Vaccines Europe reflection paper on DG Research proposal to create a European Clinical Trials capacity/platform on infectious diseases, bio-preparedness, influenza and others potential activities

European Clinical Trials capacity/platform on infectious diseases

Vaccines Europe (VE) supports the concept of creating a European Clinical Trials capacity/platform on infectious diseases but considers that pharmaceutical companies should be involved in defining the format and remit of the future platform to ensure that it responds to the needs of the industry.

The platform should develop and keep up-to-date a catalogue of clinical trial sites in EU that would allow industry to have readily access to detailed information on the site capabilities in terms of enrolment capacity but also in terms of technical expertise and logistic aspects. In particular, the catalogue should list:

- EU sites able to conduct Phase 1 clinical trials and/or studies involving products based on new technologies or containing genetically modified organisms (GMO) or microorganisms or vaccine candidates requiring biological containment level 1;
- EU sites able to perform studies in specific populations (e.g. elderly, paediatric), in specific disease areas or indications (e.g. for prophylactic or therapeutic vaccines) with information on their experience in conducting clinical studies with vaccines;
- EU sites able to perform human challenge studies with an indication of the level of biological containment setting, as needed for pathogens (BSL1, 2 etc.)
- EU sites with capabilities to stratify volunteer's baselines before vaccination (e.g. based on history of exposure to the pathogen, vaccination history or in-depth genetic background profiling using systems biology approaches) or to focus on outliers (non-responders, high reactogenic, high immune response, etc.) and to conduct the investigation over a long period of time;
- EU sites that support the development of patient longitudinal electronic medical records in order to support epidemiologic, vaccine efficacy/effectiveness and safety studies.

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, a burden that might sometimes lead to the decision of stopping/not starting a vaccine development program particularly if the R&D investments would be disproportionate to the expected returns. Another objective of the future European Clinical Trials platform could be to help secure finding funding and/or promote partnership for the development of vaccines with a low commercial attractiveness but a clear medical need. For this purpose, we encourage strong links with clinical sites and investigators in areas of high endemicity (e.g. Tropical areas).

Another challenge faced by the industry is the enrollment of subjects in clinical trials to evaluate vaccines against pathogens that are not circulating locally and that therefore do not bring any immediate benefit to study participants. VE considers that a reflection is needed on how the proposed platform could facilitate/secure the enrollment in such a case.

Bio-preparedness

In the context of bio-preparedness, VE encourages the DG Research to evaluate the need and possibility of creating an EU organization similar to Biomedical Advanced Research and Development Authority (BARDA) in the US. The mission of BARDA is "*to develop and procure medical countermeasures that address the public health and medical consequences of chemical, biological, radiological, and nuclear accidents, incidents and attacks, pandemic influenza, and emerging infectious diseases*".

Specifically, BARDA supports the advanced development and procurement of drugs, vaccines and other products that are considered priorities for national health security and supports innovation through strategic initiatives and investment in technologies and research tools that facilitate countermeasure development. BARDA's support ensures continuity of funding for medical countermeasures developed by industry or emerging from the basic research and preclinical development activities.

VE would support the DG Research to build an EU priority list of potentially emerging pathogens of higher risk for the EU citizens. The WHO list is not including antibiotic resistant pathogens (superbugs) for instance although they are potentially important threats.

Influenza

There is still a need to establish correlates of protection for influenza vaccines. Incentives to create and sponsor a network of clinical sites with the capability to conduct influenza efficacy studies aimed at establishing correlates of protection will help achieve this objective. This will require input from stakeholders in industry, academia, public sector and regulators, in order to manage and share the high burden and risk of this type of study. Collaborations by these sectors is possible, as demonstrated by the progress made, within FLUCOP, the IMI initiative, to standardize a comprehensive toolbox of bioassays needed to measure immune responses to influenza vaccination in humans.

Other potential initiatives

VE believes that the DG Research could also play a role in:

- promoting a scientific and regulatory environment facilitating clinical research with products based on new technologies and/or containing GMOs. In Europe, conducting multi-country clinical studies with products containing GMOs is very complex due to the lack of harmonized guidelines and requirements
- preparing Europe for emerging infections or combatting AMR
- supporting reduction of the impact of chronic diseases (through prevention and disease interception)
- supporting the development of new vaccines that will contribute to a healthier aging of the European citizens
- supporting the development of patient longitudinal electronic medical records in order to benefit data collection for epidemiologic, vaccine efficacy/effectiveness and safety studies.

In addition Vaccines Europe actively participated to the preparation of the first ever-strategic European roadmap for vaccines of tomorrow (**IPROVE)**. [1] [2] As an outcome, the IPROVE roadmap

[1] Medaglini, D., R. De Azero, M., Leroy, O., Bietrix, F., Denoel, P. (2018). Innovation Partnership for a Roadmap on Vaccines in Europe (IPROVE): A vision for the vaccines of tomorrow. *Vaccine*. 36 (9) p. 1136-1145. Accessible at: https://linkinghub.elsevier.com/retrieve/pii/S0264410X17316808. (Accessed on 21 February 2018).

identified 82 recommendations how to tackle challenges around 6 main areas of importance to the Vaccines R&D community in the EU. On the basis of these recommendations, the European Vaccines industry conducted an internal prioritization exercise and selected 7 specific topics of common interest to be supported by new commission research instruments in the coming years via:

- Development or reinforcement of research networks and collaborations
- Support of research, development or innovation projects.
- Identify innovative design of clinical trials and methodologies to profile volunteers earlier in the process

The seven topics are:

1. Explore emergent in-vitro bioassay technologies and improve in-vitro assay for antibody functional screening
2. Research for selection and analysis of epitopes
3. Support research on structural vaccinology
4. Create a toolbox of adjuvants with well-defined profile to shape the immune response
5. Better approach to a combined use of vectors, adjuvants, routes of immunisation
6. Identify innovative design of clinical trials and methodologies to profile volunteers earlier on in the process
7. Develop expertise and support infrastructures to perform controlled challenges in humans.

Vaccines Europe comments on funding instruments

The funding of more targeted research such as in-vitro bioassay technologies, selection & analysis of epitopes, structural vaccinology, create a toolbox of adjuvants and support infrastructure to perform controlled challenges in humans are very important.

IMI has changed vaccine research by fostering pan-European collaborations between public and industry vaccine stakeholders, while generating greater levels of transparency and trust between these parties along the way. More than 15 vaccine projects are now underway and the successes and impactful deliverables become visible. The IMI instrument is often considered as “the” instrument for any health/biotechnology project involving industry. However, the IMI model does not fit all R&I projects. For instance, collaborative projects on vaccine candidates with very low or no commercial potential require a direct support to the Industry (global health projects, emerging infectious disease projects, etc.). IMI has reached a certain limit for vaccines projects because the number of vaccine companies is limited. Moreover, the current IMI/EC rules on in-kind contribution eligibility have limited the initiation of new or more ambitious projects.

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[2] A strategic European roadmap for the vaccines of tomorrow: A joint stakeholder reflection (2016). Accessible at: http://iprove-roadmap.eu/ (Accessed: February 2018).