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The use of prior knowledge and platform approaches in early vaccine development

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Abstract

The concept of 'platform approaches' and 'prior knowledge' gained widespread prominence after the COVID-19 pandemic, where platform approaches supported the rapid development and approval of COVID-19 vaccines. Since then, multiple regulatory initiatives have been taken to optimise their implementation in drug development, including the set-up of the US Food and Drug Administration (FDA) Platform Technology Designation Program. Although 'platform approaches' and 'prior knowledge' are usually associated with marketing authorisation applications, this article will discuss how the same principles can be implemented in the early development of vaccines and accelerate their time to market.

Introduction

Vaccination is a key component of public health policy with demonstrated cost-effective benefits in protecting both human and animal populations. Vaccines can be manufactured under multiple forms and by using different technologies, including inactivated (killed), toxoid, live attenuated, virus-like particles, synthetic peptide, polysaccharide, polysaccharide conjugate (glycoconjugate), viral vectored (vector-based), nucleic acids (DNA and mRNA) and bacterial vector/synthetic antigen presenting cells.

During the development of the COVID-19 vaccines, regulatory agencies accepted reliance on already existing data from vaccines based on the same technology.[1] This leveraging of existing data, the so-called 'prior knowledge', was not new in vaccine development. For example, seasonal influenza vaccines' reliance on related authorised strains minimises data required for annual updates.[2]

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In a 2018 Joint Biologics Working Party (BWP)/Quality Working Party (QWP) workshop, the European Medicines Agency (EMA) defined 'prior knowledge' as 'including company knowledge from development and manufacturing experience (e.g., experience based on similar compounds, products and processes) as well as reference to scientific and technical publications or application of established scientific principles e.g. within chemistry'.[3]

A particular subset of prior knowledge is the 'platform approach', a term which is used throughout the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) and EMA guidance, but is described in more detail in the ICH Q11 guideline as the 'development of a production strategy for a new drug starting from manufacturing processes similar to those used by the same applicant to manufacture other drugs of the same type (e.g., as in the production of monoclonal antibodies using predefined host cell, cell culture, and purification processes, for which there already exists considerable experience)'.[4]

The World Health Organization (WHO) defines platform technology as 'a group of technologies used as a base upon which other applications, processes or technologies are developed.'[5]

Platform approaches are also referred to as 'platform manufacturing' and 'platform technology' in the framework of manufacturing, and are sometimes used interchangeably.

The use of prior knowledge and platform approaches is 'traditionally' linked with marketing authorisation applications (MAA). However, it can also be used in early stages of development, in particular in vaccines that are based on a common technology.

Nonclinical development

An early step in the development of vaccines is the evaluation of nonclinical safety. For general toxicology studies, a single repeated dose toxicology (RDT) in one species, according to the 'N+1' principle, is usually sufficient for vaccines. In principle, this study needs to be repeated for every new vaccine candidate.[6] Depending on the type of vaccines, other safety toxicology studies may also be required, including biodistribution studies and neurovirulence studies. Safety toxicology studies should be performed under good laboratory practice (GLP) conditions.

In general, there is an ethical consideration to reduce the number of animal studies based on the 3R (replacement, reduction, refinement) principle.[7]

When leveraging safety toxicology data, it is very important to assess which elements of the product are the 'drivers' of safety toxicology and if these drivers are linked to the platform or product-specific variations. For mRNA vaccines formulated in Lipid Nanoparticles (LNP), the driver of the potential toxicity is the LNP composition and, to a lesser extent, the biologic activity of the expressed antigens of the mRNA vaccine. For DNA vaccines that are based on a common backbone like, for instance, a Yellow Fever-based viral vector, the toxicity is mainly driven by the backbone itself and less by the inserted antigen. This is particularly true if the antigen used is well-known and has an already characterised safety profile.

A careful case-by-case assessment is therefore required to establish the nonclinical risk/benefit profile.

For mRNA vaccines, the leveraging of existing nonclinical data of products based on the mRNA platform is discussed in the WHO guidance on mRNA vaccines.[5] As an example, the EMA accepted a non-GLP repeated dose toxicity (RDT) study for Spikevax (Moderna mRNA Covid-19 vaccine)[8] and, for mRESVIA (Moderna mRNA RSV vaccine), accepted the omission of a recovery group[9] in the RDT study.

