the European Commission has set out a roadmap to ensure better cooperation among Member States.

Firstly, a feasibility study on the development of a common EU vaccination card began this year, with a proposal for a common vaccination document that could help EU citizens continue their vaccination across Member States, is expected in 2022.

The Commission will continue the development of safe and effective new vaccines through Research programmes Horizon 2020 and the upcoming Horizon Europe.

The bi-annual Report on the State of Vaccine Confidence in the EU started in 2018. Its role is to monitor attitudes to vaccination on a regular basis. Based on this, guidance that can support Member States in countering vaccine hesitancy will be presented by 2021.

Information is key, in particular to counteract the increasing trend on hesitancy in some of our countries. The European Centre for Disease Prevention and Control (ECDC) will establish a European Vaccination Information Sharing system and provide guidance for developing relevant and trustworthy sources of information for the public, as well as a European vaccination information portal to be launched next year.

The Commission will support countering online vaccine disinformation and develop evidence-based information tools and guidance for Member States in responding to vaccine hesitancy. Communication on vaccination, explaining the myths, misconceptions and skepticism that surround this issue will be a priority for the next College.

In the field of vaccine reserves, the Commission is considering a virtual European data warehouse on vaccine needs, which could facilitate the voluntary exchange of information on available supplies, possible surpluses and global shortages of essential vaccines. This would ensure that necessary measures are in place in the event of a pandemic.

We also want to ensure, along with industry, that a steady supply of vaccines is available, while ensuring a diversity of suppliers, and to exploit the possibilities of joint vaccine procurement. Measures such as these are already being rolled out. 15 Member States and the Commission have signed framework contracts for the production and supply of pandemic influenza vaccines guaranteeing access to vaccines in the case of a pandemic.

Recent years have shown us that the spread of contagious diseases do not respect borders. Europe has not only a responsibility to its citizens but to the global community as well, as evidenced by its work this year in central Africa. Thanks to close cooperation of Member States and the European Medicines Agency (EMA), more than 1.5 million doses of a new Ebola vaccine in the Democratic Republic of Congo have now been stocked.

Together in the EU, we have built solid foundations that will serve us well for success in the future. Let us keep up the fight to relegate further diseases to history, and ensure that following generations no longer die from preventable causes, and avoid further speeches like those of Ethan Lindenberger and Kevin Brennan.

1 https://ec.europa.eu/health/vaccination/ev_20190912_en

2 https://ec.europa.eu/health/sites/health/files/vaccination/docs/20190426_special-eurobarometer-sp488_en.pdf

A cancer vaccine: how to eradicate virus-related cancers in Europe?

Véronique TRILLET-LENOIR

Oncologist and MEP, Renew Europe, France, Member of the ENVI Committee

Some cancers are virus-induced. Among them, human papillomavirus (HPV), responsible for sexually transmitted cancers of the cervix, anus, penis, vulva and the ENT region.

The vaccine against the virus is effective: 26 studies conducted on 73,000 women and which compare the risk of cervical cancer depending on whether or not they had been vaccinated with a follow-up of up to 8 years have been compiled: the risk of developing lesions leading to cancer has been reduced by 99%. These studies do not show any side effects that can be attributed to the vaccine.

The European Centre for Disease Prevention and Control (ECDC) therefore recommends that Member States vaccinate girls aged 10-14 years with 3 doses.

However, the vaccination schedule remains an exclusive competence of the Member States.

The recommendations vary greatly from country to country in the European Union: vaccination is recommended at different ages (from 9 to 26 years), most of the time only for girls, at different doses (2 or 3 doses), and since 2017 it has been extended to boys in Italy, offered at school in Hungary and Ireland, free or partially reimbursed (France), etc.

Vaccination coverage is also very uneven: above 70% in Sweden, the United Kingdom, Northern Ireland, Spain, Portugal, Italy, Malta, Hungary, Belgium, 50-60% in Finland, the Netherlands, Denmark, Latvia, 30-50% in Germany, Slovenia, below 30% in France, Luxembourg, Greece, Cyprus, Poland, Slovakia, Romania and unknown in Estonia, Lithuania, the Czech Republic, Austria, Croatia, Bulgaria.

The gaps in coverage are due to a lesser extent to discrepancies in Member States' recommendations than to a growing phenomenon of mistrust of vaccines, largely fuelled by significant disinformation about their risks and leading to a strong hesitation from citizens regarding vaccination, in particular parents for their children.

What can the European Union do?

In order to respect gender equality regarding diseases, and given the proven efficacy of vaccination for male cancers, it is important to review ECDC's recommendations for gender-neutral programmes to include young boys.

The European Union should also encourage an increase in the number of teenagers vaccinated (ideally 90%) and guarantee fair access to vaccination by preventing the risk of shortages.

Last but not least, informing and educating people is key in order to raise citizen awareness about the issues at stake.

Updating European guidelines, working on hesitation regarding vaccination and setting up surveillance records for vaccine coverage should be part of a future European Cancer Plan.

Clinical Evaluation of vaccines

Prof. Guido RASI
Director Executif of EMA

Vaccines are arguably among the most cost-effective and successful interventions in public health. Regulatory authorities are responsible for evaluating vaccines prior to marketing authorisation and continually monitor vaccines that are placed on the market to ensure requirements for quality, safety and effectiveness are met. Robust and established criteria for evidence to be generated during vaccine development are in place and illustrated in dedicated up to date guidance documents issued by EMA. EMA also offers the possibility of scientific advice to discuss elements related to a specific vaccine, that cannot be addressed by guidelines.

Several new vaccines are currently under development. These cover pathogens for which a vaccine is not yet available or pathogens for which current options may provide further improvements. In order to efficiently advance the development of these vaccines, it has been advocated for a more conducive environment to foster vaccines research and development in the EU and retain the current vaccines expertise and infrastructure.

Innovative technologies such as nucleic acids and viral vectored vaccines, including heterologous prime-boost strategies, or alternative routes of administration such as needle-free mucosal administration, are emerging approaches requiring where an understanding of the underlining science is needed to establish regulatory requirements.

In early clinical studies, the aim is usually to determine safety and immunogenicity of the vaccine in a limited number of vaccinees, according to different doses and schedules, so to define the posology to be progressed into later clinical studies. Research geared towards gaining more insight into the immune response that confers protection after vaccination or natural exposure would help in streamlining the development of new vaccines. In addition, new generation assays for both humoral and cell mediated immune responses could facilitate antigen(s) and regimen selection, and support definition of correlates of protection with major impact on the development process.

In case there is no immune marker that can be accepted as surrogate endpoint for protection, and whenever possible, studies to determine the efficacy of the vaccine in preventing the disease in the target population is required. Depending on the incidence of the infectious disease to be prevented, often these randomised studies require large sample sizes, in the order of the thousands, to meet the study objectives.

For several diseases and pathogens, the conduct of field efficacy trials is hampered by the relative rarity of cases that can be recruited in a reasonable timeframe. In such instances, provided feasible and scientifically adequate, approaches such as human challenge studies, or inferring protection from animal models of disease, have been proposed. More in-depth understanding of these models and their surrogacy is needed to help regulators in determining their value across the different development phases.

Late stage clinical trials usually provide major contribution to the safety database of the vaccine. Besides standard requirement for the safety evaluation of medicinal products, adverse events of special interest following immunisation are proactively collected in the clinical trials. The actual size of the safety database at time of approval may vary for each vaccine depending on the identified potential risks. However, in principle the database should be sufficiently large to estimate the frequency of uncommon adverse events (occurring in-between 1/100 and 1/1000 vaccinated persons). Depending on the vaccine and the target population, there is a need to consider the number of subjects in the target population within a certain age range or belonging to any special population, e.g. immunodeficient subjects or pregnant women, to be included in the safety database.

After approval, there is a need to make sure that, vaccines are continuously monitored so that emerging information on their benefit risk balance is rapidly evaluated. To facilitate this, risk management plans are put in place at time of approval summarising, among other aspects, the activities needed to gather additional information on the safety of the vaccine. Effectiveness studies, that reflect real-world efficacy in terms of both the direct and indirect effect of the vaccine, are in certain cases required as post-approval commitments. The existence of networks that can rapidly conduct safety and effectiveness studies in the post-authorisation phase would be instrumental for a timely and efficient collection of these data. Collaboration with public health authorities is often necessary to allow the conduct of these studies, which calls for a structured and transparent collaboration among the different stakeholders. A platform that would enable the conduct of these studies across the EU would be of major public health relevance as it would support more rapid and better-informed public health policy decisions on vaccination in Europe through knowledge sharing and utilisation of common methodologies. At the same time, it would also facilitate rapid and robust regulatory decisions on individual vaccines.

Overall, provision of greater assurance on the robust evaluation of vaccine safety and vaccine effectiveness, would improve public confidence in vaccines and vaccination monitoring programmes.

Indeed, the growing phenomenon of vaccines hesitancy is negatively affecting vaccination campaigns in many countries in the EU and elsewhere in the world, with detrimental consequences on the ability to protect citizens and save lives due to the spread of vaccine preventable diseases. Regulators have a major role to play in improving transparency and providing easily accessible way information on vaccine product ingredients and the assessment of quality, safety and efficacy, including safeguarding their scientific integrity. The collaboration with ECDC, health care professionals and other authorities around the world, to raise awareness on safety and effectiveness of vaccines, and the creation of an EU vaccination portal to proactively share information on vaccines and vaccination in the EU, are important steps forward in that regard.

Improving pan-european collaboration in tackling vaccine-preventable diseases

Andrea AMMON
ECDC Director

If you could easily protect yourself from harm – wouldn't you? Taking the example of vaccines, we see that they have led to significant reductions in the number of cases of many diseases. Smallpox, for example - once the deadliest disease known to humanity - has now been completely eradicated. Polio is present in only a handful of countries, and the number of cases of measles and rubella are but a fraction of what they once were.

But despite these major achievements for public health, outbreaks of vaccine-preventable diseases such as measles continue to occur across Europe, due to insufficient numbers of vaccinated people in many countries. The target for measles elimination in 2020 will be missed, and measles vaccination coverage has fallen steadily over the last ten years. False claims about immunization threaten to undermine public confidence in the safety and efficacy of vaccines, and are being spread on the internet and social media. In addition, several European countries have experienced shortages in vaccine production and supply, which has hampered the effective implementation of their vaccination programmes.

Facilitating exchange between EU Member States

There is no simple answer how to address these challenges. But many of them can be tackled more effectively if we work more closely together at the pan-European level. Whilst each country is responsible to organise and deliver healthcare to its citizens, it makes sense to facilitate information sharing and to pool knowledge and best practice around vaccination between Member States.

Following a 2018 Council Recommendation on strengthened cooperation against vaccine-preventable diseases, the European Centre for Disease Prevention and Control (ECDC) is embarking on a new journey in the fight against vaccine-preventable diseases. One important task is to lead a new collaboration between European public health and immunisation experts. It provides a forum for experts from EU Member States and countries of the European Economic Area (EEA) to come together and discuss current priorities, issues and best practices.

This new collaboration builds on existing structures – so called National Immunisation Technical Advisory Groups (NITAGs), that are established in most European countries and whose scientific assessments form the basis of national recommendations around vaccines. These NITAGs, or equivalent expert committees, provide decision-making bodies with evidence-based advice to ensure that local policy is well informed with the latest scientific knowledge.

Improved national decision-making

The collaboration between the different NITAGs, facilitated by ECDC, will enable the sharing of published and unpublished evidence generated at national level through an online platform and through a series of webinars. It will also serve as a system for countries to work together in synthesising the evidence on vaccines and their use in immunisation programmes through conducting joint reviews of the latest evidence, and through the development of mathematical models on vaccination.

The result of such close exchange of knowledge and practice will ideally lead to more transparency, efficiency, effectiveness and consistency in the national decision-making process on vaccines and immunisation policies. It should also reduce the duplication of work that exists across countries in evaluating the evidence base, and lead to greater opportunities for sharing good practice and expertise. ECDC will also assess the feasibility of developing guidelines for a core European vaccination schedule, and work to improve vaccination coverage monitoring systems.

Building trust

The reasons why people are not getting vaccinated are manifold and complex. ECDC is helping to build and regain trust in vaccination by providing credible information to healthcare professionals, policymakers and also the wider public. One more step in that direction is the ongoing development of an online European vaccination portal to provide evidence-based information on immunisation - in plain language that everyone can understand.

Vaccines have brought tremendous health benefits to our world – much more than we often realise. ECDC is therefore committed to strengthening Europe's defences against vaccine-preventable diseases, and will continue to help Member States build confidence and trust around vaccines.

Sustain vaccination programmes through a healthier vaccine ecosystem in an interconnected Europe

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Since the emergence of vaccination, life expectancy has increased between 15-25 years, and further gains are expected. Evidence suggests that the control of infectious diseases through vaccination largely contributed to this increased life expectancy.

Many infectious diseases, which were once commonplace, are increasingly rare because of vaccination. Take smallpox, for example – an infectious disease which killed hundreds of millions of people globally. It is now eradicated thanks to vaccination, and we are on the verge of eradicating polio.

Despite the tremendous progress made, there are major trends of the global public heath context directly impacting the vaccine ecosystem:

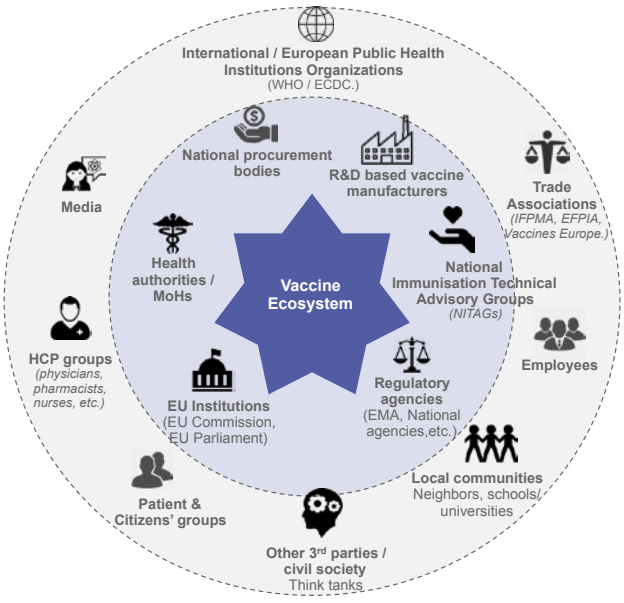
- Growing/ aging world population which challenges both national health structures and budget
- Infectious diseases still being major public health threats, with still circulating infectious agents, like polioviruses or measles, despite existing vaccines and continuous evolution of bacteria and viruses resulting in new emerging diseases (Ebola, Zika…)
- Urbanisation and increasing migration and displaced populations from areas of conflicts, which raise new vaccine prevention challenges to be addressed, including for Europe.

Continuing in the path of progress for immunisation is dependent on a healthy vaccine ecosystem.

Over the last decade, the vaccine ecosystem has proven to be vulnerable, with increasing risks of unbalances, the most visible being vaccine shortages.

The global vaccine ecosystem comprises a large variety of actors, including the European actors, both at regional and country levels, notably EU Institutions, Member states governments, healthcare professional associations, vaccine manufacturers, patients' groups, as illustrated in figure here below.

