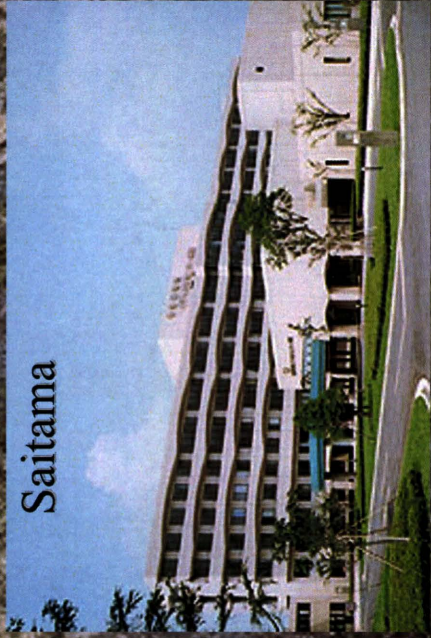


Hospitals in Kitasato



Saitama



Kanagawa



Tokyo



Players in clinical trials at Kitasato

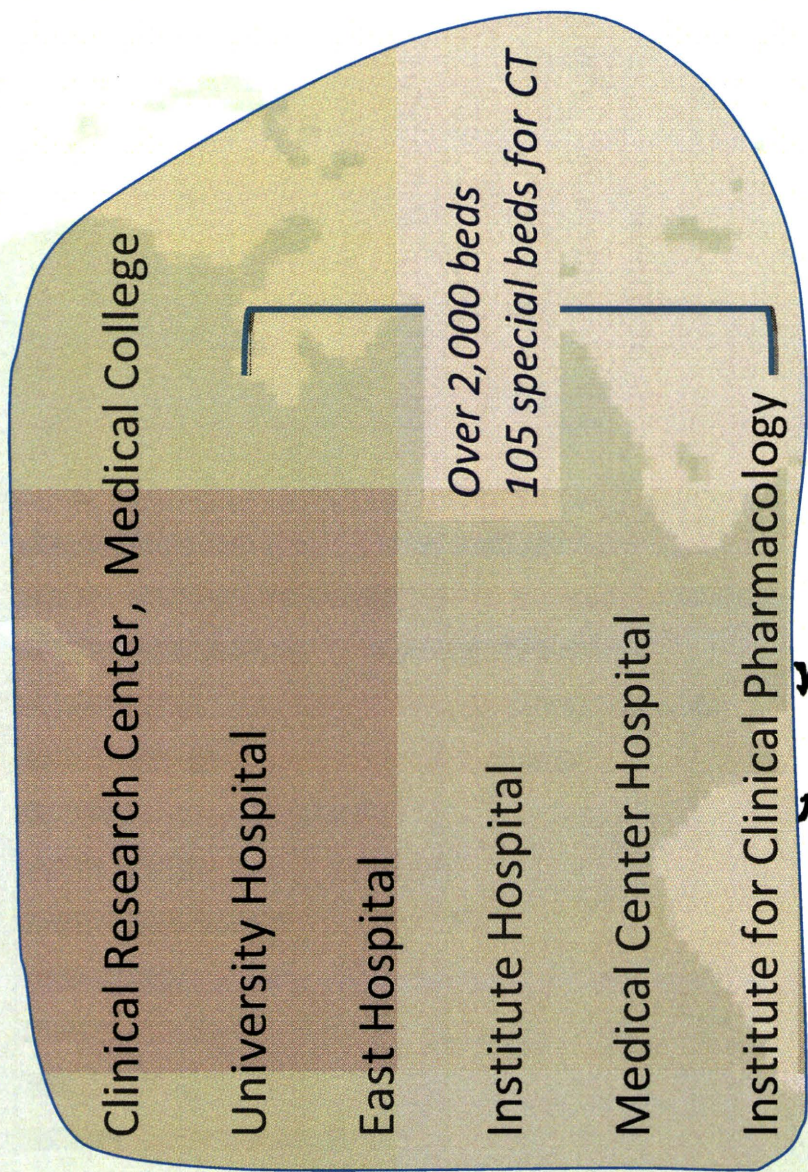
- 4 general hospitals
 - University Hospital
 - University East Hospital with 1 CP unit
 - Institute Hospital
 - Medical Center Hospital
- 1 specific center for clinical pharmacology

J-GCP requires each admin process for individual facilities.

4 IRBs are set in the Kitasato.

IND and NDA are not separated in Japan, and not a few ethics committee are in Kitasato.

