IRISH MEDICINES BOARD

Clinical trial applications–IMB procedure

Making gene and cell therapy medicines a reality

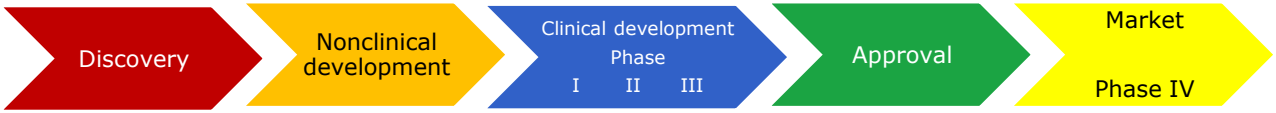
Gibson Hotel, Dublin. 11th July 2012

Dr. Una Moore,
Senior Pharmaceutical Assessor,
Irish Medicines Board.

Clinical Trials for ATMPS

What is a clinical trial?

*any investigation in human subjects intended to discover or verify the clinical, pharmacological and/or other pharmacodynamic effects of one or more investigational medicinal product(s), and/or to identify any adverse reactions to one or more investigational medicinal product(s) and/or to study absorption, distribution, metabolism and excretion of one or more investigational medicinal product(s) with the object of ascertaining its (their) safety and/or efficacy

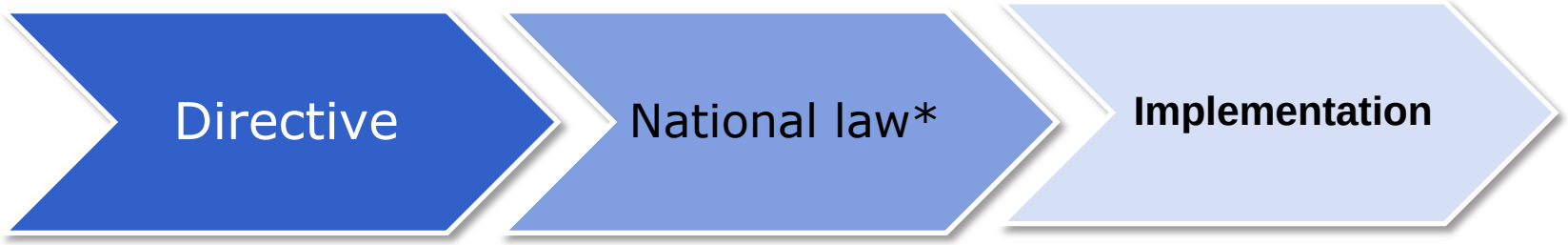


*Directive 2001/20/EC

IRISH MEDICINES BOARD

Legal Regulatory Framework for CTs in the EU

- The EU Clinical Trials Directive 2001/20/EC



*Transposed into Irish law – European Communities Regulations, 2004 (SI No. 190 of 2004)

Amendments to 2001/20/EC:
The Good Clinical Practice Directive 2005/28/EC
The Good Manufacturing Practice Directive12003/94/EC

IRISH MEDICINES BOARD

Objective of Directive 2001/20/EC

- Established to:
  - provide greater protection to subjects participating in CTs
  - ensure quality of conduct
  - Harmonisation of the regulation required to carry out a CT in EU

Point 16 of Regulation No 1394/2007 on ATMPs states that principles and ethical requirements of Directive 2001/20/EC apply to ATMP CTs

IRISH MEDICINES BOARD

Sponsor

- Sponsor:
  - *An individual, company, institution or organisation which takes responsibility for the initiation, management and/or financing of a clinical trial.
- Every trial must have a sponsor
- Based in EU or legal representative in EU/EEA
- IMB's communication is with the sponsor