Vaccine Ecosystem Interdependancies chart



Each of the actors of the ecosystem has its own role and is impacted by the behavior of the others, among others:

- For regulatory agencies, to set guidelines for high quality, safe and efficient vaccines
- For the EU and National public health institutions, to define vaccination policies/ programmes according to the epidemiology, existing vaccines and their benefit-risks at population level
- For the procurement agencies, to plan and procure vaccines based on the demand, the immunization programme and the budget defined by the governments
- For the manufacturers, to develop and produce vaccines with the required quality and regulatory standards, and supply countries according to demand signals.
- For the healthcare professionals (HCP), to implement vaccination policies and get target populations vaccinated accordingly
- For the population, to access reliable and accurate information on vaccination they need

Because of these high interdependencies, major impact on one "species" can put at risk the ecosystem balance, with consequences such as reduced access to vaccines/vaccination globally and reduced Research & Development (R&D) investments in new vaccines.

Indeed, still today, we too often see:

- Cost-containment policies and tender processes-based solely on the lowest price criteria resulting from governments and public health partners willingness to minimize vaccine budget.
- Limited visibility on the vaccines demand: knowing that it takes up to 3 years to produce vaccines, a 1-year tender contract does not allow us to anticipate the manufacturing.
- Highly specific national regulations creating delays to vaccine access. For example, to reach a Chinese baby, a vaccine lot manufactured in Europe is tested 3 times and sometimes with different test methods or norms.

These global trends are damaging for the vaccine industry, mainly the R&D based vaccine manufacturers 'species' including the ones based in Europe. We produce vaccines that have been researched for worldwide population, investing massively in development of vaccine and large-scale manufacturing biotechnologies as well as manufacturing infrastructures/ facilities. An average of 16% of our income is spent in R&D of new vaccines, complying with highest level of standards of evidence generation (eg. Efficacy Randomised Controlled Trials involving thousands of patients[1]).

In comparison, the emerging countries vaccine manufacturers produce mainly heritage vaccines for the emerging world that were researched and developed by the R&D-based manufacturers, with a clear focus on high volume and low price. They spend on average 2% of their annual income in R&D, some even benefiting from donors' or government's funding for their manufacturing infrastructures.

Over the last decade, the concentration of R&D based manufacturers was observed, with, consequently, shrinkage of R&D investments for new vaccines against new diseases. Only five companies are carrying out 63% of the most urgently needed vaccine R&D projects[2].

In addition, decisions for industry to invest in Europe are increasingly challenging as incentives are much higher in other territories like Singapore and the USA. Further loss of vaccine manufacturing capacity and capabilities in Europe would have direct consequences for the European population, with progressive loss of control over its own vaccine supply and over its biodefence. Europe would then become reliant on imported vaccines supplies and in the event of epidemics or even more worryingly, a pandemic or a biological attack, EU Member States will find themselves competing with non-EU countries for available vaccine supply, risk losing out, as local manufacturers might prioritize their home markets and geopolitical partners. This should raise concerns knowing infectious diseases evolution risks and the antibiotic resistance context.

Invigorating the vaccine ecosystem is critical to sustain vaccination programmes

Fortunately, we see encouraging EU initiatives on vaccination (i.e. Council Recommendation and the Joint Action on Vaccination) that demonstrate the strong commitment from Europe to stay at the forefront of vaccination policies & innovation, and lay the groundwork for a necessary 'healthier' vaccine ecosystem. Supply & preparedness to health threats, fight to stop vaccine misinformation dissemination, HCP coalition on vaccination are critical topics that contribute to set up a policy climate supportive of a European-based vaccine industry, with continuous investments in R&D and in manufacturing capacity for a sustainable supply of high-quality vaccines.

In a few months, Germany will take the EU presidency fora a semester, and the European Health Data Space appears to be one of their priorities. Digital transformation of healthcare systems has the potential to boost R&D and innovation in vaccines. Not only it will open a new era in vaccine innovation, but it will also create opportunities to accelerate clinical

1 https://clinicaltrials.gov/ct2/show/NCT01427309

2 2018 Stat+ - Access to Medicine Foundation report https://www.accesstomedicineindex.org/publications/2018-access-to-medicine-index

development of new vaccines or new indications and to reduce the related costs, while assessing the real-world impact of vaccines thanks to the electronic health registries.

Sanofi Pasteur is contributing and committed to engage with all vaccine ecosystem actors to address the key challenges that require coordinated efforts.

› *Sustainable supply and procurement practices*

Sanofi Pasteur has a strong legacy in vaccines and produce vaccines against 7 bacterial diseases and 8 viral diseases. More than 1 billion doses of vaccines are produced each year in 12 sites, in France, North & South America, and Asia.

We all concur on the fact that poor forecasting, inappropriate procurement mechanisms and increasing regulatory barriers are impacting ability to supply vaccines to the population.

At Sanofi Pasteur, we have conducted our own assessment of the roots causes that impact our capacity to supply our vaccines through a specific company initiative to improve supply security and we have action plans in place to optimize our Industrial affairs processes accordingly. In parallel, we actively contributes to the existing collaborative work within the trade associations at global and EU levels (IFPMA & VE), with regular interfaces with WHO on this topic. Optimising public procurement practices and better demand anticipation is also central in our discussions with Health Authorities at National levels.

› *Continuous investment in vaccine Research, development & Innovation*

As R&D remains Sanofi Pasteur's DNA, we are investing more than 500 million euros each year, with five R&D sites (Europe and North America) and employees representing 15% of the overall Sanofi Pasteur's staff.

However, due to drastic evolution of regulatory standards and requirements for pre-clinical and clinical trials, the cost of development (R&D, global licenses) and industrial equipment for a new vaccine is estimated between 0,5 and 1 billion Euros. As a result, the private sector can no longer develop new vaccines at risk, without any visibility on a possible return on investment.

Interesting new solutions approaches have emerged as either public-private partnerships. These are new sources of value sharing, coordination and cooperation for the world, as for instance for the usage of electronic health data**.** Sanofi Pasteur is committed to R&D open innovation, notably via Innovative Medicine Initiative (IMI) projects (eg. Antimicrobial resistance, healthy ageing, pertussis) in Europe and contribute to the ongoing discussions on the new Horizon Europe 2021-2027 framework.

› *Use of electronic medical records in new vaccine development*

The development of a new vaccine classically requires from 10 to 15 years with massive investment ranging from $200 million to $1 billion (including construction of manufacturing facilities).

Convinced by the fact that digital health data opens a new era in vaccine, Sanofi Pasteur is supporting the Northern California Kaiser Permanente (NCKP) vaccines research unit in the conduct of an unprecedented, innovative real-world evidence clinical study to evaluate the relative effectiveness of different flu vaccines available in the US.

The data used are generated during routine clinical practice within the NCKP healthcare system in the US, using their integrated digitalized patient record system enabling the tracking of influenza events, complications in outpatient and inpatient facilities and vaccination status. The novel approach of this pragmatic study allows the prospective inclusion and cluster randomization of a total of 1.6 million vaccinees over two years – which would, have never been possible in the traditional clinical trial setting.

Similarly, we have just started a similar pragmatic randomized controlled database trial in partnership with the Finnish Institute of Health and Welfare (THL). This study possible in a European country is one example that demonstrates the power that integrated electronic health registries can have on vaccine evaluations, allowing better understand the performance of vaccines in a real-world environment, helping to demonstrate the value of a vaccine, and providing insights for future vaccines development.

Conclusion

As recently mentioned by Professor Panos Kanavos *'In order for the vaccine ecosystem to be "healthy", all relevant stakeholders should be taken into account'*[3]*...*, including the vaccine industry.

Moving forward, we should maintain dialogue and jointly seek common solutions for:

- a more balanced and healthier vaccine ecosystem, in order to tape the full potential that vaccination has both on the sustainability of the European healthcare systems, and on releasing pressure on its health care resources.
- a favorable environment for vaccine industry investments in R&D and manufacturing in the EU countries, that provide similar incentives than other attractive regions
- an interconnected Europe that facilitates patient electronic medical data collection, including vaccination records, and enables interoperability of health information systems to connect data, for the benefits of public health and vaccines innovation.

This would contribute to a healthier Europe, where 'no one should die or suffer from a vaccine-preventable disease' and to reduce cross border health threats.

3 Professor Panos Kanavos (associate professor LSE) during the European Health Policy Forum Gastein https://www.euractiv.com/section/health-consumers/special_report/a-healthy-vaccines-ecosystem/1388050/

Looking ahead to the next decade for immunization in Europe

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Vaccination is widely recognized as one of the most successful public health interventions ever developed. Vaccines have been responsible for the eradication of smallpox and rinderpest, near eradication of polio, control of several other once ubiquitous diseases and untold millions of saved lives. Yet their full potential for preventing diseases and thereby contributing to society in broader ways, from preventing lost days at school, savings in healthcare costs, lost wages and productivity due to illness to reducing the risk of antimicrobial resistance, has not yet been realized. With the end of European Vaccine Action Plan 2015-2020 (EVAP) approaching, this is an opportune moment for the countries in the European Region to reassess progress and design a path forward that will help ensure the people of the European Region enjoy both optimal use of and the full benefits of vaccines.

In 2014, all 53 Member States of the WHO European Region (Region) unanimously committed to do more in the area of immunization and agreed on a set of key goals for their national immunization programmes. In addition to setting priorities, EVAP is a tool for the national immunization programme managers to lobby decision-makers for adequate programme funding; for ministries of health to benchmark and compare their progress to that of other countries; and for populations to gain better protection against vaccine-preventable diseases.

EVAP centers on a vision of what can be achieved through vaccination – the control, elimination or eradication of vaccine-preventable diseases. Realistic regional goals, including sustained polio-free status and measles and rubella elimination, laid out together with enabling objectives, such as financially sustainable immunization programmes, have served as a roadmap to achieve this vision.

In 2018, at the midpoint of EVAP, a detailed review was conducted to assess progress based on identified targets and milestones. What this review found was a mixed picture. Overall coverage increased, to 91% for the first dose of measles-containing vaccine in 2018, for example, but not by enough. Progress made in some countries did not match that in others: middle-income countries that lack any external donor funding or support were especially lagging behind in terms of achieving the vaccination coverage targets and providing their populations with the benefits of newer vaccines. Measles coverage in the European Region as a whole is the highest in the world (together with the Western Pacific Region), yet measles and rubella elimination will, most likely, not be achieved during the life of EVAP and large measles outbreaks have swept through communities and countries, killing over 70 people in 2018 alone.

The ongoing measles outbreaks in the Region affecting even countries with high reported immunization coverage expose dangerous immunization gaps in individual and community protection against this and other vaccine-preventable diseases. To stop the diseases that vaccines can prevent, more must be done in the Region to systematically identify the root causes leading to these coverage gaps and to devise effective responses in a tailored way to close them.

Immunization as a platform to provide other pertinent healthcare benefits, including the role of immunization in contributing to financial risk protection against health costs, will positively contribute to the concept of attaining Universal Health Coverage by the countries in the Region. With EVAP coming to an end in 2020, a strategic agenda for the next decade to amplify the efforts of countries to improve vaccination coverage and thereby protection against vaccine-preventable diseases in every community will give achievement of Universal Health Coverage a healthy boost in the Region.

A European strategic agenda for immunization for the next decade, developed by the countries in Region, will outline strategic focus areas to address the root causes of gaps in vaccination coverage in every community in the Region. The strategic focus areas will allow further strengthening of immunization systems to comprehensively reach everyone so that countries can attain and sustain the disease elimination and eradication goals of the Region in the next decade. Building on the principles enshrined in EVAP and insights gained through its implementation, the starting point for this new strategic agenda will be equity – every person in the European Region should have the same quality of opportunity to enjoy the benefits that the existing and future vaccines offer. Innovation and partnerships at all levels will be key to achieving this.

The new European regional immunization strategy will contribute to the strategic priorities outlined in Immunization Agenda 2030, a new global strategy for immunization. By aligning itself to the principles of primary health care, the new regional strategy will be anchored in a "people at the centre" approach to developing national policies.

The strategic focus areas in the new strategy will be guided by national priorities and based on local data and evidence. National immunization stakeholders will thus be in the driver's seat, both in development of the regional strategy and in its national adaptation and implementation. Only in this way can the new regional immunization strategic agenda apply to all peoples, all nations and all institutions in the Region.

Securing a robust vaccine sector in Europe

Magdalena RODRIGUEZ de AZERO
Executive Director, Vaccines Europe

Vaccination certainly constitutes one of the most cost-effective preventive measures existing today and a foundation of public health programmes in Europe and worldwide. Vaccines play a fundamental role in reducing the morbidity associated to a number of diseases, including certain types of cancer and chronic conditions. Vaccines are also part of the solutions to reduce antimicrobial resistance. Today, there is a vast range of vaccines available to protect against more than 30 infectious diseases – and there are new vaccines on the horizon with the potential to prevent even more.

Vaccination, therefore, makes a substantial contribution to health, healthcare systems, and society at large, and health is the cornerstone for a competitive economy. However, health systems are still largely built on treating illness, not promoting health. In Europe, the overall spending on primary prevention and vaccination is relatively low compared to overall healthcare spending: on average, less than 3%[1], and 0.5% of Member States' total healthcare budgets respectively is dedicated to immunization programmes.[2] The number of publicly funded vaccines included in national immunisation programs still significantly differs within Europe[3]. Moreover, only a few countries start to account for the change in demographics that we are all experiencing with many Vaccine Preventable Diseases (VPDs) remaining uncovered due to insufficient budget provision. When it comes to investing in healthcare, we should ask ourselves whether the balance is right.

Vaccines are a distinctive product for a number of reasons. First of all, they are a prevention tool administered to a large number of healthy people which is affecting the benefit-risk assessment. Secondly, compared to other medicines, vaccines are highly technical biological products with complex and lengthy manufacturing, control and release processes, starting from live micro-organisms to end with safe and sterile products. These special features mean that the development and production of vaccines are particularly time-consuming, demanding, complex and costly and expose it to numerous risks for disruption.

More broadly, the vaccine industry constitutes a strategic sector for the European economy. Europe has a long history of vaccine discovery, development and manufacturing, and benefits from a strong industrial infrastructure. While major innovative vaccine manufacturers are global in nature, many of their operations are based in Europe. 80% of vaccine doses produced by Vaccines Europe (VE) members are being manufactured in the European region and 86% of these doses are exported for worldwide use[4]. Guided by the constant pursuit of innovation, the vaccine industry scores a 16% of revenues invested in research. This high rate of investment is 50% greater than the software and computer services[5]. Keeping Europe's lead in such a key sector and ensuring that European citizens benefit from the value of vaccination requires a concerted and coordinated effort by all stakeholders.

Vaccine manufacturers strive to anticipate and respond to production issues and to continuously improve production processes, invest in new sites or expand the existing ones. A quick response to increased demand is most of the times not feasible due to the long vaccines production lead times and to the time needed to increase capacity. Since the production of vaccines involves biological processes, the manufacturing of one lot of vaccine takes between 12 months for monovalent vaccines and more than 36 months for some complex multivalent vaccines. Up to 70% of that time is dedicated to quality control. The increase of production capacities through the construction of a new plant may take between 5 and 10 years from inception to production and release of the first vaccine lot.

In contrast to the broader pharmaceutical industry, the global vaccine market is limited to relatively few manufacturers. It is due to the manufacturing complexity of biological products, the need for significant investments up front to develop new products, building and maintaining the facilities, and guaranteeing the quality of the product with increasing regulatory requirements. All this, together with a cost-driven policy that does not sufficiently incentivise research and development efforts, makes the vaccine industry a "fragilised" sector. We have seen that some European countries have divested national vaccine manufacturing (e.g. Rijksinstituut voor Volksgezondheid en Milieu (RIVM) in the Netherlands and Statens Serum Institut (SSI) in Denmark), and the same is happening in the private sector with companies leaving the vaccine space[6].

