European
Diagnostic
Manufacturers
Association

Place St Lambert 14
1200 Woluwé St-Lambert
Brussels, Belgium
+32 2 772 22 25 tel
+32 2 772 23 29 fax
edma@edma-ivd.eu
www.edma-ivd.eu

Position Paper

Software and the IVD Directive

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1. Introduction

This position paper sets out the views of industry as to which software is covered by the In Vitro Diagnostic Medical Device Directive (IVDD)[1] and what is required by that directive. The paper also describes the extent of the legal responsibility of the Notified Body (NB) as regards software in those cases where a NB is required to be involved prior to an IVD medical device being placed on the market.

This paper only addresses the provisions of the medical device directives in relation to IVD medical devices (i.e. the provisions of the IVDD) and does not deal with the provisions of those directives in relation to other medical devices for which there is a recommendation of the "Notified Bodies Medical Devices Forum" (NB-MED 2.2/Rec4).

2. Scope of the IVD Directive 98/79 EC

2.1 Software within the scope of the IVD Directive

The term "software" is not defined in any of the medical devices directives, but certain software is included in the definition of "medical device" in Article 1.2(a) of the IVDD; thus

> "1.2. For the purposes of this Directive, the following definitions shall apply:
>
> (a) "medical device" means any instrument, apparatus, appliance, material or other article, whether used alone or in combination, including the software necessary for its proper application, intended by the manufacturer to be used for human beings for the purpose of: ….. "
> [Emphasis added]

Since IVD MD is a sub-category of "medical devices" the same definition applies to IVD software.

2.1.1 "Software necessary for its proper application"

Any software which is necessary for the proper application of the IVD MD as intended by its manufacturer is covered by the Directive. Many IVD instruments and apparatus contain software as an integral part of the device and without this software the device cannot function or fulfil its intended purpose. However, the scope of the Directive ends when the manufacturer's intended purpose of the device has been achieved, i.e. when the measuring signal is available to the user in the form intended by the manufacturer. Any software that processes the analytical result beyond that point is outside the scope of the Directive.

The manufacturer's intended purpose is determined by reference only to the labelling of the device, the instructions for use and / or promotional materials (IVD Directive, Article 1.2 (h)).

[1] DIRECTIVE 98/79/EC OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 27 October 1998 on *in vitro* diagnostic medical devices

Examples of software being a constituent part of an IVD MD:

- Software used to interpolate measurement data into analytical results (such as curve fitting programs)
- Software which is necessary to control the intended function of the instrument, e.g. temperature setting, pipetting volumes or an alarm function

2.1.2 Software as an accessory to an IVD medical device

Software which is intended specifically by its manufacturer to be used together with an IVD MD to enable that device to be used in accordance with its intended purpose is an accessory to that device. As such, according to Article 1 of the IVDD, it is to be treated as an IVD MD in its own right: Article 1 provides as follows:-

> "1. This Directive shall apply to in vitro diagnostic medical devices and their accessories. For the purposes of this Directive, accessories shall be treated as in vitro diagnostic medical devices in their own right.
>
> 2. For the purposes of this Directive, the following definitions shall apply:
> (c) 'accessory' means an article which, whilst not being an in vitro diagnostic medical device, is intended specifically by its manufacturer to be used together with a device to enable that device to be used in accordance with its intended purpose."
>
> This means that the intended use of the software together with the device must still allow the device to be used in the way in which it was intended to be used by the manufacturer of the device. If it does not do this, because, for example, it somehow changes the use or performance of the device, then the software cannot be an accessory

Example of software being an accessory to an IVD MD

Software intended for the processing of raw data and calculating a specific analytical result (i.e. so called "stand-alone software" if placed on the market separately from the IVD MD).

2.1.3 Software which is especially mentioned in the IVD Directive

In Annex II, List B of the IVDD software for evaluating the risk of Trisomy 21 is explicitly mentioned.

> "- reagents and reagent products, including related calibrators, control materials and software, designed specifically for evaluating the risk of trisomy 21".

2.2 Software not covered by the IVD Directive

The intended purpose of an IVD medical device is the generation of correct analytical result(s) from a specimen derived from the human body following an in vitro diagnostic examination. The scope of the Directive does not extend beyond the point where the analytical results are provided by the device.

Examples of software that is not within the scope of the IVDD

- Software such as expert systems intended for the analysis of patient data which, wholly or in part, have not been produced by the device itself in the fulfilment of its intended purpose.
  An Expert System is computer software which imitates the thinking and approach of the expert in the field.
- Software to be used for the administrative handling of patient data or the use of data for the management of a laboratory organization (laboratory integrated management system, LIM) or the transmission of analytical results obtained.
- Software to be used for the education of medical staff

- Software made available for general laboratory use, e.g. statistical software for internal or external quality assurance systems (EQAS)
- Software used for or assisting in general maintenance of medical devices or components of medical devices (e.g. parts lists, service diagrams, and expert servicing systems).
- Software used as a tool within the overall design and manufacturing processes of the medical device.

