NCI Pediatric Early Phase Clinical Trials Network (PEP-CTN)

Malcolm A. Smith, MD, PhD

NIH NATIONAL CANCER INSTITUTE

March 2017

Background

- NCI has been primary funder of pediatric phase 1 trials through Children's Oncology Group (COG) Phase 1/Pilot Consortium
- COG Phase 1/Pilot Consortium has been productive over most recent funding period
  - 15 new trials approved by CTEP
  - Evaluations of range of novel therapies: checkpoint inhibitors, antibody-drug conjugates, molecularly targeted agents, oncolytic viruses, DDR modulators
  - Effective incorporation of PK and imaging
  - Generally favorable comments from external reviewers

Pediatric Early Phase Clinical Trials Network (PEP-CTN)

- Dedicated component focused on early phase clinical trials is critical to NCI pediatric drug development program
- Requirements for early phase clinical trials distinctive from phase 3 clinical trial requirements
  - Limited institutions
  - Intensive data collection
  - Close study monitoring
  - Detailed pharmacokinetic (and pharmacodynamic) sampling
  - Rapid development and activation of protocols using standard templates

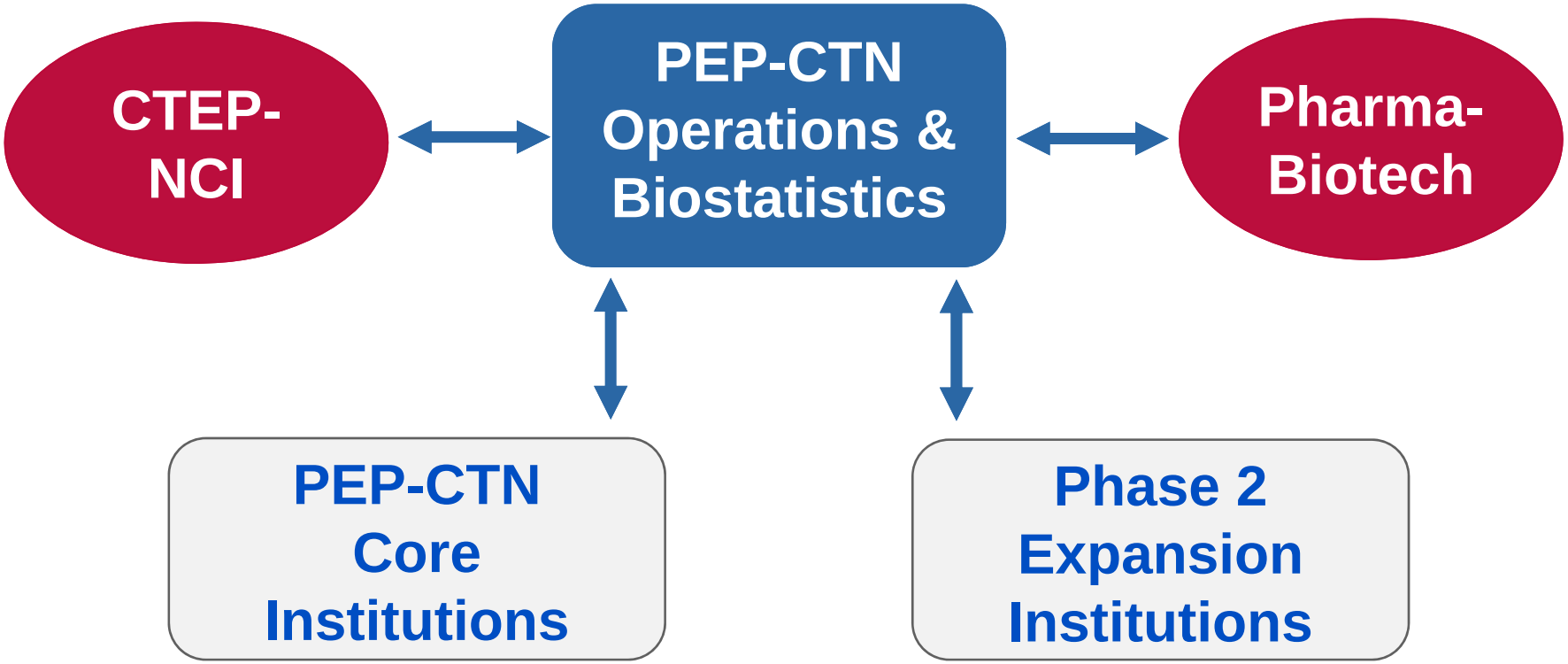
Research Opportunities in Coming Award Period

