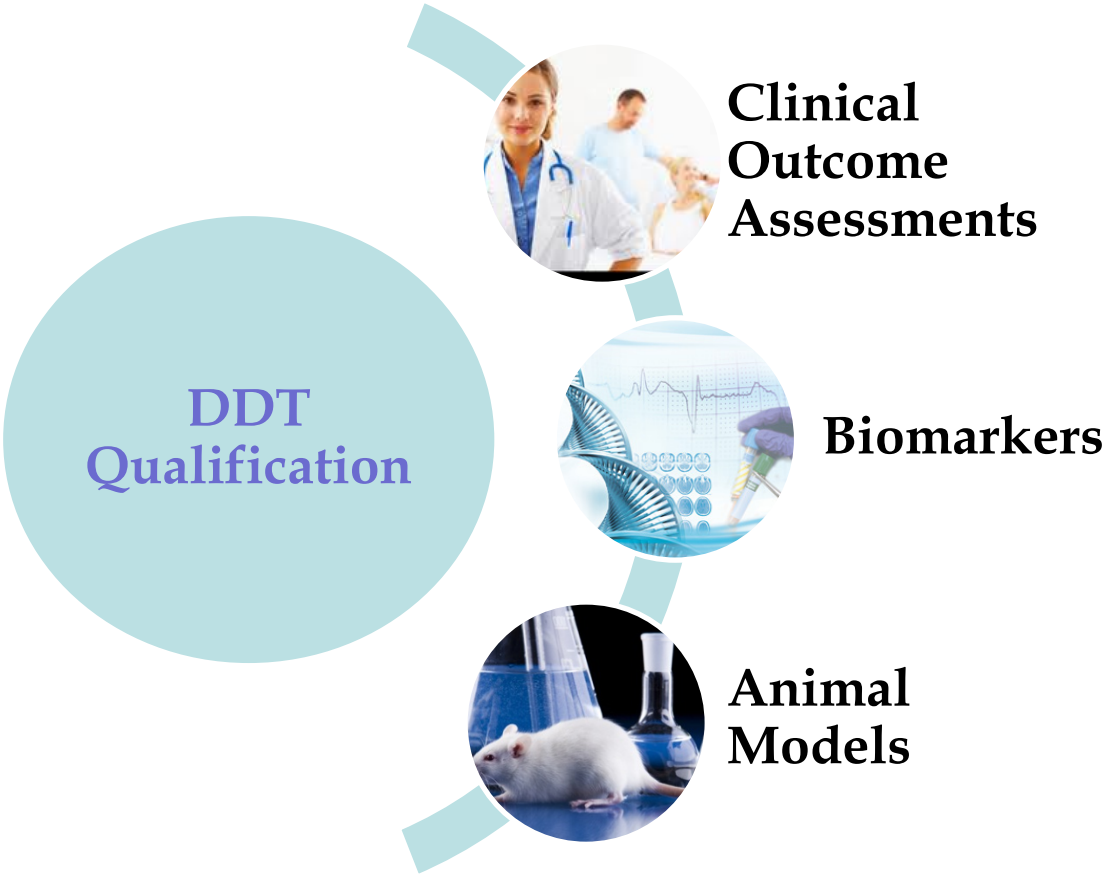
Update on CDER's Drug Development Tool Qualification Program

ShaAvhree Buckman-Garner, M.D., Ph.D.
Director
Office of Translational Sciences
Center for Drug Evaluation and Research
U.S. Food and Drug Administration

DDT Qualification Activities



What I have discussed in previous updates…

- Evolution of the DDT Guidance
- Development of the Qualification Program/Process
- Implementation Efforts Underway

Focus for Today's Discussion….

LESSONS LEARNED…….

COA Qualification Process

DDT Stage	FDA Process Activities	Content Considered During Each Stage
Initiation Stage	• DDT # assigned • LOI received • QRT formed and review meeting scheduled • LOI response letter drafted • LOI response letter discussed during QRT meeting • LOI response letter finalized and signed • LOI response letter sent • *Potential: Revised LOI requested*	• Concept(s) of interest • Context of use (disease definition; population characteristics; etc.) • Hypothesized concepts and potential claims • Hypothesized conceptual framework • COA placement within preliminary endpoint model

