FDA Update on DDT Qualification Programs

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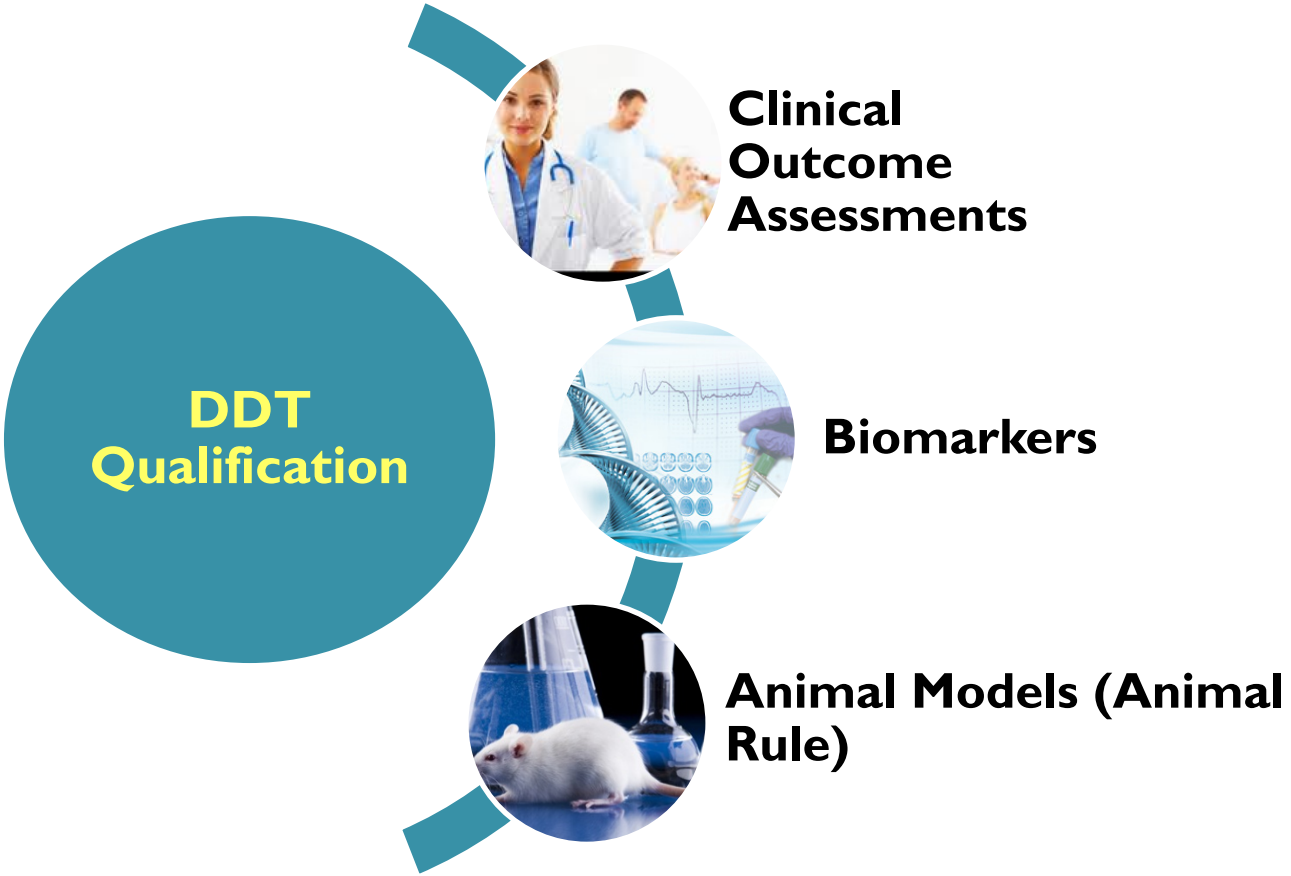
When I was here last year….

