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Ich Guidelines

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Abstract:
Regulatory agencies and the pharmaceutical sector get together to debate the scientific and technical facets of drug registration thanks to ICH, the international council for harmonization of technical criteria for pharmaceuticals for human use. The goal of the ICH is to increase global harmonization in order to ensure that pharmaceuticals are produced and registered in the most resource-effective way possible. The conduct of stability studies, establishing appropriate limits for impurity testing, and improved risk management are crucial milestones in the quality area of harmonization.

Keywords: ICH guidelines, History of ICH guidelines, ICH-GCP ,Members, Countries involved, QSEM series guidelines,

Introduction:
The ICH, or International Conference on Harmonization, is a body that coordinates technical standards for medications intended for human use. The ICH is unusual in that it brings together the pharmaceutical industry and regulatory agencies to talk about the scientific and technological aspects of drug redistribution. The ICH has gradually adjusted to the more international nature of drug research. Quality, safety, effectiveness, and multidisciplinary guidelines are included. Regulatory authorities and representatives of the research base industry from the EU, Japan, and the US are all involved in the ICH effort.
The guideline aims to provide an example of the core stability data package for new drug substances and products, but it leaves enough room for interpretation to account for the wide range of possible practical situations that may arise due to particular scientific considerations and properties of the materials under evaluation. If there are reasons that can be supported by science, alternative methods can be applied. The recommendation concerns the molecular entities and related drug products that are submitted with registration requests for new information. The information required to be submitted for shortened or abridged applications, variations, clinical trial applications, etc. is not currently covered by this guideline. This guideline does not cover the specifics of sampling and testing for individual dosage forms in their proposed container closures.[1]

Objectives-[6]
- Guidelines as Quality, Safety, Efficacy as the main criteria for authorizing new medicines and monitoring their safety.
- Electronic information for transfer the of regulatory information ;

- The Common Technical Document (CTD), a common format for quality, safety and efficacy information;
- The medical dictionary for adverse event reporting and coding of clinical trial data (MedRA), which comprises standardized medical terms to facilitate sharing of regulatory information internationally for human medicines.

History of ICH:-[2]

ICH established in 1990's as a joint initiative involving both regulators and research-based industry representatives of European Union, Japan and USA in scientific and technical discussion of testing procedures required to assess and ensure Safety, Quality, Efficacy of medicines.

- **Initiation of ICH:-**
  The birth of ICH took place at meeting on April 1990 hosted by European federation of pharmaceutical industries Association (EFPIA) in Brussels.
- **The early meeting:-**
  At the first SC meeting of ICH it was decided that the topics selected for harmonization would be divided into Safety, Quality and Efficacy groups (EWGs).
- **Commitment and Process:-**
  The commitment of ICH was set out in a steering committee statement from the meeting in Tokyo, October 1990.

Process statement deals with the :

1) Clinical trials with animals and humans.
2) Recognizing the substantial progress.
3) To look on existing issues as well as past topics and its relation with future aspects.

ICH Located:

The ICH secretariat is based in Geneva. The biennial meetings and conference of ICH steering committee rotate between EU, Japan and USA.

Purpose of ICH:-

- Ensuring quality, Safety and efficacy of drugs.
- Harmonization of drugs technical requirement.
- Avoid duplication of human clinical trials.
- Reduce use of animal testing but without a compromise on evaluating efficacy and safety of drugs.
- More economical use of human, animal and material sources.
- To eliminate unnecessary delays in the availability of new medicines.
- Aim to produce a single set of technical requirement for registration of new drug product.

GOALS:-

- To promote international harmonization.
- To make information available on ICH, ICH activities and ICH guidelines to any country or company.
- To strengthen the capacity of drug regulatory authorities and industry to utilize them.

Participants of ICH:-

ICH is comprised from six co-sponsoring parties as well as three observers and IFPMA (International Federation of Pharmaceutical Manufacturer Assosiation).

- JAPAN- MHW (Ministry of Health and Family Welfare)
  JPMA (Japan Pharmaceuticals manufacturer Association)
- EUROPE- EC (European Commision)
  EFPIA (European Federation of Pharmaceutical Industries Assosiation)
- US-FDA (United States Food and Drug Administration)
  PhRMA (Pharmaceutical Research and manufacturers of America)

Region	Regulatory Body	Research Based Industries
Japan	MHLW	JPMA
Europe	EU	EFPIA
US	FDA	PhRMA

ICH Structure:-

1) ICH Steering committee
2) ICH co-ordinators
3) ICH Secretariat and ICH working groups.
4) ICH med DRA management.