With Spikevax, the non-GLP RDT study could, in principle, be inadequate for evaluating the nonclinical safety profile. It was accepted, however, as no clear differences in toxicity were observed between this and the GLP RDT studies conducted with other non-COVID-19 mRNA vaccines based on the same platform. For mRESVIA, the platform data were considered to sufficiently characterise the safety toxicology profile, as the LNP composition – the main driver of toxicology profile – was similar to other mRNA-based vaccines. It is important to note in this context that, at the time of initial marketing authorisation, Spikevax was granted 'conditional marketing authorisation' by the EMA.

In DNA vaccines, where the gene of interest is inserted into a plasmid vector, it could be conceived that a full RDT study with a single vaccine could form the basis of a 'platform toxicology program', as the main toxicity driver would be the vector.

As an example, in a RDT study, one antigen could be sufficient to initiate early clinical trials of a vaccine based on the same platform, but with a different antigen inserted. This will, of course, be dependent on several conditions, such as the same route of administration, the same (or less) number of doses, the same dosing regimen, the same or lower doses. Additionally, the 'new' antigen should have a better or similar safety profile than the antigen that has already been included in the 'platform' toxicology trial.

For plasmid DNA vaccines, a biodistribution/persistence study to assesses the presence of plasmid collected from a panel of tissues at multiple time points is required.[10] Until recently, there was a requirement to perform a biodistribution study for each novel DNA vaccine. As studies examining plasmid biodistribution/persistence indicate that DNA vaccines prepared from a common plasmid vector but encoding different antigens behave similarly, biodistribution studies may be waived for DNA vaccines based on platform data from vaccines with the same plasmid vector, but with a different gene inserted.

For vaccines based on a Yellow Fever-derived vector, a nonclinical study is required to assess the neurovirulence.[11,12] As the potential risk for neurotropism is derived from the Yellow Fever vector and not from the inserted gene, performing such a study could be omitted if neurovirulence data from vaccines based on the same Yellow Fever vector are available.

Chemistry, manufacturing and controls

Also, during the chemistry, manufacturing and controls (CMC) development, the leveraging of existing data is possible. This can be considered in a wide range of manufacturing aspects, including process and formulation development, development of analytical procedures, specification setting, stability, and characterisation of impurities, for example.

The use of prior knowledge has been accepted previously by the EMA during the COVID-19 pandemic. This was seen, for example, with Jcovden (Janssen COVID-19 Vaccine) where, based on experience with the Ad26 vaccine platform products, critical quality attributes (CQA), critical material attributes (CMA) and critical process parameters (CPP) were assigned. A process control strategy was also developed based on extensive platform experience.[13] It is also important to take into consideration that, at the time of initial marketing authorisation, Jcovden was granted 'conditional marketing authorisation' by the EMA.

More recently, during the approval of mRESVIA,[9] the EMA also accepted prior knowledge for the development of analytical procedures.

Both the WHO[14] and the EMA[15] reference the possibility of using prior knowledge in their updated guidance on mRNA vaccines. The ICH Q2(R2) and ICH Q14[16,17] guidance of analytical method development also allows the use of prior knowledge.

The EMA toolbox guidance on quality data packages for PRIME applications offers a good framework where prior knowledge can be extrapolated in early development.[18]

It is also possible to leverage existing analytical methods developed for other vaccines based on the same platform. When an established platform analytical procedure is used for a new purpose, validation testing can be abbreviated, if scientifically justified. In certain cases, an analytical procedure can be applied to multiple products with little or no modification of measurement conditions. For a new application of such platform analytical procedures, the subsequent development can be abbreviated, and certain validation tests can be omitted based on a science- and risk-based justification.

The validation package for methods can also be leveraged between different products based on the same platform, where appropriate.

When establishing the shelf-life claim of a novel vaccine, this could be supported by existing stability data of other vaccines based on the same platform. Different parameters would need to be considered to evaluate if making extrapolations is possible, including already tested stability conditions (including stress and accelerated testing conditions), similarity of degradation profiles, potential impact of novel antigen on stability, changes in manufacturing process between the different vaccines and comparability of batch analysis data, for example.

