

The clock is ticking – MedTech Europe’s recommendations ahead of May 2025 deadline for Class D IVDs

MedTech Europe – December 2023

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Executive summary

Class D IVDs are critical for public health. They mainly fall into two categories: a) those related to blood, cells, tissues or organ screening, and b) those related to management of life-threatening infectious diseases. Under the *In vitro* Diagnostic Medical Devices Regulation 2017/746/EU (IVDR), Class D devices rely on a complex infrastructure whose elements must work together: Common Specifications¹, Expert Panel assessment², Notified Body review, and evaluation by EU Reference Laboratories³. MedTech Europe has always supported the full and early establishment of all needed infrastructure for Class D devices.

With the deadline to certify Class D devices under the IVDR arriving in only 18 months from now (26 May 2025), manufacturers wishing to transition their devices face numerous challenges in the regulatory pathway.

With this paper, MedTech Europe makes several recommendations to ensure the continuous supply of Class D devices from the transition date of 26 May 2025.

- Several European Ministers of Health at the EPSCO Council meeting of 30 November 2023, called for measures – including extended transition time and a root cause analysis of the issues – to address potential shortages in Class D devices which are not transitioning to the IVDR. Any additional time given must be used by the European Commission, MDCG, Notified Bodies and other actors to identify blockages and improve the efficiency and predictability of the system – with the goal of supporting innovation and enabling all manufacturers to transition their devices to IVDR.

¹ IVDR 2(74): “common specifications’ (CS) means a set of technical and/or clinical requirements, other than a standard, that provides a means of complying with the legal obligations applicable to a device, process or system.” These are published and entering into force in July 2024.

² IVDR 48(6): “where no CS are available for class D devices and where it is also the first certification for that type of device, the notified body shall consult the relevant experts”

³ When designated for that device

- **For devices which are today not (yet) covered by EU Reference Laboratories (EURL) – including during the EURLs transition period – Notified Bodies should strive to align their approaches for conformity assessment and batch release.**
- **For devices covered by EURLs, it is essential to plan for the inclusion of devices covered by EURLs during the transition period. Collaboration among authorities, EURLs, and stakeholders should be initiated now to ensure preparedness for mandatory activities under the IVDR. The paper outlines proposals for efficiently establishing EURLs in this context. In that regard, several proposals are made in the paper for the efficient setting up of EURLs.**
- **Prior to the end of the transition period, the Joint Research Centre should assess each EURL if it is ready to carry out the necessary batch release and performance evaluation and will be operational by the deadline. This assessment will allow the Commission to use the provision of article 100(9) of the IVDR⁴ and pause or restrict the designation of an EURL where they are not ready. Considering that the publication of an Implementing Act for this purpose will take at least three months, it is recommended that the assessment takes place three months before the end of the transition. The Joint Research Centre could seek advice from Notified Bodies when conducting this assessment.**
- **Re-classification should be considered for devices intended for the detection of the presence of, or exposure to, SARS-CoV-2, given that their pathogenic presentation is comparable to other non-class D respiratory viruses and COVID-19 is no longer considered a pandemic or a generally life-threatening condition. Also see Annex I at the end of this paper.**

⁴ IVDR100(9): *“The EU reference laboratories shall be subject to controls, including on-site visits and audits, by the Commission to verify compliance with the requirements of this Regulation. If those controls find that an EU reference laboratory is not complying with the requirements for which it has been designated, the Commission, by means of implementing acts, shall take appropriate measures, including the restriction, suspension or withdrawal of the designation.”*

Introduction – the situation for the transition of class D today

As of December 2023, many manufacturers are progressing with Class D applications and conformity assessment to CE-mark their devices under the *In vitro* Diagnostic Medical Devices Regulation (EU) 2017/746 (IVDR). At least 62 IVDR certificates already have been issued. One certificate can cover one or more devices therefore the exact number of certified devices is not known. The same is true for applications – the number of devices that are in the process of conformity assessment is unknown. The deadline to certify Class D devices is only 18 months from now: 26 May 2025. The time it takes to obtain Class D certificates varies greatly, taking 13-18 months (50% of cases) or 19-24 months (40% of cases). This means that companies should have applied by the end of 2023 in order to reach certification on time for the May 2025 deadline.

Remarks about the state of the IVDR transition were made by European Ministers of Health at the EPSCO Council meeting of 30 November 2023, including calls for an extension to the IVDR transitional periods. These calls referred to the fact that possibly a fifth of Class D devices on the market today have been applied for under IVDR as of July 2023⁵. MedTech Europe supports any measures which will keep IVDs, including Class D, available to the blood banks, laboratories, and patients who need them. Any additional time given must be used by the European Commission, MDCG, Notified Bodies and other actors to improve the efficiency and predictability of the system – with the goal of enabling all manufacturers to transition their devices to IVDR.

Small and Medium Enterprises (SMEs) may be particularly sensitive to the complexities and burden of Class D conformity assessment. They are often limited in human and financial resources, making it challenging to invest in transitioning to the IVD Regulation. MedTech Europe's IVDR survey from October 2022⁶ pointed out that 51% of Class D legacy devices belong to manufacturers who do not have an agreement in place with a Notified Body. While the ability to access to a Notified Body has improved since then, it can remain a challenge, especially for SMEs⁷.

For many manufacturers, navigating the IVD Regulation represents their first collaboration with a Notified Body. Training initiatives offered by Notified Bodies, such as those focusing on the structuring of technical documentation, are enormously helpful for manufacturers. Improving access to a Notified Body can be achieved by establishing a transparent pathway for early, well-structured dialogues between manufacturers and Notified Bodies.

⁵ assuming that there are more than 1000 Class D devices under the IVD Directive and 230 applications had been submitted as of July 2023. See slide 32 of [European Commission survey of Notified Body applications and certifications](#) (July 2023). Exact numbers are not known neither of Class D devices which are on the market under the IVD Directive nor of the number of devices covered by the applications numbers cited.