Drug Development Tools Qualification



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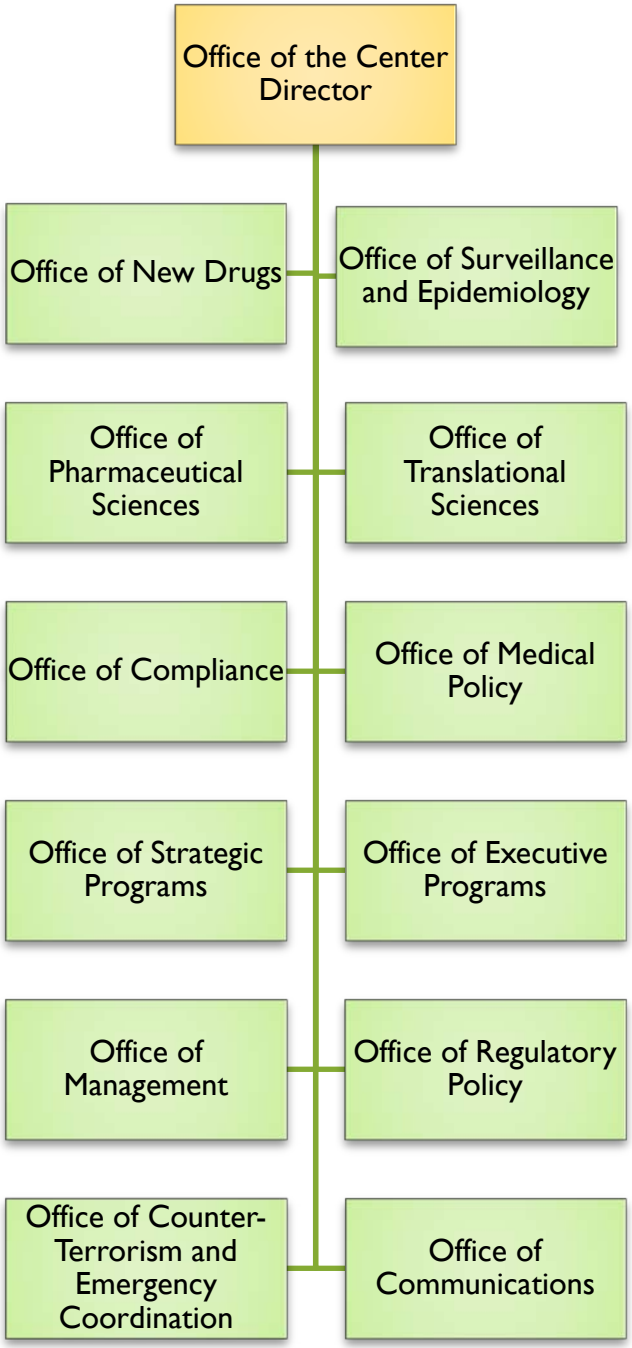

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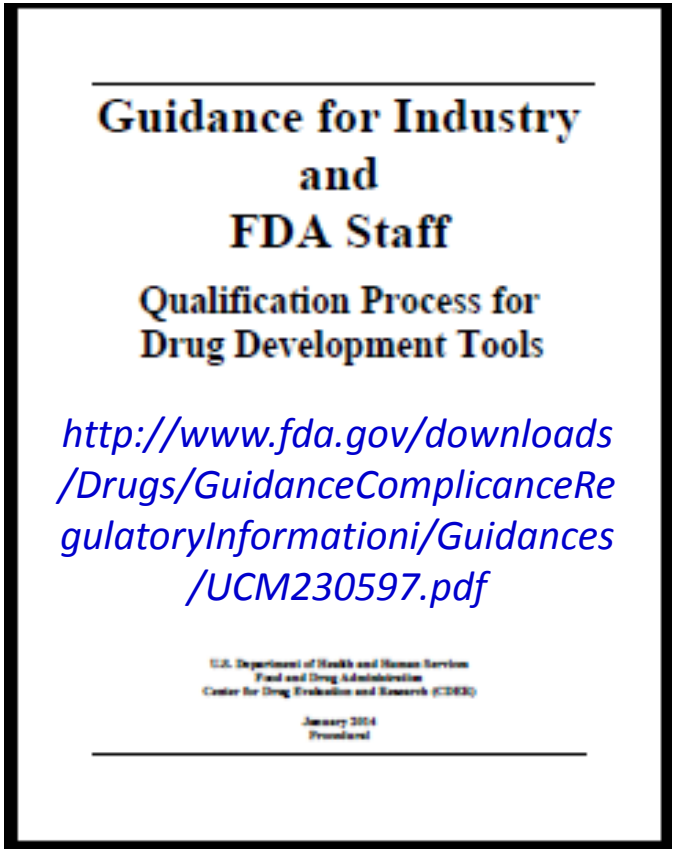
We have made progress…