*Directive 2001/20/EC

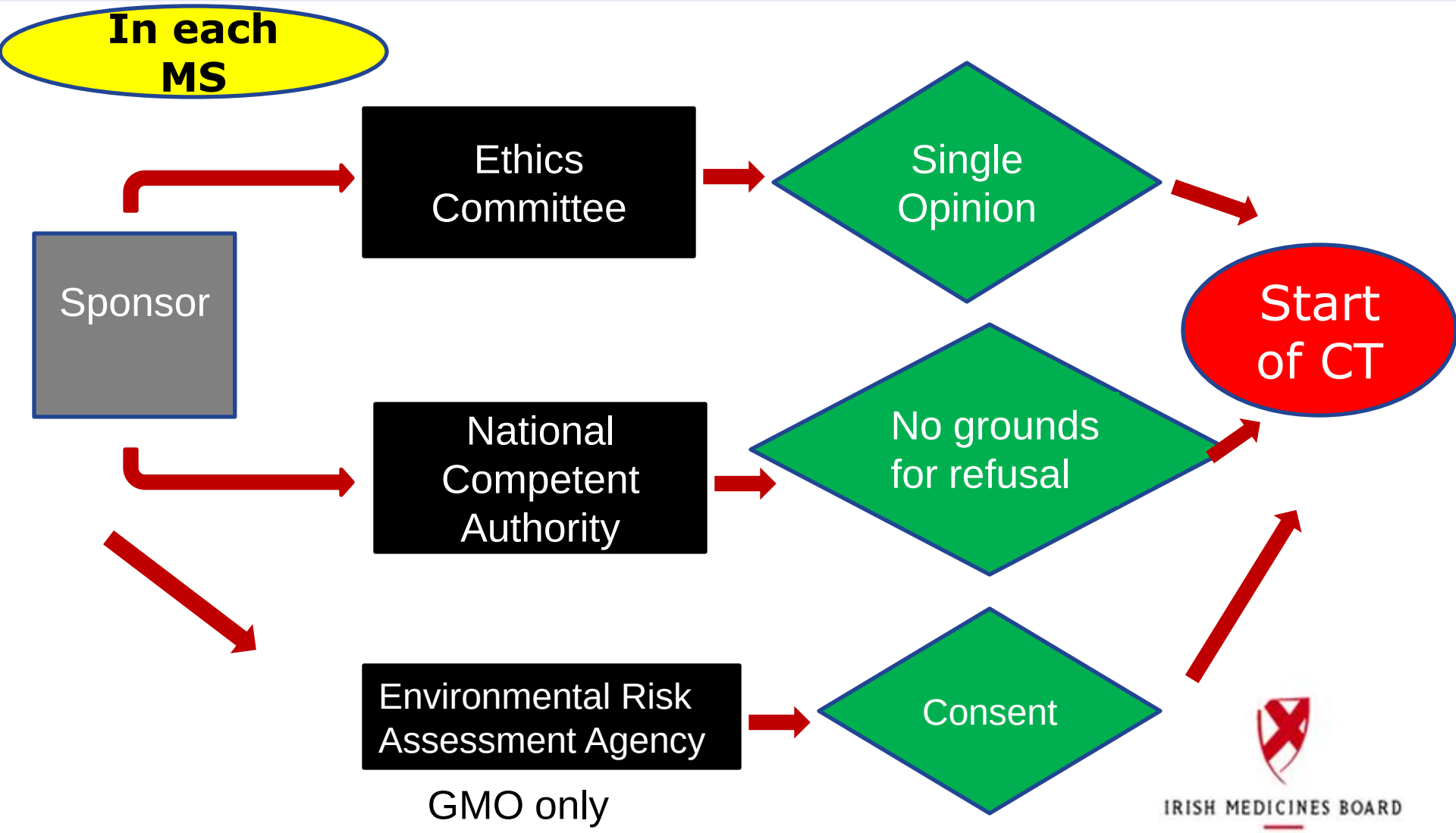
IRISH MEDICINES BOARD

Investigator

- **Investigator:**
  - Authorised health care professional responsible for conducting the investigations at the trial site.
  - If the trial is conducted by a team of individuals the investigator is the leader responsible for the team.

IRISH MEDICINES BOARD

Clinical Trials – What's required to start a CT?



Clinical Trials in Ireland

- Who regulates CT's in Ireland?
  - The IMB is responsible for the:
    - Authorisation of clinical trials and the
    - Inspection of compliance with good clinical practice
    - Pharmacovigilance for CT
  - Ethics Committees - Department of Health
  - Environmental Protection Agency (GMOs)

An Roinn Sláinte
DEPARTMENT OF HEALTH

epa
Environmental Protection Agency
An Ghníomhaireacht um Chaomhnú Comhshaoil

IRISH MEDICINES BOARD

Making a CT application to the IMB

General information:

- Covering letter
- EudraCT number
- EudraCT application form
- IMP labelling in English
- EPA Certificate (for GMOs only)

Protocol-related folder:

- Clinical Trial Protocol + synopsis
- Ethics Committee's opinion (when available)

IMP-related folder

- Investigator's brochure
- Investigational Medicinal Products Dossier (IMPD)
- Non-Investigational Medicinal Products Dossier (NIMPD)
- Scientific Advice (NCA or EMA, if any)

IRISH MEDICINES BOARD

- **EudraCT number** - Each clinical trial with at least one site in the European Union receives a unique number for identification, the EudraCT Number, must be included on all clinical trial applications

- EudraCT (**E**uropean **U**nion **D**rug **R**egulating **A**uthorities **C**linical **T**rials) is a database of all clinical trials commencing in the Community from 1 May 2004 onwards.