This is worrisome and, in this context, a well-balanced vaccine ecosystem, which recognises the true value of current and future vaccines as well as the strategic value of the EU vaccine industry is absolutely critical. What can we all do together to make sure we keep Europe at the centre of vaccine research and manufacturing in the future?

1 Gmeinder M; Morgand D;Mueller M (2017). How much do OECD countries spend on prevention? https://www.oecd-ilibrary.org/docserver/f19e803c-en.pdf?expires=1569405811&id=id&accname=guest&checksum=6744C8AF05558BA46D9F2FB79CEBD486

2 Olivier Ethgen & others https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4994728/

3 https://www.sciencedirect.com/science/article/pii/S0264410X18308727?via%3Dihub

4 https://www.vaccineseurope.eu/about-vaccines/vaccines-europe-in-figures/

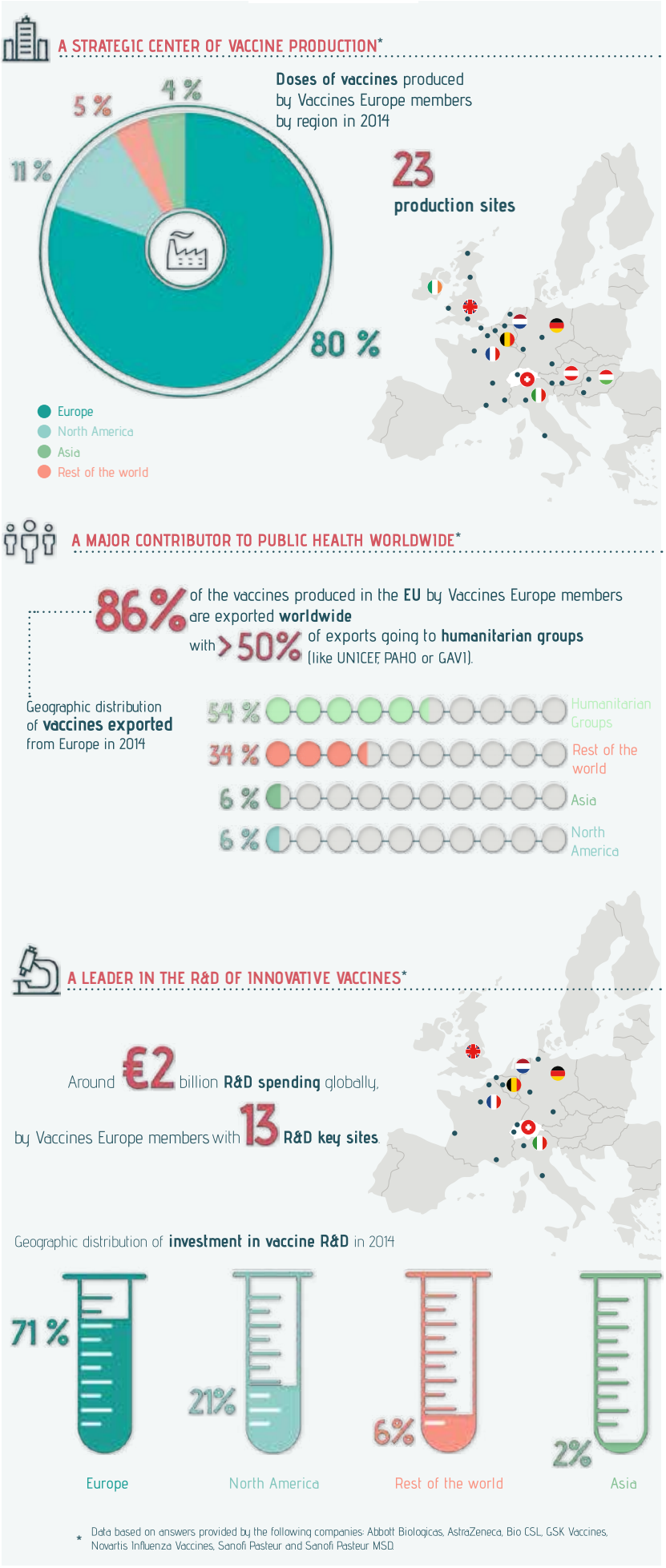
5 Data provided by WifOR Institute is based on the 2018 EU Industrial R&D Investment Scoreboardhttps://publications.jrc.ec.europa.eu/repository/bitstream/JRC113807/eu_rd_scoreboard_2018_online.pdf

6 https://www.pharmaceutical-technology.com/news/newsgsk-pharma-completes-acquisition-of-novartis-healthcares-vaccines-business-4683437/

The research-based vaccine industry in Europe continues to be committed to 1) invest in future vaccines and capacity building, to 2) seek efficiencies and innovative solutions to further improve manufacturing and supply, and to 3) work with National and European authorities and stakeholders on the solutions proposed in the Council Recommendation on strengthened cooperation against vaccine-preventable diseases and the Joint Action on Vaccination, especially on research, development and improving sustainable supply of vaccines in Europe and globally.

In addition, Vaccines Europe recommends (1) to address the lack of a stable policy environment to support vaccine innovation with appropriate pull mechanisms, together with a fair recognition and reward of vaccines value, (2) to continuously interact with all stakeholders from the earliest stages of development – especially regulatory authorities and recommending bodies to ensure that resources are not spent on developing vaccines that are unlikely to be approved and recommended, (3) to better connect and coordinate vaccine research while also focusing on research for diseases of low-income countries and pandemic preparedness to better anticipate and prepare for future health threats, which is one of the greatest challenges of our time (4) to keep the right balance between treatment and prevention when it comes to investing in healthcare and to account for the shift in demographics in Europe within the national immunisation plans.

Keeping Europe's lead in such a key sector is crucial if the EU does not want to become reliant on imported vaccine supplies and ensure that European citizens benefit from the value of vaccination.



Harnessing the power of partnerships to develop life-saving vaccines

Dr. Pierre MEULIEN

Executive Director, Innovative Medicines Initiative (IMI)

It is universally well accepted that vaccination is one of the most effective lifesaving public health interventions the world has as its disposal. So far, two mammalian diseases have been officially wiped out through vaccination campaigns. Smallpox, which plagued the human race for thousands of years (it was responsible for about 400,000 deaths in Europe every year in the 18th century) was officially eradicated in 1980. Rinderpest, which caused infections in cattle, buffalo, antelope, deer and related species, was eradicated in 2010.

Many other diseases have been and are being controlled today through massive vaccination campaigns worldwide. These include diphtheria, tetanus, polio, some forms of meningitis, otitis, whooping cough, pneumonia, hepatitis A&B, measles, rubella, mumps, chicken pox, influenza and others.

Europe plays an important part in securing the production of these vaccines. Indeed 80% of the world's vaccines are produced on European soil and we can also boast some of the best groups involved in vaccine research and development in the world.

This is one reason why so much vaccine oriented research is funded through the Innovative Medicines Initiative (IMI), a public-private partnership (PPP) between the European Union and the European pharmaceutical industry.

Vaccine research lends itself well to the PPP model because there are many areas where there is a need for collaboration between industry, academic researchers and others to create multi-stakeholder groups that have the expertise, data and resources to address major gaps and solve challenges in vaccine research and development. Only by working together in this way can we hope to accelerate the time from the research bench to clinical assessment in humans.

Over the past 11 years of IMI we have invested over EUR 430 million (from public, private and philanthropic sources) in 17 projects covering a whole host of issues. The IMI vaccine portfolio can divided roughly into two main chapters. The first includes projects covering general bottlenecks in vaccines R&D, including ways of assessing vaccine efficiency, manufacturing quality, and vaccine safety, for example. The second is about how Europe responded to the pandemic threat of Ebola in 2014.

Spotlight on Ebola

When the Ebola crisis broke in Africa in 2014, there was no vaccine, no rapid diagnostic, no anti-viral therapy; in short, nothing that we could offer patients or those at risk in order to squash the epidemic. The IMI Governing Board reacted immediately by allocating a significant budget and launching a series of Calls for proposals for European and African groups to accelerate research on vaccines, rapid diagnostics, manufacturing platforms and clinical trials platforms. To date, we have invested over EUR 300 million in this area and the resulting IMI projects have been spectacular in how they have enabled valuable implementation in the field. One vaccine went from bench to the clinic within one year, while another project worked on analysing the immune responses to another Ebola vaccine both in Europe and Africa. Three rapid diagnostics are being field-trialled as we speak and manufacturing at scale strategies have been worked out in yet another project. The project teams have also been working with social scientists and technologists to ensure public acceptance of the local campaigns through educational and outreach programmes.

Within our Ebola portfolio there are projects focused on rapid diagnostics which are badly needed for this disease. It is so important to be able to detect as quickly as possible whether people presenting with symptoms have Ebola (in which case they need to be isolated) or another illness. Four IMI projects are dealing with this issue and have mobilised laboratories in Europe and Africa as well as small biotech companies and the diagnostic industry to provide creative solutions. Currently several of the resulting prototypes have been approved to be used in field trials in the current DRC outbreak.

We have another project called ZAPI ('Zoonoses anticipation and preparedness initiative'), which brings together experts in human and animal health to create new platforms and technologies that will facilitate a fast, coordinated and practical response to new infectious diseases as soon as they emerge. The project has chosen three viruses that have been known to make the leap from animal to human. These are Rift Valley fever (usually infecting cattle, sheep, camels and goats), Schmallenberg virus (cattle sheep and goats), and Middle East Respiratory Syndrome (MERS, whose usual reservoirs include bats and camels).

Addressing some of the biggest challenges in vaccines research

The other part of the IMI vaccine portfolio deals with some hot topics in vaccinology. For example, while we know a lot about how antibodies neutralise incoming pathogens, we know a lot less about how cellular immunity works, and what potential markers of immunity could be in different settings. Here, IMI's FLUCOP project is looking at many immunological parameters to decipher which markers correlate with a protective response to flu vaccines. The results of this project are currently being used to design future influenza vaccines and could help us design the ultimate universal flu vaccine.

We are also looking at vaccine safety as the bar for safety in vaccination is set extremely

high - and for good reason - as vaccines are used mostly in prevention strategies and therefore intervening in healthy populations where safety should be paramount. Thanks to our projects, we now understand much more about the human immune system and how to harness this optimally in order to maximise the desired immune response against a specific infectious agent while minimising the risk of adverse events.

Taking action on vaccine hesitancy

Finally, we need to address the issue of vaccine hesitancy in Europe. There has been a lot of misinformation coming from the anti-vaccine lobby which needs to be countered by evidence based data covering the epidemiology of disease in Europe and the positive impact of the use of vaccines. IMI's ADVANCE project's 47 partners come from 19 EU countries and include the vaccine industry, the European Centre for Disease Prevention and Control, the European Medicines Agency, national public health laboratories and academic experts. The project has delivered a blueprint of an efficient and sustainable vaccination benefit-risk assessment tool that is acceptable to all stakeholders. This is a major achievement and provides a platform for solid monitoring of the benefits and safety of vaccines.

Recently ADVANCE has driven the creation of a not-for–profit international organisation called VAC4EU. Its goal is to provide, in a consistent and stable manner, the evidence that the European citizen and policy makers have been asking for. Hopefully this will increase the confidence that the EU citizen has in vaccines so that we can together avoid dramatic situations like the recent explosion of cases of measles in 47 European countries, solely due to a decrease in vaccination rates. We have a collective responsibility to share solid evidence on the benefits of vaccination so that our populations can remain immunised against the most deadly diseases that historically had such a devastating impact on our societies.

Introducing IMI

The Innovative Medicines Initiative (IMI) was set up in 2008 as a public-private partnership between the European Union (represented by the European Commission) and the European Federation of Pharmaceutical Industries and Associations (EFPIA).

For 2014-2020, IMI's total budget is EUR 3.276 billion. Of this, EUR 1.638 billion comes from Horizon 2020, the EU's funding programme for research and innovation. EFPIA companies have committed EUR 1.425 billion to the programme, and up to EUR 213 million can be committed by other organisations that decide to contribute to IMI as Associated Partners in individual projects.

At IMI, our goal is to improve the medicines development process and make it more efficient, and to ensure that patients will have faster access to better and safer medicines. We do this by funding collaborative projects that bring together all key groups involved in life science research. Through our projects, we are funding innovative solutions to the most pressing medical burdens of our time, including antimicrobial resistance, dementia, and diabetes.

Over a decade in, we are globally recognised as a pioneer of open innovation and an attractive model for successful public-private partnerships (PPPs) in research.

Interested? Find out more at imi.europa.eu

Vaccination, Population Health, and European Leadership

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Vaccination coverage in Europe is high in both historical and comparative perspectives. Based on available data, coverage for all antigens recommended for routine immunization by the World Health Organization (WHO)[1] has increased or remained at high levels over the last one to two decades. For most of these vaccines, Europe is at or near the top of the list for coverage in comparison with other geopolitical regions of the world.

Although there are myriad causes of morbidity and mortality, it is not a coincidence that vaccine coverage is high in Europe and life expectancy is also long. In fact, life expectancy at birth in Europe has increased five years since 2000 and is higher than in any other WHO region. Europe's high life expectancy is due in part to having the world's lowest mortality rate for children under the age of five—to which pediatric vaccination indisputably contributes—and is further bolstered by high longevity for adults who have reached the older ages—to which adult vaccination contributes.

Europe's deep commitment to vaccination coverage has also relieved some pressure on its health budgets. Prevention of infectious disease via vaccination has an important offsetting effect with respect to rising health care costs. Some of the steady creep in health spending in recent years is due to the market entrance of new, expensive treatments and procedures. Costs are further magnified by the pressure imposed by population aging and the associated mounting burden of non-communicable diseases.

The aforementioned benefits of vaccination are widely recognized and reflected in the methods used to assess both existing and new vaccines for determining inclusion in national immunization programs. However, in recent years economists and the global health community have come to recognize that vaccines confer myriad benefits beyond direct reductions in morbidity, mortality, and health care costs. These benefits (which must also reflect any adverse effects due to vaccination) fall into three categories: additional health benefits not typically assessed or measured, economic benefits, and social benefits.

One broad health benefit of vaccination that has gained prominence in recent years is its ability to help slow and mitigate the effects of mounting antimicrobial resistance—a major threat looming over the future of Europe and the world. Vaccination both directly reduces the incidence of resistant infections and indirectly curtails resistance by diminishing the need for antimicrobial treatment, which is what drives the development of resistance in the first place. At the individual level, vaccination can help prevent cascading health problems, such as secondary nosocomial infections that might take hold when an unvaccinated individual is hospitalized for a vaccine-preventable disease. Some vaccines, such as the measles vaccine, are hypothesized to protect against "immune amnesia" in which infection with one virus makes a child more vulnerable to other potentially fatal infections. Vaccination can also protect early childhood development, which has been linked to improved health outcomes later in life; at the population level, this will eventually lead to considerable health care cost savings as populations continue to age. All of these health benefits, as well as vaccination's economic and social benefits, are magnified by vaccination's ability to interrupt the transmission of disease, offering some protection to the unimmunized—a phenomenon known as "herd effects."