DDT Guidance (Final January 2014)



Guidance for Industry
and
FDA Staff

Qualification Process for
Drug Development Tools

http://www.fda.gov/downloads/Drugs/GuidanceComplicanceRegulatoryInformationi/Guidances/UCM230597.pdf

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)

January 2014
Procedural

- Describe a process NOT evidentiary standards
- Qualification process described for Biomarkers, Animal Models, and Clinical Outcome Assessments (COA)

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MDDT Guidance (Draft November 2013)

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Medical Device Development Tools

Draft Guidance for Industry, Tool Developers, and Food and Drug Administration Staff

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.

Document issued on: November 14, 2013

You should submit comments and suggestions regarding this draft document within 90 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit written comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. Submit electronic comments to http://www.regulations.gov. Identify all comments with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions regarding this document, contact Katie O'Callaghan at 301-796-6349 or by electronic mail at kathryn.ocallaghan@fda.hhs.gov.

U. S. Department of Health and Human Services
Food and Drug Administration
Center for Devices and Radiological Health

DDT Qualification Web Site

http://www.fda.gov/Drugs/DevelopmentApprovalProcess/DrugDevelopmentTools QualificationProgram/

Context of Use

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Home | Food | Drugs | Medical Devices | Radiation-Emitting Products | Vaccines, Blood & Biologics | Animal & Veterinary | Cosmetics | Tobacco Products

Drugs

Home › Drugs › Development & Approval Process (Drugs) › Drug Development Tools Qualification Program

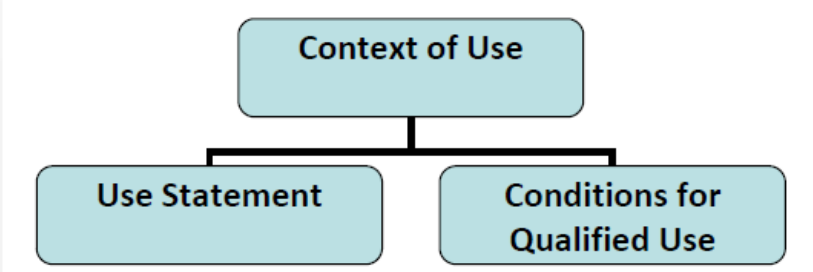
- Development & Approval Process (Drugs)
  - Drug Development Tools Qualification Program
  - Animal Model Qualification Program
  - Biomarker Qualification Program
  - Clinical Outcome Assessment Qualification Program

Biomarker Qualification Context of Use

"Context of use," or COU, is a comprehensive and clear statement that describes the manner of use, interpretation, and purpose of use of a biomarker in drug development. This document provides guiding principles in formulating a **Context of Use (COU)** statement for biomarkers being proposed for qualification through FDA's Center for Drug Evaluation and Research (CDER) Biomarker Qualification Program (BQP)[1].

A COU is comprised of a concise biomarker **Use Statement** and a comprehensive description of conditions for the biomarker to be used in the qualified setting, termed the **Conditions for Qualified Use**. (See also **Example of a Context of Use in a Qualification Recommendation for Hypothetical Biomarker**) It should be noted that biomarkers recommended for qualification prior to 2012 may not represent this current approach for specifying the use statement and conditions for qualified use.

Figure 1: Appropriately Constructed Context of Use



- **Use Statement.** The Use Statement should be concise and include the name and identity of the biomarker (s) and purpose for use in drug development.
- **Conditions for Qualified Use.** The Conditions for Qualified Use should be a comprehensive description of conditions for the biomarker to be used in the qualified setting.

