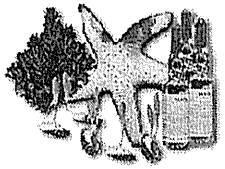
NATIONAL CANCER INSTITUTE

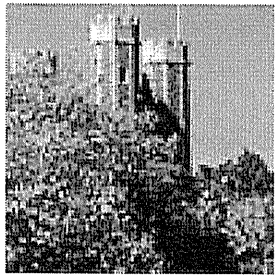
NExT (CTEP) by Numbers

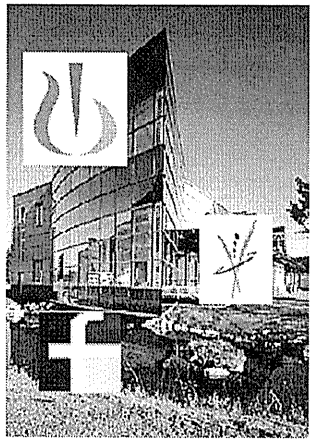
- CTEP sponsored only Investigator-Initiated Clinical Trials
- Currently sponsors over 100 INDs
- Approx. 11,000 registered investigators at over 3,300 institutions
- Over 750 active protocols
- 150-250 new protocols/year
- Approx. 30,000 patients accrued/year
- **Over 80 collaborative agreements (CRADAs, CTAs, and CSAs) with pharmaceutical companies (Collaborators)**

NATIONAL CANCER INSTITUTE

新規化合物がＮＣＩに入り臨床試験実施までの流れ:
NCI Experimental Therapeutics Program (NExT)







Biomarker →

Formulation →

Screening → in vitro → in vivo

Animal toxicology →

NExT program
SEP review

DTP

CTEP

CTEP

Clinical Trials by Academia Consortia Or Cooperative Groups

Development

SAC

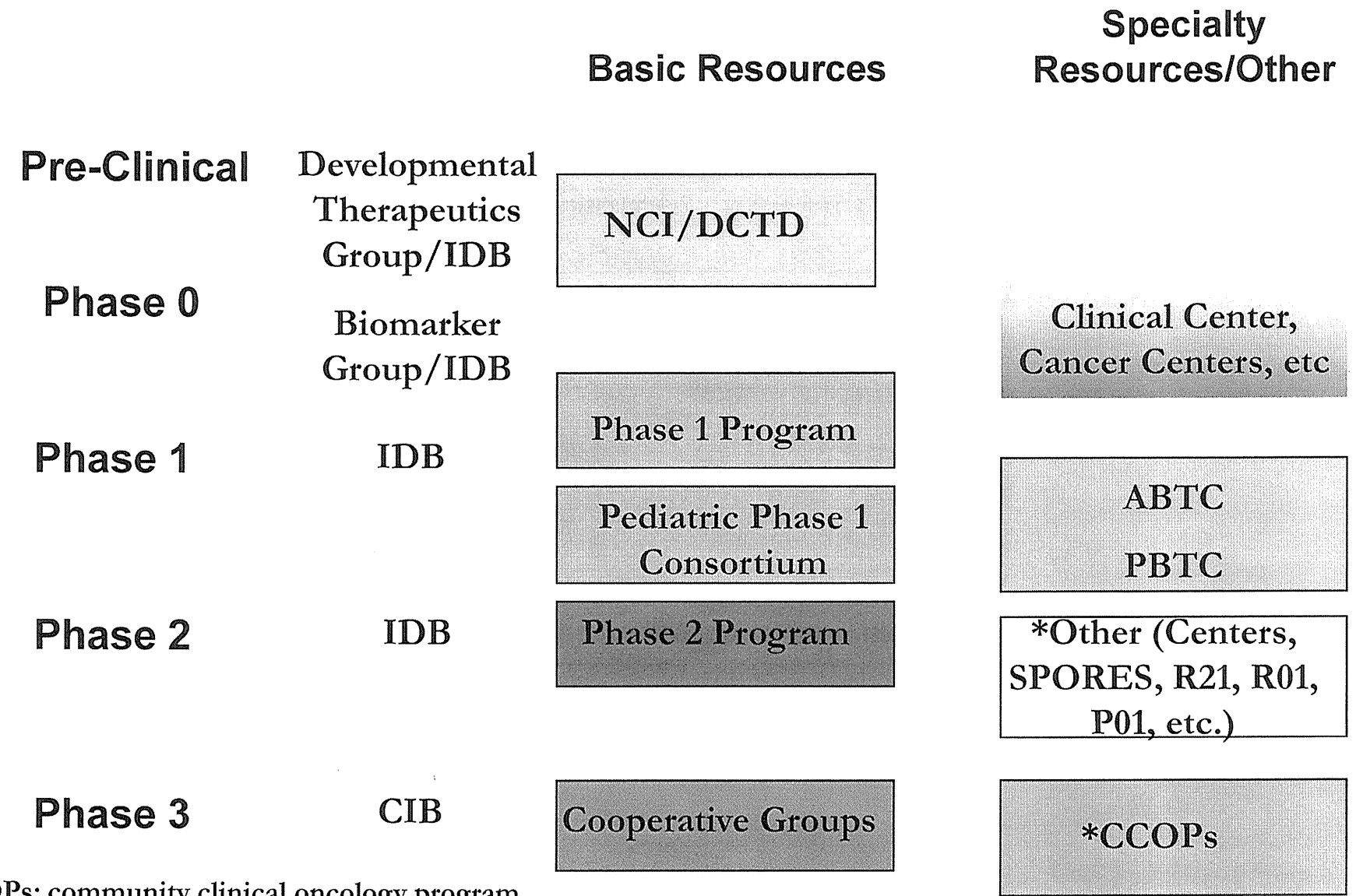
Molecular Imaging →

CTEP各部門の機能

部門	Function
OAD	CTEPのディレクター・ オフィス、各部門を統括
ARC	CTEP研究者へのAdministrative support
RAB	研究者、企業、FDAなどとの契約 **CRADA , MTA, IND.**
OIB	臨床試験がスムーズに行われるよう各部門を統括
CGCB	臨床試験の予算とプロポーザル・ マネジメント
PMB	薬剤の管理・ 搬送と症例のRandomizing
CTMB	臨床試験のモニタリング,
IDB	新規化合物の開発(早期臨床試験)
CIB	臓器別に臨床試験第Ⅲ相以降を担当

