

Translation / Original: German

General information on regulatory requirements and standards regarding in vitro diagnostic medical devices

1. General introduction

The information given here is addressed to persons and parties responsible for administration and purchasing in health care facilities and to their contacts at manufacturers or suppliers. This information wants to provide some orientation when dealing with recording sheets in procurement, focusing on **In Vitro Diagnostic** instruments (IVD instruments).

1.1 Definition of IVD instruments

IVD instruments (including software used for their proper functioning) are medical devices which act together with specific reagents – for the examination of specimens derived **from** the human body. Consequently, they are not medical devices used for diagnostic purposes **in** or **on** the bodies of patients (German Medical Devices Act (MPG), §3 (4)).

2. European legislation and German legislation

2.1 Directive 98/79/EC on in vitro diagnostic medical devices (IVD Directive)

IVD instruments – as well as their reagents, calibrators and controls – are subject, inter alia, to the European Directive 98/79/EC on in vitro diagnostic medical devices, which is the last of altogether three medical devices directives.

2.2 German Medical Devices Act (Medizinprodukte-Gesetz/MPG) and its ordinances

The MPG transposes the European IVD Directive into German national law, being in force in its new version since 7 August 2002 (last amended on 14 June 2007). Ordinances – namely the Medical Devices Ordinance (MPV), the Medical Devices Operator Ordinance (MPBetreibV) and the Safety Plan Ordinance (MPSV) - concretize national rules governing medical devices:

- MPV implements the annexes to the IVD Directive, by way of reference.
- MPBetreibV describes the responsibility of professional users or operators for the correct use of products.

- MPSV lays down, inter alia, the reporting obligations (vigilance) of manufacturers and users where a medical device led or might have led to the death of a person or to a **serious** deterioration in her/his state of health.¹

2.3 "Classification" of IVD devices

In contrast to Directive 93/42/EEC concerning medical devices, there is **no** classification in product classes (e.g. I, IIa, IIb, III) under the IVD Directive. According to the MPG (§ 13 (1)), in vitro diagnostics are exempted from allocation into classes.

But the following categorization is made pursuant to Article 9 of the IVD Directive:

- High risk and risk devices² (Annex II, Lists A and B),
- Devices for self-testing (to be used by lay persons),
- "All other" devices

All IVD instruments fall in the last-mentioned group (i.e. "all other" devices). The **only** exception (in context with the information given here) are **IVD devices for self-measurement of blood sugar** by lay persons (cp. Annex II List B of the IVD Directive).

2.4 CE marking; identification number of a "notified body"

IVD instruments, which are placed on the market according to the MPG, must have a CE marking on the device and in the instructions for use. The CE marking means that the IVD device is **safe** and **fully functioning** and that **all** relevant requirements of the IVD Directive – including requirements to electromagnetic compatibility – are fulfilled.

For **all IVD instruments for self-testing** a "notified body" is involved in the carrying out of conformity assessment procedures. This is expressed on the products by stating the identification number of the "notified body" next to the CE marking.

A "notified body" for defined products is a state-accredited and monitored institution under private law, which performs system and product audits on behalf of the public administration. Manufacturers can **freely** choose their "notified bodies" located inside the EU.

¹) See in MedizinProdukteRecht (2002) Heft 4 page 110 et seq. regarding the requirements of the Medical Devices Safety Plan Ordinance for in vitro diagnostics under the Medical Devices Act; practice-oriented help for manufacturers, authorised representatives and users in the reporting of events ("Die Anforderungen der Medizinprodukte-Sicherheitsplan-Verordnung für In-vitro-Diagnostika im Rahmen des Medizinproduktegesetzes; praxisorientierte Hilfe für Hersteller, Bevollmächtigte und Anwender zur Meldung von Vorkommnissen"). Jointly elaborated by the German Federal Health Ministry (BMGS), the Federal Institute for Drugs and Medical Devices (BfArM), the Paul-Ehrlich-Institute (PEI) and VDGH.
http://www.bfarm.de/clin_030/nn_424460/SharedDocs/Publikationen/DE/Medizinprodukte/vigilanz/AnforderungenMPSV-IVD,templateId=raw,property=publicationFile.pdf/AnforderungenMPSV-IVD.pdf

²) The group of high risk products includes solely reagents, reagent products as well as calibrators and control materials. The same holds true for the group of risk products; however, there are two exceptions (software for evaluating the risk of trisomy 21 and products for self-measurement of blood sugar by lay persons).