  Established in accordance with Directive 2001/20/EC.

  Access to EudraCT database is confidential, can only be accessed by Competent Authorities of the Member States, the EMA and the Commission.

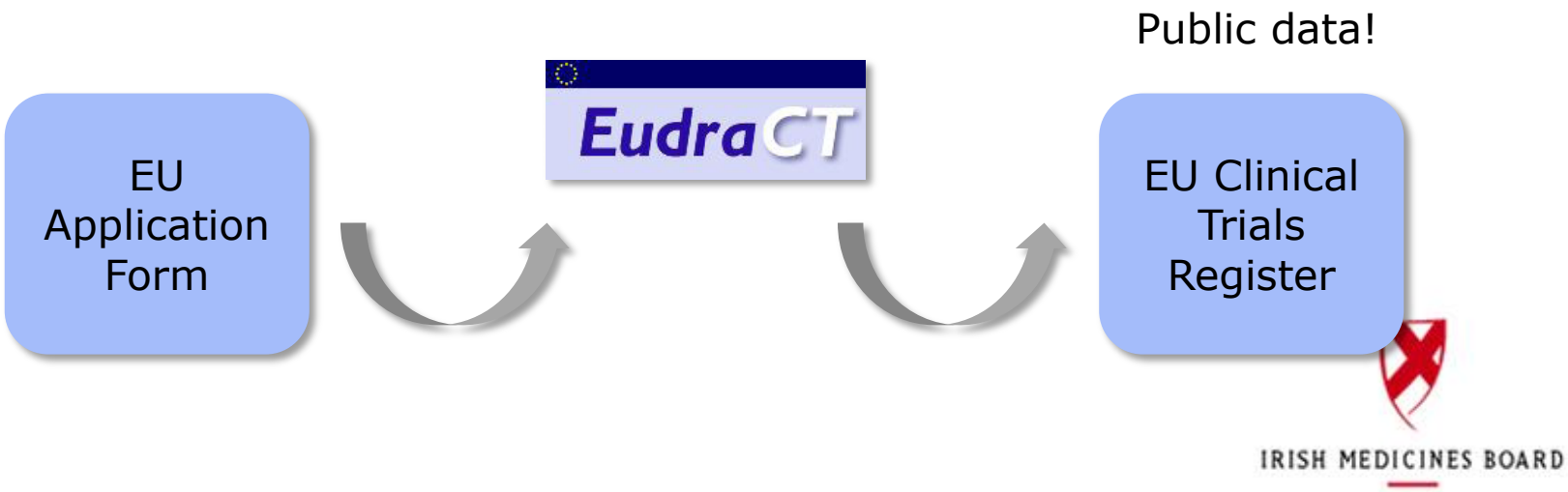
https://eudract.emea.europa.eu

IRISH MEDICINES BOARD

CT Register

- The Public Side of EudraCT- EU Clinical Trials Register (https://www.clinicaltrialsregister.eu)

Public online register gives access to information on clinical trials in the EU.



Clinical Trials – Documentation to be submitted

- *Clinical trial protocol*:

  *A document that describes the objectives, design, methodology, statistical considerations and organisation of a trial. The term protocol refers to the protocol, successive versions of the protocol and protocol amendments;

- *Investigator's brochure*

  *A compilation of the clinical and non-clinical data on the investigational medicinal product or products which are relevant to the study of the product or products in human subjects

*Directive 2001/20/EC

IRISH MEDICINES BOARD

Clinical Trials – Documentation to be submitted

Investigational Medicinal Products Dossier (IMPD)

- Provides information on the
  - Quality of the test product,
  - Comparators, placebos.
  - Site(s) of manufacture
  - Non-clinical and clinical studies

- Full IMPD
- Simplified IMPD
- Summary of Product Characteristics

IRISH MEDICINES BOARD

Investigators Medicinal Product Dossier

Full IMPD is required:

- Products which are not authorised in EU/EEA/ICH
- Placebos

Simplified IMPD or no IMPD required:

- Authorised Product - no changes - SmPC suffice
- If authorised product is blinded / modified – data to demonstrate that there is no significant effect on the quality of the product.
- Data previously assessed in the MS concerned.

