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Qualification process of drug development tools in different countries

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Abstract
Drug Development Tools are methods, materials, or measures that have the potential to facilitate drug development. Examples of these tools may include, but are not limited to: a biomarker used for clinical trial enrichment, a clinical outcome assessment (COA) used to evaluate treatment benefit, or a disease specific animal model used for efficacy testing under the Animal Rule. Qualification is a regulatory decision that means that within a stated context of use (COU), a Drug Development Tool has been demonstrated to reliably support a specified manner of interpretation and application in drug development. Qualification process of these development tools, is different in some way or other in various countries.

Keywords: drug development, qualification, drug development tool, biomarkers, clinical outcome assessment, animal models

1. Introduction

Process of drug development

For small-molecule drugs, the path to a marketed drug involves a long and exhaustive journey through basic research, discovery of the medicine, preclinical development tests, increasingly complicated clinical trials with humans, and regulatory approval by the Food and Drug Administration (FDA).

Step 1: Discovery and Development: At this stage in the process, only few compounds out of thousands of compounds may become potential candidates for development as a medical treatment. After early testing, however, only a small number of compounds look promising and call for further study.

Step 2: Preclinical Research: Before testing a drug in people, researchers must find out whether it has the potential to cause serious harm, also called toxicity.

Step 3: Clinical Research: "Clinical research" refers to studies, or trials, that are done in people. As the developers design the clinical study, they will consider what they want to accomplish for each of the different Clinical Research Phases and begin the Investigational New Drug Process (IND), a process they must go through before clinical research begins.

Step 4: FDA Review: If a drug developer has evidence from its early tests and preclinical and clinical research that a drug is safe and effective for its intended Use, the company can file an application to market the drug. The FDA review team thoroughly examines all submitted data on the drug and makes a decision to approve or not to approve it.

Step 5: FDA Post-Market Safety Monitoring: Despite the rigorous steps in the process of drug development, limitations exist. Therefore, the true picture of a product's safety actually evolves over the months and even years that make up a product's lifetime in the marketplace. FDA reviews reports of problems with prescription and over-the-counter drugs, and can decide to add cautions to the dosage or Usage information, as well as other measures for more serious issues.

2. Types of drug development tools

1. Biomarker: the drug development tools, biomarkers are one of the most widely Used & invaluable tool to enable meeting the goal by confirming the efficacy and safety of drug candidates. The term "biomarker", refers to a broad subcategory of medical signs – that is, objective indications of medical state observed from outside the patient – which can be measured accurately and reproducibly.

2. Clinical outcome assessment: Clinical outcome assessments (COAs) measure a patient's symptoms, overall mental state, or the effects of a disease or condition on how the patient functions.

3. Animal Models: Animal model is a living, non-human animal Used during the research and investigation of human disease, for the purpose of better understanding the disease without the added risk of harming an actual human being during the process.

3. Role of Drug Development Tools (DDT) in Regulatory affairs

The challenges of modern product development and globalization underscore the critical importance of modernizing and advancing regulatory science to match advances in basic and applied science and technology.
Clearly, for scientific advances to realize their full potential

for improving public health, FDA must be able to issue clear guidance, play a major role in the improvement of modern product and process development tools, and make sound regulatory decisions about risks and benefits of products that increasingly involve new technologies.

To help meet these challenges, a Strategic Plan for Regulatory Science has been developed, the science of developing new tools, standards, and approaches to assess the safety, efficacy, quality, and performance of FDA-regulated products. FDA identifies priority areas where new or enhanced investments in regulatory science research capacity will be essential to continued mission success and to public health and safety.

Rapid identification of potential therapeutic targets for medical product development has been facilitated by widely accessible biological information, sophisticated bioinformatics tools to map pathways and build systems biology models, and high throughput screening methods.

4. Regulations of drug development tools in different countries

United States

- The guidance has been prepared by the Office of Compliance in the Center for Drug Evaluation and Research (CDER) in cooperation with the Center for Biologics Evaluation and Research (CBER) and the Office of Regulatory Affairs (ORA) at the Food and Drug Administration.
- At present, FDA runs a DDT Qualification Program within its Center for Drug Evaluation and Research (CDER). The program has been described by agency officials as "a mechanism for formal review by CDER to qualify drug development tools, and provide a framework for interactions with the Center to better identify data needed to support qualification of these tools."

Europe

- In Europe, the EMA (European Medicines Agency) qualification process is a new, voluntary, scientific pathway leading to either a CHMP (Committee for Medicinal Products for Human Use) Qualification opinion or a qualification advice on innovative methods or drug development tools, which would aid in the process of drug development. CHMP qualification opinion on the acceptability of a specific Use of the proposed method (e.g. Use of a novel methodology or an imaging method) in a research and development (R&D) context (non-clinical or clinical studies), based on the assessment of submitted data.

Japan

- In Japan, the regulation made is to understand the features of the innovative statistical strategies, such as modeling & simulation and adaptive design, and to discuss their potential of Use in new drug development. PMDA (Pharmaceuticals and Medical Device Agency) considers the Use of novel Biomarkers related to drug response in development of medicines is expected to enhance and to realize creation of medicines with higher efficacy and less adverse effects.

India

- Semi-regulated countries like India still lack appropriate regulations and guidelines for drug development & qualification process for drug development tools. Clinical Practice is a set of guidelines for biomedical studies which encompasses the design, conduct, termination, audit, analysis, reporting and documentation of the studies involving human subjects. The fundamental tenet of (GCP) Good Clinical Practice is that in research on man, the interest of science and society should never take precedence over considerations related to the well being of the study subject.

ICH Guidelines

- The ICH guideline describes recommendations regarding context, structure and format of regulatory submissions for qualification of genomic biomarkers as defined in ICH E16. The Use of biomarkers has the potential to facilitate the availability of safer and more effective drug or biotechnology products, to guide dose selection and to enhance their benefit-risk profile. This guideline is based on previous experiences with submissions containing biomarker data in the various regions. These submissions have been either stand-alone biomarker qualification applications or a component of medicinal product-related regulatory process marketing applications (NDAs / BLAs / MAAs).
- The development of a consistent format for submission of biomarker data will facilitate easy review and exchange of assessments between regions. The objective of the guideline is to create a harmonized recommended structure for biomarker qualification applications that will foster consistency of applications across regions and facilitate discussions with and among regulatory authorities

5. Conclusions

- Apart from U.S, there is no regulated country specifying the tools which can be qualified to aid in the drug development process.
- Regulated countries like Japan & Europe have considered the FDA drug development tools essential to boost the development process during the clinical trials.
- Hence, it can be said that qualification process of drug development tools is essential to facilitate drug approval but semi regulated countries like India still lack appropriate guidelines for qualifying the tools.

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