2.5 Standards

2.5.1 General information

CE marking according to the IVD Directive can be lawfully affixed only if the instrument and its reagents demonstrably fulfill the essential requirements and if they provably meet quality assurance measures in their production (see in particular Annexes I and III to the IVD Directive).

Preferably harmonized standards – which are published in the European Official Journal - can be resorted to for fulfilling given requirements (where such standards exist). Where IVD instruments or certain of their safety characteristics correspond to harmonized standards, it is assumed that these products meet relevant regulatory requirements.

There is **no fundamental obligation** to use standards where at least an equivalent safety level can be achieved in a different way (see § 8 MPG).

2.5.2 Electrical-mechanical safety

IVD instruments are **not** medical-electrical instruments in the meaning of the harmonized standard series EN 60601-x ("medical electrical instruments"), because IVD instruments are **not used in or on** the body. Consequently, the standard series EN 60601-x is **not** applicable to IVD instruments.

In the standard series EN 61010-x ("Safety requirements for electrical equipment for measurement, control and laboratory use") IVD instruments fall under the definition "laboratory instruments". This standard series includes the specific part EN 61010-2-101 for "in vitro diagnostic medical equipment", which is listed as harmonized standard under the IVD Directive.

Where electrical-mechanical safety is concerned, **solely and exclusively** this part of the standard applies to IVD instruments.

2.5.3 Electromagnetic compatibility

Regarding requirements to electromagnetic compatibility, standard EN 61010-2-101 (applicable to IVD instruments) refers - with standard EN 61010-1: 2001 - to harmonized standard EN 61326 ("Electrical equipment for measurement, control and laboratory use – EMC requirements"). This standard series includes the specific part EN 61326-2-6 for "in vitro diagnostic medical equipment".

When applying **this** EMC standard EN 61326-2-6, requirements to electromagnetic compatibility (emissions and immunity) are fulfilled for IVD devices.

The requirements of EMC standard DIN EN 60601-1-2 for medical electrical equipment do **not** apply to IVD devices.

3. Existing German legislation

3.1 Calibration Regulation (Eichordnung- EichO)

The Calibration Regulation does not apply to medical measuring devices **with** absorption photometers (including those of IVD instruments). There is no marking of conformity with the "H" symbol for such instruments.

Now quality assurance is based on § 4a of the Medical Devices Operator Ordinance (MPBetreibV).

4. Further sets of rules applicable to IVD instruments

4.1 RTTE Directive 1999/5/EC

Where telecommunications equipment (e.g. modems) or radio equipment (e.g. radio Ethernet cards) are parts of IVD instruments, the requirements of Directive 1999/5/EC on radio equipment and telecommunications terminal equipment must **additionally** be taken into account for these parts. Such conformity is proven by way of a separate declaration of conformity by the manufacturer, according to Directive 1999/5/EC.

4.2 Accident prevention rules BGV A3 – Electrical facilities and operating means

Pursuant to BGV A3 (BGV = rules of employers' liability insurance associations), testing for proper condition is required prior to initial start-up (§ 5 (1)). Such initial testing is not necessary where the IVD instruments is a plug-in electrical device and where the manufacturer or installer confirms to the entrepreneur – by way of a declaration of conformity according to Directive 98/79/EC – that the IVD instruments fulfills relevant electro-technical rules.

