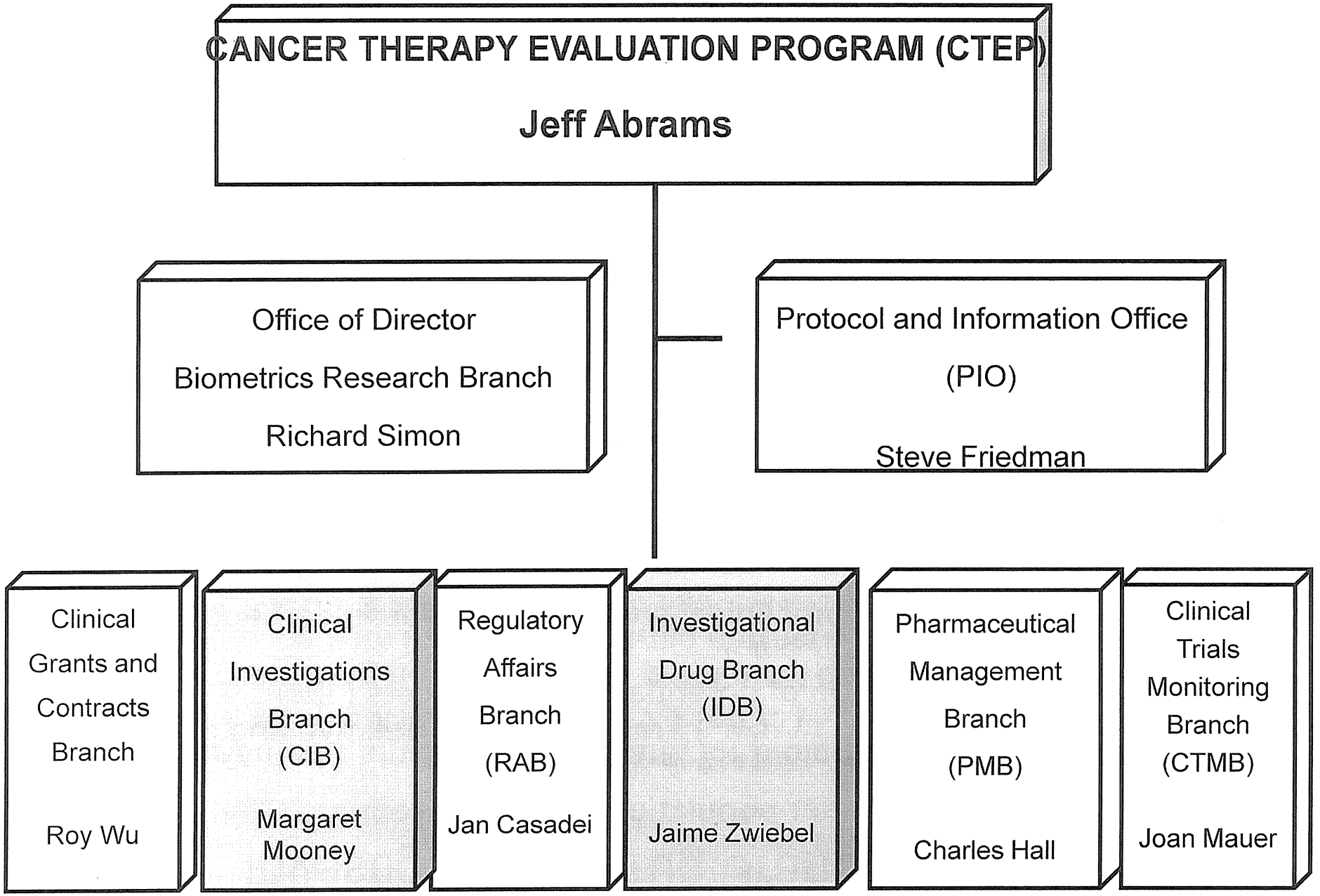

CANCER THERAPY EVALUATION PROGRAM (CTEP)
Jeff Abrams
Office of Director
Biometrics Research Branch
Richard Simon
Protocol and Information Office
(PIO)
Steve Friedman
Clinical Grants and Contracts Branch
Roy Wu
Clinical Investigations Branch (CIB)
Margaret Mooney
Regulatory Affairs Branch (RAB)
Jan Casadei
Investigational Drug Branch (IDB)
Jaime Zwiebel
Pharmaceutical Management Branch (PMB)
Charles Hall
Clinical Trials Monitoring Branch (CTMB)
Joan Mauer

