Practice-oriented summary of the most important aspects and requirements

In vitro diagnostic medical devices are subject to the European Directive 98/79/EC (IVDD). Presenting a subgroup of medical products, their market access, use, and market surveillance is regulated. The Directive is implemented in the national laws of the member states.

What are in vitro diagnostic medical devices (IVDs)?

According to the Directive, in vitro diagnostic medical devices include: reagents, reagent products, calibration materials, control materials, kits, instruments, apparatus, equipment, and systems that are intended for use in the examination of specimens taken from the human body (tissue, blood, urine, etc.) to diagnose diseases, to monitor a person’s state of health, or to monitor therapeutic procedures.

Examples of in vitro diagnostic medical devices are:

- Hepatitis or HIV tests
- Clinical chemical tests
- Coagulation test systems
- Urine test strips
- Pregnancy tests
- Blood sugar monitoring systems for diabetics
- Receptacles manufactured specifically for medical specimens

Accessories

Accessories include items that themselves are not in vitro diagnostic medical devices, but are intended specifically by the manufacturer to be used together with a device to enable that device to be used in accordance with its intended purpose. Under the Directive, accessories are treated as separate in vitro diagnostic medical devices.

Devices for self-testing

Devices for self-testing form a special IVD group. These IVDs are intended by the manufacturer to be used by laypersons in a home environment, for example pregnancy tests.

Devices for performance evaluation

Devices to be used in performance evaluation studies outside the manufacturer’s facility must also conform to the relevant requirements of the Directive.

Exceptions

Products that are used only for veterinary medicine as well as products for general laboratory use are not subject to the IVD Directive. However, sampling devices that are invasive are subject to Directive 93/42/EEC on medical devices.
Who is a manufacturer according to the Directive?
The Directive defines the manufacturer as the natural/legal person who is responsible for the design, manufacture, packaging, and labeling of a finished device for the purpose of marketing under his/her own name, regardless of whether these activities are performed by that person him- or herself or by a third party acting on his/her behalf.

The manufacturer according to the Directive will pass on the relevant requirements to suppliers of semifinished products and components. Thus, the suppliers will also be affected by a part of these regulations. Manufacturers of finished IVD products outside the EU must have a representative within the EU.

Essential requirements for in vitro diagnostic medical devices
Annex I of the Directive requires that the safety and health of patients, users, and any third party must not be endangered by proper use of the product, and that any possible product risk – compared with the associated benefit – is acceptable.

The principle of integrated safety applies, i.e. risk avoidance and risk minimization in the design and manufacture of the product, protective measures against residual risks, and appropriate information of users. The generally acknowledged state of the art must be applied. The product must be suited for the intended use, and the assigned performance characteristics must be ensured for the lifetime of the product.

In addition to these general requirements, there are other requirements that apply above all to the design and manufacture of the devices and refer to:

- Chemical and physical characteristics (compatibility with the material to be tested)
- Protection against infection and microbial contamination (processing, packaging)
- Suitability for use under the respective environmental conditions (risk minimization)
- Combination with other products, disposal
- Measuring function (precision, display)
- Protection against radiation (intentional or unintentional radiation, ionizing radiation)
- Protection against electric shocks, electromagnetic compatibility
- Protection against mechanical or thermal risks
- Use by laypersons: easy to use, low risk of incorrect interpretation of results (products for self-testing only)
- Provision of information by the manufacturer (labeling, instructions)

The requirements are further detailed and explained in:

- Harmonized standards, e.g. EN ISO 14971, EN 13640
- Common technical specifications (currently for devices according to Annex II, List A only)
- Guidance documents, e.g. MEDDEV documents
The Directive distinguishes four different groups – based on the risk associated with the use of the respective products.

List A
List A of Annex II contains the products with the highest potential risk. They include reagents, calibrators, and controls for the determination of:
- blood groups (AB0, rhesus, and Kell system)
- HIV-1/-2 infections, HTLV-I/-II infections, and hepatitis B, C, and D
- vCJD

List B
List B of Annex II contains high-risk products (reagents, calibrators, and controls unless otherwise stated):
- for the determination of blood groups (Duffy and Kidd system);
- for determination of irregular anti-erythrocytic antibodies;
- for the detection of rubella and toxoplasmosis;
- for the detection of phenylketonuria;
- for the detection of infections with cytomegalovirus or chlamydia;
- for the detection of the tumor marker PSA;
- for the determination of HLA tissue types DR, A, B;
- for the evaluation of the risk of trisomy 21, including software;
- products for self-testing of blood sugar levels, including instruments.

All products in List A and List B require the participation of a Notified Body in all aspects of the conformity assessment procedure.

