Clinical Trials Systems in Japan

Ministry of Health, Labour and Welfare

R&D Division, Health Policy Bureau

Toshio Miyata, MD

May 25, 2010
British Embassy Tokyo

Clinical Trials in a Globalized Society
-Building an Effective Cancer Clinical Trials System-

Background

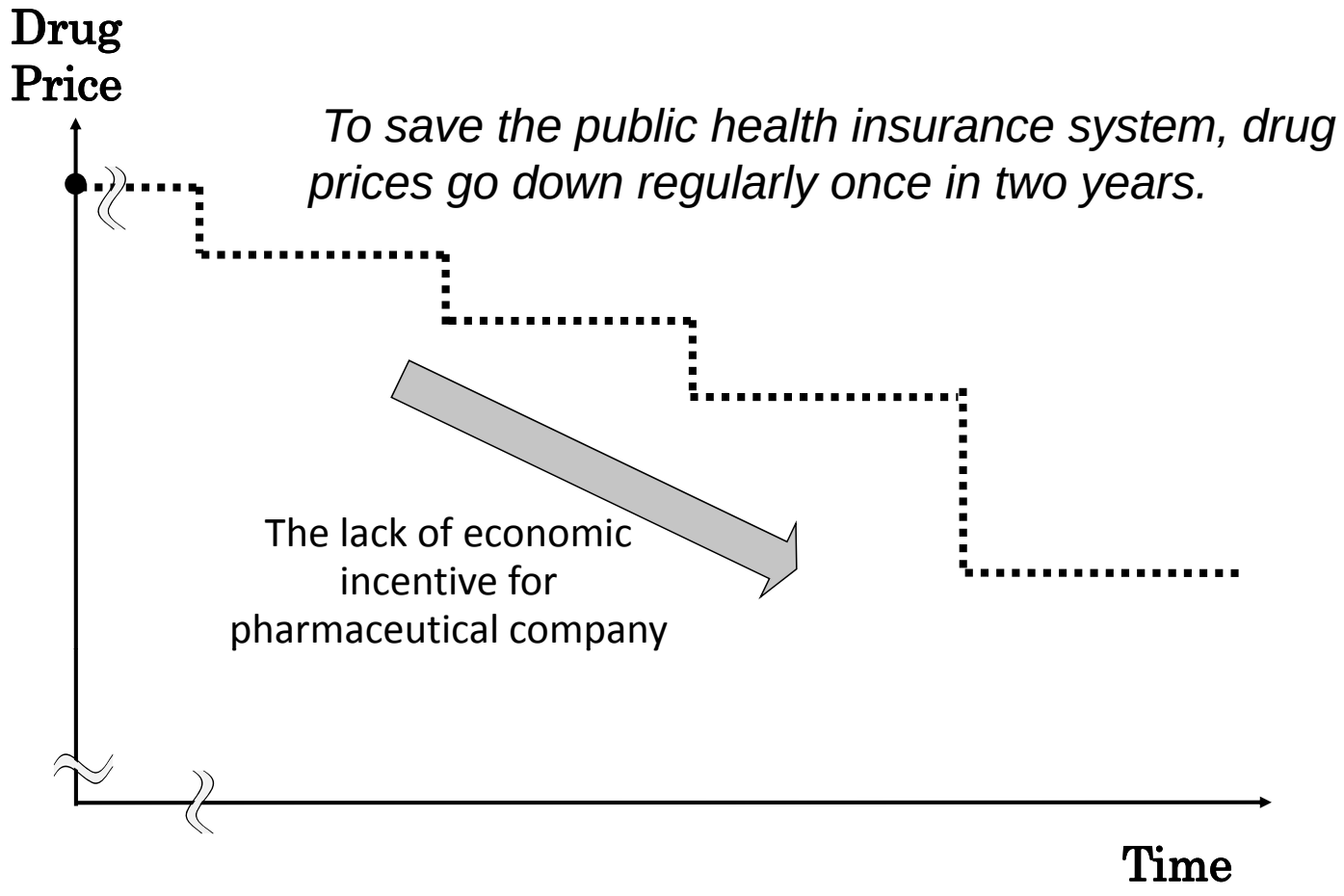
Health Care Insurance in Japan

- Public health Insurance coverage is the right of every citizen.

- All citizens have the right of free access to medical institutions authorized to treat patients with health insurance coverage.

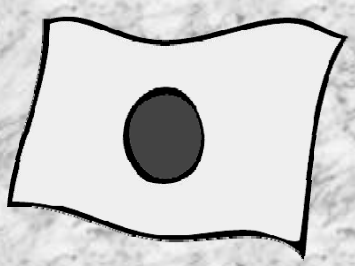
Health Insurance Law ⇨ **New diagnostic technique or treatment shall be required evidence to be covered by public health insurance.**

Pharmaceutical Affairs Law ⇨ **Pharmaceutical companies shall not market investigational new or off-label drugs and devices because of the lack of evidence.**



The bright and dark sides of Clinical Trials

World's 3rd strongest of Japanese R & D ability
Contribution through ICH activity



Drug/Device Lag
Slump of Clinical Research
Hollowing out of Clinical Trial

Patients wish to be treated with advanced medical care using investigational new drugs/devices or off-label drugs/devices

(1) Regulations of Clinical Trials in Japan

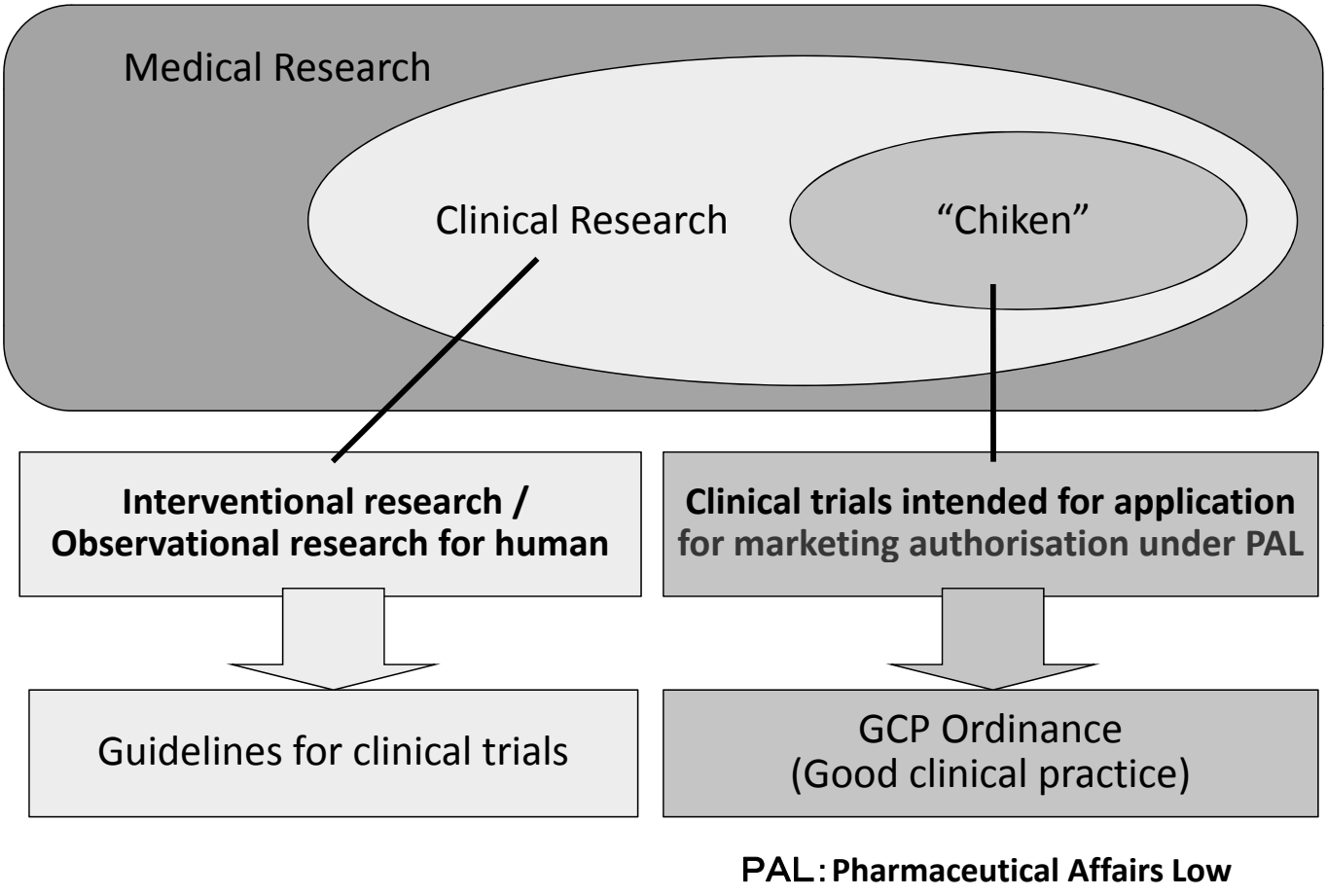
(2) New 5-Years Clinical Trial Activation Plan

(3) Promotion of Global Development and Clinical Trials

(4) Models of collaboration with industry to promote life innovation

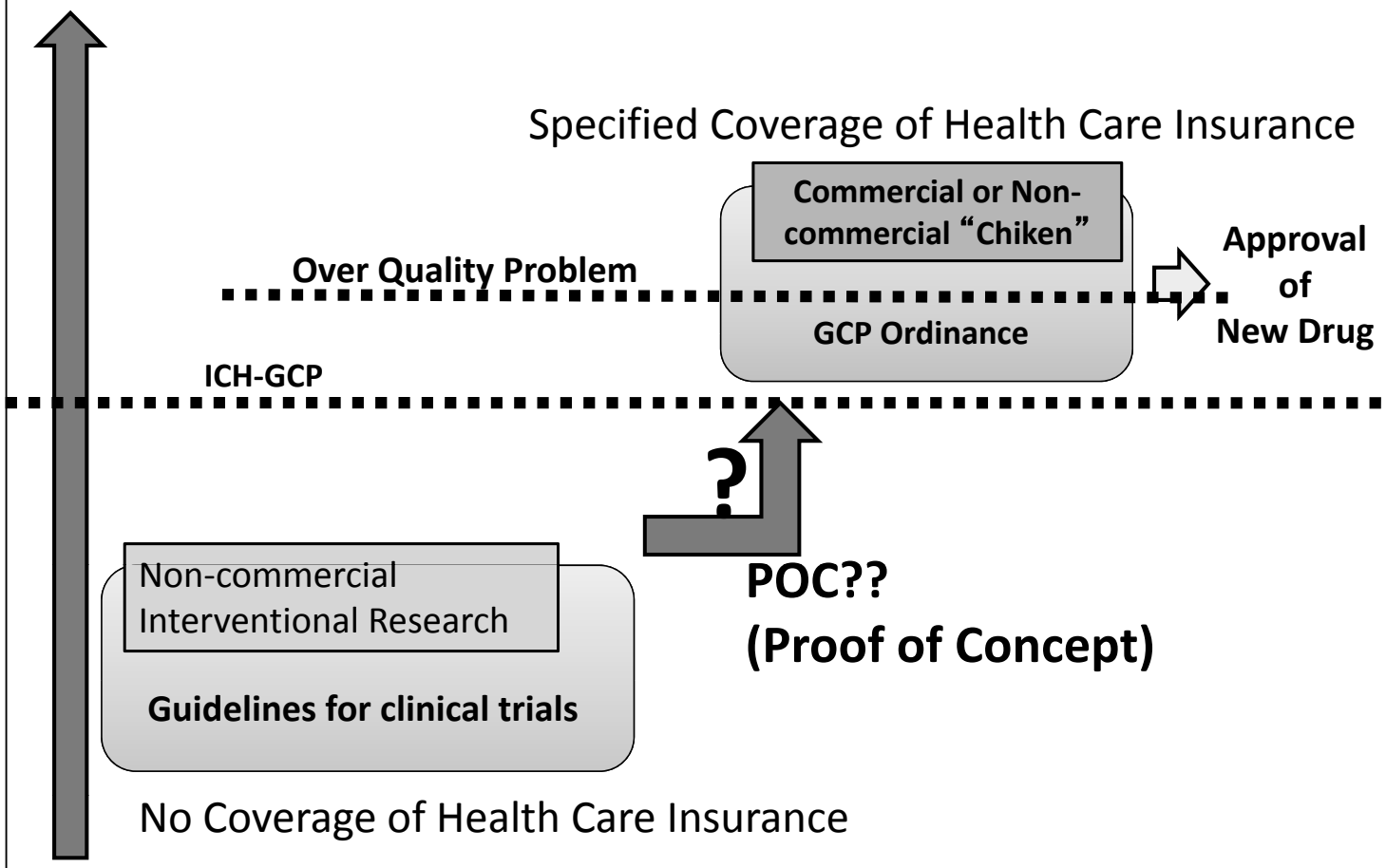
(5) Education and Knowledge Transfer

Regulations of Clinical Trials in Japan (summary)



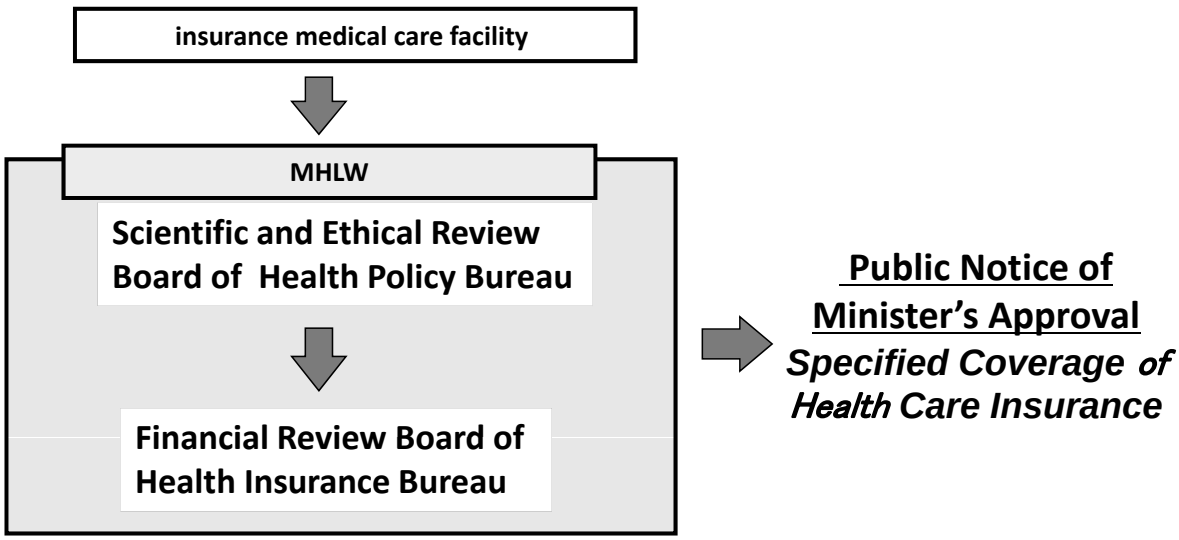
PAL: Pharmaceutical Affairs Low

Flowchart of Approval of New Drug

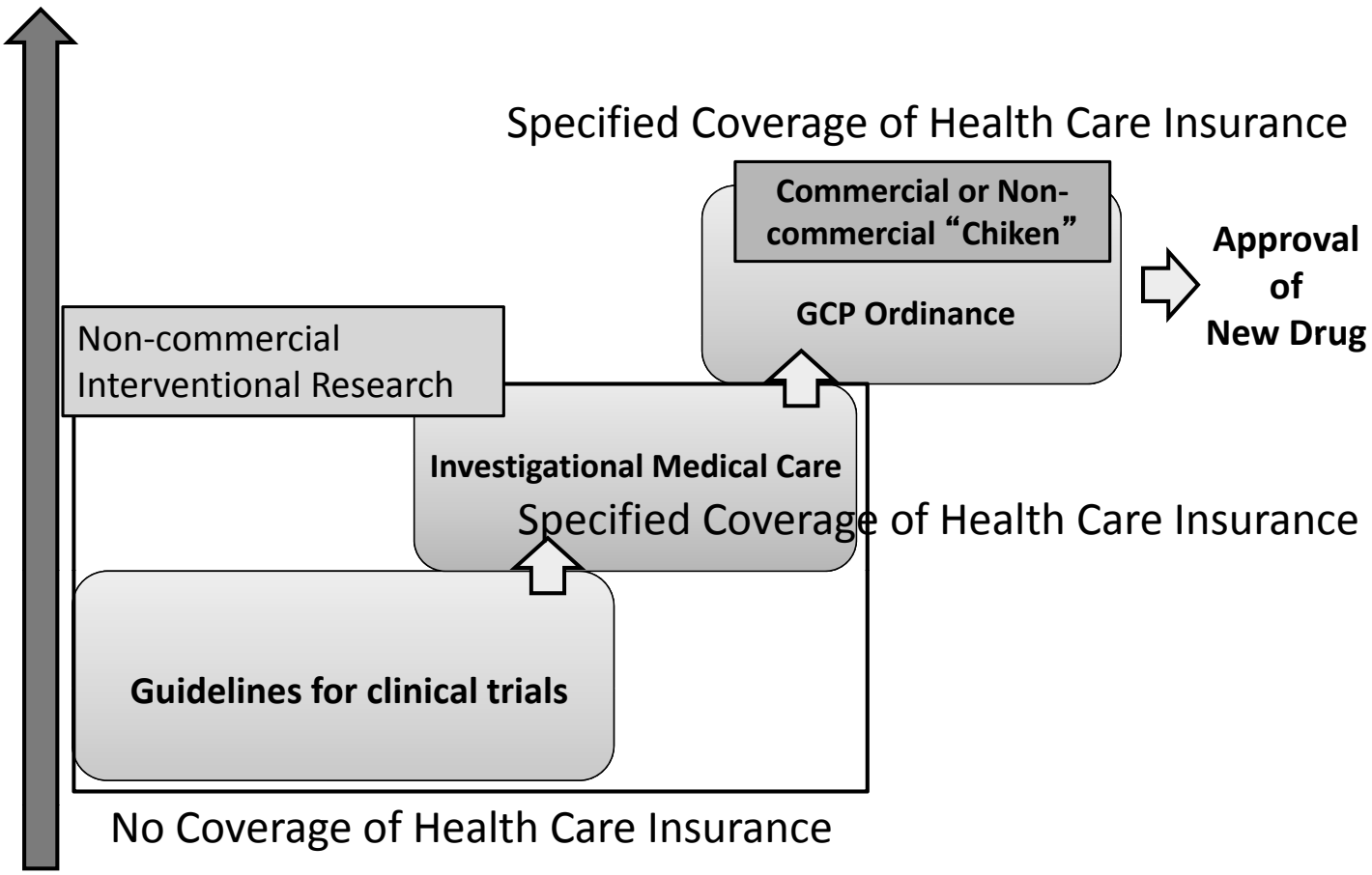


Evaluation System of Investigational Medical Care(2008～)

Evaluation System of interventional research using investigational new or off-label drugs and devices prior to final PMDA/MHLW approval under Specified Coverage of Health Care Insurance



Flowchart of Approval of Investigational Medical Care



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New 5-Years Clinical Trial Activation Plan

MEXT / MHLW
March 2007

（1） Clinical Study Infrastructure Building

- 10 core clinical research centers that are able to plan and manage multi-center trials
- 30 major clinical trial institutions that are able to perform trials smoothly

（2） Human Resource Development for Clinical Research

- Training provision for MDs, CRCs, Bio-statisticians, Data managers, etc.

（3） Public Promotion of Clinical Trial and Encouraging Participation

- Improve patient volunteers' ease to participate in trials
- Improve patient's incentive to participate in trials

（4）Efficient Clinical Research Management and Sponsors' Ease

- Harmonize administrative document formats
- Streamline administrative work share between hospitals and sponsors
- Improve transparency of hospitals' research capacity

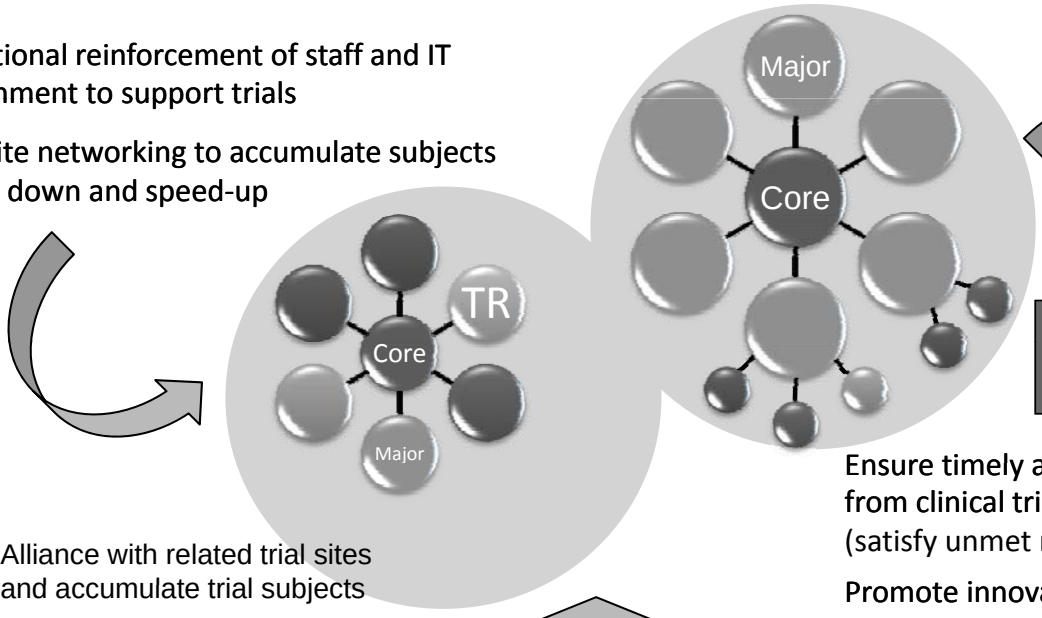
（5） Others

- Review GCP Ordinance and Clinical Research Guideline for international harmonization and patient protection

Network of clinical research centers

Institutional reinforcement of staff and IT environment to support trials

Build site networking to accumulate subjects
→ cost down and speed-up



Alliance with related trial sites and accumulate trial subjects

Expedite trial performance

Ensure timely access to new drug from clinical trial stage (satisfy unmet needs)

Promote innovation of new drug

10 Core clinical research centers

Total 1,000M¥ / year (approx. 10M$ / year)

- ○ Train human resources in-house and in the institutions in the net work
- ○ Strengthen IRB capacity
- ○ Consolidate data management system
- ○ Plan, Do, Assess clinical research

Infrastructure improvement

30 Major clinical trial institutions

Total 750M¥ / year (approx. 7.5M$ / year)

- ○ Secure Recruiting CRCs and other trial supporting staff
- ○ Support promotion of common IT plat home

Nation-wide network of TR/clinical trial centers

COE is able to plan and manage multi-center trials (MHLW)

CTC is a core center to smoothly perform trials (MHLW)

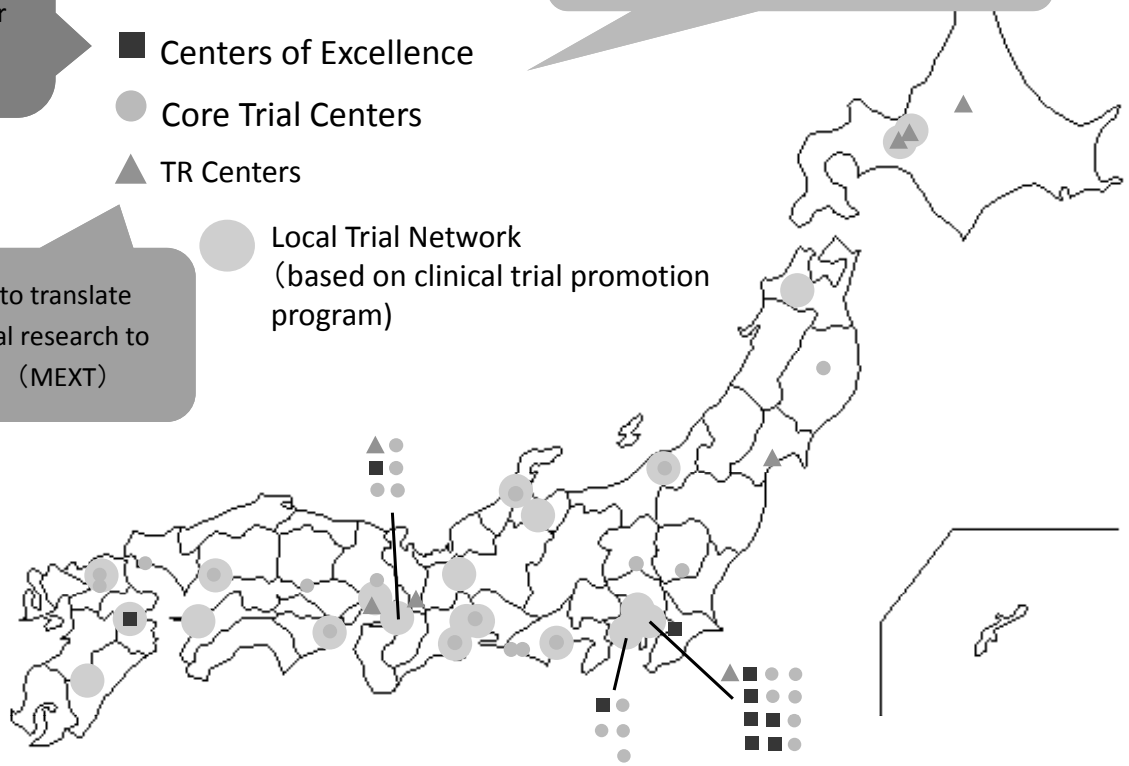
■ Centers of Excellence

● Core Trial Centers

▲ TR Centers

● Local Trial Network
（based on clinical trial promotion program)

TR center is to translate basic medical research to clinical trial （MEXT）



Midterm Review of the 5-years Plan

① Improve **cost, speed and quality** of clinical trials

② Improve **number of global MCTs**

③ Secure provision of high quality innovative medicine and **enable patient to enroll a trial safely**

"*MIERUKA*" of the final goal

(identifying problems and bringing them to the foreground)

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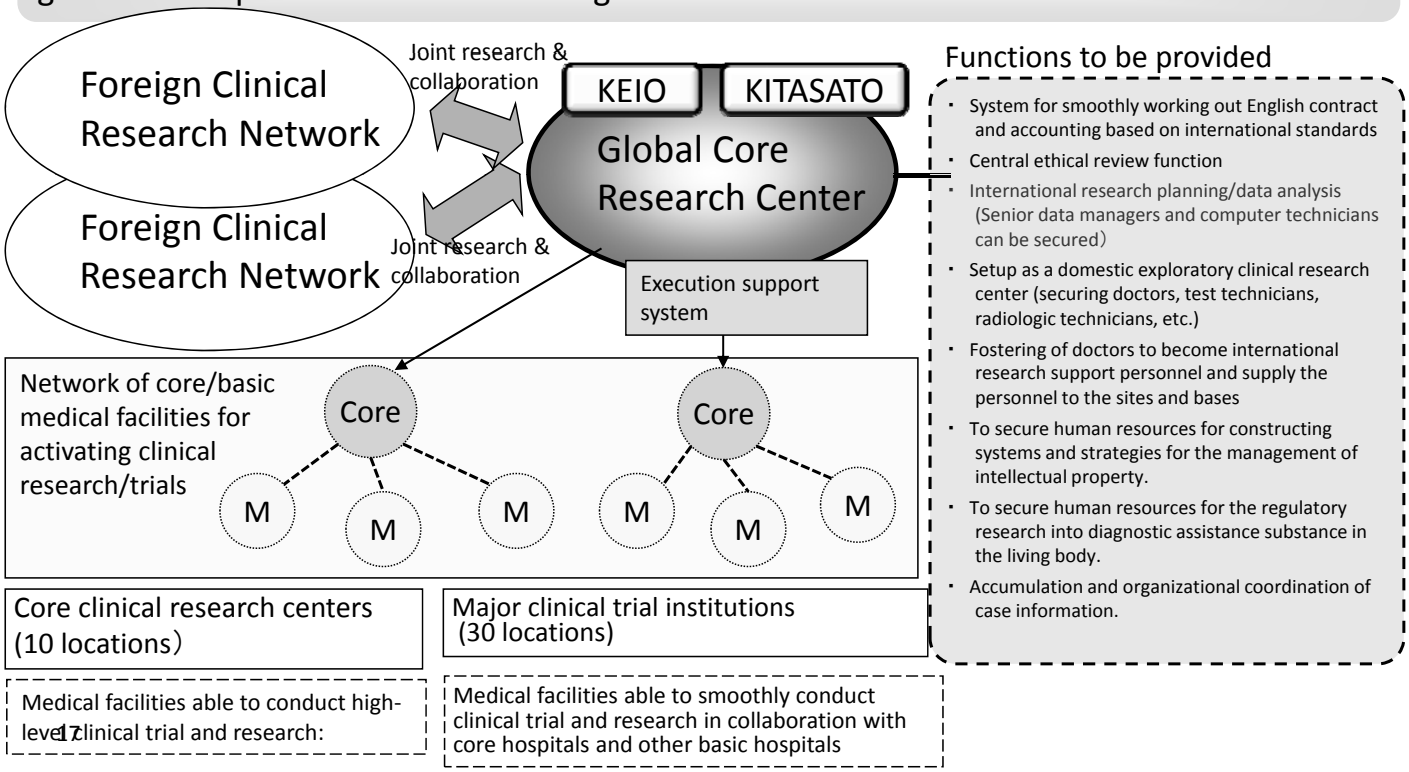
Global Core Research Center for Clinical Trial

Work begins in 2009 with budget of ¥400 million

Goal: Reinforcement of clinical trial institution in Japan and promotion of simultaneous global development of innovative drugs



Functions to be provided

- System for smoothly working out English contract and accounting based on international standards
- Central ethical review function
- International research planning/data analysis (Senior data managers and computer technicians can be secured)
- Setup as a domestic exploratory clinical research center (securing doctors, test technicians, radiologic technicians, etc.)
- Fostering of doctors to become international research support personnel and supply the personnel to the sites and bases
- To secure human resources for constructing systems and strategies for the management of intellectual property.
- To secure human resources for the regulatory research into diagnostic assistance substance in the living body.
- Accumulation and organizational coordination of case information.

