J Pharm Innov (2017) 12:185–187
DOI 10.1007/s12247-017-9280-2

PERSPECTIVE

Drug Regulation and Oversight, from Local to Global

Julie Babyar[1]

Published online: 25 March 2017

Abstract
Purpose The purpose of this perspective piece is to address the potential for drug and medical product innovation through sound regulation and strengthened international harmonization.
Methods Current literature, recommendations and guidelines in regulatory agencies assisted in this perspective review.
Results Multiple guidelines and recommendations provide for strategic planning and process improvement capabilities at local, national and international levels.
Conclusions Seeking best practice starts with identifying and improving individual nation drug regulatory bodies, including the US Food and Drug Administration (FDA). Inefficiency causes and process improvement solutions have been suggested and outlined in strategic plans at the FDA as well as with multiple stakeholder organizations and public-private partnerships. Cohesively, these groups should be tasked with formal, consistent updates on improvement as well as ongoing supportive research and evaluation of the changes implemented. Simultaneously, the international community has a tremendous opportunity to act on best practice for drug and medical product innovation by aligning sound and consistent approach to regulation.

Keywords Drug regulation · Regulatory medicine · Drug approval · International drug harmonization · Global medicine regulation

✉ Julie Babyar
jbabyar@gmail.com

[1] 415 Herondo St., Apt 332, Hermosa Beach, CA 90254, USA

Perspective

The potential for global harmonization and alliance in drug and medical product regulation continues to grow. The realization of this potential is the future, and by maximizing current recommendations for efficiency at individual national agencies, the future can become the present.

The US Food and Drug Administration (FDA), under the Department of Health and Human Services, continues to bear major scrutiny and criticism. The responsibilities for chemical analyses of products and oversight from the Department of Agriculture were initiated in the 1800s. In 1906, formal laws were set to protect consumers of food and drug products by way of the Pure Foods and Drug Act [1]. The FDA is responsible for approving and regulating drugs and medical devices, from clinical trials to marketed final product. Additionally, the FDA, alongside partnering federal agencies, oversees safety of food and drug products from international trade, importation and exportation. Similarly structured agencies are found internationally, including the European Medicines Agency (EMA).

On the discussion of FDA, efficiency and bureaucracy, there are several identified concerns that are validated in literature. Concerns have been relevant for decades, as advancement and efficiency of the FDA has become of public and congressional priority. The most overarching theme in public eye and within literature is that of new drug applications. An FDA report from 2003 declared that turnover time for new drug applications was 19 months, down from 27 months in 1993. Budget expansion and staffing have been identified as assistants to the decrease in turnaround time. FDA personnel have reported concerns at the FDA, including insufficient review times, workload issues and inability to accurately assess applications due to the stifling of scientific disagreement on decisions [2]. Additionally, between 1996 and 2001, the FDA's Center for Drug Evaluation and Research (CDER)

has published 140 policies to help reviewers in drug review processes [2]. Concerns over new drug applications and FDA administrative issues continue to be addressed and solutions approached through many avenues.

Development and approval of new drugs is not the only focus of concern. Drug components that have already been approved but potentially useful for other purposes must also undergo FDA review. One literature review found that new pediatric indictors are increasingly pursued as new uses for already approved drugs. Approval phrase times were no different in new use reviews compared to new drug applications [3]. New use drug application understanding, research and all policies should be enhanced. Along similar lines are concerns over expedited drug approvals for compassionate use, and compassionate use decisions have been linked to outdated methodology within the FDA. Recommendations for changes to compassionate use and new use are found in the literature as well as acknowledged by the FDA.

In 2004, the FDA released a report on new medical product innovation challenges and opportunities. Out of this report came several recommendations. The FDA Critical Path Initiative was launched as a result (C-Path) as a public-private partnership to accelerate pace of medical production in a cost effect manner [4]. The Clinical Trial Transformation Initiative, co-founded by the FDA and Duke University in 2007, also aims to better advancement of medicine by optimal clinical trial design [5]. Another FDA partnership is the Reagan-Udall Foundation, which was created through Congress in amendment of the Food and Drug Administration Amendments Act of 2007 [6]. Additionally, member organizations such as PHRMA weigh in with specific best practice recommendations for medical product expediency.