Consultation and Advice (C&A) Stage	• Initial Briefing Package (IBP) requested
	• Active C&A:
	  • Qualitative summary reviewed and response letter sent
	  • Quantitative summary reviewed and response letter sent
	  • Other submissions as requested
	• QRT meetings held to discuss each submission and response letters sent (using same process described in stage above)
	• *Potential: Revised submissions or additional information requested*
		• Summary of qualitative research includes documentation of content validity:
		  • Concept elicitation interview findings
		  • Item generation summary (decisions for recall period, response options and format, mode/method of administration)
		  • Cognitive debriefing interview findings
		• Summary of quantitative research includes documentation of content validity and other measurement properties
		  • Further documentation of content validity using new methods (e.g., IRT, Rasch)
		  • Confirm conceptual framework and scoring
		  • Reliability, construct validity, and ability to detect change
		  • Final instrument content (format, scoring procedures)
		• Other submissions (e.g., study protocols; interim findings) as requested by submitters

Review Stage	• Final Qualification Package requested • QRT meeting(s) held • Qualification decision made • *Potential: Revised package or additional information requested*	• Final documentation (including all primary data and detailed results) of instrument development work

Project Status Report (as of 3/31/13)

DDT Stage	Number in Stage
Initiation Stage	**16**
Initiation – DDT # assigned	10
Initiation – LOI received	2
Initiation – revised LOI requested	4
Consultation and Advice Stage (C&A)	**19**
C&A – IBP requested	6
C&A – Active	13
Review Stage	**2**
Cancelled	**3**
On Hold	**3**
Declined	**9**

What are we learning?

- Refining and streamlining processes
- Discussions regarding the evidence necessary to support COA measurement
- Providing tools to therapeutic review divisions to organize thinking about disease definitions and subpopulations


WARNING
CHALLENGES
AHEAD

Time Delays Identified

- We have identified a number of factors that contribute to time delays
  - Delays on the part of both FDA and submitters
  - Delays related to
    - Process
    - Lack of understanding or knowledge
    - Competing priorities / work backlog
    - Unable to reach internal and external agreement on COA development

Formation of QRT and Scheduling QRT meetings for each submission
Internal deliberations / senior management agreement on goals of qualification
Coordination with EMA
Drafting responses and review by QRT members-- time to think through issues
Reviewer training on what is expected of them as part of the QRT (goals, steps, timeline, etc.)

Challenge / Cause of Time Delay
Understanding the goals of the qualification process and relevance to the review process
Reviewer workload
Internal consensus on concept of interest or endpoint model
Consensus on the level of detail that should be included in submissions; multiple requests for additional information

Challenge / Cause of Time Delay
False starts because submitters due to the meaning of: Qualification, Context of Use and needed specificity, and/or Concept of Interest
Understanding of the PRO Guidance
Delays in sending updates/new submissions

Challenge / Cause of Time Delay
Instrument development process can be naturally lengthy (several years to complete)
Multi-company consortia with conflicting internal policies that take time to resolve
Submitters human resource, funding, and contracting issues
Consensus among external groups (disease consortia, scientific/clinical community, drug developers) on concept of interest or endpoint model

Challenge / Cause of Time Delay
Agreement on concept of interest, context of use, endpoint model. This is a new way of thinking about the process for both FDA and instrument developers.
Need for consensus on concept of interest, endpoint model, context of use (e.g., depression impact proposed, FDA interested in depression symptoms)
Scientific disagreements (e.g., best practices)
Agreement on disease definitions

Other DDT Qualification Challenges

- Divisions and developers may not see the need for qualification if a tool has already been used in labeling
- Existing tools risk going through the DDT qualification process and being deemed 'unqualifiable' without modifications
  - Costs to qualification process
  - Modifications to tool might provide competitors with a market advantage

How do we fix?

