Innovative Science and Technology Approaches for New Drugs (ISTAND) Program

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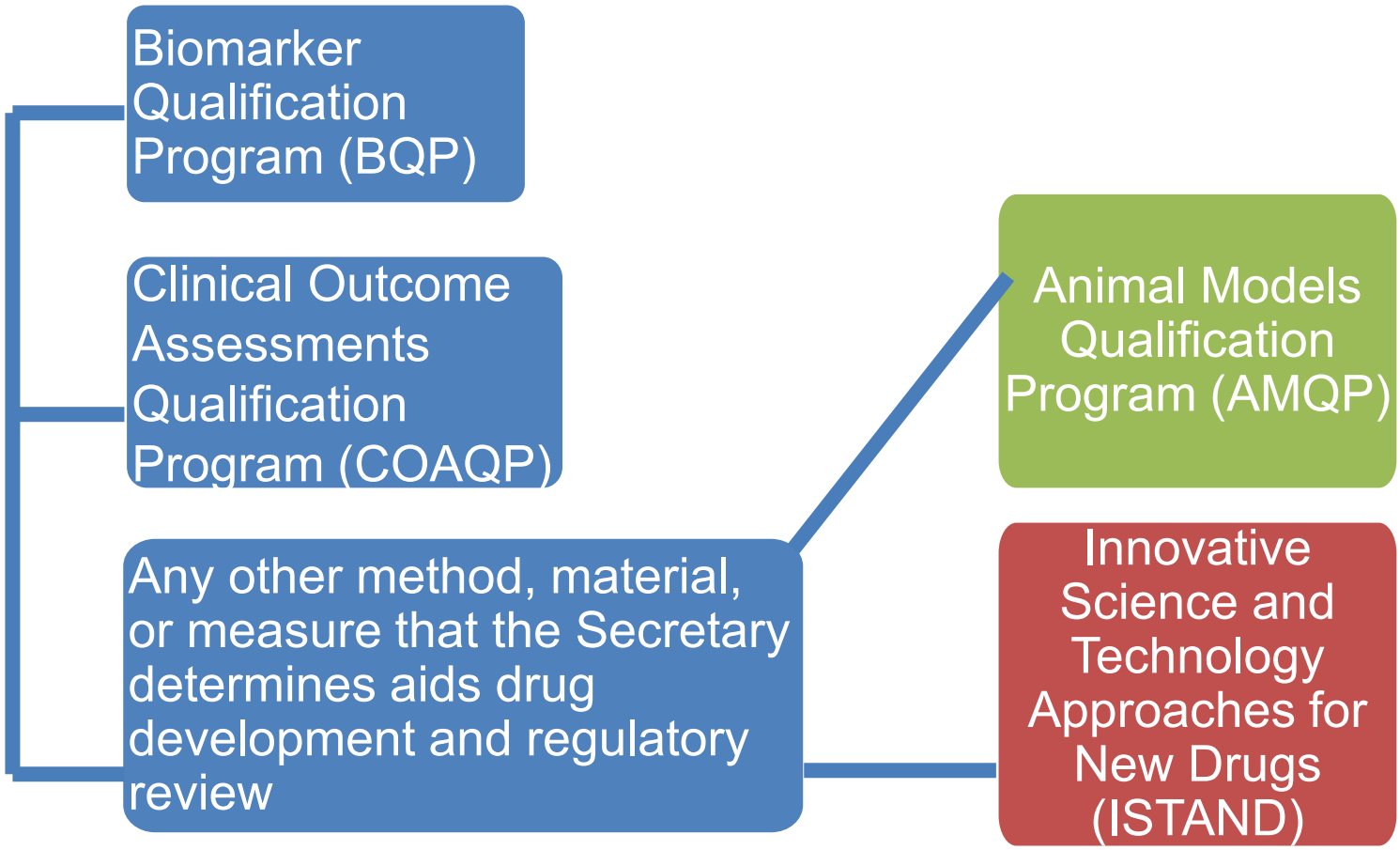
Agenda

2025 Scientific Advisory Committee on Alternative Toxicological Methods Meetings

- **DDT Qualification Programs**
- **What is Qualification**
- **ISTAND Qualification Steps**
- **ISTAND Qualification Review Team**
- **ISTAND Review Process**
- **Validation Considerations in DDT Qualification**
- **ISTAND Program Progress**
- **Considerations for DDT Qualification**

DDT Qualification Programs



What is Qualification?