Identified recommendations and solutions are common in literature pertaining to FDA and medical product best practices. C-Path has identified six key focal areas where opportunities can improve and transform medical product impact [7]. These six areas include better evaluation tools, streamlining clinical trials, harnessing bioinformatics, moving manufacturing into the twenty-first century, developing products to address urgent public health needs and specific at-risk populations. There are 76 actionable items listed that accompany these recommendations, and updates to these recommendations are listed on their website [4]. In contrast, the Reagan-Udall Foundation specifically addresses projects and partnership funding. Direct assistance from the Foundation is found in three projects: the Big Data for Patients (BD4P) which aims to train patient advocates in big data initiatives, the Critical Paths to TB drug regimens initiative (CPTR), and the Innovation for Medical Evidence Development and Surveillance (IMEDS). IMEDS aims to improve patient care and medical products through methods research agenda coordination using electronic health data. IMEDS also looks to educate on public safety, surveillance, and evaluation to sentinel tools and lessons learned in medial product assessments [6]. Together, these organizations and agencies consist of vast expertise and multiple responsibilities. Solutions and recommendations for optimal drug and medical product innovation have been identified, and organizations already responsible should be tasked with sustained improvement.

Drug and medical product regulation in the USA can be compared and improved with international partners. Strategies deployed should continue to be re-evaluated within the FDA as well as abroad. Patient-reported outcome inclusion in product analyses is a common consideration in European agencies and increasingly used in the FDA [8]. Similarly, diagnostic test requirements in patient population studies are changing under European agencies to align more similarly with the USA [9]. The FDA evaluates more frequently using a "lifecycle" approach, accounting for the drug through post-marketing periods [10]. This is a well-received approach and viewed as more comprehensive, though resource intensive. In contrast, risk evaluation and mitigation strategies used to assess risk in post-marketing evaluations were assessed and found to be lacking in evidence [10]. Safety summary analyses, required by new legislation in 2007, were found to be not very impactful in an FDA review [11]. Inefficient and non-impactful policies should be reviewed and, if applicable, removed.

What is considered acceptable evidence and how it is accepted has been a source of discussion with FDA in focus, and many scientists as well as researchers disagree on study design and evidential impact. In instance, a recent study revealed that the authors, a committee of experts in the field, found that the FDA's requirements of randomized controlled study design in various research phases may not be best for everyone involved [12].

Evaluating the FDA regulatory practice through valid methodology is possible, and this validity must be encouraged in the future. Even among literature accepted through minimal evidence, 33% of the journals revealed that the FDA had create unintended consequences from their processes, and 50% found no impact or weak impact of the FDA process [13]. Comparison studies with international partners can only strengthen and increase understanding for consistent and accurate approaches to regulation.

New and recent redesigns on an international scale support the worldwide desire for improved, expedited medical care. The World Health Organization has a significant presence in drug and medical product development, though much of this presence centers on capacity building and access for underdeveloped and developing countries [14]. In 1999, the WHO distributed a drug regulatory manual for countries, in effort to strengthen consistency and foundation. Several years later, the WHO identified that only about 50 national regulatory agencies provided transparency through online information

access. While training in regulatory practices is provided by WHO, drug regulation is ultimately the responsibility of the individual nations [14]. As such, inconsistencies and varied standards continue to create malalignment in an increasingly global market.

In effort to address continued and new regulatory incongruences, the International Coalition of Medicines Regulatory Authorities (ICMRA) was recently formed. ICMRA is a strategic, voluntary entity that aims to establish a global framework in regulatory science, prioritizing for pharmaceuticals, biologics, genetic therapies, radiopharmaceuticals, and combination products. Health Canada is the interim chair, and Ireland and Japan represent the vice chairs. Management Committee governance includes representatives from the leading drug authorities of the following countries: Australia, Brazil, Canada, China, the European Union, Ireland, Italy, Japan, Netherlands, Singapore, South Africa, the UK and the USA [15].

International alignment is important not only for innovation and safety consistency, but to have cohesive support against the counterfeit drug movement, to enhance global health access and have a voice to trade and corporate protection interests. International alignment is also important for classification of drugs in effort for optimal medical innovation. In example, the regulation process for drug abuse and classification within the USA falls under the authority of the DEA, an agency that works in conjunction with the FDA for drug approval. The DEA requests the assistance of the Assistant Secretary of Health to assist in drug approvals and classification of each drug. Within literature, it is found that this classification process is unpredictable, with some wait times as long as 11 months [16]. Minimizing internal inefficiencies can assist in optimal performance and turnaround time for drugs and medical products, and assuring international consensus on classification of drugs is crucial.