More details in CT-1

Communication from the Commission – detailed guidance on the request to the competent authorities for authorisation of a clinical trial on a medicinal product for human use, the notification of substantial amendments and the declaration of the end of the trial (CT-1).

IRISH MEDICINES BOARD

Guidance documents on the preparation of a full IMPD

Substances of biological origin:
Guideline on the requirements for quality documentation concerning biological investigational medicinal products in CTs (EMA/CHMP/BWP/534898/2008).

Guideline on virus safety evaluation of biotechnological investigational medicinal products (EMEA/CHMP/BWP/398498/2005)

Substances of chemical origin: Guideline on the requirements to the chemical and pharmaceutical quality documentation concerning investigational medicinal products in clinical trials (CHMP/QWP/185401/2004)

Advanced Therapy IMPs: medicinal products involving cell or gene therapy or tissue engineering - no specific guidance documents available
(EMA website www.ema.europa.eu/ Home – Regulatory – Human Medicines – Scientific Guidelines – Biologicals – Drug substance.

Non Clinical Studies:
ICH M3 Non-clinical safety studies for the conduct of human clinical trials and marketing authorization for pharmaceuticals (CPMP/ICH/286/95), 2009

IRISH MEDICINES BOARD

Manufacture of IMPs

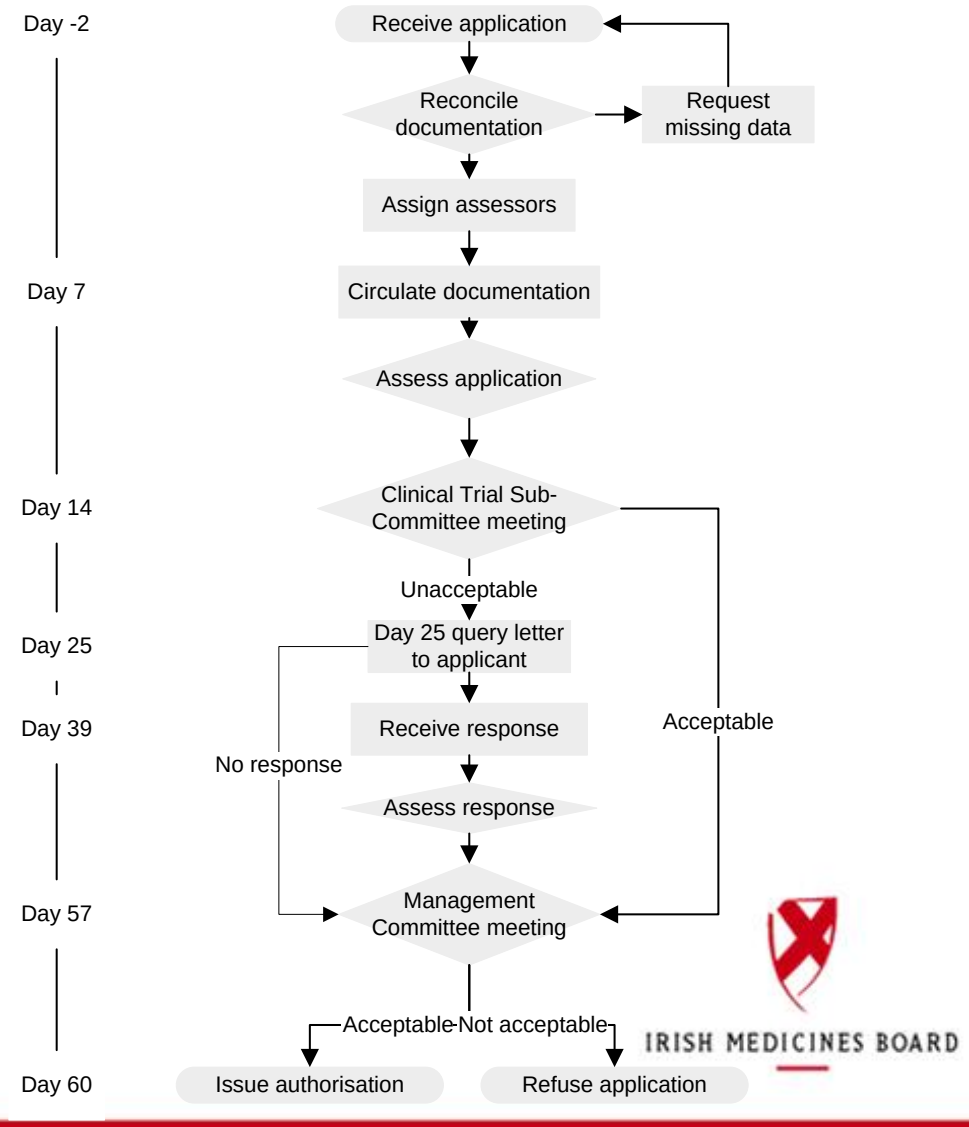
- IMP licences / QP declarations are required for:
  - All sites conducting manufacturing activities related to the unauthorised IMP / placebo (e.g. manufacture, packaging).
  - Sites performing modification/ re-packaging of authorised products (dependent on the modification proposed).
  - Release of unauthorised IMPs / placebo and modified authorised products (IMP licence).

