The European Association of Medical devices Notified Bodies

Team-NB Position Paper

Editor:	**Team-NB**	Adoption date 21/02/2024	Version 1

Team-NB Notified Bodies recommendations

on the classification of devices intended to detect the presence or the exposure to SARS-CoV-2

Background information

SARS-CoV-2 devices are currently classified as class D devices according to MDCG Classification guidance 2020-16 Rev. 2 per IVDR Annex VIII Rule 1, 2nd indent.

Rule 1 second indent

*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.***

NOTE 2: The list of high-risk agents may be updated based on quantitative analysis of new scientific evidence on the incidence, pathogenicity, burden of mortality and morbidity, and transmission dynamics of infectious agents in the population."

MDCG 2020-16 rev2 "Guidance on Classification Rules for in vitro Diagnostic Medical Devices under Regulation (EU) 2017/746" provides further explanation and guidance of the classification rules outlined in Annex VIII IVDR. MDCG 2020-16 rev2 lists in its rationale, SARS-CoV-2 devices as examples for Class D devices falling under Rule 1 second indent "*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**".*

According to rule 1 second indent two main aspects need to be considered (and fulfilled) in combination:

1. High or suspected high risk of propagation.
2. Causes a life-threatening disease.

The rationale obtains respective considerations related to potential dynamics regarding incidence, transmission, pathogenicity, mortality and morbidity based on a quantitative analysis of new scientific evidence for the relevant infectious agents, hence the two main aspects of rule 1 second indent; first "high or suspected high risk of propagation" and second "causes a life threatening disease" might be weighted differently using new scientific data which might lead into a change of the classification (Note 2 page 17 of MDCG 2020-16 rev2).

Such a dynamic could be demonstrated after the pandemic caused by this "novel" pathogen SARS-CoV-2.

For an efficient risk evaluation of this respiratory virus, the two main aspects of Rule 1 second indent are to be kept in consideration: the transmissibility, defining the associated public health

risk, and the disease severity, defining the patient specific risk.
In the opinion of the Notified Bodies these could be reconsidered by several means and factors:

- Availability of various effective vaccines (reducing serious disease, hospitalization rates and mortality)(1)
- Quite high vaccination rate for the EU/EEA population for primary course (73%), with adults (>60 years) displaying up to 91% vaccination rate(2).
- Various national recommendations of vaccination like Influenza (or even in combination with Influenza) for individuals/populations at risk(3)
- Currently no circulating variants of concerns (VOC) (defined by World Health Organisation-WHO).
- Current scientific evidence on circulating variants in the EU/EEA indicates no increased impact on immunity or severity for general population(4)

Whilst the initial device classification as class D was appropriate during the pandemic , it can now be argued whether SARS-CoV-2 would still be falling under rule 1 second indent, especially, since as of the 5th of May 2023 the WHO officially declared SARS-CoV-2 (COVID-19) is no longer PHEIC (public health emergency of international concern) and is transitioning to the endemic phase [5].

Although it is shown that the overall morbidity has significantly decreased in the main EU population, there are remaining risk factors to be considered:

- Unvaccinated people;
- Vaccinated people with comorbidities (where vaccination effectiveness might not be as high, or shows a faster decrease)
- Waning vaccination effectiveness over-time (especially if no re-vaccination occurs)
  Emerging new virus mutations/strains with potential increased transmissibility, increased impact on vaccine efficacy / immunity and ultimately increased severity
- Challenging factors in defining an overall mortality rate (different vaccination schemes, ages groups, comorbidities, immunocompromised patient groups, etc)
- Social aspects: loss of awareness, feeling of urgency from healthy population (might lead to lower vaccination frequency/rate)

Based on the considerations above, Notified Bodies consider the risk associated with devices intended to detect the presence or exposure to SARS- CoV-2 (COVID-19) should be re-evaluated and their classification, should be reassessed.
Alternative possible classifications are assessed in the next section of this paper.

Possible device classification options

1) Classification as Class B according to IVDR Annex VIII rule 6

As per IVDR Annex VIII Rule 6, class B:

*"All other devices **not covered** by **other classification rules**, where an erroneous result is **unlikely to have a significant negative impact on patient outcome**, cause death or **severe disability** or **put individual in immediate danger**."*

According to the current version of the MDCG 2020-16 (rev2), classification of SARS-CoV-2 devices as class B products appears possible if the following is taken into consideration:

- Influenza A/B virus (non-pandemic strains) are for instance listed as examples of class B mainly based on the well-established technology behind the devices and list of preventing measures that would support patient safety.
- Other classification rules may appear difficult to evaluate. Particularly, diseases not generally leading to or resulting in a life-threating situation do not fall under any rule 3 classification rules; as per exclusion, rule 6 will apply.
- Active global surveillance and an early warning system (e.g. WHO, ECDC) are in place to detect circulating or emerging strains.

