Intersection of CAN with FDA Regulatory Science Initiatives and Activities

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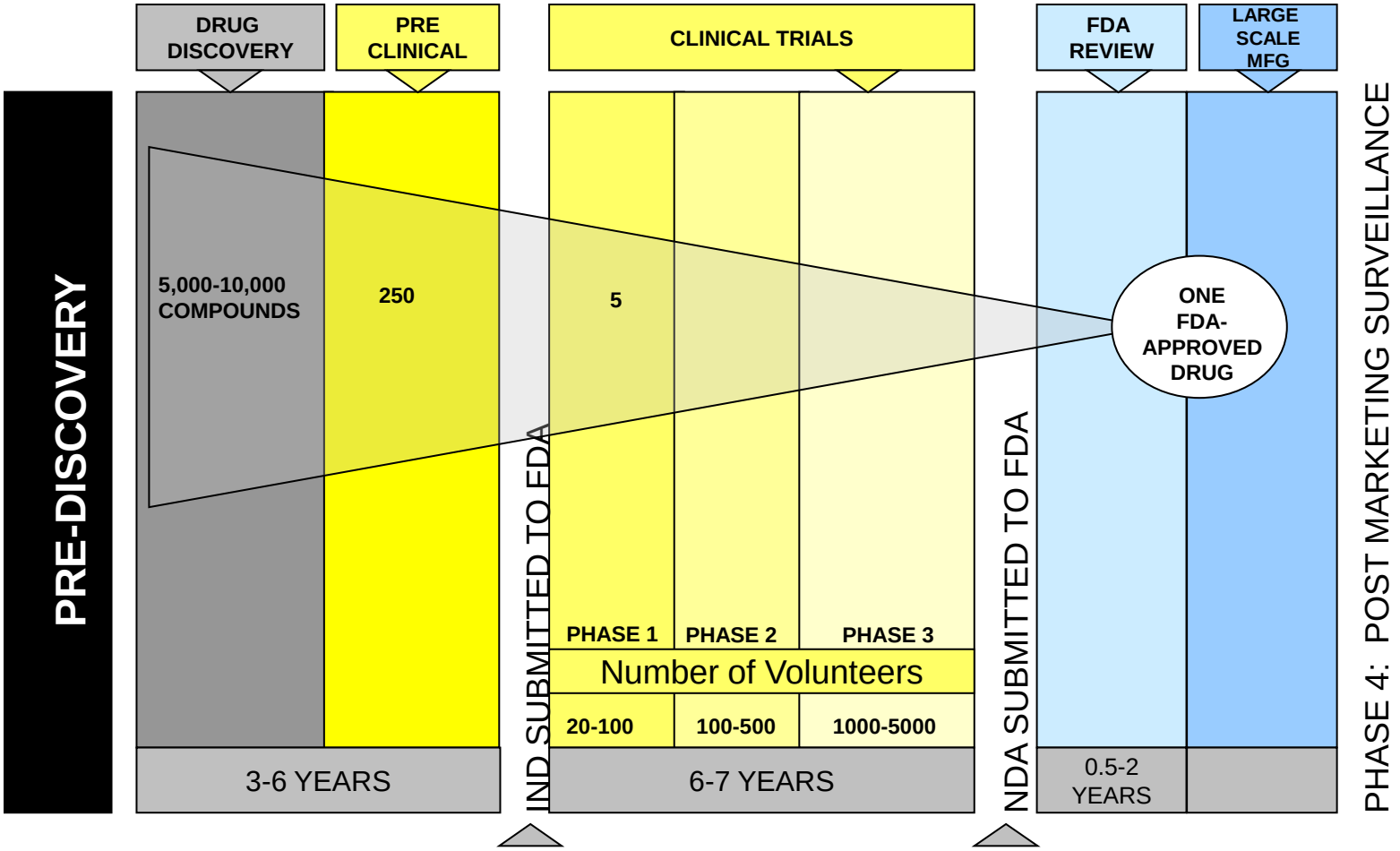
We Were Asked to Address:

- 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



SOURCE: PhRMA 2008, Stages of Drug Development Process and attrition rate of compounds as they travel through the drug development process over time.

