Clinical trial design -Prerequisites-Ethics

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Glossary/ definitions (IMP/NIMP…)

Prerequisites for first study in man
- IMPD

Good clinical Practice (GCP)
- General Considerations
- The Principles of GCP
- Ethics Committee
- Investigator
- Sponsor
- Investigator's Brochure (IB)
- Clinical Trial Protocol

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Investigational Medicinal Product (IMP)

Substance used as the test substance or reference substance (active comparator or placebo)

Non Investigational Medicinal Product (NIMP)

Substance wich are not the object of investigation but used in the trial according the protocol

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Focus on IMPD: investigational medical product dossier

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European Medicines Agency
Inspections

London, 31 March 2004
CHMP/QWP/185401/2004 final

COMMITTEE FOR MEDICINAL PRODUCTS FOR HUMAN USE
(CHMP)

GUIDELINE ON THE REQUIREMENTS TO THE CHEMICAL AND PHARMACEUTICAL QUALITY DOCUMENTATION CONCERNING INVESTIGATIONAL MEDICINAL PRODUCTS IN CLINICAL TRIALS

DISCUSSION IN THE QWP	June/Oct. 2004
TRANSMISSION TO CHMP	December 2004
RELEASE FOR CONSULTATION	December 2004
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ADOPTION BY CHMP FOR TRANSMISSION TO EUROPEAN COMMISSION	23 March 2006
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Note: This Guideline was developed by the CHMP Quality Working Party with a mandate from the European Commission, to facilitate the implementation of Directive 2001/20/EC.

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GUIDELINE ON THE REQUIREMENTS TO THE CHEMICAL AND PHARMACEUTICAL QUALITY DOCUMENTATION CONCERNING INVESTIGATIONAL MEDICINAL PRODUCTS IN CLINICAL TRIALS

TABLE OF CONTENTS

IMPD

Investigational medicinal product dossier:
Describes the chemical and pharmaceutical quality

Two chapters:

S: Drug Substance

P: Investigational medicinal product under investigation

IMPD

IMPD

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Eur J Nucl Med Mol Imaging
DOI 10.1007/s00259-008-0853-7

GUIDELINES

Guideline to regulations for radiopharmaceuticals in early phase clinical trials in the EU

Alfons Verbruggen · Heinz H. Coenen · Jean-Robert Deverre · Denis Guilloteau · Bengt Langstrom · Piero A. Salvadori · Christer Halldin

Abstract The purpose of this guideline is to help investigators by giving an overview of relevant current EU requirements concerning the quality of starting materials and final drug products (the radiopharmaceuticals), the non-clinical safety studies and dosimetry considerations whilst designing a human clinical trial which includes the use of radiopharmaceutical compounds.

Keywords Radiopharmaceuticals · Early phase · Clinical trials · Regulations · Quality requirements · Toxicology · Dosimetry

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European Medicines Agency

June 2009
CPMP/ICH/286/95

ICH Topic M 3 (R2)
Non-Clinical Safety Studies for the Conduct of Human Clinical Trials and Marketing Authorization for Pharmaceuticals

Step 4

NOTE FOR GUIDANCE ON NON-CLINICAL SAFETY STUDIES FOR THE CONDUCT OF HUMAN CLINICAL TRIALS AND MARKETING AUTHORIZATION FOR PHARMACEUTICALS
(CPMP/ICH/286/95)

TRANSMISSION TO CHMP	July 2008
TRANSMISSION TO INTERESTED PARTIES	July 2008
DEADLINE FOR COMMENTS	October 2008
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DATE FOR COMING INTO OPERATION	December 2009

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Table 3: Non-Clinical Studies to Support Exploratory Clinical Investigations

Clinical:		Non clinical:		
Dose to be Administered	**Start and Maximum Doses**	**Pharmacology**	**General Toxicity Studies**	**Genotoxicity / Other**
Approach 1: Total dose ≤ 100 µg; maximum of 3 administrations (at least one week between doses) AND Total dose ≤ 1/100[th] NOAEL and ≤ 1/100[th] pharmacologically active dose (scaled on mg/kg for i.v. and mg/m[2] for oral)	Maximal and starting doses can be the same but not exceed 100 µg	In vitro target/ receptor profiling should be conducted Appropriate characterization of pharmacology in a pharmacodynamically relevant species should be available to support human dose selection.	Extended single dose toxicity study[a] in one species, usually rodent, by intended route of administration with toxicokinetic profile or via the i.v. route. A limit dose of 10 mg/kg in rats (~6000 times the 100 µg clinical dose on a mg/kg comparison basis) can be used.	Genotoxicity studies are generally not conducted, but any studies or SAR assessments conducted should be included in the clinical trial application. For highly radioactive agents, appropriate pharmacokinetics and dosimetry estimates should be submitted
Approach 2: Total cumulative dose ≤ 500 µg, maximum of 5 administrations with a washout between doses (6 or more actual or predicted half-lives) AND each dose ≤ 100 µg AND each dose < 1/100[th] of the NOAEL and <1/100[th] of the pharmacologically active dose	Maximal daily and starting doses can be the same, but not exceed 100 µg.	In vitro target/receptor profiling should be conducted Appropriate characterization of pharmacology in a pharmacodynamically relevant species should be available to support human dose selection.	7 day toxicology study in one species, usually rodent, by i.v. route or intended route of administration, with toxicokinetics, haematology, clinical chemistry, necropsy data and histopathology. A limit dose of 10 mg/kg in rats (~6000 times the 100 µg clinical dose) can be used.	Genotoxicity studies are generally not conducted, if SAR assessments are negative. No genotoxicity assay is recommended for PET ligands. For highly radioactive agents, appropriate pharmacokinetics and dosimetry estimates should be submitted

IMPD

Example : IMPD of [^{18}F]fluormethycholine

EANM website: sharing IMPD's:

http://www.eanm.org/committees/radiopharmacy/index.php?navId=225