Sampling of class B and C IVDs under IVD Regulation 2017/746/EU

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Under the new Regulation 2017/746/EU ("IVD Regulation"), ~85% of *in vitro* diagnostic medical devices (IVDs) will be audited and certified by a notified body for the first time. The majority of these will be class B or class C and will go through a conformity assessment route based on the quality management system. Under this route, the notified body must assess at least one technical file per representative group of devices. It is important to clarify what are the 'device categories' for class B and 'generic device groups' for Class C. The depth of these groups should reflect the different risk level of the related classes.

This paper is intended for discussion with regulators and notified bodies to highlight the issue of sampling and its impact on manufacturers and the regulatory system. It makes a first proposal for an approach which could be taken, based on the legal text and on the link to the IVD Regulation nomenclature.

Note: This paper does not cover devices which may go through a conformity assessment based on the quality management system but are assessed individually rather than by representative group: class D devices, companion diagnostics, devices for self-testing and devices for near-patient testing.

Impact

80-85% of IVDs will fall under either class B or class C and are expected to undergo a conformity assessment with a notified body for the first time – for all this will mean an audit of the quality management system. The notified body must assess establish a sampling plan; this includes an assessment of least one technical file per device category for class B; and at least one technical file per generic device group for class C.

A higher risk class is expected to see more sampling than a lower risk class. The IVD Regulation follows a risk-based classification system, meaning that the higher the risk to the patient or to the European population when an IVD test gives an erroneous result, the higher the device will be classified (class A being the lowest risk class and class D being the highest). The risk class is dependent on the device intended purpose, which means that a test which is intended to screen for cervical cancer will have a higher risk class than a test to measure vitamin D levels in the blood.

How 'device categories' for class B and 'generic device groups' for class C are defined may have a significant potential impact on the notified body and the manufacturer. Because a notified body needs to assess at least one technical file per device category and per generic device group represented by the manufacturer's product portfolio, the number of technical documentation files a notified body will need to assess at a minimum is directly related to the number of these representative groups.

The assessment of 1 technical documentation file requires the following resources:

- The estimated time for a notified body to audit 1 technical documentation file can range from 3 to 5-person days depending on the notified body's capacity and the device class (an equivalent number of days for the manufacturer's employees should be expected). This does not include other auditing activities, e.g. of the manufacturer's quality management system or the creation of certificates.
- Technical documentation file assessment under the IVD Regulation is expected to be more expensive than today under the IVD Directive due to the increased amount of information to be reviewed.

How device categories (class B) and generic device groups (class C) are described can have a significant potential impact on the notified body and the manufacturer and it might have indirect impact on health care costs, in the longer period.

How to define device categories / generic device groups?

Principles to be considered

The IVD Regulation and Medical Devices Coordination Group lay out several principles or requirements which must be considered:

- During conformity assessment based on quality management system: for class B devices, the notified body should assess at least one technical documentation file per device category. For class C devices, at least one technical documentation file should be assessed per generic device group (Art. 48);
- The involvement of the notified body should be relative to the risk class, meaning that fewer technical documentation files should be reviewed for class B devices than for class C devices (recital 56);
- There are clear guidelines provided for how a sampling plan should be set up for a QMS conformity assessment (and for annual surveillance assessment). When choosing representative samples of technical files to review, the notified body must consider (Annex IX 2.3):
    - Medical Devices Coordination Group guidance
    - Novelty of technology
    - Potential impact of the device on the patient and standard medical practice
    - Similarities in design, technology and manufacturing (and sterilisation methods)
    - Intended purpose
    - Results of any previous relevant assessments;
- There should be a link between the nomenclature under the IVD Regulation and the notified body scope designation codes, the scope of quality management system certificates and the product portfolios in the mandate of authorised representatives (MDCG 2018-2: Future EU medical device nomenclature – description of requirements);

- EU QMS certificates must include the intended purpose of the devices or groups of devices covered by the certificate (Annex XII 4b).