CTEP Therapeutics Development Program

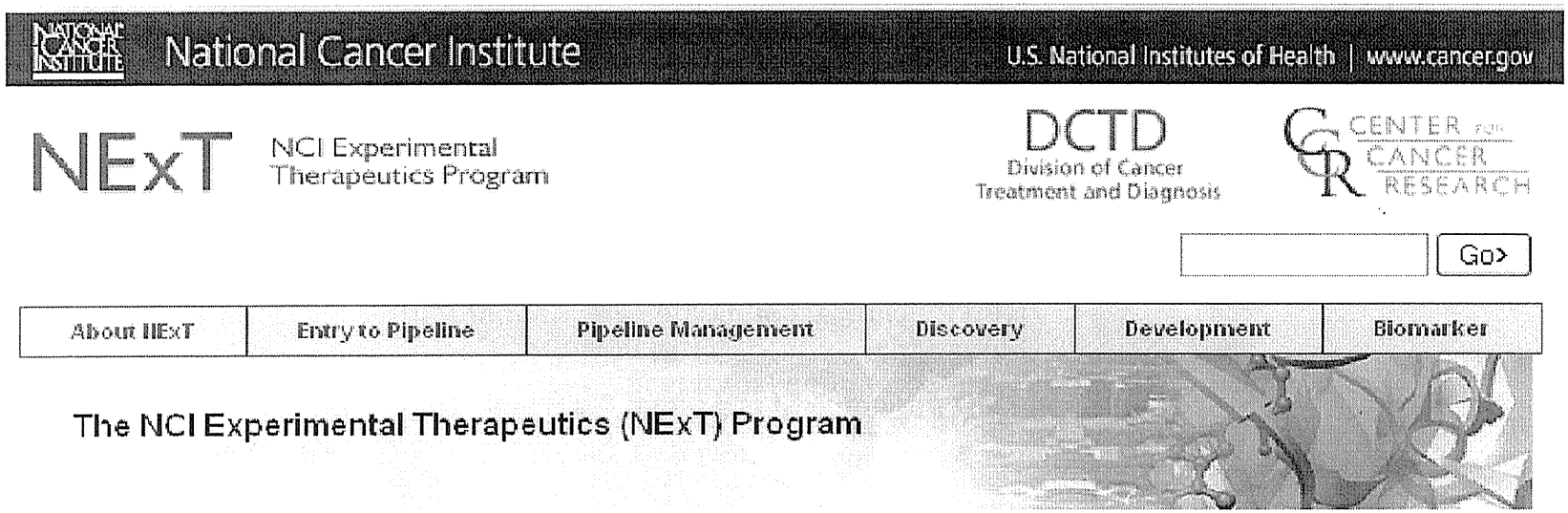
Agents Selected Through NExT Program



CCOPs: community clinical oncology program
IDB: Investigational Drug Branch CIB: Clinical Investigational Branch

*Non-CTEP Funded Resources

Access to NExT



Who: Researchers in academia, government and industry, nationally and internationally.

