



International Guidances

ICH International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use
The ICH guidances were developed by representatives from the United States, Europe and Japan.

ISO The International Organization for Standardization
ISO standards are developed by representatives from several countries. Countries can contribute to the development of an ISO standard and can incorporate ISO standards in their law. In the Netherlands, the NEN (Nederlands Normalisatie Instituut) is involved in these international standards.

Examples of ICH guidances:

- ICH E2A** Clinical Safety Data Management
- ICH E3** Structure and Content of Clinical Study Reports
- ICH E6** Good Clinical Practice (GCP)
- ICH E8** General Considerations for Clinical Trials
- ICH E9** Statistical Principles for Clinical Trials

Examples of ISO standards:

- ISO 14155 part 1** Clinical investigation of medical devices for human subjects – Part 1: General requirements
- ISO 14155 part 2** Clinical investigation of medical devices for human subjects – Part 2: Clinical investigation plans

ISO 14155 part 1 and 2 are referred to in Dutch law.

American Laws

The Food and Drug Administration (FDA) creates Codes of Federal Regulations (CFR). These CFRs are laws.

There are several departments at the FDA, amongst others:

CBER Center for Biologics Evaluation and Research
CDER Center for Drug Evaluation and Research
CDRH Center for Devices and Radiological Health

For clinical research the 21 CFR's apply, for example:

21 CFR 11 Electronic Records, Electronic Signatures

21 CFR 50 Protection of Human Subjects

21 CFR 54 Financial Disclosure by Clinical Investigators

21 CFR 56 Institutional Review Boards

Examples of clinical research laws specific for medicines:

21 CFR 312 Investigational New Drug Application

21 CFR 314 Applications for FDA Approval to Market a New Drug

Examples of clinical research laws specifically for "biologics":

21 CFR 601 Applications for FDA Approval of a Biologic License

Examples of clinical research laws specifically for medical devices:

21 CFR 803 Medical Device Reporting

21 CFR 806 Medical devices – Reports of Corrections and Removals

21 CFR 812 Investigational Device Exemptions

21 CFR 814 Premarket Approval of Medical Devices

21 CFR 822 Postmarket Surveillance – Medical Device

Sometimes there is documentation for further reference of a form or law available:

For the 21 CFR part 11:

**Guidance for Industry: Computerized Systems Used in Clinical Investigations
Guidance 21 CFR 11; Electronic Records, Electronic Signatures – Scope and
Application**

For the 21 CFR part 822:

Supporting Statement Postmarket Surveillance – Medical Device

With reference to the 'predicate rules' international guidances like the Good Clinical Practice, Good Laboratory Practice and/or Good Manufacturing Practice are meant. The 21 CFR part 312, for example, refers to the Good Laboratory Practice.

The following abbreviations are used:

IDE Investigational Device Exemptions
PMA Premarket Approval
NDA New Drug Application
IND Investigational New Drug Application
510(k) Premarket Notification

21 CFR part 11 is currently under revision. A new draft guidance Scope and Application is already available.

European Guidances

Europe has different agencies, amongst others:

EMA European Medicines Agency (Medicines, herbs and “biologics”)

Clinical Trial Directive (2001/20/EC and 2005/28/EC for non-commercial research)

Data Privacy Directive (95/46/EG)

Medical Devices Directive (93/42/EEC)

Active Implantable Medical Devices Directive (90/385/EEC)

These guidances have to be implemented in each national law of the European country members. The Netherlands are busy implementing the Clinical Trial Directive in their national law 'Wet Medisch-Wetenschappelijk Onderzoek met Mensen'.

Dutch Laws

WMO Wet Medisch-wetenschappelijk Onderzoek met Mensen

WBP Wet Bescherming Persoonsgegevens

WBGO Wet Geneeskundige Behandelingsovereenkomst

Besluit Medische Hulpmiddelen

Besluit Klinische Evaluatie Medische Hulpmiddelen

The current WMO is of 1998. It is under revision for adjustment to the European Clinical Trial Directive of 2001.

Unofficial Guidance

GCdM Good Clinical Data Management Practices

Developed by the Society for Clinical Data Management (SCDM) to promote standards of good practice within clinical data management.

The SCDM is a non-profit professional organization founded to advance the discipline of clinical data management.

When do which laws apply to clinical research?

Dependent on the country/countries where:

- the product under investigation will be applied for market approval
- the clinical research is conducted.

Laws & Guidances in daily clinical data management practice

Most important for clinical data management is the 21 CFR part 11 with its guidances, the ICH E6 GCP and/or the ISO 14155 part 1. And, if chosen by you or your organisation, the GCdM.