FDA U.S. FOOD & DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION & RESEARCH

CDER DDT QUALIFICATION: IMPACTS OF 21 CC, PDUFA VI, AND OTHER RECENT CHANGES

CHRISTOPHER LEPTAK, M.D., PH.D.
DIRECTOR, OND REGULATORY SCIENCE PROGRAM
DIRECTOR, BIOMARKER QUALIFICATION PROGRAM

Liver Forum

April 2018

Disclaimers

- Views expressed in this presentation are those of the speaker and do not necessarily represent an official FDA position

- I do not have any financial disclosures regarding products regulated by the FDA

Opportunities for Improved Integration of Biomarker Development Activities within Drug Development

Note: These pathways do not exist in isolation and many times parallel efforts are underway within or between pathways. All share common core concepts, are data-driven, and involve regulatory assessment and outcomes based on the available data.

Facilitating Biomarker Development: Strategies for Scientific Communication, Pathway Prioritization, Data-Sharing, and Stakeholder Collaboration; Published June 2016, Duke-Margolis Center for Health Policy

BEST: BIOMARKERS, ENDPOINTS, AND OTHER TOOLS RESOURCE

- A glossary of terminology and uses of biomarkers and endpoints in basic biomedical research, medical product development, and clinical care
- Created by the NIH-FDA Biomarker Working Group
- Publicly available at http://www.ncbi.nlm.nih.gov/books/NBK326791/
- BEST harmonizes terms and definitions and addresses nuances of usage and interpretation among various stakeholders, including:

- Biomedical scientists
- Translational and clinical researchers
- Medical product developers
- Patient/disease advocacy groups
- Government officials
- Clinicians

Overview of 21st Century Cures (21CC) Legislation and PDUFA VI: Impacts on DDT Qualification Activities

Highlights

- 21st Century Cures and PDUFA VI increasingly places FDA as an *active participant* in drug development, broadening our traditional regulatory role
- Requires expanded efforts to enhance drug development
  - *Patient-focused drug development*: collect / analyze patient experience, to use in designing drug development programs (endpoints), and in regulatory decision making (endpoints and risk/benefit considerations)
  - *Novel, innovative trial designs*: use of complex adaptive and other novel trial designs – and how such clinical trials can be used to satisfy the substantial evidence standard
  - *Real world evidence*: using data regarding use or potential benefits and risks of a drug derived from sources other than randomized clinical trials – in support of new indications and post-approval study requirements
  - ***Drug development tools: biomarkers and COAs***

21ST CC DDT PROCESS (SECTION 3011): WHAT'S DIFFERENT?

- New important features, but also much continuity with existing DDT programs
- Formalizes a process defined by three submissions. "Accept" or "Not Accept" decision for each:
  - Letter of Intent (LOI)
  - ***Qualification Plan (QP)***
  - Full Qualification Package (FQP)
- Requires setting and implementing "reasonable timeframes" for the FDA review of each submission type

TRANSPARENCY PROVISIONS

Under 21CC, DDT qualification becomes a transparent public process:

- All interested parties know what tools are in development, stage of development, and FDA determinations including rationale
- Information about the submission and FDA's determination including recommendations will be posted on DDT website
- For legacy projects, we plan to post only new information after transition (e.g., we will not make public information prior to legislation enactment or to agreement to transition to 507)
- De facto Letter of Support (LOS) as part of DDT engagement

21ST CC: ACCEPTANCE OF BIOMARKER INTO QUALIFICATION

- Acceptance decision for each submission (LOI, QP, FQP) based upon scientific merit:
  - Does the proposal address an impactful drug development need?
  - Is there enough information to suggest a likelihood of success?
  - What is the feasibility of the proposed analytical biomarker measurement approach?

- Prioritization of review of submissions based upon:
  - "the *severity, rarity, or prevalence* of the disease or condition targeted by the drug development tool and *the availability or lack of alternative treatments* for such disease or condition; and
  - the identification by the Secretary or by biomedical research consortia and other expert stakeholders, of such drug development tool and its proposed context of use *as a public health priority*" (italics added)

CONTENT FOCUS FOR SUBMISSION TYPES

- LOI Submission: Feasibility assessment of proposal will include information to support that measurement of the novel DDT is, in fact, possible.

- QP Submission: Project development plan from concept to information to be developed/provided to support the DDT's COU. For biomarkers, to determine clinical utility and clinical validation, important to know that the analytical validation has been completed and information submitted to QP.

- FQP Submission: Review of data to support the clinical validation of the DDT for the COU

THREE-TIERED INTERNAL REVIEW

- DDT Program Assessment and Recommendations
  - Work with requestor to clarify DDT, COU, and project proposal
  - Provide tool-specific recommendations based on past and ongoing projects

- Discipline-specific SME Assessment and Recommendations
  - Includes OND division management participation
  - Evaluate based on regulatory precedent, current disease-specific challenges, and level of impact on drug development programs

- CDER DDT Committee Assessment, Recommendations, and Decision
  - Opportunity for broad senior CDER input early and throughout in the process
  - Work towards greater consistency across therapeutic areas and divisions

THANK YOU FOR YOUR ATTENTION

U.S. FOOD & DRUG
ADMINISTRATION