

Expectations for compliance with traceability requirements of the EU IVD Directive and associated ISO standards: what is good enough?

Klaus E. Stinshoff

A decorative footer image showing a close-up of various medical devices, including what appears to be a syringe and other components, with a green and yellow gradient overlay at the bottom.

Product traceability:

the procedure by which it is possible to establish the **distribution route** of one or more identified medical devices from leaving the manufacturers premises to the end user or, if possible, the patient

(CheF Document N 38, 2000-04-26).

Metrological traceability:

property of the result of a measurement or the value of a standard whereby it can be **related to stated references**, usually national or international standards, through an unbroken chain of comparisons all having stated uncertainties

NOTE 1 Each comparison is achieved by a (reference) measurement procedure defined in a calibration transfer protocol

NOTE 2 There are several types of traceability. Therefore the term '**metrological traceability**' is used in the present text

(EN ISO 18153:2002)

Measurement standard:

a **material measure, measuring instrument, reference material or measuring system** intended to define, realize, conserve or reproduce a unit or one or more values of a quantity to serve as a reference”

(International Vocabulary of Basic and General Terms in Metrology, VIM, ISO, 1993)

Technical standard:

a **document**, established by consensus and approved by a recognized body, that provides, for common and repeated use, rules, guidelines or characteristics for activities or their results, aimed at the achievements of the optimum degree of order in a given context

(ISO/IEC Guide 2:1996)

Justice vs Microsoft



Article 3

Essential requirements

Devices must meet the essential requirements

set out in Annex I which apply to them, taking

account of the intended purpose of the devices

concerned.

Harmonized standards,
development procedure:



Annex I A.3:

The **traceability** of values assigned to calibrators and/or control materials **must be assured** through available reference procedures and/or available reference materials of a higher order

Annex I A.3:

Where appropriate, the **instructions for use** must contain information appropriate to users on the **traceability of the calibration** of the device

Annex I B.4.1:

Devices which are **instruments** or apparatus having a primary analytical measuring function must be designed and manufactured in such a way as to provide adequate stability and accuracy of measurement within appropriate accuracy limits, taking into account the intended purpose of the device and of available and appropriate **reference measurement procedures and materials**.

Annex III 3:

The **technical documentation** must allow assessment of the conformity of the product with the requirements of the Directive. It must include in particular:

.....

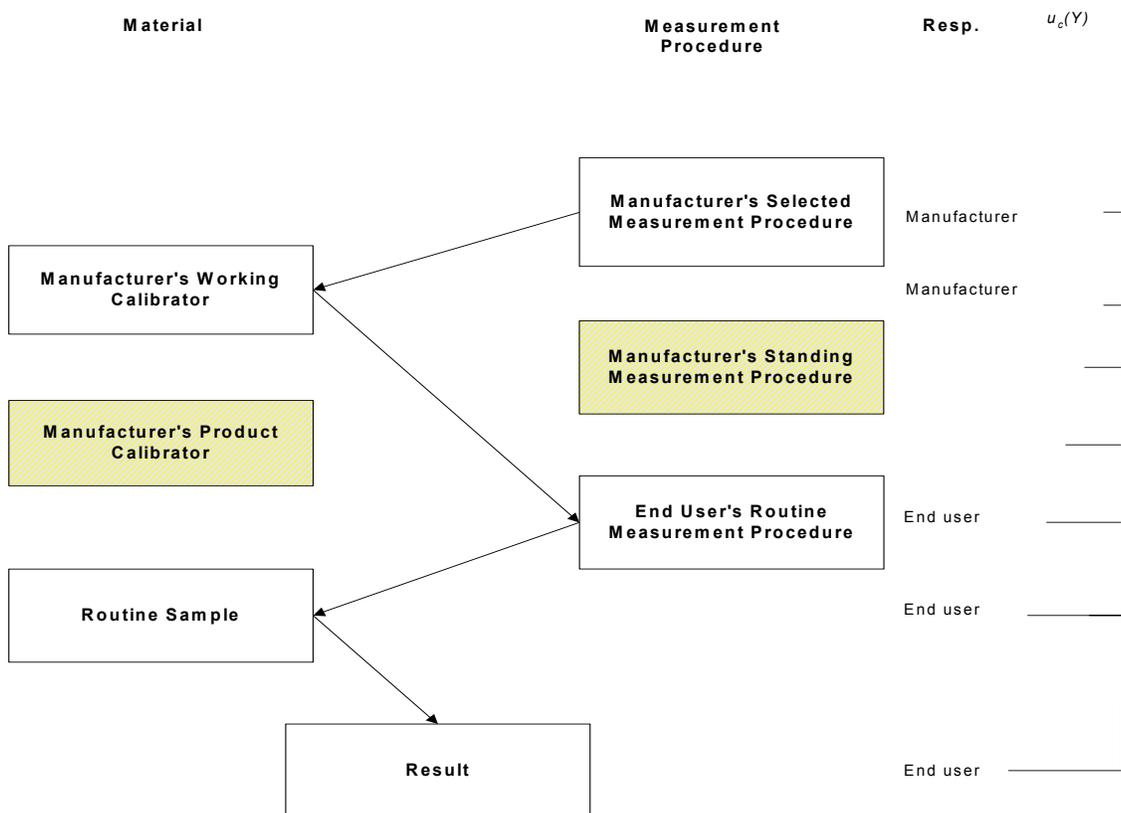
- adequate performance evaluation data showing the **performances claimed** by the manufacturer and supported by a **reference measurement system** (when available), with information on the **reference methods, the reference materials...**