Devices for self-testing
These devices are subject to special requirements which are described in Annex I, Section 7 of the Directive.

- The product must be easy to use for laypersons, and the enclosed instructions must be easy to understand.
- The risk of errors in use or in the interpretation of results must be kept as low as possible.
- Where possible, such devices must include a user control which allows verification of correct performance at the time of use.

A typical example is a pregnancy test.

Devices for self-testing require the participation of a Notified Body in the conformity assessment procedure. The aspect of self-testing is of special interest in the evaluation by the Notified Body.

Note: Products to be used by laypersons for determining blood sugar levels are exempted from this device group (see List B).

Other IVD products
Products that are neither listed in Annex II nor intended for self-testing do not require involvement of a Notified Body in the conformity assessment procedure. Typical examples are clinical chemistry tests or tests for thyroid function.
Conformity assessment procedures

The manufacturer may select the route of conformity assessment if there are different options. The different procedures are described in the Annexes of the Directive.

Conformity assessment procedure for list A products

Example: HIV test kit

Conformity assessment procedure for list B products

Example: Tumor marker PSA
Conformity assessment procedure for self-testing devices

Example: Pregnancy test

Conformity assessment procedure for other IVDs

Examples: Clinical chemistry tests, blood sugar tests for use by trained medical personnel
Overview of Annexes III to VIII

Annex III: Manufacturer's self-declaration
The manufacturer must compile and maintain a technical documentation showing that the product meets the applicable requirements. In Annex III, Section 3 general requirements for the technical documentation are listed; this list is relevant for all processes. The manufacturing process must comply with the principles of quality assurance. A system for market surveillance, reporting, document storage, etc. must be in place. After successful self-assessment without participation of a Notified Body, the manufacturer issues a declaration of conformity.

Annex III.6: Assessment of the technical documentation of self-testing devices by the Notified Body, to be performed in addition to Annex III if this way is chosen. No audit required.

Annex IV: Full quality assurance system
The manufacturer has a full quality management system (according to EN ISO 13485 including design), fulfills the additional requirements of the Directive (e.g. according to Annexes I and III), and declares the conformity of his products with the Directive. These measures are assessed in initial and surveillance audits by a Notified Body. In addition, List A devices require a product design evaluation according to Annex IV.4 and a verification of manufactured products according to Annex IV.6 by the Notified Body, focusing on lot-to-lot consistency.

Annex V: EC type examination
A Notified Body conducts a type evaluation to check the compliance of the prototype with the essential requirements of Annex I of the Directive and issues a type examination certificate.

In addition, List A devices require a verification of manufactured products according to Annex VII.5, focusing on lot-to-lot consistency.

Annex VI: EC verification
A Notified Body tests the finished products. Each product lot is tested and approved individually (not applicable to List A products).

Annex VII: Production quality assurance
The manufacturer has a quality management system for production, testing, and final inspection (according to EN ISO 13485), and he meets the additional requirements of the Directive. He ensures that the products concerned conform to the approved type and meet the provisions of the Directive (Annex I).

Annex VIII: Devices for performance evaluation
Obligations of the manufacturer including the contents of a statement to be issued for respective products are defined in this Annex.

National implementation
The Directive on in vitro diagnostic medical devices was issued by the European Parliament and the Council of the European Union on October 27, 1998, and was published in the Official Journal of the EU on December 7, 1998. The Directive came into effect on June 7, 2000. In December 2011, List A was amended by Directive 2011/100/EU to include devices for the detection of vCJD.
Future development of European IVD regulation

Based upon the results of the public consultation initiated by the Commission in summer 2010, the Commission issued a proposal for an IVD Regulation in September 2012 which initiated a legislative procedure expected to be completed in the second half of 2016. This EU Regulation will be effective directly without having to be transferred into national law and will bring a significantly changed product classification system generating reasonable consequences for the conformity assessment of many products.

TÜV SÜD Product Service: your partner for testing and certification

A long-standing experience and industry-specific know-how enable us to cover all medical products and conformity assessment procedures in accordance with Directive for Active Implantable Medical Devices 90/385/EEC (AIMD), Directive on Medical Devices 93/42/EEC (MDD), and Directive on in vitro diagnostic Medical Devices 98/79/EC (IVDD). As Notified Body for medical products, our certification body number is 0123.

We are able to provide you with the legally required testing and certification services; you can also profit from our comprehensive expertise in all phases of development – worldwide.

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In the area of in vitro diagnostic medical devices, we work together with a network of highly qualified partners who have to meet your and our quality criteria. By always working with the most qualified partners, we ensure that our service for you is always state-of-the-art.

Your contact partner at TÜV SÜD Product Service can provide further information.

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