The Clinical Trials Enterprise and CTTI

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Topics

- The Clinical Trials enterprise, current status
- FDA's Critical Path Initiative
- FDA-Duke Clinical Trial Transformation Initiative (CTTI)

The Clinical Trials System
(*per Rob Califf and Judy Kramer*)

It's great! Except it's

- Too slow
- Too expensive
- Doesn't answer many critical questions

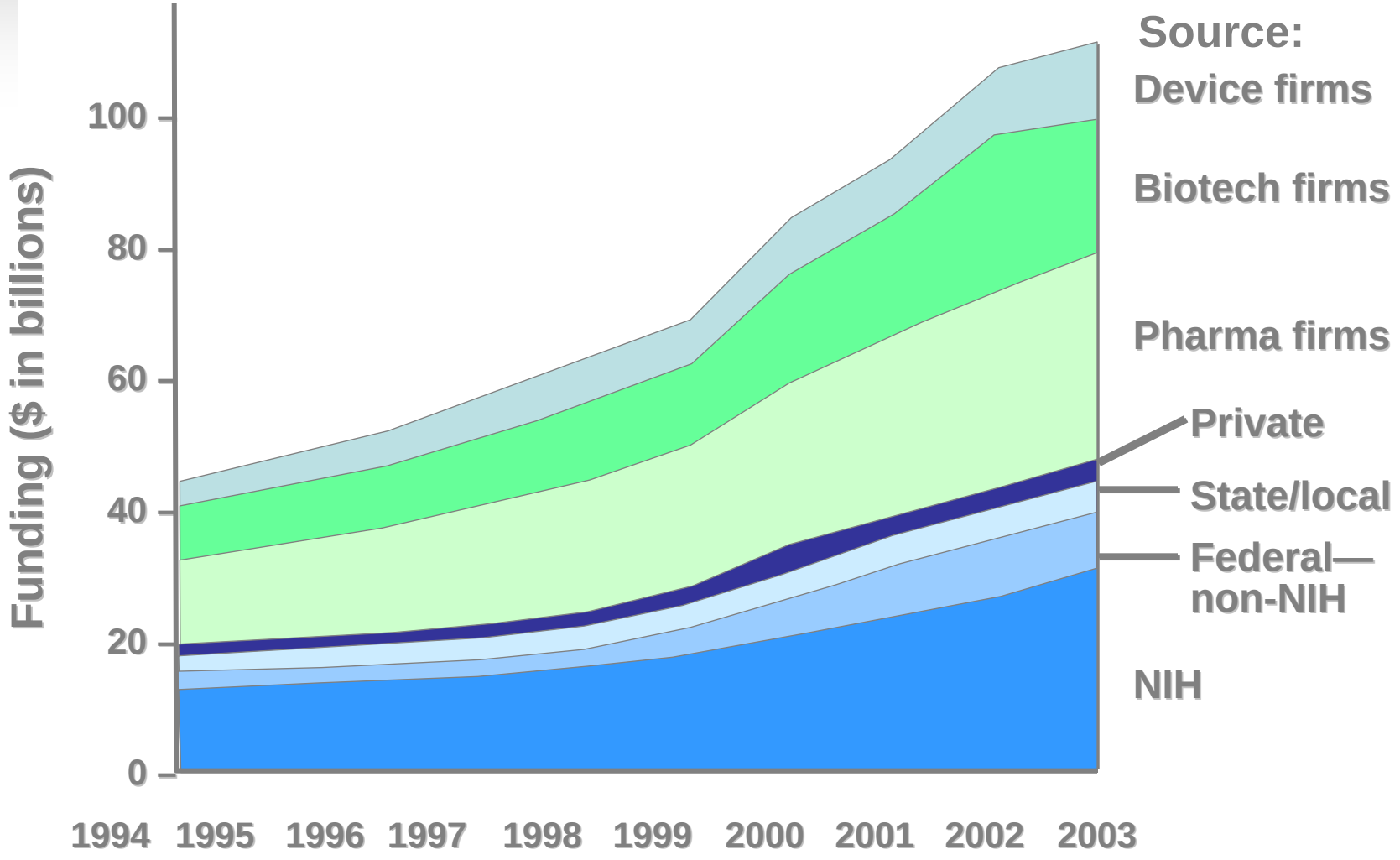
What are Some of the Problems?

- Patients and caregivers want
  - Rapid access to new drugs/devices/biologics
  - Assurance that benefits outweigh risks
- Randomized clinical trials (RCT) = the gold standard
- Systems often paper-based, slow, costly
- Problems delay access to new innovations and limit information on appropriate use of approved products

