



Review

A global regulatory science agenda for vaccines

Lindsay Elmgren^a, Xuguang Li^a, Carolyn Wilson^{b,1}, Robert Ball^{b,1}, Junzhi Wang^c, Klaus Cichutek^d, Michael Pfeleiderer^d, Atsushi Kato^e, Marco Cavaleri^f, James Southern^g, Teeranart Jivapaisarnpong^h, Philip Minorⁱ, Elwyn Griffiths^j, Yeowon Sohn^k, David Wood^{l,m,*,2}

^a Health Canada, Ottawa, Canada

^b Center for Biologics Evaluation and Research, Food and Drug Administration, Bethesda, MD, USA

^c National Institute for Food and Drug Control, Beijing, China

^d Paul Ehrlich Institut, Langen, Germany

^e National Institute of Infectious Diseases, Tokyo, Japan

^f European Medicines Agency, London, UK

^g Cape Town, South Africa

^h Institute of Biological Products, Department of Medical Sciences, Ministry of Public Health, Bangkok, Thailand

ⁱ National Institute of Biological Standards and Control, Potters Bar, UK

^j London, UK

^k Korea Food and Drug Administration, Seoul, Republic of Korea

^l World Health Organization, Geneva, Switzerland

^m Quality Safety and Standards Team, Department of Immunization, Vaccines and Biologicals, World Health Organization, Avenue Appia 20, 1211 Geneva 27, Switzerland

ARTICLE INFO

Article history:

Received 8 August 2012

Received in revised form 22 October 2012

Accepted 31 October 2012

Keywords:

Vaccine regulation

Clinical trials

Post-marketing surveillance

Vaccine quality

Correlates of immunity

Vaccine standardization

ABSTRACT

The Decade of Vaccines Collaboration and development of the Global Vaccine Action Plan provides a catalyst and unique opportunity for regulators worldwide to develop and propose a global regulatory science agenda for vaccines. Regulatory oversight is critical to allow access to vaccines that are safe, effective, and of assured quality. Methods used by regulators need to constantly evolve so that scientific and technological advances are applied to address challenges such as new products and technologies, and also to provide an increased understanding of benefits and risks of existing products. Regulatory science builds on high-quality basic research, and encompasses at least two broad categories. First, there is laboratory-based regulatory science. Illustrative examples include development of correlates of immunity; or correlates of safety; or of improved product characterization and potency assays. Included in such science would be tools to standardize assays used for regulatory purposes. Second, there is science to develop regulatory processes. Illustrative examples include adaptive clinical trial designs; or tools to analyze the benefit-risk decision-making process of regulators; or novel pharmacovigilance methodologies. Included in such science would be initiatives to standardize regulatory processes (e.g., definitions of terms for adverse events [AEs] following immunization). The aim of a global regulatory science agenda is to transform current national efforts, mainly by well-resourced regulatory agencies, into a coordinated action plan to support global immunization goals. This article provides examples of how regulatory science has, in the past, contributed to improved access to vaccines, and identifies gaps that could be addressed through a global regulatory science agenda. The article also identifies challenges to implementing a regulatory science agenda and proposes strategies and actions to fill these gaps. A global regulatory science agenda will enable regulators, academics, and other stakeholders to converge around transformative actions for innovation in the regulatory process to support global immunization goals.

© 2012 Elsevier Ltd. All rights reserved.

* Corresponding author. Tel.: +41 22 791 4050.

E-mail address: woodd@who.int (D. Wood).

¹ Additional CBER scientists who contributed to the document were: Dale Horne, Estelle Russek-Cohen, Hector Izurieta, Marion Gruber, Philip Krause, Konstantin Chumakov, Jerry Weir, Hana Golding, Sheldon Morris, Gopa Raychaudhuri, and Karen Midthun.

² The authors alone are responsible for the views expressed in this publication, which do not necessarily represent the decisions, policy, or views of the World Health Organization or any other institution whose staff have contributed to this manuscript.

