Joint Clinical Health Technology Assessment (HTA) for Vaccines in Europe

Call for integrating vaccine specificities, September 2021

Introduction

Vaccines are an important public health intervention protecting the population against infectious diseases. There is currently serious fragmentation of national and/or regional immunisation programmes across the European Union (EU), which impacts the overall protection of the population. In addition, a significant delay occurs between the licensing of a vaccine and the organisation of those vaccination programmes[1], which is exacerbated by a range of organisations undertaking assessments, often duplicating efforts and increasing the risk of heterogeneous outcomes. Health technology assessments (HTA) are increasingly adopted by European countries to inform decision-making and support best stewardship of resources in increasingly complex healthcare systems. However, there is very limited experience in applying HTA methodologies to vaccines, in particular for clinical assessments, as HTA methods and frameworks are traditionally geared towards medicines, not vaccines.

The idea for a harmonized European-wide HTA system "*to improve the sustainability of public health systems and improve patients' access to new medicines*" has led the European Commission (EC) in 2018 to propose a Regulation on a European-wide HTA methodology (the Regulation) which includes provisions for the use of common HTA tools, methodologies and procedures across the EU.

Vaccines Europe shares the European Federation of Pharmaceutical Industries and Associations' (EFPIA) concern[2] on the provisional agreement on increased EU-level cooperation between EU Member States on HTA reached by the European Parliament and Council negotiators[3] and asks to ensure no unnecessary administrative and regulatory barriers to patients' access to new medicines and vaccines will be introduced in Europe.

While it has not been publicly disclosed at which stage of the implementation of the Regulation vaccines will be included, it would need to ensure that the unique **specificities of vaccines,**

[1] Blank PR, Schwenkglenks M, Sardos CS, Patris J, Szucs TD. 589 Population access to new vaccines in European countries. Vaccine. 5902013;31:2862-7.
[2] EFPIA statement "*EU HTA; compromise but at what cost*?", https://efpia.eu/news-events/the-efpia-view/statements-press-releases/eu-hta-compromise-but-at-what-cost/ (Accessed on 18 August 2021).
[3] Press release "*Health Technology Assessment: Informal deal between Council and European Parliament*", https://www.consilium.europa.eu/en/press/press-releases/2021/06/22/health-technology-assessment-informal-deal-between-council-and-european-parliament/ (Accessed on 18 August 2021).

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in terms of process, relevant expert-stakeholder involvement as well as assessment methodology will be considered. This is important considering there is at present limited experience for HTA vaccines in several European countries[4]. In addition, Vaccines Europe wants to emphasise the need to systematically involve the vaccines companies in the future Joint Clinical Assessment (JCA) process, including scoping and appeal mechanism.

Vaccines Europe proposals

To ensure vaccine-unique features are accounted for in a future European-wide clinical HTA methodology and processes, Vaccines Europe believes that the following vaccine-specific considerations need to be realised:

1. Establishment of a European Vaccine Clinical HTA Committee

The composition of the Committee should reflect vaccine specific expertise and capacities and include all relevant stakeholders, i.e. vaccine experts, members of National Immunisation Technical Advisory Groups (NITAG)s, HTA bodies, the European Centre for Disease Prevention and Control (ECDC) and representatives of the Civil society. The Committee should ensure proper assessments through applying vaccine specific processes and assessment methodologies as well as ensuring the EU population perspective is applied consistently, avoiding local or sub-regional division. A good reference point for this Committee could be the European Medicines Agency's (EMA) Vaccines Working Party.

Apart from the Committee, **public health and vaccinology-specific experts should be involved in all stages of clinical HTA assessment of vaccines** to ensure that the direct and indirect impact of vaccines on individuals, society and public health will be properly assessed.

2. Development of vaccine specific methodologies and processes for clinical HTA assessment of vaccines

The goal of Joint Clinical Assessment (JCA) applied to vaccines should be to **support rapid implementation of effective vaccination programmes** in Europe. Specific JCA methods and processes should be developed for vaccines, including horizon scanning based on screening of new developments in vaccinology, early consultations and a dedicated vaccines clinical assessment methodology drawing on available guidance, e.g. World Health Organisation (WHO)[5].

[4] The EU HTA Regulation is built on the lessons learned from EUnetHTA, but only scarce learnings were gained for vaccines. Until now, only one joint relative effectiveness pilot assessment for a vaccine against herpes zoster (Zostavax®, 2013) has been performed by EUnetHTA. Another pilot involving EUnetHTA and some NITAGs took place in 2018 as part of an early consultations process. Consequently, EUnetHTA, the potential configurator body of the future HTA landscape for medicinal products in Europe, has limited experience with vaccines.

