Regulatory Toxicology and Pharmacology 72 (2015) 102–106

Contents lists available at ScienceDirect

Regulatory Toxicology and Pharmacology

journal homepage: www.elsevier.com/locate/yrtph

Workshop Report

Genomics in the land of regulatory science

Weida Tong [a,*], Stephen Ostroff [b], Burton Blais [c], Primal Silva [c], Martine Dubuc [c], Marion Healy [d], William Slikker [a,*]

[a] National Center for Toxicological Research, US Food and Drug Administration, Jefferson, AR, USA
[b] Office of the Chief Scientist, US Food and Drug Administration, Silver Spring, MD, USA
[c] Canadian Food Inspection Agency, Ottawa, Ontario, Canada
[d] Foods Standards Australia New Zealand, Canberra, ACT, Australia

ARTICLE INFO

Article history:
Received 7 March 2015
Available online 18 March 2015

Keywords:
Genomics
Regulatory science
Next generation sequencing

ABSTRACT

Genomics science has played a major role in the generation of new knowledge in the basic research arena, and currently question arises as to its potential to support regulatory processes. However, the integration of genomics in the regulatory decision-making process requires rigorous assessment and would benefit from consensus amongst international partners and research communities. To that end, the Global Coalition for Regulatory Science Research (GCRSR) hosted the fourth Global Summit on Regulatory Science (GSRS2014) to discuss the role of genomics in regulatory decision making, with a specific emphasis on applications in food safety and medical product development. Challenges and issues were discussed in the context of developing an international consensus for objective criteria in the analysis, interpretation and reporting of genomics data with an emphasis on transparency, traceability and "fitness for purpose" for the intended application. It was recognized that there is a need for a global path in the establishment of a regulatory bioinformatics framework for the development of transparent, reliable, reproducible and auditable processes in the management of food and medical product safety risks. It was also recognized that training is an important mechanism in achieving internationally consistent outcomes. GSRS2014 provided an effective venue for regulators and researchers to meet, discuss common issues, and develop collaborations to address the challenges posed by the application of genomics to regulatory science, with the ultimate goal of wisely integrating novel technical innovations into regulatory decision-making.

1. Introduction

We live in an era marked by significant developments in the advancement of new technologies and innovations in biomedical and food safety research fields resulting in a dramatic increase in our comprehension of genomics, biochemical mechanisms and pathogen behavior. There is a plethora of new analytical tools; some of these tools offer unprecedented high-throughput capabilities that have revolutionized the way standard laboratory experiments are performed. For example, microarray technologies enable the testing of up to tens of thousands of hypotheses at the DNA, RNA and protein levels in a single experiment (Schena et al., 1995). Notwithstanding these rapid technological advances, it may take years for the adoption and application of these innovations in regulatory decision making processes. As depicted in Fig. 1, the translation process from innovation to application usually takes several steps, often an interplay between science and perception. When a new technology is developed, its utility is primarily assessed by non-regulatory entities, usually academia and product development companies such as pharmaceutical entities. During this process, the initial enthusiasm for the new technology gives way to practical reality in a trial-and-error fashion. At the end of this process, the regulatory community finally gains a better understanding of the technology and how it can be used in a "fit-for-purpose" manner in support of regulatory objectives. While this vetting process is critical, it is not necessarily efficient or rapid. Therefore, one of the major challenges is an objective approach to platforms and mechanisms expediting the innovation-to-regulatory application pathway.

To facilitate this process, in 2010, the U.S. Food and Drug Administration (FDA) launched its Advancing Regulatory Science initiative aimed at developing "new tools, standards, and approaches to assessing safety, efficacy, quality, and performance across FDA-regulated products" (http://www.fda.gov/downloads/

* Corresponding authors.
E-mail addresses: Weida.tong@fda.hhs.gov (W. Tong), William.slikker@fda.hhs.gov (W. Slikker).

http://dx.doi.org/10.1016/j.yrtph.2015.03.008
0273-2300/Published by Elsevier Inc.

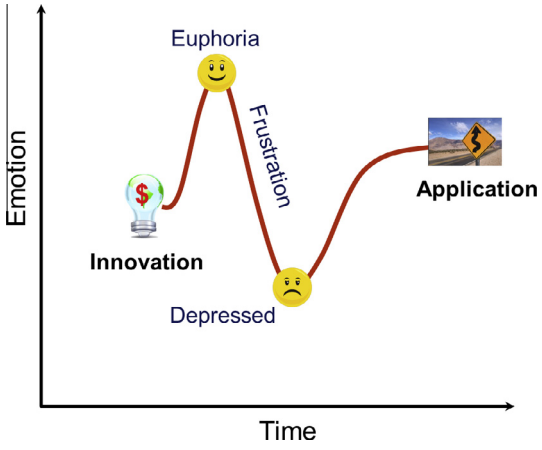

Fig. 1. An illustration of the innovation-to-application process. It usually takes 10–20 years to translate innovation to regulatory application. Therefore, one of the objectives of Regulatory Science Research is to expedite the translation process for innovation by optimizing its reproducibility, standardizing the analysis protocols and promoting data sharing.