IRISH MEDICINES BOARD

Clinical Trials – IMB Procedure for non-ATMPs

Total timetable ≤60 days

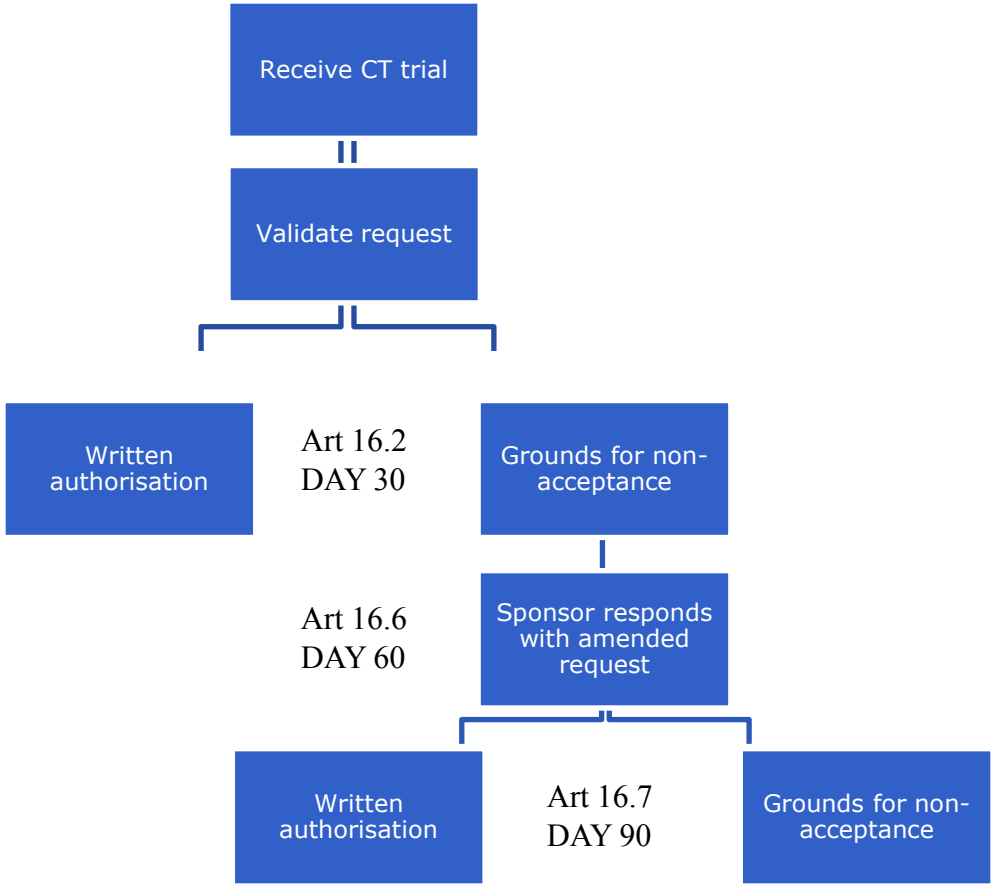
No clock stop



Clinical Trials – IMB Procedure for ATMPs

Total timetable ≤90 days

No clock stop



*Directive 2001/20/EC

IRISH MEDICINES BOARD

Clinical Trials – IMB Procedure for ATMPs (extended)