⁶ "Transition to the IVD Regulation - MedTech Europe Survey Results for October 2022"
https://www.medtecheurope.org/wp-content/uploads/2023/02/mte_public-report-ivdr-survey_27-feb-2023.pdf

⁷ Data from MedTech Europe's survey shows that 53% of SMEs and 6% of large companies do not have an agreement with a Notified Body designated under the IVDR (October 2022)

Through interviews with its members (most of which are large manufacturers), MedTech Europe can confirm that many have submitted applications for their portfolio of Class D devices. These manufacturers report that the costs associated for Class D certification have increased significantly compared to the IVD Directive. The financial and resource burden represents a challenge for all manufacturers – larger and smaller – and is expected to lead to some degree of discontinuation. **In general, a more predictable and efficient path to certify Class D devices would encourage manufacturers to persevere with the IVDR and bring both innovations and legacy devices to the European market and healthcare systems. This should be addressed as a matter of urgency in the short term. It is also essential for discussion to start now on needed reform to the IVDR across the areas of efficiency, innovation and governance (for detail, see MedTech Europe’s position on the Future Regulatory System).**

Beyond the above call to improve the pathway to certification, MedTech Europe makes specific recommendations below to address challenges in the Class D regulatory infrastructure which need careful attention to avoid the disruption of supply of critical IVD tests, especially during and after the transition period to establish EU Reference Laboratories (EURLs). This paper provides recommendations for consideration by all stakeholders including the Commission, the Joint Research Centre together with candidate EURLs, Notified Bodies, and the IVD industry, to support manufacturers who have applied for conformity assessment, still plan to apply or are struggling to engage in the IVDR CE-marking process.

Harmonisation of conformity assessment for Class D devices

(applicable during the transition period of EURLs and for areas that will not be covered by EURLs)

Notified Bodies have demonstrated agility in adapting to the evolving regulatory infrastructure for Class D devices, including an absence of EURLs. Prioritisation of Class D applications together with a pragmatic approach towards conformity assessment has resulted in progress towards Class D certification. It is estimated that by July 2023, 62 Class D certificates have been issued under IVDR⁸. One certificate can cover one or more devices therefore, the exact number of certified devices is not known.

For devices which are today not (yet) covered by EURLs – including during EURLs transition period – efforts by Notified Bodies to continue aligning their approaches for conformity assessment and batch release will be needed.

⁸ Notified bodies survey on certifications and applications results for July 2023 can be consulted on the Commission’s website: https://health.ec.europa.eu/system/files/2023-11/md_nb_survey_certifications_applications_en.pdf

It is important that the certification process continues, and Notified Body practices are aligned to provide for a level playing field. We welcome Notified Bodies' publication of the consideration paper to provide a framework for the verification process for Class D IVD medical devices in the absence of designated EU Reference Laboratories⁹. MedTech Europe is willing to engage in discussion with Notified Bodies in support of a harmonised approach, including sharing experiences from members who went through conformity assessment to help identify the aspects that can be improved and aligned.

Recommendations for the EU Reference Laboratory transition period

Today, Class D devices have a path to market which is demonstrated by the progress in the certification. Most Notified Bodies conduct conformity assessment and batch release. With their official designation¹⁰, EURLs will take on a mandatory role in conducting performance verification and batch release for Class D devices in their scope^{11,12}.

On 5 December 2023, Implementing Regulation 2023/2713/EU designated five laboratories as EURLs¹³. These newly designated laboratories will cover four out of the nine areas of Class D tests: hepatitis and retroviruses; herpesviruses; bacterial agents; and respiratory viruses that cause life-threatening diseases.

A transition period until **1 October 2024** has been foreseen by the European Commission, after which the EURLs start their role in performance verification and batch release. For devices which will not have a designated EURL, the appropriate activities will be performed by the Notified Body.

⁹ Team-NB published a Position Paper on measures for class D IVD, October 2023 <https://www.team-nb.org/class-d-measures-in-the-absence-of-eu-reference-laboratories/>

¹⁰ [Commission Implementing Regulation \(EU\) 2023/2713 of 5 December 2023 designating European Union reference laboratories in the field of in vitro diagnostic medical devices](#)

¹¹ IVDR, Annex IX, Chapter II, Section 4.9: *“Before issuing an EU technical documentation assessment certificate, the notified body shall request an EU reference laboratory [...], to verify the performance claimed by the manufacturer and the compliance of the device with the CS, where available, or with the other solutions chosen by the manufacturer to ensure a level of safety and performance that is at the least equivalent. Their verification shall include laboratory tests by the EU reference laboratory [...]*

¹² IVDR, Annex IX, Chapter II, Section 4.12: *“To verify conformity of manufactured class D devices, the manufacturer shall carry out tests on each manufactured batch of devices. [...] notified body or the manufacturer shall send samples of the manufactured batches of devices to the EU reference laboratory, where such a laboratory has been designated [...]. The EU reference laboratory shall inform the notified body about its findings.*

¹³ [Commission Implementing Regulation \(EU\) 2023/2713 of 5 December 2023 designating European Union reference laboratories in the field of in vitro diagnostic medical devices](#)

For devices covered by EURLs, it is essential to plan for the inclusion of devices covered by EURLs during the transition period. Collaboration among authorities, EURLs, and stakeholders should be initiated now to ensure preparedness for mandatory activities under the IVDR.

