



unicri

United Nations
Interregional Crime and Justice
Research Institute



The respect of Ethics and GCP in the CTs authorisation procedures in the EU

Umberto Filibeck

**Former Head of AIFA GCP Inspectorate and GCP Promotion Unit
UNICRI Consultant for Projects on GCP of CTs in developing
countries**

OPBG Clinical Trial Center Consultant

**DIRECTIVE 2001/20/EC OF THE EUROPEAN PARLIAMENT
AND OF THE COUNCIL of 4 April 2001**

**on the approximation of the laws,
regulations and administrative
provisions of the Member States
relating to the implementation of good
clinical practice in the conduct of
clinical trials on medicinal products for
human use**

laying down principles and detailed guidelines for good clinical practice as regards investigational medicinal products for human use, as well as the requirements for authorisation of the manufacturing or importation of such products

MAIN PROVISIONS

All clinical trials, including bioavailability and bioequivalence studies, shall be designed, conducted and reported in accordance with the principles of good clinical practice.

ICH-CGP PRINCIPLES

A) ETHIC GUARANTEE

- **2.1 Clinical trials should be conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki, and that are consistent with GCP and the applicable regulatory requirement(S).**
- **2.3 The rights, safety, and well-being of trial subjects are the most important considerations and should prevail over interests of science and society.**
- **2.6 A trial should be conducted in compliance with the protocol that has received prior EC approval.**
- **2.9 Freely given informed consent should be obtained from every subject prior to clinical trial participation.**

B) TECHNICAL-SCIENTIFIC GUARANTEE

- **2.4** The available nonclinical and clinical **information** on an investigational product **should be adequate** to support the proposed clinical trial.
- **2.7** 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.
- **2.8** Each individual involved in conducting a trial should be **qualified by education, training, and experience** to perform his or her respective task(s).
- **2.12** **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.

C) PROCEDURAL GUARANTEE

- **2.10** All **clinical trial information** should be recorded, handled, and stored in a way that allows its accurate reporting, interpretation and verification.
- **2.11** The **confidentiality of records** that could identify subjects should be protected, respecting the privacy and confidentiality rules in accordance with the applicable regulatory requirement.
- **2.13** System with procedures that assure the **quality** of every aspect of the trial should be implemented

A Clinical Trial may be undertaken only if, in particular, besides what foreseen by GCP principles:

- The rights of the subject to physical and mental integrity, to privacy and to the protection of the data concerning him, are safeguarded.
- The subject may without any resulting detriment withdraw from the clinical trial at any time by revoking his informed consent.
- Provision has been made for insurance or indemnity to cover the liability of the investigator and sponsor.
- The subject shall be provided with a contact point where he may obtain further information.
- No incentive or financial inducement are given.

A Clinical Trial on minors may be undertaken only if:

- The informed consent of the parents or legal representative has been obtained; consent must represent the minor's presumed will and may be revoked at any time, without detriment to the minor.
- The minor has received information according to its capacity of understanding, from staff with experience with minors, regarding the trial, the risks and the benefits.
- The Ethics Committee, with paediatric expertise or after taking advice in clinical, ethical and psychosocial problems in the field of paediatrics, has endorsed the protocol.

ETHICS COMMITTEE

‘Ethics committee’: an independent body in a Member State, consisting of healthcare professionals and non-medical members, whose responsibility it is

- to protect the rights, safety and wellbeing of human subjects involved in a trial and
- to provide public assurance of that protection, by, among other things,
 - expressing an opinion on the trial protocol,
 - the suitability of the investigators and the adequacy of facilities, and
 - on the methods and documents to be used to inform trial subjects and obtain their informed consent;

ETHICS COMMITTEE

- The Ethics Committee shall give its opinion, before a clinical trial commences.

ETHICS COMMITTEE

- In preparing its opinion, the Ethics Committee shall consider, among others:
 - (a) the relevance of the clinical trial and the trial design;
 - (b) whether the evaluation of the anticipated benefits and risks is satisfactory and whether the conclusions are justified;
 - (c) the protocol;
 - (d) the suitability of the investigator and supporting staff;
 - (e) the investigator's brochure;
 - (f) the quality of the facilities;

ETHICS COMMITTEE

- (g) the adequacy and completeness of the written information to be given and the procedure to be followed for the purpose of obtaining informed consent;
- (h) any insurance and provision for indemnity or compensation in the event of injury or death attributable to a clinical trial;
- (i) the amounts and, where appropriate, the arrangements for rewarding or compensating investigators and trial subjects;
- (j) the arrangements for the recruitment of subjects.

COMMENCEMENT OF A CLINICAL TRIAL

- EC approval
- Competent Authority authorization
- It is necessary written authorization by Competent Authorities, for all Phases CTs

AMENDMENTS

- Amendments may be made to the conduct of a clinical trial following the same procedures for CT authorization.

SUSPENSION/WITHDRAWAL OF THE CLINICAL TRIAL/MARKETING AUTHORIZATION

- When the Competent Authority (C.A.) has information raising doubts about the safety or scientific validity of the clinical trial, it may suspend or prohibit the clinical trial.
- Withdrawal of Marketing Authorisation (M.A.) when CTs have been conducted not in compliance with GCP
- Refusal of MA application based on CT performed in EU and extra-EU Countries not in compliance with GCP ethical principles.

MANUFACTURE AND IMPORT OF INVESTIGATIONAL MEDICINAL PRODUCTS (IMP)

- Manufacture or importation of Investigational Medicinal Product (IMP) must be authorized by the C.A.

VERIFICATION OF COMPLIANCE OF CLINICAL TRIALS AND INVESTIGATIONAL MEDICINAL PRODUCTS WITH GOOD CLINICAL AND MANUFACTURING PRACTICE

- To verify compliance with the provisions on GCP and GMP, the C.A. appoints inspectors to inspect the sites concerned by any clinical trial conducted, particularly the trial site or sites, the manufacturing site of the IMP, any laboratory used for analyses in the clinical trial and/or the sponsor's premises and ethics committee as well.
- The inspections shall be conducted on behalf of European Community and the results shall be recognised by all EU Member States.

VERIFICATION OF COMPLIANCE OF CTs AND IMP WITH GCP AND GMP

- GCP inspections may take place on any of the following occasions:
 - (a) before, during or after the conduct of clinical trials;
 - (b) as part of the verification of applications for marketing authorisation;
 - (c) as a follow-up to the granting of authorisation.

- Improvement and harmonisation of inspection guidance shall be achieved by the Member States, in collaboration with the Commission and the Agency, through joint inspections, agreed processes and procedures and sharing of experience and training.

*Thank you
for
your attention*