Health and Youth Care Inspectorate
Ministry of Health, Welfare and Sport

Image: ANP/Andrew Brookes

Appeal to manufacturers: please take timely action to ensure that you meet the IVDR requirements

The Dutch Health and Youth Care Inspectorate (IGJ) has conducted a survey among Netherlands-based manufacturers of in vitro diagnostic medical devices (IVDs). The IGJ wished to gain insight into how the transition to the European regulation on in vitro diagnostic medical devices (IVDR) is progressing. This publication describes the results of the survey.

What does the IGJ aim to achieve with this publication? The IGJ wants to reach out to manufacturers and:

- inform them on the extent of compliance with the IVDR requirements and on progress with the transition to the IVDR;
- motivate them to keep working to meet the IVDR requirements;
- encourage them to improve their knowledge of the IVDR;
- provide an insight into how the IGJ will monitor compliance with the IVDR during the transition period.

We have included a brief glossary at the end of the document for readers who are not particularly familiar with this subject.

Key tips for manufacturers

Improve post-market surveillance (PMS) compliance.

- If you have not already done so, take immediate steps to comply with the IVDR requirements relating to vigilance and PMS.

Do not postpone the transition to the IVDR.

- Contact an IVDR-notified body to arrange an assessment procedure. Notified bodies have indicated that they currently have sufficient capacity. Take advantage of that. A list of IVDR-notified bodies can be found in NANDO.

Avoid delays in the certification process.

- Make sure your communication with notified bodies is fast and effective.
- Make sure your technical documentation is complete, accurate and well structured.

Be transparent with health institutions.

- Provide clear and timely information to health institutions about the IVDs that will not transition to the IVDR.

For readers who are not particularly familiar with this subject.

What are in vitro diagnostic medical devices and what is the IVDR?

In vitro diagnostic medical devices (IVDs) are an important group of medical devices that are essential for diagnostics in places like medical laboratories. To ensure that IVDs are safe and effective, they must comply with legal requirements. On 26 May 2022, these requirements became more stringent, when European Directive 98/79/EC for *in vitro* diagnostic medical devices (IVDD) was replaced by European Regulation (EU) 2017/746 (IVDR).

The IVDR significantly expanded the number of requirements that IVDs must meet. The requirements also became much stricter. The changes include a requirement to provide more clinical evidence before placing an IVD on the market and an obligation to conduct more extensive safety and performance monitoring once a product is on the market. In addition, in many cases, an assessment must be conducted by a notified body before an IVD is allowed on the market.

The IVDR entered into force in 2017 and became applicable on 26 May 2022. All IVDs placed on the market for the first time after 26 May 2022, or which fall into the lowest risk class (Class A), have had to fully comply with the IVDR requirements since 26 May 2022. For existing IVDs, transitional rules apply. This means the IVDR requirements will be applied gradually, depending on the risk class into which the IVD falls. '*Legacy IVDs*' are IVDs that were first placed on the market before 26 May 2022 under the IVDD and, since 26 May 2022, have been marketed under the **transitional rules** referred to above.

It is not until 26 May 2027 that all IVDs will have to fully comply with the IVDR. This means that manufacturers of these IVDs do not immediately have to comply with the requirements, but they should be taking steps to prepare for compliance.

To gain insight into how the transition to the IVDR is progressing, the IGJ conducted a survey among Netherlands-based manufacturers of IVDs. The survey focused mainly on manufacturers of legacy IVDs.

Under two themes, we will explain more about the results of the survey and what action manufacturers can take:

Theme 1 – IVDR requirements for legacy IVDs under the transitional provisions

Theme 2 – IVDR transition for legacy IVDs

You can find more information about how the survey was conducted in the text box below. The text box also contains additional information regarding the manufacturers who responded to the survey.

More about the method and participation

The IGJ invited all Netherlands-based manufacturers of IVDs to take part in an online survey. These were manufacturers who had registered (notified) IVDs before the end of November 2022. The survey ran from December 2022 to January 2023. The response percentage was 61% (Figure 1a).