EURLs are expected to build their own environment necessary for carrying out their IVDR role. This is expected to be developed during their transition period, including:

- Form their overall network and scope-specific sub-networks and adopt rules of procedure
- Establish common assessment and interpretation criteria, agreeing on the use of same reference materials and common test specimens. As specimens, control materials and reference materials may be short-lived, the EURLs should have an acquisition plan in place to ensure their continuous availability¹⁴. They also should set scope-specific sub-networks
- Develop common procedures for carrying out performance verification and batch release, including the sets of tests and associated parameters considered sufficient to verify that the device complies with the common specifications
- Align policies on independence, conflict of interest and confidentiality
- Set up a network of national reference laboratories and publish on their website the list and their respective tasks. In order to achieve transparency with regard to the structure and level of the fees, the EURLs should lay down the rules according to which the fees are calculated, including the rules for the estimation of costs based on average costs, and make them publicly available¹⁵
- Undertake work to receive Union financial contribution etc.

It is vital that EURLs consult with Notified Bodies and manufacturers to ensure that the environment they are establishing is appropriate to carry out their tasks.

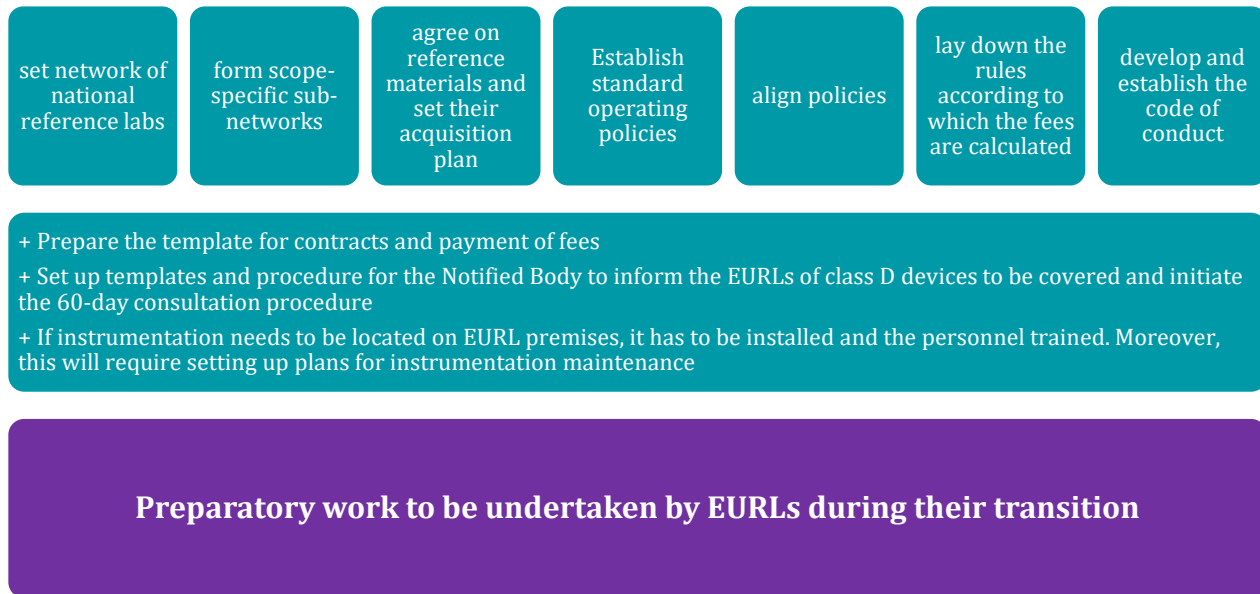
It will also be necessary to set up the necessary templates, procedures and other elements to enable EURLs, Notified Bodies and manufacturers to interact during conformity assessment and for batch release. Some manufacturers will find themselves interacting with multiple EURLs. It is critical for this to be in place before the end of the transition period, given that the time between designation and the May 2025 deadline is very limited. This includes but is not limited to:

- Preparation of template contracts and payment of fees.

¹⁴ As described in the Commission Implementing Regulation (EU) 2022/944 of 17 June 2022 laying down rules for the application of Regulation (EU) 2017/746 of the European Parliament and of the Council as regards the tasks of and criteria for European Union reference laboratories in the field of in vitro diagnostic medical devices https://eur-lex.europa.eu/eli/reg_impl/2022/944/oj

¹⁵ As described in the Commission Implementing Regulation (EU) 2022/945 of 17 June 2022 laying down rules for the application of Regulation (EU) 2017/746 of the European Parliament and the Council with regard to fees that may be levied by EU reference laboratories in the field of in vitro diagnostic medical devices https://eur-lex.europa.eu/eli/reg_impl/2022/945/oj

- Setting up templates and procedure for the Notified Body to inform the EURLs of class D devices to be covered and initiate the 60-day consultation procedure.
- If instrumentation needs to be located on EURL premises, it has to be installed and the personnel trained. Moreover, this will require setting up plans for instrumentation maintenance.



As described above, EURLs will need to put in place numerous procedures, contracts and other conditions which are necessary for their role in performance verification and batch release processes. If the transition timeline given by the implementing regulation proves to be too short, the EURLs will begin their designation without being ready to start their activities under the IVDR. This is of significant concern given that many of the procedures, contracts and other necessary conditions will require consensus and coordination between (variously) the group of EURLs, the European Commission including the Joint Research Centre, Notified Bodies and manufacturers. There will be no possibility to wait for the EURLs to become ready once the transition period ends, as Notified Bodies will be legally obliged to engage for batch release with the EURL for the devices in their scope. This carries the risk of creating a disruption in the availability of certain Class D medical tests, in case Notified Bodies cannot release the manufactured batches. The performance verification for devices whose conformity assessment is ongoing when the transition time ends will have to be conducted by the EURL. It is not known how long the conformity assessment will take under EURL. It is possible that this process will be even longer than the one today under Notified Bodies given that this is a new element for EURLs.

