BIOPROCESS ONLINE

Guest Column | February 3, 2020

Evaluating New FDA Draft Guidance: Qualification Process For Drug Development Tools

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The FDA issued its draft guidance on the qualification process for drug development tools in December 2019[1], as part of the commitment mandated by the 21st Century Cures Act. The guidance defines drug development tools (DDTs) *as methods, materials, or measures that have the potential to facilitate drug development*. Examples of DDTs may include a biomarker used for clinical trial enrichment, a clinical outcome assessment (COA) used to evaluate clinical benefit, or an animal model used for efficacy testing of medical countermeasures under the regulations commonly referred to as the Animal Rule. The agency's basis for standardization is to create broadly recognized DDTs which, within a specific context of use (COU), can be used to demonstrate key characteristics of the drug development, simplifying the review and accelerating the development and approval process of new drug therapies.

Qualifying Within Context

When the FDA qualifies a biomarker, it is qualified for a specific context of use. That is why the COU statement should describe all of the elements characterizing this purpose and manner of use as well as define the boundaries within which the available data adequately justifies use of the DDT. As data from additional studies is obtained over time, requestors of DDTs may continue working within the qualification program to submit a new project with additional data to expand upon a qualified context of use.

The guidance provides a general FAQ section to address the broader program navigational questions as they relate to the FDA's stated objectives of encouraging innovation and a shared learning environment leading to the development of new tools in the context of unmet needs and the formation of collaborative groups that increase efficiency and lessen the individual resource burden.

Qualifying Is Voluntary

Seeking qualification of a drug development tool for a specified context of use is voluntary. A drug development tool is considered qualified if the primary conclusion, based upon the stated COU, will facilitate a specific interpretation in a regulatory review based upon its role in the drug's development. A qualified DDT will be publicly available for use in any drug development program for the qualified context of use and will not require prior agreement with a review division or office on its acceptability for that specific use. Drug development tools that have not been qualified, or that are qualified for a different context of use, may still be used in regulatory applications based upon conversations with the relevant agency.

Specific FDA Qualification Programs

The guidance summarizes the FDA's three drug development tools qualification programs: the Biomarker Qualification Program (BQP), the Clinical Outcome Assessment Qualification Program (COAQP), and the Animal Model Qualification Program (AMQP). In the case of biomarker qualification, the program goals are to work with stakeholders for input and direction to support the identification and development of new biomarkers, to provide a process and framework for qualifying biomarkers used in regulatory decision making, and to qualify a biomarker for a specific COU that addresses clearly stated drug development needs.

A clinical outcome assessment (COA) may be used to determine whether a drug has demonstrated a clinical benefit. Generally, the FDA will consider qualifying a COA as part of the program if it is well defined and reliably assesses a targeted concept for a specified context of use in adequate and well-controlled investigations. For purposes of supporting new drug development, regulatory review, and labeling, a qualified COA may be used in clinical trials.

does not guarantee that it will be appropriate for all drugs or biologics under development. Other types of animal models, such as those used for proof-of-concept testing or for safety testing, are not eligible for qualification under the CDER/CBER program.

Three-Step Qualification Process

There are three steps to submitting and qualifying a drug development tool for a specific context of use:

1. Letter of Intent (LOI) – Three Months

Submitting a letter of intent initiates the qualification process. The LOI should clearly describe the drug development tool, a relevant drug development need, and a proposed context of use along with a scientific rationale in support of these elements. The FDA may return the LOI submission to the requestor if additional information is required. However, if the LOI submission is complete, the FDA will issue a reviewable memorandum to the requestor. The FDA aims to complete the LOI review within three months of issuing the reviewable memorandum. The LOI review concludes when the FDA issues the requestor a LOI Determination Letter, at which point the proposed DDT is formally considered a part of the drug development tool program.

2. Qualification Package (QP) – Six Months

The second stage of the process constitutes the comprehensive review of the submission. The QP should include all available relevant data, knowledge gaps, data collection, and the analysis plan. It should address any prior feedback from the FDA in the LOI Determination Letter, as well as any subsequent advice provided by reviewers. The package should include any planned study protocols and analytic plans along with an estimated time frame for completing data collection, data analysis, and reporting. If all needed information is contained in the submission, the FDA will issue the requestor a reviewable memorandum, thereby initiating the time frame for the QP review. The FDA aims to complete the QP review within six months of issuing the reviewable memorandum and the review concludes when the FDA issues the requestor a QP Determination Letter. The Determination Letter will include requests for data and recommendations regarding data needs for the Full Qualification package (FQP). If a QP is not accepted, a requestor may revise and resubmit, withdraw, or redirect the project focus with a new DDT and LOI.

3. Full Qualification Package (FQP) – 10 Months

The FQP is the final stage of submission in the qualification process, and it should include detailed descriptions of all studies, analyses, and results, as described in the FDA's response to a requestor's qualification package. As in prior stages, upon submission there is an initial assessment, during which the FDA assesses the FQP for completeness. If the assessment determines there are missing elements, the agency could issue the requestor a non-reviewable memorandum describing the information that is needed. If the submission is considered complete, then the FDA will send the requestor a reviewable memorandum and initiate its final comprehensive review of the FQP. The outcome of the comprehensive review could result in acceptance of the DDT for the intended COU or, based upon the data submitted, the DDT could be approved for a modified context of use. The FDA goal is to complete the FQP review within 10 months of issuing the reviewable memorandum. This stage concludes when the FDA issues the requestor a qualification Determination Letter.

Conclusion

The draft guidance provides a high-level description of the intent and content of the drug development tool qualification program, but it does not address evidentiary standards or performance criteria for purposes of DDT qualification, leaving it to industry to propose the scientific argument and data package. Considering the myriad potential of context of use applications, qualifying a drug development tool may require more than one organization to contribute to developing the required scientific data to meet the FDA's expectations. The benefits of having universally accepted drug development tools for a specific context of use could be profound in both shortening the development timeline and accelerating the review process and could have a concomitant effect of standardizing major portions of a regulatory submission to multiple major regulatory bodies. How the industry addresses the potential benefits of collaborating within specific contexts of use will tell us a great deal about the potential impact of this program. The FDA is seeking feedback on the guidance by Feb. 12, 2020 before finalizing the program.

References:

1. https://www.fda.gov/drugs/development-approval-process-drugs/drug-development-tool-ddt-qualification-programs

About The Author:

Bikash Chatterjee is chief operating and science officer for Pharmatech Associates. He has over 30 years' experience in the design and development of pharmaceutical, biotech, medical device, and IVD products. His work has guided the successful approval and commercialization of over a dozen new products in the U.S. and Europe. Chatterjee is a member of the USP National Advisory Board and is the past chairman of the Golden Gate Chapter of the American Society of Quality. He is the author of *Applying Lean Six Sigma in the Pharmaceutical Industry* and is a keynote speaker at international conferences. Chatterjee holds a B.A. in biochemistry and a B.S. in chemical engineering from the University of California at San Diego.

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