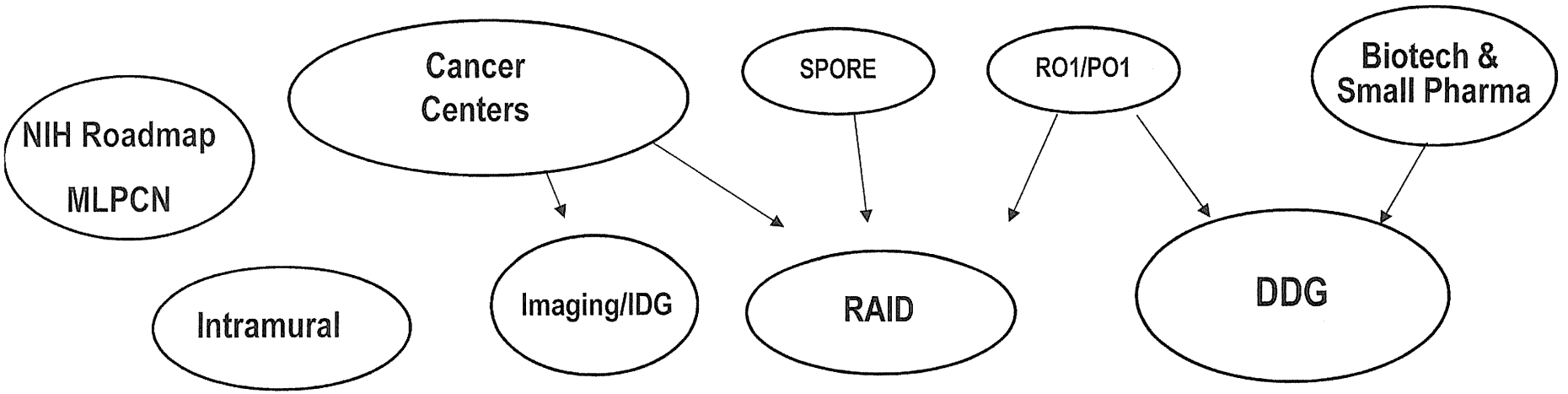
http://next.cancer.gov/

NATIONAL CANCER INSTITUTE

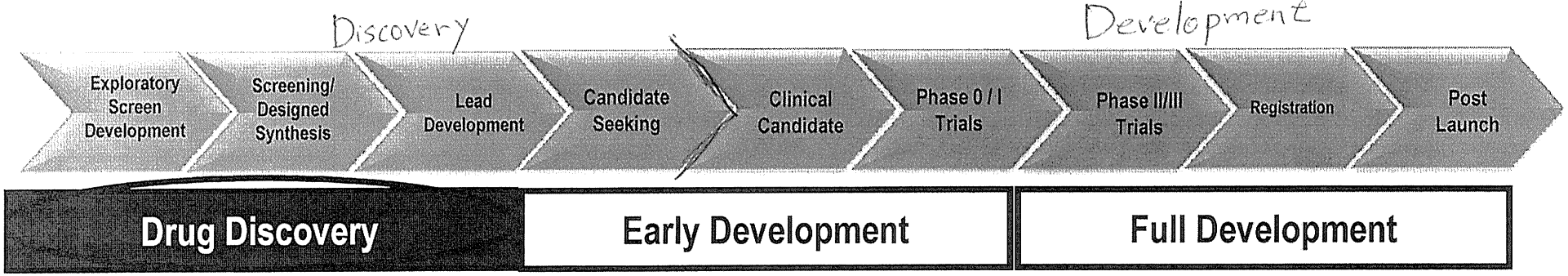
FDA Approved Therapeutics Developed by NCI *from Preclinical Stage*

Year	Agents	Role of NCI	Mechanism of Support
2010	Sipuleucel (Provenge®)	RAID project	National Cooperative Drug Discovery Grant
2010	Eribulin(Halaven)	Natural product discovery; screening; formulation of clinical product; efficacy testing; clinical candidate selection; first-in-human trial	DCTD/DTP Frederick labs;
2009	Pralatrexate	RAID project; NCI produced GMP bulk drug	DCTD/DTP contract resources for production of GMP quality bulk drug
2009	Romidepsin (Depsipeptide)	Developed safe human dosing schedule in large animals; PK and Tox; produced drug for clinical trials; conducted first-in-human trials in NIH CC	DCTD/DTP pharmacology and toxicology and drug production
2004	Cetuximab	Produced first lots for imaging and chimeric clones	DTP Contracts; Cooperative Drug Discovery Grant
2004	5-Azacytidine	Pre-clinical molecular pharmacology; produced pre-clinical and clinical drug supply; conducted pivotal trial	DTP Contracts; Frederick
2003	Bortezomib	Extensive analog screening; MOA and PD studies; PK & Tox; clinical formulation	DCTD/DTP Frederick labs; formulation, PK, Tox
2000	Temozolomide	Scale up synthesis and clinical formulation	DCTD/DTP bulk drug and formulation contracts

Transformation of the NCI Therapeutics Pipeline



The NCI Experimental Therapeutics (NExT) Pipeline: Target discovery through early stage clinical trials



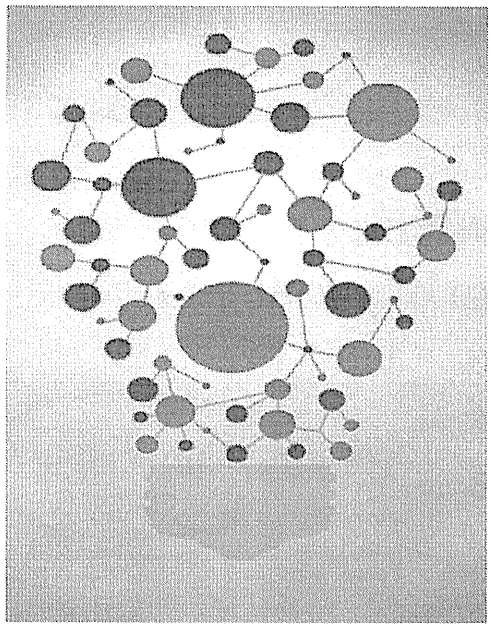
Harmonize Activities into Single Pipeline

MLPCN: molecular libraries probe production centers network,

Chemical Biological Consortium

Mission

Dramatically increase the flow of early-stage drug candidates into the DCTD therapeutics pipeline. ***Provide the extramural community the opportunity to participate in a highly collaborative drug discovery partnership with the NCI.***

