

# Intersection of CAN with FDA Regulatory Science Initiatives and Activities

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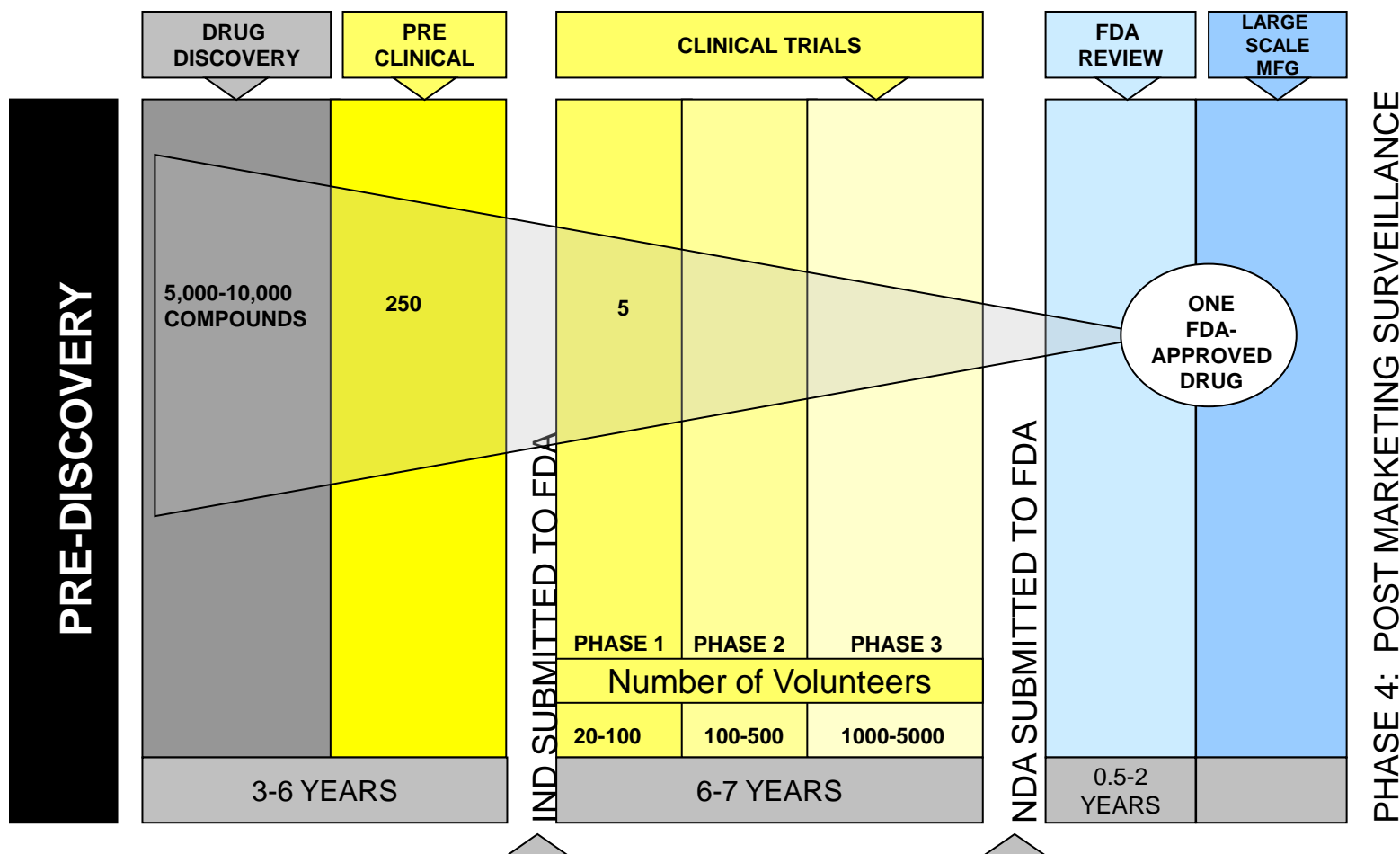
## We Were Asked to Address:

- What are the key issues and problems across the translational science pipeline that CAN could be well-situated to address that, from the regulator's point of view in approving new therapies, stand in the way of making swift regulatory decisions?
- What are the gaps – in science, competency, process, priority – that need to be addressed?
  - How can CAN help fill in the gaps, help de-risk the regulatory process, and move us toward the ideal state?