Shelf-life extrapolation would be particularly useful in the early development of vaccines, as it would avoid having to relabel clinical supplies during early clinical trials. This would be particularly true in cases where the first-in-human studies are performed in patients.

Performance of confirmatory stability studies would still be required for novel vaccines based on the same platform, but existing stability data would also support the rational design of this stability. Based on the existing experience, one could assess which release criteria remain stable over time and therefore should not be assessed at each timepoint.

When leveraging CMC data between products, it is important to have an in-depth understanding of parameters that are dependent on the platform, compared with which parameters are product-specific. Conclusive risk assessments in case product-specific data are reduced or omitted as prior knowledge will be required. It will therefore be a case-by-case decision as to whether the use of existing data will be considered acceptable.

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Integrating prior knowledge in early clinical trials

The extent to which prior knowledge/platform approaches can be used in regulatory submissions depends on the degree of similarity between the structural composition, intended effect, manufacturing process and product quality, and proposed context of use between the different vaccines based on the same platform.

The approach of using prior knowledge can, in principle, be applied to all types of biologicals, including, for example, mAbs and other therapeutic proteins, vaccines, viral vectors, cell therapy products and vaccines. However, it is acknowledged that the principle will be difficult to apply to other groups of products and formulations where data are unavailable (for example, data from mAbs are unlikely to apply in general to other types of recombinant products). For complex products in particular, the prior knowledge is expected to be based on very similar products (for example, same viral vector with a similar genetic construct carrying a different gene of similar size).

The leveraging of clinical data with other similar products can support the dose selection (including the selection of starting dose based on existing safety data), as well as the proposed dosing schedule on trials with new products. It can also support other elements of trial design, such as the selection of relevant timepoints.

Regulatory interactions

Where relevant, it is advisable to discuss the use of prior knowledge/platform data upfront with regulators during an agency meeting, in order to receive agreement on the appropriateness of the leveraging of existing data.

At the time of the Clinical Trial Application, it is essential to present and adequately justify the relevance of the use of existing data in the appropriate context.

The information should be in the appropriate part of the submission; that is, in the investigational medicinal product dossier (IMPD) or the investigator brochure (IB). The differentiation between prior knowledge and new product data should be very clear.

In this context, it is important to remember that regulators give approval for clinical trials for individual products, not for platforms. Each trial submission, irrespective of its relationship to an existing platform, is viewed as a standalone.

In the US, it also possible to cross-reference to data from other products via a drug master file (DMF). The DMF is submitted to the FDA and cross-referenced to support one or more medicinal product applications.[19] This approach provides third party confidentiality of the data and IP protection. In the EU, a similar approach is possible for small molecules via the active substance master file (ASMF), but not for biologics and vaccines.[20]

Of note, in 2022, the EMA adopted a veterinary vaccine platform technology master file (vPTMF).[21]

Platform designations

The FDA established a Platform Designation Program in 2024.[22] This designation needs to be formally requested by the pharmaceutical company to the FDA and is subject to a number of eligibility criteria. One of the criteria for this designation is that it needs to be incorporated within, or used by, an approved drug product (NDA/ANDA) or licensed biologic (BLA), which limits its use for early stage biotech companies who are developing multiple products based on the same platform.[23] It is recommended that organisations engage in formal discussions with the FDA before applying for the platform designation.

In the EU, there is currently no equivalent for the FDA Platform Designation Program. However, the newly proposed EU pharmaceutical legislation[24] proposal contains provisions for 'platform technology', which it defines as a technology or collection of technologies that is comprehensive, well-characterised, reproducible and used to support the development, manufacturing process, quality control, or testing of medicinal products or their components that rely on prior knowledge and that are established under the same underlying scientific principles.

It also introduces the notion of a 'platform technology master file' prepared by the owner of the platform technology. This would contain data of a platform technology for which the underlying scientific principles, under which the platform technology is established, have reasonable scientific certainty to remain unchanged across products and to apply regardless of components added to the platform for a medicinal product.

