

Appendix 2: International regulations for clinical investigation with medical devices

Table 1: Overview

Legislature	National Medical Device Acts
<p>European Guidelines (Directives) MDD 93/42/EEC AIMDD 90/385/EEC IVDMD 98/79/EC</p>	
<p>State of the art</p>	<ul style="list-style-type: none"> ▪ MEDDEV 2.7.1 (12/2009) "Evaluation of clinical data. A guide for manufacturers and notified bodies" (incl. Appendix 1) ▪ MEDDEV 2.7.2 (12/2008) „Guide for Competent Authorities in making an assessment of clinical investigation; notification.“ ▪ MEDDEV 2.12.2 (May 2004) "On PostMarket Clinical Follow-up"
<ul style="list-style-type: none"> ▪ ISO EN 14155 (Part 1 und 2) Clinical investigation of medical devices for human subjects - <ul style="list-style-type: none"> ▪ Part 1: General requirements ▪ Part 2: Clinical investigation plans (update in preparation) ▪ Guideline for Good Clinical Practice (ICH Topic E 6, CPMP/ICH/135/95) 	<ul style="list-style-type: none"> ▪ GHTF SG5/N2R8:2007 „Clinical Evaluation“ (final, 08.05.2007) ▪ GHTF SG5(PD)N3R7: „Clinical Investigations (Draft 23.01.2008)“ ▪ GHTF SG5(PD)N4R7: „PMCF-Studies“ (Draft 23.July 2008) ▪ Declaration of Helsinki

Some key concepts in regulations for clinical investigation with medical devices:

- *Uncertified medical devices (before certification in Europe)*

In order to conduct a clinical investigation of the performance, safety and therapeutical benefit of a treatment or method with uncertified medical devices approved medical devices or handling instructions used in off-label indications or with additional unusual burdens for the patient, a study protocol with all additional necessary documents or approvals must be prepared. Registration with or approval by the relevant national authorities may be necessary depending on the national or local law.

The results of the clinical investigation should be summarised in a clinical, biometric report containing critical comments on the study concept, the study methodology and interpretation of the results, and take into account the clinical and scientific knowledge available. The report should draw conclusions for the medical profession, the medical device manufacturer and, where appropriate, the health authorities and any other bodies. This comprehensive report constitutes part of the clinical trial and is necessary regardless of whether or not the study is to be published.



- *Certified medical devices (after certification in Europe, use according to its intended purpose)*

The conduct of clinical studies with certified medical devices used in their certified indications or 'instructions for use' are governed by minor regulatory requirements – also dependent on the current national or local law.

- *New technologies / products with new physical mode of action:*

New technologies or products with new physical mode of action or certified medical devices outside its intended purpose/use have to be proven according to the current guidelines.

The manufacturer must demonstrate that the intended purpose(s) and claim(s) made in relation to safety, performance and therapeutical benefit are achieved, as referred to in the Directives for medical devices. As a general rule, such demonstration will require clinical data (Annex X of the Medical Device Directive, MDD 93/42/EEC or Annex 7 of the Active Implantable Medical Devices Directive AIMDD 90/385/EEC). Evaluation of clinical data is particularly relevant to assessment of conformity with essential requirements given in *MDD 93/42/EEC Annex I: General Requirements, sections 1 and 3* and *AIMD 90/385/EEC Annex 1: General requirements, sections 1 and 2*. Attention should also be paid to Annex I, I.6 (MDD) and Annex 1, I.5 (AIMD).

- *Clinical Data*

Clinical data are data which are relevant to the various aspects of the clinical safety, performance and therapeutical benefit of the device. This must include data obtained from:

- published and/or unpublished data on market experience of the device in question; or a similar device for which equivalence to the device in question can be demonstrated; or
- a prospective clinical investigation(s) of the device concerned; or
- results from a clinical investigation(s) or other studies reported in the scientific literature of a similar device for which equivalence to the device in question can be demonstrated.

Clinical evaluation is based on the assessment of the risks and the benefits, associated with use of the device, through either:

- a) the literature route and/or
- b) clinical investigation route

In the clinical assessment report all clinical data will be reviewed and the clinical benefit/risk ratio will be discussed (MEDDEV. 2.7.1 April 2003 Evaluation of clinical data. A guide for manufactures and notified bodies).

- *Literature search*

The conclusion on the acceptability of a medical device is based on an assessment of risks and benefits of the literature route or the clinical trial route. In the absence of own clinical trials this analysis should be done according the literature route. Literature research has been carried out in different databases, according to the MEDDEV recommendation.

- *Metoo products / Generics:*

A lot of products for Conventional or Modern Wound Management are on the market. Nevertheless we have different product groups/families like gauzes, robes, hydrocolloids, foams, films, alginates, hydrofiber, dressings in combination with supportive/ancillary pharmaceutical compounds (like silver or polihexanide dressings).



The standard product groups/families are often referred to as “me-too” products; the European definitions related to “me-too” products can be found in MEDDEV 2.7.1 and 2.12/2 (www.ec.europa.eu/enterprise/medical_devices/meddev/meddev_index_en.htm). In these cases, the manufacturer must demonstrate equivalence in all the essential characteristics (Technical, biological and clinical properties). Special attention is paid to the performance, principles of operation and materials in comparison with existing products. If differences are identified, an assessment and demonstration of the significance these differences may have on safety and performance must be documented. Where products are essentially equivalent, considerations of cost and budget impact become more important than clinical end-points.