While the classes of generic device groups and device categories are not specified, the IVD Regulation provides a definition for 'generic device group'. These groups can be defined based on the intended purpose or technology. The definition also indicates that the devices can be grouped in a generic (i.e. simple) rather than detailed, manner.

'generic device group' means a set of devices having the same or similar intended purposes or a commonality of technology allowing them to be classified in a generic manner not reflecting specific characteristics; (Art. 2(7))

No definition is provided for 'device categories'. It seems logical that the device categories should be less detailed than the generic device groups.

Defining device categories and generic device groups

Pulling together the above principles, a logical proposal for sampling of class B and class C devices can be made.

Following guidance by the Medical Devices Coordination Group, a link between the groups on the EU quality management system certificates, notified body scope designation codes and nomenclature should be made. It seems logical to classify the representative categories and generic device groups either by considering the notified body scope designation codes or the nomenclature (or both).

This paper cannot discuss the nomenclature under the IVD Regulation as a source of grouping logic because the nomenclature has not yet been determined.

If a link is made to the notified body scope designation codes, the device categories and generic device groups could be based on the tables of codes under Annex II, Regulation 2017/2185/EU. The advantage of grouping IVDs by the notified body scope designation codes is that the groups will match the expertise of the notified body which is designated for the relevant group's code. Since the generic device groups should be based on similar intended purpose or commonality of technology, either Table I "Codes reflecting the design and intended purpose of the device" or horizontal Table 2 "IVD devices for which specific technologies are used" from Annex II of Regulation 2017/2185/EU, should be considered.

While either Table I or horizontal Table 2 would work for classifying device categories and generic device groups, MedTech Europe suggests that Table I, which generally groups devices by their intended purpose, would be the more appropriate solution. EU Quality management system certificates are required to include the intended purpose of groups of devices. Table I would serve as a consistent way to group devices and at the same time describe their intended purpose on certificates.

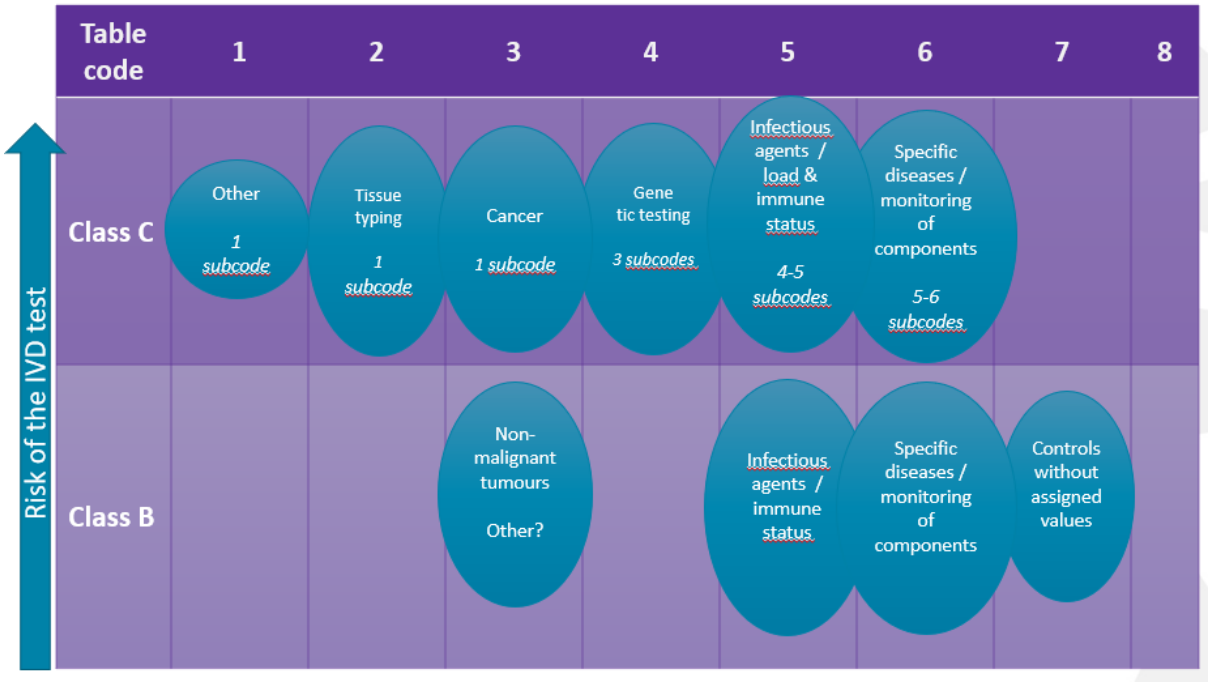
The codes under Table I, Annex II, Regulation 2017/2185/EU, are summarised here below:

Table I - CODES REFLECTING THE DESIGN AND INTENDED PURPOSE OF THE DEVICE

1. Devices intended to be used for blood grouping (6 subcodes)
2. Devices intended to be used for tissue typing (2 subcodes)
3. Devices intended to be used for markers of cancer and non-malignant tumours (2 subcodes)
4. Devices intended to be used for human genetic testing (3 subcodes)
5. Devices intended to be used to determine markers of infections/immune status (6 subcodes)
6. Devices intended to be used for non-infectious pathologies, physiological markers, disorders/impairments (except human genetic testing), and therapeutic measures (9 subcodes)
7. Devices which are controls without a quantitative or qualitative assigned value (2 subcodes)
8. Class A devices in sterile condition (3 subcodes)

The depth of the groups should reflect the different risk levels of the related classes. Taking a risk-based approach, MedTech Europe would propose describing device categories for class B by the main codes under Table I and describing generic device groups using the more detailed subcodes under Table I. The below visual shows that this would result in all class B and class C IVDs being sampled according to their representative group and according to their risk class.

Table I: Distribution of codes across device classes



Keeping the groups fairly high level would allow notified bodies to develop sampling plans which are appropriate to the manufacturer's portfolio while considering the elements under Annex IX, 2.3:

- Medical Devices Coordination Group guidance
- Novelty of technology
- Potential impact of the device on the patient and standard medical practice
- Similarities in design, technology and manufacturing (and sterilisation methods)
- Intended purpose
- Results of any previous relevant assessments (Annex IX 2.3)

It can be noted that these elements ask the notified body to consider both similarities in intended purpose/design and technology.

Final thoughts

When setting up a sampling system under a QMS conformity assessment there are further important principles which should be considered:

- This is a QMS audit, where the intention is for the notified body to sample representative devices;
- The IVD Regulation has other requirements for the notified body to assess devices across the lifetime of the QMS certificate. Class C devices will be further sampled during annual surveillance assessments and post market safety update reports will be reviewed. The notified body also carries out change control, whereby significant changes to devices are evaluated;
- Finally, if a manufacturer has any devices requiring EU technical documentation certificates, the notified body will individually review the technical files for such class B or C devices, e.g. self-tests, near-patient tests and companion diagnostics. This further informs the notified body about the ability of the manufacturer to design and manufacturer devices under the QMS.

The number and level of complexity of notified body scope designation codes has increased, from 35 to over 80, whereas the complexity in IVDs has not significantly changed. Simplicity in setting up representative categories and generic devices groups would make sense for the IVD sector. It is also essential to keep sampling simple during the transition period, when notified body resources are expected to be a challenge. According to industry feedback, the system proposed in this paper would be easy to understand and apply. There is little to no overlap foreseen between groups and there is good correspondence both to the classification rules and to NB expertise.

MedTech Europe welcomes discussion to find a clear and consistent risk-based approach that helps all stakeholders in achieving the aims of the IVD Regulation and maintain a consistent supply of products to patients.

About MedTech Europe

MedTech Europe is the European trade association for the medical technology industry including diagnostics, medical devices and digital health. Our members are national, European and multinational companies as well as a network of national medical technology associations who research, develop, manufacture, distribute and supply health-related technologies, services and solutions.

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