9 Vaccine SMEs' Needs

As in most innovative sectors, SMEs play a critical role in bridging basic discoveries from academic research to clinical development[36]. This could be seen over the last decade with the increasing amount of both business and licensing deals being signed between small players and larger manufacturers.

These innovative SMEs range from SMEs developing vaccines, SMEs specialised in standard or innovative platforms for vaccines development (3D molecular modelling services, cell lines, formulation, biologics delivery systems, etc.) and SMEs active in connected disciplines, such as biology, nutrition, immunology, mathematics, modelling, etc.) Even if limited in number, part of European SMEs are leading in some specific fields throughout the value chain, as for example (non-exhaustive list):

- Viral vectors with ArenaVax, XBrane bioscience
- Adjuvants with DUOTOL, Crossbeta Biosciences, Microbiotec
- Delivery with Sigmoid, DUOTOL, Bioneedle technologies
- CROs (Confarma, Centrial, WIL research, etc.) and bioprocess equipment developers (Sartorius, etc.)

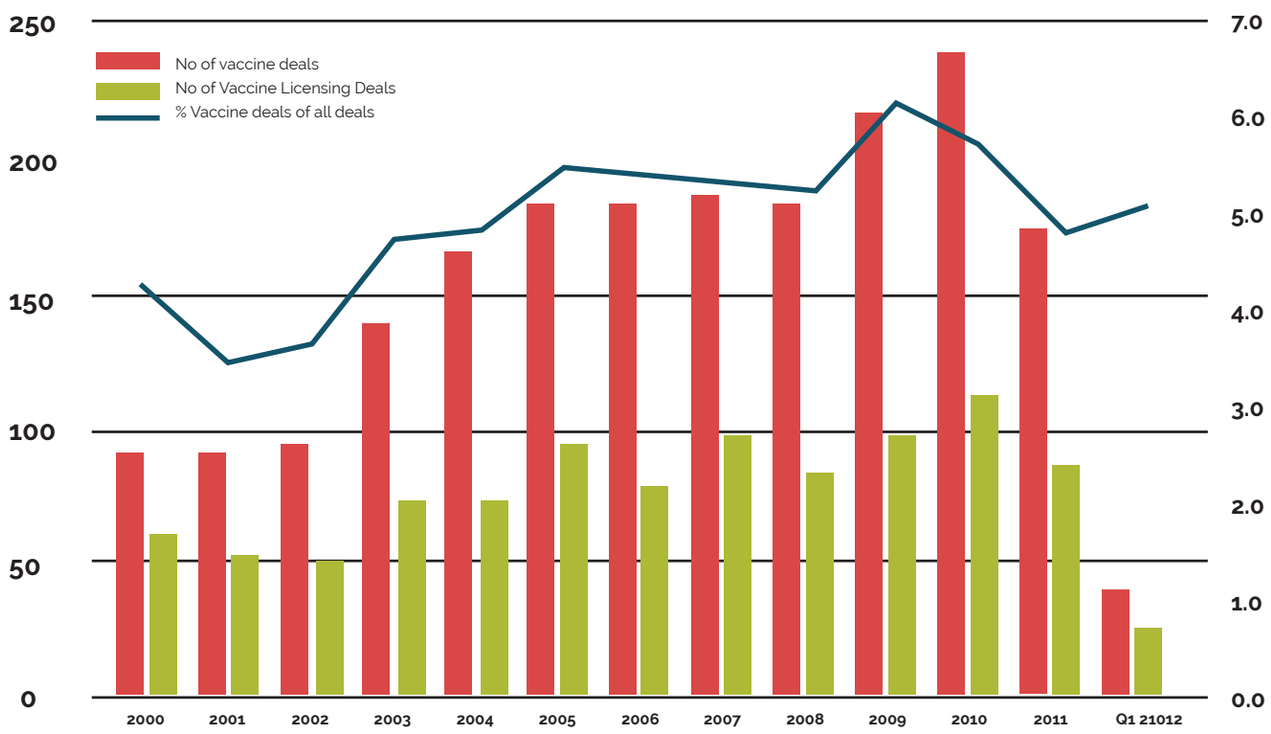
GAPS AND CHALLENGES

The number of vaccine SME players in the EU is low mainly due to the limited, fragmented nature of the European financial market to support these ventures. It was estimated by workshop participants that around 80 companies operate in the field of vaccines in the EU. Furthermore, these SMEs are mostly active at a regional level and lack visibility at EU level. The main European hubs where SMEs working on vaccine development can be found in France, Switzerland, Austria and the United Kingdom and growth trends can be seen in Hungary[37] as well.

Several gaps have been pointed out by the participants in the development phases from preclinical to proof-of-concept (PoC) through to Phase III.