# Background

# Research and Development Process



# Drug Development

- Currently takes more than 10 years and requires an investment of over \$1B to bring a single innovative drug to market
- Ongoing concern about ability of the drug development enterprise to translate innovative science and bring needed therapies to market
- Ongoing concern about the ability, and willingness, of societies to pay for novel therapies

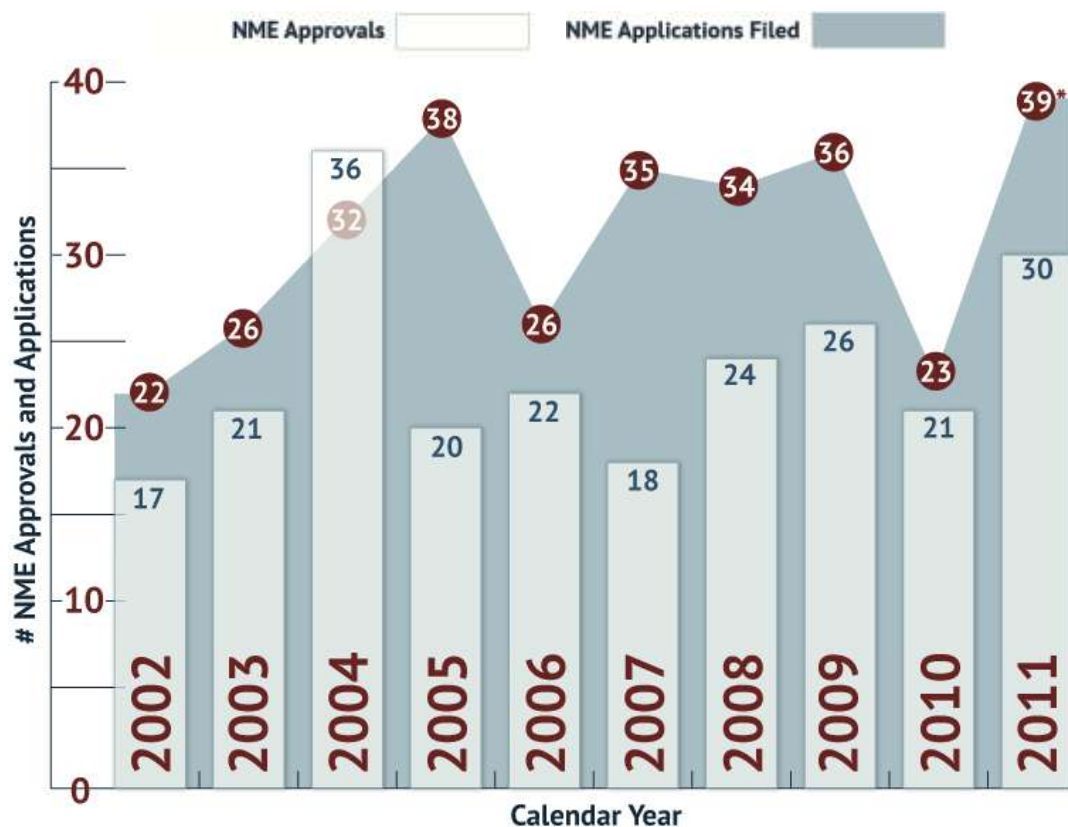
## Key Question

- How to translate the vast amount of new knowledge about human health and disease efficiently, rather than using the time-consuming, costly and inefficient methods currently in place?



# CDER's Efforts to Support Drug Development

# In 2011, CDER approved 30 NMEs, the highest total of NMEs approved in seven years



*\*The final number of NME Applications filed in 2011 is projected, pending final validation of the data and dependent outcome of 12 applications submitted in late 2011.*



# Innovation in drug approvals for 2011

## First in-Class Drugs

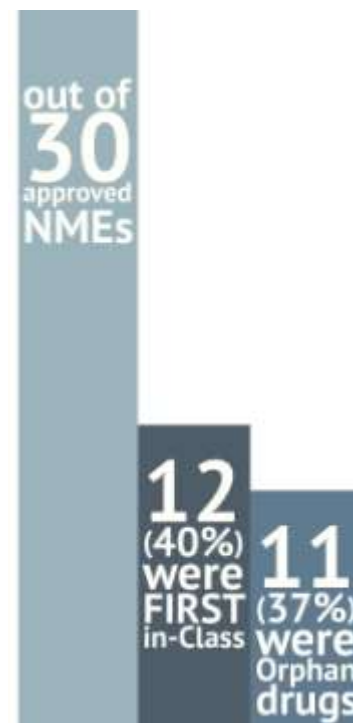
- |             |            |              |              |
|-------------|------------|--------------|--------------|
| 1. Adcetris | 4. Firazyr | 7. Potiga    | 10. Yervoy   |
| 2. Benlysta | 5. Jakafi  | 8. Victrelis | 11. Zelboraf |
| 3. Darilesp | 6. Nulojix | 9. Xalkori   | 12. Zytiga   |