It is worth considering the experience of the European Medicines Agency and the Notified Bodies, where it took roughly two years to set up the necessary procedures and templates in order to support a (relatively simple) consultation for companion diagnostics, even though the European Medicines Agency already had procedures established for other scientific consultations. As examples of specific procedures which have been established to allow for coordination with the schedules and working

methods of the European Medicines Agency, Notified Bodies must notify three months in advance of requesting a consultation for their scientific opinion and there are guidance documents, templates and specific schedules for when and how to submit requests for consultations. By now, this consultation process has been tested several times and largely works, although there still are discussions on how to structure the Summary of Safety & Performance, timing for addressing questions, and on when and how scientific opinions should be published. The situation for EURLs is considerably more complex and MedTech Europe expects more discussion, and aligned procedures will be needed between multiple EURLs and stakeholders, also given the EURL role not only in consultation for performance verification but also in batch release activities.

Several proposals are made in the paper for the efficient setting up of EURLs.

MedTech Europe calls on the European Commission to ensure that:

- Instrumentation – especially high throughput, closed-loop, or heavy instrumentation – should be kept available to the EURL and the Notified Body at the manufacturer's premises. This will ensure sustainability to maintain the equipment (insurance for risks, training for instrumentation use and training for software, logistics, maintenance, financial cost). EURL experts can visit the premises and perform testing. Many products are closed-loop systems, for each assay an instrument will be needed. This will avoid EURLs having an overcrowded space by instruments from different manufacturers, overwhelmed to operate systems from different suppliers or needing to run assays often on high throughput instrumentation to ensure their proper functioning. Moreover, if instrumentation will have to be moved often, it will not only increase the CO2 footprint but also impact the sustainability as these instruments will be more often subject to breaks and tear-off.
- For devices which had the IVDR certificate issued and devices for which an application was lodged with a Notified Body, to avoid disruption to the certification process, the performance verification should be carried out by EURLs only at the time of the next re-certification.
- Moreover, during the re-certification, the performance check may involve a smaller sample set as described in the infopack for EURL candidate laboratories published by the Commission¹⁶ “In order to verify the manufacturer's claims on the performance of a device, the EURL does not need to repeat the performance study carried out by the manufacturer. They should come up with a suitable protocol to verify the performance and compliance with common specifications/other solutions chosen by the manufacturer, which may involve a smaller sample set than that used by the manufacturer.”
- Predictability is secured in terms of timing for all stakeholders, including Notified Bodies, manufacturers and laboratories. This includes clarity on when the 60 days set time for performance verification will start and when batch release will take place.
- Consider the costs and fees of the EURLs services and how this adds up to other costs for the manufacturer: cost for Notified Body review, costs to run Performance Studies, cost for

¹⁶ https://health.ec.europa.eu/system/files/2022-12/md_candidate-laboratories_infopack_en.pdf

application for authorisation of Performance Studies. Manufacturers report that today an IVDR certification process already poses a significant financial burden compared to the IVD Directive. If EURLs will introduce additional costs, will this investment be achievable and will it encourage innovation for critically needed IVDs to test for blood safety and the fight against deadly and fast-spreading diseases?

- Following laboratories' designation, it should be avoided that they would actively start requesting financial support for their setup from manufacturers or Notified Bodies. No financial burden should be transferred to manufacturers or Notified Bodies for making the EURLs operational. Union financing should be available as set up in the implementing act¹⁷.
- The EURLs should ensure transparency in the fee structure for various services provided and make this publicly available as set up in the implementing regulation.
- During the transition period, allow EURLs carry on contractual work with third parties like Notified Bodies to continue supporting the current system including the testing of legacy devices.
- Support that EURLs carry out discussions with Notified Bodies to establish the necessary procedures and run 'fake' or pilot applications to ensure readiness.

Prior to the end of the transition period (1 October 2024), the Joint Research Centre should assess each EURL if it is ready to carry out the batch release and performance evaluation and will be operational by the deadline. This assessment will allow the Commission to use the provision of article 100(9) of the IVDR¹⁸ and pause the designation of an EURL if this is not ready. Considering that the publication of an Implementing Act for this purpose will take at least three months, it is recommended that the assessment takes place three months before the end of the transition. The Joint Research Centre could seek advice from Notified Body when conducting the assessment.

- If the EURL has not set up all processes necessary to carry out and guarantee batch release and timely performance verification for all required devices under its scope, then its designation should be deferred or restricted and the devices in scope should not be required to go through EURL procedures. The designation could be paused or a restriction could pause specific activities of the EURL such as performance verification or batch verification, depending on the circumstances. This assessment should be undertaken to prevent disruption in availability of class D tests. It should be anticipated by all actors including Notified Bodies, that if devices are no longer covered by an EURL that they do not need to go through EURL requirements until an EURL is again designated.

¹⁷ [EU/2022/945](#) Commission Implementing Regulation (17 June 2022): *Commission Implementing Regulation laying down rules for the application of Regulation (EU) 2017/746 of the European Parliament and the Council with regards to fees that may be levied by EU reference laboratories in the field of in vitro diagnostic medical devices.*

¹⁸ Article 100(9) IVDR: *The EU reference laboratories shall be subject to controls, including on-site visits and audits, by the Commission to verify compliance with the requirements of this Regulation. If those controls find that an EU reference laboratory is not complying with the requirements for which it has been designated, the Commission, by means of implementing acts, shall take appropriate measures, including the restriction, suspension or withdrawal of the designation.*

A classification update of SARS-CoV-2 can ease the burden from the Class D system

Around 40% of Class D applications may come for devices that detect SARS-CoV-2. Although many manufacturers intend to place these devices on the market, some might hold up with the technical documentation submission in the reasonable expectation that classification of devices testing SARS-CoV-2 will be revised in line with the improved epidemiological landscape. Positive developments such as a wide vaccination rate together with a low mortality and morbidity linked to COVID-19 infections, have a direct influence on the risk this pathogen poses for the individual and for the public health. Consequently, if we apply the classification rules of the IVD Regulation to devices which test for SARS-CoV-2 strains currently in circulation, these devices should fall into Class B. Discussion on the scientific data to support a discussion on re-classification of SARS-CoV-2 can be found in the Annex I at the end of this paper.