(1) Regulations of Clinical Trials in Japan

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Tools for self-learning & in-hospital training

- Educational program developed in the clinical research infrastructure project (Health science research grant)
- E-learning system developed by JMA Center for Clinical Trials, etc.

Educational Program for CRCs, Data managers, and IRB members

Object	When	Contents
CRCs (basic)	Lecture in Sep. + Practical Training from Oct. (Tokyo) (59 students took the course)	Pharmaceutical affairs law, Basic knowledge on clinical trials, Informed consent, etc.
Local Data Managers	2 days course: add on the CRCs' basic course (Tokyo) (39 students took the course)	Function, Practice, Basic knowledge of biostatistics, Management tools (incl. practical training), etc.
CRCs (advanced)	2 days course ×2 cities (Tokyo, Osaka) (November and January) (89 students took the course)	Latest GCP regulation, Multinational trials, Investigator initiated trials Education etc. (incl. group discussion)
IRB members	1 day course: (Tokyo) (77 IRB-members took the course)	Board member's function, Review points, A Mock IRB, etc.

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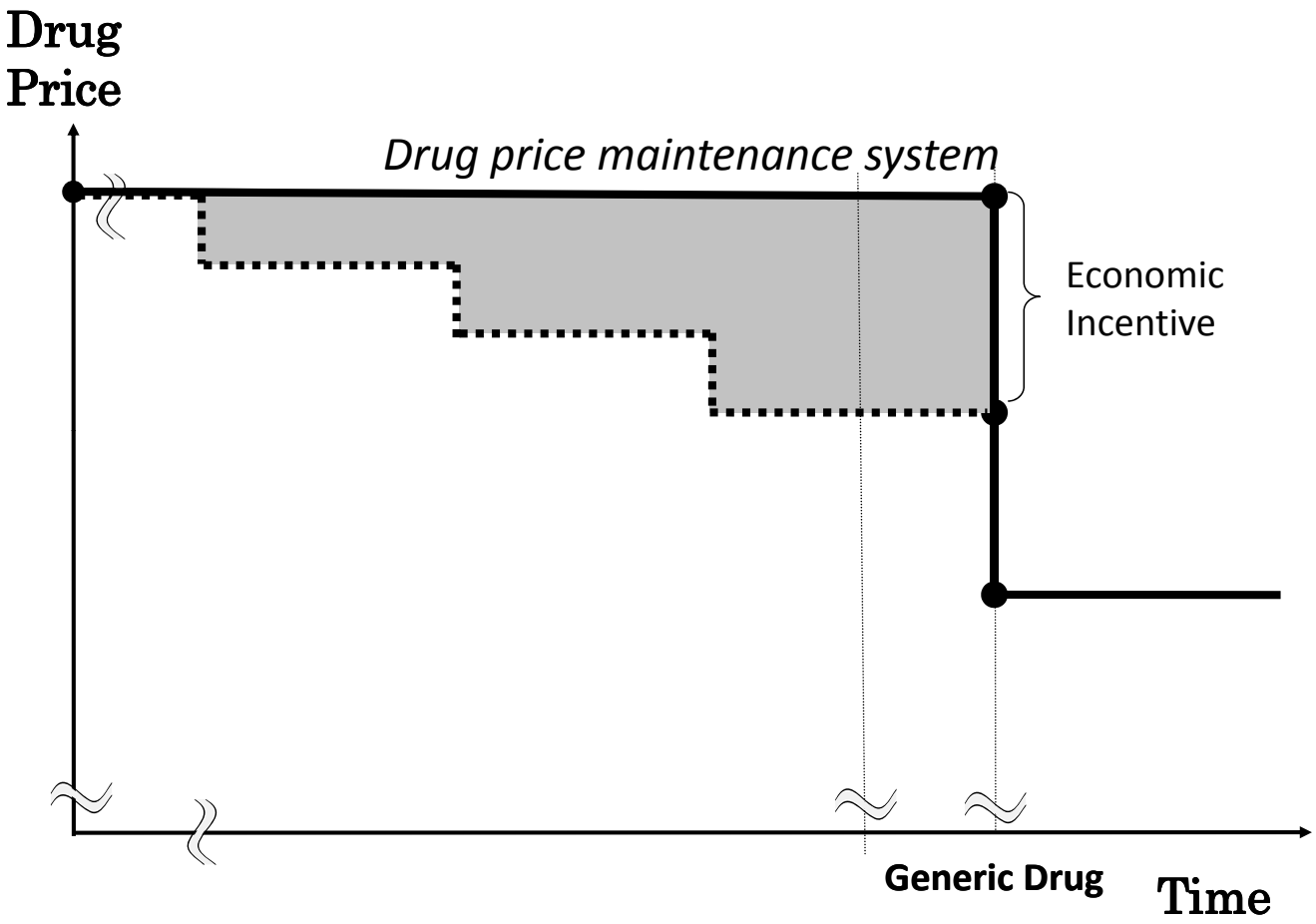
Patented Drug Price Maintenance System

- *Drug price maintenance system has been started to encourage the development of new drugs or the elimination of off-label use and address unmet medical needs from April, 2010.*

- *Drug price maintenance system is applied to drugs which are decided by scientific review board based on expert knowledge by academia.*

⇨ **MHLW requested pharmaceutical companies to develop 108 drugs. (May, 2010)**



All the players in good harmony!

" All for the welfare of patients!"

Challenges and Initiatives of PMDA

Tatsuya Kondo, M.D. ,Ph.D.

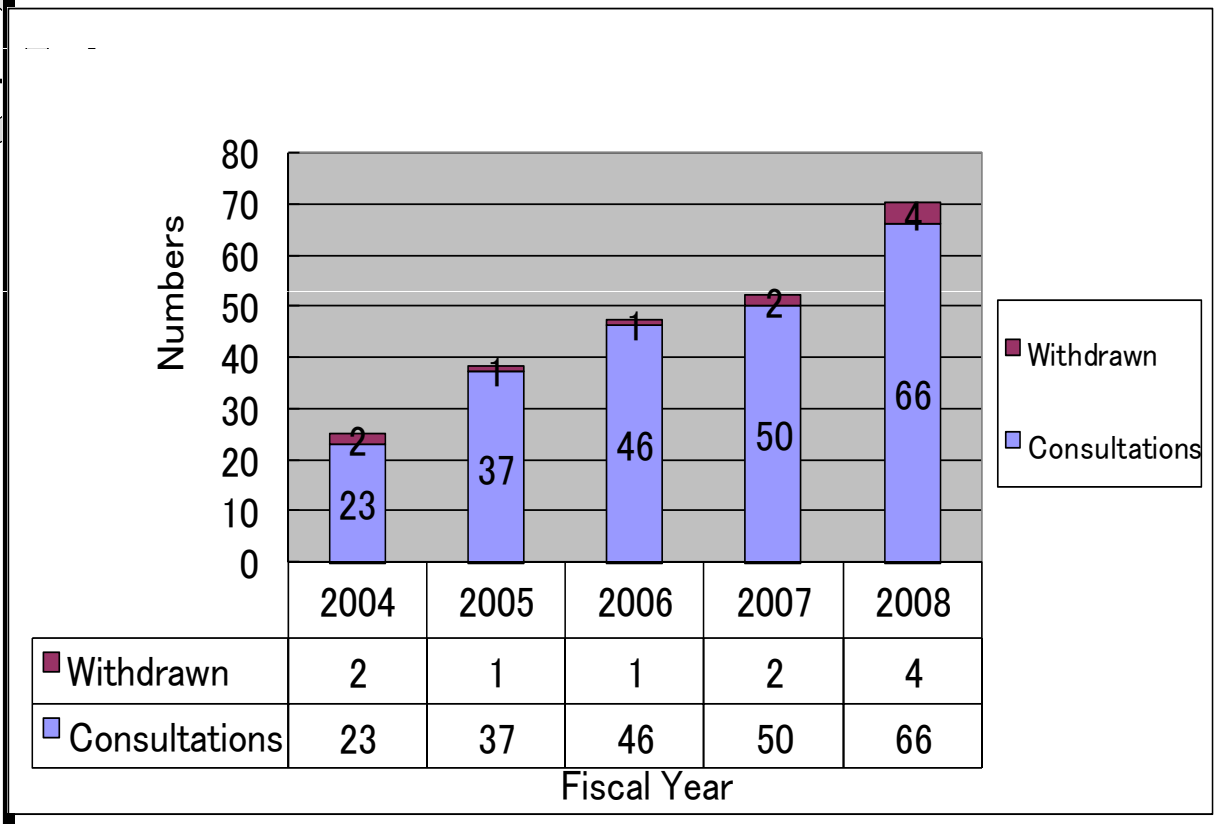
Chief Executive,

Pharmaceuticals and Medical Devices Agency

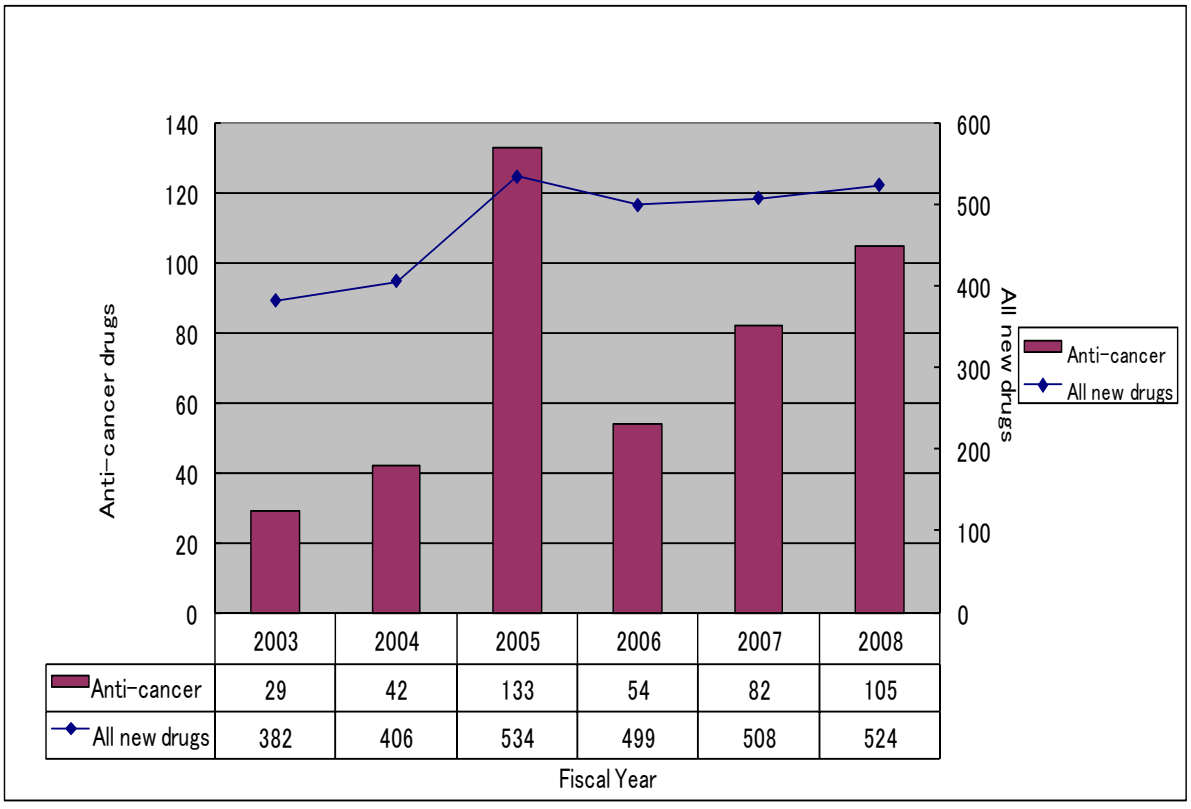
Outline

1. Current situation of anti-cancer drug development
2. PMDA initiatives on Global drug clinical trials
3. Future directions of PMDA
   - Improvement of “Regulatory Science”
   - Building of collaborative relations among International community
4. Conclusion

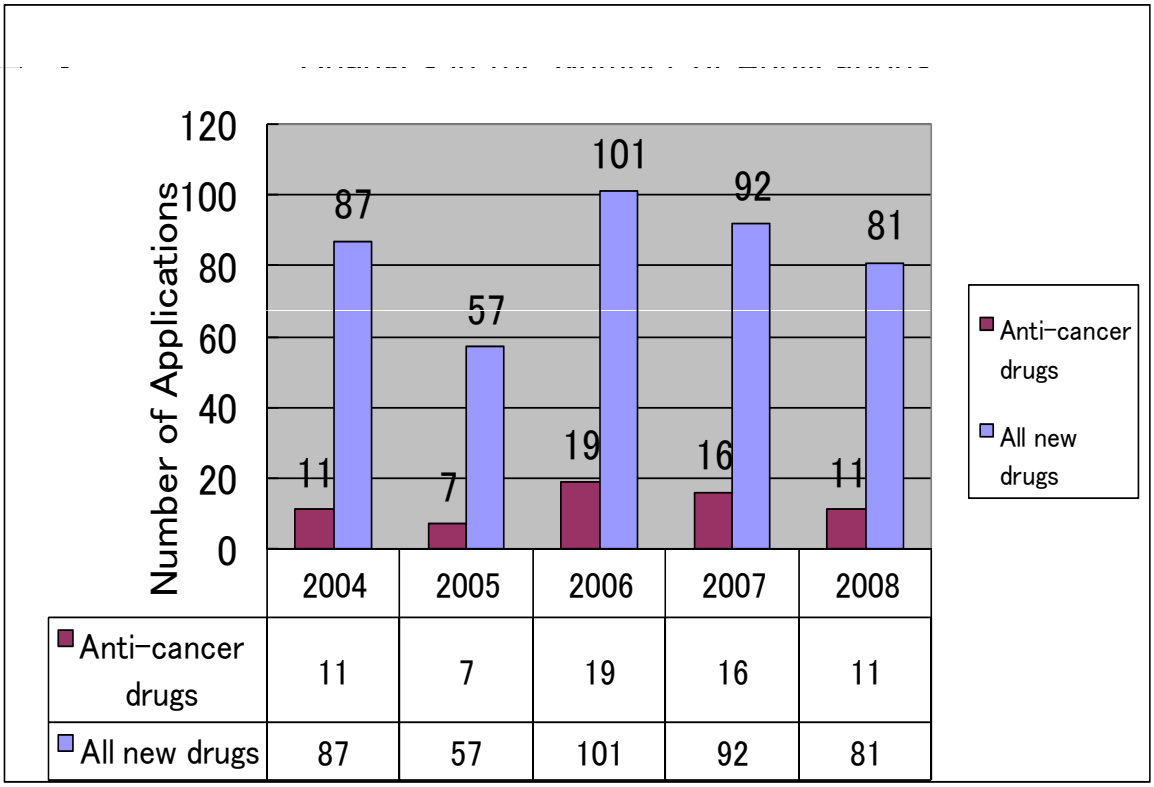
Consultations on Clinical Trial for anti-cancer drugs



Number of Notified Clinical trials for Anti-cancer drugs



Application Numbers for Anti-cancer drugs



	2004	2005	2006	2007	2008
Anti-cancer drugs	11	7	19	16	11
All new drugs	87	57	101	92	81

Fiscal Year

PMDA initiatives for promoting Global Development

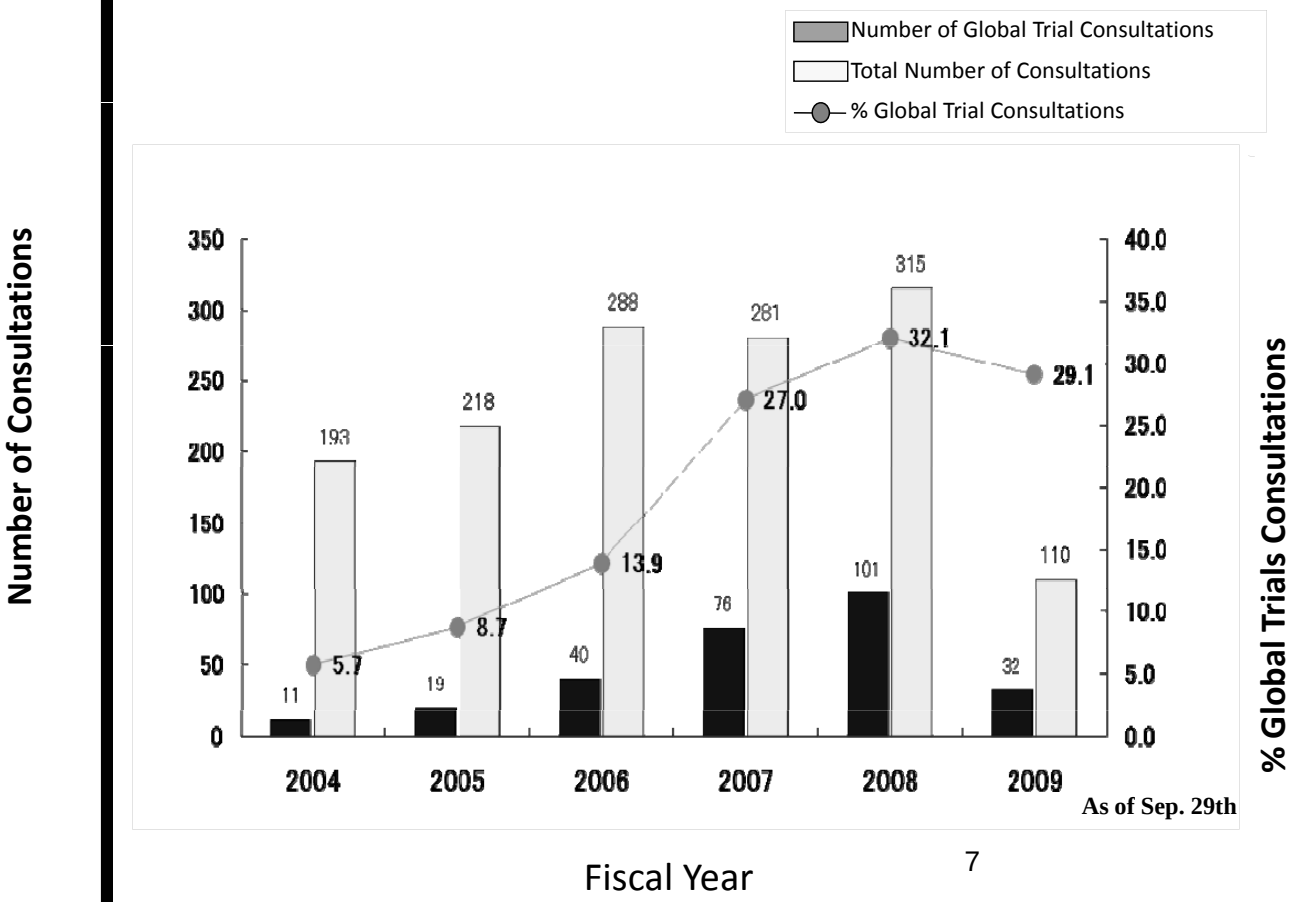
- **"Basic Principles on Global Clinical Trials "** Published on September 28th, 2007

English: http://www.pmda.go.jp/operations/notice/2007/file/0928010-e.pdf

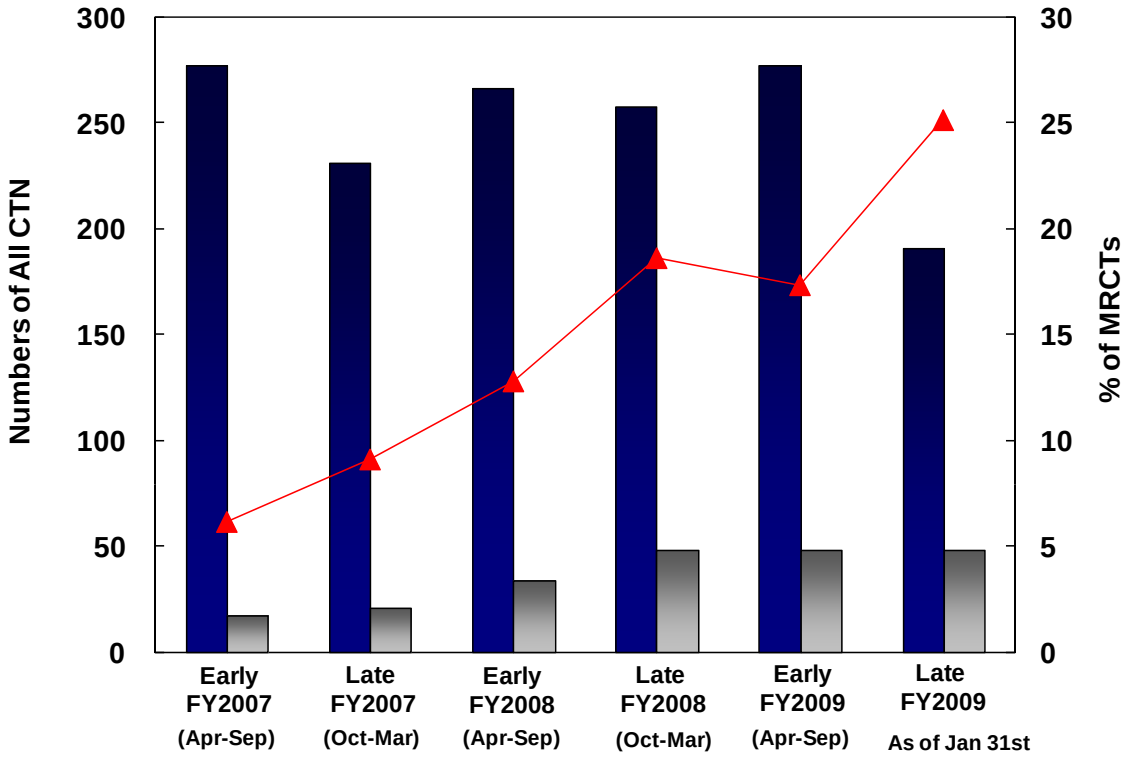
- **" Points to Be Considered by the Review Staff Involved in the Evaluation Process of New Drug"** Published on April 17th, 2008

