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European wide Innovation Procurement in Health and Care

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Deliverable

D4.2: Final procurement demands

WP	**#4**	Analysis of current status of Antibiotic use at hospital and use – opportunities – barriers of Rapid Diagnostics test considering socio-economic consequences of AMR development and defining initial criteria
Task	**#4.2**	Translation of the URS into procurement demands

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[1] Dissemination level: **PU**: Public; **CO**: Confidential, only for members of the consortium (including the Commission Services); **EU-RES**: Classified Information: RESTREINT UE (Commission Decision 2005/444/EC); **EU-CON**: Classified Information: CONFIDENTIEL UE (Commission Decision 2005/444/EC); **EU-SEC** Classified Information: SECRET UE (Commission Decision 2005/444/EC)
[2] Type of the deliverable: **R**: Document, report; **DEM**: Demonstrator, pilot, prototype; **DEC**: Websites, patent fillings, videos, etc.; **OTHER**; **ETHICS**: Ethics requirement; **ORDP**: Open Research Data Pilot
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Deliverable abstract

In WP4.2, the user requirements specifications were translated into procurement demands. We matched the clinical perspectives with the currently available innovative diagnostics based on the algorithms defined in WP4.1.
Hospital-acquired lower respiratory tract infections, such as Ventilator-Associated Pneumonia (VAP) served as an example of how the demand side from a clinical perspective can be matched with the currently available innovative diagnostics, as discussed in our previous WP4.1 report. We first analyzed online available VAP guidelines and compared the diagnostic parameters and treatment options for VAP. We also reviewed the VAP clinical scoring systems. Secondly, we defined clinical decision trees for VAP based on these guidelines. The UAntwerp developed a questionnaire to identify the product specifications for the selection of a rapid diagnostic test for the two VAP algorithms (antibiotic stewardship and detection of colonization). With the support of the European Respiratory Society (ERS), we invited seven VAP experts to fill out this questionnaire. Next, the different outcomes were identified that could be linked to these technical specifications. This resulted in a clear picture on the proposed clinical pathway for the diagnosis of VAP, the technical specification for the diagnostic test and the first draft of the URS. Finally, UAntwerp constructed a database with variables for landscaping diagnostic tests for detection of microbial and host biomarkers for diagnosis of respiratory tract infections. This landscaping is a joint initiative with another EU funded Marie Curie project (New Diagnostics for Infectious Diseases). Information collected includes: intended use, setting, performance, patient type, method, target, analysis, detection, detected pathogens, detected antimicrobial resistance (AMR), storage conditions, shelf life, kit components, volume/amount required, test preparation, sample processing, controls, calibration, maintenance, hands on time, results readout, time to result, instrumentation, instrument specifications, connectivity, waste disposal, samples per run, patient population, sensitivity, specificity, PPV, NPV, reproducibility, limit of detection, cross-reactivity, interference, training, required, on-site training, cost of kit (€), instrument availability in Europe, cost of instrument (€)/leasing possibility, calibration, maintenance/support, stage of development, market region, regulatory approval, and CLIA complexity.

Deliverable Review

	Reviewer #1: Yves VERBOVEN			Reviewer #2: Not applicable for this deliverable		
	Answer	Comments	Type*	Answer	Comments	Type*
Is the deliverable in accordance with						
the Description of Action?	☒ Yes ☐ No		☐ M ☐ m ☐ a	☐ Yes ☐ No		☐ M ☐ m ☐ a
the international State of the Art?	☒ Yes ☐ No		☐ M ☐ m ☐ a	☐ Yes ☐ No		☐ M ☐ m ☐ a
Is the quality of the deliverable in a status						
that allows it to be sent to European Commission?	☒ Yes ☐ No		☐ M ☐ m ☐ a	☐ Yes ☐ No		☐ M ☐ m ☐ a
that needs improvement of the writing by the originator of the deliverable?	☐ Yes ☒ No		☐ M ☐ m ☐ a	☐ Yes ☐ No		☐ M ☐ m ☐ a
that needs further work by the Partners responsible for the deliverable?	☐ Yes ☒ No		☐ M ☐ m ☐ a	☐ Yes ☐ No		☐ M ☐ m ☐ a

