BU Clinical & Translational Science Institute

BOSTON MEDICAL CENTER
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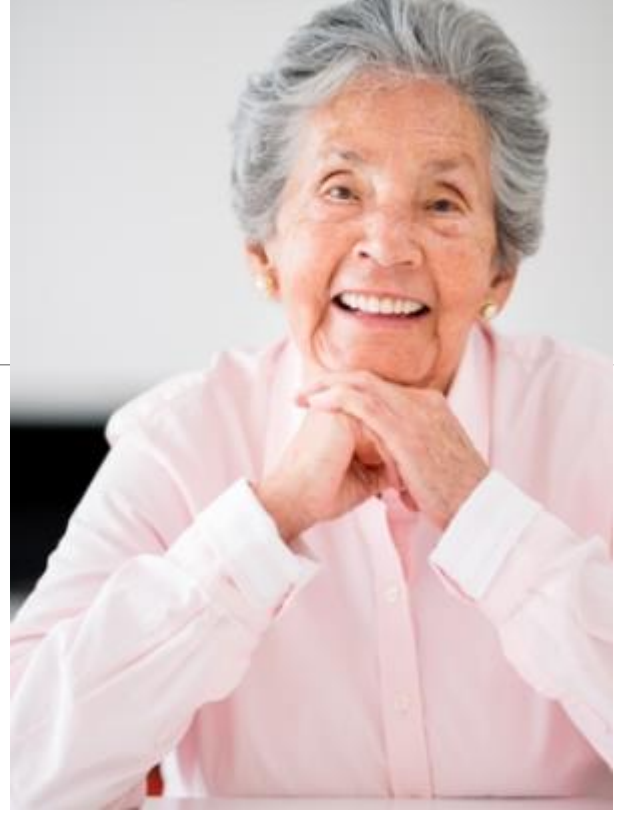
Research Professionals Network Workshop Series

SO YOU THINK YOU KNOW GCP?

Mary-Tara Roth
Director, CRRO
mtroth@bu.edu

Gina Daniels
Human Research Quality Manager
gdaniels@bu.edu




Hope

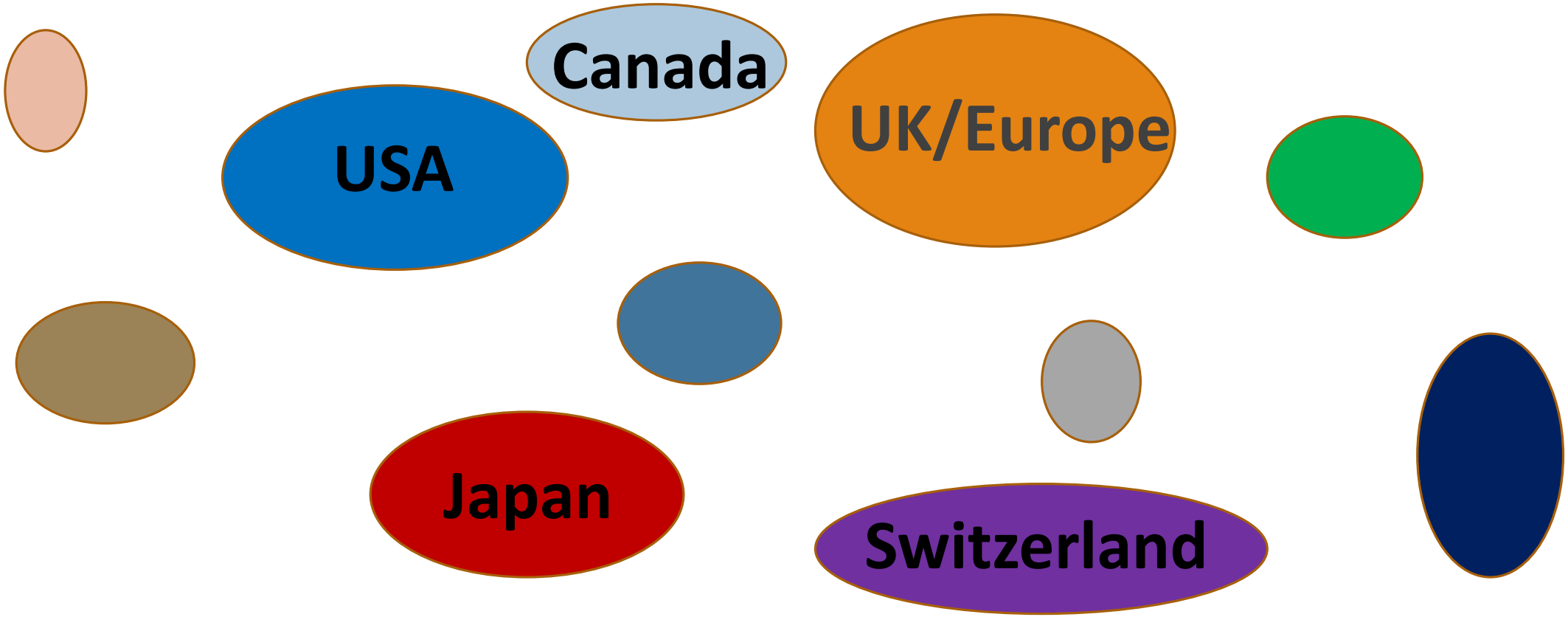
What is [ICH] GCP?