English: http://www.pmda.go.jp/english/service/pdf/points.pdf

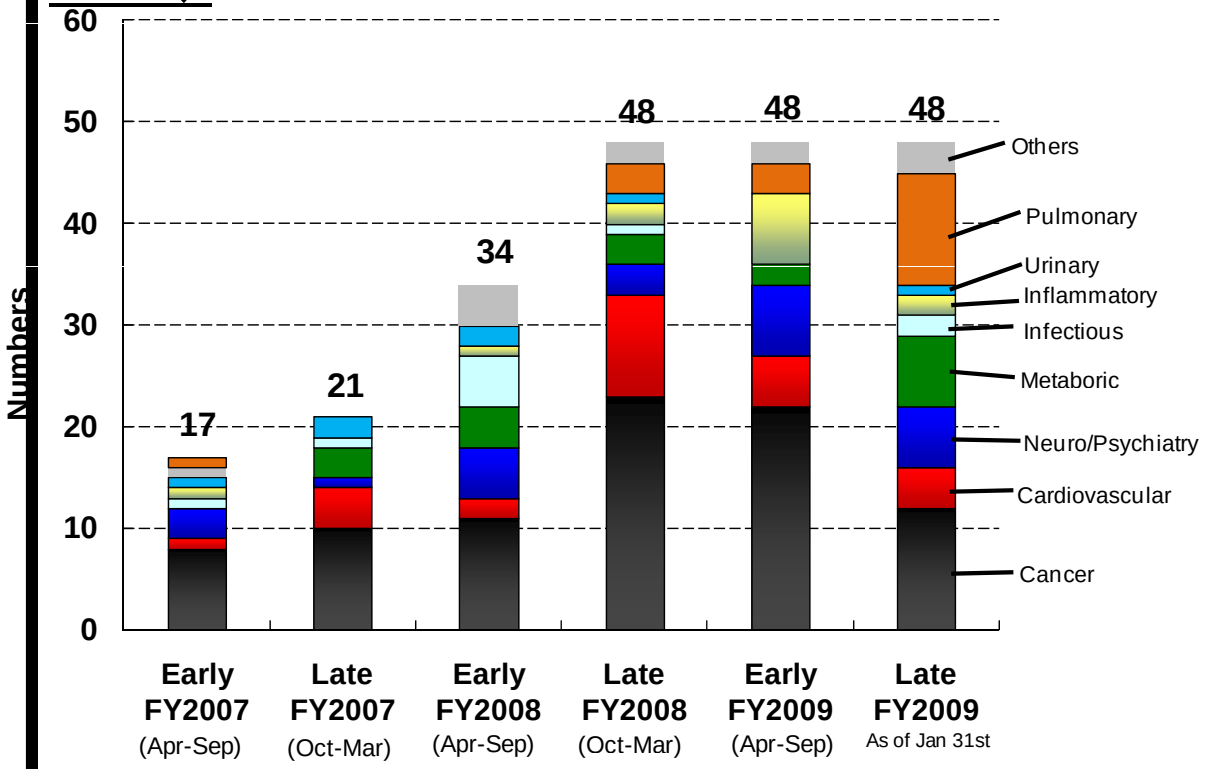
Global Clinical Trial Consultations



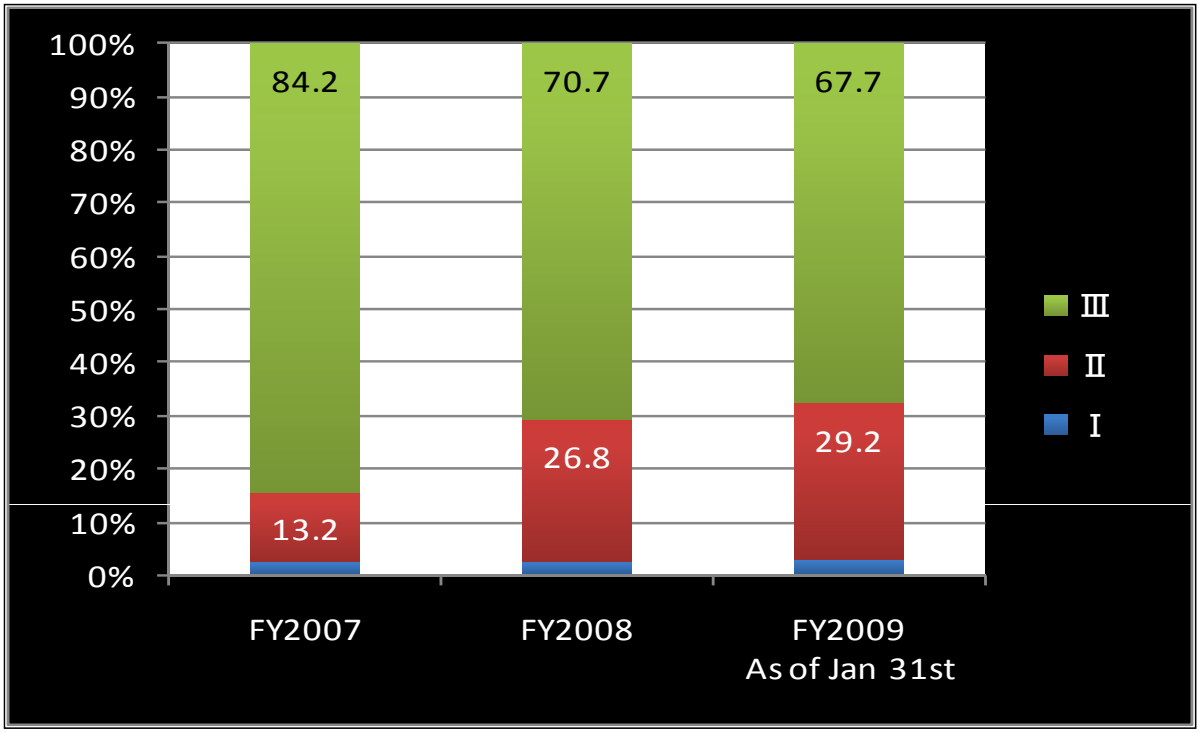
Trends in Global Clinical Trials including Japan (Percentage)



Trends in Global Clinical Trials including Japan (Target Therapeutic Area)



Trends in Global Clinical Trials including Japan (Trial Stage)

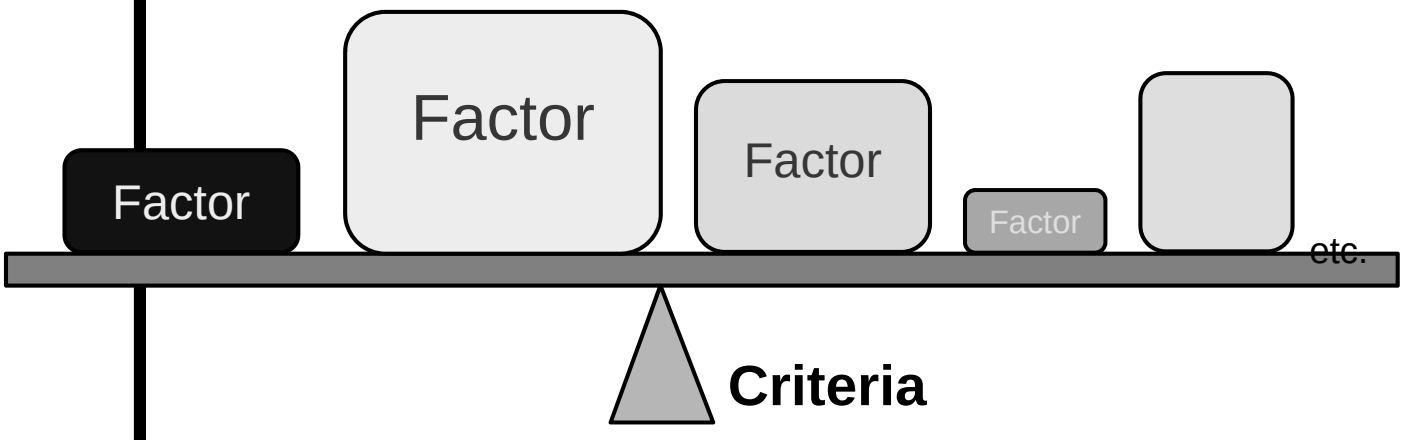


Summary of Current Situations of Global Clinical Trials in Japan

- Rapid advance: Japan has markedly increased its experience of conducting Global Clinical Trials (GCTs) since FY2007
- Almost all Therapeutic Areas are now a target for GCTs
- GCTs were mainly conducted at confirmatory stage (Phase III) in FY2007, but the phase of GCTs has shifted to an earlier stage (Phase II)

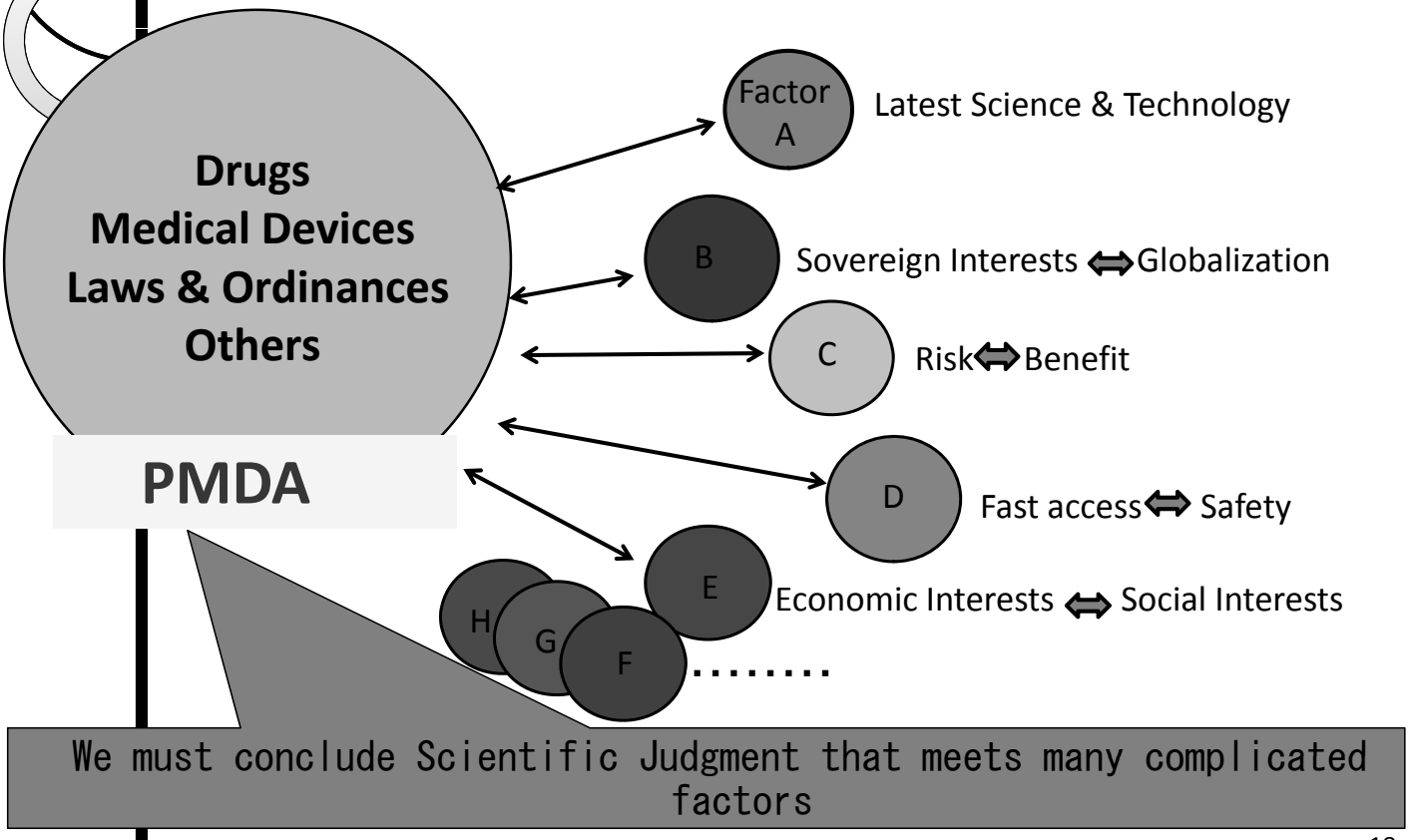
Challenge (1)

Develop comprehensive & robust disciplines in the field of "Regulatory Science"



In response to social demands,
we take balanced judgments ⇒ toward a more desirable form of society

Regulatory Science:



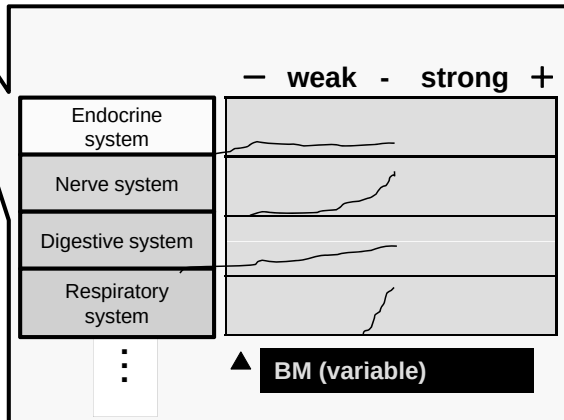
Regulatory Science ~for pharmaceuticals~

Evaluate the scientific data to determine whether an drug is "safe and effective for its intended use "

【drugs 】
- Therapeutic area and effect-efficacy
- Dosing period
- Used as the sole regimen / co-prescribing of several drugs
- GLP, GCP, GMP

【medical user of drugs（Doctors, hospital）】
- Highly specialized hospital（w or w/o medical specialist ）
- Special hospital（ w or w/o medical specialist ）
- General hospital
- Specialized clinic （ w or w/o medical specialist ）
- General clinic

【patients】
- Individual deference in Genome
- Diagnosis （single / multiple）
- severity
- Dosage ／administration route／duration of administration etc.



Therapeutic benefit vs Adverse events

PMDA's Role on Regulatory Science

Academic Science

Collaborative Graduate Studies Program

University

Research
Education

Regulatory Science

PMDA

Services
Research
Education

Regulatory Science

MHLW

Administration
Research
Education

Collaborative Graduate studies Program

Regulatory Science based approach

Clinical Research
(Medical Law)
Ethical Committee

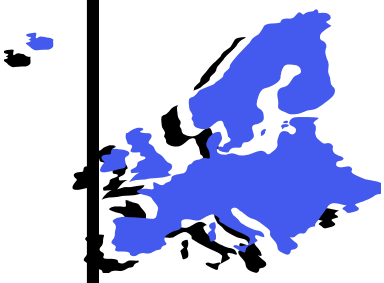
Clinical Trials
(Pharmaceutical Affairs Law)
I R B

Clinical practices
Research
Education

Hospital

Industry

Challenge (2) :
Building of collaborative relations



EC/EMA

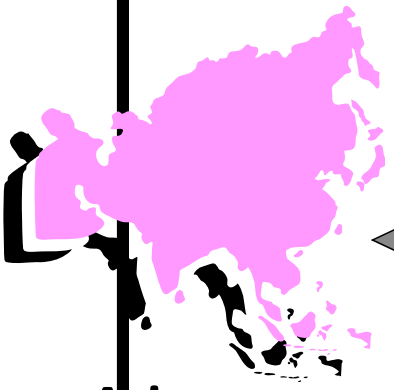
ICH, GHTF
Bilateral meeting

US/FDA

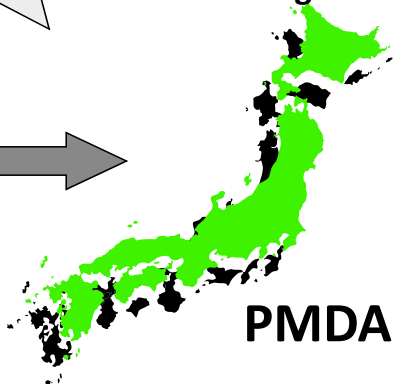
HBD

Other Main Countries :
Canada / Australia

International Organizations :
WHO,OECD



Asia



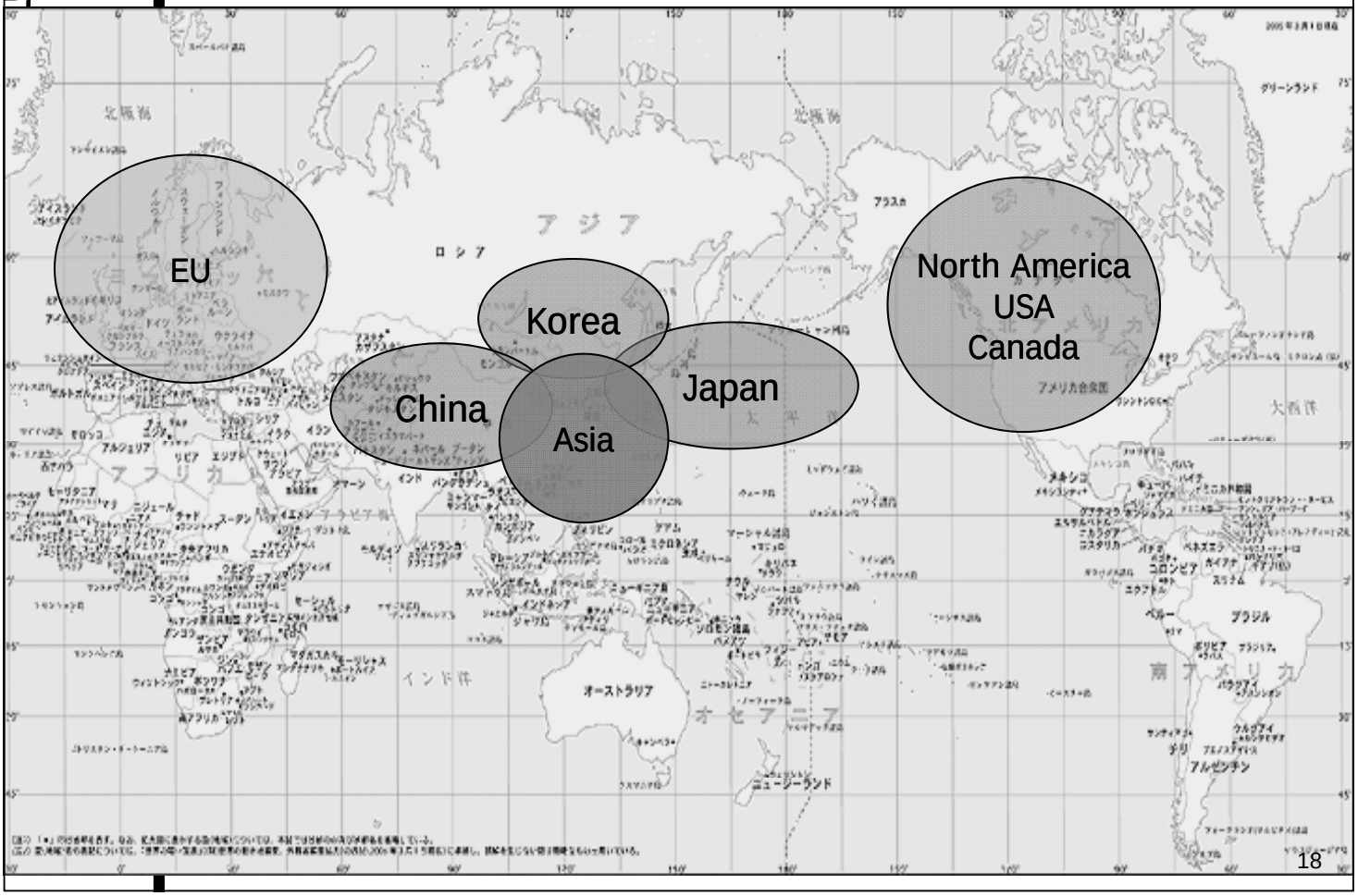
PMDA /MHLW

We must work in accordance with International standards

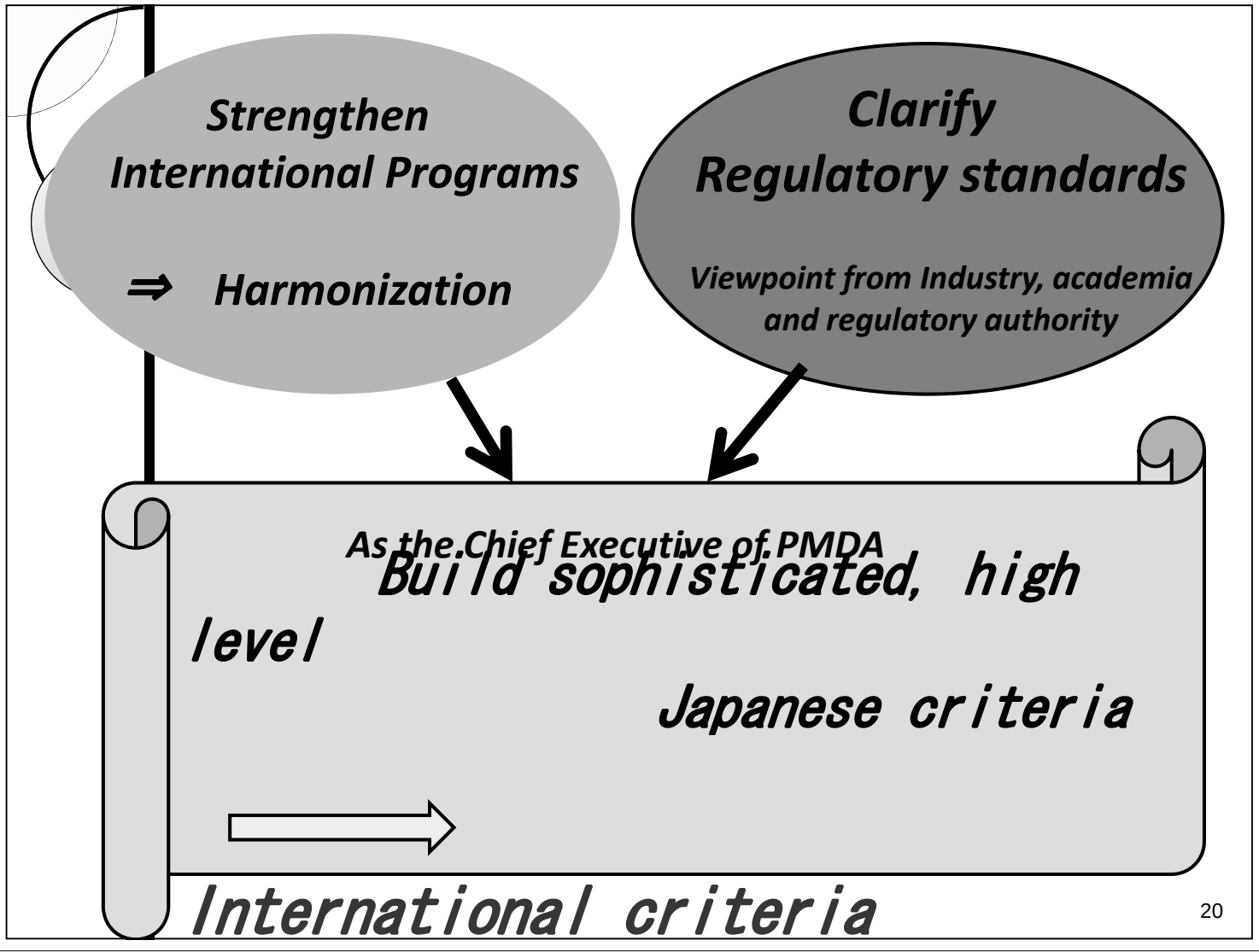
- Bilateral and executive-level talks with US FDA, EC/EMA on a regular basis
- Dispatch manager-level resident officer to Washington DC and London for a long term
- Information sharing based on confidentiality agreements

International standards
= Based on "Regulatory Science"

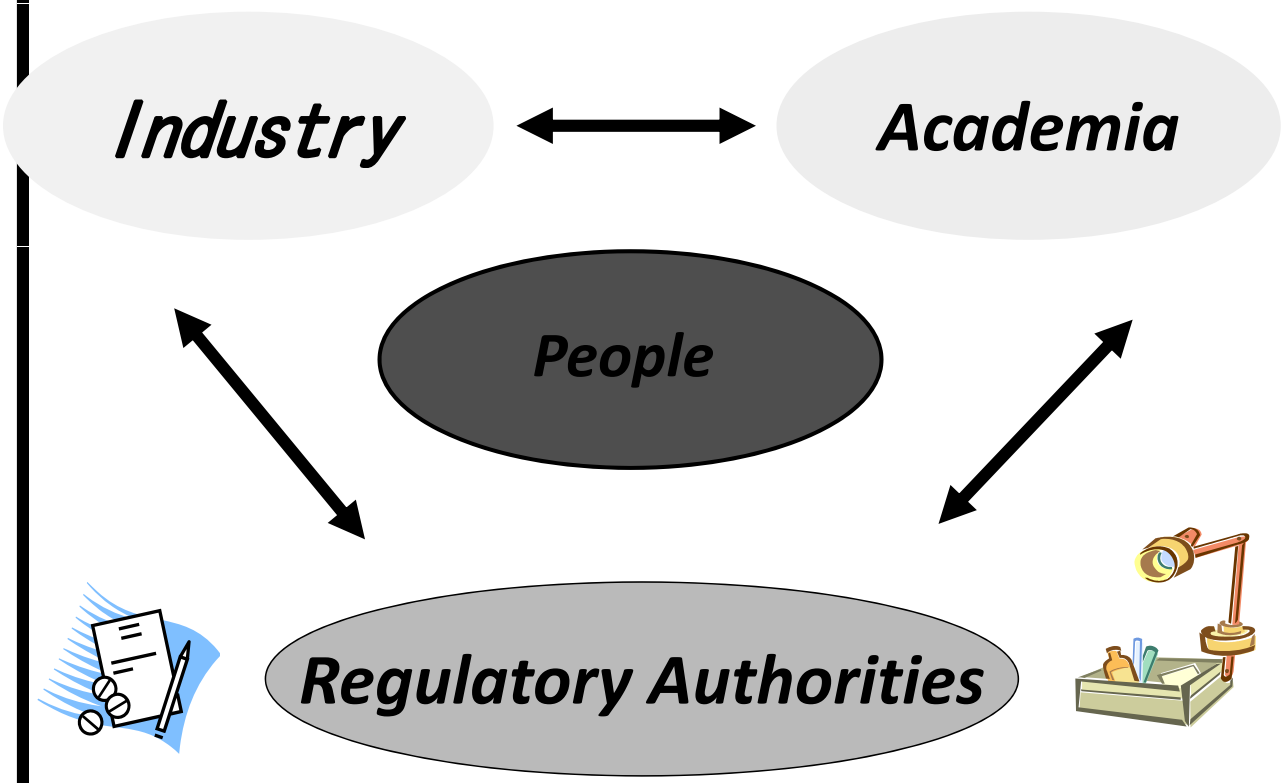
Innovative Drugs from Asia to the world



As the Chief Executive of PMDA,



Work together in a responsible manner based on “Regulatory Science”



Thank you for your attention!

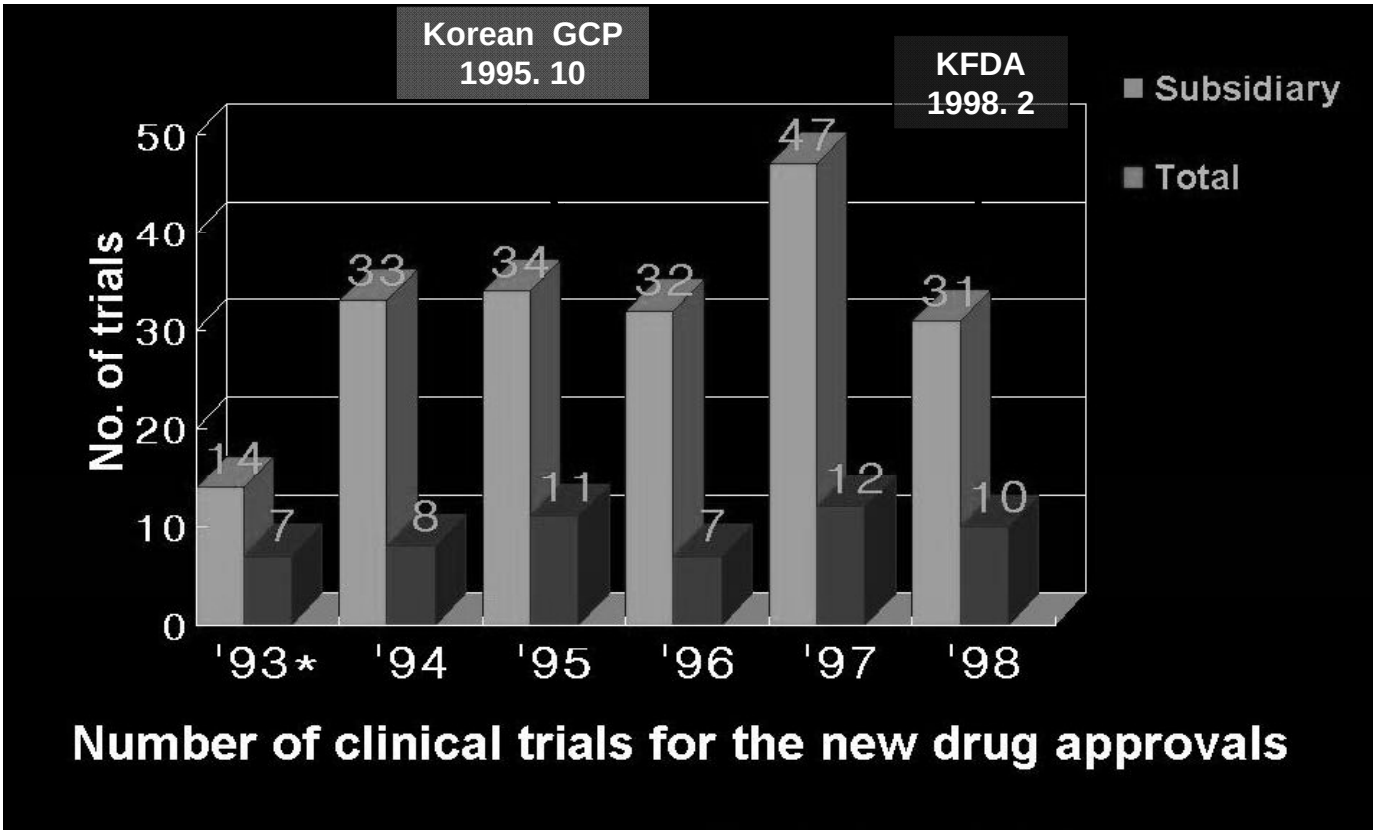
Pharmaceuticals and Medical Devices Agency

Clinical Trials in Korea

Yung-Jue Bang, M.D., Ph.D.

