

Consultation of medical devices combined with medicinal products

Authorization of combination products is based on the Medical Devices Directive (MDD: 93/42/EEC). For certification of these products by a Notified Body, the manufacturer submits all necessary documentation to the Notified Body which assesses the medical device included in the product and initiates the compulsory consultation by a Competent Authority which then arranges for the assessment of the medicinal substance. The Notified Body must consider the Competent Authority's vote in its final assessment of the combination product.

To whom is this news bulletin applicable?

Concerned are medical device manufacturers using medicinal products as specified in Annex I MDD, section 7.4 - only where the substance is liable to act upon the body with action ancillary to that of the device. The basis for deciding which regulatory regime is applicable to the authorization of a combination product is the mode of action of its constituents. A differentiation is made between primary mode of action and ancillary action. Ancillary action, in this context, refers to the component which exclusively plays a supporting role in the mode of action of the overall combination product.

What can we do for you?

Our company brings together the scientific resources of over 200 experts for all types of active and non-active medical devices and in vitro diagnostics. Our experts contribute to national and international activities regarding standardization as well as harmonization of guidelines and legislation.

The successful application for market authorization depends on well planned strategic decisions and meticulous and careful preparation of the documentation to be submitted. You may use the services of our experts for information prior to submission of the required documentation.

In addition we can provide scientific advice for companies planning the development of new combination products.

What is required from manufacturers?

The documentation is best to be provided in common technical document (CTD)-format. However a guideline for the contents is to be found in MEDDEV 2.1/3 part B:

- **General Information**
 - Description of the device (components, intended use)
 - Justification for the use of the medicinal substance (intended purpose, suitability of the substance, critical evaluation of alternatives)
 - Critical evaluation of the results of the risk analysis (potential risk in relation to the expected benefit)
- **Qualitative and quantitative particulars of the constituents**
 - Description of the substance
 - The amount of substance included in the device
 - If modifications were introduced: adequate description required
- **Description of method of manufacture**
 - Overall description of the device manufacturing process included in Design Dossiers
 - Process description for the substance is required
- **Controls of starting materials**
 - Specification of the medicinal substance derivate
 - EU Pharm to be referenced (if applicable)
 - Or national references (if applicable)
 - Drug Master File(s)
- **Control tests carried out at intermediate stages of the manufacturing process of the medical device**
 - In process controls (if applicable)
- **Control tests on finished products**
 - Qualitative test(s)
 - Quantitative test(s)
- **Stability**
 - Desired function to be maintained during shelf life
 - (Recommended storage conditions?)
- **Toxicity**
 - Toxicological profile of the substance
 - New substance: results of toxicity tests (ISO 10993)
- **Reproductive function**
 - Toxicological profile of the substance
 - New substance: results of toxicity tests (ISO 10993)
- **Embryo/foetal and perinatal toxicity**
 - Toxicological profile of the substance
 - New substance: results of toxicity tests (ISO 10993)
- **Mutagenic potential**
 - Toxicological profile of the substance
 - New substance: results of toxicity tests (ISO 10993)

- **Carcinogenic potential**
 - Toxicological profile of the substance
 - New substance: results of toxicity tests (ISO 10993)
 - To be considered: Genotoxicity, chemistry, duration of exposure
- **Pharmacodynamics**
 - Intended action of the substance with regard to the toxicity, chemistry, duration of exposure
- **Pharmacokinetics**
 - Description of the pattern of local and systemic exposure to the medicinal substance.
 - Maximum level and duration of exposure should be considered.
 - Potential level of exposure a safety concern?
 - New substance: release characteristics, subsequent distribution and elimination.
- **Local tolerance**
 - Relevant results from ISO 10993 to be provided.
 - Where appropriate: relevant literature.
- **Clinical documentation**
 - Clinical evaluation of the medical device is required. Relevant documents: see MEDDEV 2.7.1.
- **Labelling**
 - Acc. MDD.

What is assessed by the Notified Body?

TÜV SÜD Product Service as Notified Body will establish an evaluation report that is to be submitted to the Competent Authority. This report includes an assessment of the risk management, the risk to benefit analysis with regard to the intended use and the clinical need of the product, an evaluation of the sterilization process, inactivation of bacteria and other new infectious agents and the biocompatibility.

After consultation a final report will be compiled taking into account the comments of the Competent Authority and the results of the product specialists for sterilization, biological safety and other important product characteristics.

Please check for current guidelines of ICH and EMEA.



www.tuev-sued.com/mhs

If there are any open questions, please feel free to contact us.

Links to informative websites:

<http://www.emea.eu.int/>

<http://www.pheur.org/>

<http://www.pei.de/>

<http://www.ich.org/>

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