Chief among vaccination's economic benefits is its protective effect for labor force participation, hours, and productivity. When people remain healthy, they are able to work more and with greater vigor, translating into increased household income and savings, as well as, at the macro level, reduced fiscal stress. In a similar fashion, vaccination for post-retirement adults can allow them to be more productive in non-market activities, such as volunteering in the community or helping to raise grandchildren. And at the other end of the age spectrum, children who are vaccinated are able to attain higher levels of schooling with fewer absences and even enjoy greater cognition in comparison with their unvaccinated counterparts. Vaccination also helps reduce risk for households and improves peace of mind.

Finally, vaccination's social benefits include boosting social equity, insofar as the protection afforded by vaccination tends to disproportionately advantage less-well-off members of society. Within households and families, vaccination also has intergenerational effects; the human papillomavirus vaccine, for example, improves the odds that mothers will survive and be able to care for their children.

Rational, well-informed decisions about the allocation of social resources need to account for all of the sources of benefit vaccination offers, which appear to be substantial from accumulating evidence. In principle, most of the health, social, and economic impacts of vaccination can be measured, monetized, and summarized in the form of a social benefit-cost ratio. The models and tools to accomplish this are well established, and in the European context we have much of the data required to generate estimates in a reasonably rigorous fashion. Assessing vaccination's full benefits will be especially relevant for funding decisions with respect to a new generation of vaccines currently in the pipeline (such as those for clostridium difficile and respiratory syncytial virus), which are likely to be more expensive and have a moderately greater immediate budgetary impact than earlier-generation vaccines. European policymakers would do well to keep the full benefits of vaccination in mind in decisions looming on the horizon and continue Europe's impressive record of leadership in the vaccines space.

1 The WHO recommends vaccination against tuberculosis; hepatitis B; polio; diphtheriae, tetanus, and pertussis; *Haemophilus influenza* type b; pneumococcal disease; rotavirus; measles; rubella; and human papillomavirus for all immunization programs.

Raising awareness about the importance of vaccination in Europe for public health

Monika BEŇOVÁ
MEP (S&D Group),
Member of the ENVI Committee

Vaccination can surely be considered as a great success. It helped to almost exterminate such diseases as measles, smallpox, whooping cough or diphtheria that hurt or killed millions of people in the past. Vaccination saves up a huge amount of human lives every year. It also provably offers an important protection for the youngest and oldest members of our society, as well as for those people who due to their health condition cannot be vaccinated and are most vulnerable to illness. Vaccination is the crucial part of our modern public health care systems. It not only saves human lives, but also reduces health care costs.

Unfortunately, vaccination has become the victim of its own success. Suppression of some diseases started to be taken by society as for granted and society than mistakenly stopped feeling the risk of those. It is still true that diseases that can be prevented by vaccination still pose a great risk. People also have become more concerned about possible side effects of vaccination. The result is that there are doubts about the need to vaccinate and the level of coverage decreases which leads to the weakening of herd immunity.

Confidence in vaccines is crucial. Decisions of individuals not to vaccinate, affects the whole entire population. The fact is that if we want to continue in eliminating diseases and aim to protect people who cannot be vaccinated, because they are too young, too old or too sick, we all need to vaccinate.

Conducted surveys have shown that 85 % of EU citizens considered vaccination as an effective instrument how to prevent infectious diseases. Around 50 % of Europeans vaccinated in the last five years and almost 80 % of EU citizens are discussing the possibilities of vaccination with health care experts, whom they trust. On the other hand 48 % of Europeans mistakenly believe that vaccines can often cause serious side effects and 38 % think vaccines can cause them the diseases they are originally protecting them from. 34 % do not see the need to be vaccinated and 29 % think vaccination is only necessary for children.

This is one of the results of disinformation campaigns focused on vaccination, which were during this year placed by World Health Organization among the top 10 threats to public health. These data confirm that effective awareness rising and combat against the disinformation is necessary for the efforts to increase the level of vaccination. We need to support further research regarding the improvement of vaccines and the need to ensure equal access to vaccines for all. We also have to support health workers and empower them so that they can build on trust that people have to them. They are the frontline when it comes to vaccination and are helping to increase vaccine acceptance and counter vaccination myths.

Is Europe Prepared for the Future of Vaccines Innovation?

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Dr. Rino RAPPUOLI
Chief Scientist, GSK Vaccines

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Head of External R&D, GSK Vaccines

Introduction

Each year, vaccines help protect people of all ages worldwide against nearly 30 vaccine-preventable diseases. Second only to clean drinking water, vaccines save more lives (around 2-3 million) than any other public health intervention. Vaccination plays a fundamental role in helping to protect people from diseases that would otherwise decimate communities and weaken societies. That is why vaccines are widely seen as one of the best investments in healthcare that any government can make.

The recent life science revolution, the exponential growth of new insights into host-disease interactions, and the discovery of disruptive technologies are enabling us to re-think vaccinology and to develop new vaccines we could not have imagined even a few years ago. Unlocking this potential means we are on the verge of developing vaccines for more diseases and populations, faster and more efficiently than ever before.

Careful preparation is required to fully realize the potential of tomorrow's vaccines. Many current challenges related to development, licensure, and administration of vaccines must be overcome. Now is the time to for Europe to lead the way to ensure successful development of the next generation of vaccines and delivery to patients who need them.

New Vaccines Will Bring Unprecedented Health Benefits

Advancements in vaccinology, immunology, and new technologies have the potential to fundamentally change the dynamics of vaccine development by enabling us tackle new disease targets previously believed out of reach, and to test, manufacture, and deliver vaccines faster. Moreover, these breakthroughs highlight new opportunities to expand protection offered by vaccination for all stages of life, a concept we call "lifecourse immunisation" [*see Figure 1*].

Promising new technologies include antigen delivery platforms like GSK's self-amplifying mRNA (SAM), generalised modules for membrane antigen (GMMA), and bioconjugation, which can potentially speed up discovery, increase potency and efficacy, simplify and accelerate manufacturing, and reduce scale-up time and costs to make vaccines accessible to broader populations. Adjuvants – substances designed to enhance the immune response to vaccines – also create new possibilities. Adjuvants have been used in vaccines since the 1930s, but today scientists have a deeper understanding of how the human immune system interacts with pathogens. With a new generation of adjuvanted vaccines we will be able to target populations with sub-optimal immune responses, including older adults at risk of developing diseases like respiratory syncytial virus (RSV) and Chronic Obstructive Pulmonary Disease (COPD), and people living in developing countries and exposed to global killers like tuberculosis and Malaria.

These new technologies open opportunities for a step-change in vaccine discovery, and will help expand new fields of vaccine development. For example, the area of therapeutic vaccines is growing and has great potential for patients. GSK is already working on vaccines for patients suffering from chronic diseases like Hepatitis B infection, which can lead to liver cancer,[1] and COPD, a debilitating respiratory

1 Hepatitis B Foundation. Risk Factors for Liver Cancer. https://www.hepb.org/research-and-programs/liver/risk-factors-for-liver-cancer/.

Figure 1. The Transformation of Vaccine Innovation

disease that is becoming more prevalent globally.[2] In addition to therapeutic vaccines, we are also setting our sights on vaccines that address antimicrobial resistance (AMR), a growing threat to public health and modern medicine.[3] For example, GSK has begun clinical studies for a vaccine against an often-devastating infection with bacteria called *C. difficile*, a major cause of gastroenteritis-associated illness, antibiotic use, and death worldwide.[4]

Europe Can Play a Lead Role in the Transformation of Vaccine Innovation

Europe is poised to drive the transformation of vaccine innovation. The EU-funded and multi-stakeholder led Innovation Partnership for a Roadmap on Vaccines in Europe (IPROVE), outlines the science and technology investments required for vaccines innovation and charts a scientific course forward.[5] GSK contributed to this roadmap and we remain a committed partner to implement its objectives. In this spirit, we offer the following recommendations for a stronger European vaccine research and innovation (R&I) enterprise:

1. Build Upon the IMI Partnership Model

Europe has led multi-sectoral partnerships in public health and medicine with the Innovative Medicines Initiative (IMI1 and IMI2). Now in its second decade, the IMI has built an unparalleled network of public and private researchers who have translated basic immunology insights into tangible vaccine development milestones.[6] With 13 IMI projects on vaccines, GSK and other vaccine companies have contributed substantially to major advancements in vaccine R&I in Europe and beyond.[7]

The Horizon Europe and new health innovation partnership programs offer a timely opportunity to build upon this successful model for the future. To build a true partnership, we urge European Institutions to move beyond the current structure where the role of industry is often limited to a contributor rather than an integral partner in the process of bringing vaccines to the market. As we have demonstrated, industry brings unique expertise, experience and capabilities that significantly contribute to innovation, and therefore should be integrated as a key partner across the spectrum of R&I activities.

2. Commit to Transform & Accelerate Vaccine Development

Given the rapid progress in life science and vaccine technologies, concerted action is needed to realize the full potential of future vaccines. Constant innovation is needed in vaccine development, which is complex and currently takes as long as two decades or more.[8] To accelerate the critical pathway from discovery to delivery, we need to transform research, development, and licensure.

The IPROVE roadmap identified a need for a multidisciplinary approach to vaccinology. By harnessing analytical tools and data sources available today and in the future, we can identify targets and reach decision points faster, by exploiting our rapidly evolving understanding of microbiology, genetics, immunology, structural and systems biology, and bioinformatics.

We also need to take a closer look at clinical trials to identify opportunities to modernise and streamline whilst maintaining the highest safety standards. The IPROVE roadmap calls for innovative design and harmonisation of clinical trials data and development of analyses frameworks, including use of novel analytical tools to streamline data collection during trials and profile volunteers earlier in the process. Advances in immunology, disease modelling, in silico modelling, including the analysis of big data and the application of machine learning and artificial intelligence, provide opportunities to innovate, de-risk and accelerate the vaccine-development process.

In addition, more effort and collaboration are needed to develop controlled human infection models (CHIMs) which are especially helpful for the development of vaccines and can provide early evidence of clinical efficacy and samples for cutting-edge immunological research. CHIMs are particularly needed for the development of universal or broadly protective vaccines against influenza, RSV, and *C. difficile*.

Finally, we recommend expanding beyond mainly disease-driven IMI projects toward projects that encompass technology-oriented research, including vaccine adjuvants, platform technologies, antigen discovery, and systems-immunology. By doing this, Europe will more quickly open new fields of vaccine development like therapeutic and AMR vaccines for patients throughout the life course.

3. Foster a Competitive and Innovation-Friendly Environment for Vaccines

A supportive and innovation-friendly R&I environment is essential to drive the development of new vaccines. Europe has a long history of leading the world in vaccine discovery. Today, the vaccine R&I and manufacturing footprint in Europe is substantial. Continuous investment in vaccine research, development, and production represents a major public health strength and economic asset for Europe.

Ensuring a competitive and innovative vaccine development and manufacturing landscape requires commitment to policies that drive private sector investment. This requires an appropriate balance between "push" mechanisms (e.g. capacity, capability, funding, tax incentives and infrastructure) and "pull" mechanisms (e.g. clear target product profiles, more predictable and stable demand, and improved procurement policies). More fundamentally, it requires a viable and sustainable pricing and access environment for vaccines in Europe. Policy change will require sustained political will, but will ensure Europe remains a global leader in this vitally-important sector.

Conclusion

We are on the brink of a new era of vaccines in which the scientific and technological advances across the life sciences will revolutionise vaccine development. To fully enable the potential of future breakthroughs, a clear scientific roadmap of actions has been proposed that would improve the way vaccines are evaluated, licensed, used, administered, monitored, and financed. The European Institutions are positioned to be at the forefront of this transformation. What is needed now is sufficient political drive to enable this ambition, including implementation of appropriate legal, economic and structural measures that will best incentivise, reward, and accelerate vaccine innovation in Europe.

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Vaccination for patients with chronic conditions

Marco GRECO
President of European Patients' Forum (EPF)

Vaccination does not just concern children: it is something that benefits people of all ages. A life-course approach to vaccination as part of universal health coverage can enhance people's quality of life, including that of people living with chronic diseases. For society and governments, there may be significant savings for health and social systems from reducing the burden of chronic as well as vaccine-preventable diseases – for example by avoiding unnecessary hospital admissions through better management of chronic conditions in the community and by reducing the impact of antimicrobial resistance and thus costs associated to it. Vaccination should thus be considered a part of universal health coverage.

Vaccination is particularly important for patients with chronic diseases and long-term health conditions, such as diabetes, respiratory illness and heart failure. Their numbers are increasing, especially as people become older. Many of these patients are at higher risk of catching infectious diseases; complications of common infectious diseases can be much more serious for them. Vaccination recommendations exist for many conditions, but the uptake of vaccination by patients is lower than it could be.

In addition, some patients are vulnerable either because their immune systems are weakened by disease or they are undergoing therapy that weakens it. Patients with autoimmune conditions, or people with organ transplants, sometimes cannot be vaccinated at all, so they depend even more than other people on effective community (herd) immunity. Those patients are put at particular risk by the falling rates of vaccination in the population.

The European Patients' Forum started engaging its membership on this topic in 2018, first by conducting a short survey to explore awareness and attitudes to vaccination, and then by producing a toolkit of information and advocacy resources. Three national workshops have been held – two in Romania, and one in Germany. Our work has highlighted some issues, including: patients' lack of awareness of specific recommendations for their chronic condition; vaccination not being integrated properly as part of the treatment pathway; some degree of hesitancy in the patient community; and practical access barriers such as availability and cost.

Patients look to both traditional and increasingly social media for information. Many say there is not enough easy-to-find, trustworthy and easily understandable information on vaccination for specific chronic conditions. Patients also want to know more about the benefits and risks of vaccination specifically for them, i.e. understanding the benefit/risk of each vaccine in their personal context, including the risk of not being vaccinated, so that they can make an informed decision that is right for them.

The EPF Manifesto on vaccination for patients with chronic diseases calls for action to improve patients' access to vaccination, as well as better targeted information. Vaccination should be included in disease management plans and clinical guidelines, and professionals should routinely check their adult patients' vaccination status and offer vaccination if needed. Patients' barriers to access vaccination in different countries, including availability and cost, should be tackled.

Patients are also concerned about low vaccination uptake and hesitancy among healthcare professionals. Inconsistency or negative attitudes can undermine the trust relationship between patient and healthcare professional, so it is vital that professionals give a consistent, solid, evidence-based message across professional groups, and set an example. The EPF believes that developing collaborations between healthcare professionals' and patients' organisations in this regard is a vital step forward.

Vaccine hesitancy: public health emergency

Rory PALMER

MEP (S&D Group), Member of the ENVI Committee

Eradicating and tackling disease and protecting public health through vaccination is one of the most important achievements of modern medicine. Next year we will celebrate the 40th anniversary of the global eradication of smallpox, a disease which had been one of the world's most feared diseases. Moreover, thanks to the national vaccination programmes Europe is free of polio since 2002. Despite successes like these, we have been seeing an unwelcome return of some of the vaccine-preventable diseases. Today, we finds ourselves on the verge of a global public health emergency.

Measles is one such example. Since a vaccine was introduced in the UK in 1968, 20 million cases and 4,500 deaths have been averted in the UK, according to Public Health England (PHE). The UK had successfully managed to achieve World Health Organization measles elimination status, but shockingly that status has now been lost.

This is a part of a global trend. In recent years we have been seeing record-breaking measles outbreaks across Europe, even though the disease is almost entirely preventable with just two vaccination doses. Over 82 500 people were infected in 2018 - 3 times higher than in 2017 and 15 times the number of people affected in 2016.