Vice-President, Korea National Enterprise for Clinical Trials
Director, Clinical Trials Center,
Professor, Division of Medical Oncology,
Seoul National University Hospital

Clinical trials for registration before 2000



Driving forces for changes

❖ 1998 – 2000 : Comprehensive discussions among regulatory authorities, industry and academia

- KFDA - successful progress of ICH meetings
- Domestic pharma companies - new agents to be tested
- Foreign pharma companies - new drugs to be launched
- Academia - highly motivated clinical investigators

❖ 2000 : Bench-marking visit of Australia

Major regulatory changes in early 2000s

- **KGCP revision, as of January 4, 2000**
  - Harmonize with ICH guideline E6
  - Clarify the responsibility of investigators and the function of IRB
- **Adoption of the Bridging concept (E5) in 2001**
  - Diverse bridging strategies were permitted
- **Separation of IND from combined IND/NDA in 2002**

National Technology Roadmap Project* for clinical trial technology

- Experts Working Group recommend globalization of clinical trials.
  - Establishing ‘Centers of Excellence’
  - Developing educational/training programs for clinical trial professionals
  - International accreditation of IRBs
  - Regulatory reforms

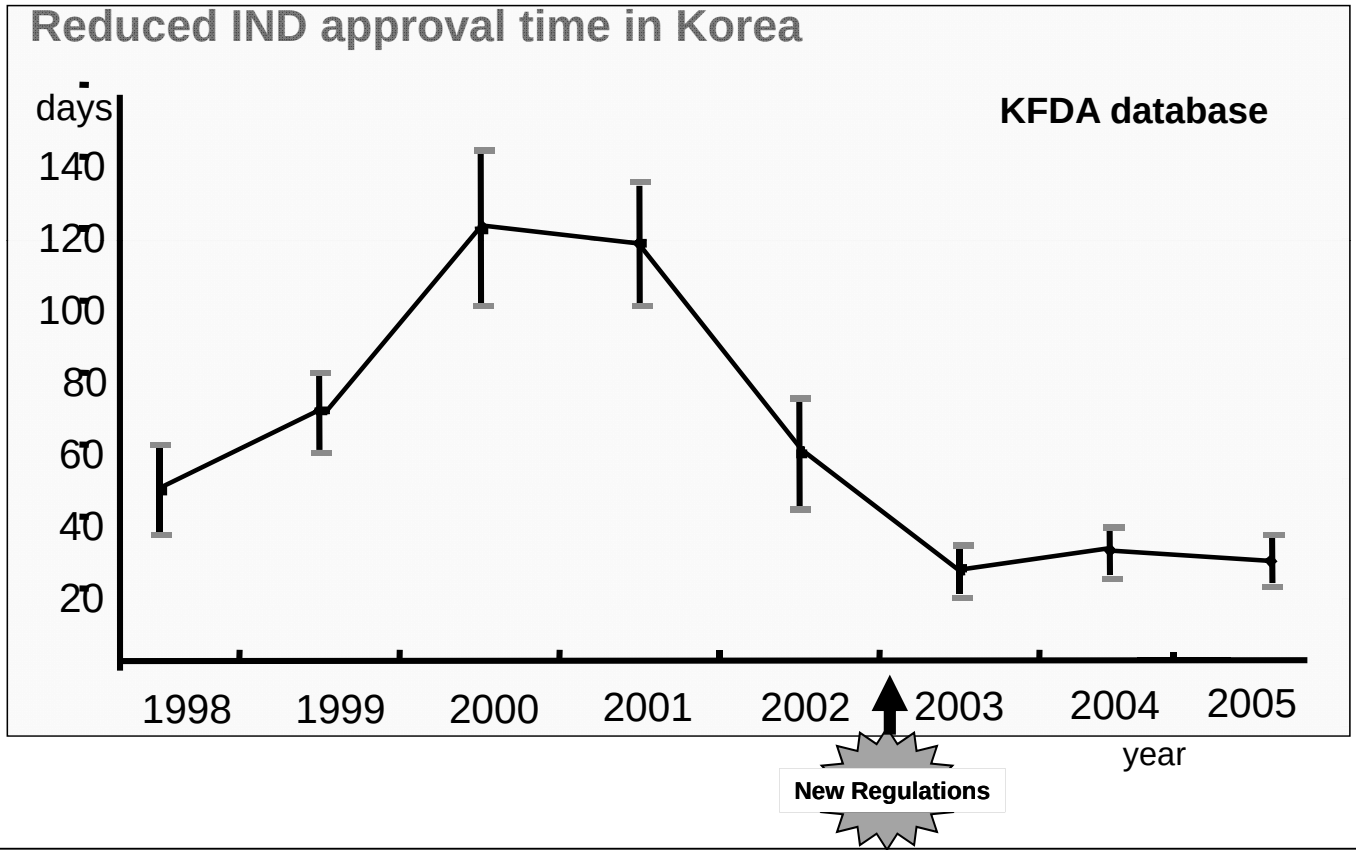
* by MOST & MOHW, in 2002

Upgrading IRBs

- Korean Association of IRB (KAIRB) in 2002
  - Non-profit organization with more than 50 IRBs
  - IRB operation guidelines, SOP
  - Education of IRB professionals
  - In 2007, endorsement from MOHW for training of IRB professionals
- International accreditation of IRBs
  - Samsung Medical Center in 2006*
  - Seoul National University Hospital, Asan Medical Center in 2006^
  - Inje University Busan Hospital, Seoul St. Maria Hospital, Chonnam University Hospital in 2007^
  - 14 IRBs as of 2009

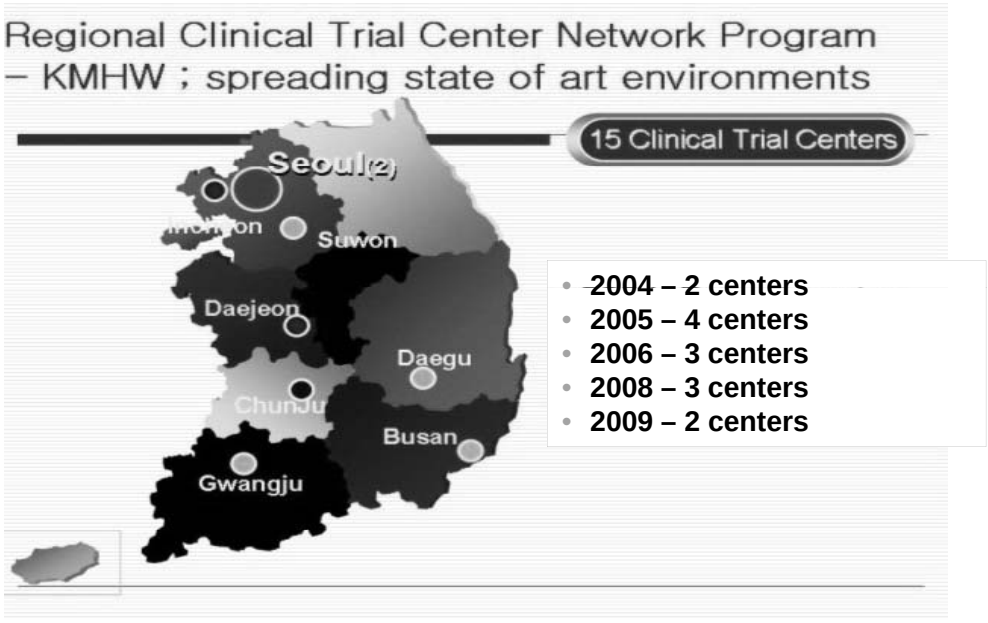
* By AAHRPP, ^ by SIDCER/FERCAP

KFDA: Streamlining of IND review system



Regional Clinical Center by MOHW

- Similar to US NIH-GCRC supporting program
- 14 centers of excellence (2004-2009)



Clinical Trials Center, SNUH

- Established on June 15, 1997
- Designated as Regional Clinical Trials Center by MOHW in 2004
- Renovation in 2007

Clinical Trials Center, SNUH

Core lab.: sample processing/storage

Outpatient clinic: 7+1 units

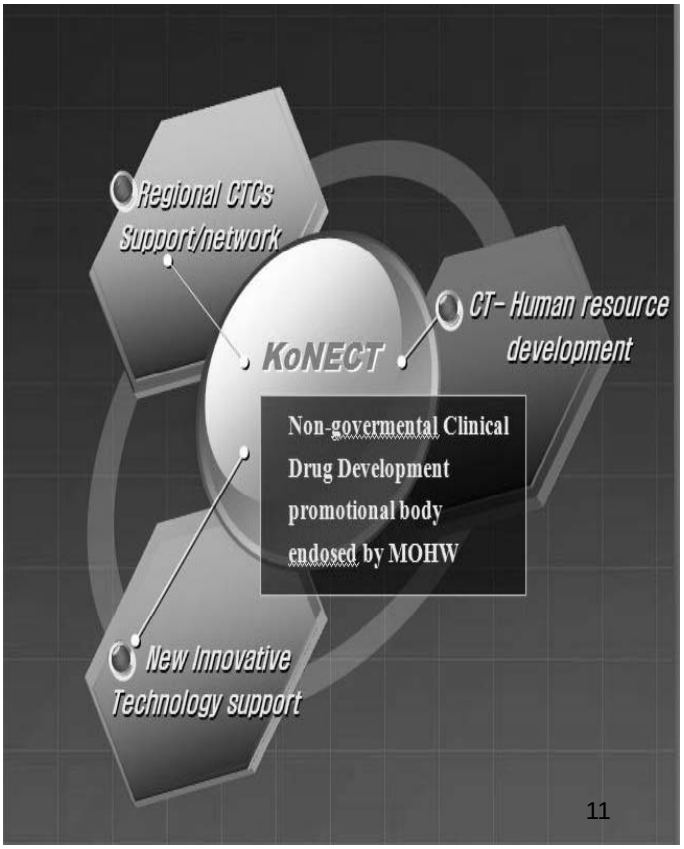
Research ward: 46 trial beds

Pharmacy

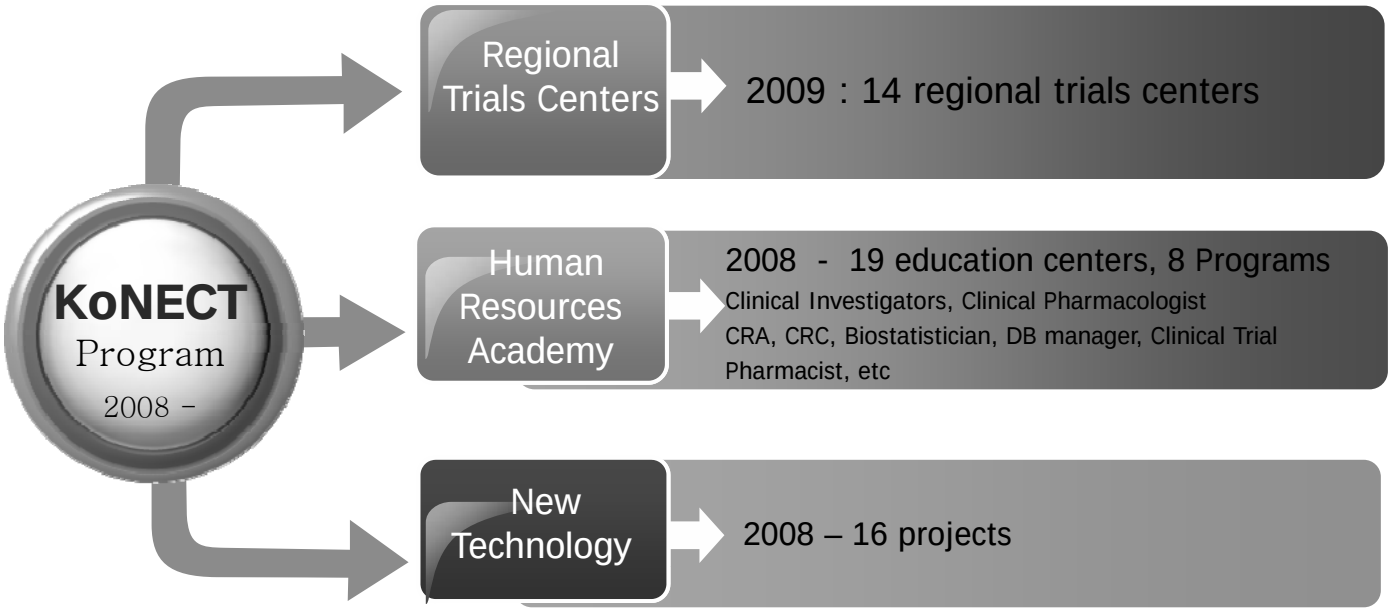
Pharmacodynamics lab.

Medical Device Evaluation

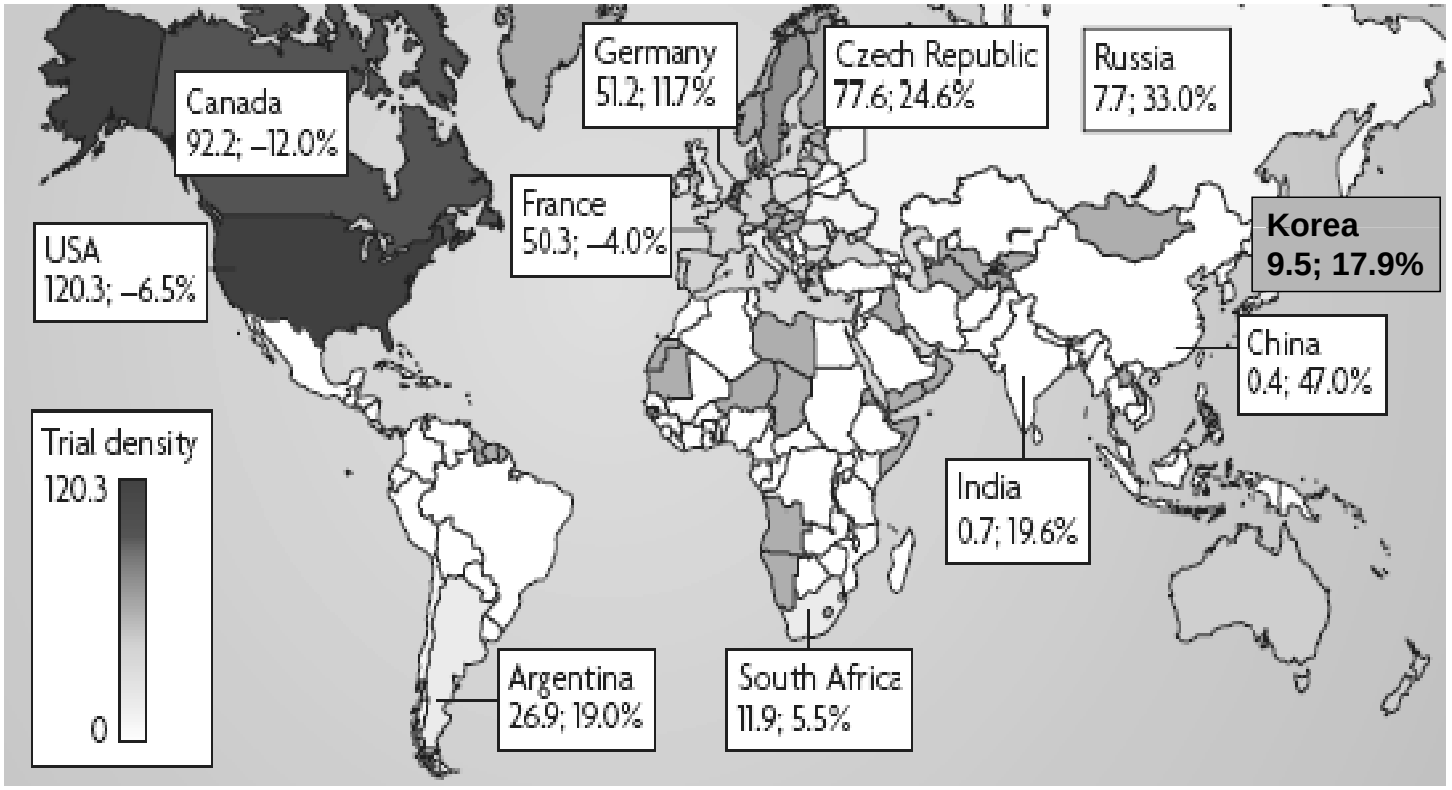
Korea National Enterprise for Clinical Trials (KoNECT) in 2007.12



Activities of KoNECT

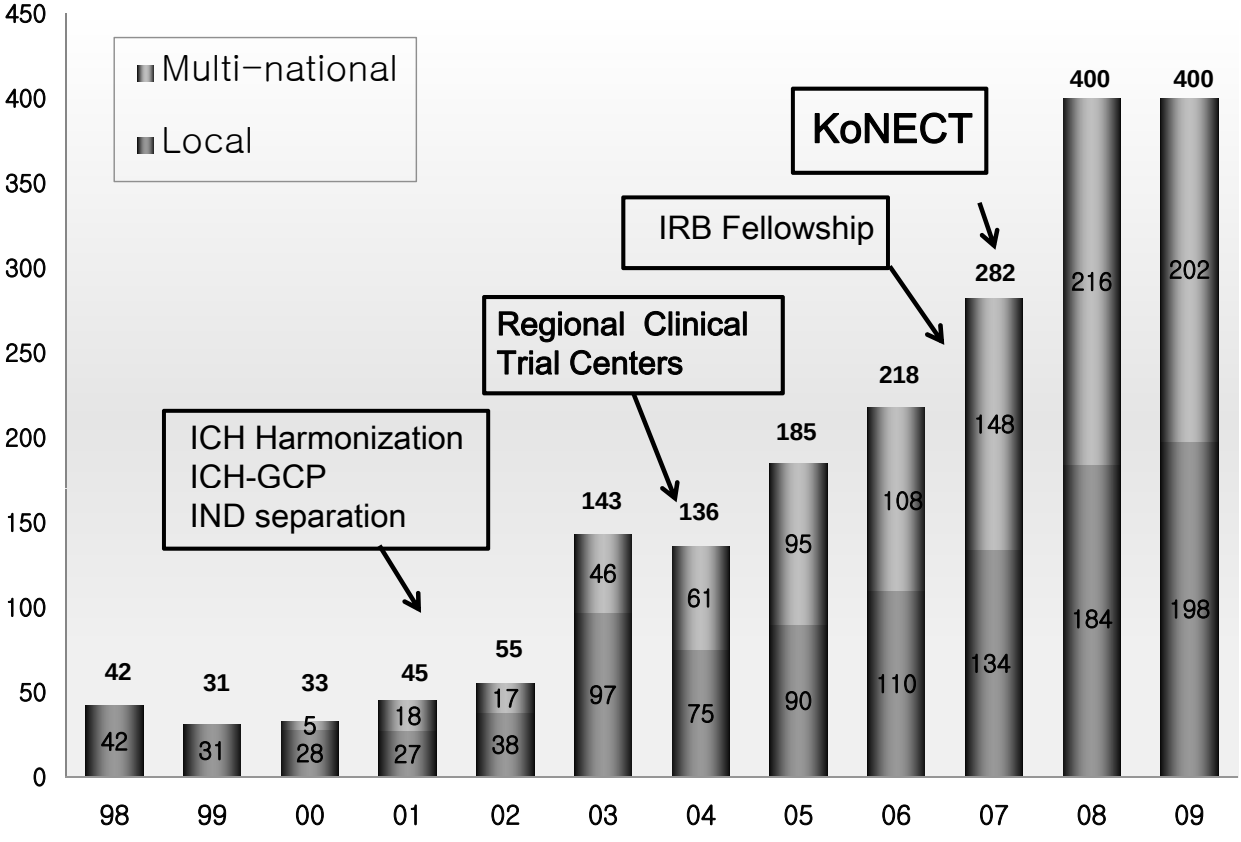


Globalization of clinical trials; trends



NATURE REVIEW 2008;7:13-14

Clinical trials approved by KFDA



Clinical trials by country

❖ *Source: www.clinicaltrials.gov, 31. Dec. 2009*

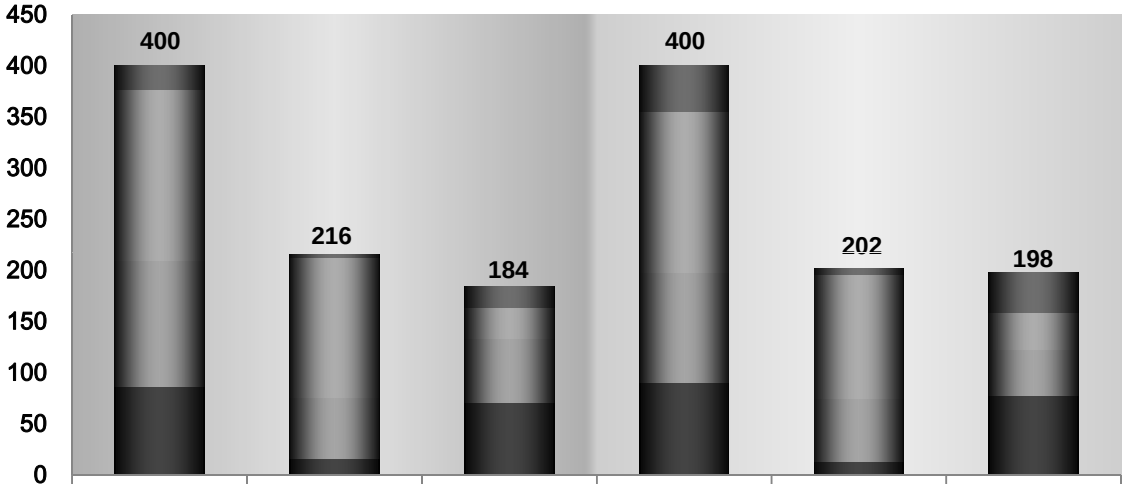
	2005 (Total 115773)			**2006** (119085)			**2007** (115975)			**2008** (142597)			**2009** (96497)		
1	US	61371	53.01%	US	60289	50.63%	US	54263	46.79%	US	62426	43.78%	US	43918	45.51%
2	Canada	5870	5.07%	Germany	7324	6.15%	Germany	12642	10.90%	France	14266	10.00%	France	8105	8.40%
3	Germany	5817	5.02%	France	5451	4.58%	France	4628	3.99%	Germany	9922	6.96%	Germany	6428	6.66%
4	France	5666	4.89%	Canada	5150	4.32%	Canada	3688	3.18%	Canada	4786	3.36%	Canada	3010	3.12%
5	UK	3107	2.68%	UK	3956	3.32%	UK	3403	2.93%	Japan	4392	3.08%	Spain	2685	2.78%
6	Italy	2807	2.42%	Spain	2961	2.49%	Spain	3281	2.83%	Italy	3776	2.65%	Belgium	2583	2.68%
7	Japan	2578	2.23%	Italy	2841	2.39%	Italy	3053	2.63%	Spain	3548	2.49%	UK	2382	2.47%
8	Spain	2321	2.00%	Japan	2321	1.95%	Japan	2200	1.90%	UK	3240	2.27%	Italy	2347	2.43%
9	Netherlands	2319	2.00%	Poland	1725	1.45%	Poland	1823	1.57%	Russia	2023	1.42%	Japan	2168	2.25%
10	Australia	2177	1.88%	Australia	1642	1.38%	Belgium	1797	1.55%	Belgium	1976	1.39%	Korea	1426	1.48%
11	Belgium	1513	1.31%	Netherlands	1591	1.34%	Russia	1792	1.55%	Poland	1963	1.38%	China	1283	1.33%
12	Poland	1328	1.15%	Russia	1588	1.33%	Australia	1530	1.32%	Netherlands	1666	1.17%	Russia	1217	1.26%
13	Sweden	1255	1.08%	Belgium	1492	1.25%	Netherlands	1374	1.18%	Korea	1582	1.11%	Poland	1120	1.16%
14	Denmark	1214	1.05%	Brazil	1181	0.99%	India	1087	0.94%	Australia	1579	1.11%	Australia	1074	1.11%
15	Norway	937	0.81%	India	1074	0.90%	Hungary	1001	0.86%	India	1497	1.05%	Netherlands	1035	1.07%
16	Russia	909	0.79%	Argentina	1064	0.89%	China	997	0.86%	China	1493	1.05%	India	953	0.99%
17	Czech Republic	906	0.78%	Czech Republic	1058	0.89%	Brazil	974	0.84%	Czech Republic	1441	1.01%	Brazil	865	0.90%
18	South Africa	861	0.74%	Austria	1027	0.86%	Korea	970	0.84%	Brazil	1348	0.95%	Sweden	831	0.86%
19	Brazil	748	0.65%	Israel	973	0.82%	Czech Republic	948	0.82%	Sweden	1216	0.85%	Switzerland	798	0.83%
20	Hungary	741	0.64%	Sweden	883	0.74%	Israel	942	0.81%	Hungary	1103	0.77%	Hungary	753	0.78%
21	Switzerland	718	0.62%	Hungary	859	0.72%	Sweden	831	0.72%	Austria	1034	0.73%	Israel	728	0.75%
22	Taiwan	717	0.62%	Denmark	853	0.72%	Austria	816	0.70%	Israel	1033	0.72%	Austria	649	0.67%
23	Finland	684	0.59%	Mexico	827	0.69%	Argentina	794	0.68%	Denmark	992	0.70%	Denmark	641	0.66%
24	Mexico	625	0.54%	Korea	820	0.69%	Ukraine	742	0.64%	Romania	992	0.70%	Taiwan	633	0.66%
25	Argentina	619	0.53%	South Africa	776	0.65%	Mexico	712	0.61%	Argentina	895	0.63%	Czech Republic	631	0.65%
26	India	618	0.53%	China	774	0.65%	Denmark	666	0.57%	Mexico	850	0.60%	Mexico	605	0.63%
27	Israel	607	0.52%	Ukraine	714	0.60%	Switzerland	656	0.57%	South Africa	800	0.56%	Slovakia	514	0.53%
28	Austria	535	0.46%	Switzerland	571	0.48%	Taiwan	640	0.55%	Greece	798	0.56%	Romania	485	0.50%
29	China	459	0.40%	Romania	526	0.44%	South Africa	607	0.52%	Taiwan	770	0.54%	Finland	477	0.49%
30	Greece	393	0.34%	Finland	470	0.39%	Greece	593	0.51%	Ukraine	744	0.52%	Argentina	451	0.47%
31	Portugal	381	0.33%	Taiwan	460	0.39%	Finland	550	0.47%	Slovakia	688	0.48%	Greece	448	0.46%
32	Korea	373	0.32%	Norway	418	0.35%	Romania	546	0.47%	Finland	623	0.44%	South Africa	434	0.45%

