EUROPEAN COMMISSION

# View in the context of the Performance Evaluation Consultation Procedure (PECP)

## Expert panels on medical devices and *in vitro* diagnostic devices (Expamed)

## Contents



## Scope of this expert view

This scientific view reflects the opinion of independent experts (MDR Article 106.1) on the performance evaluation report (PER) of the manufacturer. The advice is provided in the context of the performance evaluation consultation procedure (PECP), which is an additional element of conformity assessment by notified bodies for specific high-risk in vitro diagnostic devices (IVDR Article 48.6).

When making its conformity assessment decision, the notified body is obliged to give due consideration to the opinions expressed in the scientific view of the expert panel, where applicable (Annex IX, Section 4.9 or, as applicable, Annex X, Section 3, point (j)).

For class D devices, the notified body must provide a full justification in the case of divergent views between the notified body and the experts. This justification shall be included in the notification to the competent authority (IVDR Article 50; mechanism for scrutiny of class D devices).

# 1 ADMINISTRATIVE INFORMATION

| | |
|---|---|
| **Date of reception of the dossier** | 09/09/2024 |
| **Notified Body number** | 2797 |
| **Internal PECP dossier #** | IVD-2024-000021 |
| ***In vitro* diagnostic medical device** *(descriptive text, no nomenclature use)* | Multiplexed nucleic acid in vitro diagnostic test (Qualitative PCR) intended for the simultaneous qualitative detection and identification of multiple respiratory viral and bacterial nucleic acids, including Middle East Respiratory Syndrome Coronavirus (MERS-CoV), in nasopharyngeal swabs in transport media obtained from individuals suspected of respiratory infection by their healthcare provider. |

# 2 INFORMATION PROVIDED BY THE NOTIFIED BODY

| **Intended purpose (P)** | | |
|---|---|---|
| **P1** | **what is detected and/or measured** *please specify the analyte(s) or marker(s), e.g. SARS-CoV-2 spike protein, Kel1 (K)* | Middle East Respiratory Syndrome Coronavirus (MERS-CoV) RNA, ORF5 |
| **P2** | **function of the device** *e.g. diagnosis, aid to diagnosis, monitoring, determining the infectious load, tissue typing etc* | This test is intended for the simultaneous qualitative detection and identification of multiple respiratory viral and bacterial nucleic acids which includes the Middle East Respiratory Syndrome Coronavirus (MERS-CoV) |
| **P3** | **the specific disorder, condition or risk factor of interest that it is intended to detect, define or differentiate** *e.g. hepatitis C infection, exposure to SARS-CoV-2, risk of HIV transmission in blood transfusion etc.* | Middle East Respiratory Syndrome Coronavirus (MERS-CoV) infection |
| **P4** | **whether it is automated or not** | Automated |
| **P5** | **whether it is qualitative, semi-quantitative or quantitative** | Qualitative |
| **P6** | **type of specimen(s)** *e.g. whole blood, serum, saliva etc* | nasopharyngeal swabs (NPS) in transport media |

| | | |
|---|---|---|
| **P7** | **where applicable, the testing population**<br>*e.g. persons with specific health conditions, persons with specific symptoms, children in a certain age range* | Individuals suspected of Middle East Respiratory Syndrome Coronavirus (MERS-CoV) infection |
| **P8** | **intended user** | Trained laboratory professionals proficient in using automated platform |
| **Technology (T)** | | |
| T1 | principle of the assay method or principles of operation of the instrument<br>*e.g. real-time PCR, qualitative PCR, digital PCR, sandwich immunoassay, competitive immunoassay, immunoturbidimetric assay etc.* | Qualitative PCR |

# 3 VIEWS OF THE EXPERT PANEL

## 3.1 Information on panel and sub-group (where relevant)

| | |
|---|---|
| **Date of views** | 07/11/2024 |
| **Expert panel name** | IVD expert panel |
| **Sub-group of expert panel (where relevant)** | IVD sub-group 2024-21 |