NATIONAL CANCER INSTITUTE

Investigational Drug Branch (治験薬部門)

- **Agent-oriented : small molecules and for biologic agents** (治験薬中心の開発:主に分子標的薬と抗体、免疫治療、ワクチンなど)
- **Identify promising novel agents in preclinical development and arrange collaborations with industry/academic partners** (基礎実験にある有望な新規化合物を見出し、企業及び大学研究者と共同研究を行う)
- **Create drug development plan coordinating with industry /academic source; continually updated** (企業と大学研究者と共同して新規化合物、治験薬の開発プランを立てる)
- **Trial solicitation, review, prioritization, and monitoring** (開発プランに従いそれを実現してくれる研究者から送られてくるコンセプトを審査、選択、そして臨床試験へと発展させ、実際に試験のモニターリングの施行)
- **Strategic development plans to complement industry plans** (作戦的開発プラン)
  - **Ensure appropriate preclinical studies; bench-bedside-bench** (適切な基礎実験がおこなわれているか)
- **Science-driven evaluation of potential disease targets** (標的となる疾患がサイエンスに根ざして評価されているか) **Translational correlative and imaging studies** (探索的な基礎研究と画像的な研究)
- **Drug availability to broader populations when appropriate** (薬の適応範囲を広げる)

NATIONAL CANCER INSTITUTE

Clinical Investigations Branch (臨床試験部門)

- **Disease-oriented** (腫瘍疾患別)
- **Clinical Trials Cooperative Group Program** (Cooperativeグループ試験)
- **Organization of comprehensive programs of preliminary and definitive clinical trials of new treatments or combined modality therapy for specific malignancies**
  (特定腫瘍につき新規治療法ならびに組み合わせによる治療法を開発するために最終段階あるいはそれに近い臨床試験を監督する)
- **Multi-modality clinical research** (多方面からアプローチされる臨床研究)
- **Disease-oriented issues related to large clinical trials, *e.g.*, biomarkers, banking of clinical specimens, imaging studies** (探索的な基礎研究、臨床検体のバンキング、画像診断など)
- **International clinical trials and coordination of international planning of phase III trials** (第 3 相国際共同試験)
- **Development of research standards and harmonization of research methodologies such as outcome criteria and novel clinical trials designs** (臨床試験のスタンダード化と臨床試験のハーモナイゼーションをはかる)

Industry Cooperative Model For Enhancing The Economy

- NCI's **non-overlapping** drug **development** of agents with pharmaceutical and biotech companies will result in economical growth : a broad range of tumors, rare or orphan disease indications, different dosing schedules, biomarker studies etc.
  - If phase 2 successful, the companies will take over to conduct phase 3 study or CTEP orchestrate phase 3 study with the cooperative group with the company
  - Drug derived from CBC or NCI program will be developed and eventually licensed out to industry
  - Small biotech companies often do not have sufficient funding for pre-clinical IND filing studies, phase 1-2, dependent on NCI's capability and prioritization, these biotech companies will be able to develop drugs
    - NCI's prioritization on drug development -> recent implementation of NExT program
- NCI investment towards drug development clinical research may generate new intellectual properties resulting in potential economical growth

NCI-supported Clinical Trials Cooperative Groups

- American College of Radiology Imaging Network
- American College of Surgeons Oncology Group
- Cancer and Leukemia Group B
- Children's Oncology Group
- Eastern Cooperative Oncology Group
- Gynecologic Oncology Group
- National Surgical Adjuvant Breast and Bowel Project
- North Central Cancer Treatment Group
- Radiation Therapy Oncology Group
- Southwest Oncology Group

NCI-supported Clinical Trials N01 and UO1 groups

- N01 9 Institutions
- U01 14 Institutions

NATIONAL CANCER INSTITUTE

CTEP System for Investigator-Initiated Clinical Trials: ＣTEP が医師主導試験をスポンサーする意義 サマリー　1

- Driven by medical need and scientific opportunity

  医療上のニーズとサイエンスを極めることが推進力となりこのプログラムは運営されている
- 57% ASCO plenary presentations

  学会で発表されるプレナリーセッションの５７％を占めている
- Discovery of new treatment effectiveness

  新しい治療法の効果をみいだす
- CTEP handles complex issues e.g. combination study using different pharrma agents. Existing collaboration with more than 100 industries

