

Vaccines Europe's position paper on the EU HTA Regulation and its application to vaccines – now and in the future

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From application to collaboration – EU HTA Regulation

On 12 January 2025, the Regulation on Health Technology Assessment (HTA) became applicable, creating a new EU framework for the assessment of health technologies by fostering collaboration and coordination between EU Member States (MSs). The objectives of the HTA Regulation are to **improve the availability of innovative health technologies, ensure the efficient use of resources, strengthen the quality of HTAs, and improve business predictability.**

The European Commission (EC) put forward its proposal on 31 January 2018. Adopted in December 2021, the HTA Regulation entered into force in January 2022. During a three-year implementation period before the official application in January 2025, the EC and the MSs prepared by setting up the necessary governance structure and drafted preparatory documents to support an effective application.

As a first step, the HTA Regulation applies to new cancer medicines or advanced therapy medicinal products (ATMPs) seeking marketing authorisation from the European Medicines Agency (EMA), requiring them to undergo a joint clinical assessment (JCA) at the EU level. The rules will be extended to orphan medicinal products in January 2028 and will **as of 2030 cover all new medicinal products, including vaccines.**

The application of the HTA Regulation marks a key milestone, but its success depends on continued efforts from all stakeholders. While the EC and the HTA Coordination Group have played central roles in the implementation phase, contributions from national HTA bodies, patients, clinicians, industry, and other partners have been and will be essential. **This collaborative momentum must continue.**

Being a strategic public health tool, vaccines deserve due and urgent consideration in the EU HTA Regulation

Vaccines are specific medicinal products, and as such, their assessment within an EU HTA framework requires a tailored approach. Unlike treatments administered to individuals with diagnosed conditions, vaccines are preventive interventions given, most of the time, to healthy individuals. This population-level impact (to prevent the disease in the future) means that **vaccine HTAs must account for broader public health outcomes**, such as disease transmission, herd immunity, and long-term epidemiological, clinical and socio-economic

benefits. However, those will usually **not be available at the time of the conduct of joint clinical assessment of a vaccine**. In addition, vaccination often involves complex and heterogeneous immunisation schedules across and within EU countries, multi-cohort target groups, and unique delivery systems, all of which must be carefully considered in both clinical and economic evaluations. Therefore, **already at national level, vaccines are generally not assessed by HTA bodies but by specialised advisory groups** composed of vaccine experts and other relevant stakeholders (National Immunisation Technical Advisory Groups).

The specificities of vaccines have been acknowledged in recital 24 and article 4 of the HTA Regulation, requiring for the HTA Coordination Group to develop methodologies and procedures for performing joint clinical assessments and joint scientific consultations adapted to vaccines.

JCAs will only start for vaccines in 2030. However, Phase II and Phase III clinical trials are currently being planned for vaccines in the JCA's scope as of 2030, as designing and executing a vaccine clinical trial is particularly long (3-5 years) in part due to the large sample size and long follow-up needed. **Vaccines developers, just like developers of any other centrally approved products, are eligible to benefit from joint scientific consultations (JSCs) as of 2025**, paving the way for efficient and meaningful assessments later. Unfortunately, JSCs' relevancy to vaccines appears limited due to the lack of specific methodological guidelines that appropriately capture the preventive nature of vaccines. Additionally, there is uncertainty regarding the inclusion of appropriate vaccine-specific expertise and whether the HTA Coordination Group has the capacity to convene a sufficient number of meetings to meet demand.

Vaccines have demonstrated to be one of the most life-saving public health interventions in history, saving up to 5 million lives globally each year. They play a significant role in addressing global health threats such as antimicrobial resistance, climate change¹, and zoonoses, but also in protecting societies against the impact of geopolitical and demographic changes (e.g., population ageing). Moreover, they can offset their costs multiple times through benefits to individuals, the healthcare system, and wider society². The lack of prioritisation of vaccines, a strategic public health tool, within the HTA Regulation's framework is a missed opportunity.

Key asks addressing the HTA Regulation's implementation for vaccines

To make the HTA Regulation a real and collaborative success in the vaccines space, Vaccines Europe believes that the following key points should be addressed urgently:

1. Systematically involve National Immunisation Technical Advisory Groups (NITAGs) and the European Centre for Disease Prevention and Control (ECDC) in joint HTA activities

¹ <https://www.gavi.org/sites/default/files/programmes-impact/our-impact/Immunisation---a-critical-pillar-of-climate-adaptation.pdf>

² <https://www.ohe.org/wp-content/uploads/2024/04/Socio-Economic-Value-of-Adult-Immunisation.pdf>

National Immunisation Technical Advisory Groups (NITAGs) are multidisciplinary bodies of national experts that provide evidence-based recommendations to policy-makers and immunisation programme managers. As leading and recognised authorities in the vaccines space, NITAGs play a critical role in vaccines assessment in all 27 EU MSs as they are responsible for recommending whether a vaccine should be included in the National Immunisation Programmes (NIPs), whereas HTA bodies are involved in vaccine appraisals in only 14 EU MSs.