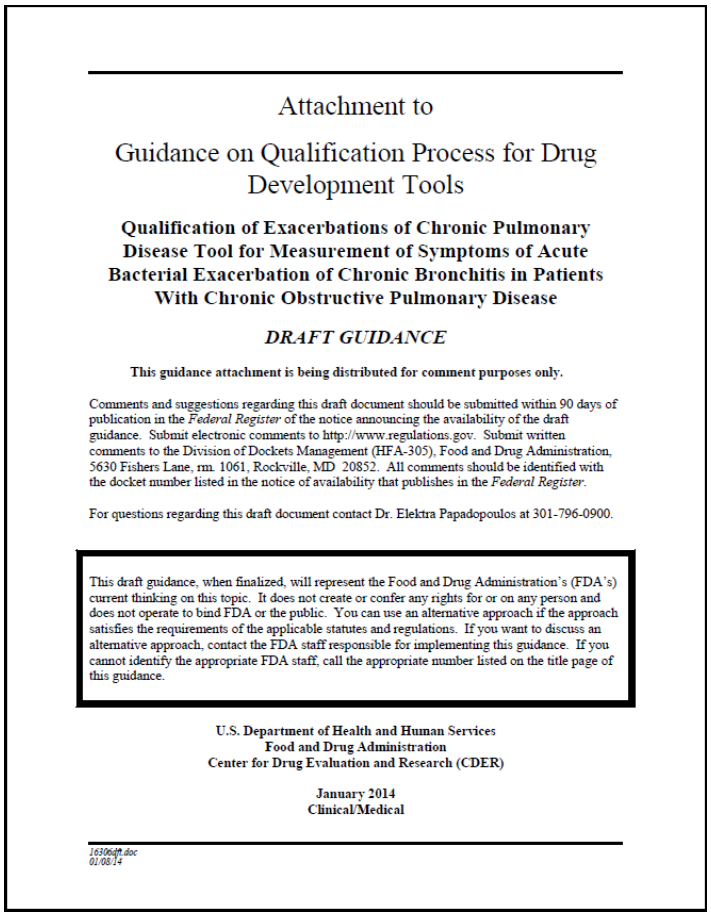
Some of the elements that should be captured in formulating a clear and comprehensive COU statement are provided in Table 1 (see below).

Elements of the COU statement, in particular the conditions for qualified use, may be not fully determined when the Letter of Intent (LOI) is submitted. Nonetheless, submitters should make the COU statement as comprehensive and clear as possible at the time of initiating interactions with the BQP. Submitters should

COA Qualification Updates

- First COA (EXACT-PRO) qualified in January 2014
- Final DDT Qualification Guidance published in January 2014
- 30+ COA projects across the various stages of the qualification process, with more on the horizon
- Slightly revised process to allow for earlier qualification and increased efficiency
- New communication tools online: wheel and spokes and roadmap diagrams

First Clinical Outcome Assessment Qualified in January 2014



Attachment to

Guidance on Qualification Process for Drug Development Tools

Qualification of Exacerbations of Chronic Pulmonary Disease Tool for Measurement of Symptoms of Acute Bacterial Exacerbation of Chronic Bronchitis in Patients With Chronic Obstructive Pulmonary Disease

DRAFT GUIDANCE

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For questions regarding this draft document contact Dr. Elektra Papadopoulos at 301-796-0900.

This draft guidance, when finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. You can use an alternative approach if the approach satisfies the requirements of the applicable statutes and regulations. If you want to discuss an alternative approach, contact the FDA staff responsible for implementing this guidance. If you cannot identify the appropriate FDA staff, call the appropriate number listed on the title page of this guidance.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)

January 2014
Clinical/Medical

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01/08/14

- EXACT
  - A PRO for the measurement of symptoms of acute bacterial exacerbation of chronic bronchitis in patients with chronic obstructive pulmonary disease

Ongoing COA Qualification Efforts

- Qualification projects actively underway for a wide variety of conditions, including but not limited to:

- *Multiple sclerosis*
- *Cancer fatigue*
- *Mild cognitive impairment*
- *Irritable bowel syndrome*
- *Asthma*
- *Cystic fibrosis*
- *Depression*
- *Non-small cell lung cancer*
- *Functional dyspepsia*
- *Community-acquired bacterial pneumonia*
- *Acute bacterial skin and skin structure infections*
- *Ulcerative colitis*
- *Crohn's disease*
- *Esophagitis*
- *Sickle Cell*
- *Muscle Wasting*