  ＣＴＥＰは複雑な問題を処理できる：ちなみに異なる企業間の治験薬のコンビネーション試験など。現在１００以上の企業とコラボレーションしている
- Consequently, the academia investigator does not have to deal with FDA for the agent related issues

  結局、大学の研究者たちは規制当局などに関連した問題などにかかわらな

NATIONAL CANCER INSTITUTE

CTEP System is a Model for Investigator-Initiated Clinical Trials: サマリー　2

- **Toxicity monitoring and reporting by CTEP**
  ＣＴＥＰによって毒性のモニターリングと規制当局への報告が行われる

- **CTEP not only support clinical trials financially but actually facilitate the clinical trial development, monitor the toxicities, and report to the FDA for the investigators.** ＣＴＥＰは臨床試験の資金だけでなく臨床試験を実際に施行するためにコンセプトの審査、プロトコールの審査、ＦＤＡとの連絡、ＩＮＤの申請承認獲得、ＦＤＡへの年次報告、安全性のモニターリング、企業との連絡、ＮＣＩで開発したＰＤマーカーアッセイなどの支援など、多岐にわたる

- **NCI is in the best position to take a lead on mandated biospecimen collections from patients in the Cooperative Group studies or CTEP sponsored studies**　　Ｃｏｏｐｅｒａｔｉｖｅ　グループ試験やＣＴＥＰスポンサー試験に登録された被験者からバイオサンプルなどを率先してコレクションすることが可能な立場にある

Study Proposals

- Letter of Intent
  - May be sent in response to solicitation
  - May be sent by investigator with interesting idea
- After LOI Approval → 30 - 60 days to submit a protocol
- If CTEP is the IND holder and sponsor of trial, CTEP monitors the trial

LOI Elements and Review

- Background & rationale
- Trial design
  - Eligibility
  - Dosing
  - Correlative studies
  - Endpoints
  - Statistical plan
  - Accrual plan

Science/Design

- Documented accrual
- Competing studies
- Source of support for clinical trial & correlatives

Feasibility

Components of a competitive Letter of Intent

http://ctep.cancer.gov/guidelines/index.html

LOI Review

1. Review and Priority Scoring of Clinical and Laboratory Components by IDB
   - Science
   - Feasibility
   - Consistency with CTEP development plan
   - Not duplicative
   - CRDL status
2. Review at Protocol Review Committee (PRC)
   - Approval pending company approval letter
3. Industry partner for review and agreement to supply agent
   - Full approval letter with protocol documents

Investigational Drug Steering Committee: Responsibilities

- **Provide strategic input into the clinical development plans for new agents: NCI IND**
- **Address critical scientific issues in early phase clinical trials**
- **Link developmental therapeutics activities with disease-specific clinical trial prioritization**
- **Assist in dispute resolution**
- **Enhance transparency of NCI's drug development process**

IDSC: Structure and Management

- **Co-Chairs: Dan Sullivan, MD (N01 PI) & Michael Grever, MD (U01 PI)**
- **Elected by U01 or N01 PI nominations**
- **Members**
  - **PI's of all NCI Phase I U01 grants and Phase II N01 contracts**
  - **Representatives from Cooperative Groups**
  - **Content experts:**
    - **Biostatistics, Industry, Imaging, Radiation Oncology, Clinical and Pre-clinical Pharmacology, Patient Advocate, FDA, NCI Staff, etc.**

- **Nine Task Forces:**
  - **Clinical Trial Design: Lesley Seymour, Don Berry, Percy Ivy**
  - **Biomarkers in Early Therapeutics: Janet Dancey, Walter Stadler, Kim Jessup**
  - **Pharmacology: Ned Newman, Merrill Egorin, Jerry Collins**
  - **Signal Transduction: Razelle Kurzrock, Steve Grant, John Wright**
  - **Angiogenesis: George Wilding, Roy Herbst, Helen Chen**
  - **Cancer Stem Cell: Pat LoRusso, William Matsui, Lucio Miele, Percy Ivy**
  - **DNA Repair and Programmed Cell Death: Robert DiPaola Miguel Villalona, Naoko Takebe**
  - **PI3K/Akt/mTOR: Afshin Dowlati, Lillian Siu, Austin Doyle**
  - **Immunotherapy: Mario Sznol, Tom Gajewski, Howard Streicher**

- **Four Working Groups**
  - **Conflict of Interest: Joe Sparano and Sherry Ansher**
  - **Meeting Planning: John Wright, Michael Carducci, Chandra Belani**
  - **LOI Review: Pat LoRusso, Michael Grever, Dan Sullivan**
  - **Metrics: Deborah Collyar and Anthony Murgo**

(Jan 2010)

Development Time vs. Accrual Performance of CTEP-Sponsored Trials

METHOD: analyzed NCI-CTEP-sponsored trials (n=553) for phase I, I/II, II, and III studies over an 8 yr period (2000-2007).