## 3.2 Summary of expert panel views

**Device description:**

The device is an in vitro diagnostic (IVD) tool designed for the qualitative detection and identification of multiple respiratory viral and bacterial pathogens, including the Middle East Respiratory Syndrome Coronavirus (MERS-CoV), in nasopharyngeal swabs from patients with respiratory symptoms. It uses multiplex PCR technology integrated with digital microfluidics, which enables automated sample processing from nucleic acid extraction to PCR amplification and detection. This setup allows for concurrent detection of multiple pathogens, which facilitates rapid diagnosis in clinical settings. As per the manufacturer, the device is an updated version of an earlier device, to which additional oligonucleotides required to detect SARS-CoV-2 were added. Due to the availability of Common Specifications for SARS-CoV-2, the expert panel focussed the review on MERS- CoV, the other class D pathogen targeted by this device (the other targeted pathogens belong to lower risk classes).

**Views on the performance evaluation report:**

**a) The scientific validity report:** The scientific validity of including MERS in the panel lacks depth, as few studies directly assess MERS detection. The literature review identifies gaps in MERS-specific scientific validation, which could be addressed by studies comparing MERS detection across devices or by providing robust evidence on the suitability of MERS primers and probes.

**b) Analytical Performance Report**: The report lacks specific data on MERS, which raises concerns given MERS' classification as a high-risk pathogen under IVDR (class D). While multiplex PCR can theoretically detect MERS, the report does not include studies confirming analytical sensitivity or specificity for this pathogen, which undermines confidence in its performance for MERS detection. A more thorough analytical validation, possibly using contrived samples or in silico analyses, would enhance the assessment of its reliability.

**c) Clinical Performance Report**: Clinical validation for MERS is limited due to its low incidence, which constrains real-world sample availability. The report relies on contrived samples to demonstrate clinical performance for MERS, but lacks detail on the sample composition, making it difficult to gauge its clinical relevance. Although the device performs well for more common pathogens, the lack of MERS-specific clinical validation weakens the overall assessment.

**Views on the specific aspects of the performance evaluation report:**

**Manufacturer's approach to clinical evidence**: The clinical evidence gathering approach appears limited, relying heavily on contrived samples due to the rarity of MERS cases. No data from MERS-prevalent regions were included, which would have strengthened the evidence for the device's clinical performance.

**Literature search, protocol and report**: The literature search is systematic but provides limited data for MERS. Only one study specifically addresses MERS, and no recent studies or comparative analyses are included. Expanding the literature review to include more MERS-related studies or in silico analyses would provide better context.

**Technological suitability and safety claims**: The multiplex PCR and digital microfluidics technologies are suitable for detecting multiple respiratory pathogens. However, while they theoretically support MERS detection, the safety and performance claims for MERS would benefit from further validation.

**Clinical evidence acceptability**: The clinical evidence is robust for other pathogens, but the lack of MERS-specific data limits its completeness.

**Views on the adequacy of the approach chosen by the manufacturer (in the absence of CS) to evaluate and ensure performance and safety of the device:**

In the absence of Common Specifications (CS), the manufacturer's approach relies on contrived samples and lacks sufficient real-world data, especially for MERS. Additional validation efforts, particularly using samples from regions with higher MERS prevalence, would help to ensure the device's performance and safety.

**Overall conclusions and recommendations on the performance evaluation report:**

The expert panel concludes that while the device demonstrates a strong potential for diagnosing respiratory infections (which was not assessed in detail), additional data specific to MERS are necessary. Recommendations include conducting in-depth analytical studies, in silico analyses, and clinical validation through comparative studies with CE-marked MERS assays to enhance confidence in MERS detection capabilities. It is also recommended to elaborate on the scientific rationale for having MERS in this multiplex, given the specific epidemiology and infection risks, and the consequences for assay performance.