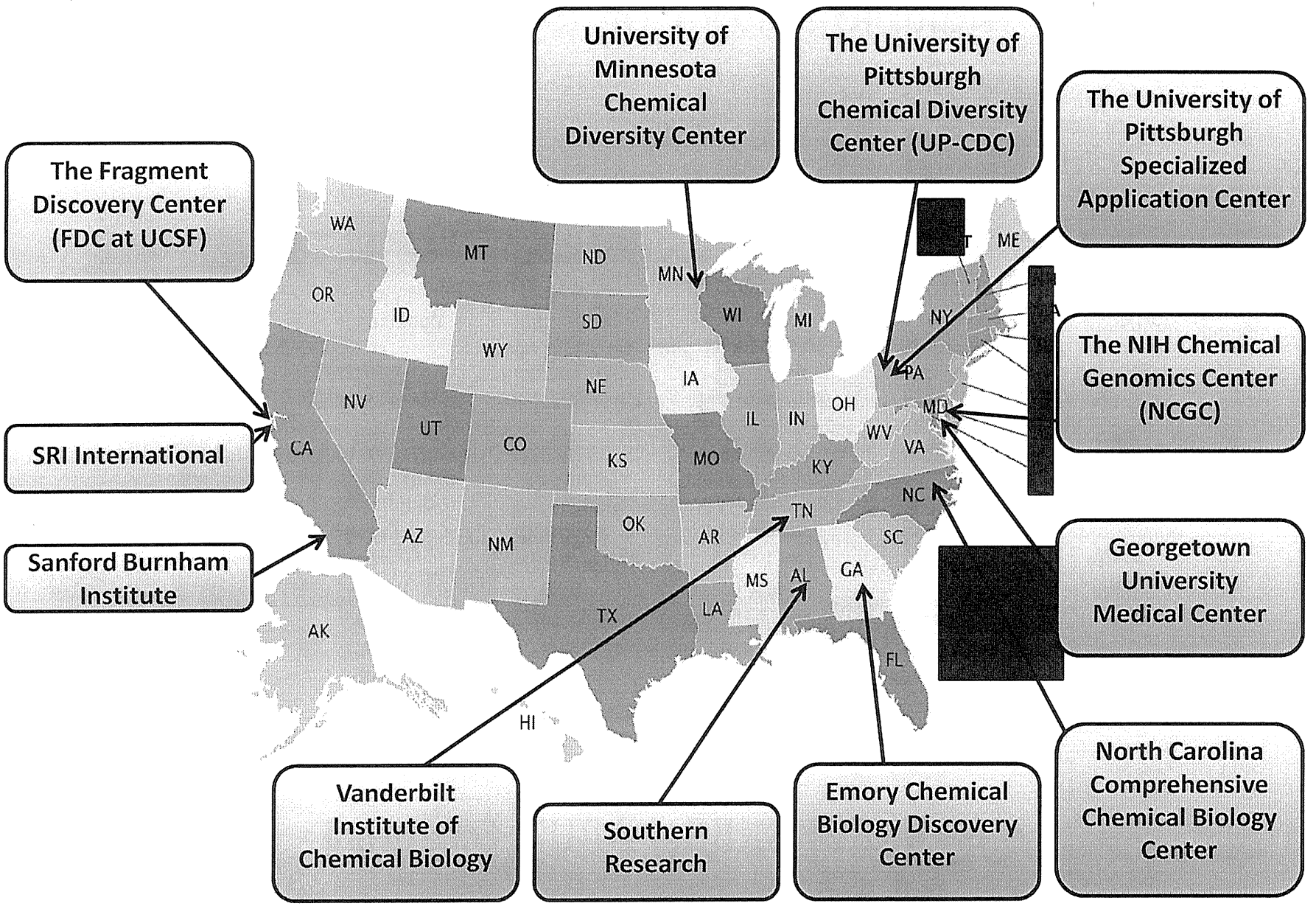


SAIC issued RFP in Oct 2008 seeking technical proposals from screening and chemistry centers to support early drug discovery activities.

August 2009 11 centers awarded contracts.

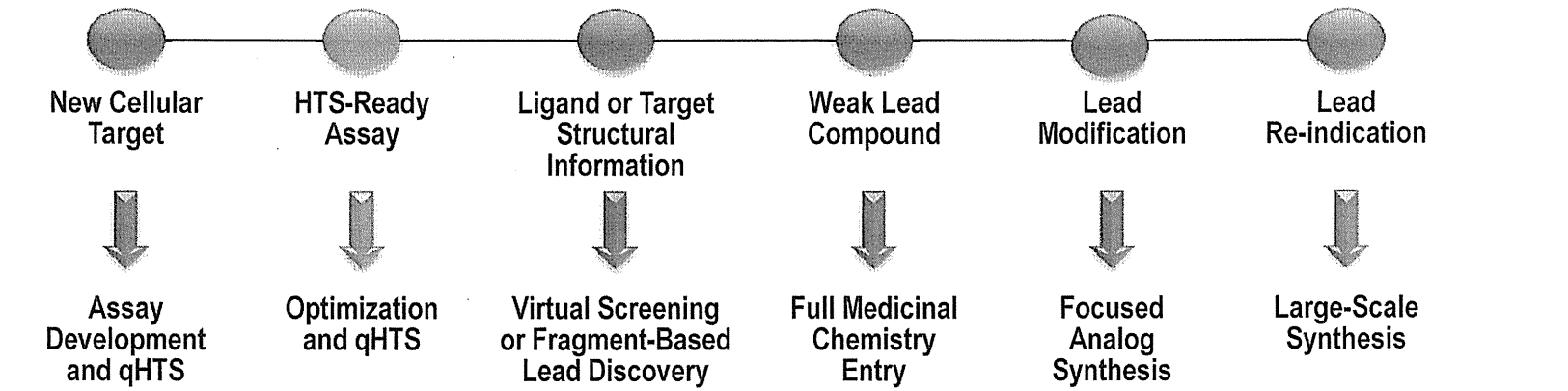
- **Comprehensive Chemical Biology Screening Centers (4)**
  - ✓ **Identify targets, develop assays and adapt these assays to HTS platforms, screen numerous compounds against a variety of different assays each year, and provide Structure- Activity Relationship (SAR) analysis**
- **Specialized Application Centers (3)**
  - ✓ **Provide expertise and experience in specific technologies needed to successfully develop and implement complex and technically difficult assays that may not be amenable to HTS**
- **Chemical Diversity Centers (4)**
  - ✓ **Capable of applying medicinal and synthetic chemistry to advance hits to lead status**

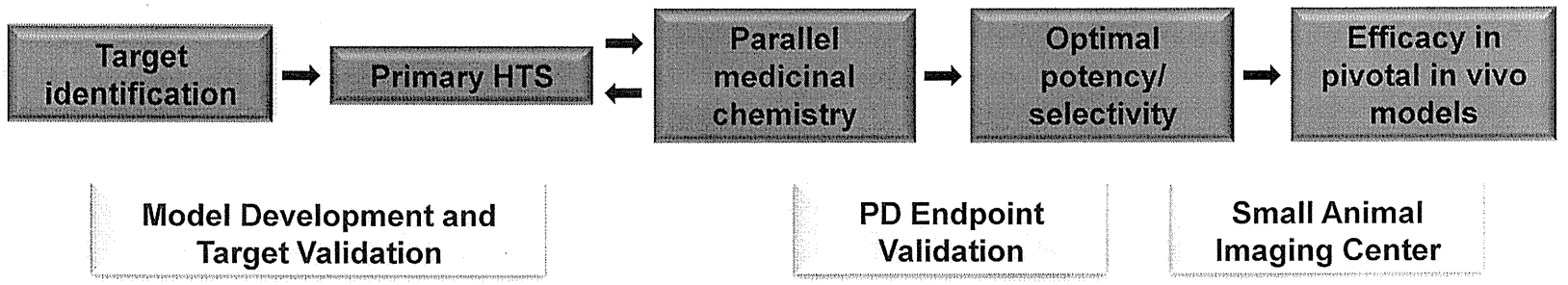
NCI Chemical Biology Consortium (CBC)