Facilities of Clinical Trials in the Kitasato Institute



Chair of trustee boards

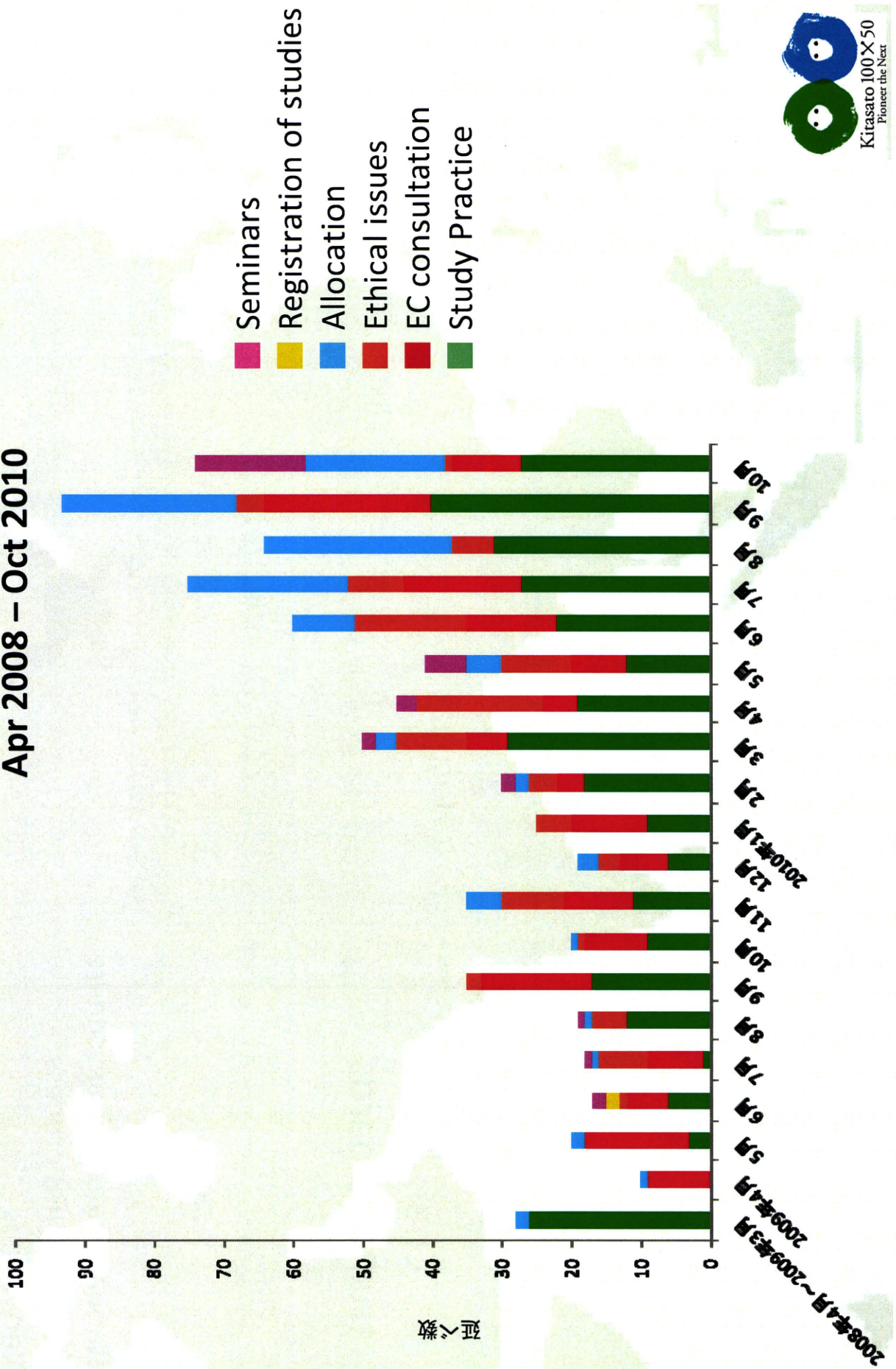
- Standardization of procedure
- Managing IRB process
- Networking
- Business development

Kitasato Academic Research Organization
(Kitasato ARO, KITARO)