## 3.3 Views on the specific reports included in the performance evaluation report (PER)

(IVDR, Annex XIII, Section 1.3.2, first paragraph)

| Views of the expert panel on the performance evaluation report of the manufacturer (PER) |
|---|
| **1. Expert views on the scientific validity report[1]** |
| The device is based on multiplex RT-PCR, a technique that can be considered state-of-the-art for detection of a panel of multiple pathogens to support the diagnosis of respiratory disease. Specifically for MERS included in the panel, RT-PCR is considered state-of-the-art. Multiplex RT-PCR or "syndromic" RT-PCR approaches are common and logical approaches for respiratory infections. Scientific validity has been evaluated through comparison to devices measuring the same analytes/markers, peer-reviewed literature containing favourable and unfavourable publications and results from other sources of clinical performance data. The scientific validity report especially mentions comparison with one other similar device on the market. However, that particular device does not cover MERS coronavirus and is in respect to this PECP not a suitable comparator. The literature search report is comprehensive but suffers from the fact that very few studies included MERS (as far as can be derived from the submitted data). Only one study mentioned MERS (Nijhuis et al 2017). In this study 2 MERS virus cultures were tested with the IVD in this review. Results were compared with an in-house developed research use only (RUO) RT-PCR, but no data on comparative detection limits are given. It is therefore difficult to truly assess the diagnostic performance regarding MERS on these two (culture) samples alone. Less favourable findings mention (among others) low pathogen load samples for especially common cold coronavirus targets that were not detected to the same extent as other competitor tests do. From the limited data submitted it cannot be excluded that the same would be true for MERS as the sensitivity and other performance characteristics cannot be assessed.<br><br>For scientific validity, there is the expectation to see a section detailing MERS-specific studies, in silico analysis, or references to validated tests for MERS. However, these are minimal or absent, and it indicates that the scientific backing for MERS in the pathogen panel is weak.<br><br>A thorough scientific validity report for MERS should include scientific literature specifically on MERS detection and its challenges, data comparing MERS detection across different devices or pathogen panels, and a clear explanation of why the primers and probes for MERS are well-designed, validated, and expected to work at a high sensitivity. Although the report provides general information on coronaviruses without deep-diving into MERS-specific issues, such as differences in genetic sequences or mutation rates, it suggests the scientific validation for MERS is not as robust as it should be. Furthermore, no information on the assay design for MERS detection could be identified, more specifically if it is based on one or more than one target region, as prescribed by the Common Specifications for another coronavirus SARS-CoV-2, characterized by high mutation rates. It is expected to easily recognize respective information on MERS assay design and the scientific rationale for the chosen approach. |

[1] Annex XIII, Section 1.2.1 of Regulation (EU) 2017/746 - Demonstration of the scientific validity

The Scientific Validity Report, while obviously more comprehensive for other pathogens, appears not thorough enough for MERS: it is recommended to include specific data or a strong scientific rationale for MERS detection beyond just theoretical assumptions.

From a scientific standpoint, there should be clear evidence that MERS is not just included in the panel as a rare target but has been rigorously validated with sufficient scientific backing, since epidemiological, infectious and clinical characteristics of the pathogen requires robust performance both in terms of sensitivity and specificity.

In summary, the scientific validity report appears not as thorough as it should be for MERS. While the inclusion of MERS into the panel is justified scientifically, the depth of evidence for its proficient detection is lacking.

**2. Expert views on the analytical performance report[2]**

The analytical performance report is extremely brief and does not contain sufficient information to be scientifically reviewed. Analytical performance studies are mainly done with a previous version of this device, e. g. data on interfering substances, specimen collection and handling, stability, precision and reproducibility are based on this previous version. Documents are referenced but not part of this documentation and can therefore not be reviewed. Other critical performance characteristics are evaluated with a combination of the two versions of the device. Reports are referenced, but again this documentation is not part of the dossier. Therefore, the expert panel is not in the situation to review all IVDR requirements that are summarized in table 1 of the analytical performance report (APR0004).

The analytical performance report lacks detailed studies or specific data on MERS, so it does weaken the confidence in the analytical performance for that target. Given that MERS is a high-risk pathogen (listed in class D under IVDR), one would expect to see at least contrived samples studies or in silico analysis convincingly demonstrating detectability, sensitivity, and specificity for this rare pathogen. Without those studies it is not possible to assess that the device has been sufficiently validated for MERS in real-world clinical or laboratory settings.