## Approved First in the U.S.

- |             |            |             |               |              |
|-------------|------------|-------------|---------------|--------------|
| 1. Adcetris | 5. Edarbi  | 9. Horizant | 13. Tradjenta | 17. Yervoy   |
| 2. Benlysta | 6. Edurant | 10. Jakafi  | 14. Victrelis | 18. Zelboraf |
| 3. Caprelsa | 7. Eylea   | 11. Natroba | 15. Viibryd   | 19. Zytiga   |
| 4. Difucid  | 8. Incivek | 12. Nulojix | 16. Xalkori   |              |

## Orphan Drug Approvals

- |             |              |            |              |
|-------------|--------------|------------|--------------|
| 1. Adcetris | 4. Ferriprox | 7. Nulojix | 10. Yervoy   |
| 2. Caprelsa | 5. Firazyr   | 8. Onfi    | 11. Zelboraf |
| 3. Erwinaze | 6. Jakafi    | 9. Xalkori |              |



# General Agreement: Development of Evaluative Tools-- A Tremendously Neglected Area

- Now: “Build an airplane and then see if it can fly”
- Better science is needed to both predict and assess safety and efficacy of investigational products
- Major causes of failure in Phase 3 clinical development
  - Lack of effectiveness against placebo or active control
  - Unexpected drug toxicity
  - Commercial non-viability (not better than existing therapy)

## Need for Evaluative Tools

- Large amount of biochemical/molecular knowledge but few ways to assess state of whole organism and impact of interventions at the organism level
- Most assessment tools are not standardized so limited ability to compare one experiment to another
- Little insight into sources of variability of treatment response, even current therapies
- As a result, most clinical development programs are “brute force” empirical efforts: extremely costly and time-consuming

# Predicting, Measuring, and Improving Efficacy Needs:

- New endpoints
- New trial designs
- Use of biomarkers to subset disease (prognostic or response predictors)
- Use of patient-reported outcomes
- Conducting natural history studies to understand disease course—particularly in rare diseases

**These have largely been great concepts...but it's no one's job to resource and solve these problems....**



**What is CDER doing to catalyze movement  
from concept to action?**

## Examples of Collaborative Efforts

- Cardiovascular Safety Research Consortium
- Serious Adverse Events Consortium
- Biomarkers Consortium
- Clinical Trials Transformation Initiative
- Critical Path Institute
  - Predictive Safety Testing Consortium
  - Patient Reported Outcomes Consortium
  - Coalition Against Major Diseases Consortium
  - Critical Path to TB Drug Regimens
  - Polycystic Kidney Disease Consortium
- Sentinel Initiative
- Analgesic Clinical Trials Translation, Innovation, Opportunities and Networks (ACTION) Initiative

# DDT Qualification Activities





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**Drugs**

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

**Drug Development Tools (DDT) Qualification Programs**

The Drug[1] Development Tools (DDTs) Qualification Program was created by CDER as part of the FDA's Critical Path Initiative (CPI) to provide a framework for development and regulatory acceptance of scientific tools for use in drug development programs. DDT qualification programs currently exist for biomarkers, clinical outcome assessments (COAs), and animal models for use under the Animal Rule.

The Drug[1] Development Tool (DDT) Qualification Programs allow CDER to work with submitters to guide them as they develop or refine a DDT for a specific context of use. CDER then will rigorously evaluate the submission for use in the regulatory process. Qualifying a DDT will allow sponsors to use the DDT in the qualified context of use during drug development without requesting that CDER reconsider and reconfirm the suitability of the DDT for the qualified context of use.

**Mission and Objectives**

- To qualify and make DDTs publicly available for a specific context of use to expedite drug development and review of regulatory applications
- To provide a framework for scientific collaboration to facilitate DDT development
- To facilitate integration of qualified DDTs in regulatory review
- To encourage development of DDTs for contexts of use with unmet needs
- To encourage the formation of collaborative groups to undertake DDT development programs to increase the efficiency and lessen the individual resource burden incumbent with DDT development
- To encourage innovation in drug development

**Development & Approval Process (Drugs)**

- Drug Development Tools Qualification Program
- Animal Model Qualification Program
- Biomarker Qualification Program
- Clinical Outcome Assessment Qualification Program