Clinical trials by city

❖ *Source: www.clinicaltrials.gov, 31. Dec. 2009*

	2005 (115773)			**2006** (119085)			**2007** (115975)			**2008** (142597)			**2009** (96497)		
1	New York	1140	0.99%	New York	969	0.82%	Houston	1266	1.09%	Houston	1165	0.83%	Houston	934	1.11%
2	Boston	1124	0.98%	Houston	910	0.77%	New York	1232	1.06%	New York	1164	0.83%	New York	792	0.94%
3	Houston	955	0.83%	Boston	849	0.71%	Boston	975	0.84%	Boston	966	0.69%	Boston	758	0.90%
4	Chicago	870	0.76%	Chicago	826	0.70%	Berlin	919	0.79%	Berlin	864	0.61%	Seoul	696	0.83%
5	Philadelphia	838	0.73%	Philadelphia	763	0.64%	Chicago	796	0.69%	Philadelphia	858	0.61%	Berlin	594	0.70%
6	Los Angeles	799	0.69%	Baltimore	760	0.64%	Philadelphia	726	0.63%	Chicago	791	0.56%	Philadelphia	572	0.68%
7	Toronto	748	0.65%	London	725	0.61%	Los Angeles	660	0.57%	Los Angeles	789	0.56%	Chicago	572	0.68%
8	Atlanta	744	0.65%	Dallas	648	0.55%	Dallas	637	0.55%	Dallas	747	0.53%	San Antonio	549	0.65%
9	Seattle	732	0.64%	Los Angeles	641	0.54%	London	631	0.55%	San Antonio	747	0.53%	Baltimore	538	0.64%
10	London	705	0.61%	Toronto	626	0.53%	San Antonio	591	0.51%	London	723	0.51%	London	532	0.63%
11	Baltimore	688	0.60%	Berlin	617	0.52%	Baltimore	581	0.50%	Seoul	696	0.49%	Paris	525	0.62%
12	Dallas	637	0.55%	Atlanta	607	0.51%	Rochester	580	0.50%	Baltimore	694	0.49%	Los Angeles	510	0.60%
13	Portland	619	0.54%	Cleveland	580	0.49%	Cleveland	570	0.49%	Paris	684	0.49%	Dallas	508	0.60%
14	Paris	611	0.53%	Birmingham	573	0.48%	Toronto	555	0.48%	Toronto	675	0.48%	Toronto	475	0.56%
15	Pittsburgh	597	0.52%	San Antonio	548	0.46%	Madrid	528	0.46%	Atlanta	652	0.46%	Cleveland	446	0.53%
16	Rochester	589	0.51%	Madrid	543	0.46%	Moscow	528	0.46%	Birmingham	623	0.44%	Rochester	444	0.53%
17	Berlin	571	0.50%	Rochester	538	0.45%	Seoul	527	0.46%	San Diego	604	0.43%	Nashville	443	0.53%
18	San Antonio	558	0.48%	Moscow	534	0.45%	Columbus	522	0.45%	Portland	599	0.43%	Portland	431	0.51%
19	Cleveland	549	0.48%	Seattle	532	0.45%	Atlanta	521	0.45%	Moscow	592	0.42%	San Diego	429	0.51%
20	San Diego	546	0.47%	Portland	510	0.43%	Seattle	518	0.45%	Cleveland	587	0.42%	Atlanta	427	0.51%
21	Birmingham	539	0.47%	Barcelona	508	0.43%	Paris	503	0.43%	Madrid	575	0.41%	Seattle	415	0.49%
22	Denver	523	0.45%	Pittsburgh	506	0.43%	Barcelona	497	0.43%	Columbus	561	0.40%	Madrid	413	0.49%
23	Cincinnati	516	0.45%	Columbus	500	0.42%	Nashville	473	0.41%	Seattle	554	0.39%	Birmingham	403	0.48%
24	St. Louis	499	0.43%	Paris	477	0.40%	Birmingham	467	0.40%	Cincinnati	549	0.39%	Cincinnati	391	0.46%
25	Montreal	497	0.43%	Indianapolis	476	0.40%	Portland	466	0.40%	Nashville	544	0.39%	Columbus	385	0.46%
26	Indianapolis	492	0.43%	Montreal	466	0.39%	Pittsburgh	461	0.40%	Rochester	521	0.37%	Barcelona	378	0.45%
27	Taipei	472	0.41%	Cincinnati	462	0.39%	Cincinnati	433	0.37%	Barcelona	521	0.37%	Moscow	359	0.43%
28	Columbus	452	0.39%	Miami	455	0.38%	Miami	429	0.37%	Miami	517	0.37%	Miami	357	0.42%
29	Kansas City	442	0.38%	San Diego	453	0.38%	San Diego	423	0.37%	Indianapolis	511	0.36%	St. Louis	345	0.41%
30	Miami	439	0.38%	St. Louis	426	0.36%	Indianapolis	419	0.36%	Pittsburgh	499	0.35%	Pittsburgh	324	0.38%
	77위 - Seoul	218	0.19%	37위 - Seoul	376	0.32%									

Nature of clinical trials in 2008-2009



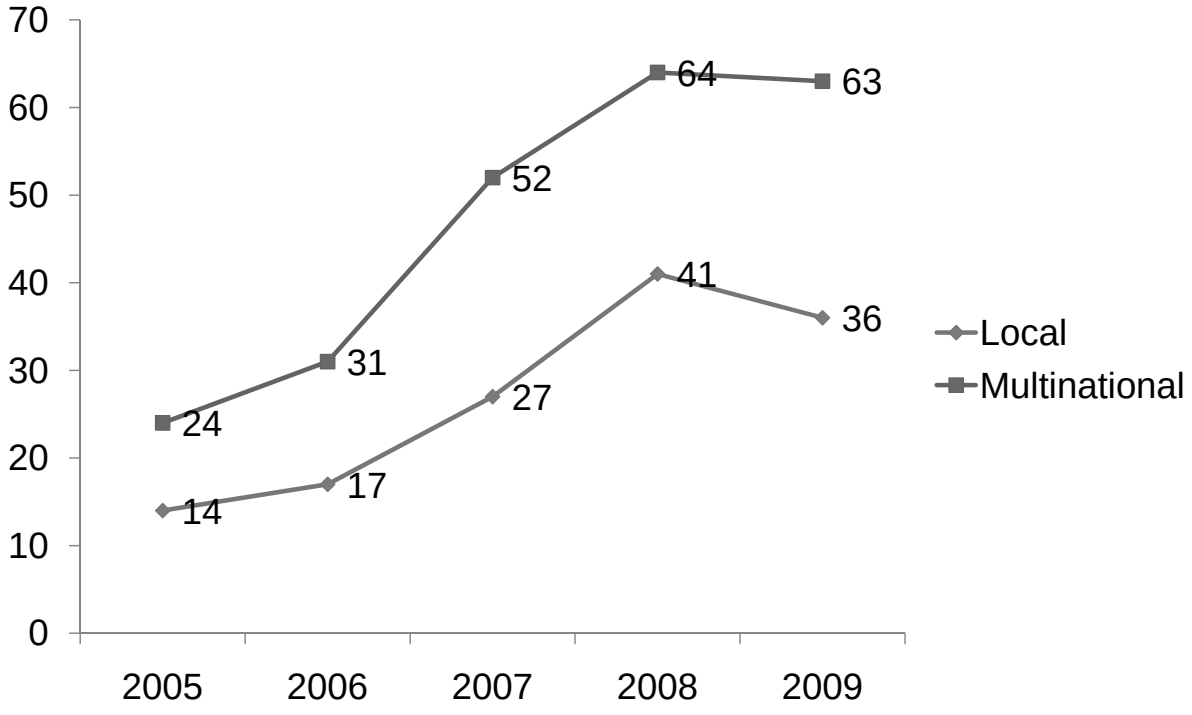
	2008			2009		
Phase IV	23	3	20	45	6	39
Phase III	167	137	30	157	121	36
Phase II	123	60	63	107	62	45
Phase I	87	16	71	91	13	78

Clinical trials by therapeutic category

Category	MNC Trials	% of MNC Trials	Local Trials	% of Local Trials	Total Trials	% of Total Trials
Oncology	69	31.9%	48	26.1%	117	29.3%
Cardiovascular	25	11.6%	28	15.2%	53	13.3%
Endocine/Metabolic	23	10.6%	16	8.7%	39	9.8%
Psychiatry	18	8.3%	11	6.0%	29	7.3%
Antinfective	19	8.8%	8	4.3%	27	6.8%
GI	4	1.9%	12	6.5%	16	4.0%
Respiratory	14	6.5%	1	0.5%	15	3.8%
Musculoskeletal	3	1.4%	12	6.5%	15	3.8%
Hematology	9	4.2%	5	2.7%	14	3.5%
Rheumatology	9	4.2%	2	1.1%	11	2.8%
Neurology	7	3.2%	4	2.2%	11	2.8%
Urology	2	0.9%	9	4.9%	11	2.8%
Immunosuppresive	4	1.9%	6	3.3%	10	2.5%
Vaccine	3	1.4%	5	2.7%	8	2.0%
Dermatology	2	0.9%	6	3.3%	8	2.0%
Opthalmology	5	2.3%	2	1.1%	7	1.8%
Stem Cell	0	0.0%	5	2.7%	5	1.3%
Antihistamine	0	0.0%	2	1.1%	2	0.5%
Other	0	0.0%	2	1.1%	2	0.5%
Totals	**216**	**100.0%**	**184**	**100.0%**	**400**	**100.0%**

Note: Based on top 500 pharmaceutical and biotech companies, Source: Evaluate Pharma® 6Apr2009

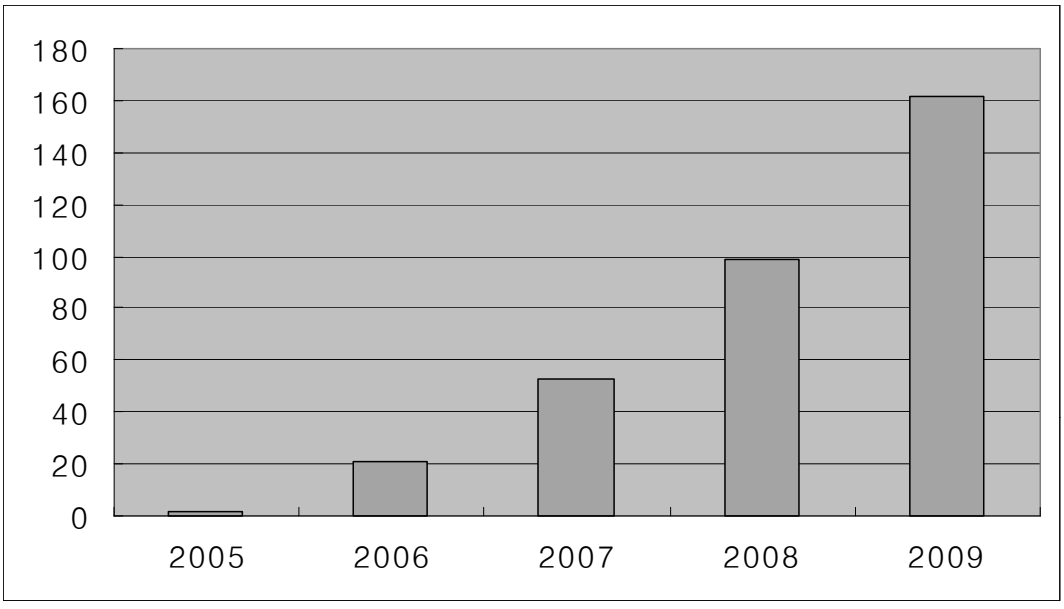
Oncology trials in Korea



2009 KFDA Data

Investigator-initiated trials in Korea

Numbers of registered trials



Year

- *Source: www.clinicaltrials.gov*

Governmental support of academic clinical trials

2004	MOHW nominated 3 Clinical Research Centers
2008	Total 11 Clinical Research Centers
2008.12	MOHW established NECA
2010.5	MOHW established NSCR under NECA

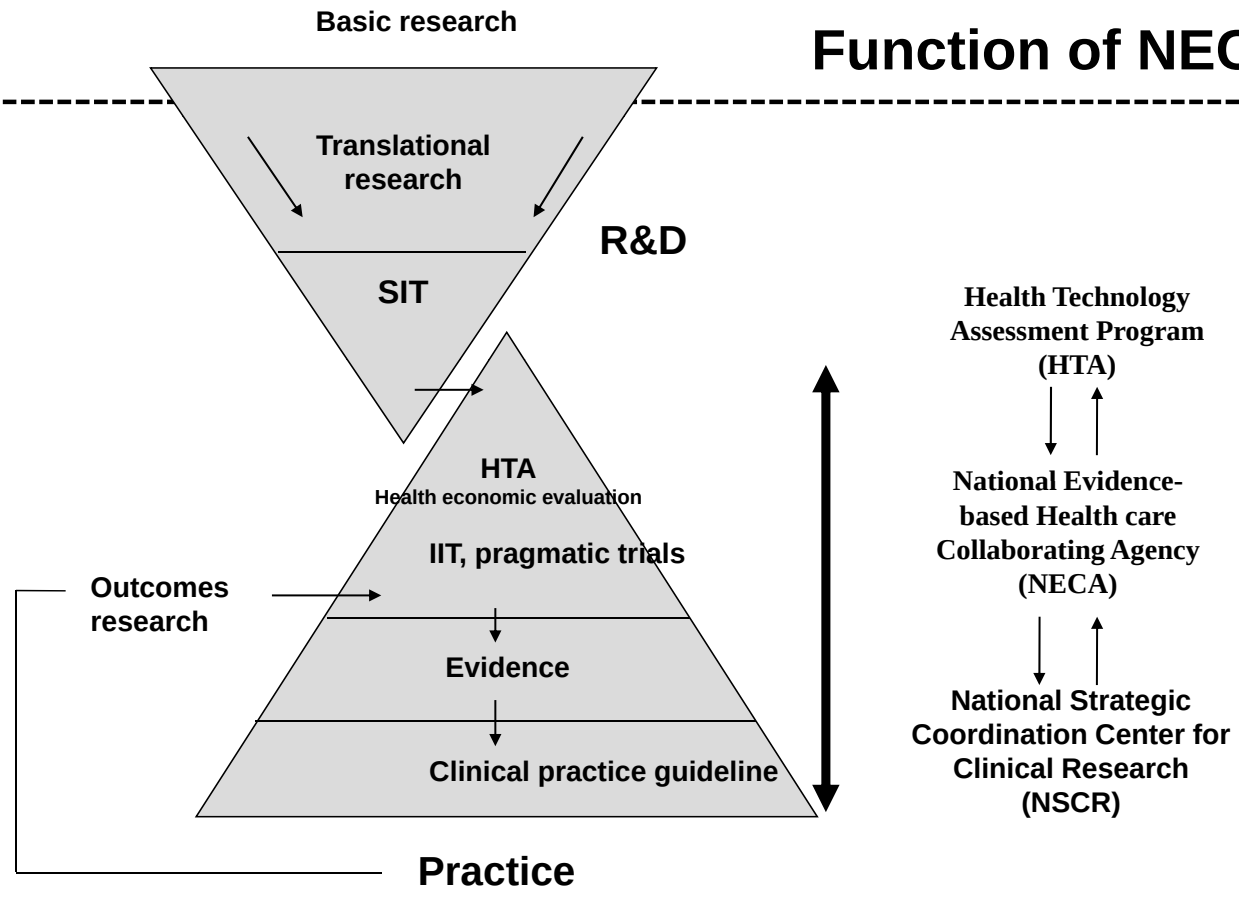
Annual Budget

National Strategic Coordination Center for Clinical Research (NSCR)	9,600,000,000 KW (8,300,000 US$)
National Evidence-based Healthcare Collaborating Agency (NECA)	5,113,000,000 KW (4,500,000 US$)
Total	14,713,000,000 KW (12,800,000 US$)

Government-supported clinical research center

	Name	Period
1	Clinical Research Center for Solid Tumor (CRCST)	´04.11
2	Ischemic Heart Disease Clinical Research Center	´04.11
3	Clinical Research Center for Chronic Obstructive Airway Disease	´04.11
4	Korea National Diabetes Program	´05.4
5	Clinical Research Center for Depression	´05.4
6	Liver Cirrhosis Clinical Research Center	´05.4
7	Clinical Research Center for Stroke	´06.4
8	Clinical Research Center for Dementia	´05.5
9	Clinical Research Center for the Appropriate Antibiotic Use	´08.11
10	Clinical Research Center for End Stage Renal Disease	´08.11
11	Rheumatoid Arthritis Clinical Research Center	´08.11

Function of NECA



National Strategic Coordination Center for Clinical Research (NSCR)

	Target	Recommendation
Topic Selection	Public interests	Reflect social needs
Clinical Trials	- Investigator-initiated trial (IIT) - Pragmatic Clinical Trial (PCT)	-Registration: Clinicaltrials.gov or equivalent -Data management: eVELOS or equivalent
Clinical Epidemiology	- Registry or cohort study - Merge with public healthcare database	Data management: eVELOS or equivalent
Clinical Practice Guideline	Public interests	-Evidence: Systematic review or adaptation -Social Consensus: Appraisal

Conclusions

- There has been a rapid growth in quality and quantity of clinical trials in Korea.
  - Governmental support for infrastructure
  - High-quality medical infrastructure
  - Highly motivated academia
- Strong points of Korea include
  - Big hospitals with huge patient volume
  - Good infrastructures for medical care and clinical trials
- Weak points of Korea include
  - Limited governmental support for academic trials
  - Limited reimbursement for clinical trials

US National Cancer Program

Naoko Takebe, MD, PhD
Edward Trimble, MD, MPH
US National Cancer Institute, NIH

US National Cancer Program

- Edward L. Trimble, MD, MPH
  - Central coordination of academic clinical trials
  - Strengths and weaknesses of academic clinical trials infrastructure
  - Education and knowledge transfer for medical professionals and medical students
- Naoko Takebe, MD, PhD
  - Models of collaboration with industry to promote life science innovation and economic growth

US National Goals

- Establish standard of care for cancer prevention, screening, treatment, and survivorship
  - Treatment: surgery, chemotherapy, radiation therapy, supportive care, symptom management
- Identify optimal use of novel agents in multi-modality cancer regimens
  - May include licensing trials, trials to expand licensing or indication

US National Goals: II

- Identify most cost-effective way to deliver good cancer care
- Facilitate study of rare cancers, less common subtypes of common cancers, cancer in patients with co-morbidities
  - Pediatric cancer
  - Cancer in older patients

US National Cancer Program

- US Department of Health and Human Services
  - National Cancer Institute: coordination & research
  - FDA: drug and device regulation
  - Centers for Disease Control and Prevention: public education, public health, breast & cervical cancer screening
  - Agency for Research on Healthcare Research and Quality: quality of cancer care, cost-effectiveness, models of care delivery

US National Cancer Program: II

- NCI-designated Cancer Centers, university hospitals, research institutes:
  - basic, translational, & clinical research; patient care, training
- Advocacy and support groups:
  - research & education
- Professional societies:
  - research & education
- Third-party payers and health care systems:
  - patient care & routine care costs for trials

Sponsorship & funding of academic cancer clinical trials in the US

- US NCI: phase I, II, and III clinical trials
  - Funding via grants, contracts, and cooperative agreements with groups ($850 million/year)
  - May include co-funding from foundations or industry
- Academia: NCI-designated cancer centers and university hospitals: phase I and II clinical trials
  - Funding from NCI grants, foundations, pharmaceutical/ biotechnology industry, institutional resources

US NCI Central Coordination

- Scientific steering committees for each major disease (gastrointestinal, breast, lung, etc)
  - Representation from academic cooperative groups, research centers with expertise in disease, community oncologists, patient advocates, NCI staff
  - Responsibility to review proposals for phase III trials, plan phase II trial portfolio, and seek international collaboration as appropriate

Strengths of US system

- Close ties between NCI, cooperative groups, Cancer Centers, universities, advocacy groups, and pharmaceutical/biotechnology industry since 1955
- Harmonization: common toxicity criteria, data elements, quality assurance, electronic data collection
- All trials meet standards of International Conference on Harmonization (ICH)
- Most parts of US health care system pay for routine patient care costs associated with academic clinical trials & pay for evidence-based care (even in absence of specific licensing indication)

Weaknesses of US system: I

- History: 11 cooperative groups; some duplication of effort; competition of trials for limited patient population; unacceptable delays in central protocol development and opening trials at local sites
- Limited public funds for per capita reimbursement to sites
  - Average $2000 per patient from NCI for academic trials while industry pays $5000-$10,000+ per patient for industry trials

Weakness of US system: II

- No centralization of cancer care for adults
- No requirement that hospitals and clinics which treat cancer patients participate in academic clinical trials
- Access to academic clinical trials limited
- Only 3% of adults with cancer enroll on NCI-sponsored academic clinical trials
  - Under-representation: older patients with co-morbidities, adolescents and young adults

Addressing weaknesses of US system

- NCI Clinical Trials Working Group recommendations, 2005
- NCI Operational Efficiency Working Group recommendations, 2010
- Institute of Medicine: A National Cancer Clinical Trials System for the 21st Century, 2010

Education and knowledge transfer

- Curricula of medical schools, nursing schools, public health & pharmacy schools includes basics of clinical trials
- University training (Bachelor, Master, Doctor) for biostatisticians
- Advanced (1-2 year) training programs in clinical trials for doctors and nurses

More educational strengths

- Basic and advanced training for clinical trials data managers
  - Certification examinations offered by the Society of Clinical Research Associates
- Short courses on clinical trials for fellows in training, junior medical faculty, nurses, pharmacists, and data managers (professional societies & universities)
- Cooperative group meetings every 6 months
- On-site audits every 3 years

Educational weaknesses

- We need to do a better job teaching doctors and nurses how to talk to patients about clinical trials.
- We need to ensure that each hospital and university active in clinical research provides appropriate support and ongoing training for clinical trials.

US National Cancer Program

- Edward L. Trimble, MD, MPH
  - Central coordination of academic clinical trials
  - Strengths and weaknesses of academic clinical trials infrastructure
  - Education and knowledge transfer for medical professionals and medical students
- Naoko Takebe, MD, PhD
  - Models of collaboration with industry to promote life science innovation and economic growth

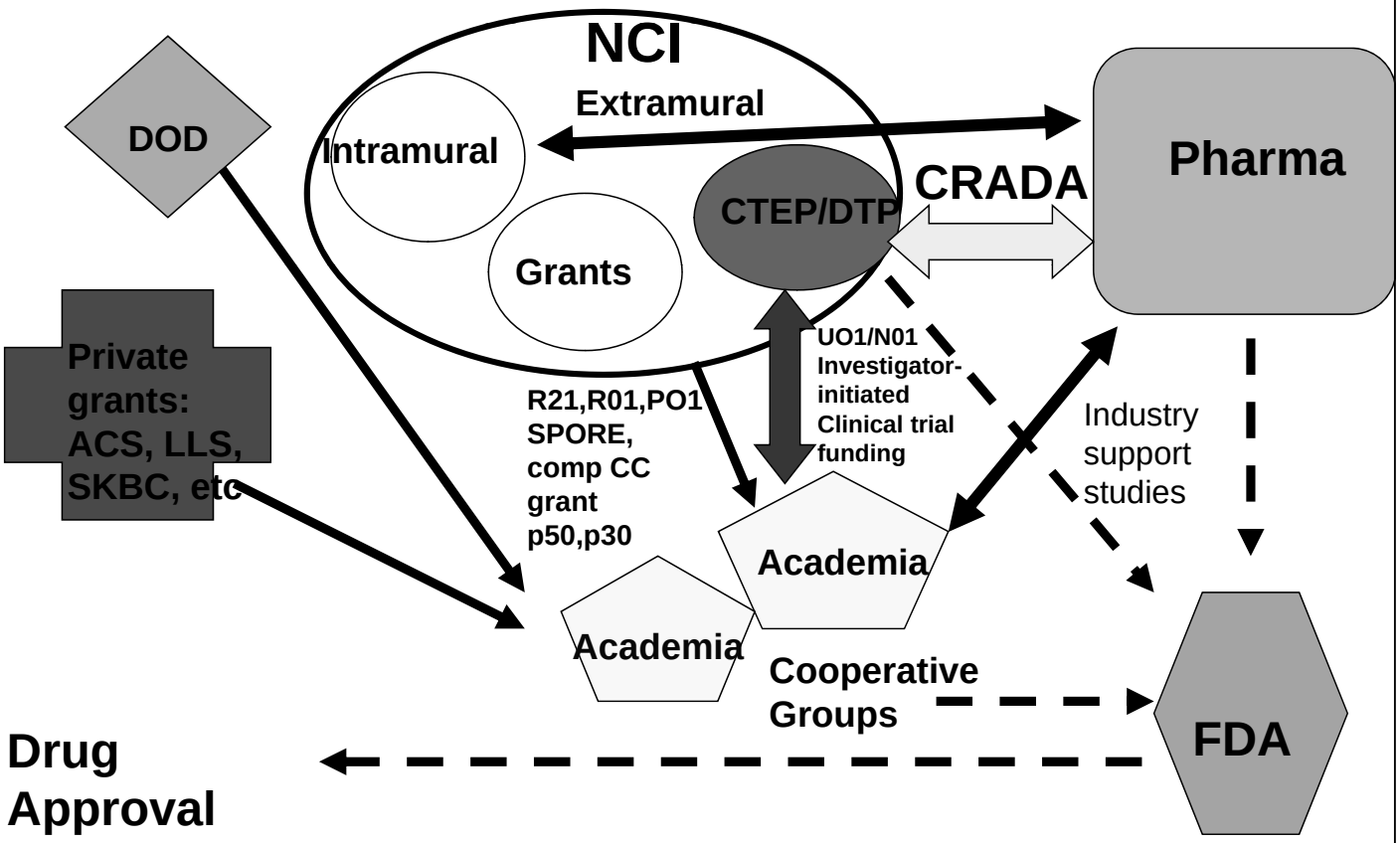
Oncology Clinical Trials In The US: National Cancer Institute Partnerships With Academia And Industry

Naoko Takebe
Edward Trimble
Cancer Therapy Evaluation Program
DCTD, NCI, NIH
January 29, 2009
Clinical Trials in a Global Society

Overview

- NCI CTEP (Cancer Therapy Evaluation Program) drug development model
  - Introduction to the NCI CTEP model
  - Model for an investigator initiated-clinical trial
  - Advantages of this model
  - Disadvantages of this model
  - Industry-Academia-Government cooperative model for enhancing the economy

Process Map Of Cancer Drug Development In The US



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

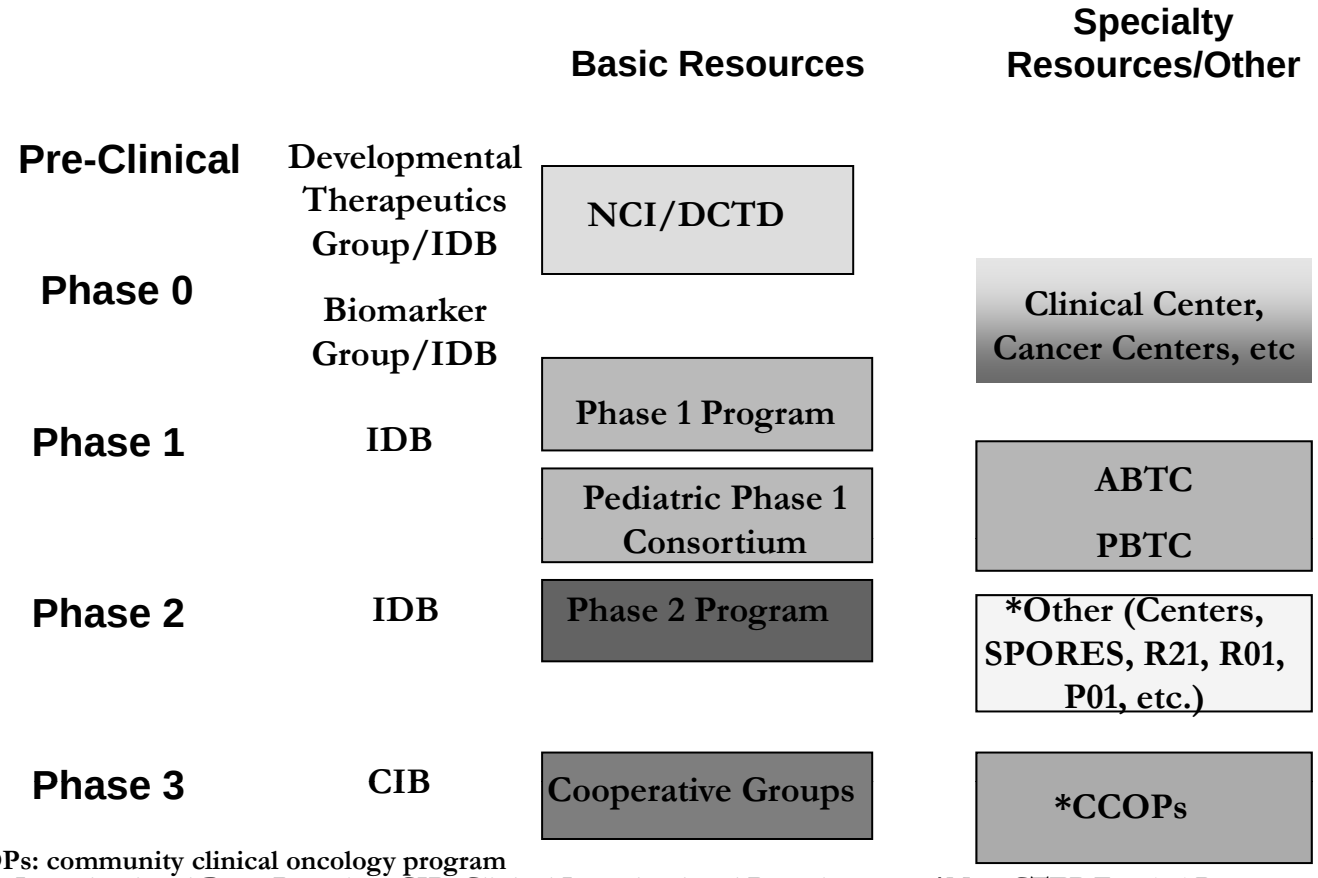
- N01 9 Institutions
- U01 14 Institutions

CTEP: Scope

- Funded clinical trial groups:
  - Phase 1 Grantees, Phase 2 Contractees, Consortia, Cooperative Groups,
- Grants, individual investigators
- Currently sponsors over 90 INDs (Investigational New Drugs)
- Numbers
  - >11,000 registered investigators at over 3,300 institutions
  - ~ 1000 active protocols
  - ~ 500 new protocols/year
  - ~ 30,000 patients accrued/year
  - ~ 80 collaborative agreements (CRADAs, CTAs, and CSAs) with pharmaceutical companies.