While PCR technology can theoretically detect MERS if well-designed primers and probes are included, the lack of concrete data makes it difficult to fully assess its performance regarding MERS. This lack of specificity could raise questions about regulatory compliance for MERS-CoV detection, particularly under IVDR standards, which require robust validation for the different assay targets.

While the technology itself (PCR, digital microfluidics) is capable and considered state-of-the-art, the absence of specific performance data for MERS in the analytical performance report is a critical shortcoming. For a pathogen with such serious implications, the expectation is that the report should provide rigorous validation, e. g. on well-characterized historical cases, cell-cultures, or contrived samples in case where real-world clinical cases are rare.

In summary the absence of analytical studies or detailed validation data for MERS in the analytical performance report is a serious weakness. While the technology might still be sound, the lack of documented validation means that based on the data submitted it is not possible to fully rely on MERS detection reflecting state of the art.

[2] Annex XIII, Section 1.2.2 of Regulation (EU) 2017/746 - Demonstration of the analytical performance

**3. Expert views on the clinical performance report[3]**

The Clinical Performance Report for the device usually draws from real-world testing or comparative studies with other diagnostic tools. However, for MERS, the clinical data is often limited simply because the number of cases is extremely low, and outbreaks are infrequent. This is why the clinical performance report lacks extensive data on MERS or only includes contrived samples rather than real patient cases. Even clinical performance data for MERS based on synthetic or laboratory-prepared samples is valuable though it does not really reflect performance in real-world clinical settings.

However, the clinical performance report relies heavily on past clinical performance studies with the previous version of the device. These clinical performance studies with the previous version are not part of the dossier submitted and therefore cannot be reviewed by the expert panel. For MERS-CoV, additional performance studies have been done with the current (new) version. These clinical performance studies for MERS-CoV appear to be based exclusively on contrived samples because of limited availability of MERS-positive clinical samples. Details of the contrived samples are completely lacking: i) composition of the contrived samples (i.e., cultured or other source), ii) matrix used, iii) origin of the material (ie virus strain), iv) concentration of the analyte, V) expected results, VI) results obtained with comparator assay(s). It is impossible for the expert panel to review the relevance of the contrived samples and thus also impossible to review the results and conclusions of the clinical performance studies. It is unclear on what data the reported PPA and NPA are based.

The documents detailing the clinical performance studies (CTP0023) are not part of the dossier and cannot be reviewed by the expert panel. Besides, clinical studies that provide evidence as "other Sources of Clinical Performance Data (CTP0013/CTR0003 and CTP0009/CTR0004)" are not provided.

The device is compared with a similar device on the market. However, this comparator device does not include detection of MERS and with respect to this review this is not a relevant or suitable comparator.

Most clinical performance reports focus on high-prevalence pathogens where robust clinical data is available, like SARS-CoV-2, influenza, or RSV. These pathogens are encountered frequently in clinical practice, so there's a wealth of clinical performance data. For a low incidence, but potentially severe disease-causing pathogen like MERS, even if it is included in the panel, the clinical performance data are sparse or absent, whereas robust substantiation of performance is of major importance. As a result, while the report might demonstrate the panel's effectiveness for more common pathogens, it is not providing enough evidence for MERS-specific clinical validation.

For MERS the dossier provided is not sufficient for a thorough evaluation. There are clinical data for more common pathogens included in the pathogen panel reassuring generic quality features of the device, but the absence of robust MERS data makes it impossible to assess quality features of the device specific for the MERS target.

In summary, the clinical performance for MERS, as described in this report, is minimal or speculative without substantial real-world data.