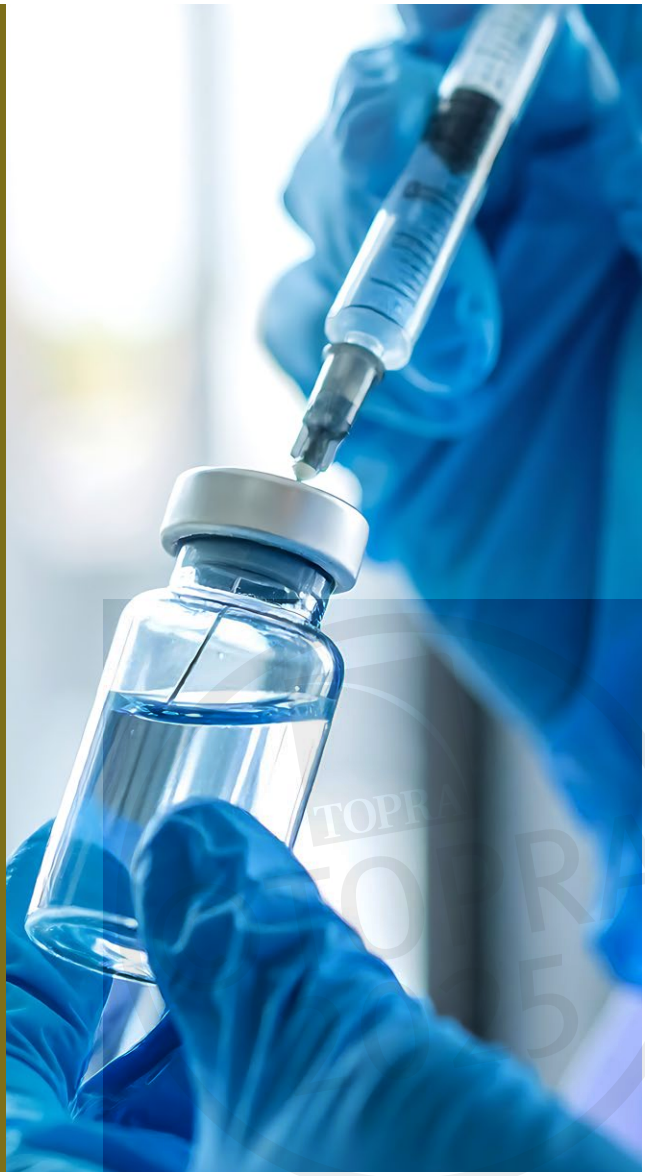
Future development

The expansion of the use of prior knowledge is currently being discussed in the framework of pandemic preparedness and in the framework of accelerated development of products for which there is a high unmet medical need.[25,26] The establishment of a regulatory framework for the use of prior knowledge could be supportive in the development of these products.

Conclusion

The use of 'prior knowledge' and/or 'platform approach' is already an established practice in vaccine development at the time of marketing authorisation. However, the same principles can be applied in the early development of vaccines. It is currently accepted by regulators on a case-by-case basis, depending on the relevance and robustness of the data with similar products. Importantly, it creates a positive environment to help accelerate the development of new medicinal products, in particular in emergency situations such as a pandemic.

Timely interaction with regulators is nevertheless essential to ensure the acceptance of existing data of other products based on the same platform.