**Resources for You**

- DDT Frequently Asked Questions (FAQs)
- DDT Glossary
- DDT Contacts and Submission Process

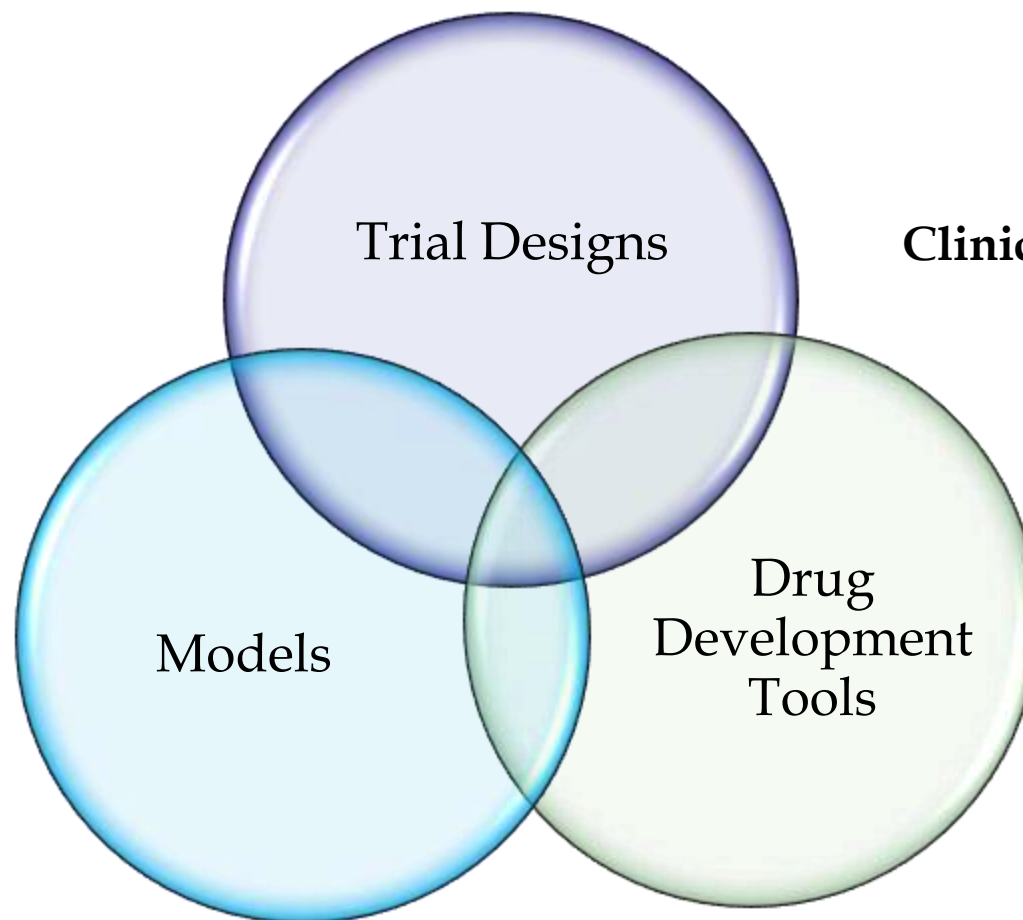
www.fda.gov/Drugs/DevelopmentApprovalProcess/DrugDevelopmentToolsQualificationProgram/default.htm



**Where should CAN play a role?**

# Current Areas of Activity

**Data Standards**



Trial Designs

**Clinical Trial Networks**

Models

Drug  
Development  
Tools

**Training**

**Data Sharing**

## Data Standards

- Uniformity in representation of data
  - Case Report Forms
  - Disease Specific Domains
- Quality
- Interoperability
- Standardized CRF templates for data collection
- Collaboration on international standards

## Data Sharing

- Facilitate pre-competitive collaboration
- Reduce barriers to access relevant information

# Creating an Integrated Workforce Training :

- Clinical Investigation
- Drug Development
- Regulatory Science
- Medical Informatics/Computational Science
- Statistics

## Developing Clinical Trial Networks

Hubs for clinical trial networks that incorporate medical practitioners and also have the capacity for integration of sophisticated bench science

# Summary

- There are major problems with current drug development paradigms
- New scientific knowledge provides a huge opportunity for improvement
- Identifying key decision points in the drug development process and prioritizing related knowledge gaps should drive CAN's investments
- To maximize the value of clinical research, an infrastructure to allow facile collection, analysis, and access to standardized data for knowledge building is essential
- Future drug development must include many innovative and agile partnerships – not re-inventing the wheel