Ongoing COA Qualification Efforts

- CDER partnering with multiple consortia, patient groups, academics, researchers, and others on COA qualification projects, including:
  - Critical Path Institute PRO-Consortium (includes 7 distinct working groups: Functional Dyspepsia, Irritable Bowel Syndrome, Non-Small Cell Lung Cancer, Rheumatoid Arthritis, Depression, Cognition)
  - FNIH Biomarkers Consortium
  - Critical Path Institute Coalition against Major Diseases (CAMD) Consortium
  - Critical Path Institute Multiple Sclerosis Outcomes Assessments Consortium (MSOAC)
  - PROOF-C Cancer Fatigue Consortium
  - Aging in Motion, a patient-advocacy organization

Ongoing COA Qualification Efforts

- CDER is collaborating with NIH to explore potential qualification of selected PROMIS measures
- CDER continues to encourage instrument development and qualification, particularly for pediatric populations, rare diseases, and other areas of unmet need

Biomarker Qualification Projects Status Report by Stage

Biomarker DDT Stage	Number in Stage
Initiation Stage	
Initiation – DDT # assigned	43
Initiation – Letter of Intent (LOI) received	43
Consultation and Advice Stage (C&A)	
C&A – Initial Briefing Package requested	28
Review Stage	**3**

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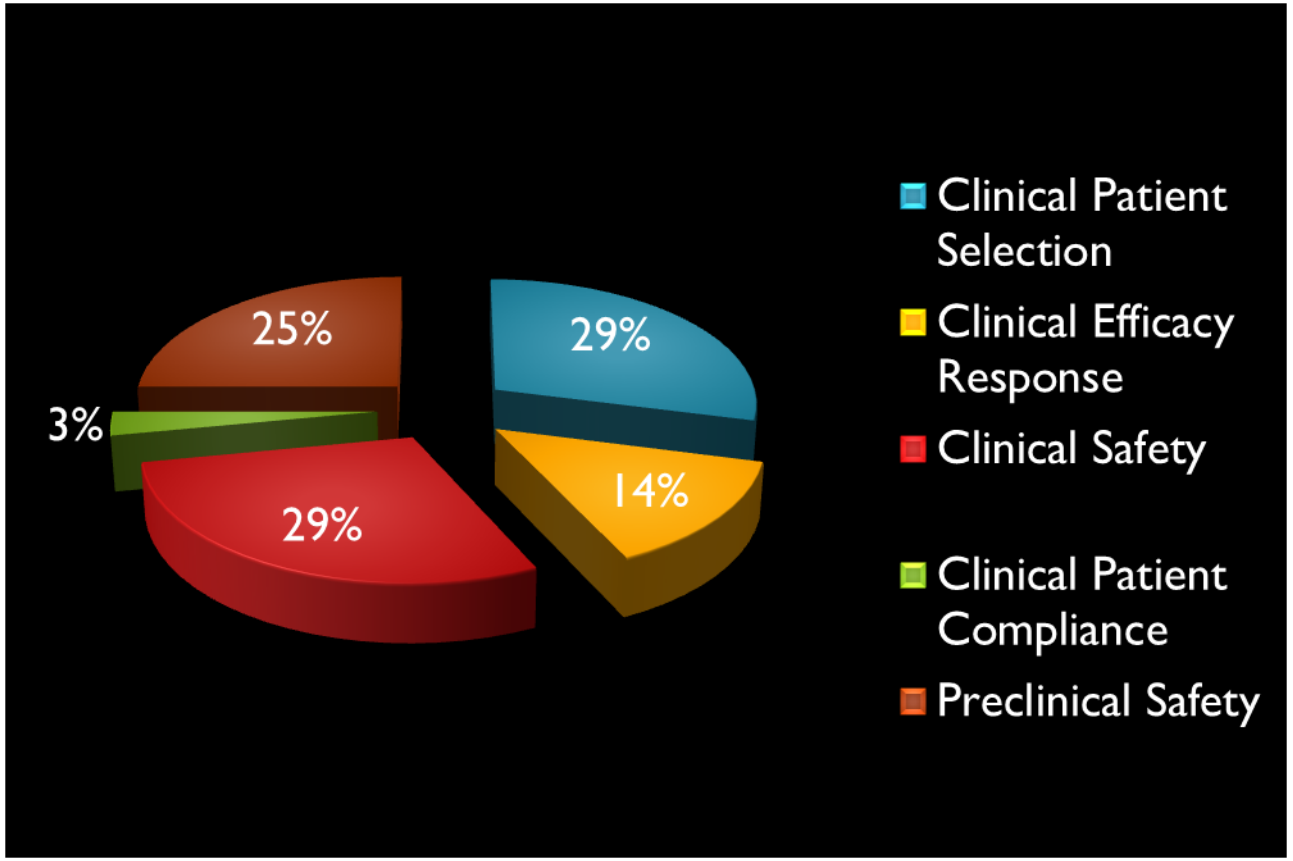
Categories of BQ Submissions (N=28)