[3] Annex XIII, Section 1.2.3 of Regulation (EU) 2017/746 - Demonstration of the clinical performance

## 3.4 Views on specific assessment aspects of the performance evaluation report (PER)

(IVDR, Annex XIII, Section 1.3.2, second paragraph)

| Views of the expert panel on the specific aspects included in the performance evaluation report of the manufacturer (PER) |
|---|
| **1. The justification for the approach taken to gather the clinical evidence** |
| The manufacturers approach to gather clinical evidence is not well justified. According to the documentation supplied there has been no efforts made to do clinical performance studies in a country where MERS is more prevalent (i.e. Kingdom of Saudi Arabia). Instead, the clinical evidence solely relies on the use of contrived samples which, based on the provided documentation, are not well defined. |
| **2. The literature search methodology, protocol and report** |
| The literature search methodology is documented to support the scientific validity of the device by gathering relevant scientific and clinical data. The primary database used was PubMed, which is a comprehensive search engine accessing the MEDLINE database of life sciences and biomedical references. Additionally, manual searches were conducted using ProQuest/Dialog® and the Wiley Online Library to ensure comprehensive coverage. The literature has been selected based on systematic reviews, meta-analyses, clinical studies, and case reports presenting relevant clinical or analytical performance outcomes for respiratory pathogen detection. Inclusion and exclusion criteria have been defined. Search results have been screened for relevance, quality, and performance outcomes, and eligible articles have been included in the report.<br><br>The manufacturer provides a table in the report with a detailed summary of 14 relevant publications, including favourable and unfavourable findings on the device and comparisons to other devices.<br><br>However, only in one publication[4] the device is compared to laboratory-developed real-time PCR assays (LDT) using only 2 different Middle East respiratory syndrome coronavirus isolates (along with previously collected clinical respiratory specimens and 29 external quality assessment (EQA) specimens). In this paper Middle East respiratory syndrome coronavirus (MERS-CoV) isolates could be detected by the device. By testing a 10-fold dilution series of both isolates, it was shown that MERS-CoV with a CT value of <30 in the laboratory-developed real-time PCR assay could be detected using the device, while detection with a CT value of >30 was achievable but was not reproducible in every instance.<br><br>The data submitted with the dossier are not sufficient to support the scientific validity of the device. |

[4] Nijhuis RHT, Guerendiain D, Claas ECJ, et al. Comparison of ePlex Respiratory Pathogen Panel with Laboratory-Developed Real-Time PCR Assays for Detection of Respiratory Pathogens. J Clin Microbiol. 2017 Jun;55(6):1938-1945. doi: 10.1128/JCM.00221-17. Epub 2017 Apr 12. PMID: 28404682; PMCID: PMC5442551.

**3. The technology on which the device is based, the intended purpose of the device and any claims made about the device's performance or safety**

The device is a qualitative nucleic acid multiplex in vitro diagnostic test for simultaneous qualitative detection and identification of multiple respiratory viral and bacterial nucleic acids in nasopharyngeal swabs (NPS) obtained from individuals exhibiting signs and symptoms of respiratory tract infection.

The **technology** of the device is based on nucleic acid amplification (specifically multiplex PCR) integrated with electrowetting-based digital microfluidics. Digital microfluidics allow for the manipulation of tiny liquid droplets using electrical fields, enabling automated sample processing from nucleic acid extraction to PCR amplification and detection.

The detection process involves PCR amplification of target nucleic acids followed by the use of ferrocene-labelled signal probes and voltammetry to generate an electrical signal for pathogen identification. This technology allows for the simultaneous detection of multiple viral and bacterial pathogens from nasopharyngeal swab (NPS) samples.

Despite the lack of extensive MERS-specific data, the multiplex PCR technology used by the device is highly adaptable for rare pathogens like MERS. PCR is a proven method for detecting coronaviruses, and if the device can accurately detect other coronaviruses such as SARS-CoV-2, it suggests that it could also reliably detect MERS-CoV. While there is limited specific information on MERS in the PER, the technology behind the device should theoretically handle MERS detection effectively based on its multiplex PCR capabilities and its performance with other coronaviruses.

The **intended use** of the device is for the simultaneous qualitative detection and differentiation of nucleic acids from multiple respiratory pathogens, including both viruses and bacteria. The panel is specifically intended for the diagnosis of respiratory infections in patients showing signs of respiratory illness, and it helps clinicians rapidly identify the causative pathogen to guide treatment decisions. It is supposed to be useful for detecting pathogens that cause influenza-like illnesses and has been modified to include targets such as SARS-CoV-2 and MERS-CoV, among other common respiratory pathogens.