- Targeted agents primarily developed for adult cancer targets
- Agents modifying DNA damage response
- Epigenetic modifying agents
- Agents targeting protein degradation
- Agents targeting fusion oncoproteins
- Antibody-drug conjugates

External Reviewer Assessments

- Highly supportive of continuing NCI-supported childhood cancer early phase clinical trials program
- Highlighted changing landscape of pediatric early phase clinical trials, with greater use of phase 1-2 designs and with less focus on studies focusing only on dose escalation
- Highlighted need for timely source data verification with the need for study monitoring in addition to the audit program
- Highlighted importance of being able to conduct studies of targeted agents restricted to patients with specific genomic alterations

Pediatric Early Phase Clinical Trials Network (PEP-CTN)



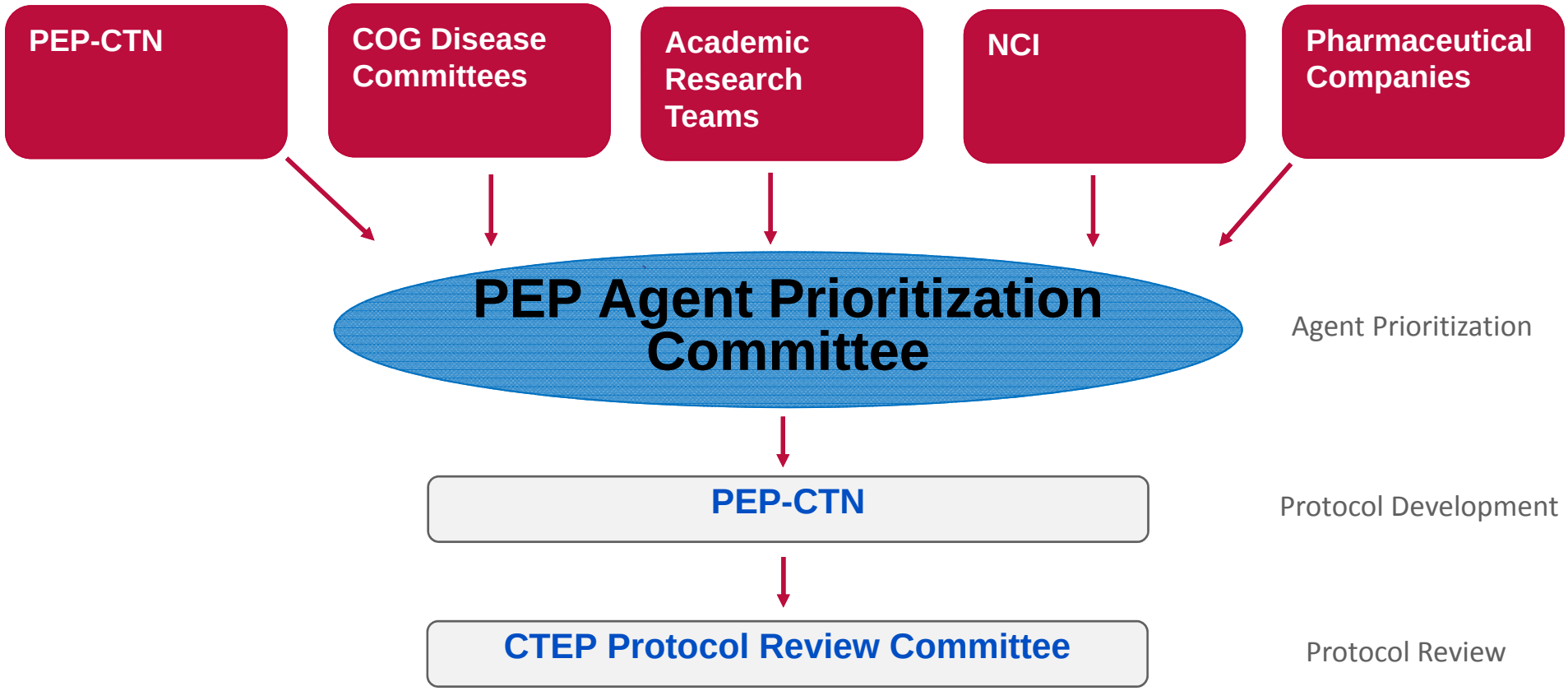
Core PEP-CTN Capabilities

- Protocol development
- Protocol implementation
- Data management
- Statistical analysis
- Pharmacokinetics
- Imaging

Changes Proposed

- Pediatric Early Phase Clinical Trials Network (PEP-CTN)
  - Core institutions for conducting phase 1 studies with intensive PK and monitoring (same institutions as existing COG Phase 1/Pilot Consortium)
  - Additional institutions credentialed for participation in phase 2 studies
  - Allows seamless phase 1 to phase 2 expansion
- Single portal for agent prioritization through Pediatric Early Phase (PEP) Agent Prioritization Committee
- Application of central monitoring to supplement onsite auditing
- Integration of genomics into PEP-CTN

Pediatric Early Phase Agent Prioritization Committee



PEP Agent Prioritization Committee: Proposed Membership

- PEP-CTN leadership (n=3)
- COG leadership and Disease Committee representatives (n=3)
- NCI (n=3)
- FDA (n=2)
- Independent researchers (n=2)
- Advocates (n=1)

PEP Agent Prioritization Committee

- Accepts and reviews applications that provide agent information and rationale for prioritization for testing in children with cancer