NATIONAL CANCER INSTITUTE

Multiple Entry Points Into CBC





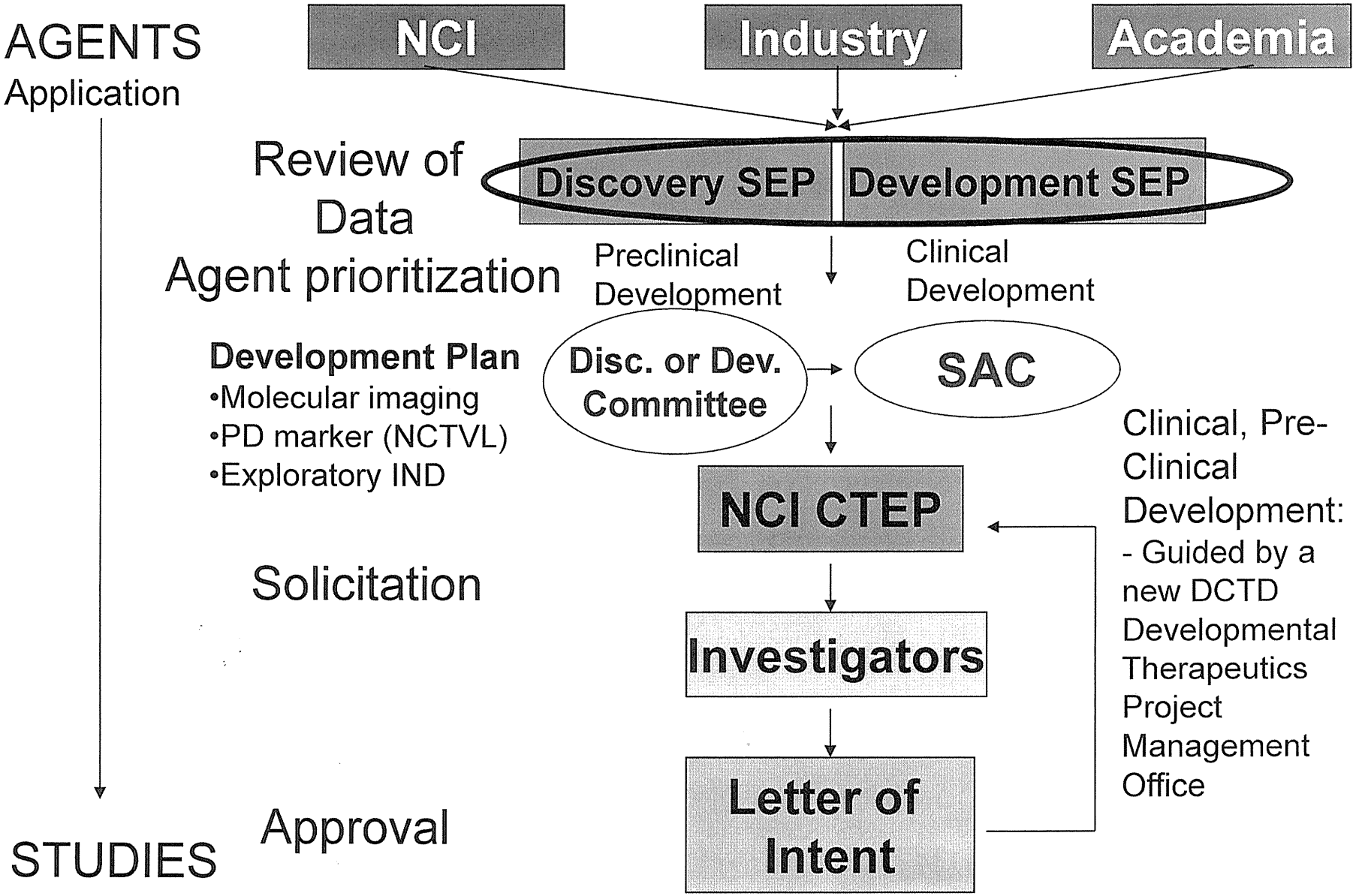
NATIONAL CANCER INSTITUTE

Early Development Platform

Contracts and in-house FFRDC Laboratory Facilities

- Pharmacokinetics/Phamacodynamics
- Toxicology
- GMP Scale-Up
- Development of PD assays during preclinical stages is supported by the Pharmacodynamics Assay Development & Implementation Section (PADIS), and during clinical stages by the National Clinical Target Validation Laboratory (NCTVL).
- Clinical Assay Development Program (CADP) to facilitate development and validation of clinical assays (including diagostics).