References

1. Kalinke U, Barouch DH, Rizzi R, Lagkadinou E, Türeci Ö, Pather S and Neels P (2022) 'Clinical development and approval of COVID-19 vaccines'. *Expert Rev Vaccines*. May;21(5):609-619.
2. Uno N and Ross TM (2024) 'Multivalent next generation influenza virus vaccines protect against seasonal and pre-pandemic viruses'. *Sci Rep.* Jan 16;14(1):1440.
3. European Medicines Agency (EMA) (2018) 'Meeting Report: Joint BWP/QWP workshop with stakeholders in relation to prior knowledge and its use in regulatory applications' (EMA/CHMP/BWP/187162/2018). (Accessed: September 2025).
4. European Medicines Agency (EMA) (2012) 'ICH guideline Q11 on Development and manufacture of drug substances (chemical entities and biotechnological/biological entities) – Scientific guideline' (EMA/CHMP/ICH/425213/2011). (Accessed: September 2025).
5. World Health Organization (WHO) (2021) 'Evaluation of the quality, safety and efficacy of messenger RNA vaccines for the prevention of infectious diseases: regulatory considerations'. (Accessed: September 2025).
6. World Health Organization (WHO) (2005) 'Guidelines on non-clinical evaluation of vaccines, Annex 1, TRS No 927'. (Accessed: September 2025).
7. European Medicines Agency (EMA) (2016) 'Guideline on the principles of regulatory acceptance of 3Rs (replacement, reduction, refinement) testing approaches' (EMA/CHMP/CVMP/JEG-3Rs/450091/2012). (Accessed: September 2025).
8. European Medicines Agency (EMA) (2023) 'Assessment Report: Spikevax'. (Accessed: September 2025).
9. European Medicines Agency (EMA) 'mRESVIA'. (Accessed: September 2025).
10. US Food and Drug Administration (FDA) (2007) 'Guidance for Industry – Considerations for Plasmid DNA Vaccines for Infectious Disease Indications'. (Accessed: September 2025).
11. European Medicines Agency (EMA) (2009) 'Quality, non-clinical and clinical aspects of live recombinant viral vectored vaccines – Scientific guideline' (EMA/CHMP/VWP/141697/2009). (Accessed: September 2025).
12. World Health Organization (WHO) (2013) 'Recommendations to assure the quality, safety and efficacy of live-attenuated yellow fever vaccines, Annex 5, TRS No 978'.
13. European Medicines Agency (EMA) 'Jcovden (previously COVID-19 Vaccine Janssen)'. (Accessed: September 2025).
14. World Health Organization (WHO) (2021) 'Evaluation of the quality, safety and efficacy of messenger RNA vaccines for the prevention of infectious diseases: regulatory considerations'. (Accessed: September 2025).
15. European Medicines Agency (EMA) (2025) 'Development of a guideline on the quality aspects of mRNA vaccines – Scientific guideline' (EMA/CHMP/BWP/82416/2025). (Accessed: September 2025).
16. European Medicines Agency (EMA) (2024) 'ICH Q2(R2) Validation of analytical procedures – Scientific guideline'. (Accessed: September 2025).
17. European Medicines Agency (EMA) (2024) 'ICH Q14 analytical procedure development – Scientific guideline'. (Accessed: September 2025).
18. European Medicines Agency (EMA) (2022) 'Toolbox guidance on scientific elements and regulatory tools to support quality data packages for PRIME and certain marketing authorisation applications targeting an unmet medical need – Scientific guideline' (EMA/CHMP/BWP/QWP/IWG/694114/2019). (Accessed: September 2025).
19. US Food and Drug Administration (FDA) (2019) 'Drug Master Files Guidance for Industry'. (Accessed: September 2025).
20. European Medicines Agency (EMA) (2018) 'Guideline on Active Substance Master File Procedure' (CHMP/QWP/227/02 Rev 4/ Corr). (Accessed: September 2025).
21. European Medicines Agency (EMA) (2022) 'Guideline on data requirements for vaccine platform technology master files (vPTMF)' (EMA/CVMP/IWP/286631/2021). (Accessed: September 2025).
22. US Food and Drug Administration (FDA) (2024) 'Platform Technology Designation Program for Drug Development'. (Accessed: September 2025).
23. Manur SV and Mateti L (2025) 'Navigating the FDA's platform technology designation: Key insights and best practices for drug manufacturers'. *Regulatory Rapporteur. 22(5). (Accessed: September 2025).*
24. European Commission (EC) (2023) 'Reform of the EU pharmaceutical legislation'. (Accessed: June 2025).
25. Vandeputte J, Saville M, Cavaleri M, Friede M, Hacker A, Mueller SO, Rizzi R, Smith D, Thirstrup S, Wagner R, Baay M and Neels P (2021) 'IABS/CEPI platform technology webinar: Is it possible to reduce the vaccine development time?' *Biologicals.* Jun;71:55-60. doi: 10.1016/j.biologicals.2021.04.005 Epub 2021 May 7.
26. Skerritt JH, Tucek-Szabo C, Sutton B and Nolan T (2024) 'The Platform Technology Approach to mRNA Product Development and Regulation'. *Vaccines (Basel)*. May 11;12(5):528. doi: 10.3390/vaccines12050528

Further resources

- Navigating the FDA's platform technology designation: Key insights and best practices for drug manufacturers
- Regulatory Framework for Platform Technologies
- Immunological considerations in the development of novel vaccines