ICH Harmonization Process:-

1) Overview
2) Initiation of Harmonization action.
3) Full ICH process for major Harmonization topics.
4) Abbreviated process for maintanance of ICH agreement.
5) Maintanance Procedure.

ICH Conference held in:-

- ICH 1-Nov 1991- Brussels
- ICH 2-Oct 1993- Oriando, Florida
- ICH 3- Nov 1995- Yokohama, Japan
- ICH 4- July 1997- Brussels
- ICH 5 – Nov 2000- San Diego-US
- ICH 6- Nov 2003- Osaka, Japan
- ICH 7- Nov 2007- Europe? Cancelled?

ICH public meetings_ICH steering Commitees
Regional meet with non-profit Organizations.

Initiation of Harmonization Action:-

1. Proposals for Harmonization action
2. Preperation of concept paper
3. Selection of procedure.

STEPS:-

The formal ICH Procedure consist of 5 steps:-

STEP 1:- Consenus Building

STEP 2:- Confirmation of six-party consenus

STEP 3:- Regulatory Consulation and Discussion.

STEP 4:- Adoption of an ICH Harmonized Tripartie Guidelines

STEP 5:- Implementation

ICH Guidelines:- (QSEM)

The ICH guidelines are covered under four headings under the acronym

QSEM:- Quality, Safety, Efficacy and Multidisciplinary.

a) Quality Guidelines:-

These Guidelines cover the areas of quality of drug products such as impurity testing and stability studies and a flexible approach to quality on the basis of GMP risk management.

b) Safety Guidelines:-

They help to detect potential risks such as genotoxicity, carcinogenicity and reprotoxicity. For example, the ICH came up with a non-clinical test methodology to evaluate QT interval prolongation which is probably the most significant reason why drugs have been withdrawn in recent times.

c) Efficacy Guidelines:-

These guidelines provide guidance about designing, conducting , safety, aspects and reporting of clinical trials for pharmaceutical products. Novel drugs products derived from biotechnology and genomics/ pharmacogenetic techniques for targeted drug delivery are also covered.

d) Multidisciplinary Guidelines:-

Topics in the pharmaceutical field that do not fit into any of the above categories are covered under this area. This guidelines also includes details of (MedDRA), CTD and standards such as Electronic standards for the Transfer of Regulatory (ESTPI).

A) QUALITY GUIDELINES:-

- Q1A-Q1F= Stability
- Q2 = Analytical Validation
- Q3A-Q3D= Impurities
- Q4-Q4B= Pharmacopieas
- Q5A-Q5E= Quality of Biotechnological Products
- Q6A-Q6B=Specifications
- Q7= Good Manufacturing Practice
- Q8= Pharmaceutical Development
- Q9= Quality Risk Management
- Q10= Pharmaceutical Quality System
- Q11= Development and Manufacture of Drug Substance
- Q12= Lifecycle Management
- Q13= Continous Manufacturing of Drugs Substances and Drug Products.
- Q14= Analytical Procedure Development

B) SAFETY GUIDELINES:-

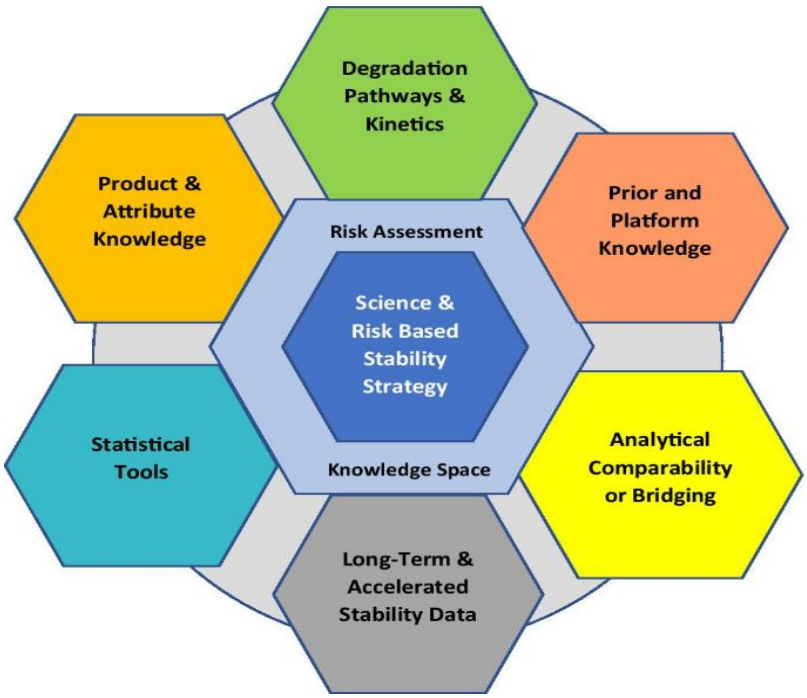
1) S1A= Need for carcinogenicity study
2) S1B= Testing for carcinogenicity of pharmaceutical product
3) S2A= Guidelines on specific aspects of regulatory genotoxicity test
4) S3= Note for guidance on toxicity
5) S4= Duration of chronic toxicity testing in animal
6) S5= Detection of chronic toxicity testing in animal
7) S6= Preclinical safety evaluation

