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Position Paper

Nucleic Acid Extraction Kits and the IVD Medical Device Directive

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The purpose of this paper is to consider:

A) In what circumstances a product (kit) placed on the market for the purpose of extracting nucleic acid from a human specimen is to be considered as falling within the scope of the IVD Directive, and

B) If and when such a kit does fall within the scope of that Directive, whether it falls within Annex II.

C) Concerns about the control of the performance of nucleic acid isolation kits.

A. Does a Nucleic Acid Extraction Kit fall within the IVD Directive?

1. Nucleic acid may be extracted from a human specimen for a variety of purposes. One such purpose is to enable research to be conducted into nucleic acid itself. Another purpose may be to obtain nucleic acid from a human specimen in order to perform an *in vitro* diagnostic examination with a nucleic acid test (NAT).

2. **Where a nucleic acid extraction kit is included in and placed on the market as a component pack of a nucleic acid test kit for human diagnostic use** (or indeed as a component part of any other IVD medical device) it is clearly intended that they are to be used together with the diagnostic reagent material(s) in the kit and **it therefore falls within the scope of the IVD Directive as an "accessory".**

3. **Where the extraction kit is placed on the market as an entirely separate product**, **it is necessary to decide whether or not it falls within the scope of the IVD Directive either**

(i) as an "*in vitro* diagnostic medical device" in its own right or
(ii) as an "accessory".

- **As to (i)**

To be an "*in vitro* diagnostic medical device" for the purposes of the Directive, the reagent, reagent product, etc., must be intended by the manufacturer to be used for the examination of specimens ……solely or principally for the purpose of providing information on the matter set out in Article 1.2(b) – emphasis added. Whether that is the intended purpose of any particular nucleic acid extraction kit has to be determined solely by having regard to the "the data supplied by the manufacturer on the labelling, in the instructions for use and/or in promotion materials" (Article 1.2 (h)). **However, since by its very nature, a nucleic acid extraction kit itself does not and cannot provide information on any matter, it follows that it cannot be an IVD medical device.**

- **As to (ii)**

To be an "accessory" for the purposes of the Directive, the nucleic acid extraction kit must be 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. **If the label, instructions for use or promotional material associated with a nucleic acid extraction kit placed on the market as a separate product exhibits such as intention, then it would be within the scope of the IVD Directive as an accessory.**

If neither (i) nor (ii) is applicable it is not an IVD within the scope of the IVD Directive.

B. Would a Nucleic Acid Extraction Kit that is within the scope of the IVD Directive fall within Annex II?

1. Throughout the IVD Directive, references to "devices" mean both "*in vitro* diagnostic medical devices" and "accessories". However, while the term "devices" is used generally throughout the IVD Directive, that term is not used in Annex II except in one indent. Instead, Annex II is applicable only to

> "reagents or reagent products, including related calibrators and control materials, for determining/detecting/diagnosing/evaluating…."

2. A nucleic acid extraction kit does not determine, detect, diagnose or evaluate anything and, therefore, **even when such a kit were to fall within the IVD Directive as an accessory, it does not fall within Annex II.**

C. Performance Considerations

1. When a nucleic acid extraction kit falls within the scope of the IVD Directive as an accessory, its performance and other characteristics must comply with the applicable essential requirements of the Directive and the requirements regarding conformity assessment.

2. **A functionality control (internal control)** for each test sample used throughout a target sequence amplification assay, including the nucleic acid extraction stage, reflects state of the art - see paragraph 3.2.1 of the CTS. This is an adequate control to ensure consistent performance of nucleic acid extraction kits and there was no need to include them in Annex II.

3. When, in the case of an amplification and detection assay that falls within Annex II of the IVD Directive, **a notified body assesses the performance evaluation data relating to that assay, it will also be able to review at the same time all the data derived from the use of the nucleic acid extraction kit(s) recommended by the manufacturer of the amplification and detection assay.**

Conclusion

In EDMA's view, a Nucleic Acid Extraction kit used with an Annex II detection assay does not fall within Annex II.

EDMA Annex II Task Force

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Note: Because of different interpretations on this issue, the position of the Commission has been requested by the Notified Bodies Group.