



VACCINES HEADS of QUALITY

White Paper

Call to Action From The Vaccine Heads Of Quality To Contribute In Reducing Vaccine Shortages And Accelerate Access To Vaccines Meeting The Highest Quality Standards

As Quality leaders of the vaccine industry at IFPMA, we are privileged to provide vaccines which eliminate diseases that know no borders. Our accountability is to ensure a state of control for the manufacturing, testing, disposition, storage, and distribution of our products. To ensure a sustainable supply of safe and efficacious quality vaccines, we must continuously improve and innovate.

We, Quality Leaders of the vaccine manufacturing industry (the Vaccines Heads of Quality) at IFPMA, are concerned by vaccine shortages. Several factors can cause vaccine shortages. Solutions are not trivial, and many require collaboration and dialogue between industry and regulators to be effective. This White Paper addresses some contributing factors to vaccines supply issues:

- the current regulatory complexity associated with Post Approval Changes (PACs)
- the increasing multiple and redundant testing of each single batch of vaccine by National Control Laboratories

Regarding the first point, national regulatory authorities set the framework within which manufacturers must operate and for issuing the license that allows a product to be commercialized in their country. As vaccine manufacturers, we seek to continually improve our products, manufacturing processes and analytical test methods as our knowledge increases, by applying innovation and science; we also need to respond to new regulatory requirements, improve Quality Control and expand production capacities, etc. Many of these activities result in Post Approval Changes (PACs) that require regulatory authority approval prior to implementation.

Today, for each PAC it can take up to several years from the first regulatory submission to final global approval because numerous countries/regions require to individually assess and approve the same change regardless of the magnitude. Furthermore, regulatory requirements and associated expectations in many countries are divergent from one to another; the same change can have different documentation requirements, review timelines vary significantly from country to country and regulatory outcomes are not always aligned. This disharmony results in

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manufacturing inefficiency and exacerbates supply chain and inventory complexity to manage multiple versions of a product to comply with individual marketing authorizations. The overall complexity has become a monumental burden for the whole pharmaceutical industry, which is a barrier to continuous improvement, discourages innovation, and augments the risk of supply interruption.

Particularly for vaccines, combined with the high degree of manufacturing and quality control complexity (it can take up to 3 years to manufacture and test one single batch of vaccine), this creates a situation where the supply of vaccines with the latest, highest and most innovative quality standards is more than ever put at risk while health authorities rightfully expect a more secured and sustained supply situation.

In addition to PACs complexity, vaccines are one of the only pharmaceutical products for which an independent testing and release step by health authorities remains before allowing distribution to the market. We have observed in the last years an increase of multiple and redundant testing of vaccines by National Control Laboratories (NCLs). Different practices are applied across the world: from testing waiver to a complete retesting through a simple documentation review. Those additional testing and heterogenous practices create an additional layer of complexity. This is exacerbated when divergent test results are obtained across laboratories, in particular when in vivo tests are performed, due to the inherent variability of such tests. Moreover, due to the time it adds in the test and release process, this has an adverse impact on the vaccines remaining shelf lives. Consequently, these additional and heterogenous local test and release activities can trigger significant supply chain issues impacting the availability of vaccines. In addition, those additional testing requirements have an impact to the availability of “precious” reagents used for testing, consumes valuable resources (both manufacturer and authority) for transfer of testing to NCLs and interpret different test results, and, last but not least, the use of thousands of animals for in vivo testing while some regulations (e.g. the 3R directive 2010/63 in the EU) rightfully requests a dramatic reduction in the use of animals for testing purposes.

Vaccines shortages are a global problem that requires a global solution. To resolve the regulatory complexity associated with PACs, we will join forces with the rest of the pharmaceutical industry to raise awareness and propose common solutions to the unintended consequences of such complexity by leveraging science and risk-based approaches based on an effective Pharmaceutical Quality System, in alignment with ICH guidelines. In addition, we will seek and propose solutions specifically for vaccines to foster a global harmonization of requirements associated with vaccines PACs by leveraging existing guidelines that are vaccines specific (e.g. WHO guideline on post approval changes for vaccines).

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Regarding the redundant testing of vaccines by NCLs, we will develop and propose solutions to progressively harmonize the release processes of vaccines with other pharmaceuticals, by reducing additional testing by NCLs to a minimum and having only one single recognized worldwide NCL batch release.

More recently, there has been an impact due to the COVID-19 pandemic. Current resources at agencies and manufacturers during this crisis have been stretched/stressed due to the increase in the pandemic related issues/etc. This can be seen in examples such as reduced manpower from absenteeism and social distancing; disruptions in supply of raw materials, protective garments and reagents as well as disruption in transportation; and increased demand for vaccines against respiratory diseases (influenza, pneumococcal and pertussis vaccines). The two points discussed in the paper have been further impacted during this time.

The solutions to these issues proposed in this paper can ease this burden in the short term and may provide further evidence about how its implementation in the long term can secure the supply of vaccines no matter which critical situation is met. Overall, the use of regulatory mechanisms based on reliance and work-sharing (as proposed above) can help prevent/mitigate shortages of supplies would be a benefit to patients and would allow agencies and manufacturers to focus all resources on critical activities.

We urge politicians and regulators globally to act beyond national borders and work with us to simplify the regulatory environment and secure the supply of vaccines for everyone who needs them.

To further bring awareness to the situation we are publishing our Quality White Paper and we will use it to engage in a dialogue with all relevant global stakeholders.

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