C) EFFICACY GUIDELINES:-

1. E1-E2F= Clinical safety
2. E3= Clinical study reports
3. E4= Dose Response Studies
4. E5= Ethinic Factors
5. E6= Good Clinical Practice
6. E7-E11= Clinical Trials
7. E12= Guidelines for Clinical evaluation
8. E14= Clinical Evaluation
9. E15-E16= Pharmacogenomics.

D) MULTIDISCIPLINARY GUIDELINES:-

- M1= MedDRA (Medical Dictionary for regulatory activities)
- M2= ESTRI (Electronic Standard for transfer of regulatory information)
- M3(R2)= Non Clinical safety studies for the conduct of human clinical trial
- M4= CTD (The Common Technical Document)
- M5= Date Element and Standards for Drug Dictionaries.[3]



ICH-GCP [4-6]

The ICH-GCP is a harmonized standard that protects the rights, safety and welfare of human subjects, minimizes human exposure to investigational products, improves quality of data, speeds up marketing of new drugs and decreases the cost to sponsors and to the public. Compliance with this standard provides public assurance that the rights, safety and well-being of trial subjects are protected and consistent with the principles of the Declaration of Helsinki, and that the clinical trial data is credible . A historical background of the reasons and the importance of GCP is summarized as follows:-

Reasons for GCP

➢ Increased Ethical Awareness
➢ Improved Trial Methods
➢ Clinical Trial Concept Better Understood
➢ Public/Political Concern over Safety Aspects
➢ Frauds and Accidents during Trials
➢ Growing Research and Development Costs
➢ Increasing Competition
➢ Mutual Recognition of Data
➢ New Market Structure Good Clinical Practice (GCP) is an international ethical and scientific quality standard for the design, conduct, performance, monitoring, auditing, recording, analyses and reporting of clinical trials. GCP provides assurance that the data and reported results are credible and accurate, and that the rights, integrity and confidentiality of trial subjects are respected and protected . It was finalized in 1996 and became effective in 1997, but was not enforced by law at that time. The Medicines for Human Use (Clinical Trials) Regulations 2004 and the European Union (EU) Directive on Good Clinical Practice changed the world perspective , and compliance with GCP is now a legal obligation in the UK/Europe for all trials involving the investigation of medicinal products. It also serves to protect the rights, integrity and confidentiality of trial subjects. It is very important to understand the background of the formation of the ICH-GCP guidelines as this, in itself, explains the reasons and the need for doing so. In this paper, we address the historical background and the events that led up to the formation of these guidelines. Today, the ICH-GCP guidelines are used in clinical trials throughout the globe with the main aim of protecting and preserving human rights.

There are 13 core principles of ICH-GCP and they are as follows: [7]

1. Clinical trials should be conducted in accordance with ethical principles that have their origin in the Declaration of Helsinki, and that are consistent with GCP and the applicable regulatory requirement(s).
2. Before a trial is initiated, foreseeable risks and inconveniences should be weighed against anticipated benefit for the individual trial subject and society. A trial should be initiated and continued only if the anticipated benefits justify the risks.
3. The rights, safety and well-being of the trial subjects are the most important considerations and should prevail over interest of science and society.

4. The available non-clinical and clinical information on an investigational product should be adequate to support the proposed clinical trial.
5. Clinical trials should be scientifically sound, and described in clear, detailed protocol.
6. A trial should be conducted in compliance with the protocol that has received prior institutional review board (IRB)/ independent ethics committee (IEC) approval/favourable opinion.
7. The medical care given to, and medical decisions made on behalf of subjects should always be the responsibility of a qualified physician or, when appropriate, of a qualified dentist.
8. Each individual involved in conducting a trial should be qualified by education, training, and experience to perform his or her respective task(s).
9. Freely given informed consent should be obtained from every subject prior to clinical trial participation.
10. All clinical trial information should be recorded, handled, and stored in a way that allows its accurate reporting, interpretation and verification.
11. The confidentiality of records that could identify subjects should be protected, respecting the privacy and confidentiality rules in accordance with the applicable regulatory requirement(s).
12. Investigational products should be manufactured, handled and stored in accordance with applicable Good Manufacturing Practice (GMP). They should be used in accordance with the approved protocol.
13. Systems with procedures that assure the quality of every aspect of the trial should be implemented.