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List of FDA-Qualified Biomarkers

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Qualified DDT:

DDT Type	Name	Submitter	Qualification Date	Link to Supporting Information
Biomarker	Seven Biomarkers of Drug-Induced Nephrotoxicity in Rats	Predictive Safety and Testing Consortium (PSTC), Nephrotoxicity Working Group (NWG)	4/14/2008	Predictive Safety Testing Consortium (PDF - 163KB)
Biomarker	Nonclinical Qualification of Urinary Biomarkers of Nephrotoxicity	International Life Sciences Institute (ILSI)/ Health and Environmental Sciences Institute (HESI), Nephrotoxicity Working Group	9/22/2010	HESI Nephrotoxicity Qualification (PDF - 234KB)
Biomarker	Nonclinical Qualification of Circulating Cardiac Troponins T and I as Biomarkers of Cardiac Morphologic Damage	PJ O'Brien, WJ Reagan, MJ York and MC Jacobsen	2/23/2012	Biomarker Qualification Decision (PDF - 144KB)

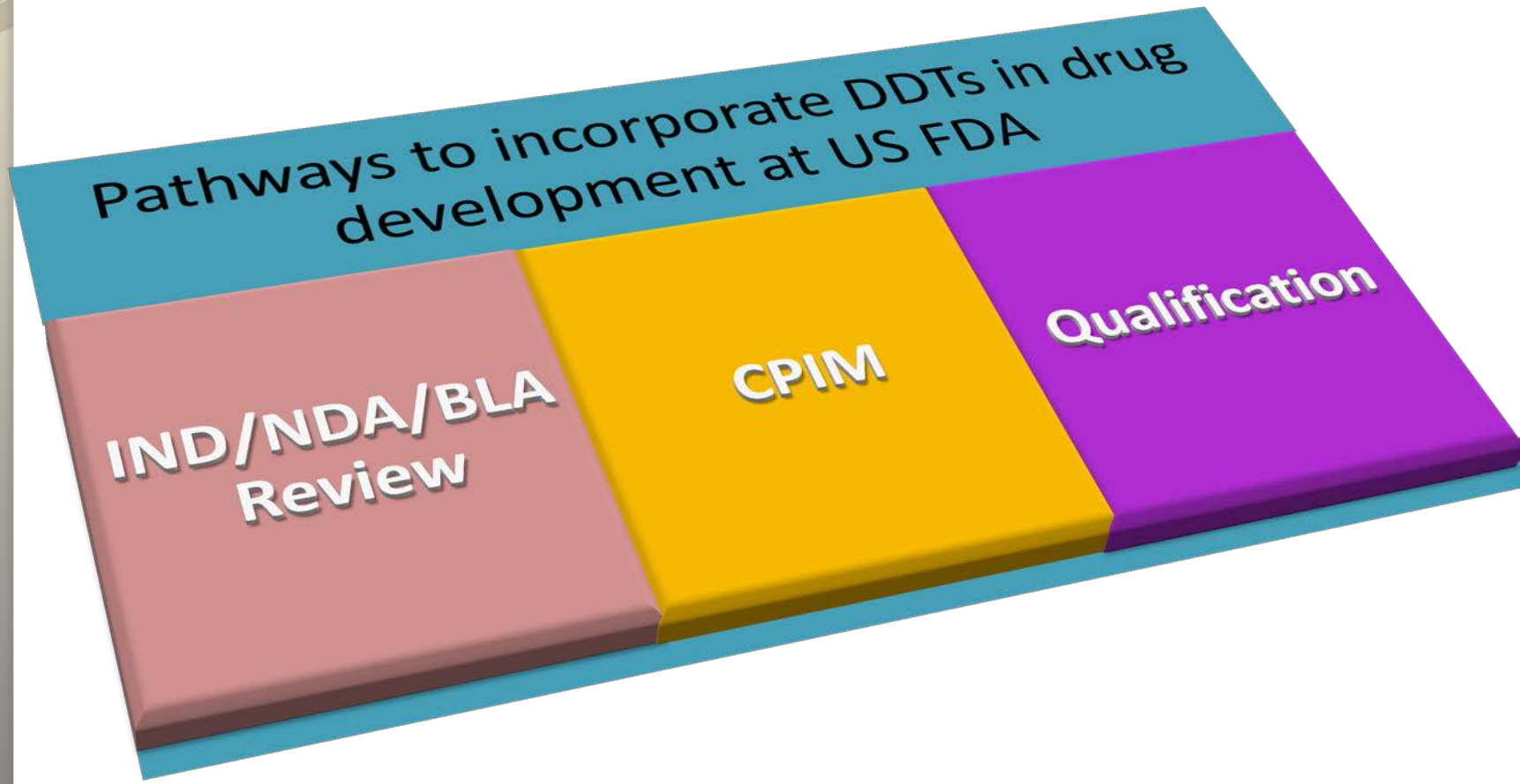
http://www.fda.gov/Drugs/DevelopmentApprovalProcess/DrugDevelopmentToolsQualificationProgram/ucm284076.htm