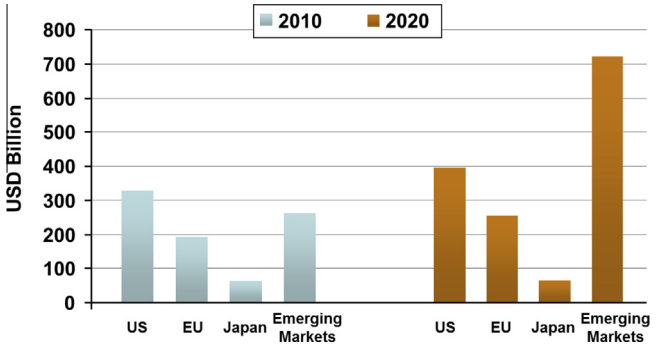

Fig. 2. Pharmaceutical sales in emerging markets are forecasted to outpace US and EU by 2020.

ScienceResearch/SpecialTopics/RegulatoryScience/UCM228444.pdf). The initiative identifies eight scientific areas that affect multiple regulated product domains. The guiding principle of the initiative is to embrace the increased adoption of emerging technologies such as genomics and bioinformatics in regulatory application. As noted by the FDA commissioner (Hamburg, 2011): "Today, we are neither effectively translating scientific discoveries into therapies nor fully applying knowledge to ensure the safety of food and medical products. We must bring 21st century approaches to 21st century products and problems." Regulatory science offers the opportunity to bridge this translational gap.

The FDA, as well as regulatory agencies in other countries, rely on science as the foundation for decision making to fulfill its mission (Woosley, 2013; FSANZ, 2013). Consequently, agencies such as the FDA continuously evaluate new tools for their potential and proper use in the review process. For example, advanced high throughput genomic technologies offer new ways to study disease and toxicity at the molecular level and for discovery of corresponding biomarkers. Even when this technology was in its infancy, the FDA had already started the discussion on how to evaluate these new data streams in supporting the safety and efficacy of new medical products (Goodsaid et al., 2010) and how to develop standards for receiving these new data and ensuring reliable and reproducible results (Tong et al., 2007).

Today's consumer products are increasingly globalized, impacting public health worldwide, posing new challenges for regulatory authorities. For example, imports of drug products into the US have tripled since 2002 (http://www.fda.gov/downloads/AboutFDA/CentersOffices/OfficeofGlobalRegulatoryOperationsandPolicy/GlobalProductPathway/UCM262528.pdf). The FDA currently regulates 300,000 production facilities in 150 different countries. As shown in Fig. 2, global pharmaceutical sales in emerging markets are anticipated to outpace sales in the US and EU by 2020, in contrast to sales in 2010. Regulatory science must confront these new realities and take an approach that emphasizes global partnerships to evaluate new technologies for regulatory application. More specifically, countries need to work together as partners and collaborate in the development of the tools and adopt technologies needed by regulatory authorities throughout the world.

To that end, the Global Coalition for Regulatory Science Research (GCRSR) was established in 2013 as an initiative of the FDA (Howard et al., 2013; Miller et al., 2013; Slikker et al., 2012) and now involves a broad range of countries and regions. The mission of GCRSR is to foster the uptake of emerging technologies by engaging global regulatory agencies. This international coalition has the objectives of facilitating education, scientific training and scientific exchanges in the field of regulatory science. It focuses on research to support regulatory decision making by identifying and promoting best practices to understand and interpret data from innovative technologies such as genomics. To date, GCRSR discussions have been focused on (1) defining the role of global research collaborations in advancing regulatory science and its impact on public health; (2) exploring the future of Regulatory Science Research as a tool for advancing regulatory science in the areas of food safety and medical products; and (3) developing strategies for training regulatory scientists in a global setting. Consequently, its main activities involve (1) holding workshops and scientific meetings to discuss the development of new technologies and their potential application in regulatory settings; (2) exchanging scholars and students for the purpose of providing education and training; and (3) enhancing the development and use of regulatory science principles. To achieve these goals, the annual Global Summit on Regulatory Science (GSRS) meeting has been instituted. GSRS conferences provide a venue for regulators and researchers to meet and develop collaborations that address the challenges and needs in the interest of advancing regulatory science. Four meetings have been conducted so far, with the first (GSRS2011) taking place in the US (Slikker et al., 2012), the second (GSRS2012) in China (Miller et al., 2013), the third (GSRS2013) in the US (Howard et al.) and the fourth (GSRS2014) in Canada (http://www.fda.gov/AboutFDA/CentersOffices/OC/OfficeofScientificandMedicalPrograms/NCTR/WhatWeDo/ucm289679.htm). Here we summarize key discussions from the most recent summit, GSRS2014, which took place in Montreal, Canada, on August 21–22, 2014, and focused on the current and future role and challenges of applying genomics in a regulatory context.

2. Genomics in regulatory science – A key focus of GSRS2014

Genomics has attracted widespread attention as an advanced means of studying the underlying molecular mechanisms of disease progression, health and pathogen behavior and relationships. It has also gained attention as an applied discipline to identify novel molecular targets and disease markers for drug development and/or diagnostic purposes, and to address regulatory challenges that are difficult to overcome by conventional methods. Genomics is recognized in the FDA Advancing Regulatory Science (http://www.fda.gov/downloads/ScienceResearch/SpecialTopics/RegulatoryScience/UCM228444.pdf) strategy as well as by regulatory agencies in other countries as a major opportunity for advancing food safety, medical product development (in terms of safety and efficacy), and precision/personalized medicine. Despite