- Committee decision options: Proceed to protocol development or defer pediatric development at this time
- Approved agents move immediately to protocol development
- Advantages
  - Single portal for entry of agents to PEP-CTN
  - Incorporates range of stakeholders in decision-making
  - Accelerates pace of agents moving into testing in children

Central Remote Monitoring

- Require inclusion of a specific monitoring plan in all PEP-CTN protocols:
  - Address the frequency of on-site audits;
  - Address various aspects related to central monitoring of data such as source data verification of the first two patients at each enrolling site for informed consent, eligibility, first two courses of treatment (drug administration and AEs), and any other key data items;
  - Tracking of Source Data Verification;
  - Timeliness of data submissions and query resolutions; and
  - Factors that may trigger more frequent monitoring or on-site audits.

Eligibility and Review Criteria

- Applications will be accepted from institutions for the PEP-CTN Operations and Biostatistics unit.
- Applicants will be required to have experience with MediData Rave, CTSU, and OPEN.
- Focus of review on the applicants' ability to provide strong scientific leadership in pediatric drug development (including for PK and biology/genomics), timely protocol development, effective data management, QA/QC including central study monitoring, appropriate statistical analysis, and image collection and analysis.

Additional Issues

- Circulating tumor DNA
- Diversity and access
- Incorporating Patient-Reported Outcomes

Budget

- Increase by 18% over FY2012 direct costs (year 11 award)
  - Implement central monitoring with support to Operations and Biostatistics component and to sites
  - Funds for molecular characterization
  - Phase 2 accrual
- Total direct costs $3,936,947 and total cost $4,091,471 in FY2018

- Scientific leadership: 10%
- Operations & Biostatistics: 42%
- Travel: 3%
- Imaging: 10%
- Site support: 30%
- PK/Genomics support: 5%

NATIONAL CANCER INSTITUTE

www.cancer.gov

www.cancer.gov/espanol