Animal Model Qualification

AMQ DDT Stage	Number in Stage
Initiation Stage	
Letter of Intent (LOI) Pending	3
Initiation – LOI Received	5
Consultation and Advice Stage (C&A)	
C&A – Initial Briefing Package requested	2
Review Stage	**0**

Link to DDT AMQP Web page:
http://www.fda.gov/Drugs/DevelopmentApprovalProcess/DrugDevelopmentToolsQualificationProgram/ucm284078.htm

Pathways to facilitate integration of DDTs in drug development



Critical Path Innovation Meetings

Goal: To foster efficient and innovative methods for drug development

- New CDER program
- Promotes understanding challenges in drug development and innovative strategies to address them
- Potential biomarkers not ready for DDT Qualification Program
- Natural history study design and implementation
- Emerging technologies or new uses of existing technologies
- Novel clinical trial designs and methods
- Nonbinding on FDA and other participants
- No advice on specific approval pathways

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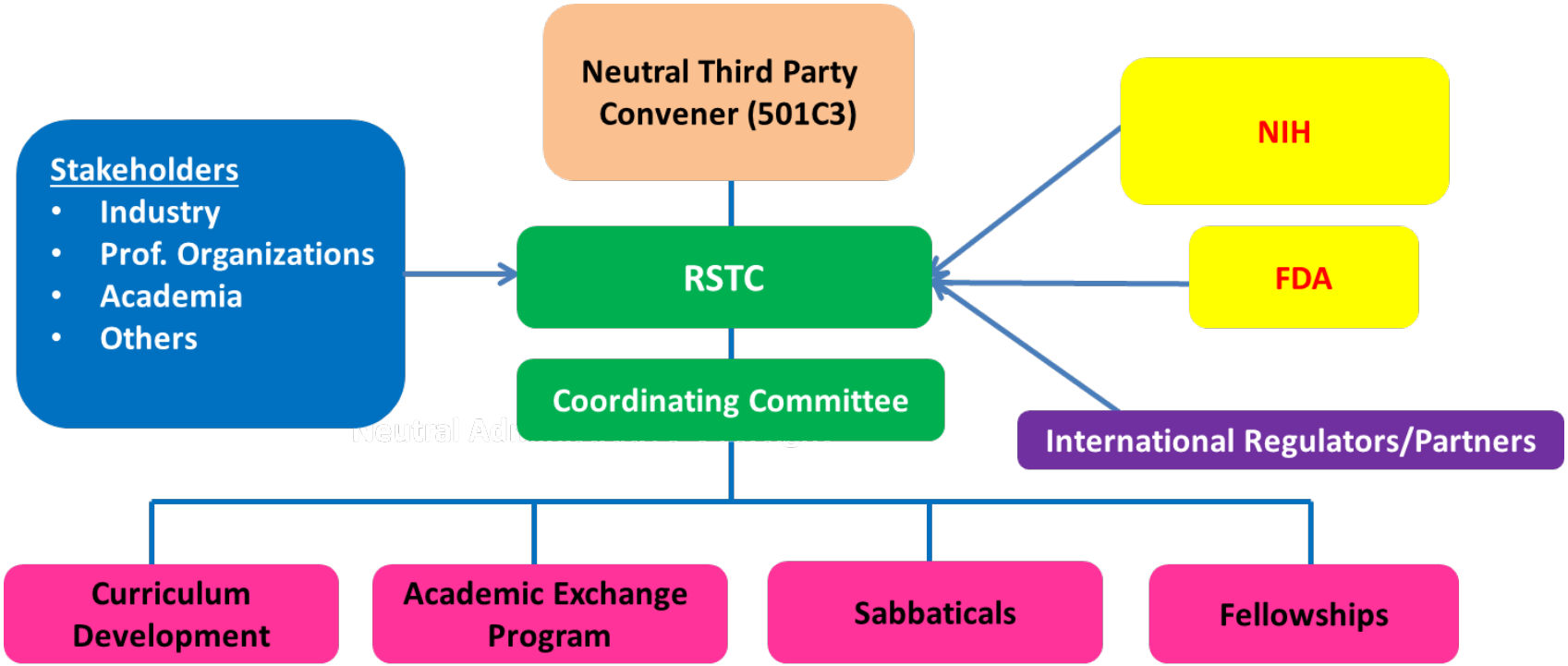
New Proposal—Training Consortium



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Building Scientific Capacity

Alzheimer's Disease Regulatory Science Fellowship

The Reagan-Udall Foundation for the FDA (RUF), in partnership with the Alzheimer's Association and the U.S. FDA, Division of Neurology Products (DNP), is offering a two-year Regulatory Science Fellowship focused in the area of Alzheimer's Disease. The fellow will have an unparalleled opportunity to receive training in regulatory science at the FDA, gaining valuable experience and knowledge working with the DNP.

Background and Goals:

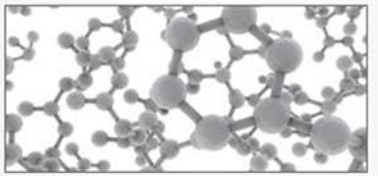