.....

Joint Committee on Traceability in Laboratory Medicine (JCTLM):

- Increasing need for a clearer and more open worldwide comparability and traceability of measurements in laboratory medicine
- Has arisen as a consequence of
 - Rapid developments in science and technology
 - The implementation and improvement in quality systems
 - The need to reduce costs
 - **New legislation, in particular the European Union IVD Directive**

Traceability Chain (no reference procedure or material of a higher order)



Minimum requirements for traceability, technical documentation

- a detailed **description of the calibration procedure**
- a detailed description of the **calibration materials** used at different steps of the calibration of a reagent or an instrument, and
- the individual and combined **uncertainties** at each step
- **SI units**, if possible

Minimum requirements for traceability, instructions for use for calibrators and control materials

- metrological **traceability of assigned values**
- to reference material or procedure of **higher order**
- (or to manufacturer's value assignment procedure, technical standards scientific literature similar appropriate documents)

Standards harmonized for traceability

EN ISO 17511

In vitro diagnostic medical devices –
Measurement of quantities in samples
of biological origin – **Metrological
traceability of values assigned to
calibrators and control materials**

Standards harmonized for traceability

EN ISO 18153

In vitro diagnostic medical devices –
Measurement of quantities in samples
of biological origin – **Metrological
traceability of values for catalytic
concentrations of enzymes assigned to
calibrators and control materials**

Standards harmonized for traceability

ISO 15193/EN 12286

In vitro diagnostic medical devices –
Measurement of quantities in samples
of biological origin - **Presentation of
reference measurement procedures**