5. Sets of rules not applicable to IVD instruments

5.1 The IVD Directive as a "separate directive"

For **all** IVD products the IVD Directive is the **specific** "separate directive", which excludes other directives – to the extent that the IVD Directive covers their protection requirements.

Consequently, the following directives do **not** apply to IVD instruments.

5.1.1 Medical Devices Directive 93/42/EEC

Products for in vitro diagnostics are exempted from the Medical Devices Directive, according to Article 1 (5a). Thus the Medical Devices Directive and **its** harmonized standards of the series EN 60601-x are **not** applicable to IVD instruments.

5.1.2 Machinery Directive 2006/42/EC

Hazards dealt with in Annex I to the Machinery Directive are specifically covered by Annex I to the IVD Directive and also in relevant existing harmonized standards for the safety of devices. Pursuant to Article 3 of the Machinery Directive, this Directive does not apply to IVD instruments.

5.1.3 Directive 2006/95/EC relating to electrical equipment designed for use within certain voltage limits

This Directive – implemented in Germany by the Equipment Safety Act (Gerätesicherheitsgesetz) – does not apply to IVD instruments, because – pursuant to Annex II to this Directive – its scope does not include "electrical equipment for radiology and medical purposes".

5.1.4 REACH

According to Title II (Registration of Substances) of REACH Regulation 1907/2006, the manufacturer (M) or importer (I) of articles (article: means an object which during production is given a special shape, surface or design which determines its function to a greater degree than does its chemical composition) must provide the European Chemicals Agency (ECHA) in Helsinki with certain items of information (**Article 7 point 4**) where a substance is pursuant to **Article 57**

- (CMR cat. 1+2 (= C carcinogenic, M mutagenic, R toxic for reproduction),
- PBT (persistent, bioaccumulative, toxic),
- vPvB (very persistent very bioaccumulative) or has
- endocrine disrupting properties + other properties that give rise to concern (**Article 57 item f**)

and **both** of the following conditions are met:

- The substance is present in articles in quantities totaling over 1 ton per producer/importer per year **AND**
- the substance is present in articles above a concentration of 0.1% weight by weight (w/w).

None of the above-said applies where the producer/importer can exclude exposure to humans or the environment during normal or reasonably foreseeable conditions of use, including disposal. Relevant decisions and possibly resulting obligations to provide evidence lie exclusively with the manufacturer.

5.2 Further requirements not applicable to IVD instruments

5.2.1 Leakage current

For medical electrical instruments the stating of and compliance with a certain patient leakage current is prescribed in the medical equipment standard EN 60601, where such instruments are used **in or on** the human body. Requirements of this standard regarding the stating of patient leakage current do **not** apply to IVD instruments, because IVD instruments are **not used in or on** the bodies of patients.

The term "patient leakage current" is **not** found in standard EN 61010-2-101, which applies for the safety of in vitro diagnostic medical equipment. Here, protection against electric shock is regulated differently ("dangerous body currents").

5.2.2 Electrical protection class

Standard EN 61010-2-101 – which applies to IVD instruments - knows **no** classification of instruments in protection classes that would prescribe types of construction for protection against electric shock. Consequently, manufacturers are unable to make relevant statements. However, the above-mentioned standard series puts manufacturers under the obligation to ensure adequate protection against electric shock by way of suitable technical measures.

The standard series EN 60601-x does **not** apply to protection classes for IVD instruments.

5.2.3 Protection type "Application parts"

Standard EN 61010-2-101 knows no "application parts", because – as per definition – IVD instruments have **no** parts for connecting **to or into** bodies of patients. For IVD instruments, this precludes **a priori** the classification of application parts by protection types.

5.2.4 Protection types "Enclosures"

EN 60529 describes degrees of protection provided by enclosures against the penetration of dust, foreign objects, humidity or water into a device.

Standard EN 61010-2-101 regulates protection by enclosures as such, but this standard includes no obligatory requirement as to compliance with a **specific** protection type and relevant classification for IVD instruments.