In summary, the foundation for harmonization in drug and medical product regulation has been established. Seeking best practice starts with identifying and improving individual nation drug regulatory bodies, and the most prominent of these is the US Food and Drug Administration in the USA. Inefficiency causes and process improvement solutions have been suggested and outlined in strategic plans at the FDA as well as with multiple stakeholder organizations and public-private partnerships. Cohesively, these groups should be tasked with formal, consistent updates on improvement as well as ongoing supportive research and evaluation of the changes implemented. Simultaneously, the international community has a tremendous opportunity to act on best practice for drug and medical product innovation by aligning sound and consistent approach to regulation. As these improvements come to fruition, the future has never been brighter.

Compliance with Ethical Standards

Conflict of Interest There are no conflicts of interest to declare.

Human and Animal Rights and Informed Consent This article does not contain previously unpublished studies with human or animal subjects performed by any of the authors.

References

1. FDA. Home Page. http://www.fda.gov/. Published 2016. Accessed September 24, 2016.
2. Office of the Inspector General (Department of Health and Human Services). FDA ' S Review Process for New Drug Applications. 2003.
3. DiMasi JA. Innovating by developing new uses of already-approved drugs: trends in the marketing approval of supplemental indications. Clin Ther. 2013;35(6):808–18. doi:10.1016/j.clinthera.2013.04.004.
4. Critical Path Institute. Who We Are. https://c-path.org/about/. Published 2016. Accessed September 30, 2016.
5. Clinical Trials Transformation Initiative. Who We Are. https://www.ctti-clinicaltrials.org/. Published 2016. Accessed September 30, 2016.
6. Reagan-Udall Foundation. About Us. http://www.reaganudall.org/about-us/. Published 2016. Accessed September 30, 2016.
7. U.S. Department of Health and Human Services. Critical Path Opportunities List. 2006.
8. Basch E, Geoghegan C, Coons SJ, et al. Patient-reported outcomes in cancer drug development and US regulatory review: perspectives from industry, the Food and Drug Administration, and the patient. JAMA Oncol. 2015;1(3):375–9. doi:10.1001/jamaoncol.2015.0530.
9. Senderowicz AM, Pfaff O. Similarities and differences in the oncology drug approval process between FDA and european union with emphasis on in vitro companion diagnostics. Clin Cancer Res. 2014;20(6):1445–52. doi:10.1158/1078-0432.CCR-13-1761.
10. Psaty BM, Meslin EM, Breckenridge A. A lifecycle approach to the evaluation of FDA approval methods and regulatory actions. Jama. 2012;307(23). doi:10.1001/jama.2012.5545.
11. Sekine S, Pinnow E, Wu E, Kurtzig R, Hall M, Dal Pan GJ. Assessment of the impact of scheduled postmarketing safety summary analyses on regulatory actions. Clin Pharmacol Ther. 2016;100(1):102–8. doi:10.1002/cpt.346.
12. National Academies Press, Practice PH. Ethical and Scientific Issues in Studying the Safety of Approved Drugs Committee on Ethical and Scientific Issues in Studying the Safety of Approved Drugs; Board on Population Health and Public Health Practice; Institute of Medicine 2012.
13. Briesacher B, Soumerai S, Zhang F, et al. A critical review of methods to evaluate the impact of FDA regulatory actions. Pharmacoepidemiol Drug Saf. 2013;22(9):11–9. doi:10.1002/pds.3480.A.
14. World Health Organization. Annual Report 2015 WHO Essential Medicines and Health Products Annual Report 2015. 2015.
15. Health Canada. Fact Sheet. http://www.hc-sc.gc.ca/dhp-mps/intactivit/drug-medicament/icmra-eng.php. Published 2015. Accessed September 30, 2016.
16. Rocha BA. Principles of assessment of abuse liability: US legal framework and regulatory environment. Behav Pharmacol. 2013;24(5–6):403–9. doi:10.1097/FBP.0b013e328363d163.