Class B Re-classification consequences

Taking into consideration the above discussion points re-classification of SARS-CoV-2 devices as class B (following rule 6) can lead to the following consequences:

- Although class B devices (non-self-test/ non-NPT) are assessed on a sampling basis, the sampling should be done on a risk/novelty basis as according to the MDCG 2019-13 sampling guidance. The notified body should justify their sampling rationale and can sample an increased number of files within a Class B device category if necessary. After issuing the certificate, the notified body continues to assess technical documentation in line with the sampling plan. When all the technical documentations have been reviewed, the notified body will focus the review of the technical documentation related to post-market surveillance.
- If the device is a self-test or near patient test the technical documentation will be reviewed in full.
- In case any new pandemic strains is detected, as per MDCG 2020-16 rule 1 second indent, Note 2, the list of high-risk agents may be updated and the corresponding devices reclassified.
- Reduction in classification from Class D to Class B will mean that Article 100 elements such as, the Common Specifications no longer apply. Despite Common Specifications no longer applying the devices will still be subject to notified body scrutiny and need to present Clinical Evidence of sufficient depth and quality to establish performance per the current state of the art in medicine.

However, it should also be considered that Performance Evaluation and Post-Market monitoring requirements would be less stringent: the IVDR mandates specific post-market monitoring for all device classes to confirm the safety, performance, and scientific validity throughout the lifetime of the device by means of PMS, continuous Performance Evaluation and PMPF activities, however, the frequency of the PMS report and Performance Evaluation Report updates for class B are defined by the manufacturer and PMPF activities can be excluded if an appropriate justification is provided.,

Furthermore it should be considered that in order to apply rule 6, all of the rule 3 classification rules need to be ruled out.

2) Classification as Class C device according to Annex VIII Rule 3c:

As per IVDR Annex VIII Classification Rule 3c

*"Detecting the presence of an infectious agent, if there is a **significant risk** that an erroneous result would cause death or **severe disability to the individual**, foetus or embryo being tested, or to the individual's offspring"*

The main aspect of applying rule 3 is the potential significant risk that an erroneous result could lead to individual health threatening situation. It is questionable if we do have sufficient data of the post-pandemic phase available to provide an objective, data derived evaluation.

Note:

SARS-CoV-2 devices intended for **self-testing (ST)** are classified as **class C** as per Annex VIII Rule 4a, if implementing Rule 1.9 does not apply, in case of several classification rules apply to the same device, the rule resulting in the higher classification shall apply (e.g. Rule 1 second indent > Class D)

SARS-CoV-2 devices intended for **near-patient testing (NPT)** are classified according to their own rule as per Annex VIII Rule 4a

- ➔ e.g., as **class D** device (under Rule 1, 2nd indent)
- ➔ or e.g., as **class B** for Influenza A/B virus, non-pandemic (under Rule 6, as examples given by MDCG 2020-16 rev 2)

According to the current version of the MDCG 2020-16 (rev2), classification of SARS-CoV-2 devices as class C products appears possible if the following is taken into consideration:

- There is a remaining risk for certain vulnerable patient groups (elderly, immunocompromised, patients with comorbidities etc.) of severe COVID-19 course when infected with SARS-CoV-2
- Rule 3c is difficult to fully exclude as it is challenging to evaluate all data published during the pandemic phase. The post-pandemic phase is considered short compared to e.g., the knowledge already gained with Influenza virus for comparison and our knowledge about e.g., Long-/Post-COVID-19 is still limited.

Class C Re-classification consequences

Taking into consideration the above discussion points re-classification of SARS-CoV-2 devices as **class C (following rule 3c)** can lead to the following consequences:

- Stricter requirements for Post-Market monitoring: manufacturers of class C devices are required to prepare PSUR at least annually; the PSUR may be reviewed by the notified body during surveillance activities. Furthermore, the continued obligation to make SSP available to the public will ensure higher transparency. The SSP will be reviewed by the notified body at least once during the certification cycle.
- Stricter requirements for Performance Evaluation monitoring: manufacturers of class C devices are required to update the PER at least annually. The output will lead to more stringent and periodically PMPF activities as well, as applicable. As a Class C device, the established CS as well as EURL scrutiny can be applied, Article 100 (2) 6 (3).
- Although class C devices (non-self-test/ non-NPT) are assessed on a sampling basis, the sampling should be done on a risk/novelty basis as according to the MDCG 2019-13 sampling guidance. The notified body should justify their sampling rationale and can sample an increased number of files within a Class C generic device group if necessary. After issuing the certificate, the notified body continues to assess technical documentation in line with the sampling plan. When all the technical documentations have been reviewed, the notified body will focus the review of the technical documentation related to post-market surveillance.
- If the device is a self-test or near patient test the technical documentation will be reviewed in full.

Conclusion for recommended reclassification

In light of the considerations above, notified body agree the reclassification from Class D to a lower risk class for non-pandemic SARS-CoV-2 is appropriate.

Taking into account the potential remaining risk for vulnerable populations (worst-case scenario) and the limited data available for the post-pandemic phase, a reclassification to Class C would be recommended: this would ensure stricter PMS & Performance Evaluation/Clinical Evidence requirements are applied and a better protection of patient safety.

A further reclassification to class B could also be considered once more data on the post-pandemic phase, especially regarding the long Covid syndrome, are available.

References

(1) 2023-WCP-0057 Draft.docx (europa.eu) ECDC communicable disease threat report KW 49

(2) COVID-19 Vaccine Tracker | European Centre for Disease Prevention and Control (europa.eu) accessed last 12/13/2023

(3) Epidemiological Bulletin 2/2024 (11 January 2024) https://www.rki.de/DE/Content/Infekt/EpidBull/Archiv/2024/02/Art_01.html

(4) ECDC Covid-19 Variants of Concern, accessed last 12/13/2023

(5) WHO News Covid-19