… an international ethical and scientific quality standard for designing, conducting, recording and reporting trials that involve the participation of human subjects.

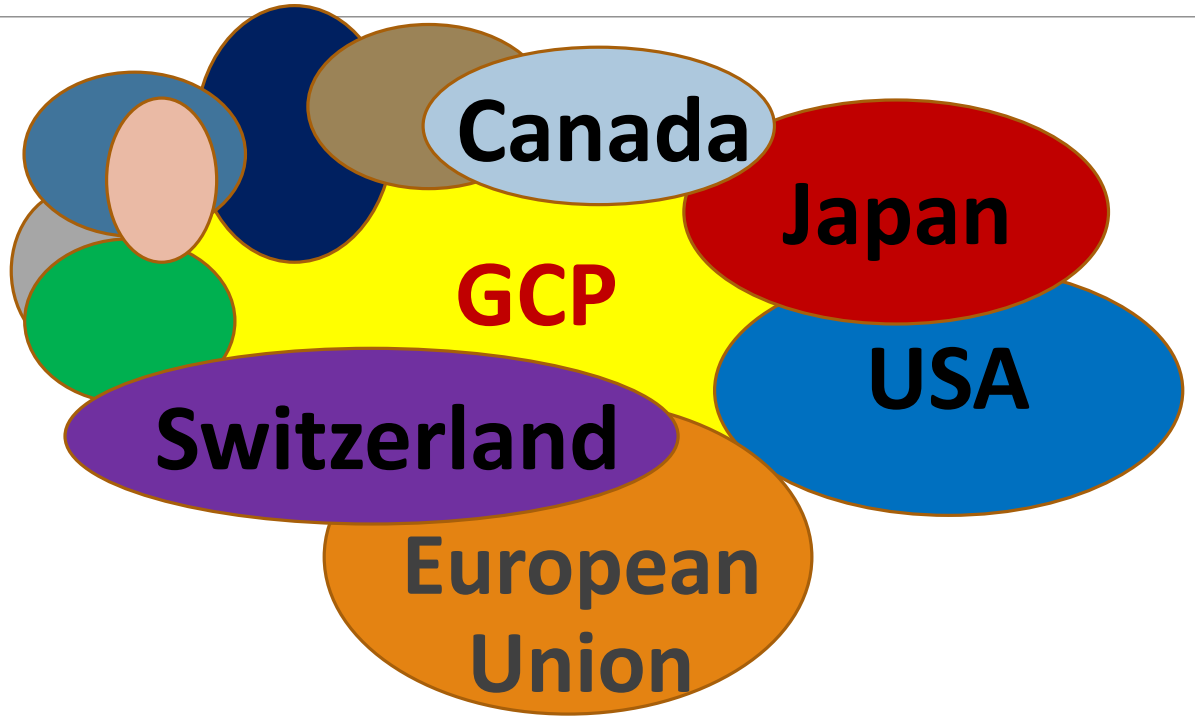
Compliance with this standard provides public assurance that the rights, safety and well being of trial subjects are protected, consistent with the principles that have their origin in the Declaration of Helsinki, and that the clinical trial data are credible.