- The survey was not mandatory, and no identifying details were shared with the Inspectorate. Because of this, manufacturers were able to freely share with the Inspectorate their experiences and challenges relating to the implementation of the IVDR.
- The survey was designed as a 'self-check'. Completing the survey gave manufacturers an indication of the extent to which they are prepared for, and comply with, the IVDR.

Figure 1a: Survey participants

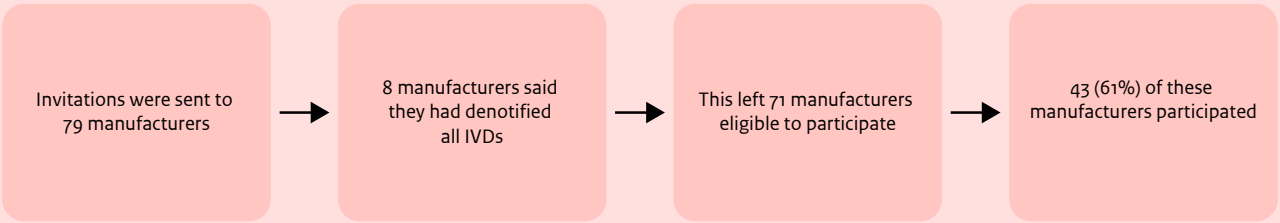


Figure 1b: Respondents by company size

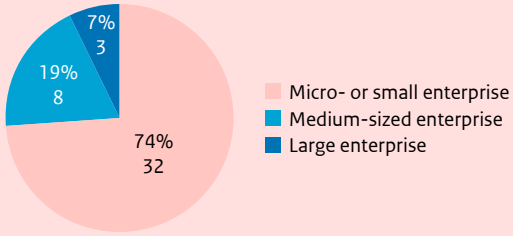
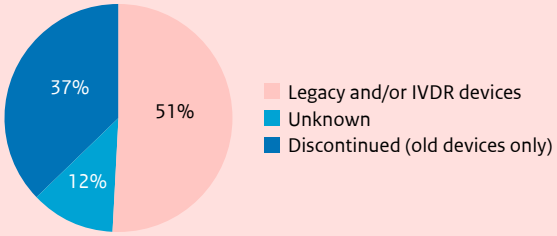


Figure 1c: Categories of IVDs that respondents had placed on the market



Key takeaways

- Most respondents (40; 93%) were from micro-, small- and medium-sized enterprises (Figure 1b). This is higher than in a recent survey from MedTech Europe, in which this percentage was 71%.
- Sixteen (37%) respondents indicated that they are no longer placing IVDs on the market at present. However, these manufacturers are known to the IGJ as manufacturers of registered IVDs. The IGJ will investigate this further.
- Twenty-two (51%) respondents are currently marketing a total of 269 IVDs.
- Of these 269 IVDs, 177 are being marketed as legacy IVDs by 14 respondents in total.
- The remaining 92 of the 269 IVDs have already completed the transition to the IVDR and are being marketed as IVDR devices. This is done by a total of 12 respondents.
  - Five of these IVDR devices are new IVDs that had not previously been placed on the market under the IVDD.
  - The remaining 87 IVDR devices had previously been placed on the market under the IVDD. These were predominantly Class A IVDs, for which no certification from a notified body is required. For that reason, they are not subject to a transition period.

Theme 1: IVDR requirements for legacy IVDs under the transitional provisions

What is this theme about?

In order for the IVDR's transitional provisions to apply, legacy IVDs must meet specific conditions.

One condition is that legacy IVDs must continue to comply with the IVDD. Another is that the design and intended purpose of the IVD must not be significantly changed after the implementation date of the IVDR. Furthermore, manufacturers of legacy IVDs must immediately comply with a number of the IVDR's requirements. These are the requirements relating to post-market surveillance (PMS), market surveillance, vigilance and the registration of economic operators and medical devices.

Under this theme, we will present the survey results relating to the extent to which legacy IVDs meet the conditions that already apply, according to the manufacturers themselves.

What is going well?