Standards harmonized for traceability

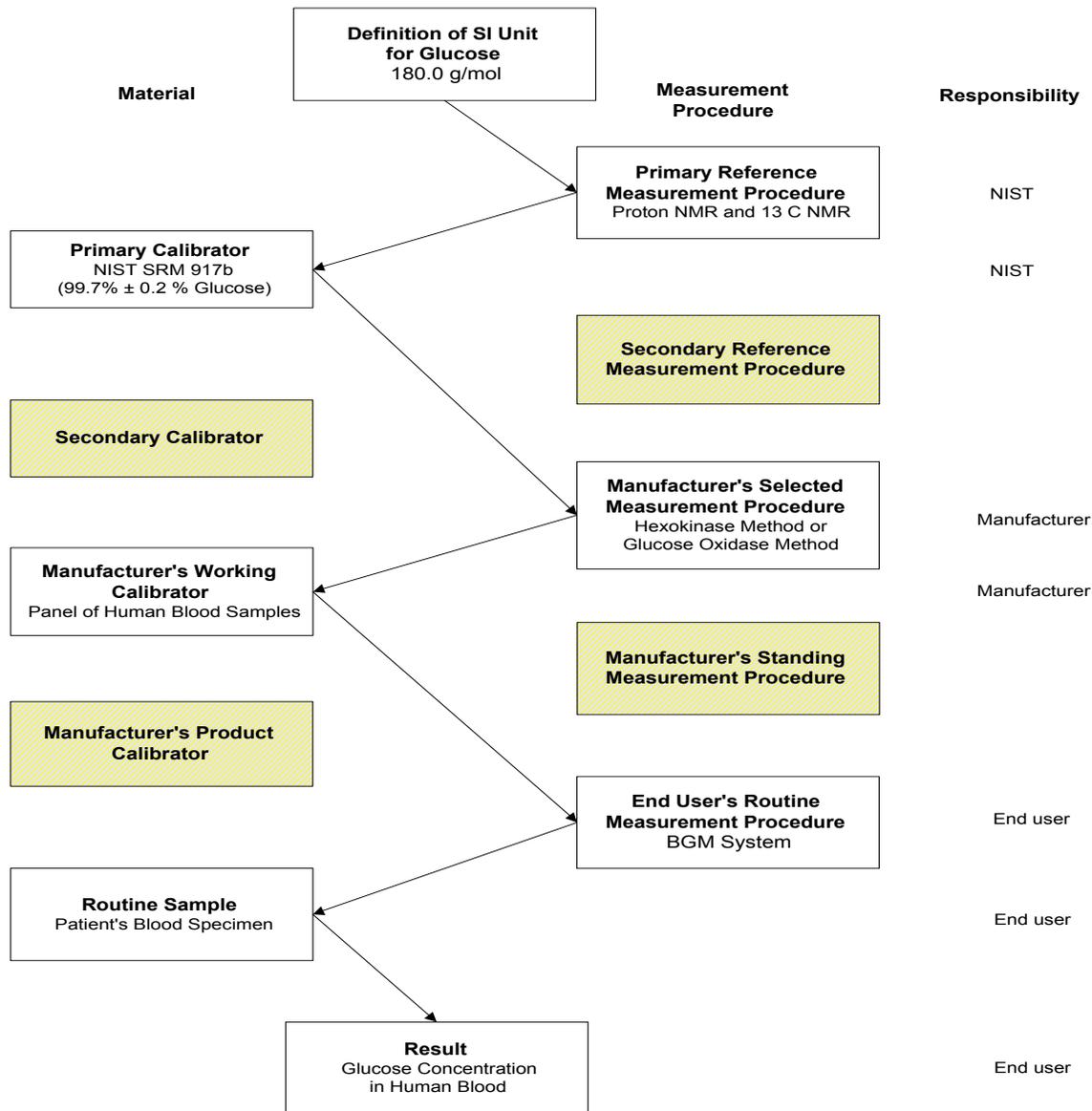
ISO 15194/EN 12287

In vitro diagnostic medical devices –
Measurement of quantities in samples
of biological origin – **Description of
reference materials**

Traceability standards

ISO 15195

Requirements for **reference
measurement laboratories**



NOTE 1 The illustration of a full traceability chain is taken from ISO 17511:2003, 4.2.2 h). Steps that are not used in this particular calibration scheme are shaded in grey.

NOTE 2 This example is not intended to represent the only possible traceability chain for a blood glucose monitoring system

Not the copyright but the technical documentation and risk management will interest Competent Authorities

The Cloning



In L'Hebdo, © Chappatte

Chief Executives of Strategic Health Authorities
Chief Executives of Acute NHS Trusts