A specific type of enclosure protection is only necessary and useful where instruments are **not** used inside a usual laboratory environment or where the **type** of use (intended use) calls for enclosure protection which goes beyond the basic requirements of EN 61010-2-101.

5.2.5 Safety technical controls (sicherheitstechnische Kontrollen/STK)

For IVD instruments there is (at present) **no** legal requirement to carry out safety technical controls, **unless** the **manufacturer** makes demands to this effect (see § 6 of the Medical Devices Operator Ordinance/MPBetreibV).

5.2.6 Biocompatibility

The IVD Directive makes no requirements as to the biocompatibility of IVD instruments, because IVD instruments are **not** medical devices for application **in** or **on** bodies of patients. Therefore, **no** statements on biocompatibility are made in the product specifications of IVD instruments.

6. Special markings beside the CE marking?

For IVD products the CE marking (in the meaning of the IVD Directive) is, in a certain way, the mark of "quality and safety" – warranting that IVD products are **safe** and **functioning** in their intended use. With the CE marking, manufacturers document that they fulfill **all** legal requirements and essential requirements (including those to electromagnetic compatibility for instruments). By affixing the CE marking, they also show that an **effective** quality management system is in place for all manufacturing processes and that obligations regarding risk analysis, documentation duties etc. are met.

Other markings or inscriptions **beside** the CE marking – which are likely to mislead third parties with regard to the meaning for safety and quality or graphics – may **not** be affixed. Given the high regulatory requirements to safety, quality and functioning of IVD products –instruments and reagents – other markings/inscriptions beside the CE marking are not only **superfluous**, they also undermine the special importance of the CE marking for **all** medical devices. No other markings/inscriptions are necessary - except e.g. the product safety marking (such as "cUL") which is needed for insurance reasons and only for the US/Canadian market, and the national approval marking (e.g. "FCC") in the use of radio technology.

All markings with a **different** meaning than that of the CE marking – such as e.g. statements on properties in environmental protection – may be affixed to the product, to the packaging or to the instruction leaflet, provided that visibility and legibility of the CE marking are not reduced (cp. IVD Directive, Article 16 (3)).

7. Disposal rules

7.1 Directive 2002/95/EC on the Restriction of the use of certain Hazardous Substances in electrical and electronic equipment ("RoHS")

Directive 2002/95/EC is transposed into German law with the Act on the Placing on the Market, Taking Back and Environmentally Sound Disposal of Electrical and Electronic Equipment (ElektroG). This piece of legislation regulates the use of dangerous substances - such as lead, cadmium, chromium VI, mercury and brominated flame retardants – in the production of such equipment. At present, relevant requirements apply only to electrical and electronic equipment of categories 1, 2, 3, 4, 5, 6, 7 and 10. According to the definition in Annex IB to Directive 2002/96/EC on waste electrical and electronic equipment (WEEE), laboratory equipment for in vitro diagnosis falls in category 8 and is, consequently, not subject to the requirements of the RoHS Directive.

According to a draft for a revision of the Directive, also IVD instruments are planned to fall in the scope of the Directive as from 1 January 2016.

7.2 Directive 2002/96/EC on waste electrical and electronic equipment (WEEE)

The ElektroG – which transposes Directive 2002/96/EC into German law – delegates the responsibility for organizing and financing the disposal of such waste equipment to manufacturers or importers. However, in so-called business-to-business (B2B) activities, the ElektroG leaves the possibility open to make other arrangements for disposal and cost assumption. Generally, the disposal of B2B products via municipal collection points is not permitted. Therefore, the information of manufacturers regarding correct disposal must be observed. Information on the course of action to be followed in disposal and the WEEE registration number – which all manufacturers must have – are usually incorporated in the instructions for use or in the general terms and conditions.

Working Party IVD instruments in VDGH,
Verband der Diagnostica-Industrie e.V.,
Frankfurt am Main, Germany
www.vdgh.de

19 December 2008