* Type of comments: M = Major comment; m = minor comment; a = advice

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1. Introduction

The diagnosis of Ventilator-Associated Pneumonia (VAP) is a challenge because the affected tissue is not accessible to sampling, the gold standard (culture) has a low specificity, and many guidelines are available recommending conflicting procedures for microbiological diagnosis. A VAP diagnosis based on clinical symptoms only might lead to over diagnosis and, hence, excessive antibiotic treatment resulting in adverse side-effects and emergence of antibiotic resistance. Rapid diagnostics might have an important role in VAP diagnosis as early detection of VAP can enhance the appropriate management of the disease, reduce morbidity and mortality [1]. In our previous report (WP4.1), we defined the clinical decision tree, focusing on detection of colonisation and antibiotic stewardship of VAP, based on the currently available guidelines and peer-reviewed literature. We identified several needs, such as the absence of reliable epidemiological data and useful prognostic biomarkers. Based on our literature study in WP4.1, we concluded that microbiology should be an important step in the decision making tree, although the current techniques have many shortcoming.

In WP4.2, the user requirements specifications were translated into procurement demands. We matched the clinical perspectives with the currently available innovative diagnostics based on the algorithms defined in WP4.1. The UAntwerp developed a questionnaire to identify the product specifications for the selection of a rapid diagnostic test for the two VAP algorithms (antibiotic stewardship and detection of colonization). With the support of the European Respiratory Society (ERS), we invited seven VAP experts to full out this questionnaire: prof. Loeches, prof. Torres, prof. Chastre, prof. Monreal, prof. Welte, prof. Timsit and prof. Shyamsundar. Next, the different outcomes were identified that could be linked to these technical specifications. We already discussed this exercise in our previous WP4.1 report, but we searched for new outcomes that were identified in literature and overlooked previously. Finally, UAntwerp constructed a database with variables for landscaping diagnostic tests for detection of microbial and host biomarkers for diagnosis of respiratory tract infections. This landscaping is a joint initiative with another EU funded Marie Curie project (New Diagnostics for Infectious Diseases). Information collected includes: intended use, setting, performance, patient type, method, target, analysis, detection, detected pathogens, detected antimicrobial resistance (AMR), storage conditions, shelf life, kit components, volume/amount required, test preparation, sample processing, controls, calibration, maintenance, hands on time, results readout, time to result, instrumentation, instrument specifications, connectivity, waste disposal, samples per run, patient population, sensitivity, specificity, PPV, NPV, reproducibility, limit of detection, cross-reactivity, interference, training, required, on-site training, cost of kit (€), instrument availability in Europe, cost of instrument (€)/leasing possibility, calibration, maintenance/support, stage of development, market region, regulatory approval, and CLIA complexity. The full database is confidential but data relevant to VAP tests for the two algorithms developed in WP4 can be extracted and shared among the EURIPHI partners.

Table 1: Overview of the different steps of D4.1 and D4.2:

DL	Planned step	Fulfilled (Yes/ No; Date)
D4.1	State of the Art	Yes (Date: 31/01/2019)
D4.1	Clinical decision tree	Yes (Date: 31/01/2019)
D4.1	Algorithms (Stewardship/ Detection of colonisation)	Yes (Date: 28/02/2019)
D4.1	Survey in Qualtrics	Yes (Date: 31/03/2019)
D4.1	Contacting theVAP expert panel	Yes (Date: 15/04/2019)
D4.2	Analysis of the technical specification questionnaire	Yes (30/07/2019)
D4.2	Overview of VAP rapid diagnostic test available on the market	Yes (15/07/2019)
D4.2	Determining the outcomes based on a review	Yes (15/08/2019)
D4.2	Final D4.2	Yes (31/08/2019)

2. State of the Art

Review and outcomes of Ventilator-Associated pneumonia (VAP)