One of the main reasons behind this resurgence is a rising tide of vaccine scepticism. Europeans are not convinced anymore about the safety of vaccination and some think it is not necessary to vaccine as the diseases appear to be 'gone'. According to this year's Eurobarometer, a third of unvaccinated Europeans do not see the need for vaccination. As for the awareness, 48% of surveyed agreed with a false claim that vaccines can produce serious side-effects and more than one third of respondents falsely believed that vaccines can cause the disease against which they protect.

How did we get here? In recent years, social media has become a "breeding ground for misleading information and negative messaging around vaccination". This is the conclusion reached by the UK's Royal Society for Public Health. Thanks to platforms like Facebook false claims around the possible side effects of the vaccines spread further and faster than ever before, despite strong scientific evidence that those fears are false. These platforms could become even more influential as generations that have grown up with these platforms become parents.

The good news is that healthcare professionals still remain the most trusted source of vaccine information for parents and they play a vital role in making parents aware of the importance of childhood vaccinations. Unfortunately, public health budgets have been hit severely by the austerity measures in the last decade. As an example, the county of Northamptonshire in my constituency, local public health budgets have been cut by 15% between 2016/17 - 2018/19. Such decisions have long-lasting impact on access to health services and the health of local populations, specifically when it comes to disadvantaged and socially excluded groups.

Diseases do not recognise borders, that is why the EU needs to show leadership on this. Vaccination programmes might be a competence of national and local authorities, but they vary from country to country, creating a confused and incoherent picture at EU level. The EU has the power to advocate for a comprehensive and harmonised approach to vaccination and to strengthen cooperation and coordination.

Changing the public perception of vaccination must be a priority and social media giants have a big role to play in clamping down on fake news and disinformation. They need to take responsibility and start promoting credible sources of information and verified, evidence-led and scientifically credible awareness campaigns.

It is also necessary to reverse the negative trend of the public health funding cuts enacted over the past decade. Resources need to be put behind empowering healthcare professionals, including midwives and school nurses, with funding, information and training in order to improve expertise and increase uptake in under-vaccinated communities.

WHO declared vaccine hesitancy is one of the main threats to global health.. We need to get all actors on board to tackle it - decision and policy makers, healthcare professionals, organisations, communities, social media platforms, the media and citizens - working together to provide comprehensive and accessible information.

Choosing not to vaccinate puts everyone at risk. It is the vulnerable who are put at most risk by falling vaccination rates - newborn babies, elders, cancer-treated patients whose immune system is weakened, or those without a fully-working immune system. This is a public health emergency, the EU's response must treat it as such.

Resilient immunisation systems: looking beyond high vaccination rates

Sibilia QUILICI
Public Policy Director, MSD

As national health budgets are under continuous pressure, the importance of successful immunisation systems becomes critical. However, we need to look beyond just achieving high vaccination rates and ensure resilient and sustainable immunisation systems are established which positively contribute to public health long term. So, where does one begin?

Responding to hesitancy

Vaccines are one of the most cost-effective and successful public health interventions available. They help prevent diseases, save lives, and improve social and economic well-being across the globe.[1] However, vaccine hesitancy threatens the global progress we have made in combatting the spread of many serious and preventable infectious diseases. For this reason, it is now becoming more important than ever that we protect the hard-fought immunisation gains, and ensure they are sustained. We have to work towards delivering high-quality vaccination services through resilient systems, which are well resourced, delivered through the life-course of citizens and which are integrated into the wider national health system.

A few months ago, the World Health Organisation (WHO) identified vaccine hesitancy among the top 10 global health threats for 2019, alongside other major health challenges, such as climate change, non-communicable diseases, antimicrobial resistance and Ebola.[2] In September, the European Commission in collaboration with the WHO, organised a Global Vaccination Summit. A major focus there was how we can rebuild trust in vaccination, which is a key factor in addressing hesitancy. The Summit ended with the adoption of an Action Plan[3], which, unfortunately leaves a lot to be desired in terms of concrete follow up, measurable goals and operational clarity. Undoubtedly, there is political will to fight vaccine hesitancy, but we also need political leadership and alignment across the multi-sector stakeholders involved in the development, implementation and delivery of a successful immunisation programme.

In addressing vaccine hesitancy, we all have our part to play. Our role as the innovative pharmaceutical industry is to research, develop, manufacture and distribute vaccines to address some of the most challenging public health concerns; infectious diseases which have the potential to put the health of all citizens at risk. Some of those most at risk include high risk and immunocompromised populations. These are the populations which rely on the community immunity achieved through large population immunization. But inventing and developing vaccines is complex, time-sensitive, and carries no guarantees. It requires an ability to produce hundreds of millions of doses of high-quality vaccines – and ensure the same quality in every single dose, every single time.

As we develop new vaccines, we think years ahead to anticipate and lessen hesitancy: Beyond conducting clinical trials to improve safety and efficacy, we are considering the type of information people need to promote confidence and reduce hesitancy when these vaccines become available. In addition, we keep investing to meet the demands of new or expanded immunisation programmes around the world, which in turn, leads to an increased global demand for vaccines. Through the sharing of our scientific work we continue to contribute to the growing body of evidence related to the safety of vaccines. Nothing is more important to us than the safety of our medicines and vaccines.

Vaccine hesitancy is creating a number of concerns for those of us who are committed to addressing public health issues. One of these concerns is the effect hesitancy has on adherence. By adherence to immunisation programmes we mean access to vaccination in due time, based on national recommendations. Ensuring the full course of the vaccination programme is delivered is critical to benefit from the full potential of vaccination. Take, for instance, the example of measles, which requires two doses. Adhering to the programme schedule and administering both doses is critical to ensure the vaccine's immunity protection. To solve the problem, we need immunisation systems that have strong infrastructure for adequate surveillance and monitoring, we also need to run public awareness campaigns, provide adequate training to healthcare professionals, and improve access. If all of this is achieved it will contribute greatly to the resilience of the programme, build public and professional confidence and increase uptake.

Creating a resilient immunisation programme

In addition to the issue of hesitancy, a major barrier to sustained high vaccination coverage and trust in immunisation programmes lies in the inability of our healthcare systems to properly prepare for and respond to crises. An example of this is the recent measles outbreaks in Europe. This crisis has focused attention on the need to start looking beyond just increasing vaccination coverage rates, and towards taking a more comprehensive approach by building resilient immunisation systems.

A resilient system is able to recover or "bounce back from adversity" following the experience of negative events, threats or hazards.[4] At its core, this concept of resilience is rooted in planning for the successful

1 https://www.who.int/immunization/sage/meetings/2014/october/SAGE_working_group_revised_report_vaccine_hesitancy.pdf?ua=1

2 https://www.who.int/emergencies/ten-threats-to-global-health-in-2019

3 https://ec.europa.eu/health/sites/health/files/vaccination/docs/10actions_en.pdf

4 WHO-EURO. Building resilience: a key pillar of Health 2020 and the Sustainable Development Goals Examples from the WHO Small Countries Initiative. 2017. http://www.euro.who.int/__data/assets/pdf_file/0020/341075/resilience-report-050617-h1550-print.pdf?ua=1

sustainability of the programme but also a quick recovery in the face of a challenge. Resilience is a state where an issue does not have an opportunity to take hold. It is where an issue or threat can be isolated quickly, dealt with and managed without it affecting the immunisation programme or other parts of the health system.

Recent research[5] [6] suggests that you can characterise a resilient immunisation system as:

a. Aware and therefore able to identify emerging risks, system weaknesses and strengths and is in a position to map out strategies for engaging strengths and reducing weaknesses.
b. Integrated and thus ensuring recognition and coordination between key system sectors.
c. Adaptive, indicating an ability to change to better position itself to succeed in warding off crises, or mitigating threats, when they do occur.
d. Capable, implying the possession of a broad range of skills, assets and resources to meet its needs.
e. Self-regulating and thus able to quickly isolate threats and minimise threats to essential services.

Building resilient immunisation systems is key to sustaining high vaccine uptake and helping communities prevent, manage and recover from hesitancy-related issues. Finding better ways to anticipate and prevent such issues will protect both individual and public health. The worrying rise in vaccine hesitancy is threatening to reverse the remarkable decades-long gains made by vaccines. Therefore, building and sustaining resilience in immunisation programmes is now critical. Take, for example, the case of France, which in January of 2018 introduced mandatory vaccination in an effort to address the worrying drop in vaccine coverage rates. They identified the issue and took action to address it demonstrating bold leadership to safeguard public health. However, the bigger question is why trust in vaccination and the immunisation system had dropped so low that this measure was required.

The need to work together

Over the past few decades immunisation programmes have expanded as a result of the introduction of innovative new vaccines and new evidence which demonstrate the benefits to wider populations. However, this creates significant complexity in the system. The complexity is mirrored in the variety and numbers of actors involved: from individual and community groups, to healthcare professionals, advisory bodies, public health institutes and policy makers to name just a few. In addition, other "non-traditional" actors and platforms which share information on vaccination, such as social media platforms and religious leaders further add to the complexity.

Acting together, each component of this vaccine ecosystem has the potential to collaborate and strengthen the resilience of the immunisation system.

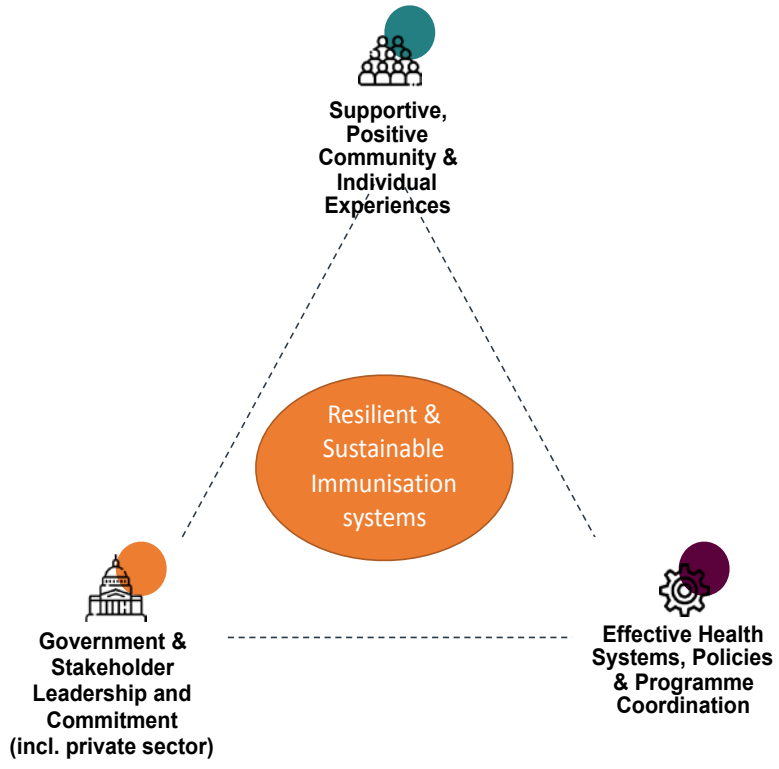
Understanding how to build a resilient and sustainable system by engaging all stakeholders, respecting their interrelationships and what roles they play in an immunisation programme may therefore be key to promoting the resilience of successful immunisation programmes.

It is time for the EU institutions and Member States to start investigating how to build and sustain resilient immunisation systems by firstly assessing the vulnerabilities and strengths within member states. Ensuring resilience assessment indicators are developed and used in a harmonised way across the European region is a good place to start. This should be central to the work already started under the EU Vaccination Roadmap going forward.

5 Kruk ME, Ling EJ, Bitton A, et al. Building resilient health systems: a proposal for a resilience index. BMJ (Clinical research ed) 2017; 357: j2323.

6 Kruk ME, Myers M, Varpilah ST, Dahn BT. What is a resilient health system? Lessons from Ebola. Lancet (London, England) 2015; 385(9980): 1910-2.

Addressing vaccine hesitancy and creating resilient immunisation systems require a multi-pronged approach



Raising awareness about the key role of health professionals - The role of physicians in vaccination

Prof. Dr Frank Ulrich MONTGOMERY

President of the Standing Committee of European Doctors (CPME)

It's a shame: People are still dying of vaccine-preventable diseases that should no longer exist in Europe. Some of them were already supposed to be eliminated but the rise of disinformation on vaccination, particularly online, the decline of people's confidence in vaccination, and inadequate access to vaccines have led to new outbreaks of diseases such as measles. More than 100 measles-related deaths and over 100,000 measles cases have occurred since 2016 in the WHO European Region. This has caused new concern for decision-makers, public health experts and healthcare professionals.

Coverage rates and the role of healthcare professionals

Due to insufficient vaccination coverage rates, the EU and its member states need to strengthen their cooperation to ensure equitable access to vaccines for all EU citizens. They have to fight disinformation and improve vaccine confidence. The Council of the EU has adopted a recommendation to strengthen the EU cooperation on vaccine-preventable diseases. The European Commission has launched a joint action on vaccination and the European Parliament has adopted a resolution expressing concerns about Europe's insufficient coverage rates and its impact on public health. However, vaccination policy as such remains a competence of national authorities.

At the same time doctors and other healthcare professionals have faced a new challenge to tackle the declining coverage rates, not only in the EU, but across the whole world. Healthcare professionals play a crucial role in delivering facts based on scientific evidence and increasing public awareness about the benefits of immunisation. Doctors are often the most trustworthy source of vaccination information and therefore important advocates to drive vaccine acceptance.

However, there is evidence that some doctors and healthcare professionals feel ill-equipped to answer questions or engage in difficult conversations on vaccination, particularly with reluctant patients and parents. In addition, healthcare professionals' own confidence in vaccination is not always high.

Education about vaccination facts and vaccination myths

Education of medical students is essential to enable new doctors to effectively communicate with their patients. Currently, education about vaccination during medical school is not yet optimal in all European countries. Vaccination should also be better addressed in continuous professional development. New skills are needed to address vaccine hesitancy and discuss vaccine-related concerns with patients. Particularly good communication skills are needed to improve trust between doctors and patients. Vaccine hesitancy is not a new phenomenon, but nowadays it spreads fast on the internet. The small but vocal group of anti-vaxxers can influence normal people through different social media platforms. Doctors and other healthcare professionals should be equipped to explain the difference between misinformation and the facts.

Raising awareness of parents should be started already during prenatal care. Healthcare professionals should also acknowledge that there is a small possibility of risks related to some vaccines for some individuals. Moreover, the collective interest of vaccination should be highlighted. Herd immunity works only when almost all people in the population are immunised. At EU level this means that one country's immunisation weakness puts the health and security of other countries at risk.

Role of the European Union and European umbrella organisations

European policies should support healthcare professionals and empower them to provide effective, transparent and objective information to the public and fight false and misleading information. The EU could undertake Europe-wide awareness campaign(s) on vaccination, propose common EU wide vaccination schedules and support education to improve communication on immunisation. EU actions should however be done under consideration of different settings in different member states.

The Standing Committee of European Doctors (CPME) is co-chairing a new Coalition for Vaccination together with the European Federation of Nurses Associations (EFN) and the Pharmaceutical Group of the European Union (PGEU). This Coalition gathers around 20 relevant European healthcare professionals' and students' associations to commit to delivering accurate information to the public, combating myths and exchanging best practices. The Coalition members can potentially outreach to millions of healthcare professionals, as many of them are major European umbrella organisations.

CPME has a long-standing commitment to affirming that the prevention of communicable diseases through vaccination is safe and effective. Immunisation through vaccination is the best protection against serious infectious diseases but also one of the most successful and cost-effective public health interventions.

