The International Conference on Harmonization (ICH) and its Relevance to Cell Therapy

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A Unique Approach

- ICH was created in 1990
- Agreement between the EU, Japan and the USA to harmonize different regional requirements for registration of pharmaceutical drug products
- Unique because joint effort by regulators and associated pharmaceutical industry trade associations

ICH Objectives

- Elimination of the need to duplicate studies to meet different regulatory requirements
- More efficient use of resources in the R&D process, as a consequence
- Quicker access for patients to safe and effective new medicines

Principles of ICH

- Development of scientific consensus documents through discussions between regulatory and industry experts
- Wide consultation of the draft consensus documents through normal regulatory channels before a harmonized text is adopted
- **Commitment** by regulatory parties to implement the ICH harmonized texts

STATEMENT BY THE ICH STEERING COMMITTEE TOKYO 1990

- The Conference will not only look at existing issues but will, based on past experience, seek to minimize future divergence of new registration requirements, as a consequence of technical progress.

Who are the members?

- Founding members: Reps from the six co-sponsoring parties from the United States, the European Union, and Japan
- Observers: World Health Organization (WHO), the European Free Trade Area (EFTA), Canada (each observer has a seat on the steering committee as a non-voting member and participates in EWGs)
- The International Federation of Pharmaceutical Manufacturers Associations (IFPMA): represents 56 countries (non-voting member of SC and runs the ICH secretariat)

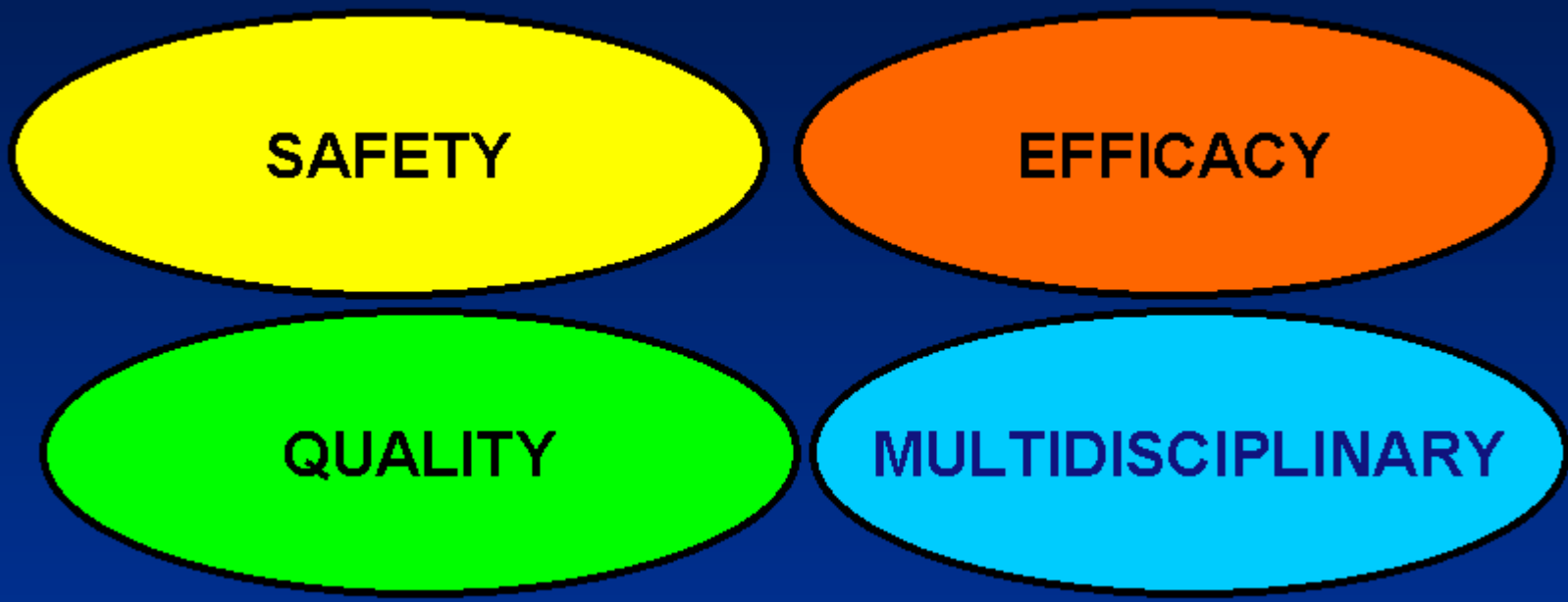
Six parties directly involved in the decision making process