- 40% (n=221) of CTEP-sponsored trials failed to achieve accrual goals
- 49% of Phase III trials failed to achieve 25% of accrual goals
- 8,723 patients accrued to the incomplete trials
- Trial development time was an important predictor of accrual success

Cheng et al., ASCO, 2009

Consequences.....

- Only about 3 to 5 percent of adults diagnosed with cancer enroll in a clinical trial.

- 40 percent of trials fall short of their accrual goals.

- Trials that don't meet accrual goals may close without answering the scientific questions they were designed to address.

- 14 of 15 trials (93%) that take over 2 years to activate are never completed.

- Failed trials may delay getting potentially beneficial new cancer treatments to patients.

- Resources spent on clinical trials that do not enroll sufficient patients are misappropriated because the underlying scientific objectives are not met.

NCI Education For Post-Graduate And Medical Students

- A month rotation or sabbatical at CTEP/NCI (junior faculties and medical or surgical oncology fellows, FDA fellows, Government officers from U.S., Canada, Italy, Japan, etc.)
- A seminar aimed at junior faculties during ASCO meetings to teach how to write a career development clinical trial proposals
- CTEP senior investigators have to assist junior faculties who submitted their career development letter of intent (LOI) for clinical trial development
- Organize workshops for clinical trials: e.g. 1st US-Japan Clinical Trial Workshop in DC in June 2010

Resources - Mozilla Firefox

History Bookmarks Tools Help

http://ctep.cancer.gov

ctep.nci.nih.gov

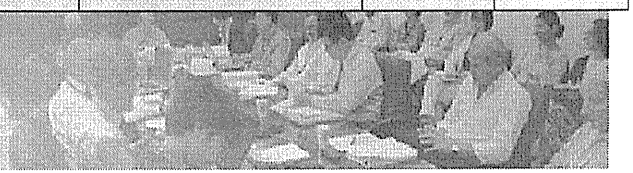
Latest Headlines

National Cancer Institute U.S. National Institutes of Health | www.cancer.gov

CTEP Cancer Therapy Evaluation Program

Home | Sitemap | Contact CTEP Go>

Home | Investigator Resources | Protocol Development | Industry Collaborations | Initiatives / Collaborations | More Links | About CTEP