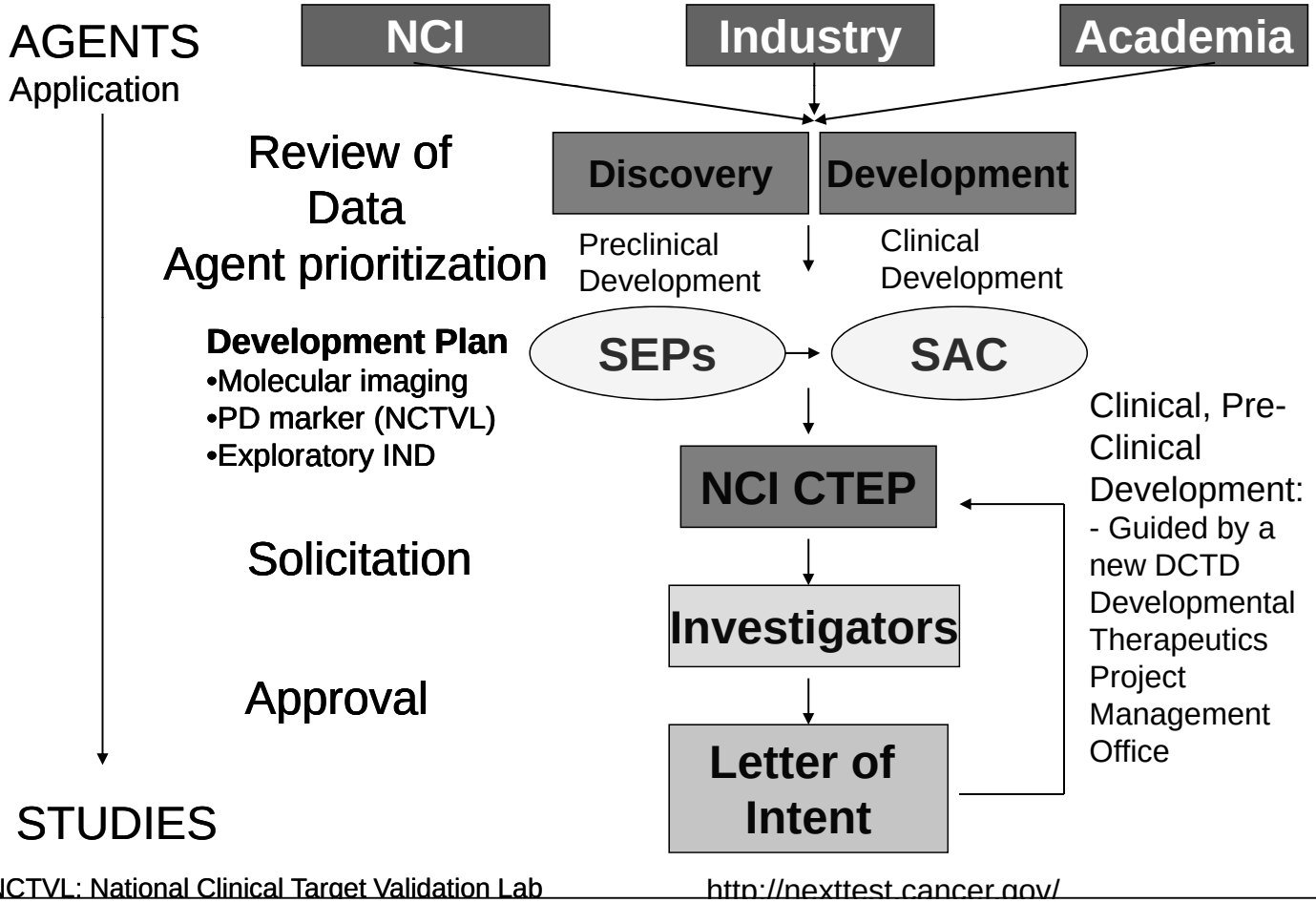
CTEP Therapeutics Development Program

Agents Selected Through NExT Program



CCOPs: community clinical oncology program
IDB: Investigational Drug Branch CIB: Clinical Investigational Branch *Non-CTEP Funded Resources

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/

1) CTEP Support Contracts: Estimate of Annual Costs for one IND (avg. 8 trials)

	Year 1	Additional Years
Contractor Costs	$319,670	$319,670
OIB	$158,740	$158,740
CTIS	$155,740	$155,740
PIO	$3,000	$3,000
PMB	$8,526	$8,526
CTMB	$1,048	$1,048
RAB	$59,356	$35,421
IDB/TRI	$30,000	$30,000
Total	$736,080	$712,145

Based on costs for past 5 years - 137 active INDs

2)Research Grants and Contracts Cost Estimates (UO1,N01, Cooperative Group)

Type of trial	Phase 1	Phase 2	Phase 1/2/3
Funding mechanism	UO1	NO1	Cooperative Groups
Avg cost/patient	$8,000 -$9,000	$7,000	$2,000

Clinical Trial Cost Estimates

Estimated Costs per trial

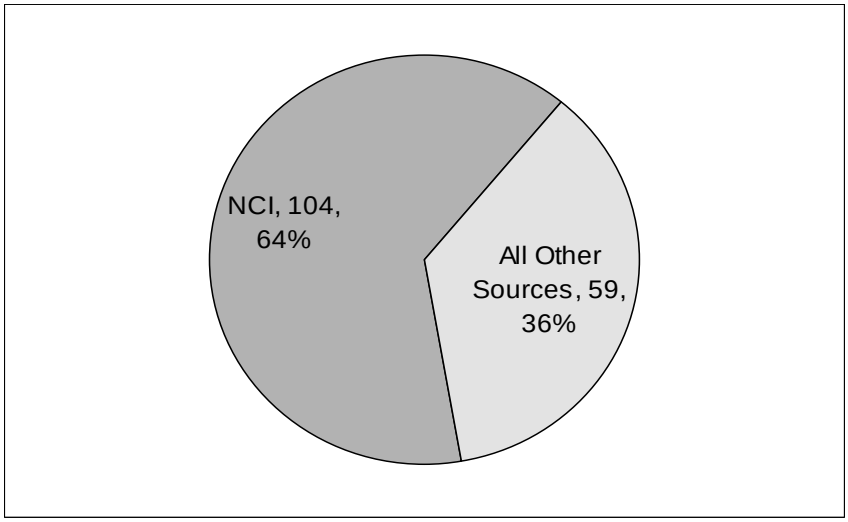
	Phase 1 (avg 18 months, 36 patients)	Phase 2 (avg 24 months, 50 patients)	Total
CTEP support contracts	$136,519	$181,028	
Clinical Trial (UO1,N01, Cooperative Group)	$306,000	$350,000	
Total	$442,519	$531,028	$973,547

Note: Costs are covered by previously awarded grants and budgeted contracts and do not represent supplemental costs to NCI

A Model For An Investigator-Initiated Clinical Trial

- **Driven by medical need and scientific opportunity**
- **57% ASCO plenary presentations**
- **Discovery of new treatment effectiveness**
- **CTEP handles complex issues e.g. combination study using different pharma agents. Existing collaboration with more than 100 industries**
- **Consequently, the academia investigator does not have to deal with FDA for the agent related issues**
- **Toxicity monitoring and reporting by CTEP**

Combination Cancer Trials For Proprietary Agents With Diverse Ownership – Total Trials Completed and Underway

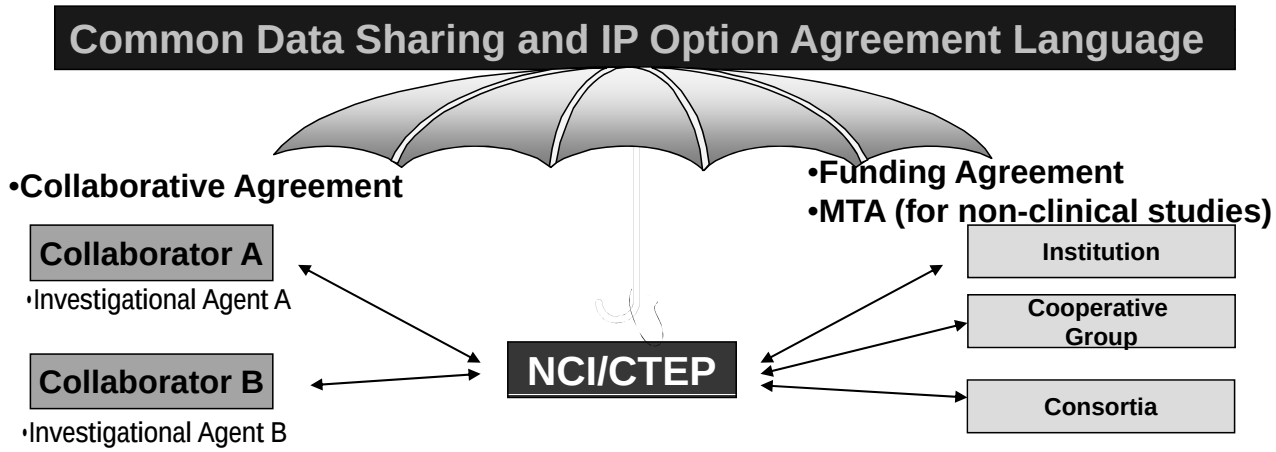


NCI・CTEPを介してならば、普通では不可能である他社の未承認薬剤同士のコンビネーショントライアルが可能

Source: www.ClinicalTrials.gov

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



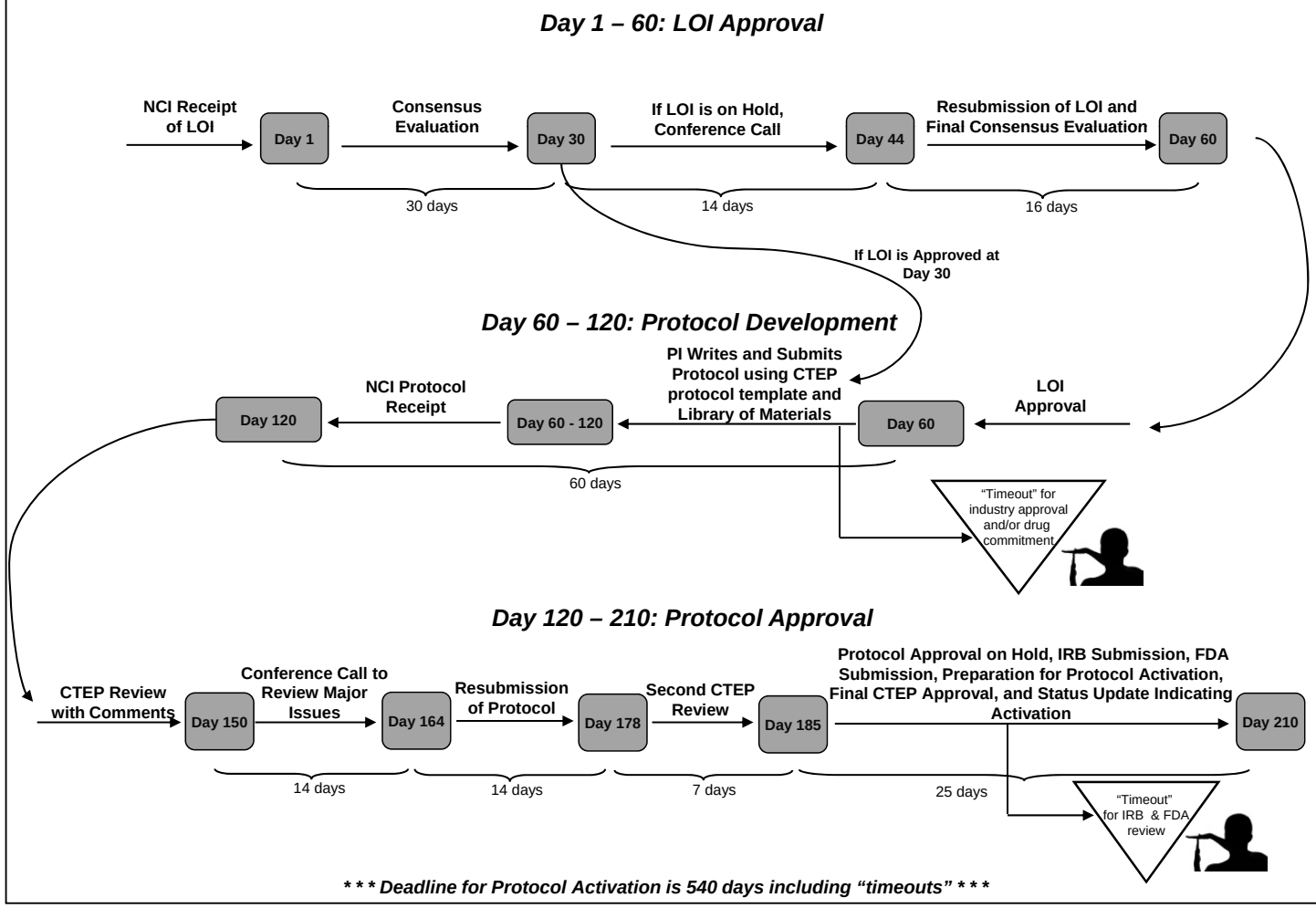
Accepted by collaborators. → > 120 trials combining investigational agents

Advantages Of This Model -1

- NCI in the best position to lead other Federal agencies, FDA, academic centers, community practices, and pharmas in optimizing the drug development process.

- Current Cooperative Group program and U01/N01 are **slow and inefficient** in the design, launch, and conduct of clinical trials
  - Recent critiques by the Institute of Medicine for Cooperative Groups
  - To improve the inefficient protocol activation process, NCI stood up the Operational Efficiency Working Group (OEWG) in order to make protocol development coordinated and streamlined

Phase 1/2 Timeline: Unsolicited LOI's



Advantage Of This Model-2

- 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
  - Need to establish SOP - a national inventory and peer-review process for accessing specimens for the study
- NCI's clinical trial **prioritization** may improve the quality and speed of clinical trial – **avoid duplicative** studies
  - CTEP sponsored investigator initiated studies have been under this prioritization. It should be extended to the Cooperative Group studies
- NCI's needs to provide appropriate financial support to improve clinical investigator participation rate

Disadvantage Of This Model

- Not every pharmaceutical industry agrees with CRADA, particularly intellectual property issues

- NCI's new agent prioritization process may be a rate limiting step
  - e.g. NExT program takes approximately 6 months to obtain an institution official approval for the drug development. CRADA negotiation will take at least 6 months from the time of approval. NCI drug development plan execution by means of mass solicitation readiness will take at least 6 months after CRADA completion.

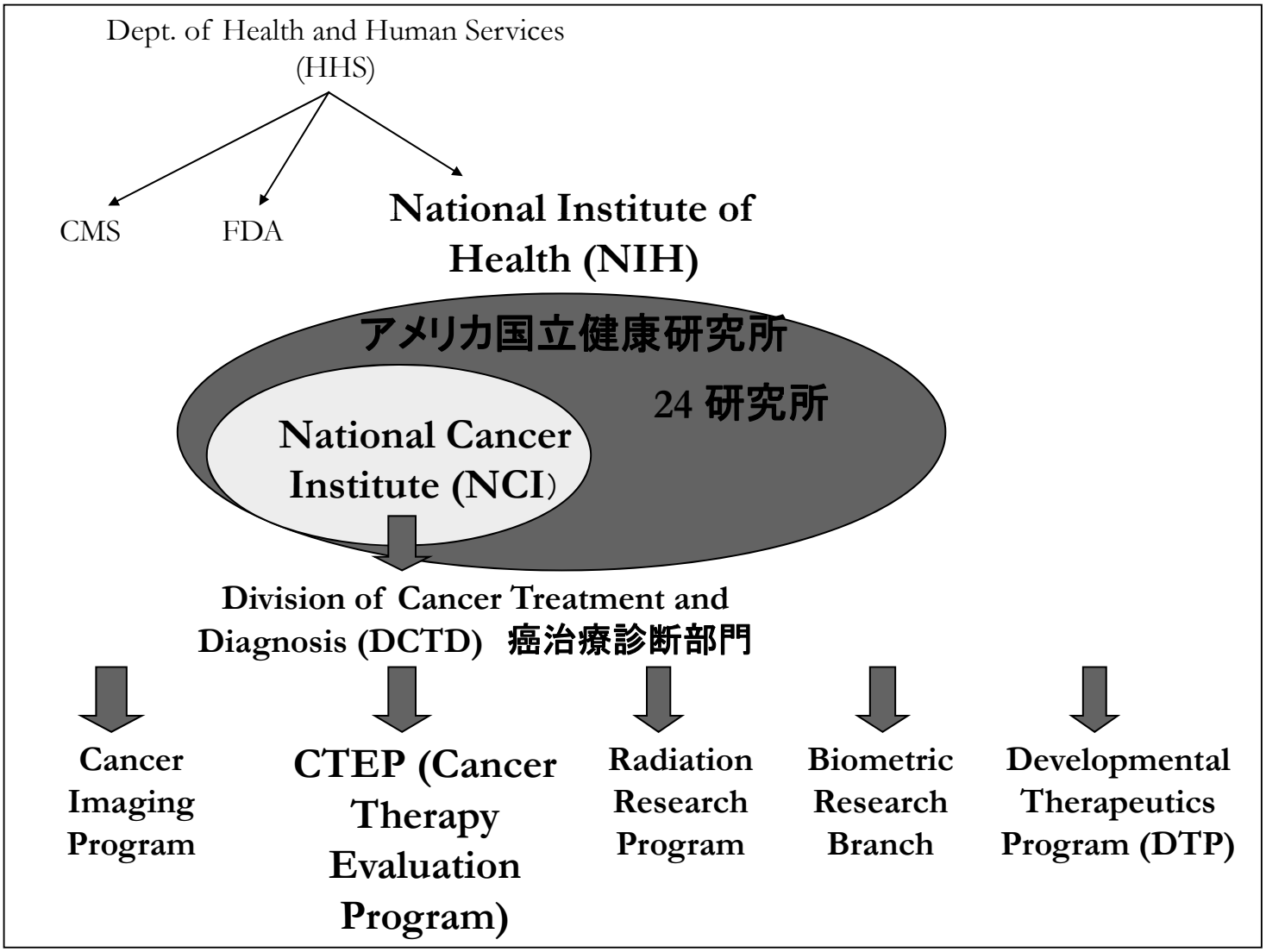
Industry Cooperative Model For Enhancing The Economy

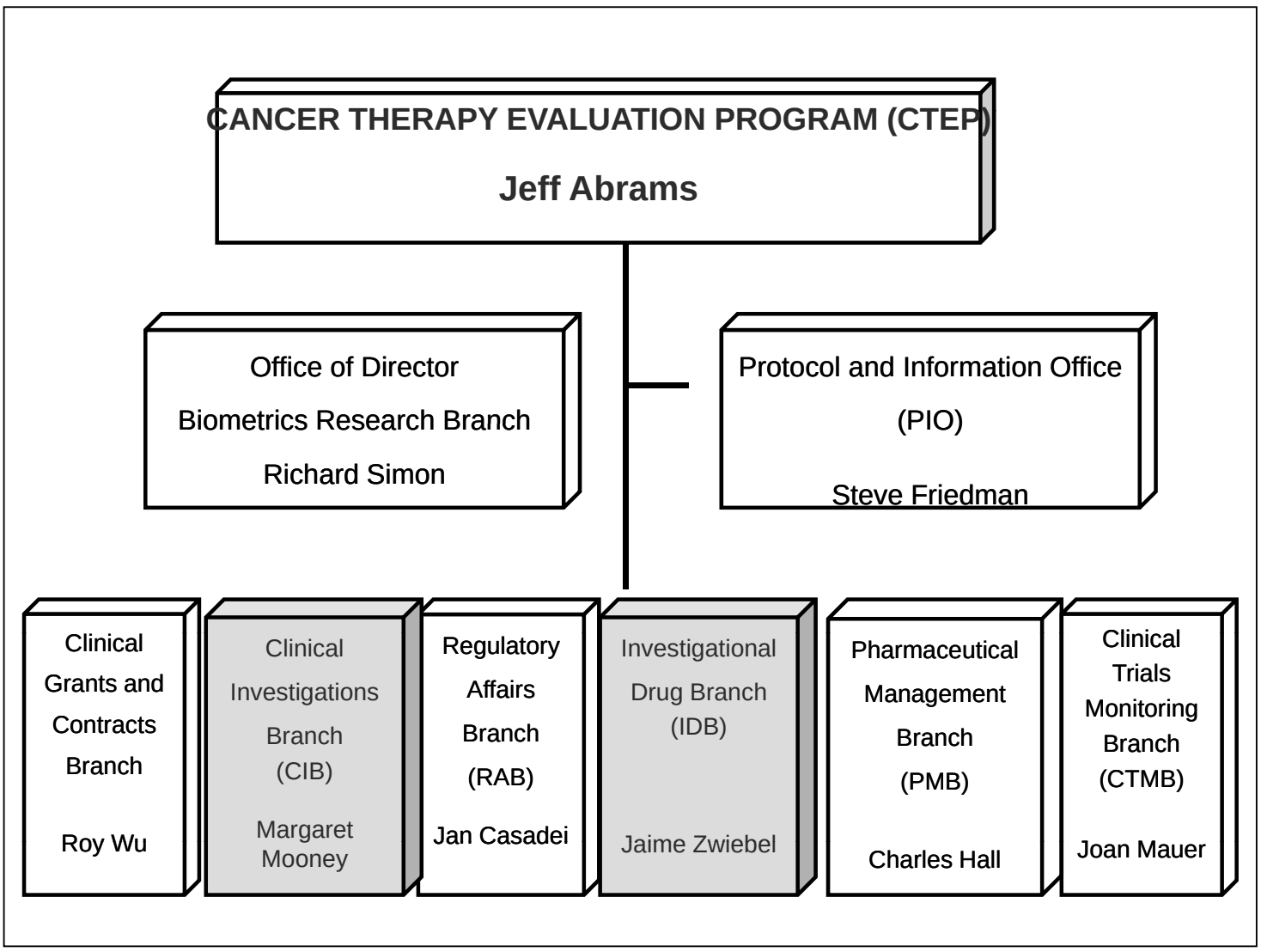
- NCI's **non-overlapping** drug **development** of agents with pharmaceutical and biotech companies will result in economical growth : a broad range of tumors, rare or orphan disease indications, different dosing schedules, biomarker studies etc.
  - If phase 2 successful, the companies will take over to conduct phase 3 study or CTEP orchestrate phase 3 study with the cooperative group with the company
  - 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

CTEP On The Web -http://ctep.cancer.gov/

- **Program information.**
- **Funding Opportunities**
- **CTEP IND agents/contacts –IDB Senior Investigator's contact info**
- **Informatics initiatives - AdEERS, CDUS.**
- **CTCAE Active CTCAE Version (Active as of 10/1/2009) link.**
- **Investigator's manual**
- **Forms and Documents**
  - **LOI Forms**
  - **Protocol Templates**
- **Guidelines**
  - Components of a competitive Letter of Intent
    - **http://ctep.cancer.gov/guidelines/index.html**
  - Correlative study and tissue banking
- **Model agreements - CDA, MTA, CTA, CRADA and CRADA appendices.**
- **Recent solicitations**

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)


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

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 <u>strategic input</u> into the <u>clinical development</u> 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**
- **<u>Enhance transparency</u> 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)

Solicitations Nov 2008~Dec 2009

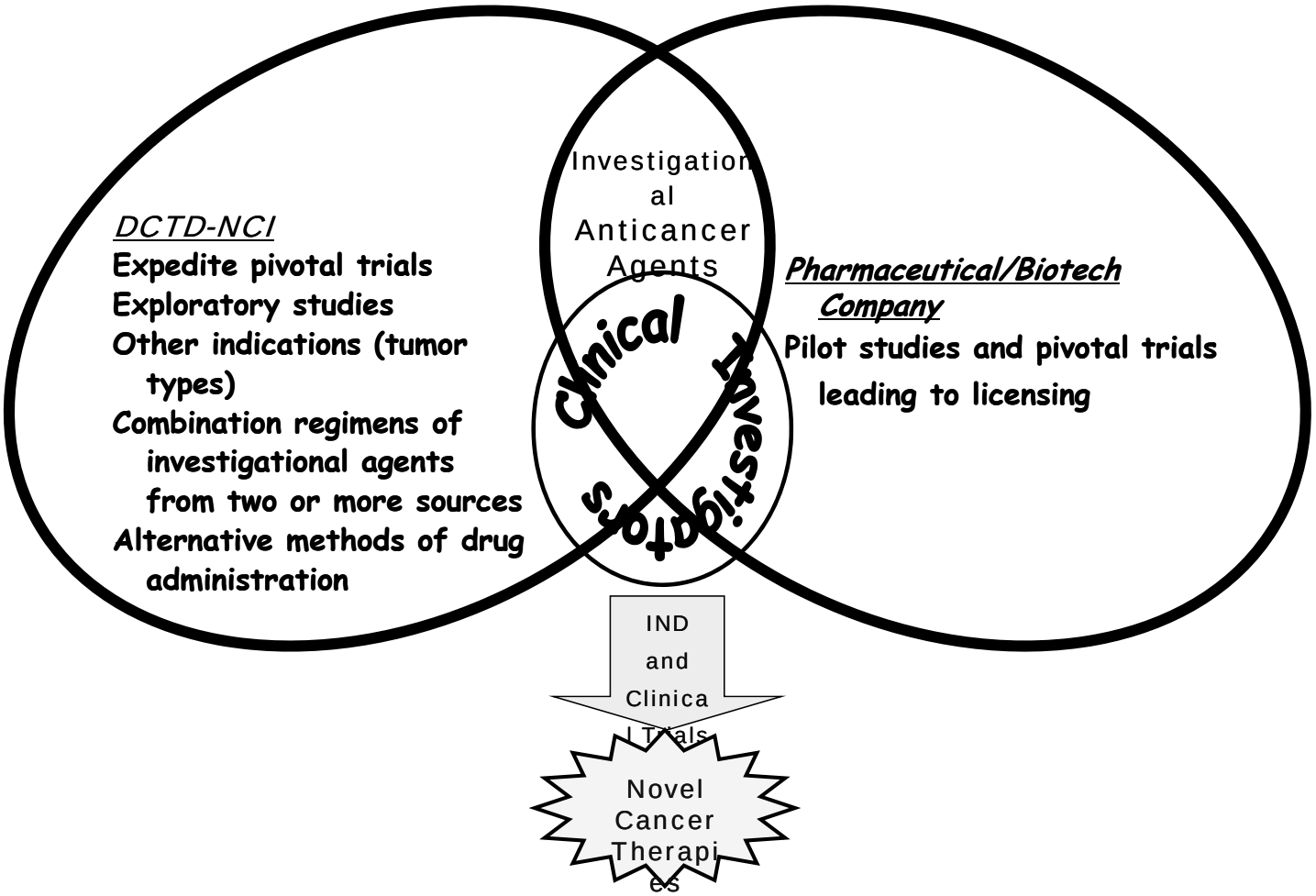
- **GDC0449 (Smo antagonist), Hh signaling inhibitor Genentech (Issued Nov 2008, Review in 2009)**
  - Single agent phase 2 studies in glioblastoma multiforme, pancreatic cancer, multiple myeloma, chondrosarcoma, prostate, gastric
  - Novel-novel combination phase 1 trials of GDC0449 + RO4929097, R1507
  - Food effect study
  - medulloblastoma (adult and peds), small cell lung cancer (randomized), erlotinib+GDC
  - Unsolicited 2010 ~triple negative, BC metastasis to BM, Future interest: endometrial carcinoma, Cervical ca., melanoma, radiation, CML. Sensitization, novel-novel combo.