There are currently no drugs available to prevent Alzheimer's Disease (AD) or even slow its course. A recent series of high-profile late stage drug failures have led those in Alzheimer's research to begin to rethink many of the underlying hypotheses related to drug development including therapeutic targets, trial design, appropriate patient populations, biomarkers, and clinical outcome measures. Patient groups, academic researchers, pharmaceutical manufacturers, and other stakeholders have formed a wide array of consortia and initiatives to examine many of these issues. A primary goal of this fellowship is to facilitate communication and collaboration between DNP and the various AD stakeholders and to help identify opportunities for DNP participation in relevant partnerships and activities to address critical issues in AD research and product development.

Fellowship Activities:

The fellow will work with DNP to identify opportunities advance the development of treatments for Alzheimer's and related diseases. Activities will include:

- Develop a comprehensive understanding of the regulatory review process.
- Learn current challenges facing Alzheimer's drug development and regulation.

Building Scientific Capacity



Learn More About Our Work

The Reagan-Udall Foundation leads and collaborates on programs, projects and other initiatives that advance its mission in support of the FDA. **Find Out More »**

Learn About Our Commitment to Regulatory Science

Separate of the FDA, the Foundation identifies and supports research and collaborations that can help achieve a more efficient development and approval process while ensuring product safety. **Find Out More »**

Stay Updated on the Latest FDA Regulatory Science Initiatives.

Next Steps…

- Internal CDER MAPPs (general and program-specific) underway
- Continuing to streamline programs to build review efficiency
- Continuing to clarify the concept of context of use—as it drives level of evidence needed
- Evolving concept of expanding qualification over time as evidence increases
- Working with international colleagues on templates

To contact us:

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