INVESTIGATOR RESOURCES

- CTEP Home

CTEP Branches and Offices

Office of the Associate Director

Clinical Grants and Contracts Branch

Clinical Investigations Branch

Clinical Trials Monitoring Branch

Investigational Drug Branch

Last Updated: 02/17/09

Investigator Resources

Investigator Registration Packet

- Investigator Registration Packet

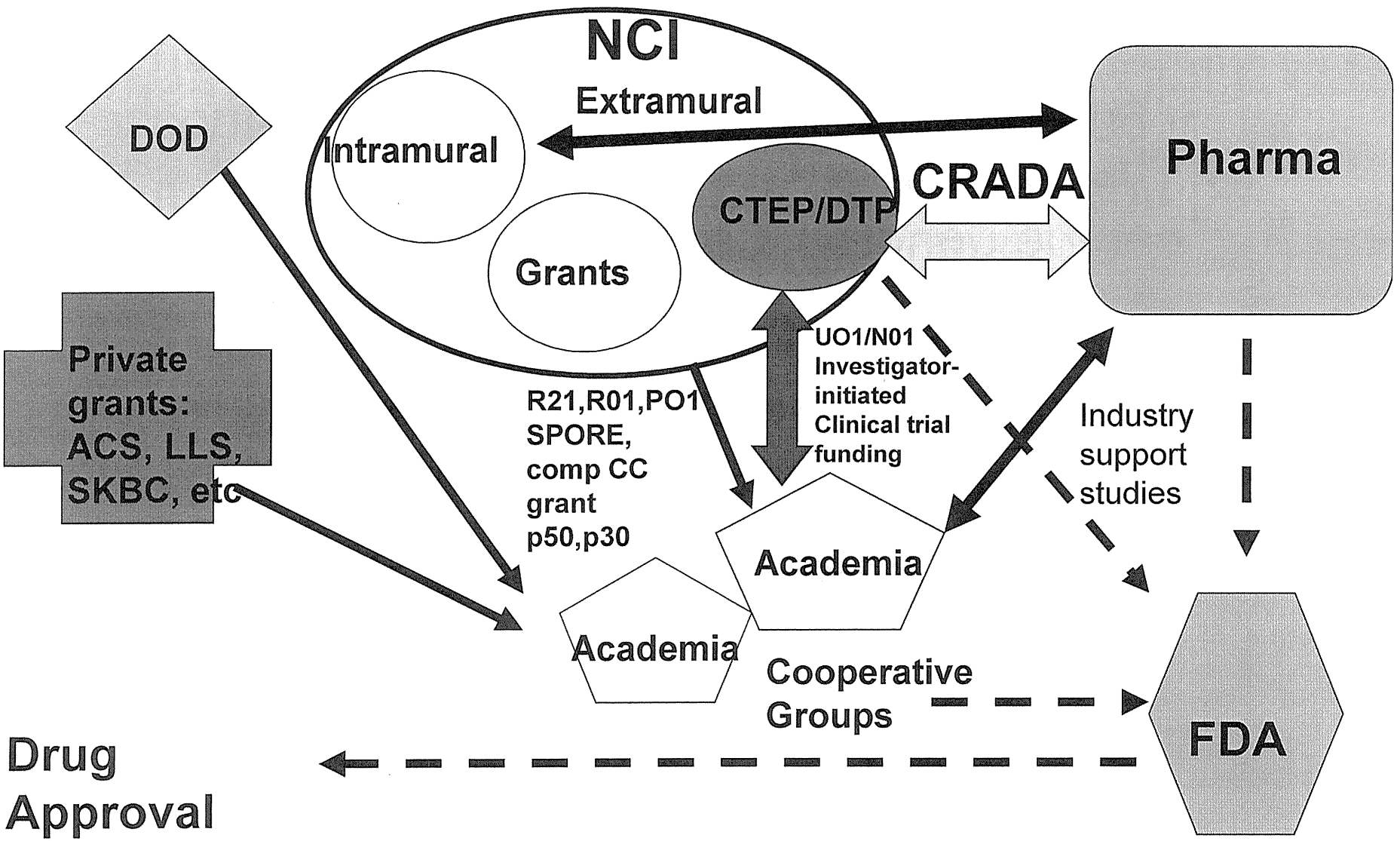
Investigator's Handbook

- Investigator's Handbook
- CTEP's Review Types and Decision Tree (MS Word)
- CTEP Review Flow for Cooperative Group Phase 3 Trials

Cancer / Clinical Trial Information

- Cancer Information Service (CIS)
- NCI's PDQ® database of cancer clinical trials
  1-800-4-CANCER
- ClinicalTrials.gov

Process Map Of Cancer Drug Development In The US



NATIONAL CANCER INSTITUTE

Early Stage - CBC

- Utilizes the CBC Agreement mechanism
  - The advantage of this system is that all work can be done under a single agreement that includes provisions for confidentiality
  - The disadvantage is that no tangible Intellectual Property rights or options can be conferred under this agreement, making it unsuitable for late stage development

NATIONAL CANCER INSTITUTE

Mid Stage Projects – Lead Compound through Phase 0/1

- NExT MTA
- "Not-to-file" language in these agreements for NCI internal studies
- Non-SAIC Contractors have language in their contracts wherein they are required to offer the first option to negotiate an exclusive or non-exclusive license
- SAIC contractors subject to third party language described in the DEC(determination of exceptional circumstances)

Late Stage Projects – CTEP Sponsored Clinical Trials

- Utilizes CRADA's, CTA's and CSA's to bring in agents for clinical studies
- IP terms for both NCI use and for cooperative group trials (CTEP IP Option), new language may have some reach through on downstream inventions.
- CTA's – quicker but many collaborators dislike them due to the lack of IP terms on NCI inventions (IP Option still applies), we may not bring in money under a CDA either (other than direct payments to contractors
- CRADA's – time consuming but allows the NCI to bring in funding support from Collaborators and offer licensing rights to the Collaboration