Vaccination in Pharmacies

Michał BYLINIAK

President of PGEU (The Pharmaceutical Group of the European Union)

In the light of the declining vaccination coverage rates across Europe, European societies depend now more than ever on a strong and unified healthcare workforce to help combatting the issues of low vaccination confidence and trust, misinformation and the remaining barriers to convenient access.

Community pharmacists have always advised patients on the importance and/or appropriateness of immunisation, identified and reminded target groups for vaccination, and of course dispensed and advised on vaccines. Most pharmacists in Europe would regard that as part of their core activity. But we are now seeing in recent years this going a stage further with pharmacists carrying out immunisation themselves within the pharmacy, as a complementary service to existing vaccination services.

More than two-thirds of Europeans can access a pharmacy within five minutes, following which they can consult a community pharmacist without any appointment. For instance for flu vaccination, this offers a tremendous opportunity to reach parts of the public that have not received a flu vaccination before.

Numbers from Ireland have shown that since pharmacists first started vaccinating in 2011, flu vaccine deliveries through the National Immunisation Office (NIO) have increased overall by 48% and, within that, deliveries to general practitioners are up by almost 23%, demonstrating that when pharmacists vaccinate, public awareness increases and vaccination rates increase.[1] In addition, statistics show that provision via Irish community pharmacies increases coverage for people who had never received the vaccination before (one in six), with 99% of patients indicating that they would return to the pharmacy for their next vaccination. Patient satisfaction with the service is very positive with 93% of patients rating the service either 9/10 or 10/10.[2]

Outside Ireland, many other established examples can be found across Europe where pharmacists are having a hands-on role in administering vaccines, such as in Denmark, Portugal, Switzerland and the United Kingdom. In addition to administering flu vaccinations, community pharmacists administer other vaccinations (for example, pneumococcal, shingles, human papilloma virus (HPV), travel vaccinations) in five European countries.

France has been the most recent country in Europe (March 2019) that has allowed pharmacists to administer flu vaccinations in the pharmacy following a very successful pilot project.[3] All community pharmacists in the French territory are now eligible to administer flu vaccines in the pharmacy, subject to the conditions that they have followed the required training programme and that the pharmacy has the appropriate premises and equipment to ensure a private and qualitative service provision.

Similar requirements for training and appropriate premises/equipment are in place in all other European countries where pharmacists are allowed to administer vaccines. In Portugal for example:

1. Pharmacists must complete mandatory training on vaccination;
2. Recertification must take place regularly (every five years in Portugal);
3. Pharmacists must provide evidence of continued activity;
4. Pharmacists must obtain a certification on Basic Life Support.

Pharmacies must as well have an adequate room for providing the vaccination with all necessary equipment, and be able to manage any anaphylactic event (for example, use of adrenaline to be administered by the pharmacist).[4]

In many of the other European countries, there exist also additional opportunities to closer engage community pharmacists in the fight against lowering vaccination rates and increasing vaccination hesitancy. With their rigorous scientific educational background and an established position as a pillar of the local community, (often with life-long relationships with their patients and communities), community pharmacists are an excellent resource for providing evidence-based, unbiased and balanced information on the benefits and risks of vaccination. It is crucial that information provision to the public on vaccination is done as part of an integrated, consistent and multidisciplinary approach across the different healthcare setting so that wherever people access the healthcare system, they receive qualitative information on immunization and that they can be identified as a potential risk/target group for vaccination. Shared electronic vaccination/health records could improve the efficiency of such communication in the future.

To summarise, European community pharmacists can improve access and convenience to vaccination information and delivery to citizens as a complementary service to established vaccination services. To increase vaccine coverage and help tackling vaccine hesitancy it is crucial to make better use of pharmacist-delivered vaccination services as an integral part of national vaccination programmes. Pharmacists across Europe are ready to work closely work together with their fellow healthcare professional colleagues and the authorities to ensure that the implementation of vaccination policies in practice can reach their full potential and can ensure a maximum increase in both coverage rates and public trust in vaccination across Europe.

1 http://ipu.ie/wp-content/uploads/2019/08/IPU-Review-AUG2019-WEB.pdf

2 https://www.thepsi.ie/Libraries/Pharmacy_Practice/Report_on_Patient_Feedback_on_the_Flu_Vaccination_Service_Provided_in_Pharmacies.sflb.ashx

3 http://www.ordre.pharmacien.fr/Les-pharmaciens/Champs-d-activites/Vaccination-a-l-officine

4 https://www.pgeu.eu/wp-content/uploads/2019/07/180403E-PGEU-Best-Practice-Paper-on-Communicable-Diseases-and-Vaccination.pdf

Independent control contributes to ensuring vaccine quality

Susanne KEITEL
Director of the EDQM, Council of Europe

Since 1994, the EU Official Control Authority Batch Release (OCABR) network has played a key role in ensuring vaccine quality. This network of state laboratories, Official Medicines Control Laboratories (OMCLs), is part of the General European OMCL network, which is supported by the EU Commission and the Council of Europe (CoE) and co-ordinated by the European Directorate for the Quality of Medicines and HealthCare of the CoE. OCABR, which is also applied to human blood-derived medicinal products, is an integrated part of the medicines regulatory system in the European Economic Area (EEA) as foreseen by the codified EU Directive for Human Medicines, 2001/83/EC, as amended. The Directive includes provisions for marketing authorisation, obligations to comply with good manufacturing practice and oversight through inspection, pharmacovigilance and market surveillance by the authorities.

Specifications for the quality of medicines, including vaccines, are defined in their marketing authorisation dossiers, which are assessed by experts at the European Medicines Agency or national competent authorities as part of the licensing procedure. They should comply with the monographs of the European Pharmacopoeia, which sets the legally binding quality standards for medicines in its member states, including the EEA. OCABR (article 114 of the Directive) allows a member state to verify through testing at an OMCL that the quality of each licensed batch of vaccine conforms to the approved specifications, independently from the release tests performed by the manufacturer and before the batch reaches the patient.

OCABR is therefore an additional guarantee of the quality of these important products. It includes a review of the manufacturer's batch documentation and testing of a pre-defined set of critical quality parameters that have been agreed by the network experts. To avoid impacting the timing for availability on the market the procedure is generally done in parallel to the manufacturer's own production and release procedures.

Article 114 specifies that OCABR results from one member state must be recognised in all the others, thus avoiding the duplication of work, conserving vaccine samples for use in patients and reducing the burden on manufacturers. Compliant batches, which have been evaluated by an OMCL according to codified procedures and under an externally audited quality system, receive an EU OCABR certificate which is then recognised throughout the EEA to allow release to market. These certificates are also recognised outside the EEA as a sign of quality. If a batch is not compliant, all member states are informed to ensure that the batch is not placed on the market.

Since OCABR is carried out in real time on every batch, the OMCLs can monitor trends in results and take preventive action if needed. Thanks to this surveillance, OMCLs regularly identify issues which, with the input of the regulatory authorities and manufacturers involved, can be corrected so only the batches with conformant quality reach the patient.

One strength of the OCABR network is communication. The information gained during the OCABR process is available to the responsible authorities in all member states and can be used to help ensure the continued high quality of these medicines. Maintenance of experimental testing at OMCLs secures expertise independent from the manufacturers. Since OMCLs have hands-on experience with vaccines from different manufacturers, they have a unique insight and contribute to the establishment of common methods and standards which helps both authorities and manufacturers to provide the best quality products. OCABR also allows the authorities to have an overview of the products that will be available, or not, on the market and thus potentially help them to anticipate possible shortages.

In 2018, through efficient work sharing, OMCLs from 12 different member states tested over 4000 final lots of vaccines to the benefit of patients in all member states. OMCLs are constantly evolving to face new challenges, such as vaccines with an ever-higher number of components and complex and sophisticated new testing methods, as well as the logistical challenges linked to manufacturers' increasingly global production strategies.

According to the World Health Organization an estimated 2-3 million lives are saved ever year thanks to vaccines. Despite the accumulated evidence of the benefit of vaccines, vaccination coverage in the EEA is sub-optimal. In April 2018 the European Commission communicated (COM(2018) 245/2) a strategy to address this issue, highlighting vaccine hesitancy as one of a complex set of contributing factors, amongst other issues including vaccine supply management. The Council recommendation of 7 December 2018 on strengthened cooperation against vaccine-preventable diseases (2018/C 466/01) sets out a number of important recommendations. Support for the EU OMCL Network to ensure that vaccines placed on the market are of high quality is among them.

The quality of vaccines is important both for the individual patient and for public confidence to foster adherence to vaccination programs. OCABR is an independent control system that helps to ensure that no matter where a patient is in the EEA, they benefit from the same high standards. OCABR certificates facilitate the movement of vaccines within Europe, which is beneficial for vaccine supply management. The contribution that OMCLs and the OCABR system make to ensuring good quality vaccines merits support. Like vaccination, OCABR is a preventive measure that is good for public health.

Healthcare distribution: facilitating optimal access and uptake of vaccines in Europe

Monika DERECQUE-POIS
Director General of GIRP

Vaccination is a story of success in the field of medical science. Since the first vaccine was administered over 200 years ago, vaccination has helped to reduce or even eradicate widespread infectious diseases across the globe. Vaccines nowadays prevent millions of deaths worldwide each year and significantly reduce costs for healthcare systems dealing with uninoculated diseases.

Making vaccines available on a large scale requires complex production methods, meticulous quality control and reliable distribution channels that ensure the products are potent and effective when patients receive them. Guaranteeing availability and effective delivery of the product also requires strong partnerships between manufacturers and their supply chain partners. This is where healthcare distributors make a crucial contribution to facilitating optimal access to vaccines in Europe.

Vaccine distribution: a delicate matter

The European Union puts great emphasis on supporting and strengthening the role of vaccines in European healthcare systems as one of the most cost-effective and efficient public health measures available to prevent serious diseases. The EU also applies strict rules for the approval of vaccinations to be allowed on the European market and follows up with post-authorisation surveillance of vaccinations to ensure maximum safety for patients.

This is especially important, as vaccines are delicate and sensitive medical products. They vary in stability, which means their potency and effectiveness can be altered easily by influence of environmental factors such as overheating or freezing and they naturally biodegrade over time. This may result in the failure of the vaccine to create the desired immune response and consequently provide poor protection. An essential part for many of the vaccines supplied across Europe thus is the maintenance of the so-called cold-chain, which is refrigerated transportation, between the manufacturer and the end-user.

Adding value to vaccines supply

Healthcare distributors are essential partners when it comes to the safe and efficient distribution of vaccines. Because the supply process must be robust, reliable and routinely monitored for possible deviations at all points of the value chain, with their state-of-the-art distribution systems, healthcare distributors play a crucial part in the vaccination process.

Equipped with the latest refrigeration technologies for both storage and transportation of vaccines, temperature monitoring equipment and meticulously planned, mapped, and risk-assessed transport routes according to current European regulations they support industry in getting their medicine to the right place at the right time while guaranteeing all products are kept safe and effective.

By assuming a quantity-based buffer function for healthcare providers, which means stocking vaccines under the right conditions and in sufficient quantities for their geographical area of activity, healthcare distributors can bridge bottlenecks in peak demand times and are in a unique position in the supply chain to pre-finance bulks of essential vaccination supplies that ultimately enable pharmacists and physicians to focus fully on the patient and to provide superior clinical care.

Healthcare distributors also assume vital and important bundling functions of vaccines that draw together supplies from several different manufacturers into one delivery pool. This function is of high value to pharmacies as it reduces the time spent by an individual pharmacy on ordering, receiving and processing invoices from the various manufacturers whose vaccines it buys from. With this, healthcare distributors add value to the sustainability of healthcare systems across Europe and contribute to a secure and stable system of supply.

Supporting confidence in vaccines

Despite the obvious positive contribution vaccines have made to European healthcare systems and the overall public health in the last decades, vaccine confidence has slowly been decreasing in popular opinion and disinformation on vaccination continued to rise across Europe.

Thus, it has become even more important for healthcare distributors to ensure end-users can trust that their supply chains work impeccably and robustly. Healthcare distributors have been stepping up to assure to their customers and patients that their continuously and professionally monitored cold-chains are up to the challenge to keep vaccines safe and secure.

GIRP, the European Healthcare Distribution Association, is the umbrella organisation for pharmaceutical full-line wholesalers and distributors of healthcare products and services in Europe. It represents over 750 pharmaceutical wholesalers serving 34 European countries. GIRP members employ over 140,000 people and distribute around 15 billion packs of medicines as well as a wide range of healthcare products per year. As the vital link in healthcare, they are committed to developing and providing innovative and efficient healthcare products and services to improve health and wellbeing of patients across Europe.

Vaccine distribution in Europe

AIM calls for European Action with regard to Vaccination Hesitancy

Christian ZAHN

President of AIM (International Association of Mutual Benefit Societies)

Vaccination is one of the most successful and cost-effective interventions to improve health outcomes of people. High uptake rates have allowed to eliminate, and in some cases eradicate, a number of diseases. And yet, the last decade has been characterized by outbreaks of measles, mumps, or polio in some countries where those diseases had previously been controlled or extinct. Vaccination and vaccine safety have consequently become a priority at European and Global level. A debate has been launched on whether and how vaccination could be organised at EU level. At the same time an EU-wide campaign has started to fight against vaccine hesitancy. At AIM, we are convinced of the added value of European action in this field. More than reimbursing healthcare costs as payer organisations, our members have a mission of general interest and have the responsibility of striving for better public health, an aim for which vaccination is a sine-qua-non condition.

Accessibility to vaccines is key for high coverage rates

One of the key aspects of accessibility is of financial nature and thus linked to reimbursement. AIM is convinced that vaccines included in vaccination schedules should be fully reimbursed so as to remove any potential financial obstacle. To guarantee patient safety but also safeguard citizens' trust, it is key for those schedules to be established on the basis of scientific recommendations taking different groups of people and risks into consideration. Moreover, it is important that the reimbursement of those vaccines does not fall solely on health insurance institutions but is also borne by the State as vaccination is a public health responsibility.

Vaccination should be allowed outside clinical settings under certain conditions

By allowing vaccination outside clinical settings, the most vulnerable in society could be reached and as a consequence, health inequities could be tackled. Pharmacists, nurses or public health workers (e.g. carers) may be, depending on national legislation, entitled to vaccinate as well. However, before allowing such practices, their added value must first of all be investigated. Furthermore, if vaccines are to be made available outside clinical settings, the administrator must be properly trained to communicate with the patient in order to provide him with comprehensive information without inducing fear, and to respect safety measures.

Safety of vaccination should be always guaranteed

Vaccines are administered to people who are usually healthy and in most cases to children. Therefore, a higher degree of safety is often expected for vaccines than for other pharmaceuticals or other healthcare interventions. To ensure the safety of vaccines, we believe it is important to improve spontaneous reporting of adverse event(s) following immunization (AEIF) and pooling of AEIF data globally in order to reduce time to identify rare vaccine reactions. AIM sees a clear need for standard methodologies for active surveillance and a standard reporting format for AEIF should be developed. This would help ensure a proper monitoring of vaccines after their use. AIM welcomes the work done under the EU Pharmacovigilance system. If this collaboration between European Commission, Member States and the European Medicines Agency is of utmost importance, the proper dissemination of its outcomes to the general public is equally crucial. AIM would call for making the information on vaccination resulting from the EU Pharmacovigilance system more visible and accessible to the general public. Indeed, perceived safety is a key challenge and vaccine hesitancy a growing issue across the EU.