Conclusion

The role that EURLs will play in the availability of Class D products means that their effective establishment is critical to patients, manufacturers and other stakeholders. Until EURLs are fully operational, the industry and Notified Bodies should work together to establish efficient and harmonised solutions for Class D certification. This paper lays out key steps that can be taken to mitigate short-term challenges to allow safe and effective approval of high-risk devices as well as their ongoing performance verification. It also suggests the introduction of EURLs in July 2025 or only when they become fully established, to benefit laboratories and manufacturers and ultimately patients across the EU. Finally, it is important that the efficiency and predictability of the path to certification be improved to enable all manufacturers who still need to do so, to apply for their Class D devices.

ANNEX I

CONSIDERATIONS UNDER THE IVD REGULATION FOR RECLASSIFICATION OF IVD DEVICES TESTING FOR SARS-COV-2

Introduction

It is important that the MDCG Guidance on Classification is updated to reflect the current epidemiologic status of an infectious agent.

SARS-CoV-2 was first described in 2019, when it was associated with an outbreak of pneumonia in Wuhan, China. SARS-CoV-2 is responsible for Coronavirus disease 2019 (COVID-19), whose clinical outcome is variable, but often includes fever, cough, headache, fatigue, breathing difficulties, and loss of smell and taste. The elderly and persons with underlying conditions such as hypertension, diabetes and obesity are at highest risk for severe disease and death. However, most cases of COVID-19 are mild to moderate and do not require hospitalization or advanced medical care. A small sub-set of patients may experience long-term symptoms referred to as 'Long COVID'. These symptoms usually occur three months from the onset of the disease, with symptoms that last for at least two months and that cannot be explained by an alternative diagnosis (e.g., respiratory, neuropsychiatric or cardiovascular manifestations).

Since its emergence, SARS-CoV-2 has been linked to over 676 million reported cases of COVID-19 and nearly 6.8 million deaths worldwide¹⁹. The high rate of propagation and mortality observed at the beginning of 2020 provided the basis for COVID-19 to be declared a pandemic by the World Health Organization (WHO) on 11 March 2020²⁰. During the briefing, it was mentioned that "WHO has been assessing this outbreak around the clock and we are deeply concerned both by the alarming levels of spread and severity, and by the alarming levels of inaction."

Announcing COVID-19 as a pandemic was essential to raise awareness at the political level. Actions were taken to fight the disease, increase the capacity of public health systems and raise public awareness. As a consequence, in Europe the *In vitro* diagnostics devices (IVDs) used to test for the presence of, or exposure to, SARS-CoV-2 were assigned the highest risk and included in the Class D category. This was re-affirmed by including SARS-CoV-2 as an example of high-risk device in the MDCG

¹⁹ John Hopkins Resource Centre Covid-19 Map – 22 July 2023 <https://coronavirus.jhu.edu/map.html>

²⁰ WHO Director-General's opening remarks at the media briefing on COVID-19 – 11 March 2020

<https://www.who.int/director-general/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19---11-march-2020>

guidance MDCG 2020-16 Rev.2 ²¹ : “devices intended to be used for the following purposes are classified as class D: ...SARS CoV and SARS-CoV-2.”

In May 2023, WHO announced the end of the emergency phase of COVID-19 ²² . “During the deliberative session, the WHO Committee members highlighted the decreasing trend in COVID-19 deaths, the decline in COVID-19 related hospitalizations and intensive care unit admissions, and the high levels of population immunity to SARS-CoV-2. The Committee’s position has been evolving over the last several months. While acknowledging the remaining uncertainties posted by potential evolution of SARS-CoV-2, they advised that it is time to transition to long-term management of the COVID-19 pandemic.”

To date, significant progress has been achieved in the fight against the spread of SARS-CoV-2 in Europe. A high immunization rate, low mortality rate, and development of innovative vaccines and therapies allowed governments to re-install a sense of normalcy where the pathogen can be considered under control.

Following the positive developments, stakeholders including Notified Bodies and the IVD industry, consider that the level of risk associated with devices which are used to identify the presence of, or exposure to, SARS-CoV-2 has decreased. Therefore, an assessment of the current situation is needed to adjust the classification of these IVDs according to the state-of-the-art and in line with the rules stipulated in the IVD Regulation 746/2017 Annex VIII.

MedTech Europe's analysis described here affirms that devices for SARS-CoV-2 should be classified as Class B. We ask that MDCG IVD amend guidance on classification MDCG 2020-16 to include the relevant examples under Class B. We note that this refers to the COVID-19 strains which have been in circulation until now. If a more pathogenic and virulent strain emerges in the future, this will be independently assessed and assigned into the correct IVDR class.

Discussion

To assess the current threat represented by SARS-CoV-2, intrinsic key parameters must be considered: ability to evolve, transmission rate, and minimal infecting dose.

Table 1 summarizes those parameters for main respiratory viruses and highlights the up-to-date comparability of SARS-CoV-2 with them.