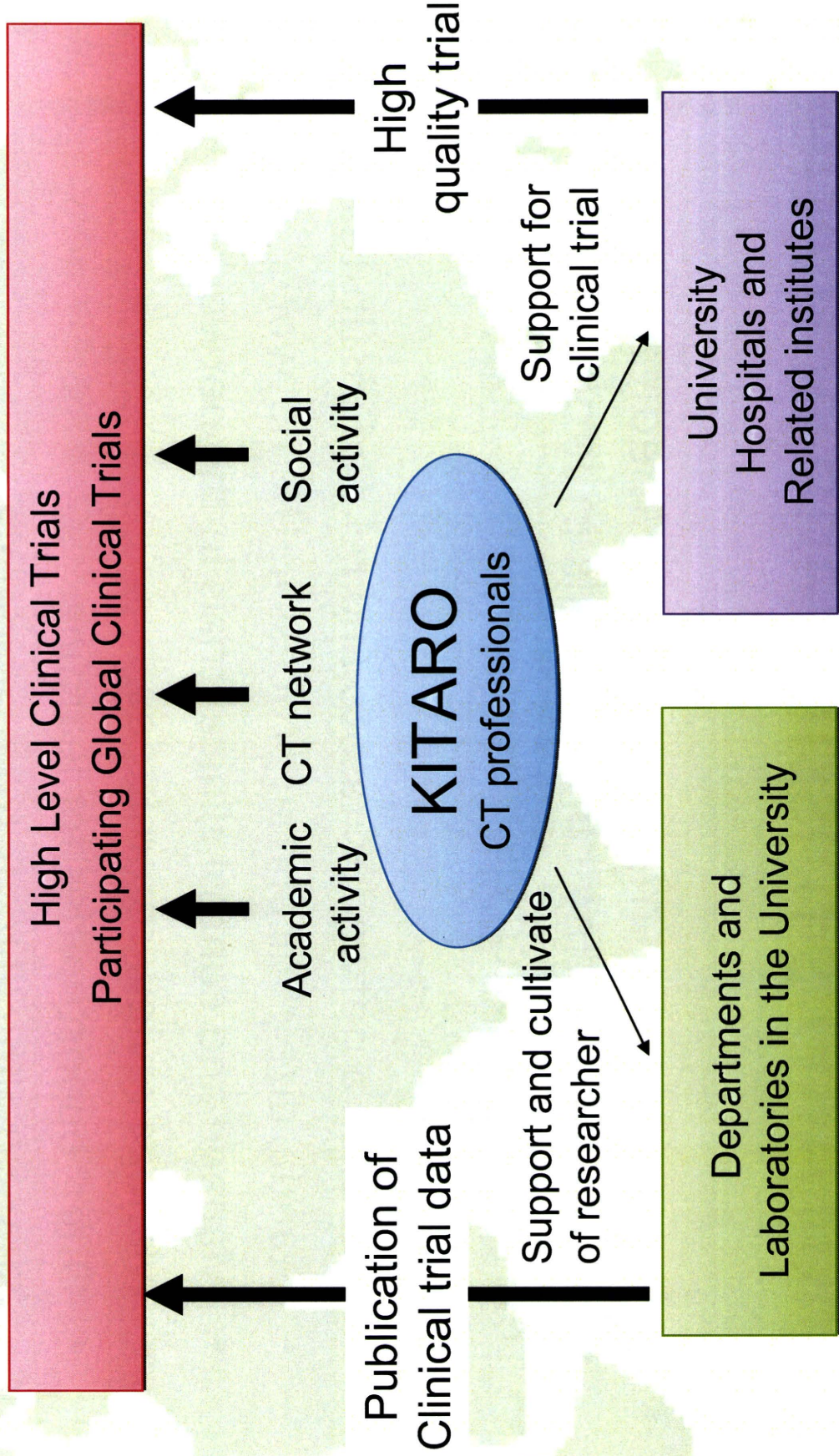


Activity of Kitasato Clinical Research Center

Apr 2008 – Oct 2010



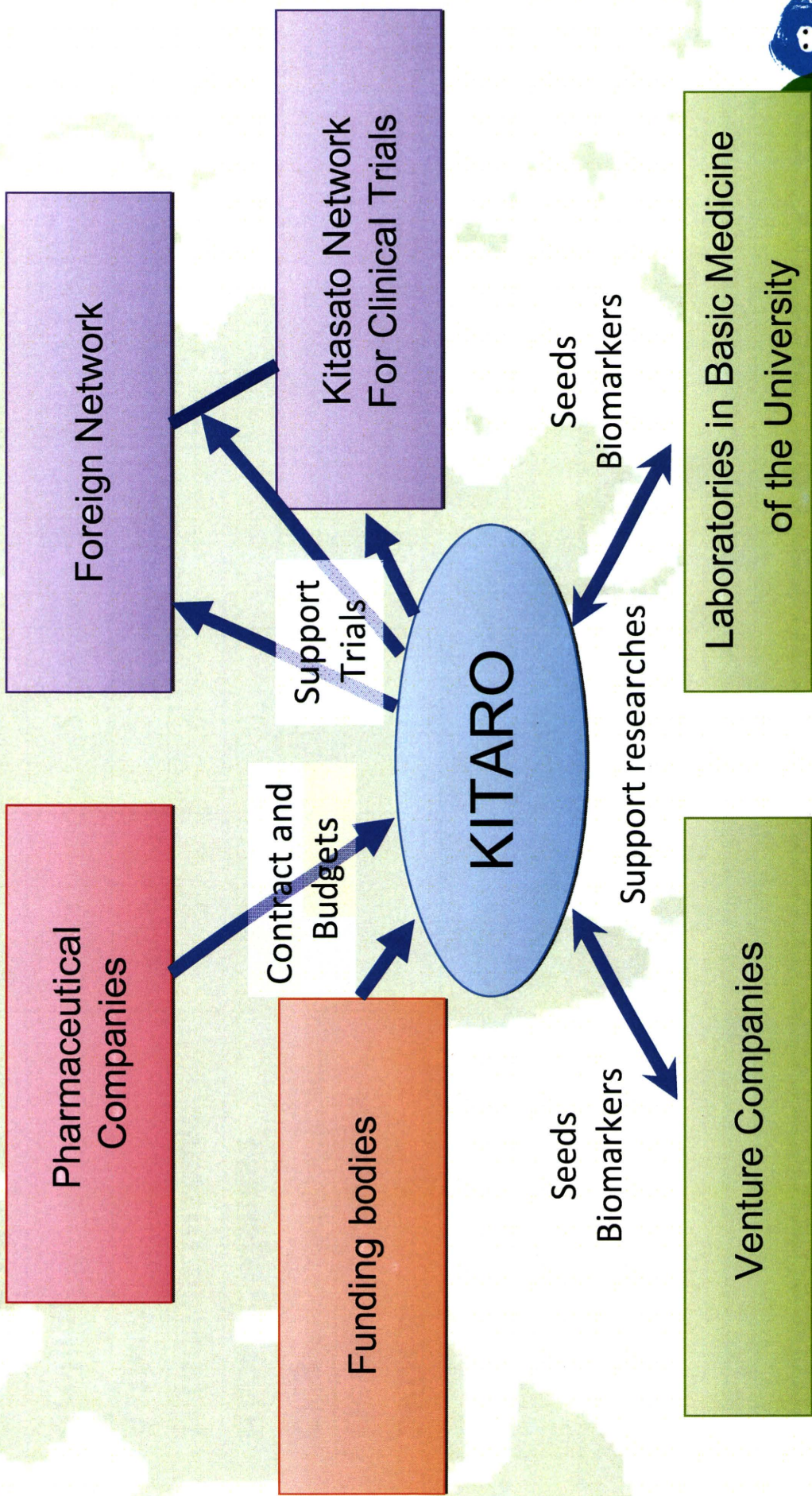
Role of KITARO in Kitasato University



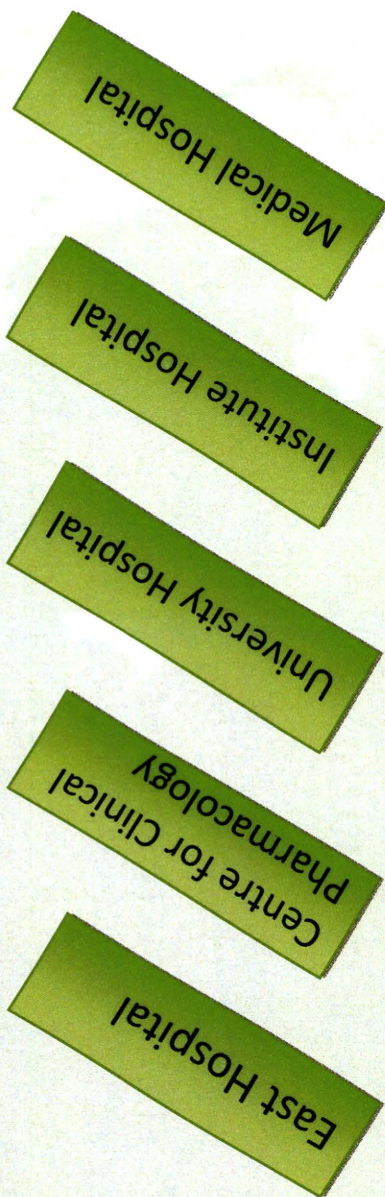
KITARO's mission and activities

- To contribute to improvement in medical quality through promoting clinical trials in Japan and Asia by the activities such as,
 - Establish a network Kitasato and related institutes in Japan.
 - Standardize clinical trial process in the network.
 - Manage and control clinical trials in the network.
 - Manage review committees.