[5] https://www.who.int/publications/m/item/WHO-TRS-1004-web-annex-9.

3. Phased approach for vaccines

Given the need to develop appropriate processes and methodological guidelines addressing the specificity of vaccines, JCA for vaccines should be considered in the later stage of the phase-in period of the potential implementation of the Regulation.

4. Continuous Vaccines Industry engagement

The Vaccines Industry should be closely involved in the development of a vaccine specific clinical assessment methodology and processes, e.g. in the implementation phase of the Regulation, the development of a methodology, the evaluation of a new system, and the hearings during the assessment.

Broad value of vaccination

Vaccines are unique for a variety of reasons, especially due to their broad ranging and positive impact on society which is usually not considered in clinical assessments. Among those benefits of vaccination - especially from a clinical assessment perspective are:

- Reducing mortality and protecting individuals against up to 20 infectious diseases and related cancers (with multivalent vaccines helping to protect individuals against several diseases in 1 shot).
- Reducing, as viruses know no borders, cross border threats to health and enabling cross-border travelling in the EU where free movement is a fundamental principle.
- Reducing disease transmission and inducing herd immunity thereby protecting the unvaccinated who may not be directly protected through vaccination (e.g. immunosuppressed persons).
- Reducing the time and quality of life burden imposed on the parents and carers of otherwise affected patients.
- Reducing the potential emergence of antimicrobial resistance (AMR).
- Generating broader country level societal benefits arising from infectious disease control, elimination, eradication and societal peace of mind.
- Minimizing the risk of unpredictable outbreak scenarios, which can result in high costs, temporary capacity constraints across the health system and/or affected communities, e.g. schools or remote at-risk communities.

Further, vaccines are unique due to their broad economic and socioeconomic impact such as maintaining individual and household productivity, taxation revenue and keeping economic sectors such as tourism open. In any future methodology and vaccine value assessments, this

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broad value of vaccines should be considered, also leveraging the value-based approach methodology applied to vaccination[6].

Core Vaccine Features to be Considered

Vaccines Europe has identified a series of core vaccine features that we think should be considered in a vaccine clinical HTA framework. These are oriented towards the four main Relative Effectiveness Assessment (REA) domains: health problems/unmet need, technical characteristics of the technology, clinical effectiveness and safety.

Health problem/unmet need

- Short- and long-term consequences of disease and associated burden on the patient, family/household and caregivers including consideration of impact of vaccine preventable disease on non-communicable conditions (i.e., downstream effects) and impact on long-term functional ability and independency.
- Disease burden at individual and population level (transmission).
- Identification of target population for routine vaccination, based on risk factors and transmission patterns.

Technical characteristics of technology

- Targeted biological nature of the product (complexity of research and development process).
- Goal, scope, and intensity[7] of the immunisation strategy within the healthcare system.
- Implementation (Dosage and scheduling) of vaccination to secure high uptake.
- Storage requirements of the vaccine.

Clinical effectiveness

- Clinical endpoints relevant to vaccines with special consideration of composite and surrogate endpoints:

  - Composite endpoints such as burden of illness scores allow for robust estimation of the vaccine impact on health-related quality of life.

  - Surrogate endpoints are necessary where clinical endpoints of interest cannot be directly observed in a clinical trial (e.g., long-term benefits of HPV or HBV vaccination on cancer, or efficacy data for new pneumococcal vaccines or meningococcal vaccines).

[6] Results of The VIHTALI project "The value(s) of vaccination: building the scientific evidence according to a Value-Based Healthcare approach", https://drive.infomaniak.com/app/share/141741/8c4e56c4-6620-4c77-8095-e967707d8c8a/preview/pdf/21716 (Accessed on 18 August 2021).

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- Population-based modelling at initial evaluation (to simulate transmission, population dynamics, direct and indirect effects including also impact on reduction on antibiotic consumption, healthcare resource utilization and thus transmission of AMR and long-term effects).
- Increased relevance of real-world data to support confidence in effectiveness of preventive vaccines and impact in the population based on clear vaccine effectiveness standards and benefits associated with each condition prevented.
- For all the above points, quality of the evidence must be assessed and robust analyses using rigorous standards must be considered

Safety

- Consideration of regulatory requirements specific to vaccines to avoid duplication.
- Public views on the safety of the vaccination.

Considering especially the insights from COVID-19 pandemic and vaccination against Sars-Cov-2, additional vaccine features beyond the four domains such as the prevention of inequities should be thoroughly assessed for their potential inclusion in clinical HTA.

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