²¹ Update - MDCG 2020-16 Rev.2 - Guidance on Classification Rules for in vitro Diagnostic Medical Devices under Regulation (EU) 2017/746 - February 2023 (europa.eu) https://health.ec.europa.eu/latest-updates/update-mdcg-2020-16-rev2-guidance-classification-rules-vitro-diagnostic-medical-devices-under-2023-02-10_en

²² Statement on the fifteenth meeting of the IHR (2005) Emergency Committee on the COVID-19 pandemic (who.int) [https://www.who.int/news/item/05-05-2023-statement-on-the-fifteenth-meeting-of-the-international-health-regulations-\(2005\)-emergency-committee-regarding-the-coronavirus-disease-\(covid-19\)-pandemic](https://www.who.int/news/item/05-05-2023-statement-on-the-fifteenth-meeting-of-the-international-health-regulations-(2005)-emergency-committee-regarding-the-coronavirus-disease-(covid-19)-pandemic)

	Mutation rate (mutation/site/year)	Infecting dose* (PFU)	Transmissibility (R0)
SARS-CoV-2	1.10 ⁻³	9	2 - 9
Influenza	1.10 ⁻⁵	0.4 - 2.1	1 - 21
Adenovirus	8.10 ⁻⁵	0.35	1 - 22
RSV	1.10 ⁻³	70	1 - 5
hMPV	7.10 ⁻⁴	1	5 - 8

Table 1: Comparative Parameters of Concerns or Main Respiratory Viruses

PFU: plaque-forming units, RSV: Respiratory Syncytial Virus, HMPV: human MetaPneumoVirus 23

*Route of administration: aerosol

Altogether, these pathogenesis data make the SARS-CoV-2 virus comparable to other respiratory viruses from a virological standpoint. Differences in clinical features should then be investigated on the recipient side, specifically in at-risk patients, by considering the current countermeasures represented by primary prophylaxis and treatment efficiency. These will impact the mortality rate. Interestingly, transmissibility and virulence did not exhibit significant changes between 2020 and 2023. There is consensus in stating that the main driver in lowering severity is the modifications of host susceptibilities thanks to both immunisation and effective management.

²³ [Cilloniz, C. et al., \(2022\)](https://err.ersjournals.com/content/31/166/220051.short): Respiratory Viruses : Their importance and lessons from COVID-19. European Respiratory review. <https://err.ersjournals.com/content/31/166/220051.short>

[Mikszewski, A. et al., \(2022\)](https://www.sciencedirect.com/science/article/pii/S1674987121001493): The airborne contagiousness of respiratory viruses: A comparative analysis and implications for mitigation. Geosciences Frontiers, Vol 13, Issue 6. <https://www.sciencedirect.com/science/article/pii/S1674987121001493>

[Karimsadeh, S., Bhopal, R., Tien Nguyen, T., \(2021\)](https://www.cambridge.org/core/journals/epidemiology-and-infection/article/review-of-infective-dose-routes-of-transmission-and-outcome-of-covid19-caused-by-the-sarscov2-comparison-with-other-respiratory-viruses/8607769D2983FE35F15CCC328AB8289D) : Review of infective dose, routes of transmission and outcome of COVID-19 caused by the SARS-COV-2: comparison with other respiratory viruses. Cambridge University Press. <https://www.cambridge.org/core/journals/epidemiology-and-infection/article/review-of-infective-dose-routes-of-transmission-and-outcome-of-covid19-caused-by-the-sarscov2-comparison-with-other-respiratory-viruses/8607769D2983FE35F15CCC328AB8289D>

[Markov, P., et al., \(2023\)](https://www.nature.com/articles/s41579-023-00878-2): The evolution of SARS-CoV-2. Nature Reviews Microbiology. <https://www.nature.com/articles/s41579-023-00878-2>

Transmissibility, vaccination and mortality

SARS-CoV-2 transmission rate evolved from beta variants to delta variants, with a rate estimated of 1.5 to 2.5.²⁴ The impact on the population was different due to dramatic improvements both in prevention and treatment as discussed below.

Currently, the European Medicines Agency²⁵ has validated a number of medicinal products for the treatment of COVID-19.

- Early stages of infection: people at risk could benefit from a combination of nirmatrelvir-ritonavir, or from antiviral monoclonal antibodies (e.g., sotrovimab, regdanvimab, casirivimab and imdevimab).
- Hospitalised patients: remdesivir or immunomodulators (tocilizumab, anakinra, or baricitinib).

Dozens of other drugs are currently under research and development and under evaluation in clinical trials.

Availability and efficiency of vaccines is the second factor mitigating the life-threatening aspect of SARS-CoV-2. Immunization against COVID-19 is effective in preventing severe illness, and hospitalisation, as it creates a high level of herd immunity that contributes to the protection of vulnerable population.

As of 26 October 2023, more than 75% percent of the EU population have received at least one dose of vaccine against COVID-19²⁶.

²⁴ Trobajo-Sanmartin, C., et al., (2022) : Differences in Transmission between SARS-CoV-2 Alpha (B.1.1.7) and Delta (B.1.617.2) Variants. *Microbiology Spectrum*. <https://journals.asm.org/doi/10.1128/spectrum.00008-22>

²⁵ Covid-19 medicines European Medicines Agency (EMA). <https://www.ema.europa.eu/en/human-regulatory/overview/public-health-threats/coronavirus-disease-covid-19/covid-19-medicines>

²⁶ European Centre for Disease Prevention and Control (ECDC) Week 42 (2023)- *Archive of Covid-19 country overview and surveillance reports – this page contains an archive of ECDC country overview and surveillance reports published since 10 July 2020, new reports are added on a weekly basis.* <https://covid19-surveillance-report.ecdc.europa.eu/archive-COVID19-reports/>

The percentage of vaccination uptake is notably higher for 18-60 years and those over 60 years of whom 84.8% and 92.4% have received at least a single does respectively (Figure 1) ²⁷.