The Facts Are Distressing

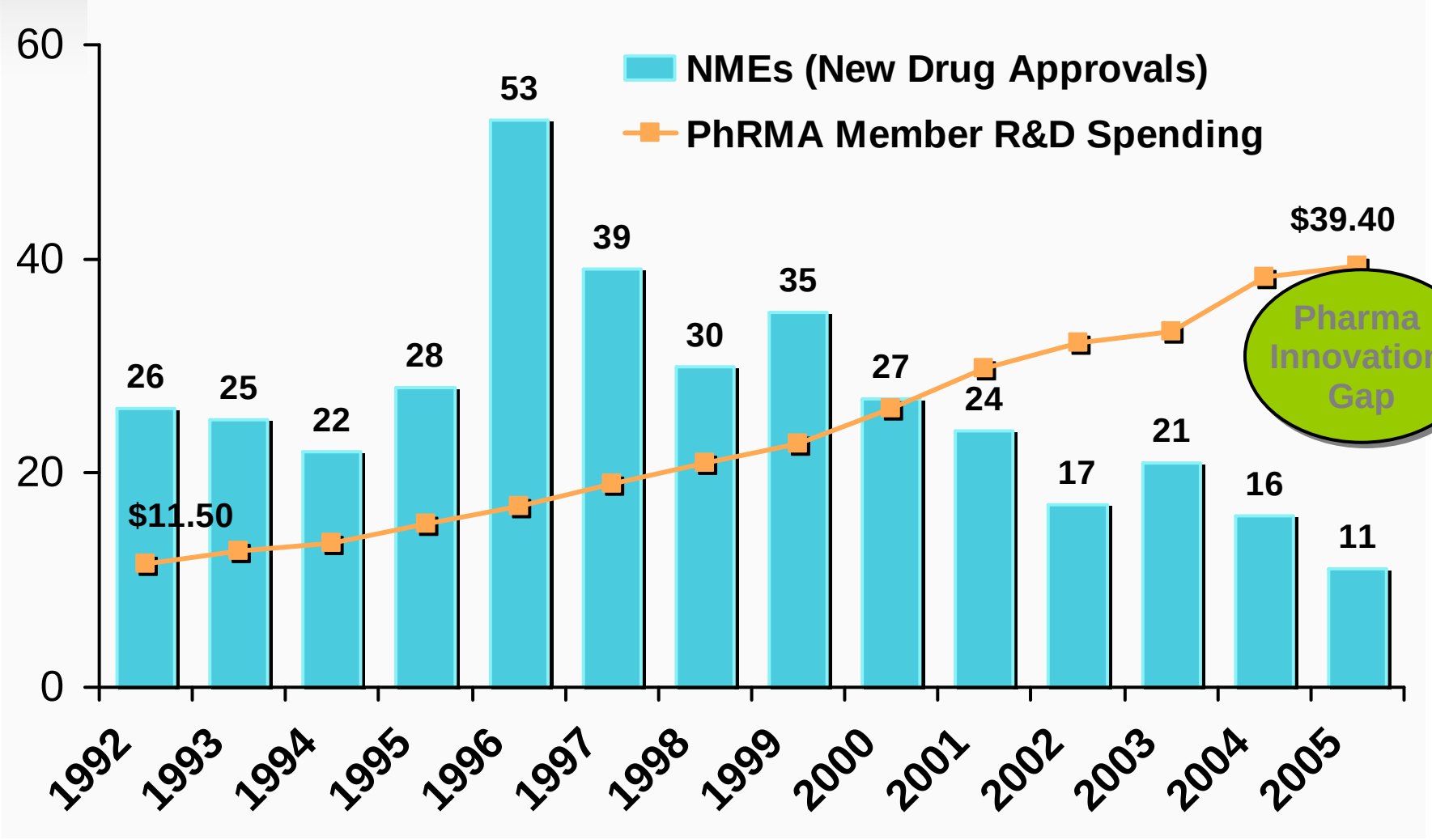
(Special thanks to Rob Califf and Judy Kramer
for the use of their slides)

Investment in Biomedical Research



Moses et al., JAMA 2005;294:1333-42

Innovation Gap Growing



Burrill & Company

What is the “Critical Path”?

- In its 2004 report FDA identified the critical path of medical product development that stretches from candidate identification to commercial production

- The “critical path sciences” involve serial *evaluation* of product performance through preclinical testing, clinical evaluation, and manufacturing

- FDA’s Critical Path Initiative focuses on ***these sciences***
  - Medical Product Development Tools
  - Technical Standards
  - Regulatory Policy and Scientific Standards

Critical Path Initiative (CPI) – Brief History

- Innovation/Stagnation: Challenge and Opportunity on the Critical Path to New Medical Products
  - Released March 2004
  - http://www.fda.gov/oc/initiatives/criticalpath/whitepaper.pdf
  - Evaluated the slowdown, instead of the expected acceleration, in innovative medical therapies reaching patients.