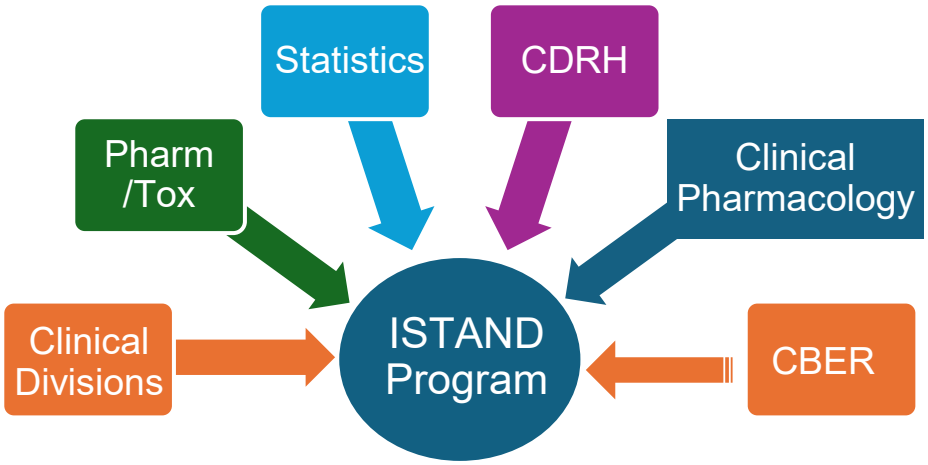
- Qualification is a conclusion that within the stated context of use, the DDT can be relied upon to have a specific interpretation and application in drug development and regulatory review. Once qualified, DDTs will be publicly available to be used in any drug development program for the qualified context of use.

- Additionally, the qualified DDT generally can be included in IND, NDA, or BLA submissions without needing FDA to reconsider and reconfirm its suitability.

ISTAND Qualification Steps and Review

Letter of Intent	Is a request for the qualification of a specific biomarker for a proposed context of use (COU) in drug development
Qualification Plan	Describes biomarker development plans for the COU and provides data on analytical validation of the biomarker measurement
Full Qualification Package	Contains all accumulated data to support the qualification of the biomarker for the proposed COU
Qualification Determination	Is FDA's determination on qualification of the biomarker for the proposed COU based on a comprehensive review of the full qualification package.

ISTAND Qualification Review Team



ISTAND Review Process

Step 1 Initial Assessment

(Target: 30 days from date FDA receives submission)

- **Submission and Initial Screening**
- **Requestor submits proposal**
- **Preliminary reviewability assessment is conducted by ISTAND Team**
- **Reviewability memo is issued to requestor**

Step 2 Comprehensive Review

(Target: within 3 (LOI), 6 (QP), and 10 (FQP) months, respectively, from the date of the reviewable memorandum)

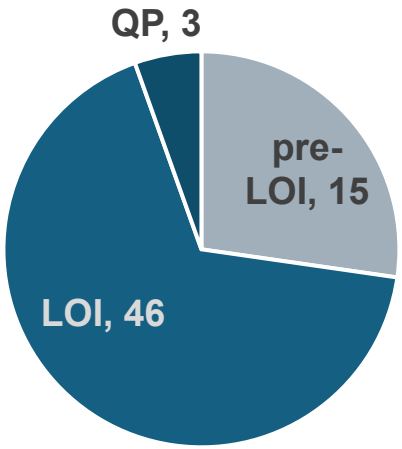
- **In-depth Evaluation/Review of the submission**
- **Qualification Review Team is formed for consultation with subject matter experts**
- **If information request (IR) is issued the review clock stops**

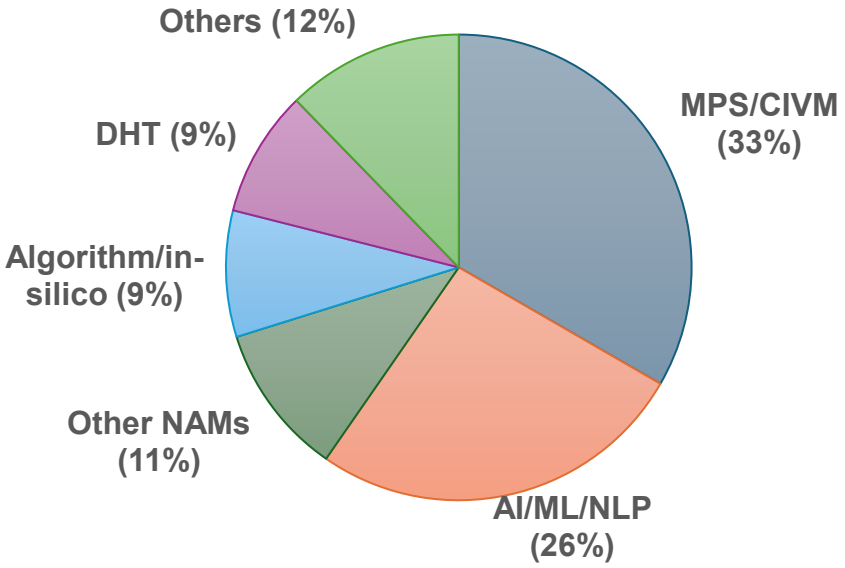
Step 3 DDT Committee Determination

(Target: 20 days within the 3-, 6-, and 10-month timeline, respectively)

- **Decision and implementation**
- **Acceptance or rejection of ISTAND Submission, or qualification nor qualification**
- **Issuance of Determination Letter for LOI and QP submissions or Qualification Letter for FQP submissions to the requestor and DDT Transparency Database Update**