 - Offer opportunities for learning.
 - Support clinical trials from academia.
 - Establish collaboration with foreign bodies.

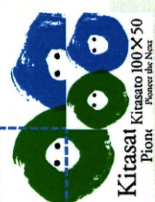
KITARO in Drug Development



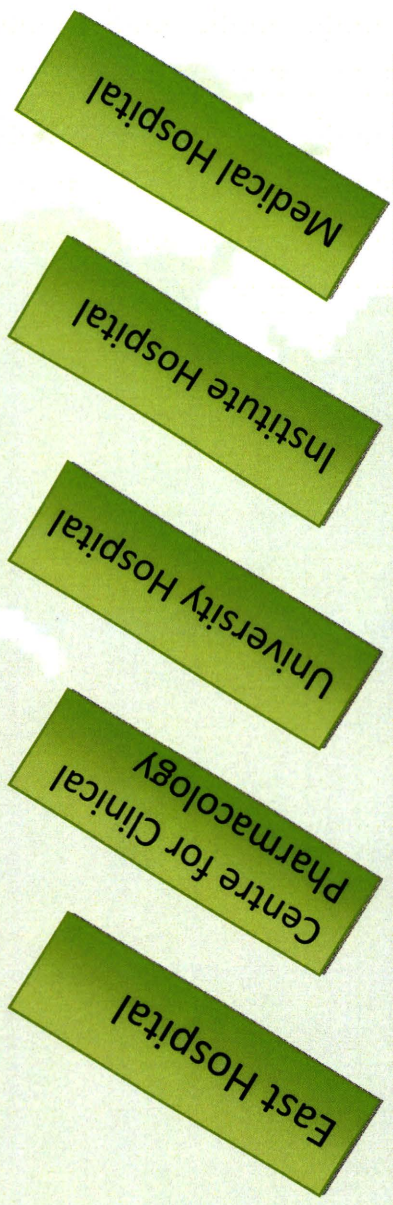
Studies Conducted in Kitasato Clinical Facilities in FY2010



	East Hospital	Centre for Clinical Pharmacology	University Hospital	Institute Hospital	Medical Hospital
CVDr & Metabolic Disease	4	2	2	1	—
CNS	12	10	7	—	4
Hepatic Disease	1	0	—	—	—
Infection Disease	2	4	—	1	—
Asthma	3	2	—	1	—
Urology	2	2	3	0	—
Oncology & Hematology	7	1	5	0	—
Other Area	9	10	—	—	—
Diagnosis	1	0	2	—	—