All respondents indicated that they are able to determine whether changes to the design or intended purpose of a legacy IVD are considered significant. Eighty percent stated that they have a procedure in place for this assessment. Manufacturers who do not have such a procedure indicated that they rely on MDCG Guidance 2022–06 on significant changes or seek support from an IVDR consultant.

In addition, the majority of manufacturers stated that, for their legacy IVDs, they are fully complying with the already applicable IVDR requirements relating to vigilance and PMS. Eighty percent have amended their vigilance procedure to reflect the IVDR requirements. The percentage of respondents who have a PMS system, a PMS plan and a post-market performance follow-up (PMPF) plan was slightly lower, at 70%.

Table 1: Percentage of manufacturers who stated that all legacy IVDs comply with the IVDR requirements

IVDR requirements	Respondents (%)
Assessment of significant changes	100
Vigilance procedure	80
PMS system	70
PMS plan	70
PMPF plan	70

What needs to be improved?

Seventy percent of manufacturers stated that their legacy IVDs fully comply with the IVDR requirements relating to vigilance and PMS. However, this number is based on the manufacturers' own assessments. It has not been independently checked by the IGJ. At the same time, at least 30% of manufacturers admitted that they are not fully complying with the requirements. Reasons given by these manufacturers included the investment in time and resources required and having other priorities.

Manufacturers must comply with the IVDR requirements relating to vigilance and PMS. This obligation has been in place since as early as 26 May 2022. It is important that manufacturers detect and report adverse events and any defects in their IVDs in a timely manner. Likewise, such issues must be resolved quickly and appropriately. In addition, the performance requirements for IVDs are constantly changing. Corona-tests may need to detect new variants of the coronavirus, for example. Accordingly, manufacturers must ensure that IVDs are always in line with the most recent insights, even after they have placed the product on the market. This is what the PMS provisions are about.

Not complying, or not fully complying, with these requirements means that the safety and performance of these IVDs are not fully guaranteed after they are introduced onto the market. This could lead to delays in identifying possible defects in IVDs or to incomplete action being taken to remedy the defects, which could have immediate and serious consequences for diagnostics and patient safety. Furthermore, in the long term, it could mean that patients are not being offered the most up-to-date and high-quality tests.

What can manufacturers do?

Avoid problems: make sure you meet the IVDR requirements

- √ Manufacturers who do not yet fully meet the legal requirements should take immediate action to rectify the situation.
- √ For more information on interpreting the PMS requirements, you can use the WHO Guidance for PMS of medical devices, the Nederlandse praktijkrichtlijn NPR-CEN-ISO/TR 20416 on PMS of medical devices and Vormgeven van PMS (in Dutch), a document drafted by a working group representing manufacturers, health institutions and authorised representatives.
- √ MDCG guidance on PMS and vigilance is still in development and is expected to be released later this year. Keep an eye on the European Commission website for updates.

What will the IGJ do?

The percentage mentioned above (30%) of surveyed manufacturers who said they are not complying with key IVDR requirements that are already in effect is concerning to the IGJ.

Starting in September 2023, the IGJ will therefore carry out random inspections of Netherlands-based manufacturers. During these inspections, we will assess whether the manufacturers are complying with the IVDR requirements relating to PMS and vigilance. The criteria that the Inspectorate will check are described in the post-market surveillance (PMS) assessment framework (in Dutch). If manufacturers are not complying with the legal requirements, the IGJ will impose a measure (in Dutch) to encourage or compel compliance, such as an order or administrative fine. You should therefore make sure you are in full compliance with the legal requirements as soon as possible.

Theme 2: IVDR transition for legacy IVDs

What is this theme about?

Transitioning legacy IVDs to the IVDR is a process in which manufacturers go through all the steps for each IVD until it fully complies with the more stringent requirements of the IVDR. Once an IVD is fully compliant with the IVDR requirements and has completed the correct conformity procedure, it may be marketed under the IVDR.

Under the IVDD, only a relatively small number of IVDs (around 8%) came under the surveillance of a notified body. Under the IVDR, around 80% of all IVDs are subject to conformity assessment by a notified body, the vast majority for the first time.