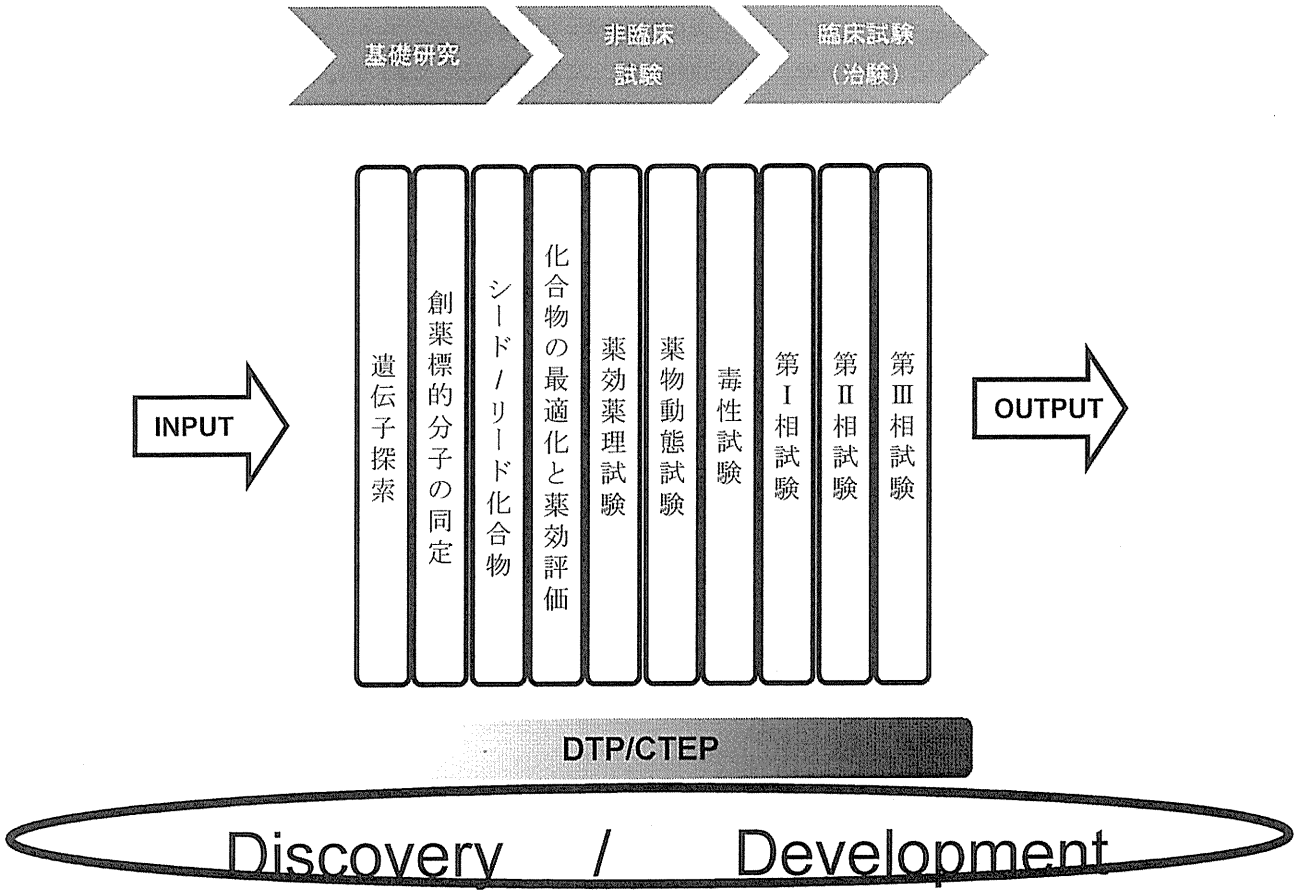
From Bench to Bedside: NCI Experimental Therapeutics Program (NExT)- Collaboration Between DCTD and Center for Cancer Research



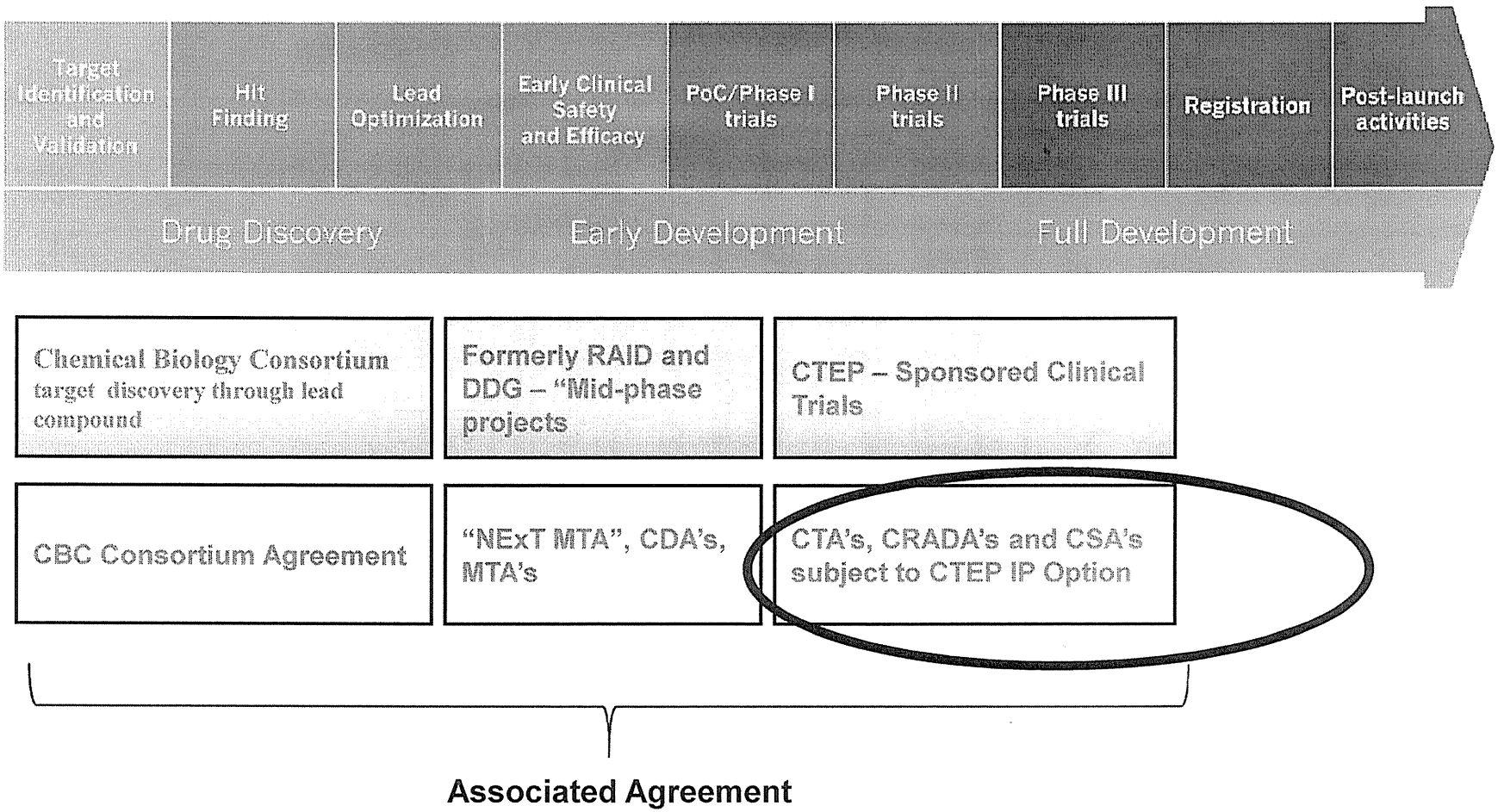
NCTVL: National Clinical Target Validation Lab