- **US Food and Drug Administration (FDA)**
- **Pharmaceutical Research and Manufacturers of America (PhRMA)**
- **European Commission - European Union (EU)**
- **European Federation of Pharmaceutical Industries and Associations (EFPIA)**
- **Ministry of Health, Labor and Welfare, Japan (MHLW)**
- **Japan Pharmaceutical Manufacturers Association (JPMA)**

ICH Steering Committee

- Determines the policies and procedures for ICH
- Selects topics for harmonization
- Monitors the progress of harmonization initiatives
- Has two members for each of the six co-sponsors, the IFPMA and Observers

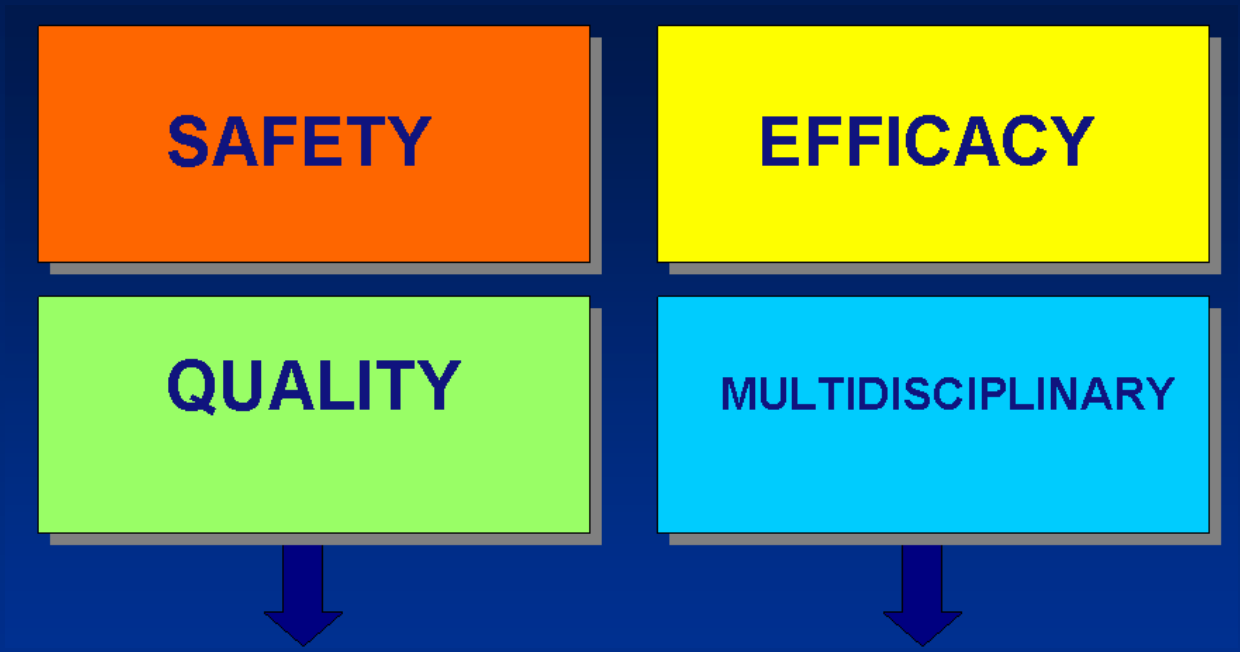
Harmonization topics divided into categories



