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GUIDELINES ON MEDICAL DEVICES

IVD GUIDANCE : Research Use Only products

A GUIDE FOR MANUFACTURERS AND NOTIFIED BODIES

Note

The present Guidelines are part of a set of Guidelines relating to questions of application of EC-Directives on medical devices. They are legally not binding. The Guidelines have been carefully drafted through a process of intensive consultation of the various interest parties (competent authorities, Commission services, industries, other interested parties) during which intermediate drafts were circulated and comments were taken up in the document. Therefore, this document reflects positions taken by representatives of interest parties in the medical devices sector.

"RUO" Labelled Products and the IVD Directive 98/79/EC

01. Introduction

This document has been developed as a result of the outcome of initial discussions on "research only products" at the Medical Devices Expert Group (MDEG) meeting of July 2003. It aims to clarify a number of issues raised by Competent Authorities with regard to products labeled as "For Research Use Only" (RUO) and their potential misuse by diagnostic laboratories.

02. Legislation

This document is written in the context of the Directive 98/79/EC of the European Parliament and of the Council of 27th October 1998 on *in-vitro* diagnostic medical devices. Reference is clearly made in recital 8 of the above Directive to "research use only" products as follows:

"whereas instruments, apparatus, appliances materials or other articles, including the software which are intended to be used for research purposes, without any medical objective are not regarded as devices for performance evaluation".

In summary for a product to be categorized as an RUO product it must have no intended medical purpose or objective.

Article 1 point 2.5 of the Directive should also be noted where it states that "This Directive shall not apply to devices manufactured and used only within the same health institution and on the premises of their manufacture or used on premises in the immediate vicinity without having been transferred to another legal entity. This does not affect the right of Member State to subject such activities to appropriate protection requirements".

Examples: *enzymes used in Polymerase Chain Reaction, gel component agars, primers designed by the institution scientific experts used in in-house techniques.*

03. Definitions

The following are the key definitions that should be noted:

"*In-vitro* Diagnostic Medical Device" means any medical device which is a reagent product, calibrator, control material, kit, instrument, apparatus, equipment or system, whether used alone or in combination, intended by the manufacturer to be used in vitro for the examination of specimens, including blood and tissue donations, derived from the human body, solely or principally for the purpose of providing information:

- Concerning a physiological or pathological state, or
- Concerning a congenital abnormality, or

- To determine the safety and compatibility with potential recipients, or
- To monitor therapeutic measures.

Article 1, 2 (e) defines **a device for performance evaluation** as follows:
"device for performance evaluation' means any device intended by the manufacturer to be subject to one or more performance evaluation studies in laboratories for medical analyses or in other appropriate environments outside his own premises";

04. "Research Use Products" versus "Devices for Performance Evaluation"

As per EN 13612, **"Performance Evaluation"** means an investigation of the performance of an *in-vitro* diagnostic medical device based upon data already available, scientific literature and / or performance evaluation studies.

If a device is in a performance evaluation phase it can be made available to institutions or laboratories to be subject to one or more evaluation studies intended to gather information on performance evaluation parameters mentioned in Annex I of the Directive, which would be used for its conformity assessment.

In this situation the manufacturer has to draw up a statement "*that the device conforms to the requirements of the Directive, apart from the aspects covered by the evaluation and apart from those specifically itemised in the statement, and that every precaution has been taken to protect the health and safety of the patient, user and other persons*."

As per Recital 30 of IVDD 98/79/EC *"...it is essential that manufacturers notify the competent authorities of the placing on the market of "new products" with regard both to the technology used and the substances to be analysed or other parameters; whereas this is true in particular of high-density DNA probe devices (Known as micro-chips) used in genetic screening".*

Therefore "*new"* parameters or technologies placed on the market by the manufacturer with an intended medical purpose are within the scope of the Directive.

Recital 8 of the IVD Directive 98/79/EC states:

"Whereas instruments, apparatus, appliances, materials or other articles, including software, which are intended to be used for research purposes, without any medical objective, are not regarded as devices for performance evaluation."

Therefore once a medical device is intended by the manufacturer to be used for medical purposes it must either fall under the category of a product undergoing performance evaluation for the purpose of CE marking or be a product which is CE marked. 'For research use only' products do not have an intended medical purpose. When a medical purpose has been established based on sufficient and broadly agreed upon scientific, diagnostic and clinical evidence, then the product must comply with the requirements of the Directive before the manufacturer can place it on the market with an intended IVD use.

05. Potential Situations where "RUO" Labeled Products could be used

The following are a list of possible situations where RUO products could be used and which therefore fall outside the scope of the IVD Directive.

(a) *RUO products used for Basic Research:*
These are products used for research conducted to study all aspects of human life in an attempt to better understand all underlying mechanisms. In such studies / experiments animal and / or human models are used. No medical purpose is defined, as the specimens taken are not being used for the purpose identified in the definition of an IVD device in the IVD Directive, article 1 2(b). In such practice there is no potential to misuse RUO products.

(b) *RUO products used in Pharmaceutical Research:*
This is research conducted to find new drug compounds. The RUO products are used to verify the reactions to compounds in animal and / or human models. In such practice there is no potential to misuse RUO products.

(c) *RUO products used for a better identification and quantification of individual chemical substances or ligands in biological specimens:*
These products usually react with substances in a specimen through specific bindings or chemical reactions e.g. monoclonal or polyclonal antibodies. The RUO products are not sold by the manufacturers with an intended use within the definition of an IVD as defined by the IVD Directive in article 1 2(b). They may more appropriately fall under the category of products for general laboratory use. They may be used as an element in a home brew diagnostic testing plan to determine the possibility of their potential future use as IVD's.

(d) *In house manufacturing of so called "home brew kits" by a legal entity for the purpose of research*:
This may involve the use of laboratory tools such as primers to improve the performance of an existing IVD within a healthcare institution. The IVD Directive does not cover this type of research

06. Other Situations

There are a number of other points which should be clarified, as follows:

(a) *Use of raw materials which are labelled 'for research use only' but which are incorporated into a finished product:*
Raw materials, which are used in this manner are a component of the end product and as such are not regarded as IVD's in their own right. For the finished product to be placed on the market as an IVD it will have been through conformity assessment in line with the legislative requirements and will thus bear the CE mark. In this case the raw material should not be labelled "for research use only"

(b) *So called 'research use' products being tested against a comparator IVD product that bears the CE mark:*
In this case the fact that the so-called 'research use' product is being assessed against an existing CE marked IVD medical device implies a medical purpose and therefore in this case the product more rightly is undergoing a performance evaluation. It should not therefore be classified as an RUO product

(c) *Market studies / Feasibility studies:*
These are carried out to determine the suitability of the product prior to CE marking for its intended use i.e. the medical purpose is clearly defined at this point. In case of a market study the product is undergoing a performance evaluation rather than a usage for basic research and therefore these studies fall within the scope of the IVD Directive.

Market studies may also take place after CE marking. As long as the manufacturer remains within the intended use of the CE marking, there is no issue with such studies. However a manufacturer may decide to carry out a limited feasibility study with a view to finding a new or expanded intended use. If the results are to be used for inclusion in a future performance evaluation study then this study will fall within the scope of the IVD Directive.

07. Labelling

It is recommended that products which clearly fall within the remit of "performance evaluation should be labelled as such to clearly distinguish them from products that fall outside the scope of the IVD Directive.