

An Approach for the Total Amendment of 'Ethical Guidelines for Clinical Studies' in Japan

-Development of a Systematic Educational Program-

CPS 4C Ethical Issues

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Outline of Today's Talk

- Review: CPS in 2006
Clinical Trials in Japan
"Un-notified trials" ?
- Total Amendment of 'Ethical Guidelines for Clinical Trials' in Japan
- Systematic Educational Program
- Summary/Conclusion

A striking contrast in Japanese clinical trials with new drugs

IND trials (*Chiken*)

- Strictly regulated by the Pharmaceutical Affairs Law and MHLW ordinance
- Necessary for notification to PMDA
- Participants' bodily injury must be compensated
- Insurance package prepared by casualty insurance co.
- Public healthcare system can be applied

"Un-notified trials"

- No legal regulation "ethical guideline" (2003)
- IEC level varies among the institutions
- No compensation for participants' bodily injury
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- The National Research Act is required

Murayama, et al. 27th Annual Meeting SCT, CPS Ethical Issues, Orlando, 2006

Intervention Study = Clinical Trial in Japan
prevention / diagnosis / treatment / care

- Authorized trials under ICH-GCP
- Industry-sponsored IND Trial
 - Investigator-initiated IND Trial (since 2003)

Industry-sponsored PMS under GPSP

Investigator-initiated Trial ("Un-notified Trial")

Clinical Trials with new drugs in JAPAN

- IND trial (*Chiken* in Japanese)
Clinical trials intended for the approval of production and distribution of new drugs (NDA)
- 'Un-notified trial' to the Authority ≠ concealed trial
Clinical trials not intended for NDA; new drug is administered as an in-house drug only in the institution where the trial is conducted

"Un-notified trials" in JAPAN

- No legal regulation
(Ethical Guidelines since 2003)
- An MD investigator can administer any investigational product to the patient under his discretion without the notification to authority, unless it is intended for NDA
- Institutional Ethical Committee (IEC) is required to act as a substitute for the authority

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Discussion & Criticism in Orlando, 2006

- How do investigators and the government consider ethical issues in Japan?
→ They don't take the issues seriously, though I point out and try to persuade them.

But as you know, Japan is very sensitive to external pressure from foreign countries. If I take your criticism back home, the situation may change. Please support me.

→ Sure we do!

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Your support has worked!

- ✓ Criticisms have been cited in
- ✓ Journal articles
- ✓ Academic conferences
- ✓ Public comments to the guidelines
- ...

The situation has been changing.

Total Amendment of 'Ethical Guidelines for Clinical Trials' in Japan (1)

- Amended in July 2008
- Enforced in April 2009
- Yet Not the law

Total Amendment of 'Ethical Guidelines for Clinical Trials' in Japan (2)

- Responsibilities of Investigator
- ✓ Compensation for participants' bodily injury related to clinical trials
- ✓ Education of research ethics & necessary knowledge prior to clinical trials operation

Total Amendment of 'Ethical Guidelines for Clinical Trials' in Japan (3)

- Responsibilities of PI
- ✓ Advanced registration of trials to the specified public databases
- ✓ Informing the director of research institution of clinical trial progress and results

Total Amendment of 'Ethical Guidelines for Clinical Trials' in Japan (4)

- Responsibilities of Director of Research Institution
- ✓ Preparation of SOPs
- ✓ Informing the MHLW of unforeseeable SAE related to the trials
- ✓ Self-assessment and inspection of compliance to the ethical guidelines

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Investigator-initiated trials in Japan

Function as project sponsor



Function as PI

Patient information leaflets, Recruiting, IC, Adverse effects, CRF

Strengthening the capacity of project sponsors in academia

☆ fund 2009-2012

"Developing an educational program to build infrastructure for clinical trials within the Special Research Initiative" subsidized by MHLW

☆ program development & implementation

"Super Special Consortium for Supporting the Development of Cutting-edge Medical Care" ("tokku")

24 projects were adopted in 2008

Summary

- 'Ethical Guidelines for Clinical Studies' have been fundamentally revised, and the regulation of un-notified trials with new drug comes near to those of IND trials in Japan.
- An educational program has just begun to be developed, which is focused on sponsor-side function in the frame of Special Research Initiative.

Conclusion

- Although the amended guidelines went into effect in April 2009, the development of infrastructure has remained to be completed in research institutions over Japan. We must extend networking to share the necessary information and continue the discussion about clinical trial systems in Japan.

Thank you for your support.

Any input is welcome to
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