

# Assuring Vaccine Quality by Strengthening Regulatory Agencies: The Work of the World Health Organization

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## INTRODUCTION

A functional and robust national regulatory authority (NRA) underlies the sustained supply of vaccines of assured quality. Guarantee of vaccine quality cannot be provided by the manufacturers alone; adequate regulatory oversight is critical to assure this. According to the World Health Organization (WHO), a vaccine is of known good quality (assured quality) (1) provided that

- the NRA independently controls the quality of the vaccine in accordance with the six specified functions defined by WHO and
- there are no unresolved confirmed reports of quality-related problems.

For this reason, WHO has focused its efforts on strengthening regulatory capacity and expertise worldwide.

Access to high-quality vaccines in the developing world depends on two additional related activities: providing pre-qualification services for vaccines and assuring that vaccines targeted primarily at the developing country market are appropriately regulated. WHO's recent work has been focused on ensuring that all three approaches are followed. This chapter will outline the components of vaccine regulation, define why and how it differs from the regulation of defined chemical medicines, provide a history of vaccine regulation, analyze the components and impacts of the WHO strategy, including the impacts on new vaccine development and access to innovative products, and finally, examine the prospects for the future.

## Regulation of Vaccines: Why Are Vaccines Different?

It is useful to enumerate the functions involved in vaccine regulation and to consider how they might differ from the regulation of chemical medicines, since these two activities are generally performed by the same branch of a national agency, and sometimes by the same staff. Six basic functions have been defined for an NRA by WHO's Expert Committee on Biological Standardization (ECBS), a global committee of experts in biologicals regulation convened annually by WHO, which develops norms and standards for vaccine quality and regulation,

as follows (2): (i) marketing approval, (ii) monitoring of adverse effects following immunization, (iii) lot release, (iv) access to a control laboratory, (v) regulatory inspections for monitoring processes and compliance with Good Manufacturing Practice (GMP), (vi) consideration of clinical trial data to demonstrate field performance. These must be supported by underlying legislation and regulations to form a regulatory system.

- Although aspects of these six functions are present for chemical medicines, some of them have different intents. For example, lot-by-lot release of product is inherent in the characteristics of a vaccine as a biological product, synthesized by or related to a living organism, and thus subject to change depending on external conditions such as temperature and pH. Chemical medicines are generally able to be chemically defined and so content and structure can be determined simply by physical and chemical tests; therefore, lot release is less important. In the case of clinical trials, outcome measures will differ considerably. For vaccines, these are generally directed at immunological response and/or efficacy in preventing disease, while for chemical medicines, key outcomes could be concentrations at the site of activity and clearance times, as well as improvement in clinical status. For all products, however, a system of marketing authorization, compliance with GMP, post-marketing surveillance of performance, and some kind of testing protocols will be needed.

## Brief Description of WHO Inputs

As noted earlier, WHO has used three approaches to assure the quality of vaccines in all countries. These include (i) an initiative to strengthen NRAs; (ii) the prequalification process, important for countries for which vaccines are not procured directly or produced within their borders, but increasingly having more far-reaching impacts; (iii) an initiative to ensure the appropriate regulation of innovative vaccines destined for the developing market. These three activities are firmly rooted in the need for strong regulation, and all depend on the normative activities of WHO, that is, the development of written and physical standards.