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

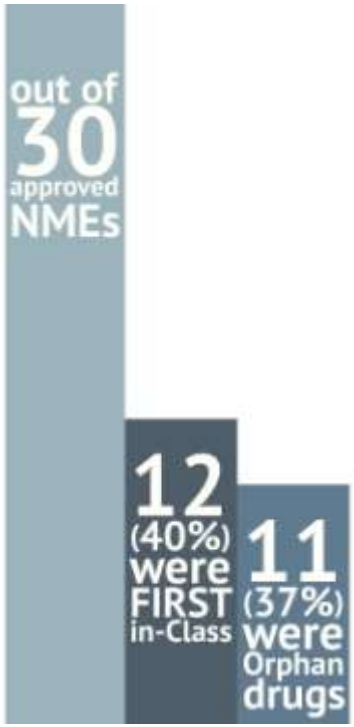
1. Adcetris
2. Benlysta
3. Darilesp
4. Firazyr
5. Jakafi
6. Nulojix
7. Potiga
8. Victrelis
9. Xalkori
10. Yervoy
11. Zelboraf
12. Zytiga

Approved First in the U.S.

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

Orphan Drug Approvals

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



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

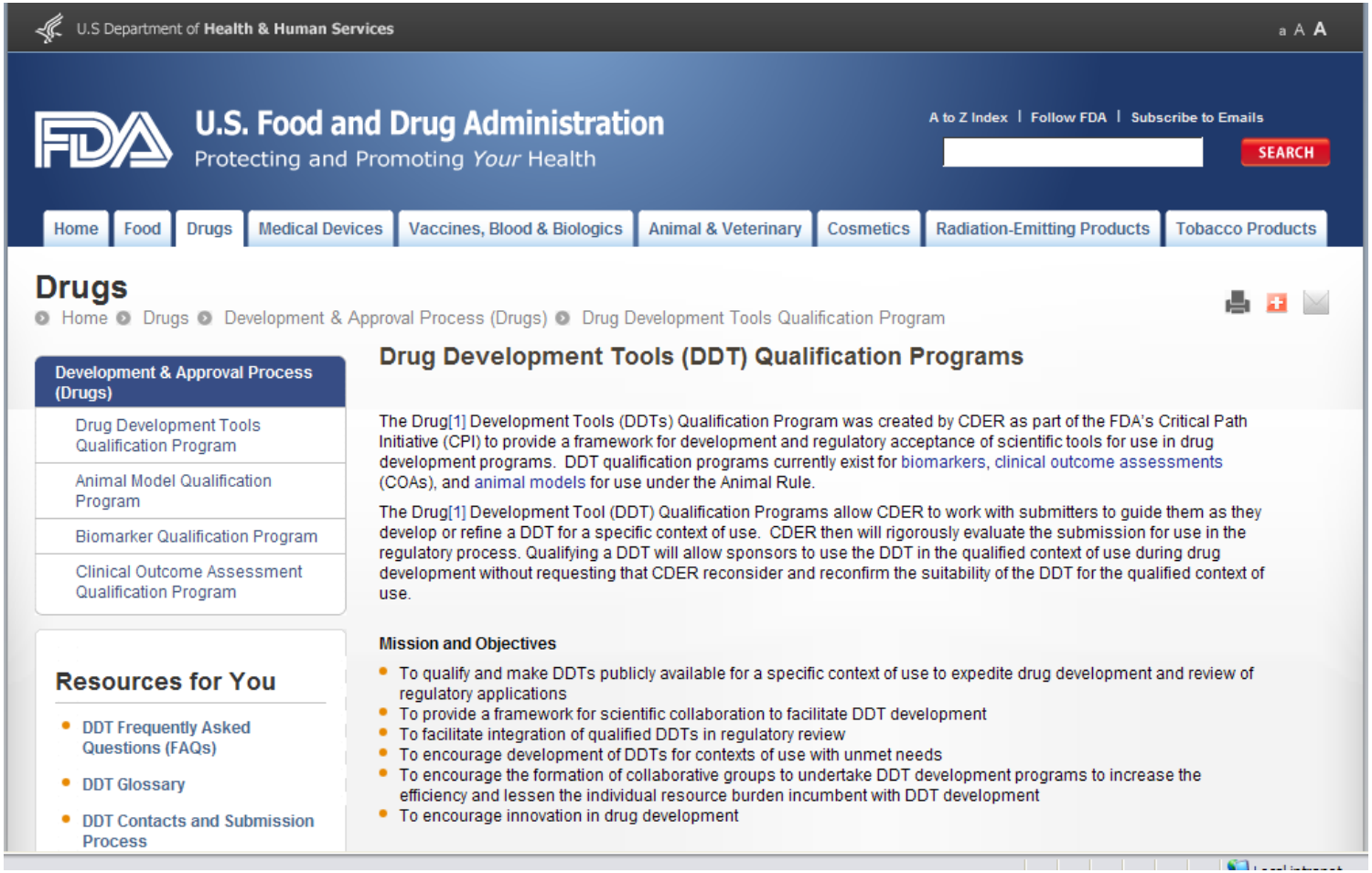
These have largely been great concepts…but it's no one's job to resource and solve these problems….