Total timetable ≤180 days

No clock stop

Receive CT trial

Validate request

Request to ACHM or SC +90 days

Art 16.4

Written authorisation

Art 16.2
DAY 120

Grounds for non-acceptance

Art 16.6
DAY 150

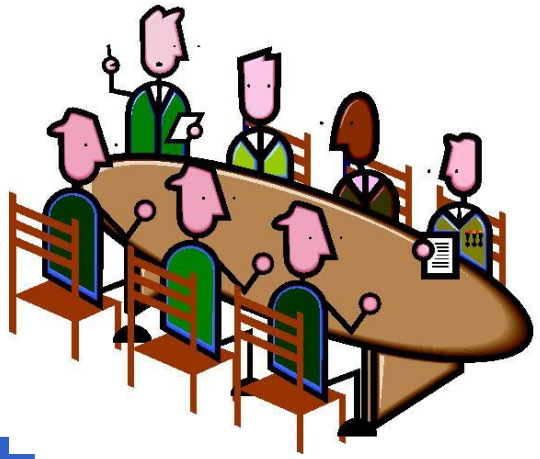
Sponsor responds with amended request

Written authorisation

Art 16.7
DAY 180

Grounds for non-acceptance

Expert Group/committee



*Directive 2001/20/EC

IRISH MEDICINES BOARD

Clinical Trials – IMB Procedure for ATMPs

Non ATMP CT	ATMP CT
No meeting required	Pre-submission meeting with IMB required (IMB requirement)
Maximum 60 day assessment timetable	60 day timetable can be extended to 90 days on IMB request
No extension to timetable permitted	Assessment timetable can be extended to 180 days if IMB needs to consult with group/committee
Written authorisation not always required before commencement of a CT	Written authorisation is always required before commencement of trial (also biological products)
Not applicable	If GMO containing CT – consent from environmental agency required

IRISH MEDICINES BOARD

IMB Fees for CT

Commercial
Pharmaceutical
Companies

Non-commercial
Hospitals
Universities
Researchers

Fees:
538 to 2889 Euro

No Fees

IMB Guide to fees for human products- fee codes 341-347

IRISH MEDICINES BOARD

Clinical Trials Guidelines - Volume 10

Chapter I

- The dossier for the competent authority (CT1)
- The dossier for the ethics committee

Chapter II

- Pharmacovigilance

Chapter III

- Pharmaceutical data

Chapter IV

- Inspections

Chapter V:

- GCP, EudraCT

Chapter VI:

- Legislation

IRISH MEDICINES BOARD

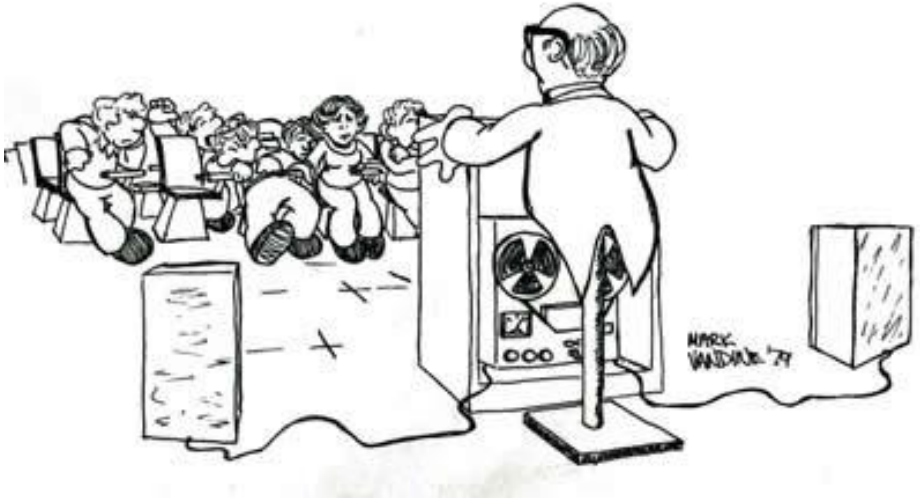
Important Web Addresses

- IMB website: www.imb.ie
- EMEA website: www.emea.europa.eu
- European Commission: http://ec.europa.eu
- ICH: www.ich.org
- European Pharmacopoeia: www.edqm.eu

IRISH MEDICINES BOARD

Clinical trial applications–IMB procedure

Thank you for your attention



IRISH MEDICINES BOARD