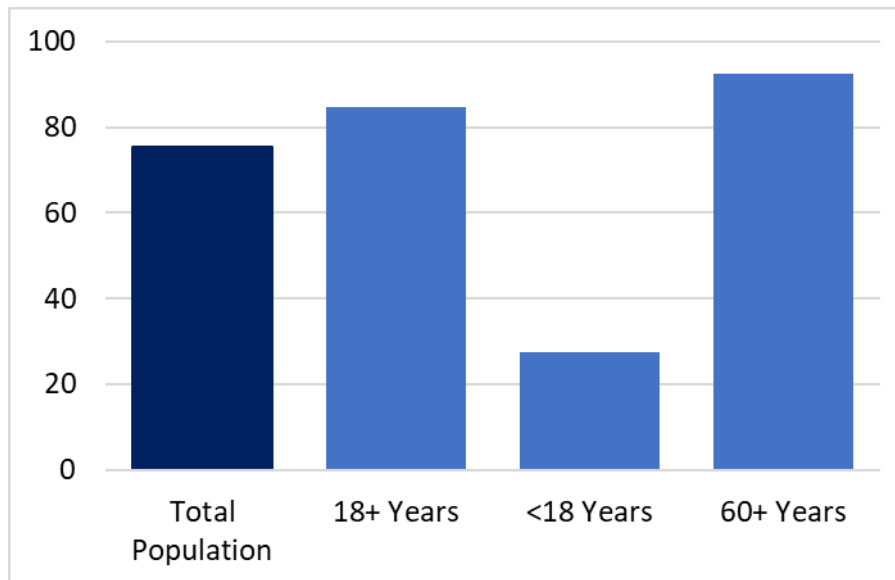


Figure 1: Cumulative Uptake (%) of at Least One Vaccination Dose Among Different Age Groups

In the EU, the combination of active drugs and global immunization greatly impacted the number of individuals requiring hospitalization due to COVID-19 has decreased significantly. It now amounts to 3.2 per 100k cases, while the number of hospitalized patients admitted to ICU is less than 0.2 per 100k ²⁸ (Figure 2).

²⁷ European Centre for Disease Prevention and Control (ECDC) Week 42 (2023)- *Archive of Covid-19 country overview and surveillance reports – this page contains an archive of ECDC country overview and surveillance reports published since 10 July 2020, new reports are added on a weekly basis.* <https://covid19-surveillance-report.ecdc.europa.eu/archive-COVID19-reports/>

²⁸ European Centre for Disease Prevention and Control (ECDC) Week 42 (2023)- *Archive of Covid-19 country overview and surveillance reports – this page contains an archive of ECDC country overview and surveillance reports published since 10 July 2020, new reports are added on a weekly basis.* <https://covid19-surveillance-report.ecdc.europa.eu/archive-COVID19-reports/>

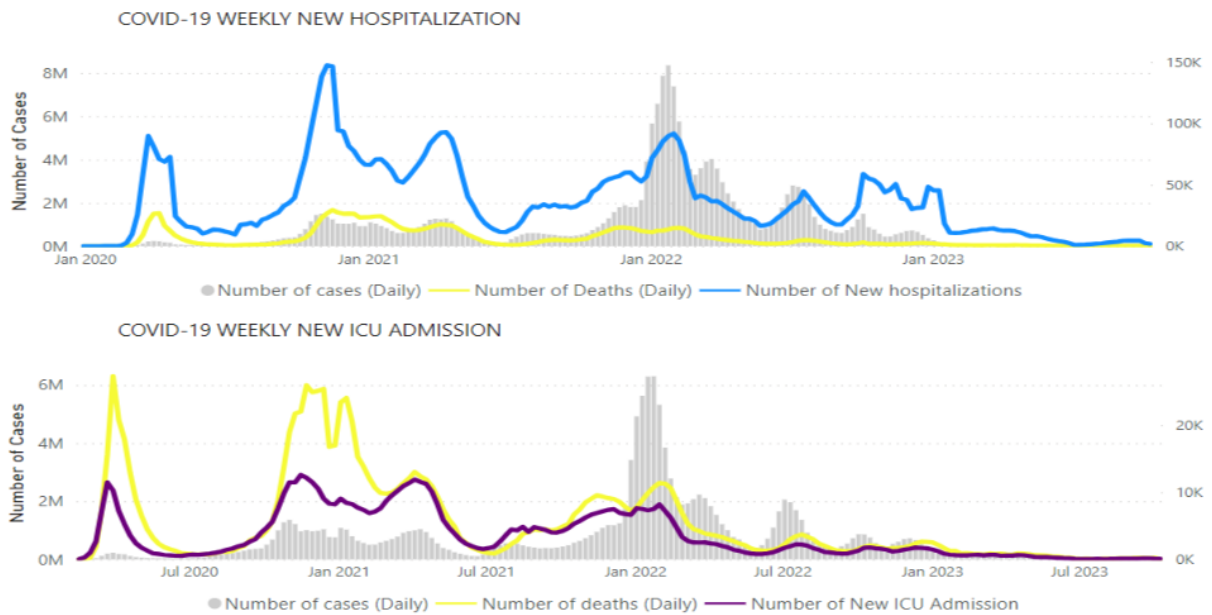


Figure 2: Shows a steady decrease in Hospitalization and ICU Admission Rate for COVID-19 European Region (EUR)²⁹

The mortality rate of individuals who died from COVID-19 among those infected is an essential indicator of the threat. As of 25 October 2023, the mortality amounts to 3 cases per million, suggesting that COVID-19 no longer represents to be a public health and death threat³⁰.

SARS-CoV-2 no longer meets the definition of a life-threatening pathogen as defined by MDCG Guidance 2020-16 rev.2, which reads as follows ³¹ :

“Life-threatening” are diseases, conditions or situations that in general result in death. These are often untreatable, treatment options are limited or require major medical interventions.”