Studies Conducted in Kitasato Clinical Facilities in FY2010

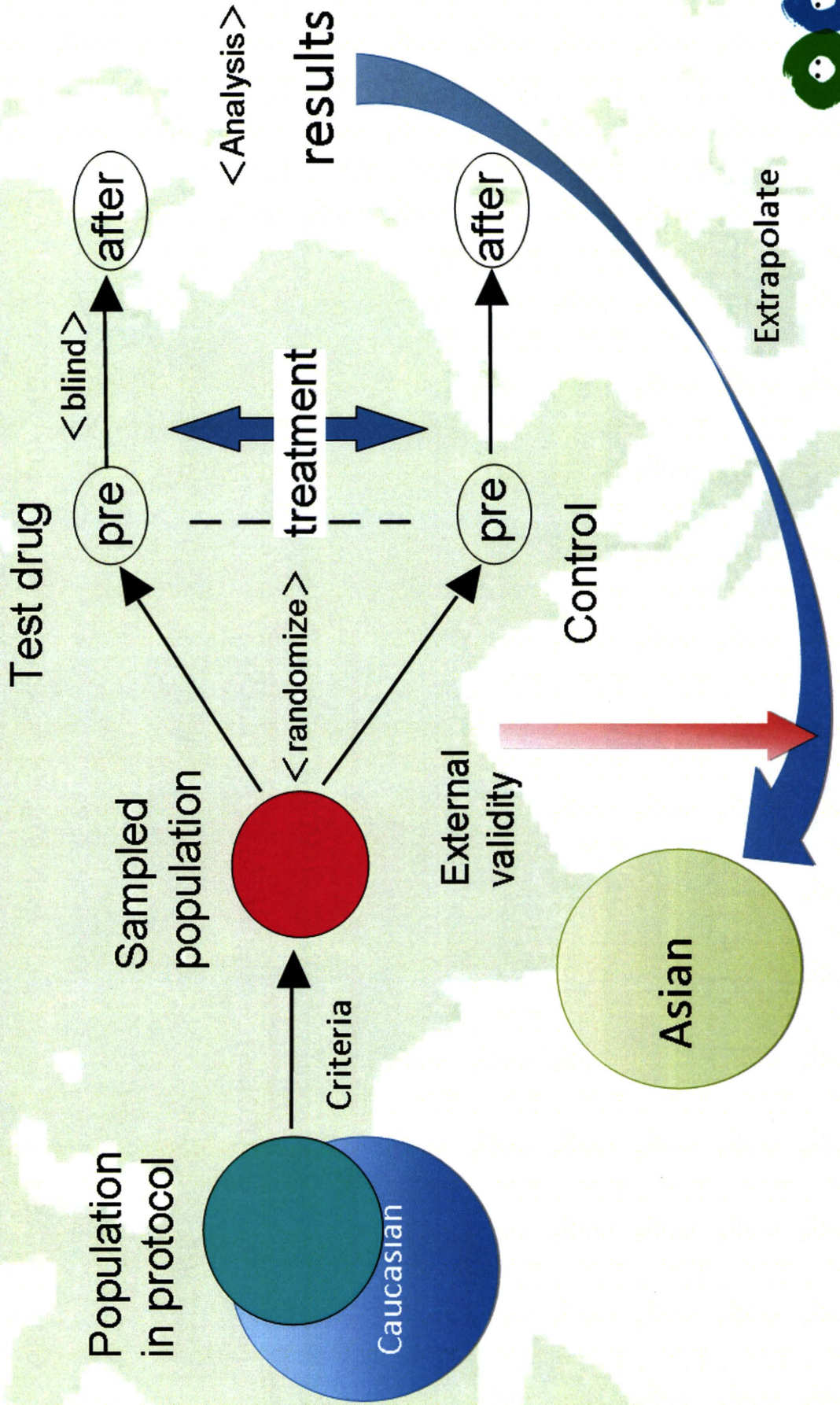


Phase-I	13	11	2	1	0
Phase-II	2	1	3	2	0
Phase-III	9	1	13	0	4
Phase-IV	0	1	2	0	0
Bioequivalency	1	11	0	0	0
Clinical Pharmacology	1	1	0	0	0
Pharmacokinetics	2	4	0	0	0
Drug Interaction	0	1	0	0	0

Why koNECT and KITARO?



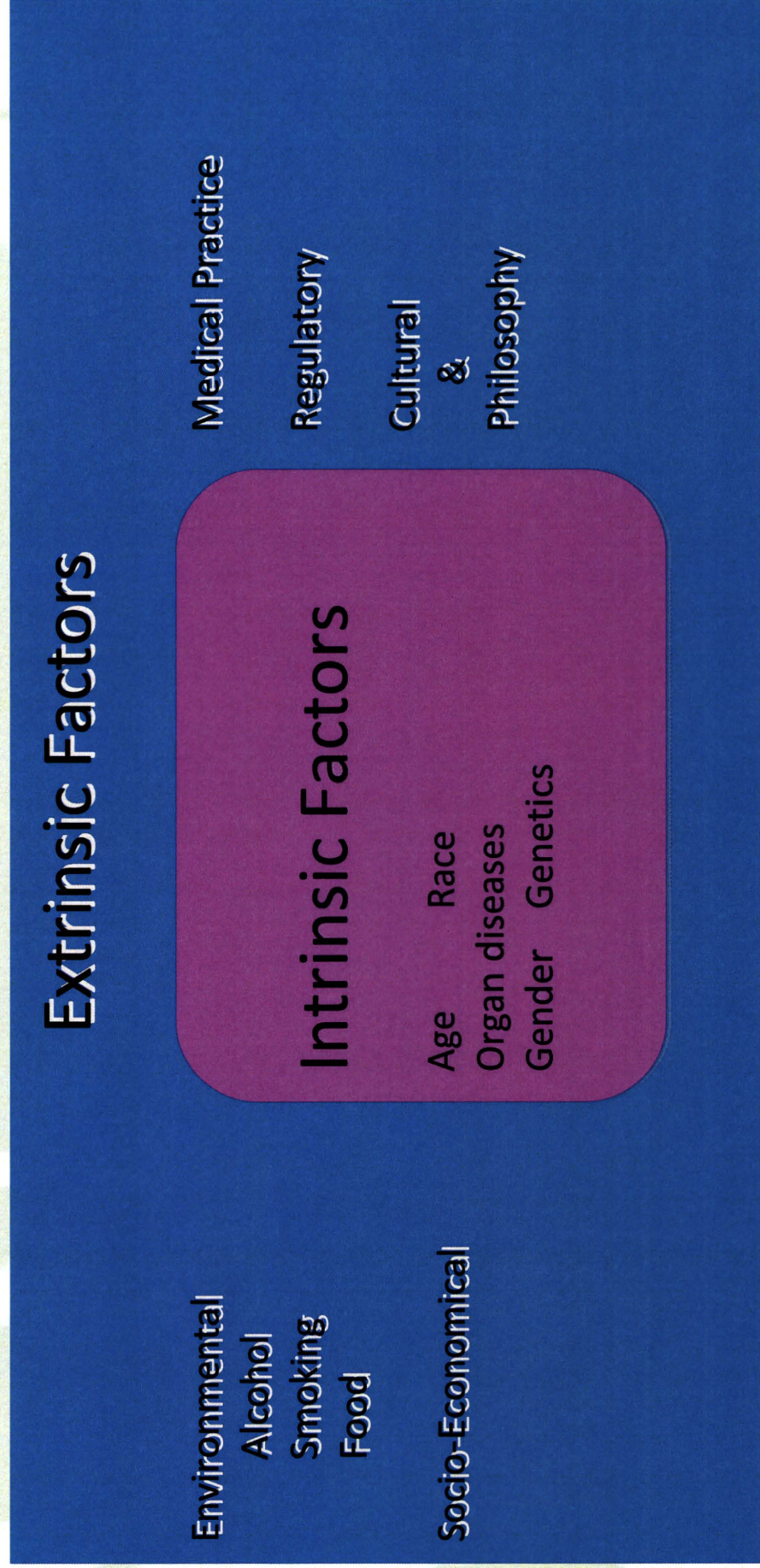
Can the results be applied to Asian?