Regarding the **safety claims,** the device has undergone risk assessments to ensure that its use is safe and that the benefits outweigh any potential risks. It is also subject to continuous post-market monitoring to evaluate safety, identify emerging risks, and ensure ongoing compliance with safety standards. The technology is well-established in clinical diagnostics, ensuring minimal risk of false results (false positives/negatives) through validated processes. Given the low a priori chance of MERS infection in the EU, the specific exposure requirements and the potential impact for both the patient and public health when missing the right diagnosis, the performance of the assay should be robust and reliable. Inference from other data or generic assumptions from other (seasonal) coronaviruses pose a potential safety risk as epidemiological, virological and clinical characteristics that may have consequences for clinical performance are not comparable.

**4. Acceptability of clinical evidence (clinical data and performance evaluation results) against state of the art in medicine**

The Performance Evaluation Report discusses the acceptability of clinical evidence by comparing the device clinical data and performance results against the state of the art in medicine.

Regarding Clinical Data and Performance Evaluation, the Clinical Performance Report (p. 69-119) compares the results obtained from the current version of the device and the previous version with comparator methods, including CE-marked devices as well as traditional methods like PCR/qPCR amplification assays. The Scientific Validity Report includes a detailed analysis of peer-reviewed scientific literature, comparing the panel's performance to other devices measuring the same analytes, thereby confirming its clinical utility. This appears acceptable for most of the other targets (not reviewed in detail), but not for MERS target (under specific review in this PECP).

The device can be confirmed as representing state of the art due to its rapid detection capabilities, ability to handle multiple respiratory targets, and its high accuracy in comparison to existing diagnostic methods. Multiplex nucleic acid amplification tests (NAATs) are considered state-of-the-art in the diagnosis of respiratory infections. These tests offer superior sensitivity and specificity compared to older methods like antigen testing or culture.

Experts are aware that there are global and European guidelines on respiratory infection diagnostics, which underscore the need for rapid, accurate molecular diagnostics, particularly in the context of outbreaks (e.g., COVID-19 and MERS-CoV). MERS-CoV is a beta coronavirus that can cause severe respiratory disease with a high fatality rate (~40%), primarily in people with underlying health conditions. Although rare, MERS is included in the panel due to its serious public health implications. However, the lack of information regarding MERS makes it impossible to assess this device regarding MERS.

Experts are also aware that multiplex PCR is one of the most advanced and reliable techniques for detecting multiple pathogens from a single sample. This is crucial in clinical settings where time and accuracy are essential. The ability to identify several viruses and bacteria at once, including important pathogens like SARS-CoV-2 and MERS-CoV, places the device at the forefront of diagnostic technology. It not only allows for rapid diagnosis but also contributes to better patient management, helping clinicians quickly determine the cause of infection and choose the appropriate treatment.

The incorporation of digital microfluidics is an innovative step forward. This technology is relatively new and provides a highly automated, precise, and miniaturized platform for handling biological samples. It allows laboratories to reduce manual steps, decrease human error, and achieve faster processing times. This kind of advancement reflects the ongoing trend in diagnostics toward automation and point-of-care testing, which is becoming increasingly important in healthcare.

In today's healthcare landscape, where speed and accuracy are paramount—especially in the face of pandemics or outbreaks—having a diagnostic tool that can deliver results in under two hours with high sensitivity and specificity is critical. Faster diagnostics can significantly reduce the time to treatment and improve patient outcomes, especially in acute care settings. From a clinical and operational perspective, this makes the technology stand out compared to more traditional, slower methods.

The ability to adapt to emerging pathogens—for example, incorporating SARS-CoV-2 into the panel—is a sign of flexibility and innovation. Devices that can quickly integrate new targets are key to keeping pace with evolving healthcare needs, especially as we face new and unpredictable viral outbreaks. However, the decision to include a new pathogen into the panel should depend on a sound assessment of rationale and need, also in terms of assay expectations (screening, confirmation).