http://nexttest.cancer.gov/

NExT Pipeline – Phases of Development and Associated Oversight



NExT Pipeline – Phase and Agreement Types



Slide Graphic courtesy of Barbara Mrockowski

Collaborative Research and Development Agreement (CRADA) For An Agent X

Pharma

- Provide the agent
- Support for proprietary assays (e.g. PK)
- CRADA fund
- Supplemental fund (optional) to sites for additional data or correlative studies

CTEP

- Develop scientific strategy; solicit clinical trial concepts and develop biomarker assay available to public in collaboration with DTP
- Sponsor the trials (IND holder, funding and monitoring the trial)
- Support infrastructure of clinical trial network
- Device master IP, contract language

Investigators:

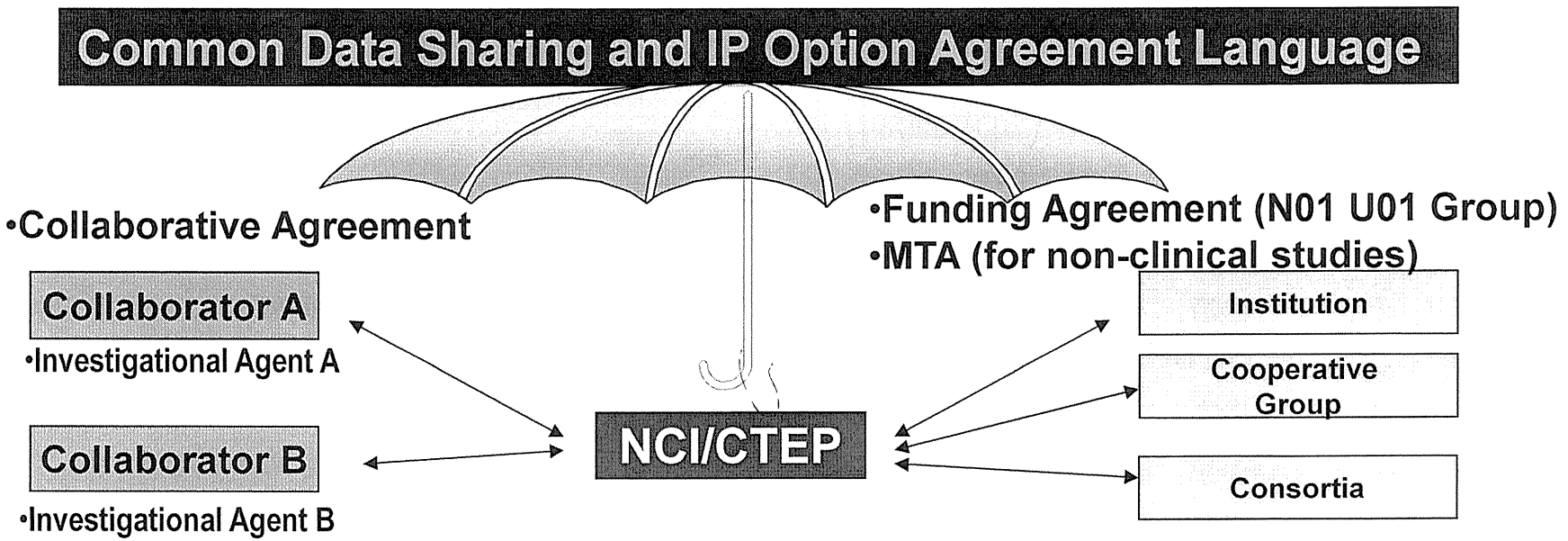
- Propose and conduct clinical trials

CTEP clinical trial network

- Phase I/II trial consortia, academic institutions; NCI intramural program
- Cooperative groups (ECOG, SWOG, CALGB, NCCTG, NSABP, RTOG, GOG, COG ..)
- Community based oncology programs
- Ex-US sites (Canada, Europe, Southeast Asia-Pacific, Japan, Korea, Latin America, Israel, Saudi Arabia, others)

Industry-NCI/CTEP-Investigator Agreements

- **Master agreement designed to encourage companies to contribute investigational agents for combination studies**
  - **IP option:** Each collaborator receives fully paid, non-exclusive, royalty-free licenses to any inventions from the combination studies