Examples of recent FDA drug product labeling that included ethnicity or genetic information

Drug products	Ethnicity information	Genetic information
Isosorbide dinitrate-hydralazine (BiDil)	Indicated for self-identified blacks	
Angiotensin II antagonists and ACE inhibitors	Smaller effects in blacks	
Rosuvastatin	Lower dose for Asians	
Tacrolimus (Protopic)	Higher dose for blacks	
Warfarin	Lower dose for Asians	Lower initial dose for CYP2C9- and VKORC1-sensitive variants
Carbamazepine (Tegretol)	Box warning for Asians with variant alleles of HLA-B*1502	Box warning for Asians with variant alleles of HLA-B*1502

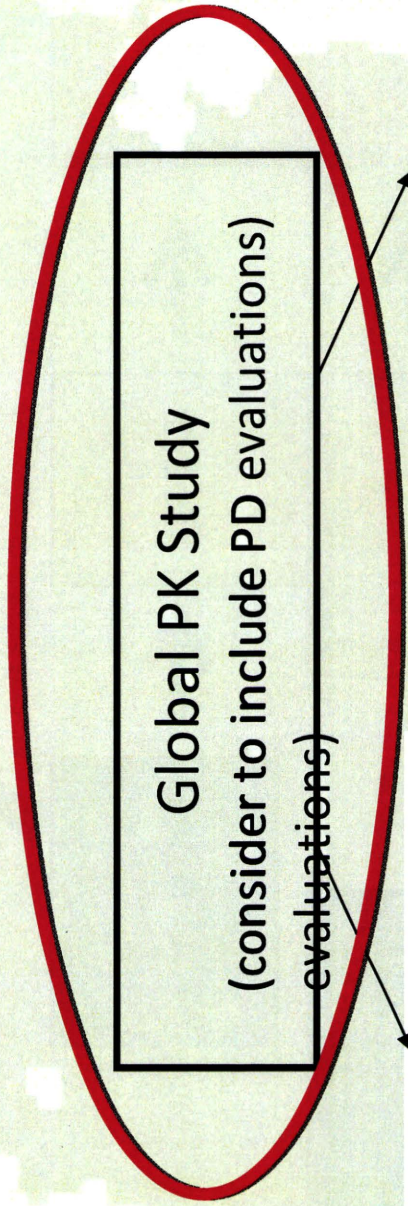
Intrinsic and Extrinsic Factors



Similarity between countries

- Intrinsic factors;
 - Genetics
 - Disease epidemiology
 - Body size
- Extrinsic factors;
 - Culture chopsticks!
 - Food
 - Level of science, social life

Importance of PK-PD Trial



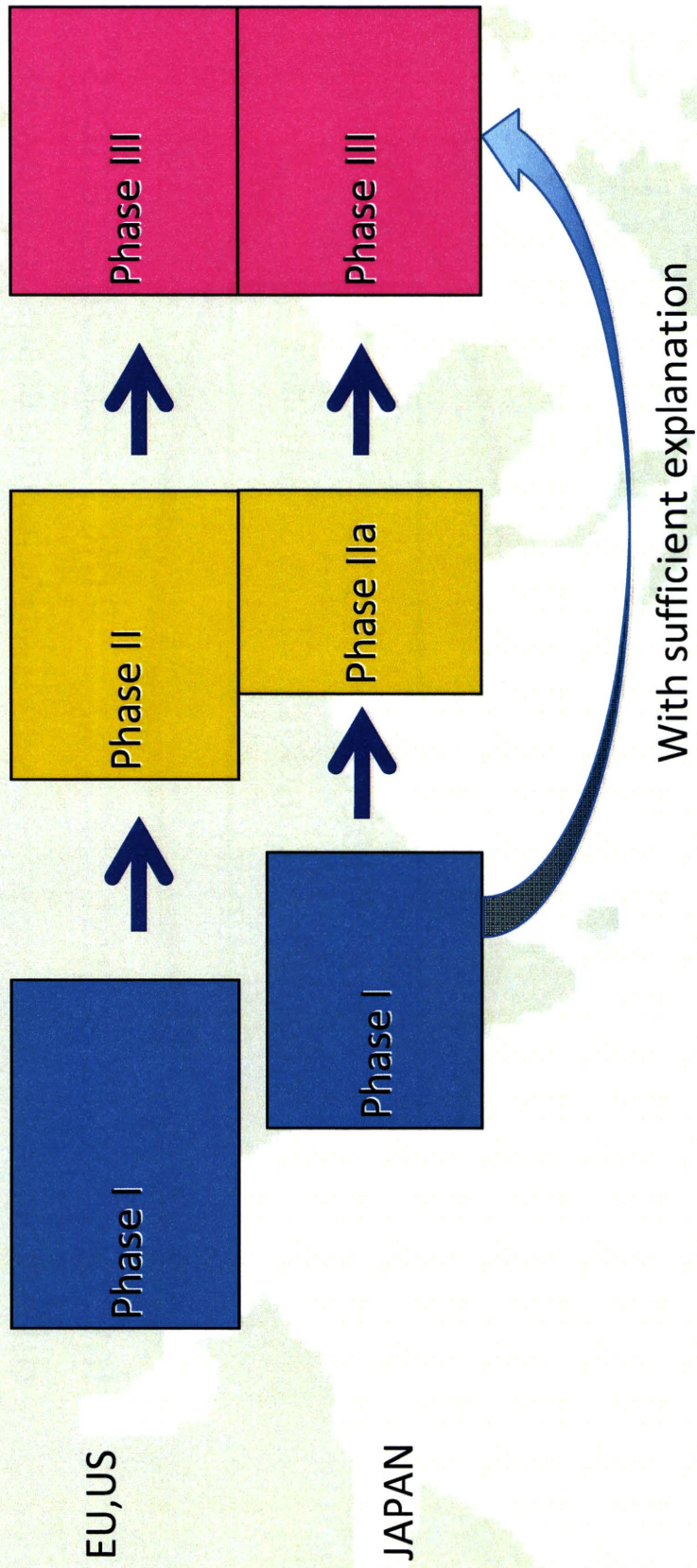
Impossible to adjust differences

Adjustable Differences
(Including cases to show PK similarity and correlation of PD and clinically relevant PD)

