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Meeting report

Report of the International Regulatory Forum on Human Cell Therapy and Gene Therapy Products☆

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ABSTRACT

The development of human cell therapy and gene therapy products has progressed internationally. Efforts have been made to address regulatory challenges in the evaluation of quality, efficacy, and safety of the products. In this forum, updates on the specific challenges in quality, efficacy, and safety of products in the view of international development were shared through the exchange of information and opinions among experts from regulatory authorities, academic institutions, and industry practitioners.

Sessions identified specific/critical points to consider for the evaluation of human cell therapy and gene therapy products that are different from conventional biological products; common approaches and practices among regulatory regions were also shared. Certain elements of current international guidelines might not be appropriate to be applied to these products. Further, international discussion on the concept of potency and in vivo tumorigenicity studies, among others, is needed.

This forum concluded that the continued collective actions are expected to promote international convergence of regulatory approaches of the products.

☆ This article may be the work product of an employee or group of employees of Health Canada, Japan Pharmaceutical Manufacturers Association, Medicines and Healthcare Products Regulatory Agency (UK), National Institute for Child Health and Development (Japan), National Institute of Health Sciences (Japan), Pharmaceuticals and Medical Devices Agency (Japan), and other organizations. However, the statements, opinions, or conclusions contained herein do not necessarily represent the statements, opinions, or conclusions of any government agency or organization. The use of commercial product names is for comparative purposes only and does not constitute endorsement by any of the authors, organizations, or agencies.

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Abbreviations

ARM	Alliance for Regenerative Medicine, USA
ATMPs	advanced therapy medicinal products
BLA	biologics license application
CBMPs	cell-based medicinal products
CMC	chemistry, manufacturing, and controls
CPFs	cell processing facilities
CPPs	critical process parameters
CQAs	critical quality attributes
EC	European Commission
EDQM	European Directorate for the Quality of Medicines and HealthCare
EU	European Union
FDA	Food & Drug Administration
FD&C	Federal Food, Drug, and Cosmetic (Act)
FIRM	Forum for Innovative Regenerative Medicine, Japan
GLP	good laboratory practice
GMP	good manufacturing practice
GTiP	good tissue practice
hCTPs	human cell therapy products
HSA	Health Science Authority, Singapore
IABS	International Alliance for Biological Standardization
ICH	International Conference on Harmonization
IPRF	International Pharmaceutical Regulators Forum
iPSC	induced pluripotent stem cells
JPMA	Japan Pharmaceutical Manufacturers Association
JSRM	Japanese Society for Regenerative Medicine
JST	Japan Science and Technology Agency
MCP	minimum consensus package
MFDS	Korean Ministry of Food and Drug Safety
MHLW	Ministry of Health, Labour and Welfare
MHRA	Medicines and Healthcare Products Regulatory Agency
MOA	mode of action
MSCs	mesenchymal stem cells
NGO	non-government organization
NIBIOHN	National Institute of Biomedical Innovation, Health and Nutrition
PEI	Paul Ehrlich Institute, Germany
PHS	Public Health Service (Act)
PMA	pre-market application
PMDA	Pharmaceuticals and Medical Devices Agency
POC	proof of concept
QRM	quality risk management
TFDA	Taiwanese Food and Drug Administration
UK	United Kingdom
USA	United States of America

1. Introduction

Over the last decade, new products based on human cells and genes have emerged and been authorized for marketing globally, including Canada, EU countries, South Korea, Japan, and the USA, among others. Alongside the accelerated research on and developments of human cell therapy products (hCTPs) and gene therapy products (GTPs), different types of regulations as well as national and regional requirements have been in place or under development.

The International Alliance for Biological Standardization (IABS), Pharmaceuticals and Medical Devices Agency (PMDA), National Institute of Biomedical Innovation, Health and Nutrition (NIBIOHN), and Japan Science and Technology Agency (JST) jointly sponsored a workshop held in Tokyo, Japan, from February 18 to 19, 2015 [1]. At the conclusion of the workshop, two suggestions were raised that aimed to contribute to regulatory progress in the cell therapy field. First, several participants suggested that a matrix of requirements by the EU, FDA, Japan, China, and Korea be developed to be able to identify points of agreement and divergence that will be the basis for further discussion. Second, those may identify points that can facilitate or inhibit cell therapy product development. Participants at the workshop also acknowledged the progress in research and development in the field of cell therapy. Such progress has been achieved through the collective efforts among regulators as well as industry and academic societies to provide safe and effective products that benefit patients globally. Sharing common challenges in hCTPs and GTPs regulations from an international perspective is valuable to the stakeholders.

The International Regulatory Forum of Human Cell Therapy and Gene Therapy Products followed through on the discussion on the challenges raised at the IABS workshop. The forum was held in Osaka, Japan, on March 16, 2016 with support from the PMDA, NIBIOHN, and Japanese Society of Regenerative Medicine (JSRM). The forum also obtained support from Japan's Ministry of Health, Labour and Welfare (MHLW), Forum for Innovative Regenerative Medicine (FIRM), and Japan Pharmaceutical Manufacturers Association (JPMA).

The objectives of the forum were to 1.) identify regulatory points/issues to consider for specific types of products; and 2.) determine critical points/issues for various types of products that have to be resolved, improved, and/or developed in terms of sound scientific regulation to facilitate the availability of products in a rational and timely manner, and which will be valuable globally to public health. From a global point of view, the specific issues that need to be aligned scientifically as common principles among regulators at the international level must be discussed. Such alignment of common principles shall allow each regulator certain flexibility to decide on a case basis and a risk-based approach. Participants were also expected to explore future regulatory dialogues and discussions to pursue a data package under minimum consensus for the global development of hCTPs. The facilitation of converging regulatory approaches will enhance the evaluation of hCTPs in a smooth, efficient, and timely manner.

The forum brought together an outstanding and diverse group of speakers from regulatory agencies, industry players, and academic societies. All speakers are at the forefront of the cell therapy field. The forum aimed to identify the regulatory elements of