- Innovation/Stagnation: Critical Path Opportunities List and Report
  - Released March 2006
  - http://www.fda.gov/oc/initiatives/criticalpath/reports/opp_report.pdf
  - http://www.fda.gov/oc/initiatives/criticalpath/reports/opp_list.pdf
  - Describes specific areas of opportunity for improvement

Guiding Principles of CPI

- Facilitate infrastructure and “toolkit” development – ***Not*** focus on development of specific products
- Encourage *collaborative efforts* among government, academia, industry, and patient groups
- Develop relevant standards (regulatory and data)
- Build support for academic science bases in relevant disciplines
- Create opportunities to share existing knowledge and databases

Wide Spectrum of Collaborations

- **International efforts**
  - Data standards
  - Global alliance for TB drug development
  - WHO and antimalarial drug development
- **With Fellow Feds**
  - Developing internet portal for submission of adverse event information (*MedWatch*^{Plus})
  - Piloting single repository of investigatory information (*Firebird*)
  - Public repository of all prescription drug labeling (*DailyMed*)
- **Sentinel**
- **Public-private consortia**
  - Data standards (HL-7, CDISC, CDASH)
  - CPath Institute
    - Predictive safety testing consortia
    - Genetic basis of AE
  - DCRI
    - Cardiac safety (ECG warehouse, DES/DAP study)
    - CTTI

CTTI

- **Established out of shared vision**
  - Current problem (clinical trials enterprise is being strangled and, therefore, cannot answer the pressing questions facing society)
  - Path forward (focus on the enterprise as a quality system, e.g., ‘product’ must be fit for use)
  - Mutual need (no one entity can fix this alone and certainly not in a timely manner)
- **MOU between Duke and FDA announced in FR 11/2007**
  - Duke and FDA share an interest in HSP and modernizing the clinical trials enterprise
  - Duke to convene a PPP with FDA and Duke as founding partners that will include a broad coalition of stakeholders

CTTI Mission/Scope

- To identify practices that through broad adoption will increase the quality and efficiency of clinical trials

What Is Quality?

"Quality" is characterized by the ability to

- Effectively and efficiently answer the intended question about the benefits and risks of a medical product (therapeutic or diagnostic) or procedure

while

- Ensuring protection of human subjects

Scope, *cont.*

- Generate evidence about how to improve the *design* and *execution* of clinical trials
- Projects about design will address principles generally applicable to clinical trials to ensure that they will accomplish their intended purpose

Scope, *cont.*

- May study other types of clinical research (e.g., registries) that can provide data to regulatory agencies
- May seek to identify practice improvements that can be applied internationally

CTTI Executive Committee

- ***FDA*** Rachel Behrman (OC, Co-chair); Bob Temple (CDER); Bram Zuckerman (CDRH)
- ***Duke*** Rob Califf (Co-chair)
- ***NIH Liaison*** Lana Skirboll
- ***Industry*** Glenn Gormley, Jay Siegel, Susan Alpert, Alberto Grignolo
- ***Academia*** David DeMets
- ***Patient Rep*** Nancy Roach (cancer advocate)
- ***At-large Rep*** Ken Getz
- ***Non-US Regulatory Liaison*** rotating; to be appointed
- ***Executive Director*** Judy Kramer
- Chair of Steering Committee-ex officio

Member Organizations

Category	# organizations
Pharmaceutical companies	7
Biotechnology companies	5
Device companies	5
Contract research org.	7
Academic institutions	4
Professional societies	4
Regulatory (FDA)	4 (CDER, CBER, CDRH, GCPP)
Other government	2 (CMS, NIH, OHRP)
Clinical investigator groups	2
Trade organizations	2
Regulatory law firms	2
Private equity firm	1
Patient representatives	2 (TBD)

Steering Committee*

- Responsibilities include:
  - Review, evaluate, and recommend projects for approval by Executive Committee
  - Assemble teams to plan and implement projects
  - Manage conflicts of interest
  - Keep abreast of parallel initiatives
  - Develop strategies to synthesize recommendations from completed projects
  - Promote adoption of CTTI recommendations within the clinical research enterprise

* Includes one representative each per member organization

Principles

- In seeking to protect and promote the public health by generating adequate and timely information about prevention, diagnosis, and treatment of disease, the clinical trial enterprise must hold paramount the need to protect human subjects, including their privacy.

- All interested entities must work together to move the system forward; we encourage the input and participation of all stakeholders. No single constituency will have a controlling influence.

Projects

- Information about the process for submission, review, and approval of projects available at CTTI Web site:

  https://www.trialstransformation.org/projects

- Priority areas defined by Executive Committee:
  - Design principles
  - Data quality and quantity (including monitoring)
  - Study start-up
  - Adverse event reporting

Approved Project Concepts

Improving the System of Reporting and Interpreting Serious Adverse Events (SAEs)

- Focus: SAEs that must be reported in an expedited manner
- Goal: to improve ability of system, including investigators, institutional review boards, industry and FDA, to identify and communicate SAEs in a more efficient and informative manner

Approved Project Concepts

Clinical Trial Monitoring

- Goal: Identify best practices and provide sensible criteria for effective monitoring while eliminating practices that may not be of value in ensuring reliable and informative trial results or human subject protection

Approved Project Concepts

Quality of clinical trial results: Consensus for Interpreting and Communicating Clinical Data in the Public Domain

- Goal: Develop principles for interpreting and communicating clinical data in the public domain (outside the peer review system)

Industry Best Practices for Oncology Clinical Data Management

- Goal: Identify and document best practices for the management of data collected in oncology clinical research

For more information….

- CTTI Website-Home
  - https://trialstransformation.org
- Member organizations
  - https://trialstransformation.org/members/member-organizations/
- Steering Committee representatives
  - https://trialstransformation.org/Org/steeringcommittee/members/

Thank you