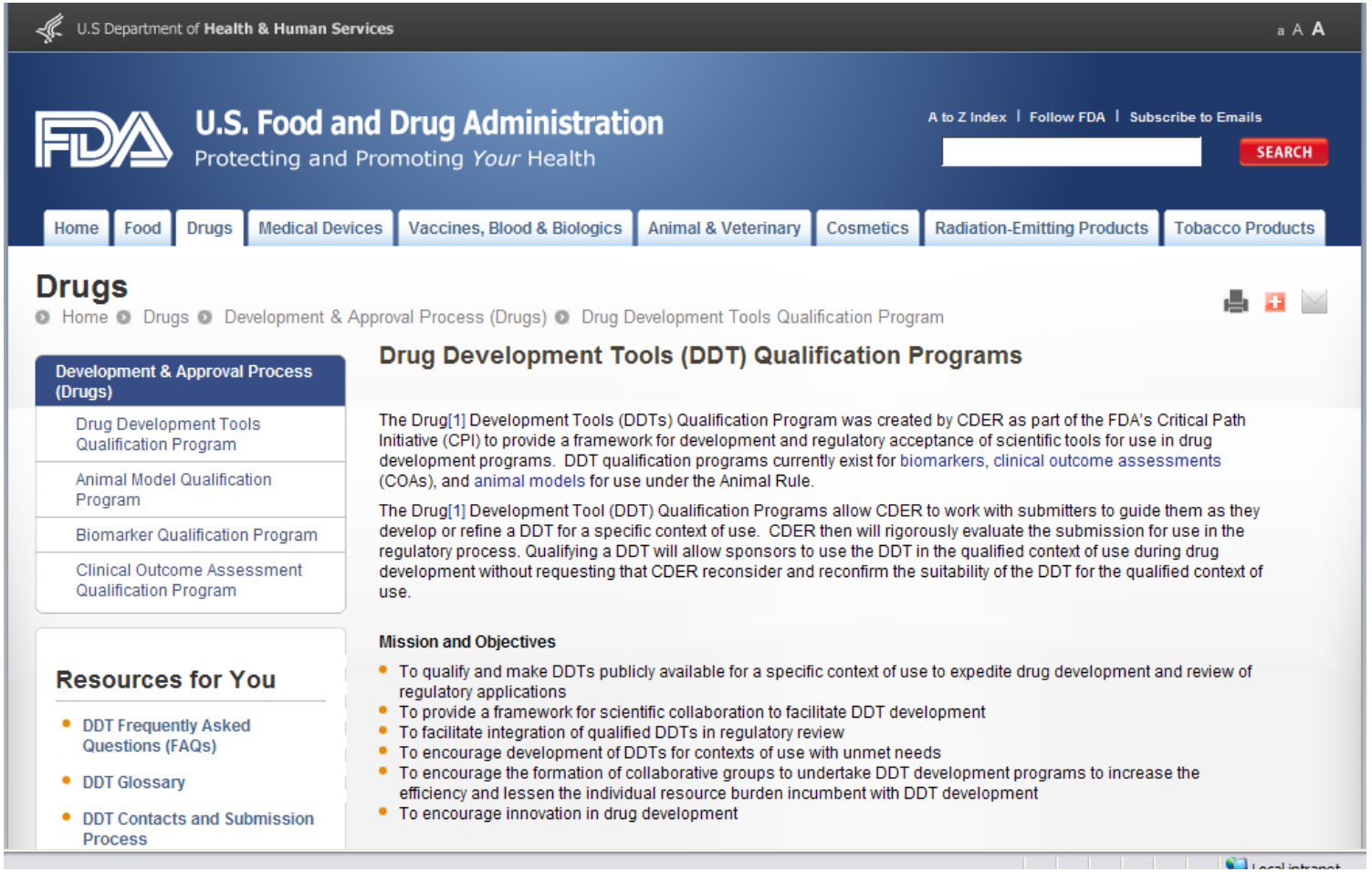
- Enhanced/early communication internal and external
- Clear communication of context of use
- Enhanced training for reviewers
- Liaisons to help address questions from submitters
- Identify narrow context of use for qualification that can subsequently be expanded…
- Streamline processes/identify time bottlenecks
- Development and dissemination of office specific MAPPs

What are we working on currently?

- Finalizing the DDT Qualification Draft Guidance
  - Definition of "Context of Use"
  - Letter of Intent and Briefing Package Materials
- Finalizing CDER MAPPs (general and program-specific) in development
- Knowledge management and electronic filing tools/capabilities established
- Qualification Review Teams forming
- EMA and FDA are having discussions about the COA qualification process
  - Aim to harmonize submission templates during both the Advice and Consultation as well as the Review Stages
  - E.g., both use the same process for all COA—PROs, ClinROs, ObsROs
- Under our MOU, EMA and FDA having discussions about specific COA qualification projects that are under concurrent review by the two agencies and we encourage concurrent submissions.

How can you help?

- Give us constructive feedback
- Review our guidance documents
- Ask questions early and often
- Watch our website



www.fda.gov/Drugs/DevelopmentApprovalProcess/DrugDevelopmentToolsQualificationProgram/default.htm

Summary

- CDER is committed to continuing to support the DDT Qualification Program
- We appreciate the dedication of the PRO Consortium members
- We understand that this is uncharted territory
- We are learning as we go
- We look forward to the outcome of producing qualified publicly available tools which serve to enhance the drug development process

To contact us:

Office of Translational Sciences/CDER/FDA
301-796-2600

shaavhree.buckman-garner@fda.hhs.gov