ISTAND Program Progress





*include all submissions - LOI, QP, pre-LOI as of 06/23/2025

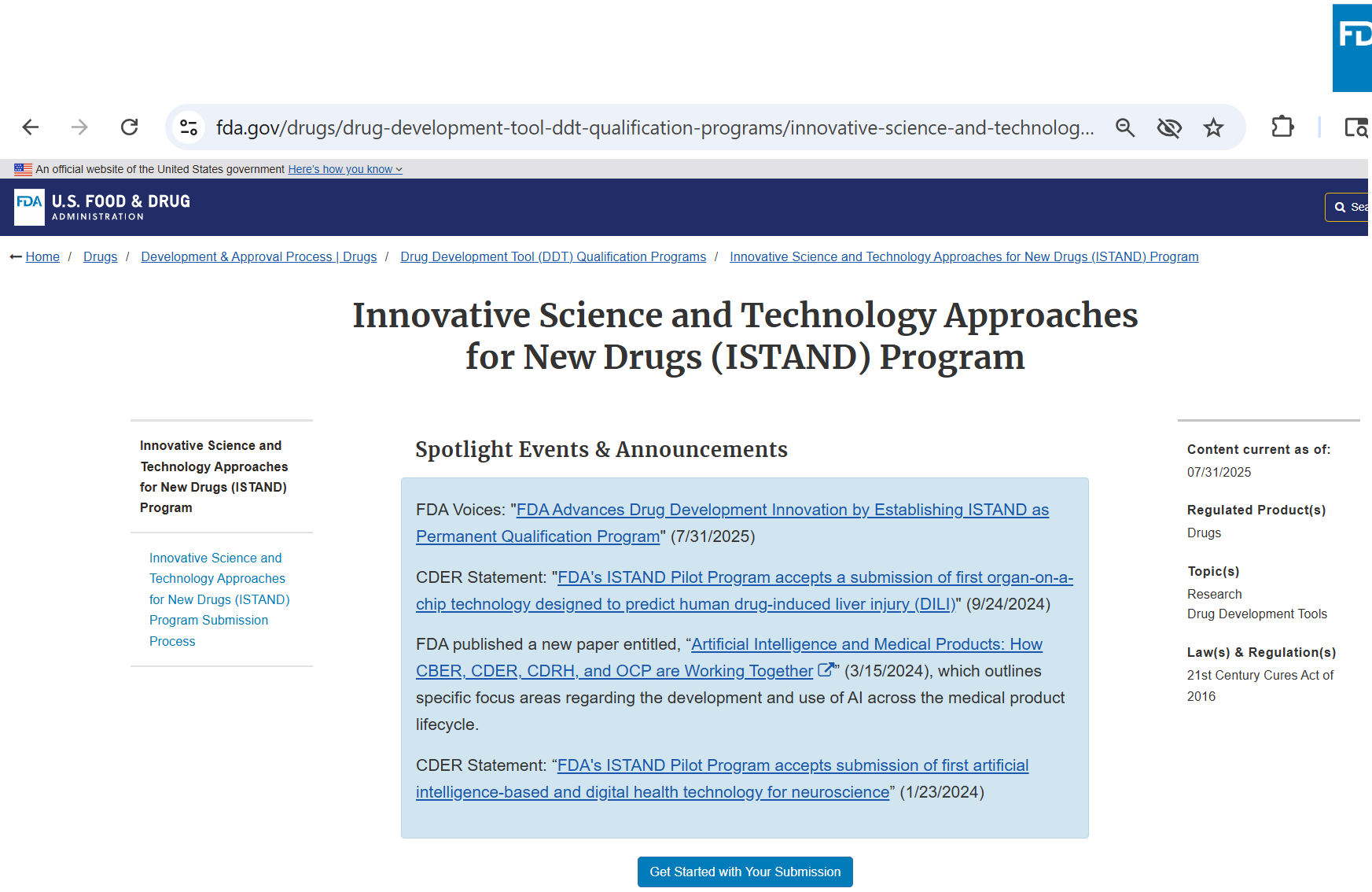
As of 6/23/2025, ISTAND has accepted 8 LOI submissions, including three AI-based DDTs, two tools that assess preclinical safety that do not involve the use of animals, two novel methods to assess tissue cross-reactivity of monoclonal antibodies, and one novel statistical approach

Considerations for DDT Qualification

- CDER's ISTAND program recognizes the need to evaluate and utilize new approach methodologies (NAMs) to improve our ability to predict safety risks in humans and to the principles of the "3Rs" (replace, reduce, and refine) of animal testing
- Context of use can address a *gap* pertinent to regulatory decision-making, e.g., where current models leave uncertainty
- An acceptable context of use may provide the same information as obtained with a current method if it addresses the "3Rs" or is better in some other way

However:

- Methodologies and tools that pertain to internal decision-making by pharmaceutical companies are generally out-of-scope for qualification program



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https://www.fda.gov/drugs/drug-development-tool-ddt-qualification-programs/innovative-science-and-technology-approaches-new-drugs-istand-program