These principles are self-explanatory and, when summarized, simply mean:

All clinical trials should be conducted in accordance with ethical principles, sound scientific evidence and clear detailed protocols. The benefits of conducting trials should outweigh the risks. The rights, safety and well-being of trial participants are of paramount importance and these should be preserved by obtaining informed consent and maintaining confidentiality. The care must be given by appropriately qualified personnel with adequate experience. Records should be easily accessible and retrievable for accurate reporting, verification and interpretation. Investigational products should be manufactured according to Good Manufacturing Practice.

Role of ICH in Clinical trials in human medicines:[8]

The European Medicines Agency (EMA) relies on the results of clinical trials carried out by pharmaceutical companies to reach its opinions on the authorization of medicines. Although clinical trials are authorized at national level in the European Union (EU), EMA plays a key role in further developing the EU as a competitive Centre for innovative clinical trials, and in maintaining IT systems for the coordination of clinical trials**.**

SOP:

A standard operating procedure (SOP) provides clear-cut directions and detailed instructions needed to perform a specific task or operation consistently and efficiently. Often seen in a myriad of industries, SOPs aim to achieve uniformity in execution, reduce miscommunication, and adhere to regulatory standards.

Importance of SOP:

- Standard operating procedures provide the policies, processes and standards needed for the organization to succeed

- They can benefit a business by reducing errors, increasing efficiencies and profitability, creating a safe work environment and producing guidelines for how to resolve issues and overcome obstacles.
- Consistency and quality control.
- Productivity and performance.
- Safety and compliance.
- Knowledge transfer.
- Knowledge transfer.

Advantages of SOP:

- Achieve Consistency. Even simple processes are susceptible to various interpretations.
- Improve Quality Assurance and Safety
- Save Time and Money.
- Simplify Employee Management.
- Avoid Knowledge Loss.
- Simplify Audits.
- Enhance Autonomy.[9]

// Shri Datta Krupa //
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(Approved by Govt. of Maharashtra, DTE, MSBTE, BATU, & PCI, New Delhi)

STANDARD OPERATING PROCEDURE
NAME OF INSTRUMENT= HOT PLATE

PROCEDURE:-

1. Plug the MAINS cord to appropriate switch
2. Maintain aseptic conditions throughout the test procedure
3. If you want to use magnetic stirrer,

   A. Put the container with sample on the plate

   B. Put the stirrer into the container

   C. Turn the magnetic stirrer knob

4. If you want to use heater,

   A. Put the container with sample on plate

   B. Turn the heater knob

5. If you want to use magnetic stirrer and heater,

   A. Put the container with sample on plate

   B. Put the stirrer into container

   C. Turn the magnetic stirrer knob

Name	Mr.Md Azim .S . N	Ms.Ulka Mote	Dr.Uttekar P .S
	User Department	**Department Head**	**Head Unit QA**
Signature			

BMR BATCH MANUFACTURING RECORD [10]

The batch manufacturing record (BMR) is a document containing the instructions that must be followed when manufacturing medication. It includes information like product name, weight and count of each component in the medication, a list of all processes and procedures to follow, and the expected yield of each batch

Importance of BMR:-

- Establishes a Product's Quality Standards
- Batch manufacturing records document the step-by-step processes used to manufacture a product
- This information can then be used to set quality standards that must be met during production.
- Batch records indicate that the batch conforms to the current Good Manufacturing Procedures (GMP).
- By reviewing the batch record, QA and operations teams have the opportunity to catch errors before the product is released to the public.
- One of the most important aspects during the review of an executed batch record is the documentation of any unexpected or atypical events that may have occurred.

