Accelerate non-animal batch release testing for human vaccines

Year 1 Report

AIM

The project, which is financed by the Bill & Melinda Gates Foundation, aims to accelerate the implementation and regulatory acceptance of non-animal approaches for human vaccine batch-release testing.

With a focus on developing countries, it means to advance the dialogue toward global regulatory alignment, and support the engendering and increase of local competencies, direct experience and confidence in change.

The end goal is to contribute to the acceleration of the uptake of more efficient, cost-effective, relevant and humane approaches to safety assurance, to increase access and lower costs of vaccines for Low-Mid Income Countries (LMICs).

ROADMAPS

Significant efforts will be devoted to the creation of stakeholder- and/or country-specific roadmaps or plans to include non-animal testing opportunities in the local regulations, pharmacopoeias, and in the human vaccine manufacturers' quality-control routine testing.

HUMANE SOCIETY INTERNATIONAL

The project targets a number of legacy human vaccines – all relying on animals for batch release testing – including Diphtheria-Tetanus-Pertussis combined vaccines, Rabies, Hepatitis (B/A), and IPV, for which a number of potency replacement opportunities and safety tests removals have been identified.

SELECTED COUNTRIES

Brazil, India, China, South Korea, Indonesia have been prioritized due to the relevance of their respective internal markets and the import of their local vaccines manufacturers which supply significant swathes of international markets. Other countries of interest, may be engaged should appropriate opportunities arise in the course of the project.

OUTREACH

Outreach activities are planned to engage key local, regional, and international stakeholders, to stimulate discussion, produce alignment on needs and priorities, and agree actions and roadmaps.

HSI's direct involvement will be related to:

- elaboration of dedicated, country-specific local stakeholder engagement and alignment strategies.
- establishment of *ad hoc* local working groups to amplify the effect of the local discussion. The individual stakeholders engaged (or the *ad hoc* local working group, if established) will be guided in their discussions, mapping exercises, prioritization efforts, and planning by the HSI-led International Steering Committee.

HSI will concentrate on securing publicly shared plans and actions for the implementation of non-animal testing methodologies in the countries of reference, and whenever possible, on the practical instantiation of new collaborations and projects for the testing of implementations of new or alternative methods.

FIRST YEAR OUTCOMES

1. International Steering Committee (ISC)

The ISC provides the expert knowledge hub of the project, with members representing different countries and world regions, all established professionals within national and supra-national bodies, international organizations, and manufacturers. They will contribute their competences and endeavour to foster and facilitate networking opportunities.

The ISC meets online every quarter to:

- Discuss global and regional strategies, and approaches for the promotion of dialogue, implementation and regulatory alignment of alternatives to animal testing for human vaccine batch release testing
- Advice on possible solutions to challenges to the implementation of replacement opportunities at global, regional or local level
- Support in the engagement of other experts
- Provide recommendations and ideas for events (webinars, workshops, face to face meetings) that can be organized within the scope of the project

ISC Participating Experts' Organizations

National Regulatory Agencies & Pharmacopoeias

Health Canada (Canada)
FDA Center for Biologics Evaluation and Research (USA)
European Directorate for the Quality of Medicines (EU)
Indian Pharmacopoeia Commission (India)

International Organizations

International Alliance for Biological Standardization (IABS)
PATH (USA)
Vaccines Analytics on behalf of the Bill & Melinda Gates foundation (USA)

Manufacturers Associations

International Federation of Pharmaceutical Manufacturers & Associations (IFPMA)
European Federation of Pharmaceutical Industries and Associations (EFPIA)

Developing Countries Vaccine Manufacturers Network (DCVMN)
Korea Biomedicine Industry Association (KoBIA)

National Control Laboratories

Paul Ehrlich Institut (Germany)
UK National Centre for 3Rs (NC3Rs)
Austrian Agency for Health and Food Safety GmbH – AGES (Austria)

Manufacturers

Biological E (India)
BioFarma (Indonesia)
Butantan Institute (Brazil)
GlaxoSmithKline (GSK)
Johnson & Johnson (The Netherland, Cina)
Merck (USA)
Sanofi (France)

2. Joint Position Statement

The ISC has been instrumental in the definition of a Joint Position Statement for the project.