²⁹ WHO Director-General’s opening remarks at the media briefing on COVID-19 – 11 March 2020

<https://www.who.int/director-general/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19---11-march-2020>

³⁰ European Centre for Disease Prevention and Control (ECDC) Week 42 (2023)- *Archive of Covid-19 country overview and surveillance reports – this page contains an archive of ECDC country overview and surveillance reports published since 10 July 2020, new reports are added on a weekly basis.* <https://covid19-surveillance-report.ecdc.europa.eu/archive-COVID19-reports/>

³¹ Update - MDCG 2020-16 Rev.2 - Guidance on Classification Rules for in vitro Diagnostic Medical Devices under Regulation (EU) 2017/746 - February 2023 (europa.eu) https://health.ec.europa.eu/latest-updates/update-mdcg-2020-16-rev2-guidance-classification-rules-vitro-diagnostic-medical-devices-under-2023-02-10_en

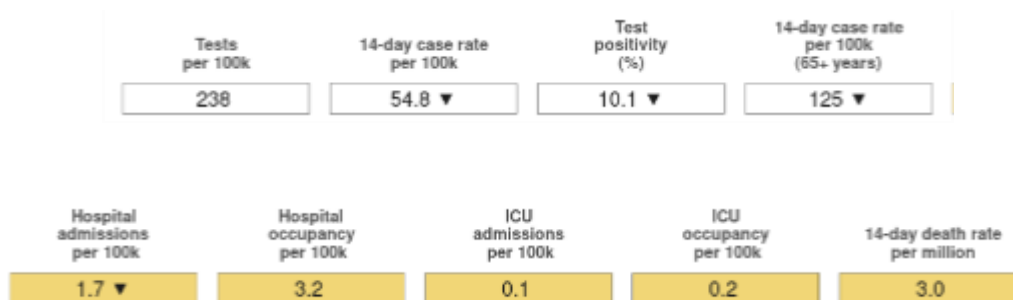


Figure 3: Statistics of Key Indicators from European Centre for Disease Prevention and Control, week 42³².

IVDR Classification Rules - Where does SARS-CoV-2 fit?

Currently, SARS-CoV-2 devices are seen as “Devices intended to be used for the detection of the presence of, or exposure to, a transmissible agent that causes a life-threatening disease with a high or suspected high risk of propagation” and are classified as Class D under Rule 1.2 within MDCG 2020-16 rev.2.

According to this classification rule, for a device to fall under this definition, it is paramount to fulfil both the “life-threatening” and “high-risk of propagation” conditions.

While the current classification was appropriate during the pandemic and back when MDCG 2020-16 rev.2 was published, the clinical landscape of COVID-19 has since changed dramatically and the overall population and individual risks have continued to decline with increasing therapeutic options, vaccination rates and naturally acquired immunity.

The 15th International Health Relations Emergency Committee³³ determined on 4 May 2023 that Covid-19 no longer presents a public health emergency concern.

³² European Centre for Disease Prevention and Control (ECDC) Week 42 (2023)- *Archive of Covid-19 country overview and surveillance reports – this page contains an archive of ECDC country overview and surveillance reports published since 10 July 2020, new reports are added on a weekly basis.* <https://covid19-surveillance-report.ecdc.europa.eu/archive-COVID19-reports/>

³³WHO Director-General’s opening remarks at the media briefing on COVID-19 – 11 March 2020

<https://www.who.int/director-general/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19---11-march-2020>

Therefore, is the current IVDR classification for SARS-CoV-2 devices as Class D still applicable or should a re-evaluation be considered?

Considering the scientific data presented and reviewing the IVDR classification Rules 1, 2, 3 and 4 in the MDGC 2020-16 guidance³⁴, it is clear that devices for the detection of the presence of or exposure to SARS-CoV-2 do not meet the conditions to fall under the designation of a Class D or C as set out in IVDR Annex VIII.

The most appropriate risk class for SARS-CoV-2 non pandemic strains according to IVDR and current state-of-art, is Class B.

Moreover, MDCG guidance 2020-16 includes under Rule 6 (Class B) those IVDs that detect infectious agents that present a moderate risk to the individual and are not easily propagated, mentioning as examples the devices intended for the detection of Influenza A/B virus (non-pandemic strain).³⁵

EU Digital COVID Certificate policy was not extended

To restore mobility and to facilitate free and safe movement during the COVID-19 pandemic, the European Parliament and the Council adopted a Regulation on the EU Digital COVID Certificate on 14 June 2021³⁶. The certificate applied from 1 July 2021 and was set to expire on 30 June 2022 before it was extended for an additional year. The EU Digital COVID Certificate Regulation finally expired on 30 June 2023³⁷. The fact that the Regulation has not been extended further indicates a clear change in how COVID-19 is seen at both political level and health management level.

³⁴ Update - MDCG 2020-16 Rev.2 - Guidance on Classification Rules for in vitro Diagnostic Medical Devices under Regulation (EU) 2017/746 - February 2023 (europa.eu) https://health.ec.europa.eu/latest-updates/update-mdcg-2020-16-rev2-guidance-classification-rules-vitro-diagnostic-medical-devices-under-2023-02-10_en

³⁵ Update - MDCG 2020-16 Rev.2 - Guidance on Classification Rules for in vitro Diagnostic Medical Devices under Regulation (EU) 2017/746 - February 2023 (europa.eu) https://health.ec.europa.eu/latest-updates/update-mdcg-2020-16-rev2-guidance-classification-rules-vitro-diagnostic-medical-devices-under-2023-02-10_en

³⁶ [EUR-Lex - 32021R0953 - EN - EUR-Lex \(europa.eu\)](#)

³⁷ [EU Digital COVID Certificate \(europa.eu\)](#)

Conclusion

The pathogenic presentation of SARS-CoV-2 is comparable to other respiratory viruses and COVID-19 is no longer considered to be a pandemic or a generally life-threatening condition.

Therefore, given the current low risk of severe disease development thanks to several effective therapeutic options and to the broad availability of vaccinations in the EU, Class B is the most appropriate rule to apply to IVDs that detect the presence of, or exposure to, SARS-CoV-2. Should the Medical Devices Coordination Group IVD wish to take a precautionary approach, examples of specific variants could be included under Rule 6 of the Classification Guidance.

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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For more information, please contact:

Petra Zoellner

Director Regulatory Affairs, IVDR & MDR

MedTech Europe

p.zoellner@medtecheurope.org

Judith Kalina

Senior Manager, Government Affairs & Public Policy

MedTech Europe

j.kalina@medtecheurope.org