The end date for the transition period depends on an IVD's risk class (see Table 2). IVDR risk class D is the highest risk class with the shortest transition period and the most stringent marketing authorisation procedure. For this class, the transition period will end in May 2025. IVDR risk classes B and A sterile have the longest transition period, which will run until May 2027. IVDs that do not comply when the transition period ends are no longer allowed to be placed on the market after that date.

Under this theme, we will present the survey results relating to how the transition of legacy IVDs to the IVDR is progressing, according to the manufacturers.

Table 2: IVDR transition periods

IVDD classification	IVDR classification	Transition period end date	Notified body approval required
Other	Class D	26 May 2025	Yes
Other	Class C	26 May 2026	Yes
Other	Class B	26 May 2027	Yes
Other	Class A (sterile)	26 May 2027	Yes
List A, List B, self-tests	B, C and D	26 May 2025	Yes
Other	Class A	N/A 26 May 2022	No

What is going well?

Classification and transition periods

All manufacturers who participated in our survey indicated that they have classified their legacy IVDs in accordance with the IVDR. This enabled them to determine the applicable transition periods as well as what they have to do to make the devices fully compliant with the IVDR.

Table 3: The IVDR risk classes in which respondents have classified their legacy IVDs.

IVDR classification	Number of IVDs
Class A sterile	0
Class B	93 (62%)
Class C	27 (18%)
Class D	30 (20%)
Not classified	0

What could be improved?

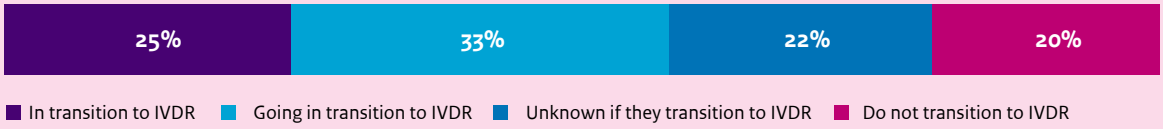
Very few legacy IVDs in IVDR transition

At the time of the survey, most legacy IVDs were not yet in the process of being transitioned to the IVDR (see Figure 2).

Although notified bodies have indicated that they currently have sufficient capacity, capacity issues may arise in the future. If manufacturers wait too long before submitting applications, there is a risk of a surge in certifications just before the transition period ends. This situation would create a challenge for both manufacturers and notified bodies. It is therefore in the interest of manufacturers and notified bodies alike to take this into account as much as possible.

There is a relatively large group (20%) of legacy IVDs that are classified as Class D (see Table 3). The certification process for this group can take up to two years. If manufacturers have not yet started the IVDR transition process for IVDs in risk class D, there is a chance that these IVDs will not obtain a CE certificate before the end of the transition period in May 2025.

Figure 2: Percentage of legacy IVDs being transitioned to the IVDR.



Uncertainty around the availability of IVDs may create risks in the healthcare sector

The percentage of legacy IVDs that will transition to the IVDR is only 58%. For 20% of legacy IVDs, manufacturers already know that they are not going to make the transition to the IVDR. For 22%, this question is as yet unresolved. Factors such as the high cost of meeting the IVDR requirements, limited market potential or the availability of new versions of the device all play a role. Some manufacturers may decide to leave these legacy IVDs on the market until the end of the transition period. This could result in an acute availability issue at the end of the transition period, particularly for niche products and IVDs that detect rare diseases. The exact nature and scale of this availability issue, and the extent to which patients will be affected, are still unclear.

Health institutions have told the Inspectorate that the lack of clarity around which legacy IVDs will make the transition to the IVDR is already a significant problem. Healthcare providers must be informed, in a timely manner, about which devices are going to remain on the market, not least because of the time required to responsibly switch to a comparable, CE-certified IVD. Or, if no such device is available, to switch to one developed in house by the health institution itself.

Agreement with a notified body for a certification process

Manufacturers with legacy IVDs they want to transition to the IVDR must complete a conformity assessment procedure (certification process) involving a notified body. At present, it seems that 30% of manufacturers have not yet made contact and 40% do not yet have an agreement with a notified body. This is in line with a recent survey by MedTech Europe, which revealed that 53% of small and medium-sized enterprises did not yet have an agreement with a notified body.