Contents

1.	Introduction	B164
2.	How has regulatory science contributed to improved access to vaccines?	B164
2.1.	New tests for evaluation of the live-attenuated oral poliovirus vaccine (OPV): Mutant analysis by PCR and restriction endonuclease cleavage (MAPREC) and transgenic mouse tests	B164
2.2.	Development and use of alternative potency evaluations for release of pandemic H1N1 vaccine	B165
2.3.	Defining international consensus values for serological correlates of immunity for pneumococcal vaccines	B165
2.4.	Improved methods to do near real-time surveillance of health care databases facilitates safety evaluation of vaccines post-marketing	B165
3.	Gaps that could be addressed by a global regulatory science agenda: Evaluating the quality of vaccines	B165
3.1.	Development of new potency assays for inactivated influenza vaccines	B165
3.2.	Research on standardization for quality control and immunogenicity of a new enterovirus 71 vaccine	B166
3.3.	Novel vaccine production technologies	B166
3.4.	Development of new analytical methods	B166
4.	Gaps that could be addressed by a global regulatory science agenda: Non-clinical evaluation of vaccines	B167
4.1.	Assays for novel adjuvanted vaccines	B167
4.2.	Identification of correlates of immunity through non-clinical evaluation	B167
5.	Gaps that could be addressed by a global regulatory science agenda: Clinical evaluation of vaccines	B167
5.1.	Identification of [additional] correlates of immunity	B167
5.2.	Development of correlates of safety	B168
5.3.	Innovative clinical trial design	B168
5.4.	Developing mathematical models for safety data requirements across the product development lifecycle	B169
6.	Gaps that could be addressed by a global regulatory science agenda: Post-marketing surveillance of vaccines	B169
6.1.	Enhancing post-marketing surveillance of vaccine safety	B169
7.	Gaps that could be addressed by a global regulatory science agenda: Cross-cutting research	B169
7.1.	Benefit-risk methodologies	B169
8.	Global regulatory science agenda: challenges	B170
8.1.	Updating benefit-risk analyses throughout the lifecycle of a product: Scientific and regulatory management following post-licensing discovery of signals for possible viral adventitious agents in live viral vaccines	B170
8.2.	Articulating the value of regulatory science in supporting global access to safe and efficacious vaccines	B170
8.3.	Research on regulatory processes	B171
8.4.	Limited pool of regulatory science expertise for vaccines	B171
9.	Proposed cross-cutting strategies and actions to support a global regulatory science agenda	B171
9.1.	Sample repositories	B171
9.2.	International, regional, and national reference preparations	B171
9.3.	Active safety surveillance in selected low- and middle-income countries when new vaccines are introduced	B172
9.4.	Coordination of regulatory science efforts	B172
9.5.	Global regulatory science exchange and capacity-building	B172
10.	Conclusions	B173
	Conflict of interest	B173
	References	B173

1. Introduction

Regulatory science is the foundation of regulatory decision-making and is used to assess the quality, safety, and efficacy of human and veterinary medicines throughout their life-span. The domains covered by regulatory science are considered to include both basic and applied biomedical sciences (such as microbiology, genetics, pharmacology, and biostatistics), clinical trial methodology and epidemiology, and social sciences (such as decision sciences, risk assessment, and communication). Regulatory science aims to contribute to the development of new tools, standards, and approaches to assess the safety, efficacy, quality, and performance of regulated products.

2. How has regulatory science contributed to improved access to vaccines?

The impact of regulatory science on improved vaccine access can be illustrated through some recent examples.

2.1. New tests for evaluation of the live-attenuated oral poliovirus vaccine (OPV): Mutant analysis by PCR and restriction endonuclease cleavage (MAPREC) and transgenic mouse tests

The OPVs that have brought the Global Polio Eradication Initiative close to success were developed by Dr. Albert Sabin by

passage and testing in non-human primates. Expensive, technically demanding tests in old-world monkeys [1] were the main safety tests initially used to assure against increased virulence of the vaccine on growth for production purposes. Two outcomes of regulatory science research have revolutionized testing for revertants: (1) a molecular-based assay that used knowledge gained from studies of mutations associated with attenuation in vaccine strains; and (2) a transgenic mouse model that expresses the human poliovirus receptor, allowing viral replication and pathogenesis, similar to non-human primates and humans.

In the 1980s, major efforts were made to understand the molecular basis of attenuation, and thus neurovirulence, in poliovirus vaccines. The molecular procedure termed MAPREC was developed to measure the proportion of revertants in vaccine bulks [2] and validated through an international collaborative study, to become an official method [3] which provides a more precise assessment of vaccine batch consistency than the monkey test, and is more easily performed.

At the same time that MAPREC was being developed, the cellular receptor for poliovirus was identified [4]. The poliovirus receptor cDNA was used to prepare transgenic mice which, unlike other mice, were sensitive to poliovirus infection and developed clinical signs of infection analogous to monkeys [5]. This alternative animal model to the monkey was validated using vaccines of varying degrees of virulence comparing results to those found in monkeys [6]. A standard operating procedure was developed, and the mouse

Download English Version:

<https://daneshyari.com/en/article/10967223>

Download Persian Version:

<https://daneshyari.com/article/10967223>

[Daneshyari.com](https://daneshyari.com)