

UNIT-IV

ICH GUIDELINES FOR PHARMACOVIGILANCE



CENTURION
UNIVERSITY
*Shaping Lives...
Empowering Communities!*

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Introduction

- ICH is the “International Conference on Harmonization” of technical requirements for the registration of pharmaceuticals for human use.
- To assure safety, quality and efficacy of medicines, the members of ICH who include members from drug regulatory authorities and research based industries of European Union, US and Japan will discuss on the technical procedures and documents required.

History

- In 1956 Thalidomide was approved for marketing in Europe and Africa for treating morning sickness in pregnant women.
- Lack of proper policies, Legislations and guidelines to ensure the safety, efficacy of the drug, 10,000 to 20,000 babies suffered from birth defects like phocomelia
- This disaster has initiated many policies, Legislations and amendments in acts to ensure the safety, efficacy, quality of the drugs, thus leading to the formation of International conference on harmonization in 1990.

Need for harmonization

- The difference in the technical requirements and the procedures followed by different countries made the global marketing of drugs as time consuming and expensive
- To reduce the cost and time required for the global marketing of drugs
- Harmonization of technical requirements has been promoted
- Special guidelines have been framed to ensure the quality, safety and the efficacy of the drugs

Objective of ICH

- To promote international harmonization of technical requirements to develop safe, effective, and high quality medicines.
- To reduce the registration cost.
- To promote public health
- To prevent the duplication of clinical trials in Humans
- To minimize the animal use without compromising on the safety and quality of drugs

Goal of ICH

- Promote international harmonization by bringing together representatives from the three ICH regions (EU, Japan and USA) to discuss and establish common guidelines
- Make information available on ICH, ICH activities and ICH guidelines to any country.

Members of ICH

- ICH is comprised of representatives from six parties that represent the regulatory bodies and research based industry in the European Union, Japan and the USA
- In Japan, the members are the Ministry of Health, Labour and Welfare (MHLW), and the Japan Pharmaceutical Manufacturers Association (JPMA)
- In Europe, the members are the European Union (EU), and the European Federation of Pharmaceutical Industries and Associations (EFPIA).

Members of ICH

- In the USA, the members are the Food and Drug Administration (FDA), and the Pharmaceutical Research and Manufacturers of America (PhRMA).
- Additional members include Observers from the World Health Organization (WHO), European Free Trade Association (EFTA), Canada

ICH steering committee

- Governs ICH
- Determines the policies and procedures for ICH
- Selects topics for harmonization
- Monitors the progress of harmonization initiatives

ICH coordinators

- The Coordinators are fundamental to the smooth running of the ICH and are nominated by each of the six parties of ICH. Coordinator acts as the main contact point with the ICH Secretariat.
- Operates from the IFPMA offices in Geneva, Switzerland

ICH coordinators (Responsibilities)

- Provides support to the ICH Steering Committee.
- Documents the meetings of the steering committee.
- Promotes coordination between Working Groups.
- Provides information on the ICH guidelines and ICH process.
- Provides administrative support for MedDRA management board.
- Provides administrative support for Global cooperation Group.

ICH global cooperation group

- Formed on March 11, 1999, as a subcommittee of ICH steering committee to Globalise the ICH and its guidelines
- One representative from each of the six parties of ICH steering committee
- ICH secretariat at IFPMA

ICH working groups

- Expert Working Group
- Implementation Working Group
- Informal Working Group
- Discussion group

ICH guidelines for pharmacovigilance

- This document gives standard definitions and terminology for key aspects of clinical safety reporting
- Gives guidance on mechanisms for handling expedited (rapid) reporting of adverse drug reactions in the investigational phase of drug development.
- The ICH has published a number of documents setting standards for safety, both clinical and pre-clinical.
- Pre-clinical guidelines have an “S” designation e.g. S1, S2 etc.
- The clinical safety guidelines are designated as “E”, standing for “Efficacy”

ICH guidelines for pharmacovigilance

- E1 The Extent of Population Exposure to Assess Clinical Safety for Drugs Intended for Long-Term Treatment of Non-Life Threatening Conditions
- E2A Clinical Safety Data Management: Definitions and Standards for Expedited Reporting
- E2B (R2) Maintenance of the Clinical Safety Data Management including Data Elements for Transmission of Individual Case Safety Reports
- E2B (R3) Clinical Safety Data Management: Data Elements for Transmission of Individual Case Safety Reports

ICH guidelines for pharmacovigilance

- E2C (R1) Clinical Safety Data Management: Periodic Safety Update Reports for Marketed Drugs
- E2C (R2) Periodic Benefit-Risk Evaluation Report
- E2D Post-Approval Safety Data Management: Definitions and Standards for Expedited Reporting
- E2E Pharmacovigilance Planning
- E2F Development Safety Update Report

Expedited Reporting

- In the EU post-marketing environment, an Individual Case Safety Report (ICSR) may involve a serious or non-serious adverse reaction – regardless of expectedness.
- Such cases must be submitted to the regulatory authorities within 15 days or 90 days respectively.
- A Marketing Authorisation should be fully versed in each change to the drug safety laws in concerned territories around expedited reporting as and when it happens.