Involving NITAGs in all joint HTA activities (JCA, JSCs, horizon scanning, methodologies development) could increase alignment between the JSC, JCA, and national assessment processes, reduce duplicate efforts and ensure relevant expertise in countries is properly leveraged. Especially, NITAGs' early participation in the JSC process would enable NITAGs to anticipate innovative vaccines and allow their views to be incorporated into the advice provided to vaccine developers, including on appropriate evidence generation plans. This could be done via, e.g. considering NITAG members as assessors/co-assessors in the JCA & JSCs processes; providing training to NITAGs on the HTA Regulation; ensuring that NITAGs provide input into the scoping process at a national level.

Coordination with the ECDC is crucial for horizon scanning and evidence sharing. Formal ECDC involvement will bolster NITAG collaboration, providing access to broader data and expert oversight, while promoting collaboration with other key EU health authorities like the Health Emergency Preparedness and Response Authority (HERA) and EMA to streamline and enhance vaccine assessments.

2. Implement appropriate terminology and methodologies for joint clinical assessments (JCAs) of vaccines

The goal of JCAs applied to vaccines should be to support rapid implementation of effective vaccination programmes in Europe. Unfortunately, the guideline documents adopted to date by the HTA Coordination Group are largely therapeutic medicine-oriented and do not sufficiently account for the unique nature of vaccines (preventive intent, long-term benefits, population-level effects). The lack of appropriate methodologies poses **a significant risk of data misinterpretation in JCAs, leading to underestimation of vaccines' full value and ultimately negative impact on access to and confidence in vaccination**. This is particularly concerning when studied alongside the limited involvement of vaccine experts (see point 1 on the NITAGs).

The unique characteristics of vaccines are well-reflected in their evaluation processes and the methodological approaches at national level. For some vaccines, approval may be granted on the basis of randomized clinical trials with immunogenicity endpoints instead of efficacy ones. However, in most cases, there is no defined correlate of protection³, hindering the comparison with other vaccines. Moreover, while RCTs are considered the gold standard for vaccine assessment prior to licensure, vaccine effectiveness studies based on real-world data (RWD) can provide additional information on vaccine performance in real-world settings, but these studies are often not part of the initial clinical assessment. As of today, the HTA Coordination Group's guidelines on indirect comparison don't consider these vaccine specificities, which might result in incomplete or inappropriate assessments.

For example, there is limited data on the duration of protection at the time of assessment and clinical trial follow-up is often not adequate to fully capture it. Mathematical modelling can

³ Correlate of protection (ICP) is defined as a type and amount of immunological response that correlates with vaccine-induced protection against an infectious disease and that is considered predictive of clinical efficacy, EMA's Guideline on clinical evaluation of vaccines, https://www.ema.europa.eu/en/documents/scientific-guideline/guideline-clinical-evaluation-vaccines-revision-1_en.pdf?utm_source=chatgpt.com

estimate the duration of protection beyond the clinical trial follow-up period, however data used may be limited because of e.g., vaccine characteristics, differences in NIPs, seasonality. Real-world evidence (RWE) is instrumental in refining national decision-making processes on immunisation programmes, and hence, could still be used in local HTA following the JCA procedure or in the updates to the JCAs, e.g., by optimising dosing regimens and enhancing guidance on target populations.

Vaccine-relevant aspects of assessment, such as the use of immunogenicity, correlates of protection, surrogate endpoints, epidemiological modeling, and indirect comparisons should be clearly acknowledged and defined in the HTA Coordination Group's methodological guidelines, as well as the role of RWE in measuring vaccine effectiveness and duration of protection.

3. Improve the collection and interoperability of real-world data, including robust surveillance

For years, the vaccines community has been advocating for **improved and harmonised data collection on vaccination across EU Member States**—data that is vital for informing evidence-based decision-making, monitoring vaccine impact, and responding swiftly to public health threats. Despite these efforts, significant gaps remain, particularly in the availability of real-world effectiveness and coverage data.

The EU HTA Regulation presents an opportunity to strengthen this aspect of the evidence ecosystem. While the Joint Clinical Assessments (JCAs) of vaccines will likely proceed without such data (due to their limited availability at the time of assessment), establishing robust and consistent data collection mechanisms at EU level is essential to support consecutive national assessments and enable meaningful updates to JCAs in the future.

This can be achieved by **leveraging the European Health Data Space, paired with dedicated, sustainable funding for the digitalisation of immunisation information systems via the Multiannual Financial Framework and national health budgets**. With these means, data collection registries could be developed to generate RWD beyond phase III trials, fostering collaboration and ensuring the relevance, comparability, and sustainability of joint clinical assessments over time.

Moreover, **the ongoing evaluation of the European Centre for Disease Prevention and Control (ECDC) provides a unique opportunity to boost the agency's capacity** and address the existing key gaps in vaccination coverage data, real-world effectiveness and epidemiological forecasting at the EU level. In addition, the agency could issue EU guidance on, inter alia, the use of RWD studies, collecting vaccine coverage data and conducting post-licensure follow-up, encompassing safety, immunogenicity, efficacy, and long-term protection.

All of the above, and potentially more, is critical to achieve one of the most important objectives of the HTA Regulation – improving the availability of innovative therapies, in this case – vaccines across the EU. It is not an impossible mission, as long as we work together and we start now and not wait until 2030.