Figure 6: PharmaDeals - Vaccine deal trends 2000 – 2015[38]

Source: PharmaDeals



[36] European Commission (2013)- DG Research vaccine SMEs workshop, March 20th 2013
[37] IPROVE vaccine SMEs' needs workshop (2014); 15 May 2014
[38] Courtesy of GSK – Philippe Denoel (2014) IPROVE workshop on vaccine SMEs' needs; 15 May 2014

These gaps can be clustered around two main challenges identified as the main bottlenecks for SMEs investing in vaccines development to grow further:

- The multiple skills challenge
- The funding challenge

The "multiple-skills" challenge

Although placed right in the 'middle' of the pipeline, i.e. in between academia and industry, SMEs lack resources and capacity to implement their projects. Vaccine development requires from the beginning **specific and broad know-how** for tests, production, and clinical trial settings but also to deal with regulatory constraints and requirements. These skills are concentrated within a handful of large pharma companies, few national institutes and academic platforms. This often leaves SMEs 'out of the game'. There is currently a gap in **securing SMEs access to translational platforms** (public and/or private) that have specific expertise for vaccines. This is indeed one of the key levers to overcome the access to the "skills bottleneck".

Similarly, the consultation of European SME representatives revealed that clinical trials remain extremely challenging for SMEs in Europe, because timelines for regulatory and ethical committees' clearance are long, and perceived deficiencies in the regulatory framework are moving leading-edge technologies elsewhere.

Hence, SMEs **need enhanced collaboration across stakeholders** in order to bridge the expertise/skills gaps they face at specific development stages and to validate the industry's perceived value of SMEs innovation early on. Currently this step is left to individual initiative and could be made more effective through cooperation at EU level.

The funding challenge

The consultation pointed out two recurrent causes of difficult access to private investors for vaccines SMEs: the lack of strong support for vaccines acceptance and the perception of a static environment slow in accepting and embracing innovation. As for **EU funding**, there is a need to better tune existing EU instruments to the specificities of SMEs and vaccines.

Overall, despite the large amount of public funds, several participants stressed that some characteristics of existing funding schemes **do not favour SME research** in vaccine development.

- Funding for promising, early-stage vaccine candidates ready to make the step towards clinical development is very scarce. Financing (possibly through use of a voucher system) directed at feasibility studies to assess GMP manufacturing potential and design coherent clinical development plans would be of great value. However, current SME instruments do not fund products that envisage more than 2-3 years to commercialisation, thereby excluding such projects.
- Follow-up funding of such projects of ca. 3 year duration, allowing scale-up to GMP early clinical trials would fill a current gap
- Also, funding for Phase 2 clinical trials is critical but not part of current SMEs instruments
- Repayment of loans is not fit for actual vaccine research, as the payback timings are lengthy. The loan scheme may only be valid for technology platforms

The assessment criteria to access the existing funding instruments are perceived as inappropriate for vaccine SMEs:

- Up to now, the viability check for SMEs is counter-productive, since many biotechonology companies are only investing in research and the absence of revenue is perceived as a risk requiring additional guarantees or imposing restrictions in accessing funding.
- The same applies to Technology Readiness Levels (TRLs) mechanism, which is inadequate for vaccines developed by SMEs. Vaccine SMEs are rarely or not at all able to deliver a product on the market within 2-3 years and are therefore excluded from most funding instruments.

More broadly, SMEs remain convinced that **more private investors** could be involved to improve the overall financing situation.

RECOMMENDATIONS FOR EU LEVEL ACTION

Five main recommendations arose from the consultation.

1. **Map out and create spaces for structured and unstructured networks: EC support is needed to build a network and structure the community:**

- Create opportunities/forums to push innovation, increasing interaction and discussing success stories as well as examples of failures to learn from a scientific, regulatory, and market point of view and to facilitate early matchmaking

- Such a network would serve innovation in two complementary aspects:
  - First, it would allow SMEs to engage and share knowledge and expertise to drive innovation, and would constitute a forum for gathering EU SMEs voice and allow the EC to better understanding of their specific needs
  - Second, it would ease dialogue with big players and academics, enabling match-making mechanisms and advisory activities tuned to SMEs specific strategies

2. Ease SMEs access to scientific/technical resources and skills, at the most critical phases:

- Pushing and driving support for innovation by identifying innovative ways to facilitate SMEs access to new technologies to reduce R&I costs and timing through collaborative projects and open calls for commissioned research: secured budgets, 'fast track' like processes for innovative SMEs
- Facilitating collaborations between SMEs, large pharma and universities:
  - EC should support effective matchmaking facilitation mechanisms enabling large companies to provide adequate feedback on initial discussions and extend bilateral collaboration to academia where appropriate
    - As an example: A process set-up at EU level to support SMEs in improving their value proposition/ enabling early assessment of SMEs technology/ research innovation with large pharma. Create a pull mechanism by providing better support to the interaction between the two, creating meetings with more time available to discuss and explore partnerships
- In the mid-term, create a vaccines innovation community portal in order to:
  - Improve the exchange of information and facilitate the development of a platform/hub
  - Strengthen the visibility of available opportunities/ services/infrastructures at EU level