Certification process delays

Of the manufacturers who are yet to certify their devices under the IVDR, 57% reported delays in the certification process. There are several reasons for these delays, including capacity issues on the part of the manufacturer or the notified body or the amount of time required for the notified body to assess the technical documentation. In addition, the numerous adjustments manufacturers have to make in response to the findings of the notified body can cause delays. According to notified bodies, delays mainly arise when information required to complete a conformity assessment is missing from the technical documentation, or when the documentation is unclear or lacks a coherent structure.

Further details of manufacturers concerns/difficulties

Experience to date has taught us that the transition to the IVDR can be a long and complex process. This is partly because not everything that is needed for an efficient conformity assessment is currently available. For example, guidelines are still being developed, and EU reference laboratories (EURLs) are yet to be designated. Although companies want to engage in the transition as soon as possible, a range of difficulties are making it hard to get the process off the ground. The IGJ understands that manufacturers are seriously concerned. A number of the challenges/concerns that emerged from the survey are explained in more detail below.

Uncertainty around the designation of notified bodies under the IVDR

√ Not all of the notified bodies that were designated under the IVDD have applied for designation under the IVDR. Other bodies are still going through the designation process, and it is not yet clear whether they will meet the requirements to be designated as a notified body. This uncertainty presents a challenge for manufacturers, since switching from one notified body to another is a major decision.

Lack of EURLs

√ The survey also revealed that manufacturers are concerned about the lack of EURLs in the certification process for Class D IVDs. Manufacturers are concerned that EURLs cannot currently perform laboratory tests to independently confirm the safety and claimed performance of IVDs.

Gathering clinical evidence

√ Manufacturers are concerned about gathering clinical evidence under the IVDR's requirements, which are more stringent than those of the IVDD. Due to the lack of guidelines and international coordination, it is challenging for manufacturers to meet the clinical evidence requirements within the set transition periods. For example, each Member State has a different process for the notification of performance studies for manufacturers to follow.

What can manufacturers do?

Do not postpone the transition to the IVDR

√ Notified bodies have indicated that they currently have sufficient capacity for assessment procedures. Take advantage of that by starting the certification process with a notified body as soon as possible. This is important to prevent a surge in applications shortly before the transition periods end, which would create a risk of IVDs no longer being available for the healthcare sector.

√ For Class D IVDs in particular, waiting for EURLs to be designated is not a sensible strategy. Notified bodies have the power to certify Class D IVDs in accordance with the IVDR. If no EURLs have been designated, they can do so even without an EURL. Notified bodies are currently finding various ways of dealing with this issue, as described in the NB position paper on approaches to testing in the absence of EURLs.

√ The European Commission is currently working hard to set up EURLs. See MDCG Guidance 2021-4 for more information.

Be transparent with health institutions

√ Provide your customers with clarity as soon as possible regarding the devices that will not make the transition to the IVDR, or for which the process will not be completed in time.

√ The manufacturer trade organisations, FME, FHI, Nefemed and Diagned, have published a declaration of intent (in Dutch) regarding the security of supply of products used in the healthcare sector. The IGJ urges all manufacturers to abide by the intentions expressed in that document.

Avoid delays in the certification process

√ Delays in the certification process are preventable. For instance, it is important to provide complete and detailed information when submitting technical documentation to a notified body. You should also make sure your technical documentation is clear and has a coherent structure. Good communication with the notified body about the certification process is helpful, both before submitting an application and during the process.

√ It is advisable to use the available best practice and other guidance documents, so that the technical documentation is aligned as closely as possible with the expectations of the notified body and the requirements of the IVDR. An example of such a guidance is the Best Practice Guidance for the Submission of Technical Documentation under Annex II and III of In Vitro Diagnostic Medical Devices Regulation (EU) 2017/746.

√ Team-NB is also running training sessions for IVD manufacturers on the content of the technical documentation, with the aim of ensuring compliance with the IVDR requirements.

What is the IGJ going to do about these challenges?