ICH Harmonised Guideline Integrated Addendum to ICH E6(R1): Guideline for Good Clinical Practice, E6(R2)

Imagine, back just after some of the big ethical/safety breaches in human research in “recent” history… (Tuskegee, sulfanilamide, thalidomide…..)



Creation of a “unified standard”



Facilitates mutual acceptance of data from clinical trials by regulatory authorities from other jurisdictions.

Some history…..

ICH: International Council for Harmonization
(formerly International Conference on Harmonization)

- Pre-ICH: Development of country-specific regs and guidelines in 60's – 80's
  - Realization in different parts of the world that independent evaluation of medicinal products must take place before they are allowed to be marketed
  - Required duplication of studies to be accepted in new markets
  - Rising costs + public expectations of minimal delays → need to harmonize
- ICH – first meeting in April, 1990 – Europe, USA, Japan
- ICH GCP E6 (R1) – 1996 (Europe, USA, Japan)
- 2015 – Operational and organizational changes in ICH
- ICH GCP E6 (R2) – 2016 (Europe, USA, Japan, Switzerland, Canada)

ICH GCP: Guideline E6

- **Quality (Q):** related to chemical and pharmaceutical Quality Assurance (stability, impurity testing, etc.)
  - 10 guidelines
- **Safety (S):** in vitro and in vivo pre-clinical studies (carcinogenicity testing, genotoxicity testing, etc.)
  - 9 guidelines
- **Efficacy (E):** clinical studies in human subjects
  - 15 guidelines
    - **E6 – Good Clinical Practice: "ICH GCP"**
- **Multidisciplinary (M):** topics which don't fit into one of the above categories
  - 5 guidelines

FDA Good Clinical Practice

- 21 CFR Part 11 – Electronic records; Electronic signatures
- 21 CFR Part 50 – Protection of Human Subjects (Informed Consent)
- 21 CFR Part 50, subpart D – Additional Safeguards for Children in Clinical Investigations of FDA-regulated Products (Interim rule)
- 21 CFR Part 54 – Financial Disclosure by Clinical Investigators
- 21 CFR Part 56 – Institutional Review Boards
- 21 CFR Part 312 – Investigational New Drug Application
- 21 CFR Part 812 – Investigational Device Exemptions
- 42 CFR Part 11 – Clinical Trials Registration and Results
- FDA Guidance Oct. 2009 – Investigator Responsibilities – Protecting Rights, Safety and Welfare of Study Subjects
- FDA Guidance Jan 2009 – AE Reporting to IRBs – Improving Subject Protections
- FDA Guidance April 1996 – E6 Good Clinical Practice: Consolidated Guidance
- FDA Draft Guidance June 2015 – Integrated Addendum to ICH E6(R1): Guideline for Good Clinical Practice E6(R2)

ICH GCP and FDA regs

"Staff at the Division of Scientific Investigations participated in the development of the ICH E6 guideline, which is the official FDA guidance on GCP. Compliance with ICH GCP ensures compliance with FDA regulations."