The harmonization output document is called a “guideline”

An ICH Guideline *is* FDA Guidance

Expert Working Groups



STEERING COMMITTEE

Monitors and Facilitates EWGs

An EWG has 6 Topic Leaders - one from each ICH party

Examples of Guidelines

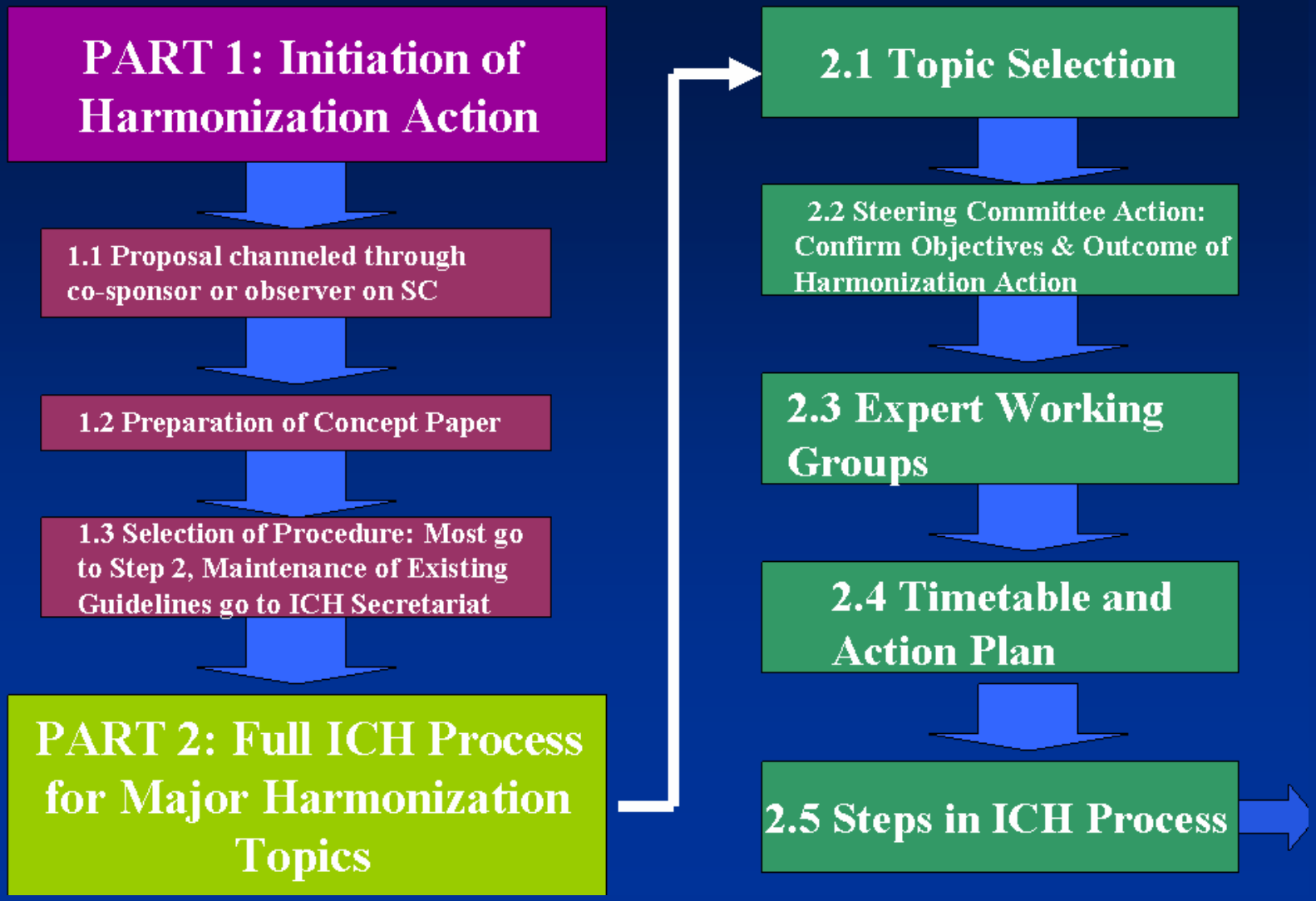
Q1A(R2): Stability Testing of New Drug Substances and Products (Second Revision)