3. Supporting SMEs early access to regulatory expertise

- Help with establishing early stage contacts with regulatory bodies, large companies, organisations providing services. Furthermore training initiatives on when to interact with regulatory bodies can be developed teaching how to use existing opportunities. This would serve to give more rapid and formal scientific feedback and aid openness towards the evaluation of new technologies
- Enhance visibility of services that regulatory agencies can provide. Although these services exist, their visibility and accessibility to SMEs could be strengthened

4. Foster competitive collaborative projects between SMEs and larger vaccine companies

- In order to foster collaborative models with large pharma, participants considered that the Commission could be supporting the following activities, within the existing funding mechanisms:

- Develop an **advising mechanism** that could provide SMEs with easier access to existing facilities and platforms across EU, enabling SMEs to benefit from new technologies. Furthermore it could reduce R&I costs, risks and timings, and help large companies in devising risk management plans to favour a greater extent of collaboration with SMEs[39]
- **Commercial contact-making workshops**, which should be a good source of leads
- A platform or a forum at EU level to facilitate **early contact** making with new models of co-development
- New instruments allowing SMEs to share R&D projects on the 'Bio-Europe' partnering model
- Initiatives to support large pharma to provide scientific advice and evaluate projects presented by SMEs
- An EC "window" awards to successful large pharma-SMEs R&I collaborations, contributing a share of pre-agreed milestones payments upon their achievement: funds should be targeted to successful projects only.

5. Sharpen financial instruments and attracting risk capital towards SMEs:

- The overarching recommendation in this area is to **make the ecosystem more receptive** to innovation for SMEs, reducing the level of bureaucracy and risk:
  - Invest in improving the public perception of vaccines as a strategic public health tool, fighting back anti-vaccination activists. Uncertain market demand automatically creates uncertainties for researchers and investors and there is a need to ensure that there is a healthy market for vaccines
  - Supporting **early contact with big pharmaceutical companies** (at least in a consultative role), e.g. by developing EU tailored programmes or call concepts focused on end of pre-clinical and phase I stages

[39] Further elaborated in the infrastructure section of the roadmap

- Better **adjusting public investment to development timelines**, and allowing for funding extension upon development success (US-SBIR-alike system) instead of the current project grant system. Such system is expected to positively bolster innovative SMEs in two ways: reducing risks of gaps in funding, by financing the full development process and helping to drive private investment as a risk sharing approach

- In addition, the consultation proposed to **better adapt current** instruments to vaccines SMEs needs.
  - Foster a dedicated instrument to draft 'calls for proposals' that are relevant for both SMEs and large companies (H2020, IMI). As for IMI specifically, define IMI topics enabling large companies to work with SMEs in the competitive sphere, including in phases 1-2.

Vaccine SMEs

GAPS & CHALLENGES	Recommendations
The multiple skills challenge: vaccine development requires specific and broad know-how for tests, production and clinical trial settings.	➤ **Establish a network of vaccines SMEs involved in human vaccine R&D at EU-level** + Create forums and a European network to push innovation, share knowledge and experience, as well as to conduct a comprehensive needs assessment + Create a vaccine innovation community portal to improve the exchange of information, opportunities, services and infrastructures at EU level ➤ **Ease SMEs access to scientific and technical resources and skills at the most critical phases** + Facilitate SMEs access to new technologies to reduce R&I costs and timing + Effective matchmaking and interaction between SMEs and large companies ➤ **Support better SMEs early access to regulatory expertise** + Facilitate the establishment of early stage contacts with regulatory bodies + Enhance the visibility of services that regulatory bodies can provide at national and EU level ➤ **Foster competitive collaborative projects between SMEs and larger companies** + Develop an advising mechanism to provide SMEs with easier access to existing facilities and platforms + Organise commercial contact-making workshops + Set-up new instruments allowing SMEs to share R&D projects on the 'Bio-Europe' partnering model + Establish an EC "window" awards to successful large pharma-SMEs R&I collaborations
The funding challenge: throughout the development phases from preclinical to proof-of-concept (PoC) and then in Phase III	➤ **Sharpen financial instruments and attracting risk capital towards SMEs** + Invest in improving the public perception of vaccines as a strategic public health tool + Better adapt current instruments to vaccines SME needs: project duration adapted to development timelines, more flexibility in funding extension, publish specific topics enabling large companies to work with SMEs in the competitive sphere, including in phases 1-2