(Joseph Salewski, CDER DSI deputy director, SoCRA Source, 8/05)

"To the extent possible, the principles of GCP should generally apply to all clinical research involving human subjects, and not just research involving pharmaceutical or other medical products…"

Handbook for Good Clinical Practice, WHO, 2002

13 Principles of ICH GCP

Ethics

- … conducted in accordance with ethical principles that have their origin in the Declaration of Helsinki and are consistent with GCP and applicable regulatory requirements
- Before trial, foreseeable risks and inconveniences should be weighed against the anticipated benefit for the individual subject and society. Anticipated benefits must justify risks.
- Rights, safety, and well-being of subjects prevail over interests of science and society

13 Principles of ICH GCP *(cont'd.)*

Protocol and Science

- Nonclinical and clinical information supports the proposed trial
- Trials should be scientifically sound and described in a clear detailed protocol

Responsibilities

- IRB/IEC approval prior to initiation
- Medical care/decisions on behalf of subject made by qualified physician/dentist
- Each individual is qualified (education, training, experience) to perform his/her tasks

13 Principles of ICH GCP *(cont'd.)*

Informed Consent

- Freely given from every subject prior to participation

Data Quality and Integrity

- All trial data should be recorded, handled, and stored in a way that allows its accurate reporting, interpretation, and verification
- Protects confidentiality of records

ICH GCP 2.1 – 2.13

13 Principles of ICH GCP *(cont'd.)*

Investigational Products

- Manufacture, handling, storage should conform to Good Manufacturing Practice (GMPs) and used per protocol

Quality Control/Quality Assurance

- Implementation of systems with procedures to ensure quality of every aspect of the trial

ICH GCP 2.1 – 2.13

Getting to Know GCP

Protocol compliance:

- ICH GCP 4.5

Investigator qualifications:

- ICH GCP 4.1

Elements of informed consent:

- ICH GCP 4.8.10

Documentation of informed consent:

- ICH GCP 4.8.8

Delegation of tasks:

- ICH GCP 4.1.5 & 4.2.4

GCP in Action!

“Each individual qualified by training, education, experience…..”

- records include CVs, licenses (IF necessary), training logs for protocol-specific training
- delegation log that shows that tasks are appropriately delegated (demonstrating oversight of PI)

“All trial data should be recorded, handled, and stored in a way that allows its accurate reporting, interpretation, and verification”

- Follow ALCOA: Documentation should be Attributable (record identifies who created/modified record), Legible, Contemporaneous (recorded in real-time, and signed/dated accurately), Original, Accurate (collected and recorded honestly and completely)
- Source documents must make it clear *who* collected/updated the data and *when*, and reasons for changes if necessary….
- Storing records per protocol and institutional policy
- Review and implement GCP Section 8: Essential Documents Before, During, After trial

“Informed consent freely given…”

- well-trained staff ensuring complete information is supplied to and understood by potential subject

CRRO can help!

Consultations, PLUS templates for documentation……

Research Subject Eligibility Assessment Form: Helps you document individual research subject eligibility assessments.

Documentation of Informed Consent Tool: Tool that will guide you through documenting the informed consent process.

Documentation of Pregnancy Testing: This tool will help you document pregnancy testing or the determination that pregnancy testing is not required.

Note-to-File Template

Regulatory Binder Tabs: A set of 15 tabs to help set up your Regulatory Binder

Regulatory Binder Tab Inserts: A list of customizable templates of logs used for regulatory record-keeping.

- Task delegation/signature log, staff straining log, AE tracking logs, Test article accountability….

And much more!

How do I know if I [must] follow [ICH] GCP?

Look in your protocol: Study Conduct/Ethics/ Regulatory Considerations section(s):

Protocol excerpt:

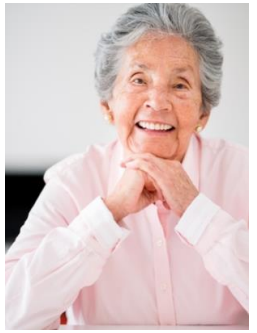
"This study will be conducted in accordance with the ethical principles that have their origin in the current Declaration of Helsinki and will be consistent with International Conference on Harmonization Good Clinical Practice (ICH GCP) and applicable regulatory requirements."

GCP – A final emphasis

Compliance with this standard provides public assurance that…..

- the rights, safety and well being of trial subjects are protected, consistent with the principles that have their origin in the Declaration of Helsinki,
- and that the clinical trial data are credible.



Questions?