Post marketing phase

- Any clinical trials including post authorisation studies during the post marketing phase of a product will need to be correctly processed and expedited according to regulatory requirements.

What should be reported

- Single Cases of Serious, Unexpected ADRs
- Other Observations

What should be reported

- Single Cases of Serious, Unexpected ADRs
- This applies to reports from spontaneous sources and from any type of clinical or epidemiological investigation, independent of design or purpose
- The source of a report (investigation, spontaneous, other) should always be specified.
- It also applies to cases not reported directly to a sponsor or manufacturer (for example, those found in regulatory authority-generated ADR registries or in publications).

What should be reported

- information that might materially influence the benefit-risk assessment of a medicinal product or that would be sufficient to consider changes in medicinal product administration or in the overall conduct of a clinical investigation represents such situations.
- Examples include: a) For an "expected," serious ADR, an increase in the rate of occurrence which is judged to be clinically important. b) A significant hazard to the patient population, such as lack of efficacy with a medicinal product used in treating life-threatening disease. c) A major safety finding from a newly completed animal study (such as carcinogenicity)

Reporting time frames

- **Fatal or Life-Threatening Unexpected ADRs:** Within 7 days after first knowledge by the sponsor that a case qualifies, followed by as complete a report as possible within 8 additional calendar days.
- **All Other Serious, Unexpected ADRs:** Serious, unexpected reactions (ADRs) that are not fatal or life-threatening must be filed as soon as possible but no later than 15 calendar days after first knowledge by the sponsor that the case meets the minimum criteria for expedited reporting.

Minimum criteria for reporting

- Information for final description and evaluation of a case report may not be available within the required time frames for reporting outlined above. Nevertheless,
- for regulatory purposes, initial reports should be submitted within the prescribed time as long as the following minimum criteria are met: an identifiable patient; a suspect medicinal product; an identifiable reporting source; and an event or outcome that can be identified as serious and unexpected, and for which, in clinical investigation cases, there is a reasonable suspected causal relationship.

Minimum criteria for reporting

- The minimum information required for expedited reporting purposes is: an identifiable patient, the name of a suspect medicinal product, an identifiable reporting source, and an event or outcome that can be identified as serious and unexpected and for which, in clinical investigation cases, there is a reasonable suspected causal relationship.
- Attempts should be made to obtain follow-up information on as many other listed items pertinent to the case.

How to report

- The CIOMS-I form has been a widely accepted standard for expedited adverse event reporting.
- Initially it is important that certain basic information/data elements, when available, be included with any expedited report, whether in a tabular or narrative presentation.
- The listing in Attachment 1 addresses those data elements regarded as desirable; if all are not available at the time of expedited reporting, efforts should be made to obtain them.
- All reports must be sent to those regulators or other official parties requiring them (as appropriate for the local situation) in countries where the drug is under development.

Individual case safety reports

- It is a document providing the most complete information related to an individual case at a certain point of time. ICSRs, sometimes referred to as safety reports, are used for reporting suspected adverse reactions to the Eudravigilance database, to a medicinal product that occur in a single patient at a specific point in time
- An individual case is the information provided by a primary source to describe suspected adverse reactions/suspected unexpected serious adverse reactions related to the administration of one or more medicinal product/investigational medicinal products to an individual patient at a particular point of time.

General reporting requirements

- Marketing authorization holders shall report, within 15 days of the day on which the holder concerned gained knowledge of the event, all serious suspected adverse reactions that occur, to the competent authority of the Member State on whose territory the incident occurred and shall report all serious suspected adverse reactions that occur on the territory of a third country to the Agency and, if requested, to the competent authorities of the Member States in which the medicinal product is authorised

General reporting requirements

- These safety reports include individual case safety reports (ICSRs), and other related documents (ICSR attachments) for each adverse drug experience.
- An ICSR is a description of the adverse drug experience that includes the basic elements, or facts, of each reportable event for an individual patient or subject.
- Under the current regulations, persons who submit safety reports on paper must use the approved reporting form for ICSR_s

15 day alert report

- FDA regulations require manufacturers, packers, distributors, and applicants to submit an ICSR on FDA Form 3500A, or its equivalent, for each postmarketing adverse drug experience that is both serious and unexpected to the agency within 15 calendar days of initial receipt of information about the adverse drug experience
- In addition to the ICSR, 15-day Alert reports frequently include related documents, such as medical records, hospital discharge summaries, or other documentation related to the event (ICSR attachments)