Member States have the competence with regard to compulsion

In that context, compulsion seems to be the perfect quick-fix to increase coverage rates and achieve herd immunity. Yet, compulsion is against the values of freedom and democracy on which the European Union was built. Furthermore, Member States have the competence regarding the decision on compulsion and should keep it. In the case of "non-compulsion", it is of utmost importance that citizens are empowered by tailored and comprehensive information describing the risk-benefits balance. They should be able to make well-informed decisions and to avoid unreasonable fear of side effects. One solution to ensure to reach a higher coverage could be to envisage a policy option such as opting-out of vaccination. An opt-out would be subject to a formal process through which awareness about risks of not being covered is built.

An EU passport for vaccination is needed

Citizens need clear, non-biased and trustful information on vaccines and clarity about vaccination schedules. An EU-wide schedule, providing minimum standards, and an EU vaccination passport would allow to reduce confusion around diverging schedules and lack of consistency between and within Member States. It would also be an added value in the case of cross-border care, cross-border movement, joint procurement of vaccines and to generate much needed statistics at EU level. Of course, such a proposal raises many challenges, notably regarding the electronic vaccination registers and their interoperability. Healthcare institutions and all healthcare professionals involved in vaccination must have the capacity to electronically register the vaccination status and information of citizens, without being subject to a duplication of work at national level. Those challenges and the others previously described (also mentioned in our position paper) can only be tackled through EU collaboration and with the involvement of all actors, governments, doctors, hospitals, pharmacists, parents, patients, and, of course, healthcare payers.

Vaccines - The educational and preventive role

Sara CERDAS
MEP (S&D Group),
Member of the ENVI Committee

Worldwide, people are living longer. In fact, in the last 100 years, human life expectancy increased by 30 years.

There are a multitude of factors that account for this increase in human's life expectancy, but one cannot deny the role public health measures had. Access to safe drinking water and water waste management, the discovery of antibiotics and vaccines.

Human beings stopped being exposed to microorganisms that otherwise would be fatal to them through life's most ingested substance, water. If a person did indeed, through any transmission mode was infected, bacteria could be fought hand in hand with antibiotics, medicines that actively target the harmful microorganisms that would otherwise translate in high death rates by most communicable diseases. And vaccines, the scientific breakthrough wonder substances, if you had the chance to be vaccinated your immune system will be in contact with a short (or a dead) part of the pathogenic microorganism and consequently, if you got in contact with the real pathogenic microorganism, your own cellular army called immune system would fight them off in a stronger and efficient way.

The combination of these three public health measures did indeed contributed for a massive transformation in human life. We live longer, and healthier. Our children are born and have the best chances of surviving than ever before in human history. Eighty percent of children worldwide are vaccinated for at least one disease.

However, history took an unthinkable twist. Somehow, in countries were vaccines are easily accessible, adults stopped vaccinating their children.

It is important to understand that in medicine, as in any decision in life, there are risks. However, risks are to be balanced with well-informed access to scientific evidence. If today, most of the world recognizes the harmful effects of climate change, that cannot be said for the benefits of vaccines. Despite consensus in the medical and scientific community, Europe is facing an ever increase number of outbreaks, for diseases that we can be protected for; they are called vaccine preventable diseases. And it is only with concerted action by the different players, that this untruthful and fake-inspired wave of the anti-vaccination movement can be overcome. It is not through strength; it is not through mandatory laws. Public Health professionals must be called into action and step up for this emergency; and must be equipped with the best tools we have at our disposal: evidence-based information.

And policy makers must clear up the way and guarantee that all actors commissioned to the task are provided with the best resources. Otherwise, we will fail.

We must not forget that not everyone can have the luxury to be vaccinated; there are people that live in remote areas of the globe that do not have access to the recommended vaccination programs; there are persons all around the globe that, even though they are vaccinated, their cellular army is not properly function; they are immune suppressed and of high risk of being infected. In high risk of perish from a preventable disease. It is a community effort, and one where everyone plays a role, spreading the most accurate and evidence-based information.

In an era where antimicrobial resistance is earning an emergency status, where climate change is making access to safe water harder, in an era were vaccines are safer than ever and work, action is needed. Today.

The EU research programmes in support to vaccine Research & Innovation

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Vaccines: their power, their challenges

Vaccination is among the most impactful and cost-effective medical interventions ever introduced for prevention of infectious diseases. Each year vaccines prevent 2-3 million deaths from diseases like diphtheria, tetanus, pertussis and measles[1], as well as prevent infection-related cancers and protect the health of the vulnerable. Promising research on therapeutic vaccines also opens new horizons for the treatment of diseases. Nonetheless, several countries are having a comeback of vaccine-preventable diseases[2], with mistrust in vaccines playing a key role in this phenomenon. Additionally, for a number of major infectious diseases suboptimal or no vaccines exist. Currently, the many challenges faced in vaccine research and development make the development of vaccines lengthy, complex and with a high risk of failure.

What is the EU doing in the area of vaccination

The EU is actively involved in the global efforts to overcome these challenges. The political commitment in support of vaccination is laid down in the Commission Communication and Council recommendation on *strengthened cooperation against vaccine-preventable diseases*[3] adopted in December 2018, aiming to increase vaccination coverage, foster support to research and innovation, and strengthen EU cooperation on vaccine-preventable diseases. Among the many actions proposed is the establishment of a European Information Sharing System; the creation of a European vaccination information portal by 2019; and an increase in the effectiveness and efficiency of EU and national funding for vaccine R&D[4].

What the EC does to overcome challenges in vaccine research and innovation

A number of scientific challenges to developing new and better vaccines remain, as well a need to understand and address the determinants for the decrease in vaccine uptake. The Commission is strongly committed to providing solutions to these challenges, as well as to strengthening the involvement of all relevant stakeholders in the research process (e.g. patient community, social scientists) and supporting the generation of high quality data for evidence-based recommendations.

Through the current framework programme for research and innovation, **Horizon 2020** (H2020), so far over **€620 million** have been invested on vaccine R&I[5]. A significant amount of this EU investment went to large consortia performing translational collaborative research spanning work from discovery to first-in human studies, with projects generating results such as predictive tools as well as promising vaccine candidates against HIV, TB and malaria. Horizon 2020 has also provided funding for the development of

1 WHO Immunization coverage. http://www.who.int/mediacentre/factsheets/fs378/en/

2 https://ecdc.europa.eu/en/about-uswho-we-aredisease-programmes/vaccine-preventable-diseases-programme

3 https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32018H1228(01)&from=GA

4 https://ec.europa.eu/health/sites/health/files/vaccination/docs/2019-2022_roadmap_en.pdf

5 https://cordis.europa.eu/projects/en

vaccines against several neglected-infectious diseases and influenza, as well as Ebola.

The H2020 portfolio also includes projects tasked to evaluate vaccine effectiveness. The **I-MOVE+**[6] project developed a platform to measure and compare the effectiveness and impact of influenza and pneumococcal vaccines, as well as vaccination strategies in the elderly. The generated data provided useful insights to public health authorities on these vaccines and on how to use them effectively. The Commission is also supporting the second phase of **TRANSVAC**, a collaborative infrastructure project which supports innovation for both prophylactic and therapeutic vaccine development and functions as leverage and innovation catalyst between vaccine R&D stakeholders.

The Commission has also supported research to understand behaviours towards vaccination. The TELL ME[7] collaborative project provided evidence and developed models for improved risk communication and strategies addressing vaccine-hesitant groups, among others. The **E-com@EU**[8] project developed communication plans for Under-Vaccinated Groups (UVGs), a tool useful for health professionals, health agencies and Institutes of Public Health (IPH) in periods of outbreaks.

In addition to the direct investment through H2020, a number of partnerships and initiatives have been created to enable for more effective types of cooperation, covering different needs in vaccine R&I, and creating incentives for industry investment in vaccine development.

To accelerate the development of medical products, including vaccines, for poverty-associated and neglected infectious diseases, in 2003 the **European and Developing Countries Clinical Trials Partnership**[9] (EDCTP) was launched. A partnership between African and European countries and the EU, it is currently in its second phase (2014-2024), with a budget of **€1.3bn**.

The **Innovative Medicine Initiative**[10] (IMI), a partnership between the EU and European Federation of Pharmaceutical Industry and Association (EFPIA), was created to speed-up the development of, and patient access to, innovative medicines. Now in its second phase and with a budget of **€3.27bn**, IMI is substantially supporting vaccine research. Through IMI's Ebola+ programme, with a budget of over €200 million, Ebola vaccine candidates have been funded, as well as tools to facilitate the deployment and acceptance of such vaccines, which are now being used in the Democratic Republic of Congo (DRC) and neighbouring countries in the global effort to contain the current epidemic.

The 2014 Ebola outbreak evidenced that the current market processes did not aid the development of products for diseases with epidemic potential. To help tackle this challenge, the **Coalition for Epidemic Preparedness Innovations**[11] (CEPI), an innovative global alliance supported by H2020, was established in 2016 with the aim to finance and coordinate the development of new vaccines to prevent and contain infectious disease epidemics.

Due to the high failure rate during the product development stages, investment in vaccine R&I is risky, therefore giving financial incentives an important role to play in overcoming this challenge. In 2015 the Commission launched the **InnovFin Infectious Diseases Financial Facility** (IDFF)[12], jointly with the European Investment Bank (EIB), to facilitate and accelerate access to finance for innovative businesses and other innovative entities in Europe.

A glance on the future

Horizon Europe, the new EU research and innovation programme, is now under preparation. Its three pillars (Excellent Science; Global Challenges and European Industrial Competitiveness; Innovative Europe) and activities targeted to widen participation and strengthen the European Research Area, will build on the efforts and successes of the previous programme. Horizon Europe will provide new models and opportunities to boost and improve vaccine development and will be instrumental in further stimulating cross-fertilisation and international collaborations to bring public health benefits to the citizens.

6 http://www.i-moveplus.eu/

7 https://www.tellmeproject.eu/content/project-summary

8 http://ecomeu.info/

9 http://www.edctp.org/

10 https://www.imi.europa.eu/

11 https://cepi.net/

12 https://www.eib.org/en/products/blending/innovfin/index.htm

Vaccination in Europe – the crucial role of the health care provider

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Introduction

Immunization has been a great health success story. Consistent widespread use of vaccines has proven successful in controlling or even eliminating disease. Indeed, diseases that commonly killed infants, children, adolescents and adults only decades ago are now virtually unknown in many countries. However, many young people and even health care providers (HCPs) are not aware of these diseases that have been eliminated and others may not fully comprehend the value of vaccines and the importance of herd immunity. Moreover, no matter how strong the science may be and how large and uniform the expert consensus, young adults and adolescents are far more likely to be influenced by the opinions and actions of a friend or peer, or a message on twitter or facebook, particularly in the digital age. Over the past decade, an increasing number of studies have documented a rising amount of people in both high–income and low-income countries who are losing confidence in vaccines, to the point of choosing not to vaccinate their children (https://wellcome.ac.uk/reports/wellcome-global-monitor/2018/). According to organizations such as the WHO and UNICEF, gains in the world's fight against vaccine-preventable diseases are at risk. The WHO has specifically identified vaccine hesitancy – which the organization defines as 'the delay in acceptance or refusal of vaccines despite the availability of vaccination services' – as one of the top ten health threats to the world in 2019.

Therefore recognizing and identifying champions who can inform, communicate and encourage confidence in immunization is key. Partnering with future and current HCPs is a good opportunity to promote the importance of vaccination.

Health care providers in Europe

HCPs are among the most trusted sources of immunisation information, and therefore are a core group to address low or declining public confidence in vaccination. However, reliance on HCP to provide optimal guidance to target population may be jeopardised if HCP, themselves, have doubts about vaccines or if they do not communicate effectively with their clientele. A qualitative study among HCP from four different European countries (Croatia, France, Greece and Romania (Karafillakis et al, 2016) showed that, in general, while the benefits of vaccination were appreciated there were also risks considered to be important such as the fear of side-effects, especially for new vaccines, and the HCP's responsibility for these side-effects if they should occur in their patients. While some HCP see it as their role to respond to hesitancy and have impact one their patients' decision, others feel they should remain neutral, and leave it to the patients to decide. In general, it was felt that vaccine confidence could be improved by more information (e.g. on side-effects) and training (e.g. communication skills), as well as stricter legislation.

Larson et al (2018) showed in a large-scale survey that there is a positive correlation between the GPs believes about vaccines and the public confidence. This recent study assessed the overall state of confidence in vaccines among the public in all 28 EU member states and among general practitioners (GP) in ten EU member states. The survey found that overall GPs are confident in the safety, importance and effectiveness of vaccination and have higher levels of confidence than the general population (except for 1 country). While these results are re-assuring and confirm results from other studies that only a minority of health care providers have concerns about vaccines (Karafillakis et al, 2016; Paterson et al, 2016), confidence of GPs in MMR vaccination is lower in certain countries in the survey.

Overall this illustrates that HCPs can play a crucial role in addressing vaccine hesitancy and in communicating with vaccinees or their parents. Paterson et al (2016) reviewed a number of studies from which it is clear that a good knowledge is related to a better confidence and improved recommendations. Evidence suggests that improved knowledge through training also improves vaccine confidence in HCPs. In addition, HCPs who are vaccinated themselves are more likely to recommend vaccines to others; they also lead by example or role model (Maltezou et al, 2019). In agreement with these findings Paterson et al (2016) report that a lack of preparedness for advising patients about vaccination and a lack of training act as inhibiting factors for recommending the vaccine.

Unfortunately a lot of work remains to be done in Europe to well educate and train our future HCP, nurse, pharmacist and midwife. In order to estimate the current basic knowledge of EU medical students towards vaccines and vaccination policy in Europe, a large web-based survey was performed among the students of the European Medical Student Association (2018): overall, 73% indicated to have courses in vaccinology in their curriculum, ranging from 1-2hours up to several courses. Up to 20% of last year medical students never had had vaccinology teaching in their curriculum!

To assist HCPs in obtaining up-to-date knowledge and information on vaccines and vaccination programmes, increasingly post-graduate courses and in-service trainings are being organized at a national, regional and international level. In an attempt to list all available courses on vaccinology worldwide, a global vaccinology e-portal was set up recently (https://www.global-vaccinology-training.com/) (Duclos et al, 2019).

Conclusion

HCPs serve as the most trusted advisors and influencers of vaccination decisions. A lack of knowledge among HCPs is considered one of the most important factors for vaccine hesitancy. Major efforts are needed to prepare and assist our EU HCP through pre- and in-service training.

Maternal vaccination: A new and highly effective policy to improve European pertussis immunisation programmes

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Hidden potential of full benefit of vaccines lies in immunization policies. This is highlighted by maternal immunization against pertussis. Originally developed for improving the acceptability of pertussis immunization in children, the new generation of pertussis vaccines, so called acellular pertussis vaccines (aP), are now used in pregnant women for eliminating the residual cases of pertussis infant mortality.

The pre pertussis vaccine area

Before vaccines became widely available in the 1950s, pertussis was one of the most common childhood diseases worldwide. 80% of cases occurred in children < 5 years and less than 3% in persons aged ≥15 years. Pertussis was and is still a severe disease particularly in infants with a case fatality rates estimated to be 0,20%, in low-mortality countries explaining that the first objectives of pertussis vaccination is the prevention of severe disease and deaths among infants below 12 months of age.

The first pertussis vaccines

The first vaccines developed against pertussis were the whole-cell pertussis vaccines (wP), which are suspensions of killed *B. pertussis* organisms. The vaccines were introduced for children widely in industrialized countries in mid-20th century and included in the Expended Programme of Immunization since 1974.

