Memorandum of Clarification and Understanding

CE Marking of general laboratory use pipettes

Countries covered: EU and UK

Regulations addressed: EU IVD-Directive 98/79/EC (IVDD) and EU-IVD Regulation 746/2017 (IVDR)

September 10th, 2021

Executive Summary

1. General laboratory use pipettes should NOT be IVD-CE marked neither per the EU IVD-Directive nor per the EU IVD-Regulation.
2. Pipettes which are specifically made to support the use of clearly identified IVD devices, being reagents and/or instruments, can be rightfully IVDD or IVDR CE marked and they fall in Class A as per classification rule n. 5(a).

Note: For the purposes of simplifying this document reference to CE marking should be taken to include IVD-CE, UKCA and UKNI marking throughout this document under the regulations relevant to such marking.

1. Background Information

This paper should provide a clarification and obtain an EU-wide understanding between involved parties on whether general laboratory use pipettes should be CE marked according to either the EU IVD Directive 98/79/EC (IVDD) or the EU IVD regulation 2017/746 (IVDR).

The directive 98/79/EC on In Vitro Diagnostic Medical Devices (IVD) provides the regulatory framework for manufacturers and for authorised representatives who wish to place in vitro diagnostic (IVD) products on the EU market. Products that satisfy the regulatory requirements are permitted to carry the CE IVD mark. The EU IVD regulation 2017/746 (IVDR) is the new EU legislation applicable to IVD medical devices which entered into force on the 25 May 2017 with a five-year transition period. The IVDR replaces the IVDD.

2. Situation analysis and history

Both the EU legislative system currently applicable to IVDs (the Directive and the Regulation) allow manufacturers to IVD-CE mark general laboratory "products" but only when they are specifically intended for in-vitro diagnostic use. This is supported by the evidence of the several general laboratory products (mostly instruments) which are IVD-CE marked and which can be seen in use in various IVD labs all throughout Europe. Pipettes are such instruments.

The legislative texts that made this possible are the two following ones:

IVD-Directive 98/79/EC, Art. 1(2 b) last paragraph
Products for general laboratory use are not in vitro diagnostic medical devices unless such products, in view of their characteristics, are specifically intended by their manufacturer to be used for in vitro diagnostic examination;

IVD-Regulation 2017/746 – Art. 1 point 3:
This Regulation does not apply to: (a) products for general laboratory use or research-use only products, unless such products, in view of their characteristics, are specifically intended by their manufacturer to be used for in vitro diagnostic examination;

Since such products under the IVD-Directive framework were in the "self-declared" category (Annex III), it is true that the EU market (but also several non-EU markets) have been flooded with general laboratory use products IVD-CE marked. This happened essentially for the following three main reasons:

1. The fact that public hospitals and companies in the field of laboratory medicine in general throughout Europe give preference to IVD-CE marked devices with respect to non IVD-CE marked ones. This is

particularly evident in the public tenders where the presence of the IVD-CE mark was, and still is, a strong positive factor.

2. The value of the IVD-CE mark in non-EU markets (some Asian and African markets).
3. The fact that, apparently, IVD-CE marked devices are subject to a more favourable taxation in some of the non-EU countries.

Even if the above products were IVD-CE marked by their manufacturers purely following a self-certification process, they still had to be notified to the respective Competent Authorities of the Member State where the EU manufacturer (or the Authorized Representative) was located. Some of these Competent Authorities, as the former Belgian Health Authorities: Scientific Institute of Public Health (WIV-ISP), have always been reluctant to accept such notifications (as IVD devices) for products of general laboratory use unless a clear link to a specific diagnostic procedure was stated and demonstrated.

In 2012, a corrective action concerning the status of automatic pipettes and pipette tips for general laboratory use was agreed within the Compliance and Enforcement (COEN) group of the European Commission, in order to have a harmonised European implementation of the provisions of the Directive 98/79/EC. Therefore, in France the Agence nationale de sécurité du médicament et des produits de santé (ANSM) asked the French manufacturers to remove the CE mark and reference to Directive 98/79/EC from all information supplied by the manufacturer on the labelling, in the instructions for use and/or in promotional materials.

Other Member State Health Authorities did not challenge the notification as IVD CE marked devices of those general laboratory devices.

However, the above practice of IVD-CE marking general laboratory devices not particularly linked to specific in-vitro diagnostic examinations, didn't go unnoticed by the EU Commission and by several of the EU Health Authorities and, as a consequence, the Health Authorities of the EU Member States and also the IVD Notified Bodies have become more sensitized to this issue and more strict in demanding clear and documented evidence that such devices are indeed linked to specific in-vitro diagnostic examinations before accepting their notification as IVD-CE marked devices.