The document, agreed unanimously, is an expert call by leading experts for concerted efforts by all stakeholders engaged in the vaccine supply chain, to accelerate the implementation of existing and innovative non-animal-based testing strategies an methods whever possible, and to realize a wider regulatory alignment that can help them be accepted and implemented worldwide, with a view to succeeding within the next 10 years.

The Position Statement also marks a significant step forward, in that it states clearly the need to move beyond the 3Rs principle as the essential foundation of a transition away from animal use for vaccine batch release and testing: the authors unanimously expressed the conviction that a transition away from animal-methods needs be grounded and effected on purely scientific grounds, and should not be withheld whenever non-animal methods provide more precise, more reproducible, and overall technically better tools to ensure the quality and consistency of vaccine batches.

The Position Statement **is slated for publication on *Biologicals***.

3. Face-to-Face Meetings

While the ISC acts as a centralized hub of expertise and networking, each geographical region has been supported in the establishment of local working groups, or bilateral stakeholders relationships, where the discussion can be focused on the local specificities and issues to ensure evaluations and efforts are grounded in the objective reality of the differing countries and regions.

Two face-to-face meetings have already taken place:

- India, October 6th 2023
- Brazil, November 6th 2023

South Korea and Indonesia meetings will follow in 2024.

The discussions within the local meetings have already produced a number of extremely meaningful considerations for the local implementation of non-animal methods. Some of the most important are that:

- similar replacement opportunities often receive different level of prioritization from different actors in differing realities.
- there is a need for local, regional and global alignment on further investment for method development (DTaP, DTwP) and on sharing expertise and experience on available methods (Rabies g-ELISA, MAT, rFC, NGS for adventitious agents tests).
- there exists a generalized preoccupation with the availability and affordability of reagents and new technologies.

The project will now focus on two directrixes: the organization of regional and global discussions on the identified priorities; supporting the continuation local discussions with *ad hoc* calls to foster the development of local implementation plans.

Experts will be engaged in the local, regional and global discussions to overcome the identified technical challenges.

4. Planning Tools

To support and help streamline the process for the consideration, evaluation, and implementation of alternatives to animal-based methods, HSI has begun the development of two Excel-based types of instruments that it means to share with the manufacturers, National Control Laboratories and any other interested stakeholders.
The tools capture different dimensions and data, and enable cogent evaluations and a guide for tracking time, open and hidden costs, and results.

The first tool, the *Global Implementation Tracker Template*, captures a project-wide perspective, allowing for the generation of an overall impression of the strategy, steps and effects of transitioning to a non-animal method for release or stability testing.

It allows a roadmap generation and tracking of the implementation process through control gates and regulatory acceptance activities and progress.

The second tool, *Specific Implementation Index Cards*, is actually a *family* of tools, all meant to tackle the transition from the *bottom up*: each card presents the essential informations on a specific method for a specific vaccine, and is meant to assist in the necessary considerations to properly evaluate the feasibility of the switch, in terms of requirements and alternatives, costs, animals, all the way to raising awareness on non-financial costs.

5. Webinars

Technical webinars, open to all the stakeholders from industry, academia, regulatory authorities, NCLs, and any other interested parties, are planned for 2024.

The first will focus on the **Transition to non-animal based vaccine batch release testing. Policy and regulations theoretical aspects and case studies**, including a discussion of the most representative case studies and the available mechanisms of dialogue and collaboration between industry and regulatory agencies.

The second will be about **DT-containing vaccines replacement opportunities. Status of methods development and possible next steps. Specific and separate sessions on aP and on wP to be included**, and it will focus on providing a detailed review of the current state of development and validation of invitro methods for the potency testing of Diphteria and Tetanus components of combined pediatric vaccines.

A third webinar will deal with **Monocyte Activation Test: overcome product specific challenges towards global implementation and regulatory alignment**. During the webinar, developing countries' stakeholders will be invited to share their work on the theme and discuss the country specific complexities, while MAT experts will present solutions implemented to similar difficulties.

A fourth webinar on **Global availability of critical reagents for biologicals testing. Current status, challenges and possible solutions**, as the availability and affordability of critical reagents and standards to be used for production and release testing has emerged as a significant criticality. It will be a collaboration of HSI and the International Alliance for Biological Standardization (IABS).

A number of local webinars are also planned for 2024, for South Korea, India, Brazil and Chinese stakeholders.