The IGJ encourages manufacturers to accelerate the transition to the IVDR, to the extent that they are able to do so. However, we are concerned about how the transition to the IVDR is currently progressing and the issues that have arisen.

Together with the Ministry of Health, Welfare and Sport, the IGJ will continue its efforts to identify, raise and help resolve bottlenecks at both the national and EU level. The IGJ will also offer its support with the drafting of MDCG guidance documents, to prevent delays. In addition, the IGJ has contributed to the timely designation of notified bodies and will continue working to ensure continuity in this process. A joint effort by all parties concerned is needed to achieve a rapid transition to the IVDR.

Glossary

In vitro diagnostic medical devices

In vitro diagnostic medical devices (IVDs) are tests done on samples taken from the human body, such as blood, tissue and urine. IVDs can be used to detect diseases, monitor the course of an illness or predict the effect of therapy. Examples of IVDs include blood glucose meters (used to determine blood sugar levels), devices to determine blood group, pregnancy tests or tests that indicate whether someone has a hereditary disease. IVDs are mainly used in hospital laboratories, but there are also IVDs that consumers/patients can use at home (self-tests) or that healthcare providers can use on patients in their homes or in a general practice setting ('point-of-care' or 'near-patient' tests).

IVD categories in this publication

- '*Old devices*' are IVDs that were placed on the market or put into service under the IVD Directive (IVDD), before the IVDR became applicable on 26 May 2022, and that remained on the market or in use after that date. See MDCG Guidance 2002-8 on legacy devices.
- '*Legacy IVDs*' are IVDs that remained on the market under the rules of the IVD Directive (IVDD) after the IVDR became applicable on 26 May 2022, taking advantage of the transitional rules set out in Article 110 of the IVDR. These devices must continue to comply fully with the IVDD and must also comply with a number of provisions in the IVDR.
- '*IVDR devices*' are IVDs that have been placed on the market in full compliance with the IVDR.

Risk classes

The legislation divides IVDs into four risk classes: A, B, C and D, with the risk increasing from Class A (lowest risk) to Class D (highest risk). The purpose for which the device is intended and the associated risks determine the risk class into which an IVD falls. For example, an HIV test falls into the highest risk class (Class D), and a urine container falls into the lowest risk class (Class A). The higher the risk class, the more stringent the requirements that the IVD must meet. If an IVD falls into classes B, C or D, or is a Class A IVD that is sterile or has a measuring function, a manufacturer cannot simply place it on the market. A notified body must first assess whether the IVD complies with the regulation.

Notified body

A notified body is a certifying authority that manufacturers must engage to check that their devices and their manufacturing and quality assurance procedures comply with the applicable regulation. If all requirements are met, the notified body will issue a CE certificate and the manufacturer may place the device on the market. Once the device is on the market, the notified body will conduct regular audits of the manufacturer. In the case of an IVD, the notified body will check that the device continues to meet the requirements of the IVDR. Not all IVDs must be assessed by a notified body. This requirement applies only to IVDs in risk classes B, C and D and to Class A IVDs that are sterile or have a measuring function.

Notified bodies are designated by EU Member States and work for the entire European market. That means that devices certified by a Dutch notified body may be placed on the market in all EU countries. The European NANDO database lists all the notified bodies designated by Member States.

EU reference laboratories (EURLs)

EURLs are laboratories within the European Union that have been designated to conduct laboratory tests to verify whether the actual performance of a device matches the performance claimed by the manufacturer. They also check whether batches (or samples) of the device comply with certain specifications. As part of the conformity assessment of a high-risk IVD (Class D), a notified body may need to ask an EURL to test the device.

Enterprise categories in this publication

- A microenterprise is an enterprise that employs fewer than 10 persons and has an annual turnover and/or annual balance sheet total not exceeding EUR 2 million
- A small enterprise is an enterprise that employs fewer than 50 persons and has an annual turnover and/or annual balance sheet total not exceeding EUR 10 million.
- A medium-sized enterprise is an enterprise that employs fewer than 250 persons and has an annual turnover not exceeding EUR 50 million and/or an annual balance sheet total not exceeding EUR 43 million.

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