Dear Chief Executive

In Vitro Diagnostic Medical Devices (IVD) Directive : In House Manufacture

As you probably know the In Vitro Diagnostic Medical Devices Directive (IVDD) came into force on 7 December 2000 (provisions to be applied from 7 June 2000), with a transition period which ends on 7 December this year in respect of new devices being placed on the market. The IVDD requires manufacturers and other institutions that place IVD kits on the community market or put them into service to meet certain requirements relating to their safety, quality and performance. Failure to comply with these requirements may constitute a criminal offence. The IVDD has been transposed into UK in the Medical Devices Regulations 2002 (SI 2002 No.618). Over the past few months the MHRA has been working hard to ensure that those likely to be affected by these Regulations are fully aware of their possible impact. Thus for example we have held a series of Study Days for NHS Laboratory Staff and others and made various presentations at conferences etc. This work will continue. Nevertheless, we have recently received a number of requests for information relating to the applicability of the Regulations to IVD test kits that are manufactured and used within the same healthcare institution. The purpose of this letter is to outline how we see the Regulations working in this context.

In general, the IVDD and the transposing Regulations, apply to all manufacturers placing IVDs on the market, or putting them into service. "Putting into service" includes the use of a device in a professional context for the purpose of medical analysis, even if the device is not marketed. However, there is an exemption that applies to health institutions set out in Article 1.5 of the IVDD. This says that the IVDD does not apply to devices that are "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". The IVDD does not define "health institution" but we interpret it to include an NHS Trust. Bearing this in mind, we have identified four basic scenarios that may apply to your Trust. These are set out below, with our interpretation of how the IVDD and Regulations apply.

Scenario 1: A health institution manufactures an IVD in-house and uses that IVD in-house, to test samples provided by patients within that healthcare institution, either on the premises of manufacture of the IVD or on nearby premises.

We believe this scenario falls squarely within the exemption allowed for by Article 1.5 of the IVDD and therefore the IVDD and Regulations do not apply.

Scenario 2: A health institution manufactures an IVD in-house and uses that IVD in-house, to test samples provided by patients within that healthcare institution, but not on the premises of manufacture of the IVD or nearby premises.

Because the IVD is not used on the premises of its manufacture or on nearby premises the exemption does not kick in and the IVDD and Regulations will apply.

Scenario 3: Health Institution A manufactures and uses an IVD to test patient samples provided by another legal entity.

In this case the device is not being used "within" the same health institution because it is being used for the provision of services to a third party (ie the testing of third party samples). Our view is therefore that the IVDD and Regulations apply and Health Institution A will need to comply with the relevant requirements. This remains our view regardless of whether or not it is providing this testing service as part of a commercial transaction.

Scenario 4: A health institution manufactures an IVD and transfers it for use to another legal entity, either free or in return for payment.

In this case, it is our view that the IVDD and Regulations apply, since the IVD is effectively being placed on the market by its transferral to another legal entity.

We have also been asked how the IVDD applies to an organisation, which is not an health institution, but which manufactures and uses an IVD without actually placing the device on the market. An example would be a commercial testing centre which provides pregnancy testing services direct to the public.

This situation is outside the scope of the exemption for health institutes referred to in Article 1.5 of the IVDD and therefore the organisation would have to comply with the provisions of the IVDD and Regulations.

I hope this clarifies the situation. Inevitably the scenarios set out above are in general terms only and I appreciate that there may be more specific instances unique to your own Trust on which you would appreciate further elaboration. If such is the case we will be happy to respond to any requests, subject to the caveat that our advice cannot be taken to be a definitive statement of the law. That can only be given by the courts. Where appropriate therefore you should normally consult with your own professional advisers.

Finally, you may wish to note that it is my intention to arrange for the above advice to be posted on the MHRA's web page and updated with additional scenarios as we come across them.

Yours sincerely,

Dr David Jefferys
Head of the MHRA's Device Sector

..... If such is the case we will be happy to respond to any requests, subject to the caveat that **our advice cannot be taken to be a definitive statement of the law. That can only be given by the courts.** Where appropriate therefore you should normally consult with your own professional advisers.....

Thank you for your attention!

Klaus E. Stinshoff

Swissmedic

Medical Device Section

Erlachstrasse 8

3000 Bern 9

Switzerland

Phone +41-31-323 58 59

Fax +41-31-322 7646

Email: klaus.stinshoff@swissmedic.ch