Whole-cell pertussis vaccination have been highly successful. It was estimated that without vaccination there would have been >1.3 million pertussis related deaths globally in 2001. In the 1980's due the dramatic reduction of the number of cases of pertussis and rising safety concerns regarding the vaccine, acceptability of the vaccination has dramatically decreased in some developed countries leading to a lower rate a vaccine coverage rate and the resurgence of pertussis.

The second generation of pertussis vaccines

Acellular pertussis vaccines were developed in response to those issues. They contain purified components of *B. pertussis* such as inactivated pertussis toxin either alone or in combination with other *B. pertussis* components. If the relative protective efficacy of the best wP and aP vaccines are comparable, safety studies of the aP have invariably found the acellular vaccines to be better tolerated than the wP vaccines. Consequently, since 1996, aP vaccines have gradually supplanted the use of wP vaccines in industrialized countries for children immunization.

Although routine pertussis vaccination of infants and young children reduced the incidence by more than 99%, the disease persists today. In addition, there has been a shift in the age-specific disease profile with an increased proportion of cases among infants below 1 year of age too young to be vaccinated and among individuals above 15 years of age. This shift has been attributed to the waning of vaccine-induced immunity, because wP vaccines can't be used for booster immunization in individuals > 7 years of age due to local reactions which increase with age and the number of injections.

Additional strategies for preventing early infant mortality

The availability of aP vaccines, better tolerated, provided the opportunity to consider booster doses in adolescents and adults for preventing early mortality in infants too young to be vaccinated.

The first strategy is the indirect protection of infants by reducing the risk of infection through booster on regular basis in adolescents and adults or targeted on the close contacts of infants (i.e. "cocooning" strategy). However, widening coverage with pertussis vaccines appears to have had limited impact in preventing transmission or on the resurgence of periodic epidemic peaks in some countries. In 2017, 42 242 cases of pertussis were reported in EU/EEA countries. Individuals ≥ 15 years of age accounted for 62% of all cases reported and infants < 1 year were the most affected age group.

The second strategy the direct protection of new-borns and infants thanks to maternal immunization. As natural infection does, it has been known for a long time that vaccination during pregnancy, referred to as maternal immunization, can provide protection for the new-born through maternal antibodies actively transferred *via* the placenta.

In response to the national outbreak in 2012, with 14 deaths among 429 infant cases infected with pertussis, the United Kingdom, was the first country in Europe to initiate a maternal vaccination programme. Pregnant women were offered a single dose of aP vaccine between 28- and 38-weeks' gestation. Of note, despite the theoretical basis, the effectiveness of this new immunization policy in the prevention of infant disease had not been established prior the implementation. In addition, according to regulatory information, the vaccine chosen to run the programme was not recommended during pregnancy, due to limited post-marketing information on the safety. Studies carried out for assessing the new policy found that maternal vaccine effectiveness was 90–93% against pertussis and 95% against infant death. Large safety studies didn't show significant increased risk of recognized maternal conditions or of adverse events in infants born from vaccinated women. Since then, Belgium, Czech Republic, Greece, Ireland, Italy, Portugal and Spain have introduced similar maternal vaccination programmes [ECDC] joining several non-European countries (e.g. Argentina, Israel, New Zealand, UK, USA).

Considering that vaccination of pregnant women is likely to be the most cost-effective additional strategy for preventing disease in infants too young to be vaccinated, World Health Organization encourages countries to consider vaccination of pregnant women. And recently, despite moderate to severe local reactions associated with combined tetanus and diphtheria antitoxin (Tdap vaccine) and the lack of monovalent aP vaccine (i.e. standalone), the USA has recommended that pregnant women receive Tdap boosters during each pregnancy considering the potential benefits of maternal pertussis immunization.

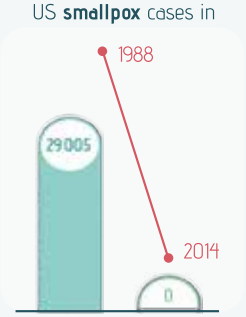
In summary, the success of the implementation of maternal pertussis vaccination in several European countries with a vaccine originally developed for infant immunization and with limited data of its use in pregnant women highlight the importance of immunization policies and their active follow-up to fully benefit from new vaccines.

PUBLIC HEALTH BENEFITS

Vaccines Europe
An industry for healthy lives

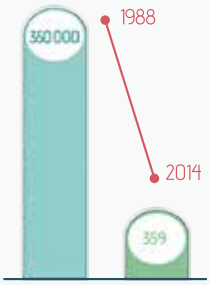
VACCINATION REDUCES ILLNESS & DEATH

US **smallpox** cases in



ERADICATED
(cf ref Back cover B.3)

Global **polio** cases in



NEARLY ERADICATED
(cf ref Back cover B.4)

VACCINATION PROTECTS PATIENTS WITH CHRONIC DISEASES

E.g. **Influenza vaccination**

-50% Heart attack occurence

-28% Death in diabetic patients

-24% The risk of strokes after respiratory diseases

VACCINATION HELPS FIGTHING AGAINST ANTIMICROBIAL RESISTANCE (AMR)

E.g. The use of conjugate **pneumococcal vaccine** reduces the use of antibiotics.
(cf ref Back cover B.6)

ECONOMIC BENEFITS

VACCINATION IS ONE OF THE MOST COST-EFFECTIVE PUBLIC HEALTH INTERVENTIONS

-86% PROJECTED CASES over lifetime in **HPV** related cervical cancers. =

Between £7 500 & €14 500 per quality-adjusted-life-year saved

(cf ref Back cover B.7)

18 YEARS of universal **Hepatits B** vaccine. =

€580 Million in net savings

(cf ref Back cover B.8)

€96 Million SAVED by avoiding **715 000** lost days of work and productivity thanks to **Influenza vaccination**. +

25 000 lives spared / year

(cf ref Back cover B.9)

SOCIETAL BENEFITS

GOOD VACCINATION COVERAGE PROVIDES HERD PROTECTION

Herd protection can indirectly protect individuals with poorer access to healthcare or vaccination programmes, as well as those who cannot be vaccinated (eg. newborns too young to be vaccinated, the immunocompromised, the immunosenescent).

PROTECTING YOURSELF IS ALSO ABOUT PROTECTING OTHERS

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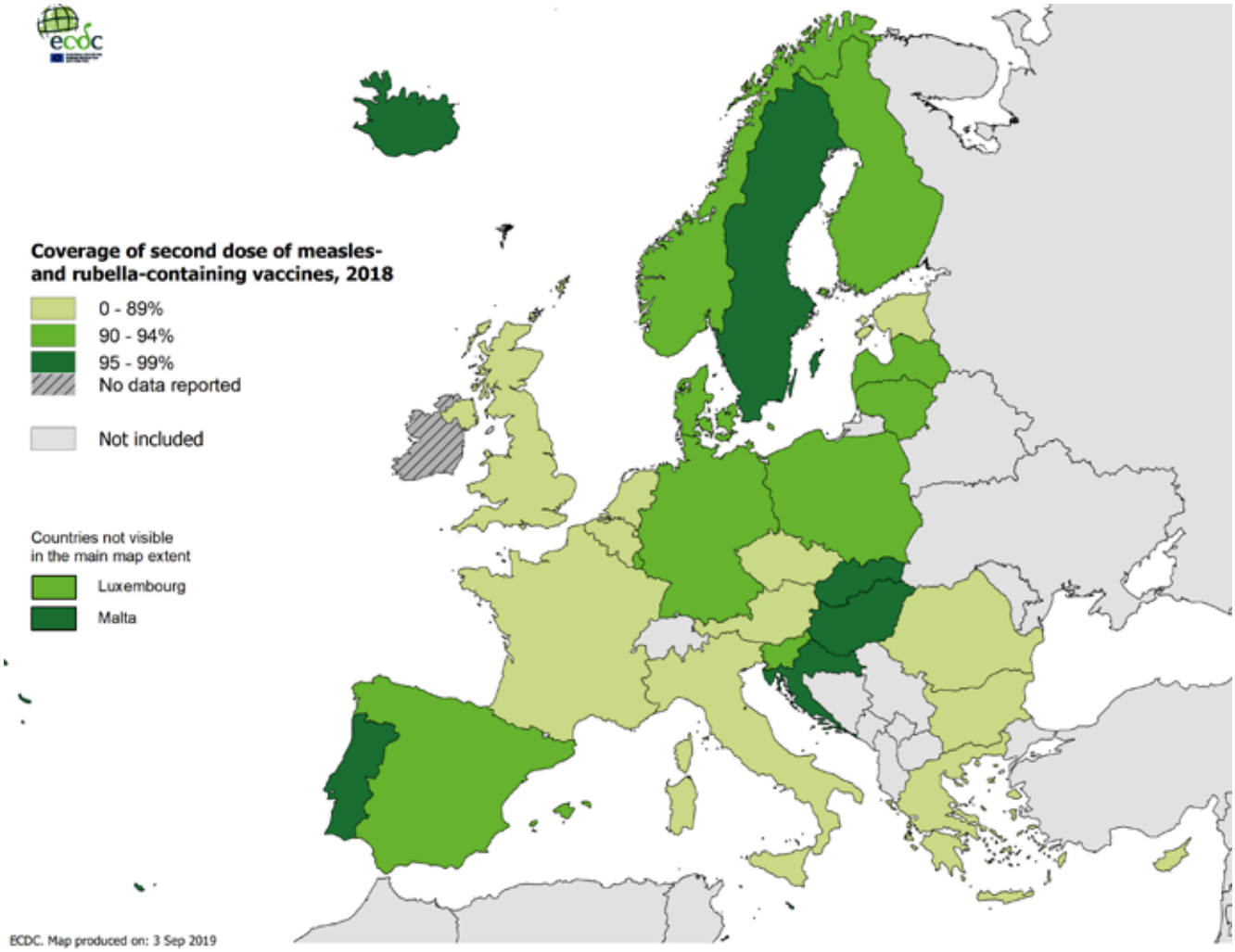
ecdc



ECDC. Map produced on: 3 Sep 2019

European Commission

VACCINE CONFIDENCE IN THE EU

TRUST IS KEY, LET'S ACT TOGETHER

THE EU HAS AMONG THE **LOWEST CONFIDENCE** IN THE **SAFETY** AND **EFFECTIVENESS** OF VACCINES WORLDWIDE

SAFETY
«I think vaccines are safe»

- 69.9% France
- 68.2% Latvia
- 66.3% Bulgaria

82.1% EU

EFFECTIVENESS
«I think vaccines are effective»

- 74.9% Poland
- 72.7% Bulgaria
- 70.9% Latvia

86.5% EU

IMPORTANCE
«I think vaccines are important»

- 85.5% Slovakia
- 78.4% Bulgaria
- 75.9% Poland

90% EU

Older age groups are more likely to be confident than younger age groups.

THE DOCTORS' VIEWS

Overall **confidence in vaccines** is high among general practitioners; especially in Germany, Romania, Spain and the UK.

Female doctors in Germany and Poland are less likely to believe the **seasonal influenza** vaccine is safe.

In Poland and Spain general practitioners with **more years in the profession** are less likely to believe that **measles-containing vaccination** is important and safe.

Enhanced EU coordination to:

- Ensure **access** to vaccination in all European countries.
- Make sure new and existing vaccines follow the **highest safety standards.**
- Share **independent transparent** information.
- Carry out more **research** and **innovative new vaccines.**

Source: State of Vaccine Confidence in the EU 2018 report

LONDON SCHOOL of HYGIENE &TROPICAL MEDICINE

VACCINE CONFIDENCE PROJECT™

For more information: ec.europa.eu/health/vaccination

Learn about the confidence in your country with the Interactive Country Data Viewer: http://www.vaccineconfidence.org/

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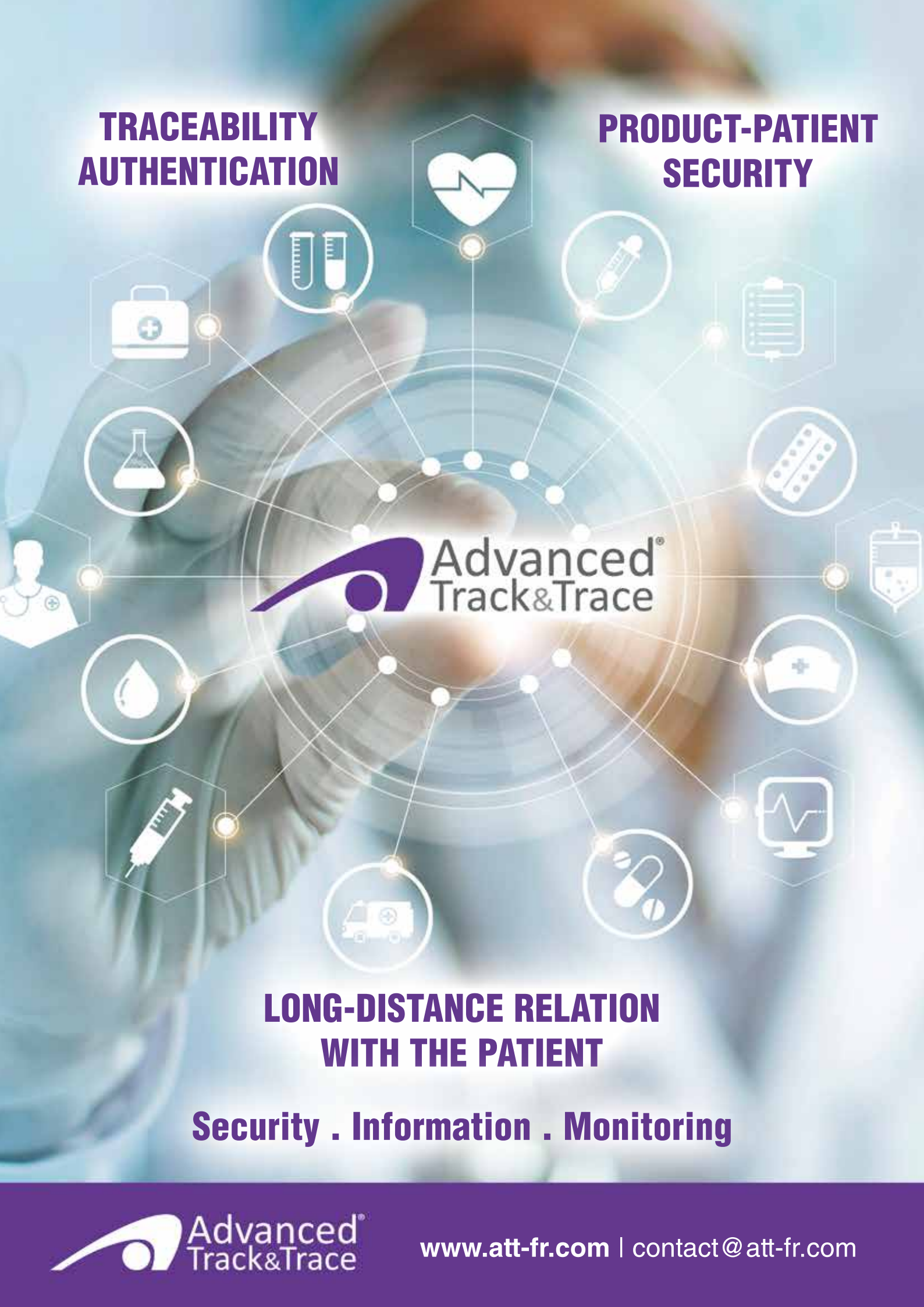
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