Global Dose Finding Trial
(Dose-Relationship comparison)

Global Confirmatory Trial

Possible Approach to Acceleration



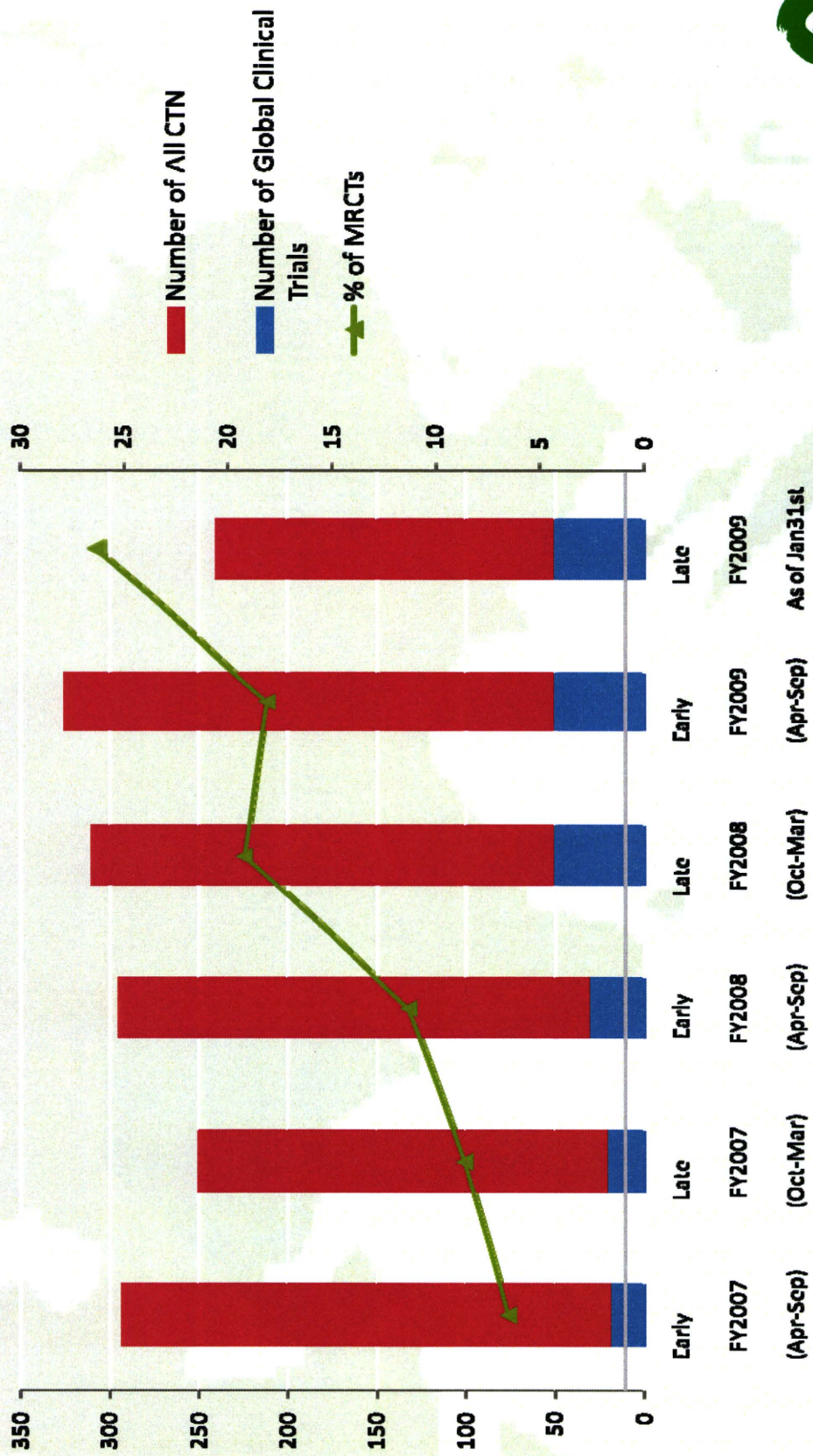
Future Strategy for Global Development



Key of success may be

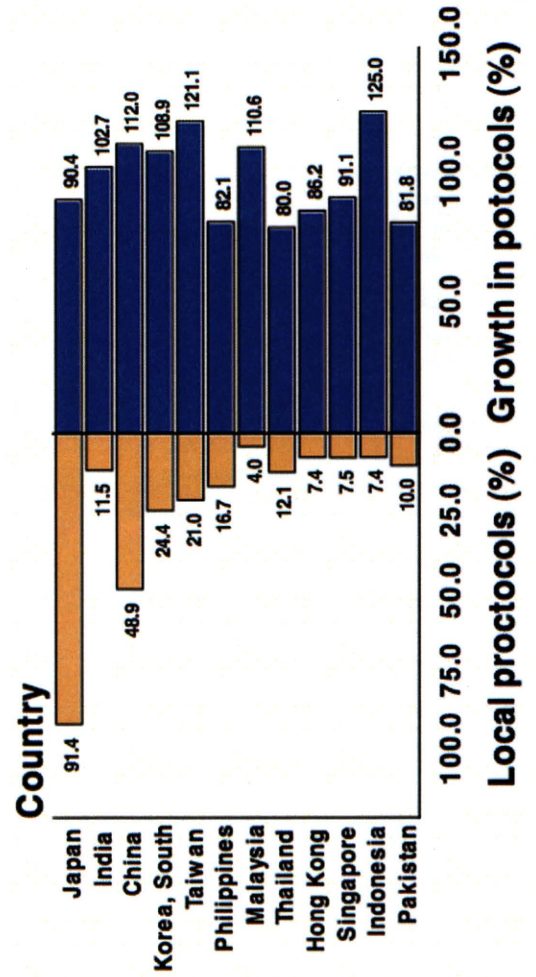
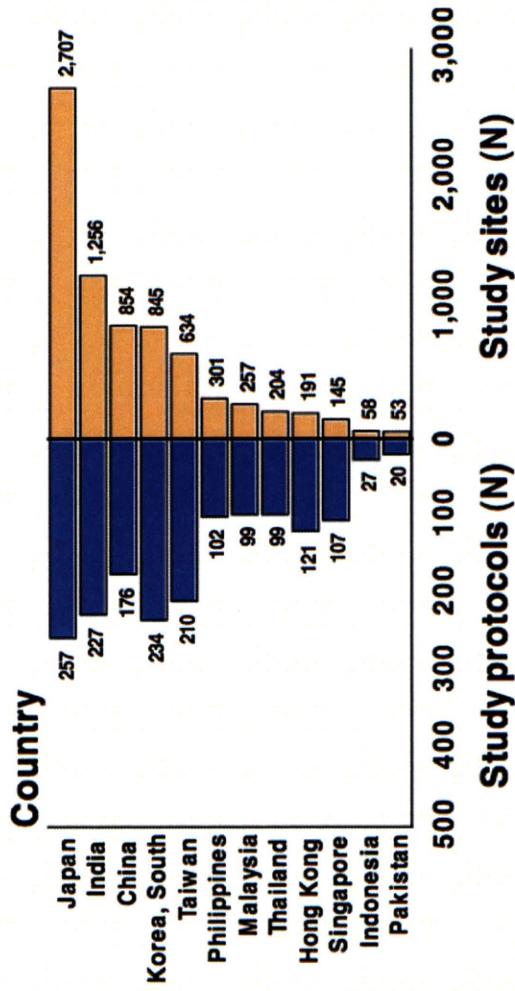
0. Preparation for global development at preclinical stage
1. Simultaneous development in each area
2. PK/PD bridging among ethnicities using biomarkers

Trends of Global Clinical Trials including Japan — Percentage —