3. Conformity assessment and need for a Notified Body involvement

3.1 General

All IVD MD must fulfil all the relevant requirements of the IVDD, such as the essential requirements, and those relating to risk analysis, and to technical documentation as well as the requirements imposed by a Quality Management System. These requirements must be observed whether or not a NB is required to be involved in the assessment of conformity of the device.

Annex I. A.3 requires a manufacturer to ensure that his device - including the software - is designed and manufactured in such a way as to achieve its performances in terms of analytical sensitivity, diagnostic sensitivity etc. And the same requirements would cover software intended to control the steps of the analytical procedure such as identification, preparation and distribution of specimens, if such software would be either a constituent part of the analyser or an accessory to it.

If a self-testing device includes software, which is necessary for the proper application of the IVD MD as intended by its manufacturer, the design examination or the verification of the full quality management system[2], respectively, will include those software aspects which are relevant for the generation of the analytical result.

The conformity assessment procedure of the IVD MD includes the software in the same way as it includes any other component part of the IVD MD. The underlying rationale is that such software, like other components of the IVD MD, could influence the functioning of the IVD MD and in consequence the analytical results which it generates.

3.2 Legal responsibility of the Notified Body

Within the scope of the IVDD, three clearly defined cases are relevant for assessment by a NB.

a) Software for Evaluating the Risk of Trisomy 21

This software is mentioned in Annex II, List B and is specifically designed for evaluating the risk of Trisomy 21.
This addresses the combination of defined reagents and the pertinent software together with other factors of risk. The algorithms included in such software are key to the risk factor calculation. Different software – or different combinations of reagents but with the same software - could give different results. In this system, where the final result is a risk factor, the software is essential to the proper calculation in combination with the analytical results of the IVD reagents.

b) Self testing device for the measurement of blood sugar

Annex II, List B comprises expressly one IVD MD for self-testing:

"- the following device for self-diagnosis, including its related calibrators and control materials: device for the measurement of blood sugar."

If such a device incorporates or uses software which is necessary for the proper application of the IVD MD as intended by its manufacturer, that would be covered by the IVDD.

c) Self-testing devices

All self-testing devices whether or not they incorporate software are subject

[2] IVD Directive Annex III, Section 6 or Annex IV, respectively.

to the involvement of a NB according Annex III Section 6 or to other conformity assessment procedures according Art. 9 para 1.

3.3 Conformity Assessment by a Notified Body

Article 9 of the IVDD specifies the conformity assessment procedures appropriate to the different "groups" of IVD MD. There are no special conformity assessment procedures laid down for “software” or "combinations of IVD MD and software". Therefore, the general rules as to conformity assessment procedures will apply to the IVD MD according to whether the device is or is not covered by Annex II or is intended for self-testing.

Where a NB is required to be involved in the conformity assessment procedure, it is important to note the defined scope of the responsibility of the NB. The legal responsibility of the NB is limited to the three cases as outlined in 4.2 to the assessment of the device or the quality system. However, the NB may well require from the manufacturer information or data regarding, for example, those aspects of the software that could affect the performance of the system.

A NB would not be concerned with the compliance of the software as such. However, the NB could well be concerned to see technical documentation relating to any aspect of the software that could influence the results obtained with device.

4. Replacement or change of Software

Where software (which is a constituent part of an IVD MD or an accessory to it) is intended to replace damaged or lost software, and does not alter the intended use and/or performances of the IVD MD, the declaration of conformity remains valid and that replacement does not need a new CE-marking”

If, on the other hand, the replacement software is an updated or upgraded version it must be verified whether the change could affect the conformity with the essential requirements of the Directive or whether the change would alter the intended use.

In the case of an IVD MD whose conformity assessment requires the involvement of a NB, if the software is substantially changed,[3] an additional approval by the Notified Body taking the form of a supplement to the EC design-examination certificate would be required.

If the software is changed, the manufacturer must ensure that

- the device after the change is still in compliance with the Essential Requirements
- the changes have been documented by means of the configuration management system
- the configuration management results in the clear identification and control of software versions.
- the changes have been validated and approved.
- compatibility with (new) hardware or existing software, or both have been assessed.
- the requirements for reporting to the NB, if involved, are complied with in case of substantial changes (including changes of the use intended by the manufacturer) or minor changes are listed.

EDMA IVD Directive Committee

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[3] NB-MED/2.5.2/Rec2 “Reporting of design changes and changes of the quality management system”