One-fourth of critically ill patients at the intensive care unit (ICU) require mechanical ventilation by placing an endotracheal tube (ETT) in the trachea to assists the normal breathing cycle. However, the intubation process increases the risk of developing pneumonia ~6 to 20 fold [2,3], which originate most frequently from bacterial colonisation of the ETT by endogenous flora or exogenously acquired pathogens. An endotracheal tube will interfere with the natural host defence mechanism by suppressing the cough reflex of the glottis and larynx and bypasses the pathogen-clearing function of the tracheal epithelial cilia [4]. The pulmonary microbiome is maintained by an intricate balance between microbial immigration through inhalation and aspiration, elimination by host defence systems and local bacterial growth [5]. When host defences are not intact, such as during aspiration, catheter insertion or surgery, the natural lung microbiome is disrobed which might result in pathogenic colonisation of the trachea [5]. Additionally, it will also induce clinical complications, such as sinusitis and nasopharyngeal trauma, biofilm formation and microaspiration of the oropharyngeal particles. Through microaspiration of bacterial particles from the ETT, the infection can progress in ventilator-associated respiratory infections (VARI) such as ventilator-associated tracheobronchitis (VAT) or VAP, of which VAP is the most prominently occurring subtype [6,7]. The incidence and mortality are heavily dependent on the studied population and can vary between 9-27% and 8-76%, respectively [6]. In the hospital, VAP presents itself as a major threat to patients and accounts for approximately 50% of the antibiotics use. In addition, VAP is associated with prolonged ventilation and hospital stay, as well as increased hospitalisation costs [8,9]. As indicated by the great variety in incidence and mortality, accurate diagnostic criteria of VAP have not yet reached an absolute consensus in the literature. However, certain implications and symptoms are generally accepted as indications for the infection and present as an acute inflammation of the lung parenchyma. Pulmonary samples such as an endotracheal aspirate, broncho-alveolar lavage and protected specimen brush can be used to diagnose VAP semi-quantitatively (excessive bacterial growth when cultured) and quantitatively (>10^3 colony-forming units/ml, depending on the sample). Further, VAP is accompanied by pneumonia-related symptoms such as increased respiratory rate, sputum production and chest pain, as well as nonspecific systemic signs such as fever, muscle ache, fatigue and lack of appetite [10].

Clinical practice guidelines of VAP

Diagnoses

Clinical practise guidelines serve as a framework for physicians to support the best practice for optimizing patient care. Ideal, pneumonia diagnosis should be based on the combination of clinical criteria, circulating and lung-specific host-response biomarkers and pathogen detection by an ultra-rapid highly accurate pathogen identification and AST testing resulting in an automated decision for optimal antibiotic prescribing, de-escalation and stewardship [11]. But, for the moment, there is no consensus on the diagnostic, therapeutic and preventive strategies of VAP and thus different strategies for diagnosing VAP are available, all having variable sensitivities and specificities [12].

The clinical diagnosis of VAP has been based on chest radiology. Although this method is sensitive, it is also non-specific and thus, an association needed to be made with other clinical signs. The oldest diagnostic criteria were published by Johanson et al. [13]. These diagnostic criteria were the presence of new or persistent infiltrates on X-ray and at least two of following clinical symptoms; Febrile > 38.3; leukocytosis or leucopenia (>11 or < 3.5) and/ or purulent tracheobronchial secretions. The sensitivity and specificity were 69% and 75%, respectively [14]. Despite this relatively low accuracy, these criteria were recommended by the American Thoracic Society. More recently, the Clinical Pulmonary Infection Score (CPIS) by Pugin were based on six symptoms (fever, leukocytosis, tracheal aspirates, oxygenation, radiographic infiltrates and semi-quantitative cultures of tracheal aspirates with Gram stain) [15]. The original study showed a high sensitivity of 93% and specificity of 100%, but it was only tested on a low number of patients. Further studies showed a high variability of the CPIS studies, with a sensitivity of 72- 93%, and specificity of 42-85 % [16–19]. CPIS does not have good discrimination and calibration for predicting mortality compared to APACHE II, but it stayed the most widely used clinical scoring system for VAP [18]. Other clinical scoring systems are APACHE II (acute physiology and chronic health evaluation II); MPM72 II (mortality probability model II); SAPS II (simplified acute physiology score II); MODS (multiple organ dysfunction score); SOFA (sequential organ failure assessment); VAP-PIRO