Number of CT sites in Asian countries

Source: Clinical Trial Magnifier Vol. 1:5 May 2008



CT activity in Asian cities

Source: Clinical Trial Magnifier Vol. 1:5 May 2008
www.ClinicalTrialMagnifier.com

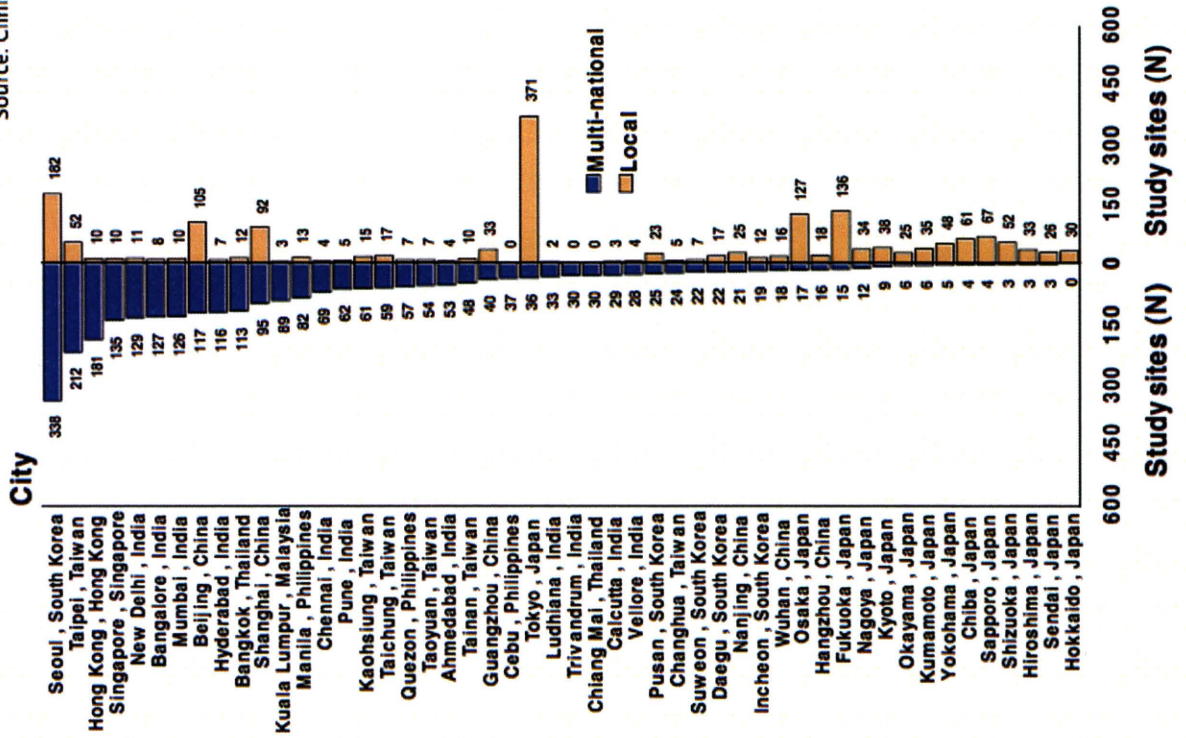


Figure 4. The chart includes the number of study sites for both multi-nationally (ranking measure) and locally conducted industry sponsored clinical trials for each of the top 50 most active Asian cities (from Table 5).