- **RO4929097 (gamma secretase inhibitor) Notch signaling inhibitor**
  - New PK data showing auto-induction of metabolism of RO when>30mg dose (3 on 4 days off vs. continuous)
  - Solicitation for Phase 1 combination trials with standard agents or novel-novel combination including ovarian ca

- **ABT263 (BH3 mimetic), bcl-2 inhibitor Abbott**
  - Single agent phase 1/2 in pediatric ALL
  - Combination phase 1 in pediatric ALL, ovarian ca with paclitaxel submitted, sorafenib combination in HCC and RCC,
  - Combination P2 in pancreatic ca with gemcitabine, P2 in ovarian ca with paclitaxel (GOG) after P1

- **MK-2206 (AKT inhibitor), Merck**
  - P2 single agent ovarian ca submitted, P2 single agent endometrial ca submitted, Peds P1, AML,NHL, BC, gastric ca, HCC and biliary, pancreatic, RCC,
  - P1 combination, lapatinib, paclitaxel,

Doing Battle Against Cancer - A Collaborative E



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.

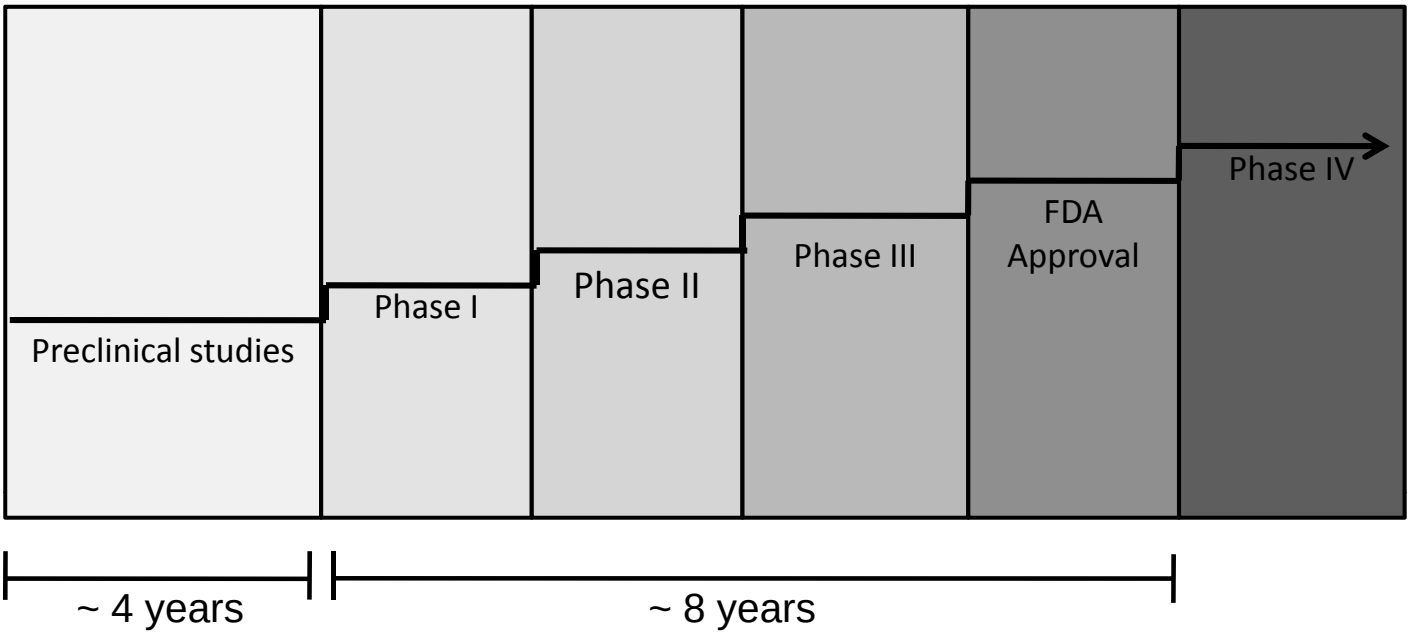
• Trials that don't meet accrual goals may close without answering the scientific questions they were designed to address.

• 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.

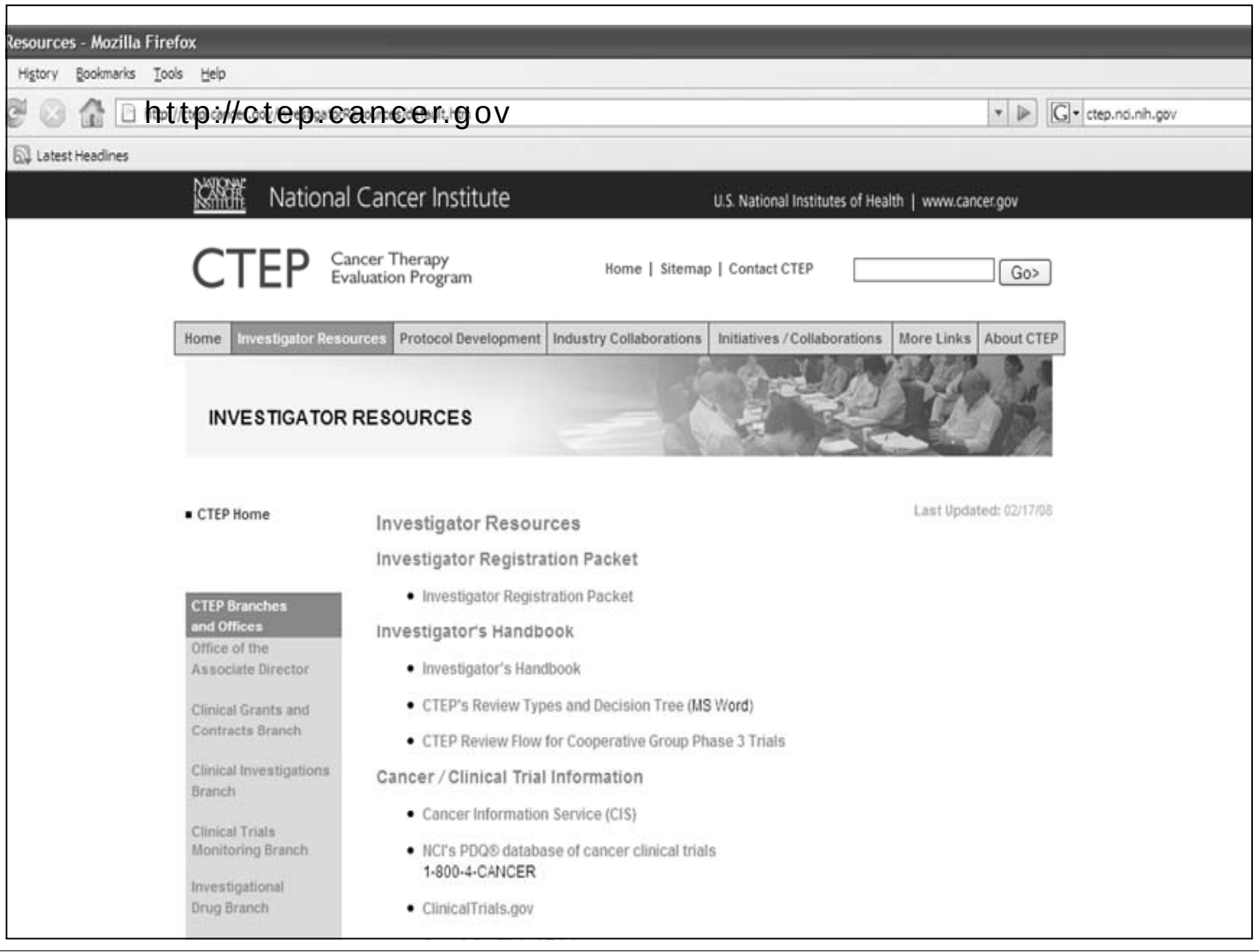
How Long Does it Take to Develop a New Cancer Drug?



Total ~ 12 years!

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



Models of National Trials Systems

Kate Law

(Cancer Research UK)

and

Jonathan Ledermann

(Cancer Research UK & UCL Cancer Trials Centre

University College London)

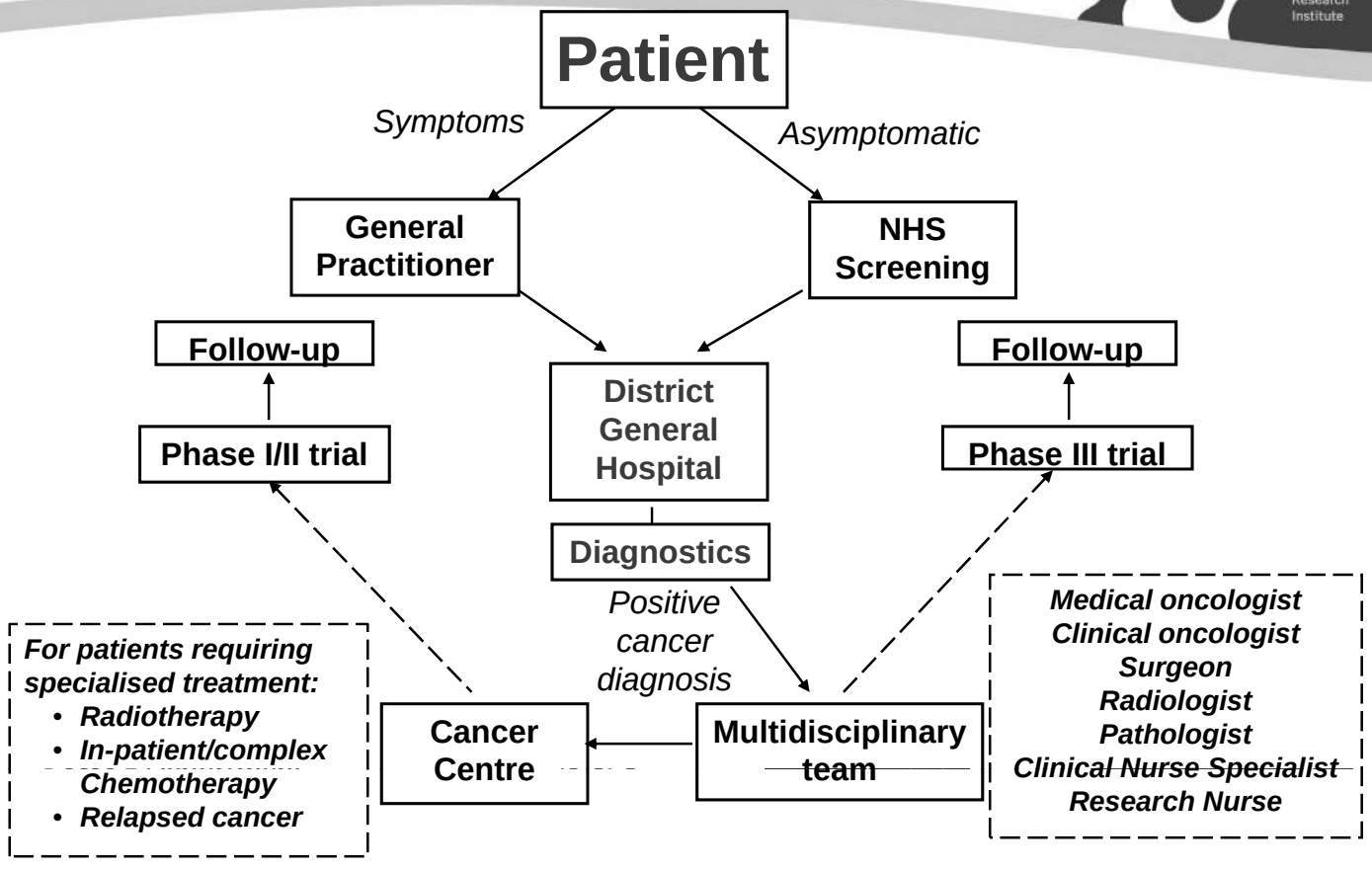
Summary

- Cancer Research UK
- Cancer treatment and cancer research in the UK
- How clinical trials are developed, managed and reviewed
- How the UK government supports clinical trials
- Partnerships with industry
- Achievements of the UK system

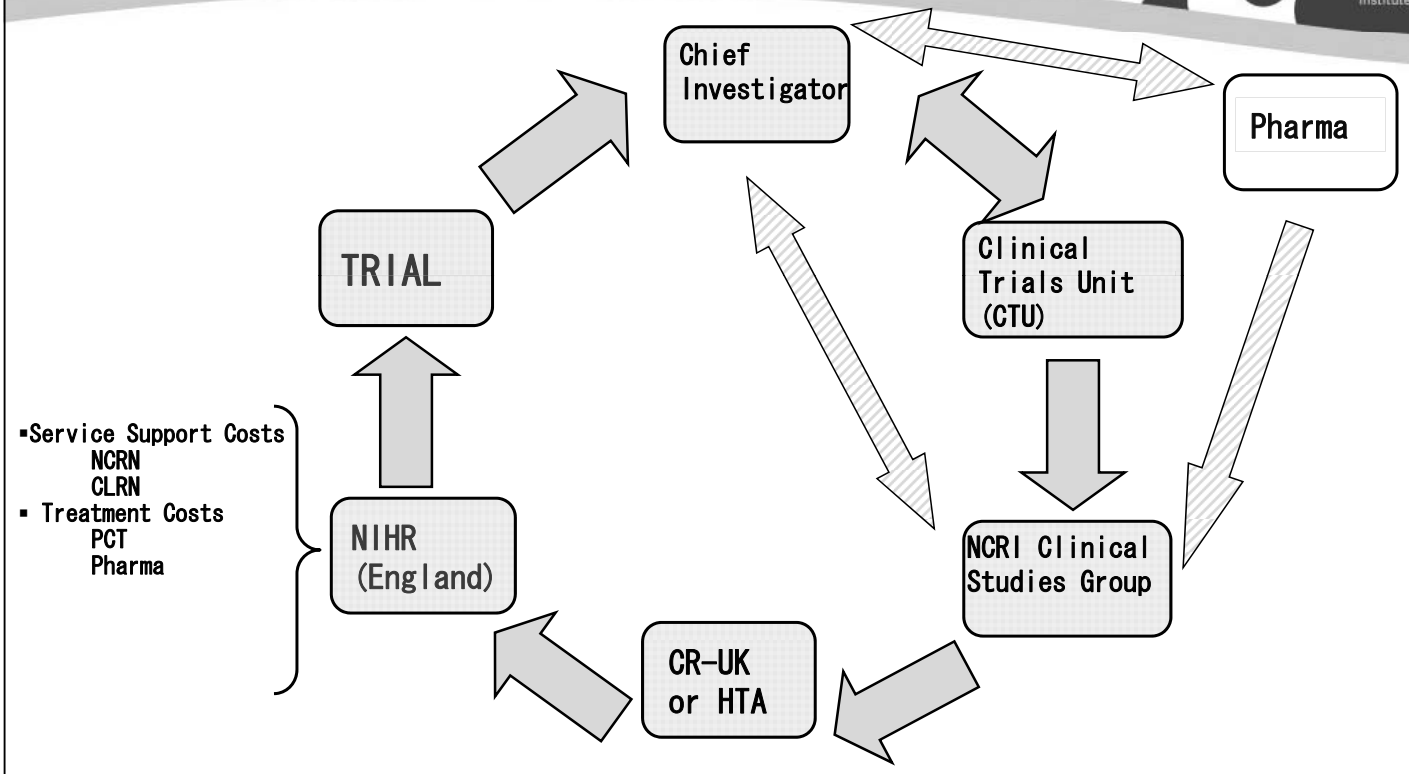
A bit about Cancer Research UK

- Cancer Research UK supports over 500 research groups in 38 towns and cities
- We are the largest charity funder of cancer research in the UK, spending £355m on research in 2009/10
- All funds are raised from the public
- We support five core funded Institutes:
  - London, Oxford, Cambridge, Manchester, Glasgow
- We spend around £18m directly on late phase trial grants
- We fund >200 nurses and >100 doctors
- More than 100,000 patients have been involved in our trials in the last 15 years

The patient journey in the National Health Service



Funding Clinical Trials in the UK

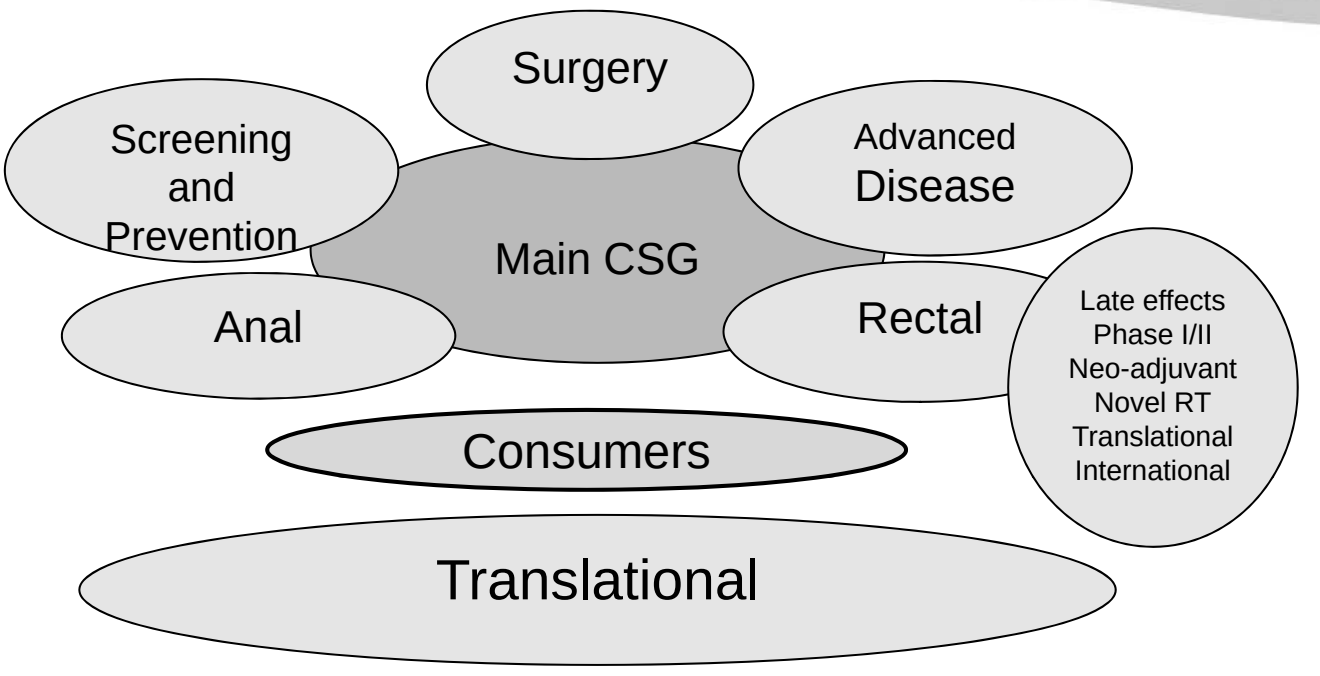


21 Registered Units with an interest in cancer

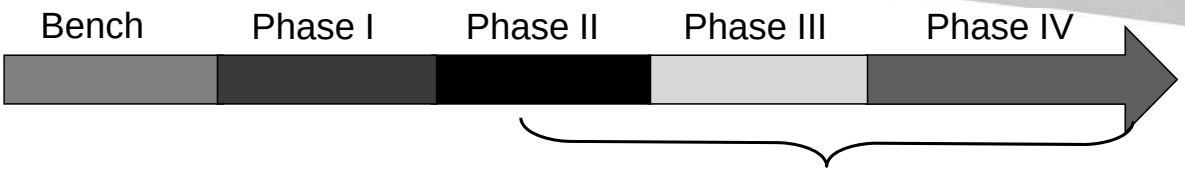
NCRI Clinical Studies Groups

- 22 Groups
- Expert involvement from across UK
- Central support under NCRN management
- User input on every group
- 15 tumour site specific
- Correlative Science
- Palliative Care
- New development groups:
  - Primary Care
  - Psychosocial Oncology
  - Complementary Therapies
  - Teenagers & Young Adults
- Consumer Liaison Group

NCRI Colorectal Cancer Clinical Studies Group



Clinical Trials Advisory & Awards Committee



Scheme: Clinical Trials project grants

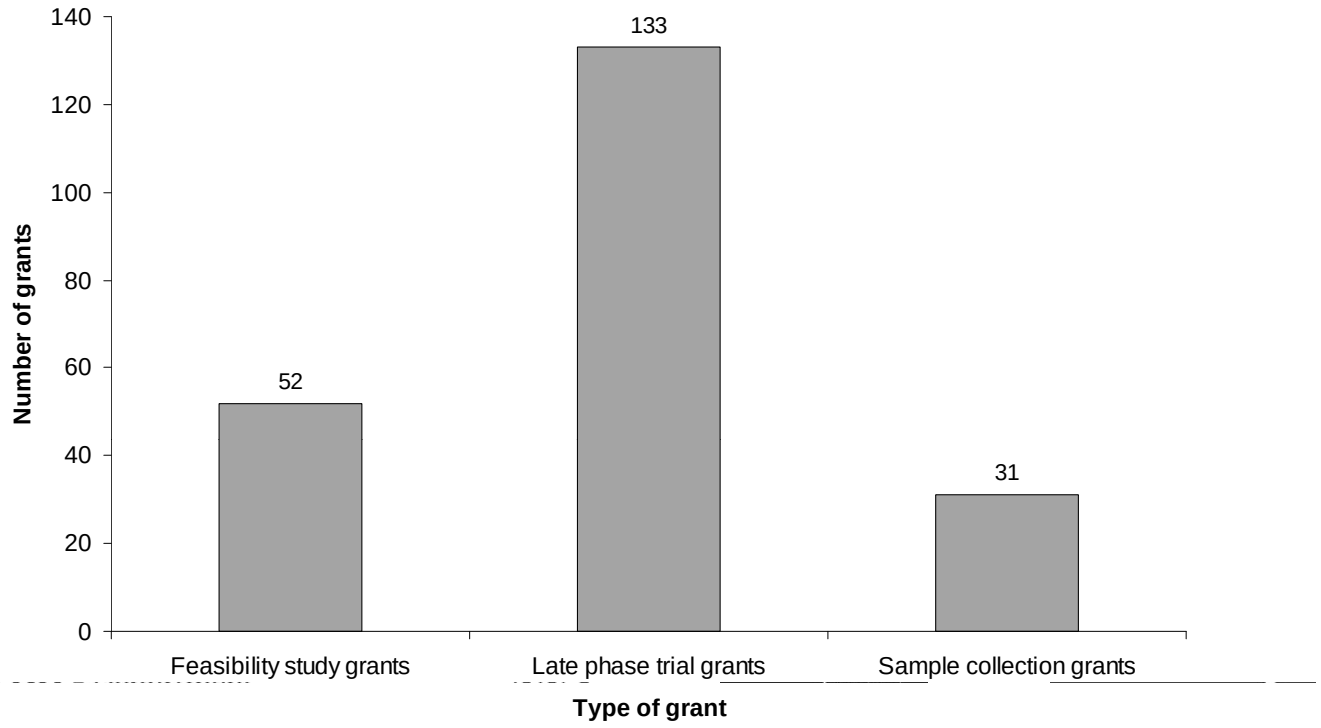
Length of funding: 2-10 years.

