EMA's updated guideline to include broader coverage on Human Challenge Trials

The European Medicines Agency (EMA) published an updated Guideline on clinical evaluation of vaccines (EMEA/CHMP/VWP/164653/05 Rev. 1). This guideline was updated following EMÀ s experience in the past decade with new vaccines applications, including the approval of the COVID-19 vaccines.

These applications have raised several issues for vaccine clinical development programmes that were not addressed in the previous guideline. EMA also encountered requests for scientific advice on vaccine clinical development programmes that have pointed to the need to provide updated or additional guidance on some issues. For example, on considerations for conducting vaccine efficacy trials, identification of immune correlates of protection, vaccines intended to be used in heterologous prime-boost regimens and vaccines to be administered to pregnant women to protect their infants during the first months of life.

The updated guideline also clarifies the role **Human Challenge Trials (HCT)** or Controlled Human Infection Models (CHIM) can play in the development of vaccines. Next to the use as proof-of-concept (PoC) trial in early clinical development, it particularly highlights the possibility to use a Human Challenge Trial to support the development of vaccine in a number of cases like:

When there is no appropriate nonclinical model (eg, when a candidate vaccine is intended to protect against an infectious disease that is confined to humans)

No possibility of comparing immune responses between a candidate vaccine and a licensed vaccine for which there is documented efficacy or effectiveness

When there is no known immune correlate of protection (ICP) or threshold value that could be applied to interpret immune responses.

When vaccine efficacy field trials are not feasible.

The guideline also offers the possibility to use HCT to assist in dose and/or regimen selection.

Recent examples of the use of HCT in vaccine development are:

- The WHO pre-qualification of **Typbar-TCV**, a typhoid conjugate vaccine based on immunogenicity studies and the data on efficacy from the human challenge study
- The Marketing Authorisation of **Vaxchora** a live oral cholera vaccine intended to prevent cholera disease in travellers based on a HCT as pivotal efficacy trial.
- The PRIME and Breakthrough designation of the **Bavarian Nordic RSV vaccine** based on immunogenicity and HCT

Discussions with regulators in an early stage of development are paramount in order to speed up development to ensure the most appropriate development route is chosen.

EMA guideline:
https://www.ema.europa.eu/en/documents/scientific-guideline/guideline-clinical-evaluation-vaccines-revision-1_en.pdf

VIEW GUIDELINE

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