In 2012 the European Commission Directorate General for Health and Consumers issued guidelines on certain products to clarify the position on CE IVD marking. The guidance "Guidelines on medical devices Borderline and Classification issues"[1] resulted in most manufacturers removing CE marks from their devices in response to the following clauses:

"If, however, the product does not possess specific characteristics that make it suitable for one or more identified in vitro diagnostic examination procedures, then the manufacturer is not allowed to qualify its product as an IVD. A manufacturer is not allowed to affix the CE mark on a piece of general laboratory equipment as a marketing claim. Merely adding the statement "for in vitro diagnostic use" to a product is not sufficient to qualify a product as an IVD.

CE mark Not permitted

Pipettes General purpose pipettes (e.g. single or multiple pipettes, plastic pipettes, Pasteur pipettes)

IVD CE mark permitted

Blood coagulation pipettes with automatic timing (Accessory of coagulometer)"

[1] https://ec.europa.eu/docsroom/documents/10322/attachments/1/translations/en/renditions/native

3. General laboratory use pipettes vs. Pipettes which are specifically made to support the use of clearly identified IVD devices

The above position and interpretation of the European Commission has also been reflected in the Classification Rule 5 a) of the EU IVDR 2017/746 which states as follows:

2.5. Rule 5

The following devices are classified as class A:

(a) products for general laboratory use, accessories which possess no critical characteristics, buffer solutions, washing solutions, and general culture media and histological stains, intended by the manufacturer to make them suitable for in vitro diagnostic procedures relating to a specific examination;

The addition of the term "specific" before "examination" reflects the position of the EU Health Authorities who wanted to underline that, if a generic laboratory device is indeed connected/linked/related-to a specific in vitro diagnostic examination, then it is perfectly possible to IVD-CE mark such a laboratory device.

In this case a separate product line must be established. Because an intended purpose other than the one for which the conformity assessment was carried out is not permitted (IVDR Art.7 (d)).

If one has a general laboratory pipette, which can be used according to the manufacturer for any use according to the manufacturer, (e.g. in botanical studies, chemistry, forensic, physics, zoology, pharmacology, in-vitro diagnostics etc.) then, such pipette, can only be classified as a general laboratory instrument and thus cannot be IVDD or IVDR CE-marked.

Alternatively, if a manufacturer manufactures a specific single and/or multi-channel pipette capable of delivering the exact volume specifically required by an IVD assay and the intended purpose of such pipette (stated in the Instructions for use) would link its use with such IVD reagents or IVD instrument, it would be possible and justified to IVD-CE mark such pipette either under the IVDD or IVDR. This corresponds to (EU) 2017/746 article 2 (4) for accessories for in vitro diagnostic devices: the product is intended by the manufacturer to be used together with a specific diagnostic medical device to enable the in vitro diagnostic medical device to be used in accordance with its intended purpose(s) or to specifically and directly assist the medical functionality of the in vitro diagnostic medical device in terms of its intended purpose(s).

In such a case the pipette and test reagents and other equipment shall be CE marked as a whole system.

Examples:

- An IVD assay requires the simultaneous dispensing of 30 µL of a particular reagent into an entire strip (8 wells) of a microtiter plate. Then a pipette manufacturer produces a pipette that has 8 parallel tips and is pre-set to deliver only 30 µL of that specific IVD reagent.
- The diagnostic system also requires that 20 µL human blood needs to be dispensed and to do this another validated pipette is needed with intended use and specifications only for 20µl of blood. The pipette manufacturer supplies these pipettes declaring that they are specifically made for such IVD purpose. These would be pipettes that can be IVD-CE marked.

Alternatively, both dispenses can be done with one pipette *for general laboratory use* if the user has validated that to their system, but such pipette would not be IVD-CE marked.

The MDCG 2020-16 „Guidance on Classification Rules for in vitro Diagnostic Medical Devices under Regulation (EU) 2017/746“ from November 2020 confirms this interpretation (see page 38/39).

4. Conclusion

Based on the above explanations our conclusion is the following:

The current law and guidance states that a pipette marketed for general use shall not be CE marked. Dedicated, solely intended devices for IVD use only may remain CE marked.

The majority of manufacturers have now completed or are in the process of the removal of CE marking from their manual pipettes which are also marketed for general laboratory applications. A common understanding and approach in the EU should be achieved in the interests of equal treatment. Therefore, the industry published this Memorandum of Clarification and Understanding to promote a common EU-wide procedure for the CE Marking of general laboratory use pipettes.

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