Vaccines Europe
An industry for healthy lives

Reflection Paper

Vaccine Innovation – Towards a sustainable and integrated development and implementation of new prophylactic vaccines

Background and problem statement

It is generally accepted that vaccines designed to prevent infectious diseases are one of the most cost-effective health care interventions. The World Health Organization estimates that existing vaccines prevent approximately 2–3 million deaths per year[1]. Vaccines have also indirect economic and social benefits such as improved labour productivity and cognitive development, as well as averted treatment costs.

Today, close to 30 diseases are preventable by vaccination but there remain many unmet needs, for example:

- infectious diseases that have an important medical impact and for which safe and effective vaccines remain elusive (e.g. cytomegalovirus, *Chlamydia trachomatis*, *Clostridium difficile*, *Staphylococcus aureus*);
- infectious diseases for which vaccines are already available but for which the efficacy should be further improved (e.g. seasonal influenza, tuberculosis, herpes zoster);
- specific populations that could be better protected (e.g. elderly, immunocompromised patients, travellers).

By preventing infections and so reducing the need to use antibiotics, prophylactic bacterial and viral vaccines are reducing our dependence on antimicrobials. A paper published recently by the independent Review on Antimicrobial Resistance[2] highlights that many vaccines that would play a crucial role in tackling drug resistance are not on the market or even in early stages of development and concludes that there is a need for a much more robust pipeline of new vaccines to help contain rising drug resistance.

In addition and in view of the ageing of the population, new vaccines, for instance with adjuvants that specifically target the aged immune system, could help to overcome the limitations of immunosenescence and ensure a better protection of the vulnerable elderly population.

As further explained in this paper, there is a real risk that innovative vaccines, for which there is a medical need, will not be developed and made available to the citizens in the EU and the rest of the world.

The non-conducive environment in the EU and elsewhere with increasing regulatory requirements, pressure on the healthcare spending and the tendency towards vaccines commoditisation, has made increasingly difficult for companies to engage in long-term investments needed to enable new vaccines to become developed and accessible to the populations in need.

Importantly, in a context characterised by a relatively limited number of vaccine manufacturers supplying for global public health needs, the non-conducive environment in the EU is also hampering the development of vaccines for the rest of the world, as the EU today

[1] *WHO Factsheet - "Immunization coverage" (Reviewed March 2016)*
[2] *"Vaccines and alternative approaches: reducing our dependence on antimicrobials" – The review on Antimicrobial Resistance (Chaired by Jim O'Neill) – February 2016*

still takes a leading position in development of vaccines for global use and is seen by many countries as a reference (basis for WHO PQ and local marketing authorisation).

Europe has a long history of vaccine discovery, development and manufacturing. More than 80% of vaccines from the major research manufacturers are produced in Europe and of this, 86% is exported for worldwide use. This makes Europe a long-standing leader in both vaccines and public health.

Europe with numerous centres of excellence in vaccinology and related disciplines has the capacity and capability of continuing to lead the discovery of next generation vaccines capable of addressing unmet medical needs. Keeping Europe's lead in such a key sector requires a concerted and coordinated effort to better pool and leverages its capacity and capability.

There is therefore a fundamental need to explore how barriers/blocking factors to the development of these vaccines could be overcome, especially in a context of changing demographic structure of the EU population and rising threats of emerging medical needs such as antimicrobial resistance, which has been identified as a major public health priority at European and worldwide levels[3,4].

A multi-stakeholder reflection appears needed to understand the factors blocking the development of innovative vaccines to address unmet medical needs although technologies are available. This reflection should also broach whether an early and continuous dialogue throughout development could be established with all relevant stakeholders (regulators, HTA bodies, payers….).

Why are some vaccines not being developed although there are medical needs?

As for new antibiotics, the time has come to understand why some innovative vaccines are not developed, what are the R&D, regulatory, implementation and economic barriers obstructing new vaccine development.

The vast majority of the vaccines that are now on the market have been developed through rather straightforward and traditional research models. The complexity of many of the remaining targets necessitates substantial investment of capital and human expertise, making the development of the next generation of innovative vaccines much more complex, challenging, costly and risky.

When designing the R&D plans for a new vaccine, a company has no other choice than to make its own assumptions on the vaccine profile and future medical needs with no possibility to assess whether the candidate vaccine will actually meet the expectations from all relevant stakeholders. This means that vaccine developers have to take an increasingly high level of risks at a very early stage in development in the current challenging economic environment.

Vaccines Europe believes that an open multi-stakeholders discussion is needed to more clearly define the priorities in terms of development of innovative/improved vaccines in Europe and explore how barriers to the development of these vaccines could be overcome to speed access to the population in need.

Policy approaches to developing a sustainable and efficient vaccine ecosystem should encourage long-term investment. Where necessary, some forms of incentives should also be

[3] WHO's first global report on antibiotic resistance reveals serious, worldwide threat to public health - 30 April 2014

[4] Factsheet- AMR: a major European and Global challenge

considered to address situations where the R&D investments would be disproportionate with the expected returns, e.g. for vaccines targeting diseases linked to poverty, bioterrorism or other emerging threats.

Could an early and continuous dialogue throughout development be established with relevant stakeholders?

Vaccine developers should have opportunities to continuously interact with all stakeholders from the earliest stages of development onwards, to ensure that resources are not spent on development activities for vaccines for which approval, recommendation and use are unlikely. Today, in the absence of such a systematic early and continuous open dialogue, vaccine companies pursue their efforts to develop safe and efficacious vaccines, some of which may ultimately never be included in the national/regional immunisation programmes.

It is important for vaccine developers to be aware of the positions of recommending bodies/payers in the different Member States on the product profiles they would consider of interest for their country or region. For example, a vaccine authorised by regulators on the basis of a demonstrated high level of efficacy may not necessary be considered attractive from a public health perspective if it does not contain some antigens (e.g. does not target some serogroups) and thus may not be recommended in certain countries/regions.

Another challenge is that the data generated to support the marketing authorisation of a vaccine are not necessarily the same as the data (usually cost-effectiveness data based on local epidemiology and standards of care) that recommending bodies/payers in the different EU Member States want to have available prior to their decision making.

Considerable efforts are being made at the EU level to foster early dialogue with regulators (RA) and health-technology-assessment (HTA) bodies through parallel scientific advice procedures.

However, for vaccines, multidisciplinary groups of national experts (National Immunisation Technical Advisory Groups [NITAGs]) are responsible for providing independent, evidence-informed advice to health authorities on policy issues related to immunisation and vaccines. The roles of NITAGs and HTAs in the decision making process vary from country to country. Now that parallel RA/HTA scientific advices have shown their added value for drug developers, it appears needed to explore the possibility to involve NITAGs in parallel RA/HTA/NITAG scientific advices for prophylactic vaccines.

Thoughts on a possible way forward

Vaccines Europe believes that EMA has an essential role to play on this debate in the light of all the Agency's efforts to encourage development and timely access to novel medicines and all its efforts to increase partnership with relevant stakeholders within and outside the EU.

Vaccines Europe would like EMA to consider organising a workshop on how to sustain the development of vaccines targeting unmet medical needs by bringing together the various key stakeholders involved in vaccine development, marketing authorisation, recommendation and implementation. This should hopefully allow to reconcile the various points of views, and establish new mechanisms or leverage existing initiatives to support sustainable vaccine innovation in the EU while keeping vaccine safety, efficacy and quality at the core of all activities.

VE 15.12.16