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 (ACTTION) Initiative

DDT Qualification Activities

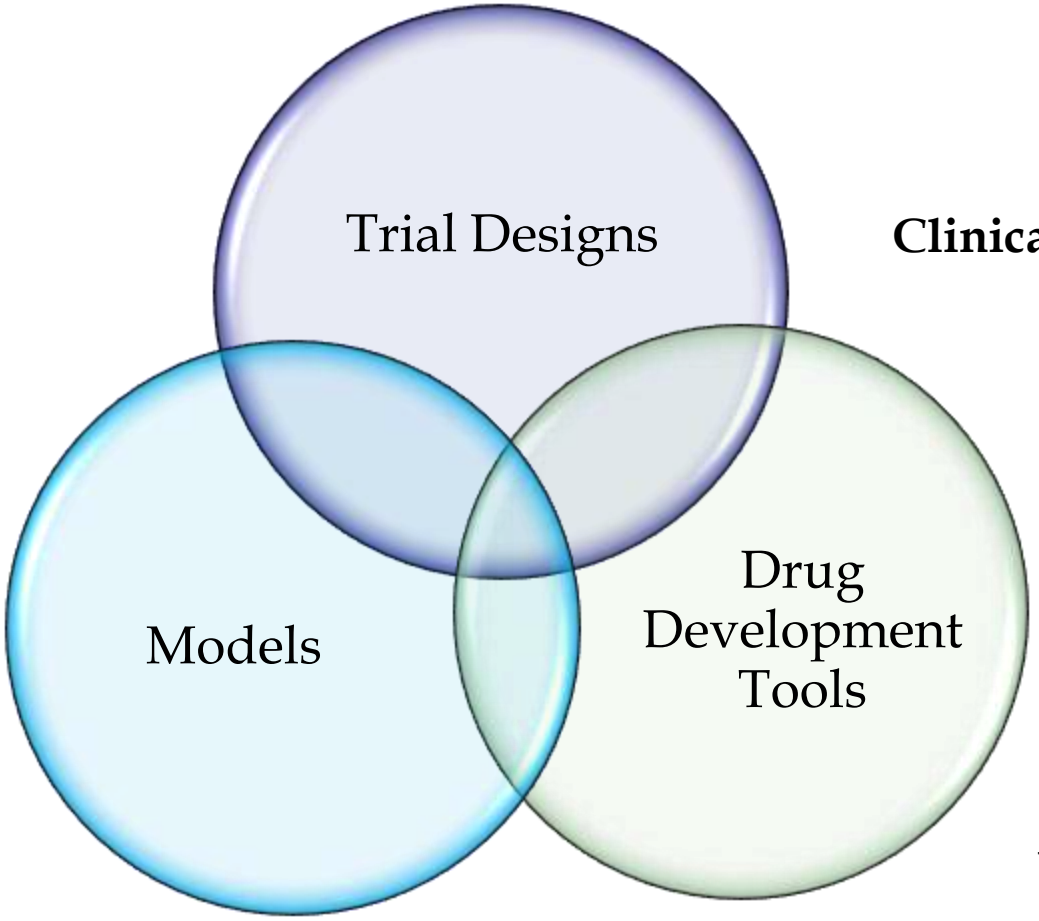


www.fda.gov/Drugs/DevelopmentApprovalProcess/DrugDevelopmentToolsQualificationProgram/default.htm

Where should CAN play a role?

Current Areas of Activity

Data Standards



Clinical Trial Networks

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