From a practical standpoint, having a comprehensive, fast, and reliable diagnostic tool can greatly improve healthcare delivery, not just in specialized labs but also in more general hospital settings. The widespread clinical utility of such a device in diagnosing respiratory illnesses, which are among the most common medical issues, positions it as a cutting-edge tool for modern medicine.

In summary, the technology behind the device is state-of-the-art. Its use of multiplex PCR, digital microfluidics, and rapid, automated detection sets it apart as a leader in diagnostic technology. This kind of innovation aligns with the future of medicine, which is moving toward faster, more precise, and automated diagnostics. However, in the case of MERS, specific data are key to evaluate this specific target, clinical data, analytical performance and scientific validity.

**5. Any new conclusions derived from PMPF reports, where applicable**

The manufacturer considered that PMPF was not necessary at this time. This decision was taken considering that the technology used by the device is well-established and widely accepted as a standard testing method for respiratory pathogens and that the device meets the state-of-the-art in medicine, including compliance with applicable regulatory standards.

The manufacturer also mentions that the device is subject to continuous post-market monitoring through several channels, including complaint and complaint trend evaluation, monitoring of scientific literature for new findings that could affect performance and customer feedback acquisition through frequent interactions with users and key opinion leaders in the medical field.

While the device is not currently undergoing a formal PMPF, the manufacturer states that the continuous monitoring process ensures that any emerging risks or performance issues should be promptly identified, what would prompt a (re)-evaluation of the need for a PMPF.

## 3.5 Overall conclusions and recommendations

**Overall conclusions and recommendations on the performance evaluation report**

In terms of evaluating MERS detection by the device, the lack of real-world data is an important limitation. The principal inclusion of MERS in the pathogen panel appears justified, meaning that the device has the capability to test for MERS, e. g. in high-risk populations, residing in the Middle East or in individuals returning from travel).

The manufacturer claims that the only difference between the current device version and its predecessor are the additional oligonucleotides required to detect SARS-CoV-2. Equivalence studies are summarized in TSR0302 (Device Performance Characterization) not provided in the documentation; therefore, respective evidence cannot be confirmed.

For SARS-CoV-2 and targets specific for the CE-IVD (MERS, *Legionella pneumophila*, and Human Bocavirus), results from the clinical performance studies are documented in CVP0004, (Device Clinical Validation Protocol) which was not provided.

**Recommendations:**

In relation to MERS-CoV, the manufacturer should perform studies and provide additional data on:

1) Analytical performance, (analytical sensitivity, analytical specificity, dynamic range, etc).
2) In silico analysis of primers and probes against publicly available sequence data
3) Composition of the contrived samples used in the clinical performance studies
4) (Attempts of) inclusion of clinical samples from MERS prevalence regions in the performance evaluation studies
5) Data on the contrived samples used in the clinical performance studies
6) Comparison studies with other CE-IVD MERS assays, based on RT-PCR or other NAT technology; preferentially devices CE marked under IVDD.

If in the future a new pathogen target is included into the panel, this should depend on a sound assessment of rationale and need, also in terms of assay expectations (screening, confirmation).

## 3.6 Stakeholder information, where available

| **Relevant information provided by stakeholders, if applicable[5]** |
|---|
| **Has the Secretariat provided information from stakeholders?** |
| ☐ YES ☒ NO |
| **If yes, please summarise the information and how it was taken into account.** |
| Not applicable |

## 3.7 Divergent positions in case no consensus can be reached

| **In case no consensus on the views can be achieved[6], please indicate how many of the experts of the panel had divergent positions** |
|---|
| No divergent views. |
| **Please summarise those divergent positions, if applicable** |
| Not applicable |

[5] According to Article 106.4 of Regulation (EU) 2017/745, expert panels shall take into account relevant information provided by stakeholders including patients' organisations and healthcare professionals when preparing their scientific opinions.

[6] According to Article 106.12 of Regulation (EU) 2017/745, when adopting its scientific opinion, the members of the expert panels shall use their best endeavour to reach a consensus. If consensus cannot be reached, the expert panels shall decide by a majority of their members, and the scientific opinion shall mention the divergent positions and the grounds on which they are based.