S1B: Testing for Carcinogenicity of Pharmaceuticals

E4: Dose-Response information to Support Drug Registration

M2: Electronic Standards for the transfer of regulatory information

How to become a bona fide guideline



Steps in the ICH Process

Example Guidelines from ICH Website www.ich.org

Q1E: Evaluation of Stability Data

The tripartite harmonised ICH guideline was finalised (Step 4) in February 2003. This document extends the main guideline by explaining possible situations where extrapolation of retest periods/shelf-lives beyond the real-time data may be appropriate. Furthermore, it provides examples of statistical approaches to stability data analysis.

Q1E	Implementation (Step 5) : **EU**: Adopted by CPMP, March 2003, issued as CPMP/ICH/420/02 **MHLW**: Adopted June 3, 2003, PFSB/ELD Notification No. 0603004 **FDA**: Published in the Federal Register / Vol. 69, N° 110, Tuesday June 8, 2004, pages 32010-32011	Status : Step 5 February 2003

S8 : Immunotoxicology Studies for Human Pharmaceuticals

The Guideline was released for consultation under *Step 2* of the ICH process in November 2004.
This guideline addresses the recommendations on nonclinical testing for immunosuppression induced by low molecular weight drugs (non-biologicals). It applies to new pharmaceuticals intended for use in humans, as well as to marketed drug products proposed for different indications or other variations on the current product label in which the change could result in unaddressed and relevant toxicologic issues. In addition, the guideline might also apply to drugs in which clinical signs of immunosuppression are observed during clinical trials and following approval to market. The term immunotoxicity in this guideline will primarily refer to immunosuppression, i.e. a state of increased susceptibility to infections or the development of tumors.
It is beyond the scope of this guideline to provide specific guidance on how each immunotoxicity study should be performed.
General guidance is provided in Appendix 1.

S8	Consultation (Step 3) : **EU** : Transmission to CHPM December 2004. Transmission to Interested Parties December 2004. Issued as EMEA/CHMP/167235/2004-ICH. Deadline for comments : April 2005. **MHLW** : Released for consultation on 28 December 2004, PFSB/ELD, deadline for comments 28 March 2005. **FDA** : Released for consultation, published in the Federal Register, Vol. 70, No. 25; February 8, 2005; pages 6697-6698. Deadline for comments : April 11, 2005.	Status : Step 3 November 2004

Website shows which formal ICH step each group has completed

Elements of a Concept Paper

- Type of action proposed: Is this a new guideline or amendment to an existing one?
- Perceived problem: In the case of a new field of science, consider problems if harmonization action is not taken
- Background information
- Type of Expert Working Group: Will the EWG be comprised of only the six-party group, or will the group be extended?

Relevance to Cell Therapy

- ICH is a forum for regulatory agreement from multiple countries
- Cell therapy specific guidelines have yet to be written
- The concepts from other harmonized guidelines are applicable to cell therapy, and it is important to have a vision of where quality, safety, and efficacy fit into a framework for successful treatment

Examples

- Q6B: Specifications: Test Procedures and Acceptance Criteria for Biotechnological/ Biological Products
- Q5D: Derivation and Characterization of Cell Substrates used for Production of Biotechnological/Biological Products
- Q5E: Comparability of Biotechnological/ Biological Products Subject to Changes in their Manufacturing Process
- S6: Preclinical Safety Evaluation of Biotechnology-Derived Pharmaceuticals