Advantages of BMR:-

- Streamlined production workflow. ...
- Company-wide integration. ...
- Improved efficiency. ...
- Increased accuracy and reduced waste. ...
- Real-time updates. ...
- Data-backed decision-making. ...
- Optimized reporting. ...
- Regulatory compliance

Disadvantages of BMR:-

- High WIP inventory levels
- Possible high cost of errors
- Increased idle time
- Batch production facilities should have a lot tracking system in place to ensure traceability and regulatory compliance

COMPANY NAME	BATCH MANUFACTURING RECORD			Page: 2 of 8
Department : Production	Title : Tongkat Ali Tablet			Batch Record : BMR-001
	Name	Signature	Date	Revision No. : 0
Prepared by :	Production Manager			Effective Date : 1 January 2016
Approved by :	QA Manager			

SOP – 028: Ribbon Mixer
SOP – 032: B2 Strokes Tablet Press

4. Raw Materials

Description	Part Number	Quantity Required (kg)	Lot No.	Qty Staged	Exp/ Retest	Performed By / Date	Verified By / Date
Eurycoma Longifolia	R-0122	25.00					
Lactose Monohydrate	R-2323	19.34					
Gelatin	R-7896	4.80					
Corn Starch	R-5858	2.40					
Methocel	R-0326	1.00					
Magnesium Stearate BP/USP	R-9696	0.46					

5. Processing Equipments

Equipment Description	ID No.	Previous Calibration	Calibration Required	Performed By / Date	Verified By / Date
Weighing Balance 150 kg	WB-01				
Tray Oven	OT-01				
Grinding and Milling Machine	GM-01				
Cube Mixer	MX-03				
Ribbon Mixer	MX-02				
Cadmill	GM-02				
B2 Strokes Tablet Press	TP-01				
Stainless Steel Container	CS-03				
Mechanical Sieve (Mesh No: 12)	SM-01				

6. Area Clearance

Batch No: TT 1606001	Manufacturing Date : 10 July 2016	Expiry Date : 9 July 2017

MFR MASTER FORMULA RECORD:

Master formula record (MFR) is a master document for any pharmaceutical product. It contains all information about the manufacturing process for the product. MFR is prepared by the research and development team of the company and all other documents like BMR and BPR are prepared using MFR by the manufacturing units.

Importance of MFR:-

- ✓ It can minimize the errors
- ✓ Content uniformity
- ✓ Avoids recalculation
- ✓ Saves lots of efforts and time
- ✓ Maintain the quality of product
- ✓ Approved from head department and QA head

Advantages of MFR:-

- ➢ Helps improve on-time delivery to the pharmacy and reduces potential out-of-specification (OOS) investigations.
- ➢ Analysis of the sample, and/or reporting of the results.
- ➢ The name of the intermediate/API/formulation being manufactured and an identifying document reference code, if applicable
- ➢ The methods, or reference to the methods, to be used for preparing the critical equipment (e.g., cleaning, assembling)
- ➢ Sampling instructions and in-process controls, with their acceptance criteria, where appropriate
- ➢ Time limits for completion of individual processing steps and/or the total process, where appropriate

Disadvantages of MFR:-

- ➢ The main disadvantages were cost, implementation resources, and the in-built obsolescence of manufacturing software systems.[11]

Form Number MF-001-V1 Date Original Issue: JULY 2021 Date Revised: Page 1 of 1	**MASTER FORMULA**

PRODUCT NAME:			
FORMULA REFERENCE:			
FORM PREPARED BY:			
		LOT NUMBER:	
		THEORETICAL YIELD:	
START DATE:		FINISHED PRODUCT SIZE:	
MIX TANK:		BATCH SIZE IN LBS:	

PRODUCT DESCRIPTION: Example: Anhydrous emollient skin balm, white in color. Bulk product is manufactured by xxx and packaged in white stick with orange cap. Then sent to third party for label and tag application and shipped to client from there.
RESPONSIBILITY: The person in charge of making products is responsible for making this product. This formula is confidential, and should not be shared with others outside the company.
MATERIALS/EQUIPMENT/SUPPLIES: 1. Mix tank 3 2. Scale X 3. Bowls 4. Blender 5. Measuring cups/beakers 6. Thermometer

INGREDIENTS:		
Phase A		%
Phase B		%
Ingred #		
Ingred #		
Ingred #		
Ingred #		
Ingred #		
Ingred #		
TOTAL		100.00

Conclusion:

The primary regulatory body for the pharmaceutical sector, the ICH International Conference on Harmonization, is the subject of this essay. Their primary responsibilities, objectives, history, and current scope are all discussed, along with the branches and all potential ICH types. It is a significant regulatory body with significant power and authority that provides all countries with high-quality standard standards for the production of the best possible drugs. It also contains information on the function of ICH in good clinical practices (GCP). The foundation of all drug-related global metrics is ICH.

Japan, Europe, and the USA were the key participants, and for the benefit of public health, these countries produced a set of universal guidelines. These are primarily intended to address the whole world to produce safe, effective and high quality drugs and dosage forms.

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