Accepted by collaborators. → > 120 trials combining investigational agents

Summary

- Public-industry-investigator collaboration is an important strategy to expedite and expand the cancer drug development
- CTEP experience indicated that such collaboration can be productive, and beneficial to investigators, the company, and most importantly, to patients
- NCI's **non-overlapping** drug **development** of agents with pharmaceutical and biotech companies will result in economical growth by generating new intellectual properties
- Each partner in drug development can provide unique and valuable contribution to the process. Concerted effort is critical and should continue to address the most challenging tasks in modern day oncology drug development
  - Optimize the efficacy of new drug development, amongst many targets and many agents(NCI example , clinical development is performed in collaboration with government support for PD, PK, imaging, and Clinical Diagnostic groups etc.)
  - Better understanding and characterization of the tumor biology and heterogeneity
  - Prioritize and develop rational combination studies especially molecular targeting agents. CRADA makes it possible to combine novel-novel drugs in clinics
  - Biomarker studies to enable personalized medicine for minimizing toxic treatment exposure to only patients with predicted efficacy

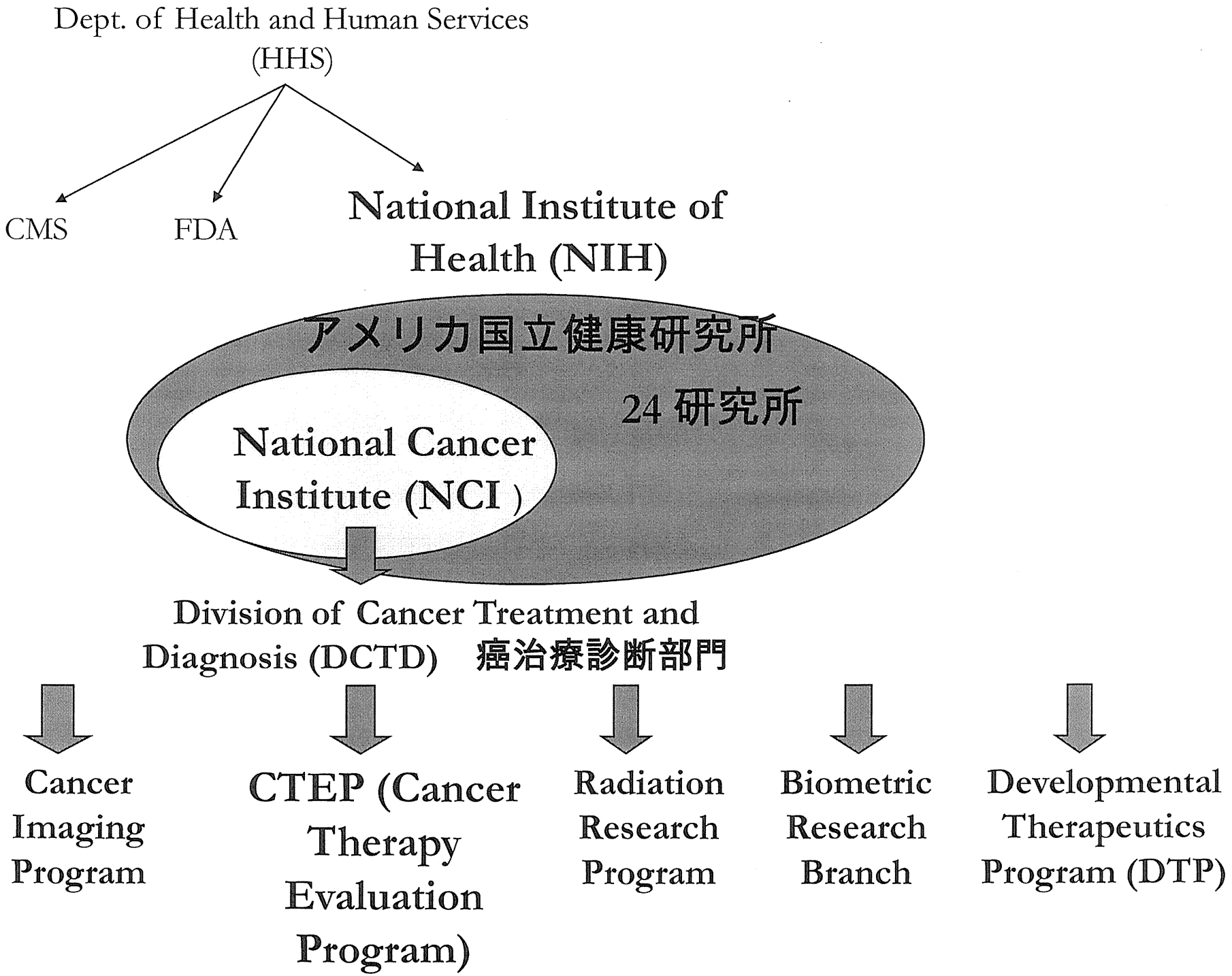
Acknowledgement

- CTEP
  - James Zwiebel, M.D. Percy Ivy M.D., Helen Chen M.D. Investigational Drug Branch
  - Sherry Ansher, Ph.D., Regulatory Affairs Branch
- NExT Program
  - Dr. Barbara Mroczkowski PhD, Special Asst to the DCTD Director at NCI
  - Jason Cristofaro J.D. PhD., Intellectual Property Advisor DCTD

Naoko Takebe Takeben@mail.nih.gov

NExT Program: http://next.cacner.gov/
CTEP website: http://ctep.cancer.gov
Clinical trials: www.ClinicalTrials.gov

Backup slides


Dept. of Health and Human Services
(HHS)
CMS
FDA
National Institute of Health (NIH)
アメリカ国立健康研究所
24 研究所
National Cancer Institute (NCI)
Division of Cancer Treatment and Diagnosis (DCTD) 癌治療診断部門
Cancer Imaging Program
CTEP (Cancer Therapy Evaluation Program)
Radiation Research Program
Biometric Research Branch
Developmental Therapeutics Program (DTP)