European Medicines Agency

March 1998
CPMP/ICH/291/95

ICH Topic E 8
General Considerations for Clinical Trials

Step 5

NOTE FOR GUIDANCE ON GENERAL CONSIDERATIONS FOR CLINICAL TRIALS

(CPMP/ICH/291/95)

TRANSMISSION TO CPMP	November 1996
TRANSMISSION TO INTERESTED PARTIES	November 1996
DEADLINE FOR COMMENTS	May 1997
FINAL APPROVAL BY CPMP	September 1997
DATE FOR COMING INTO OPERATION	March 1998

7 Westferry Circus, Canary Wharf, London, E14 4HB, UK
Tel. (44-20) 74 18 85 75 Fax (44-20) 75 23 70 40

GENERAL CONSIDERATIONS FOR CLINICAL TRIALS

ICH Harmonised Tripartite Guideline

Table of Contents

1. OBJECTIVES OF THIS DOCUMENT

In the three ICH regions, the evolution of drug development strategies and evaluation processes has led to the establishment of regional guidances on general considerations for clinical trials and the process of clinical development of pharmaceuticals for human use. This harmonised guideline is derived from those regional documents as well as from ICH Guidelines.

The ICH document "General Considerations for Clinical Trials" is intended to:

a) describe internationally accepted principles and practices in the conduct of both individual clinical trials and overall development strategy for new medicinal products.

b) facilitate the evaluation and acceptance of foreign clinical trial data by promoting common understanding of general principles, general approaches and the definition of relevant terms.

c) present an overview of the ICH clinical safety and efficacy documents and facilitate the user's access to guidance pertinent to clinical trials within these documents. The relevant ICH documents are listed in Annex 1.

d) provide a separate glossary of terms used in the ICH clinical safety and efficacy related documents that pertain to clinical trials and indicate which documents contain them.

For the sake of brevity, the term "drug" has been used in this document. It should be considered synonymous with "investigational (medicinal) product", "medicinal product" and "pharmaceutical" including vaccines and other biological products. The principles established in this guideline may also be applied to other clinical investigations (e.g. radiotherapy, psychotherapy, surgery, medical devices and alternative therapies).

2. GENERAL PRINCIPLES

2.1 Protection of clinical trial subjects

The principles and practices concerning protection of trial subjects are stated in the ICH Guideline on Good Clinical Practice (ICH E6). These principles have their origins in The Declaration of Helsinki and should be observed in the conduct of all human drug investigations.

Before any clinical trial is carried out, results of non-clinical investigations or previous human studies should be sufficient to indicate that the drug is acceptably safe for the proposed investigation in humans. The purpose and timing of animal pharmacology and toxicology studies intended to support studies of a given duration are discussed in ICH M3. The role of such studies for biotechnology products is cited in ICH S6.

Throughout drug development, emerging animal toxicological and clinical data should be reviewed and evaluated by qualified experts to assess their implications for the safety of the trial subjects. In response to such findings, future studies and, when necessary, those in progress should be appropriately modified in a timely fashion to maintain the safety of trial participants. The investigator and sponsor share responsibility for the protection of clinical trial subjects together with the Institutional Review Board/Independent Ethics Committee. The responsibilities of these parties are described in ICH E6.

2.2 Scientific approach in design and analysis

Clinical trials should be designed, conducted and analysed according to sound scientific principles to achieve their objectives; and should be reported appropriately. The essence of

rational drug development is to ask important questions and answer them with appropriate studies. The primary objectives of any study should be clear and explicitly stated.

Clinical studies can be classified according to when the study occurs during clinical development or as shown in Table 1 by their objectives. (The illustrative examples are not intended to be exhaustive). The cardinal logic behind serially conducted studies of a medicinal product is that the results of prior studies should influence the plan of later studies. Emerging data will frequently prompt a modification of the development strategy. For example, results of a therapeutic confirmatory study may suggest a need for additional human pharmacology studies.

The availability of foreign clinical data should obviate the need to generate similar data in an ICH region if the ICH E5 and ICH E6 guidelines are followed. (see ICH E5).

Table 1 - An Approach to Classifying Clinical Studies According to Objective

Type of Study	Objective of Study	Study Examples
Human Pharmacology	• Assess tolerance • Define/describe PK[1] and PD[2] • Explore drug metabolism and drug interactions • Estimate activity	• Dose-tolerance studies • Single and multiple dose PK and/or PD studies • Drug interaction studies
Therapeutic Exploratory	• Explore use for the targeted indication • Estimate dosage for subsequent studies • Provide basis for confirmatory study design, endpoints, methodologies	• Earliest trials of relatively short duration in well- defined narrow patient populations, using surrogate or pharmacological endpoints or clinical measures • Dose-response exploration studies
Therapeutic Confirmatory	• Demonstrate/confirm efficacy • Establish safety profile • Provide an adequate basis for assessing the benefit/risk relationship to support licensing • Establish dose-response relationship	• Adequate, and well controlled studies to establish efficacy • Randomised parallel dose-response studies • Clinical safety studies • Studies of mortality/ morbidity outcomes • Large simple trials • Comparative studies
Therapeutic Use	• Refine understanding of benefit/risk relationship in general or special populations and/or environments • Identify less common adverse reactions • Refine dosing recommendation	• Comparative effectiveness studies • Studies of mortality/morbidity outcomes • Studies of additional endpoints • Large simple trials • Pharmacoeconomic studies

[1]Pharmacokinetics
[2]Pharmacodynamics

DOCKET ALARM

Explore Litigation Insights

Docket Alarm provides insights to develop a more informed litigation strategy and the peace of mind of knowing you're on top of things.

Real-Time Litigation Alerts

Keep your litigation team up-to-date with **real-time alerts** and advanced team management tools built for the enterprise, all while greatly reducing PACER spend.

Our comprehensive service means we can handle Federal, State, and Administrative courts across the country.

Advanced Docket Research

With over 230 million records, Docket Alarm's cloud-native docket research platform finds what other services can't. Coverage includes Federal, State, plus PTAB, TTAB, ITC and NLRB decisions, all in one place.

Identify arguments that have been successful in the past with full text, pinpoint searching. Link to case law cited within any court document via Fastcase.

Analytics At Your Fingertips

Learn what happened the last time a particular judge, opposing counsel or company faced cases similar to yours.

Advanced out-of-the-box PTAB and TTAB analytics are always at your fingertips.

API

Docket Alarm offers a powerful API (application programming interface) to developers that want to integrate case filings into their apps.

LAW FIRMS
Build custom dashboards for your attorneys and clients with live data direct from the court.

Automate many repetitive legal tasks like conflict checks, document management, and marketing.

FINANCIAL INSTITUTIONS
Litigation and bankruptcy checks for companies and debtors.

E-DISCOVERY AND LEGAL VENDORS
Sync your system to PACER to automate legal marketing.