Level of support: Average of £85,000 per year

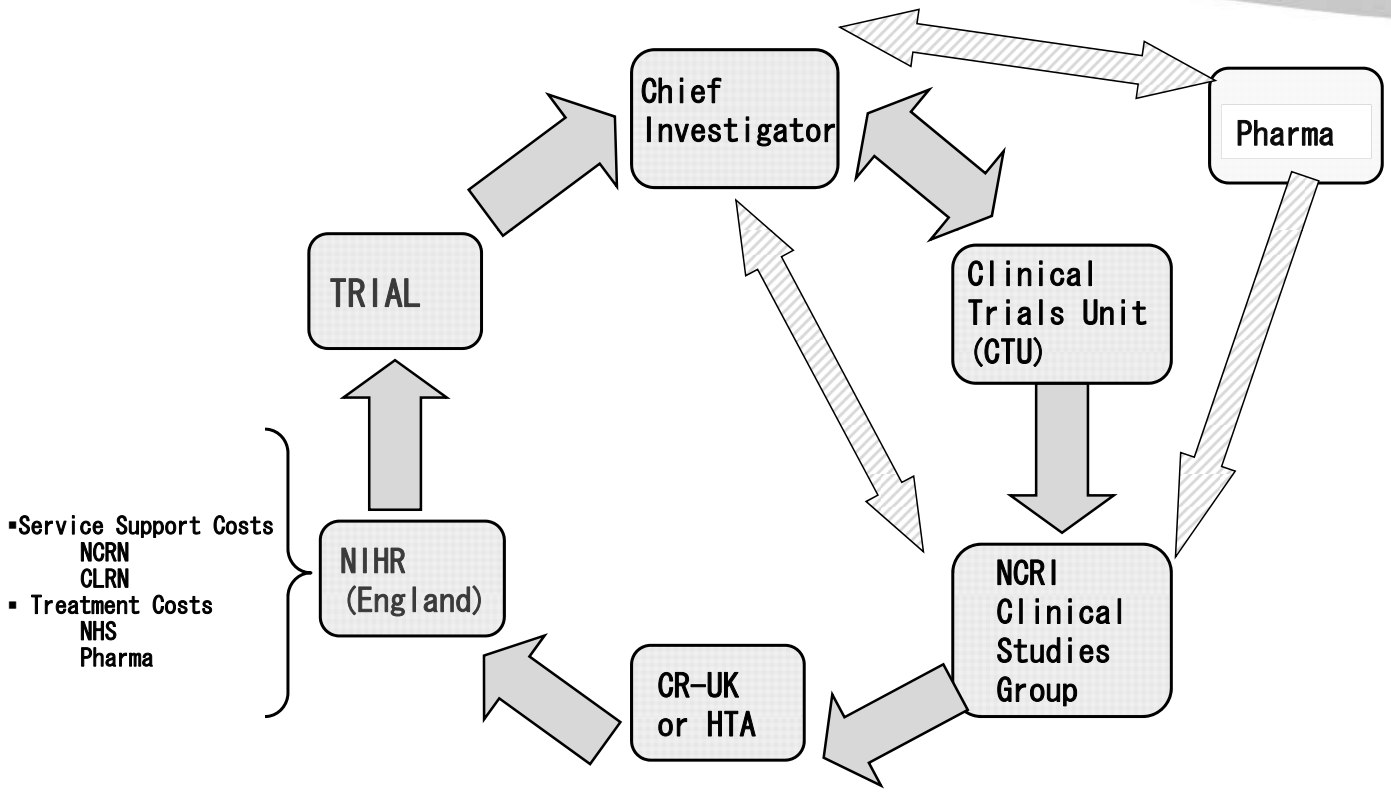
Remit of scheme: Phase II/III/IV clinical trials for all modalities and tumour types.

Portfolio: CRUK trials account for 70% of academic trials in UK (80% of RCTs)

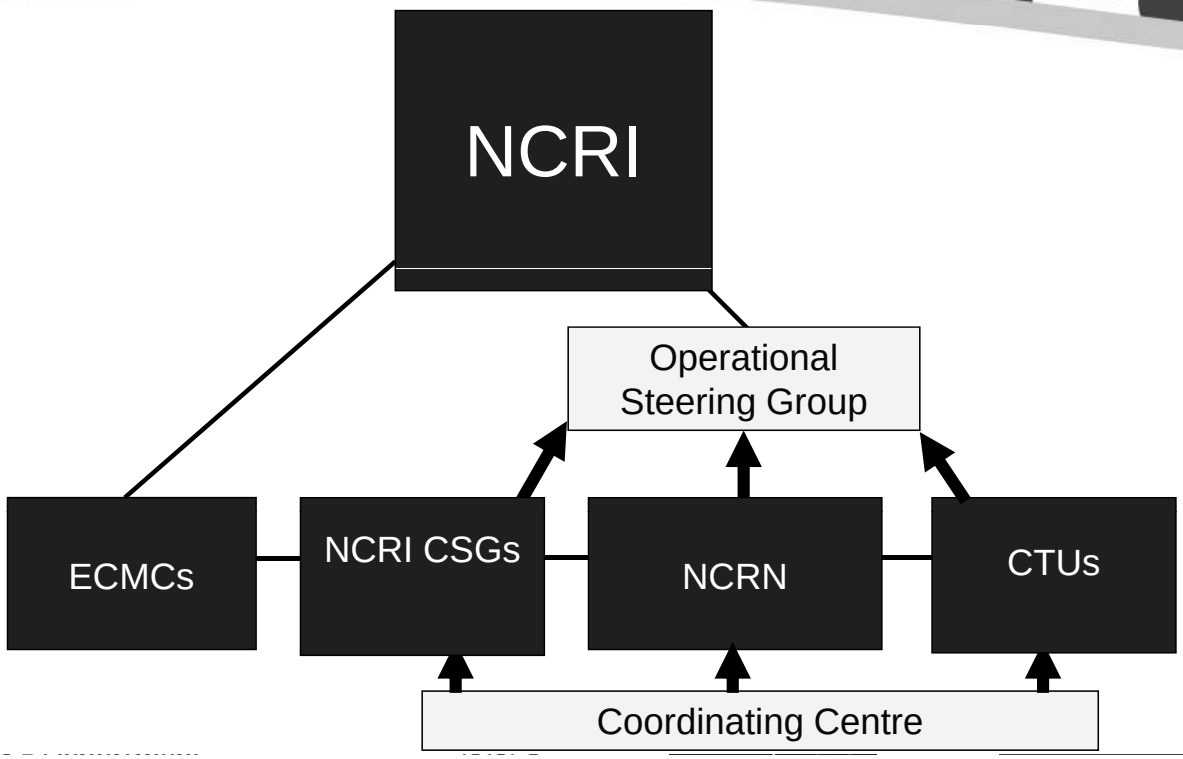
CTAAC Portfolio Summary (n = 216)



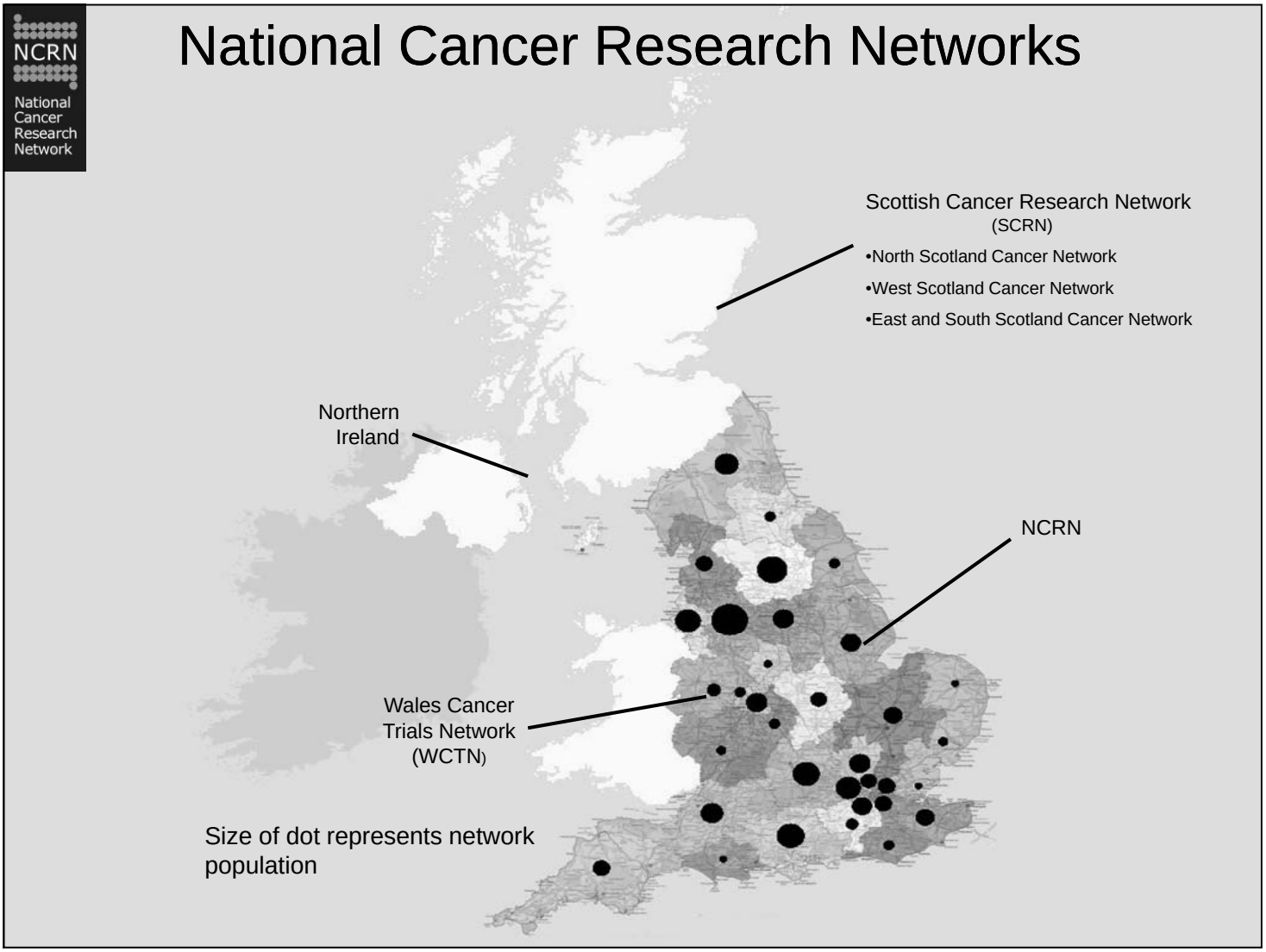
Funding Clinical Trials in the UK



Cancer Research Framework



National Cancer Research Networks



National Cancer Research Network

Aims

To ensure that patients and healthcare professionals from all parts of the country are able to participate in and benefit from clinical research.

•To integrate health research and patient care.

•To improve the quality, speed, and co-ordination of clinical research by removing the barriers to research in the NHS.

•To strengthen research collaboration with industry and ensure the NHS can meet the health research needs of industry.

National Cancer Research Network

Purpose

- To provide a world-class health service infrastructure to support clinical cancer research.
- To support and conduct randomized controlled trials of interventions (including prevention, diagnosis, treatment, and care) and other well designed studies for commercial and non-commercial sponsors. This includes pivotal licensing studies undertaken for industry on a transparent full-cost recovery basis.
- To play a key role in promoting the active involvement of patients and the public in research.

NCRN- Research Infrastructure

- Core support - £200,000 per million population
  - £16million across England, similar in Wales/ Scotland
- Mapped onto clinical practice networks
  - Centres and Units
  - Research becomes an agenda item
    - » Cancer Service Boards
    - » Individual tumour groups
- Multi-disciplinary team meetings/tumour boards
  - Discuss all NHS patients
  - Trial entry considered at this point

Clinical Research in NHS

- **Costing**
  - Research cost
  - Service support
    - » Accrual, safety reporting/tests
  - Treatment cost
    - » Cost of standard of care including diagnostics
- **Types of study**
  - Commercial – pay everything
  - Academic
    - » **Research cost** paid by research funder
    - » **Service support** paid by networks (NCRN)
    - » **Treatment cost** paid by NHS commissioners/Hospitals

Study Types

Pure academic funding

- Costs met entirely by charity (usually Cancer Research UK) or government grant (eg Health Technology Appraisal) and NHS

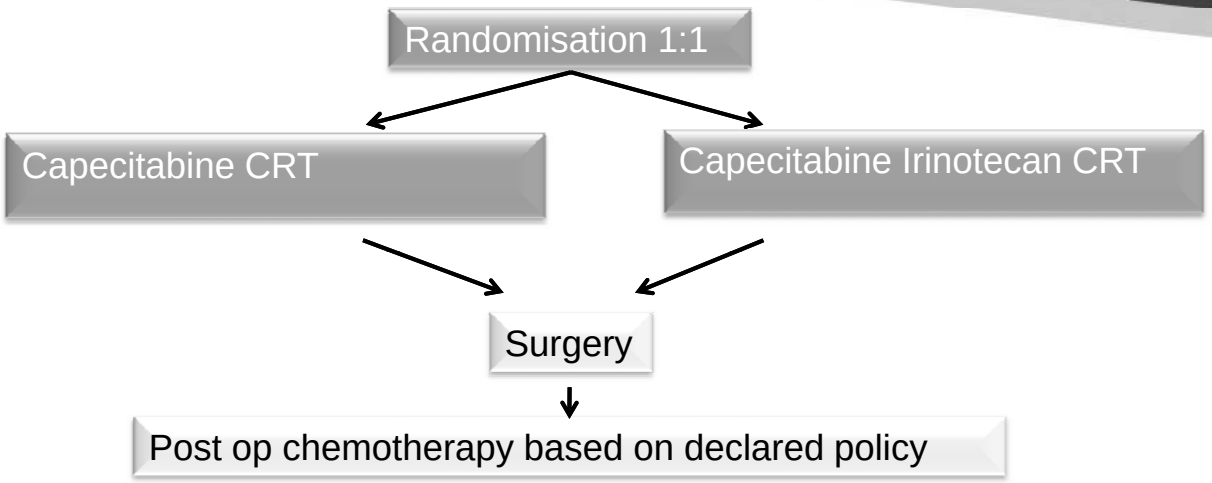
Academic with industry support

- Investigator initiated studies with drug supply met by industry. Possibly small grant to supplement charity and NHS
- NCRN-Industry partnership (AstraZeneca)

Commercial trial

- Adopted by NCRN
- Run independently of NCRN and NHR within UK hospitals

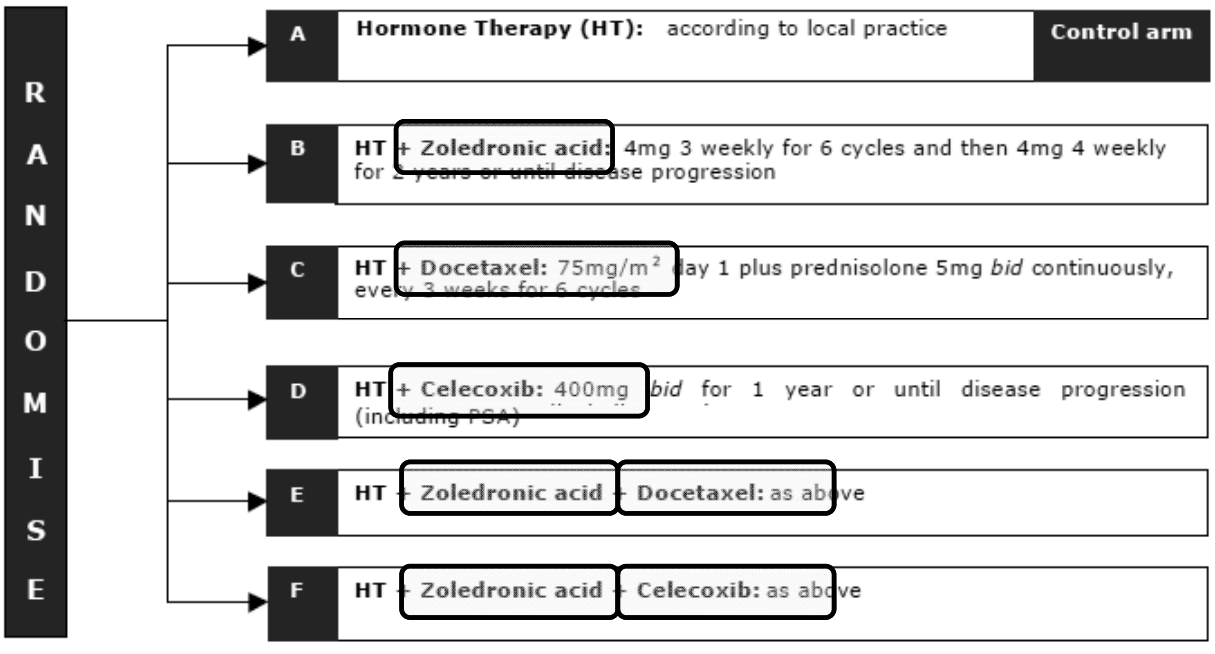
ARISTOLE - for locally advanced Rectal Cancer



- No commercial support
- Trial management funded by CR UK
- Drug supply from hospital stock

STAMPEDE

Systemic Therapy in Advancing or Metastatic Prostate Cancer: A 5-stage 6-arm Randomised Controlled Trial



Industry Trials in NCRN

- Effective collaboration with the UK pharmaceutical, biotech & device industries is a founding principle of NIHR (now a parent organisation of NCRN)
- Trials need not come though or use the networks, but it is intended to be advantageous to do so
- NIHR working with UK Dept of Health and industry partners to improve the clinical research environment for industry in the UK – and in the process improve the research environment for all clinical research
- **Investigator-led trials** and **Industry-led** within the same overall portfolio

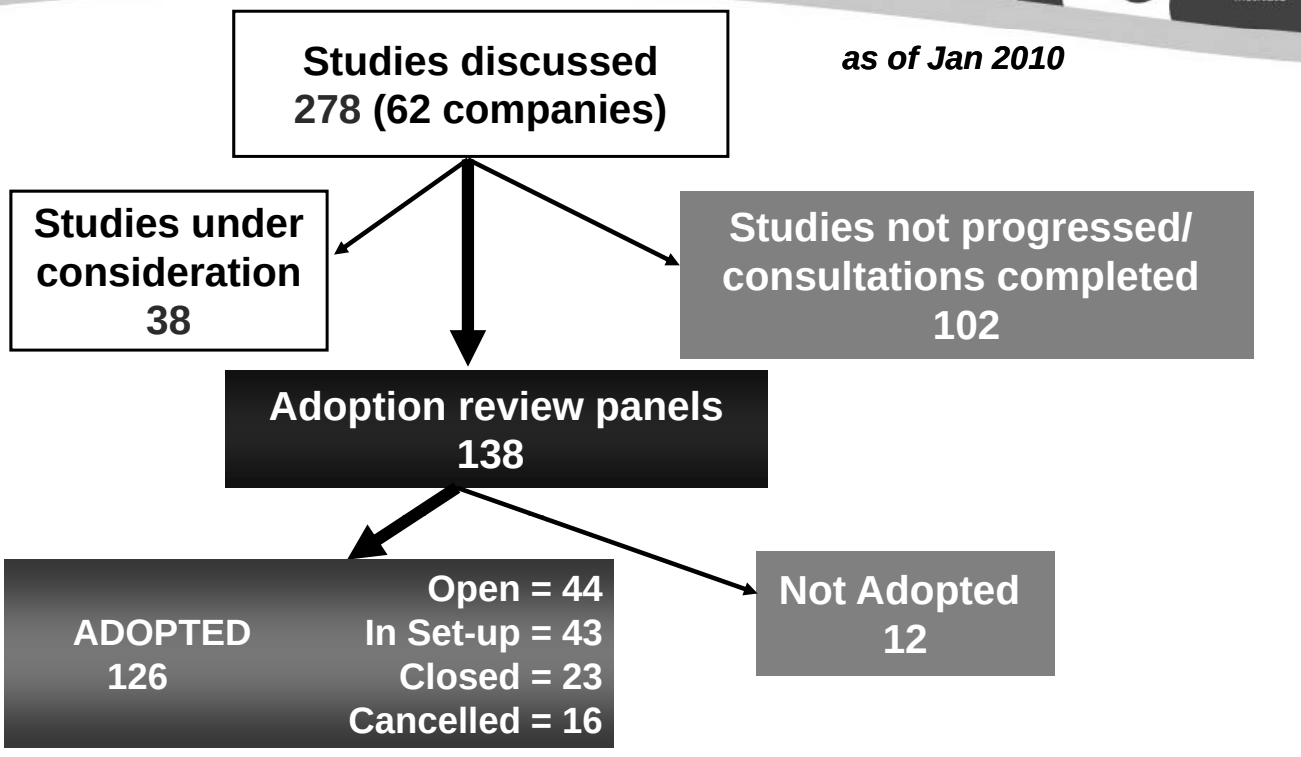
NCRN- AstraZeneca Initiative

- Partnership for access to novel agents that provide reasonable promise for advancing therapy, particularly where there are special opportunities
  - Outside primary AZ development plans
  - Primarily randomised phase II trials- Investigator Initiated Trials ~10-15 per year
  - Earlier phase studies, especially combinations
  - AZ supply drugs, knowledge of compound and partial funding
  - NCRN (CSGs/CTUs/ECMCs) provide intellectual expertise and operational capability

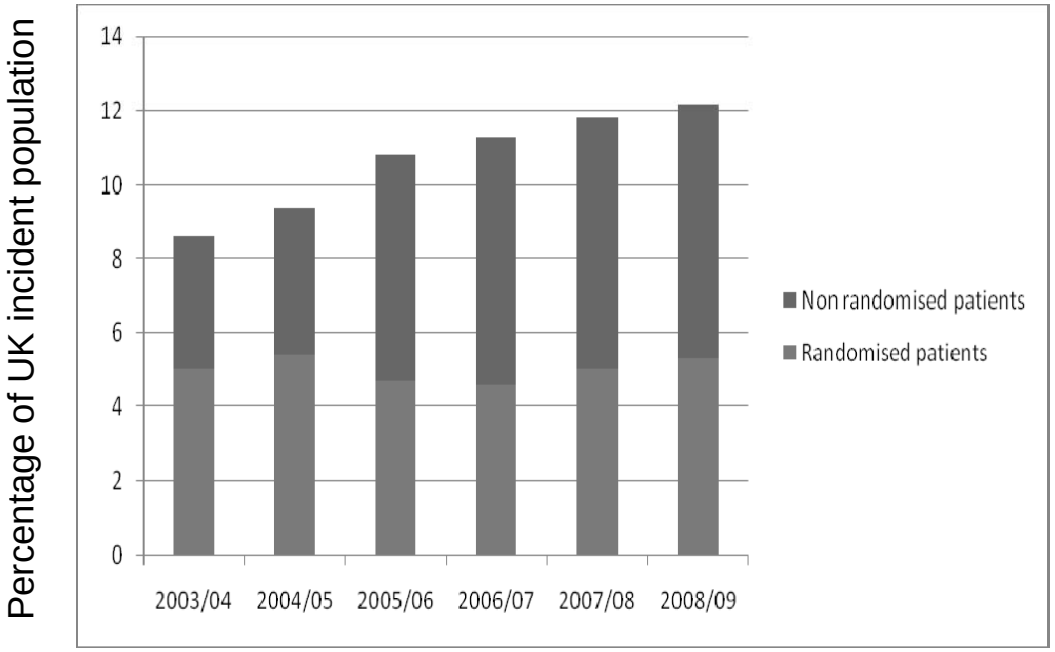
ABC-03
Advanced Biliary Tract Cancer

- Academic study, sponsored by University/Trust
- Managed through CTU
- Funding support (Research) Cancer Research UK/Astra Zeneca
- NIHR portfolio study with service support and treatment costs NHS

NCRN Industry-led Adoption Activity

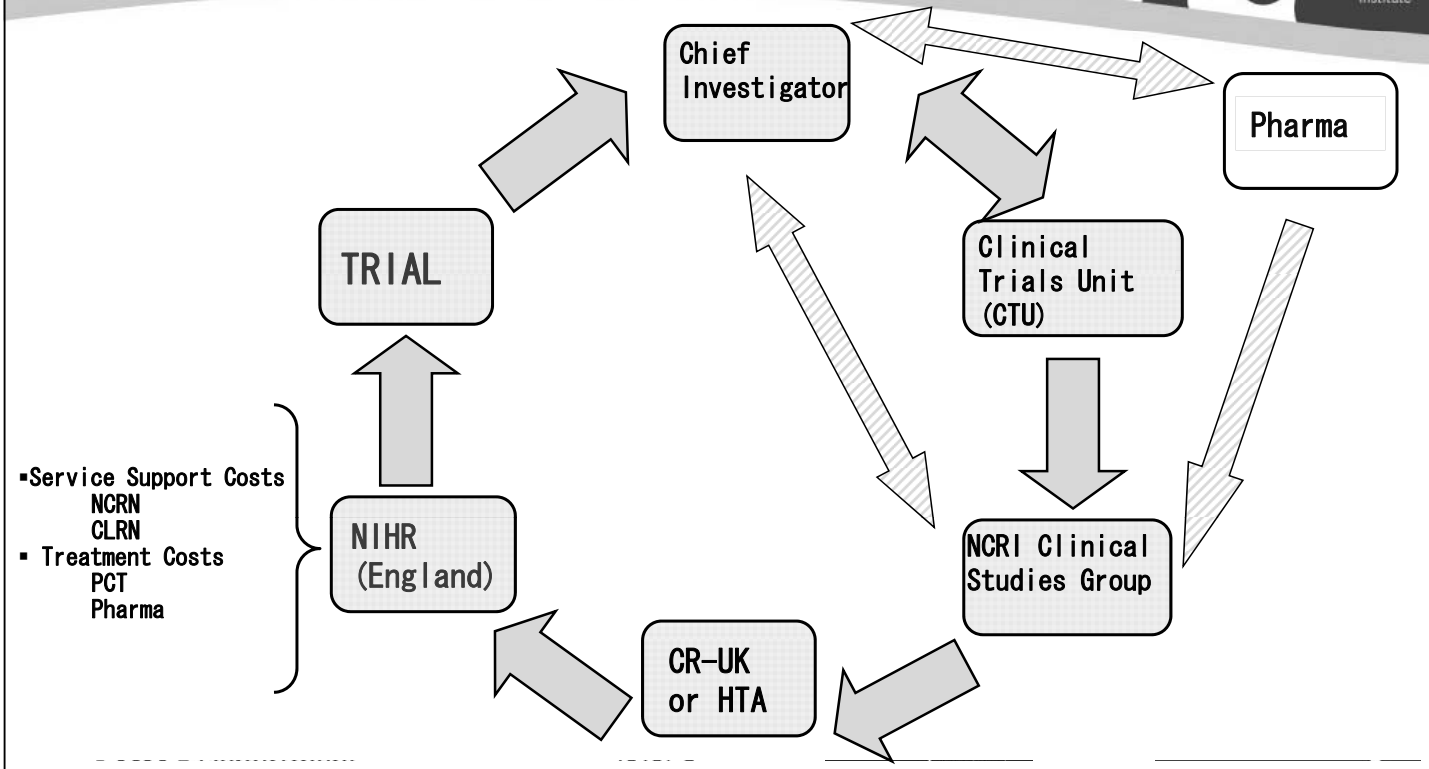


Demonstrated capability



336 open studies including 176 randomised trials in over 170 sites

Funding Clinical Trials in the UK



UK Advantages – NCRN studies

- DH funded core research staff infrastructure embedded in NHS
- A high degree of coordination via national forums for strategic planning, but local priority setting
- Highest rate of cancer trials accrual of any country
- A trials ‘culture’: ~14% of cancer patients in trials
- Strategic alignment of charity & government funders
- DH and NCRN commitment to industry partnership
- One unique UK role is testing novel agents in settings with little exposure to other recently licensed agents

Also:

- Potential for nationwide clinically annotated specimen resource
- Potential for comprehensive epidemiological, demographic, outcomes, & resource utilisation data

NCRI Partners

abpi

AICR
Cancer knows no boundaries. Fortunately, neither do we.

bbsrc

wellcome trust

Leukaemia & Lymphoma Research
BEATING BLOOD CANCERS

CHIEF SCIENTIST OFFICE

BREAST CANCER BREAKTHROUGH

breast cancer CAMPAIGN
researching the cure

WE ARE MACMILLAN. CANCER SUPPORT

E·S·R·C ECONOMIC & SOCIAL RESEARCH COUNCIL

Fighting Britain's biggest childhood cancer
CHILDREN with LEUKAEMIA

LUDWIG INSTITUTE FOR CANCER RESEARCH

THE ROY CASTLE LUNG CANCER FOUNDATION

tenovus
the cancer charity

HSC Public Health Agency

Marie Curie Cancer Care

Llywodraeth Cynulliad Cymru
Welsh Assembly Government

yorkshire cancer research

DH Department of Health

MRC Medical Research Council

CANCER RESEARCH UK