(ventilator-associated pneumonia predisposition, insult, response, organ dysfunction). Studies have shown that using a single clinical criterion has low specificity; therefore there is a need to use a combination of clinical symptoms [20].
The value of bacteriological data in establishing the diagnosis of VAP has been evaluated by many studies. Different sampling methods (invasive, non-invasive, quantitative and non-quantitative) have been tested, but no gold standard was reached [12]. It has been noticed that adding these methods, the sensitivity for the diagnosis of VAP will not increase [21,22]. Also, a Cochrane review didn't show any evidence for the use of quantitative cultures of respiratory secretions results in reduced mortality, reduced time in ICU and on mechanical ventilation. They observed similar results when invasive strategies were compared with non-invasive strategies [23]. Although the conclusions of both EU and USA guidelines described microbiology input as important for VAP diagnoses, they prefer different strategies. The USA prefers non-invasive techniques in combination with semiquantitative culture to avoid overidentification [24]. On the other hand, European guidelines prefer invasive techniques with quantitative culture as this will avoid false positivity and over antibiotic treatment [12,24]. In literature, Gram staining is also regularly discussed as it will be positive for pneumonia patients and negative in other cases, but subclassification is not possible [12]. The main problem of culture is that this method takes days before results are available, and has a limited sensitivity especially due to prior antibiotic use and low specificity because of colonisation with potential VAP pathogens [25]. Chastre et al. (2002) suggested two diagnostic strategies for VAP, namely a clinical and bacteriologic strategy. Here a gram stain of tracheal aspirate can be used for direct initial empiric antimicrobial therapy. When using the clinical approach, the patient will be treated for pneumonia when another infection might be responsible for the clinical symptoms. This technique is thus oversensitive and leads to more antibiotic therapy [12]. On the other hand, the bacteriologic strategy used quantitative cultures of respiratory samples. The pitfalls of choosing this approach are a missing threshold for the different samples used and false negative culture that can lead to failure of the treatment.

Several host and microbial biomarkers have been described for improving the current diagnosis of VAP although the European and USA guidelines advice to use biomarkers only in case of multiple drug resistance (MDR) and the absence of currently useful biomarkers. CRP, PCT, copeptin and MR.-proANP are associated with low mortality; but no clinical trials have confirmed this [21]. PCR is very effective in differentiating viral from bacterial infection but is too nonspecific for diagnoses of VAP [26]. Further studies are needed to fully understand the role of biomarkers in the diagnoses of VAP.

Antibiotic Stewardship

Appropriate antibiotic therapy needs to be based on the pharmacokinetics and -dynamics, adequate dosages with enough penetration in lung tissue and adapted to local antibiotic susceptibility profile [27]. It is also recommended that the de-escalation of therapy starts as soon as the patient is stable and microbiology data are available. Both European and USA guidelines prefer to treat a patient for 7-8 days.
Each treatment of VAP patients starts with empiric treatment unless low clinical susceptibility or negative culture. This treatment should be based on the local pathogens presents; antibiotic resistance pattern, risk factors of the patient and the type of care.

Clinical decision tree

Based on the currently available guidelines we defined two clinical decision trees, focusing on diagnosis and stewardship. In these trees, we identified several needs; such as the presence of epidemiology data and the absence of useful prognostic biomarkers. Considering the clinical symptoms, there is a lack of specificity and sensitivity; and most likely, these symptoms alone are not enough for starting the antibiotic treatment. Microbiology should be an important step in these decision trees, although the current techniques are slow and different methods having similar outcomes are available. It is also important to assess how the diagnosis will guide stewardship, especially to avoid overuse of antibiotics.

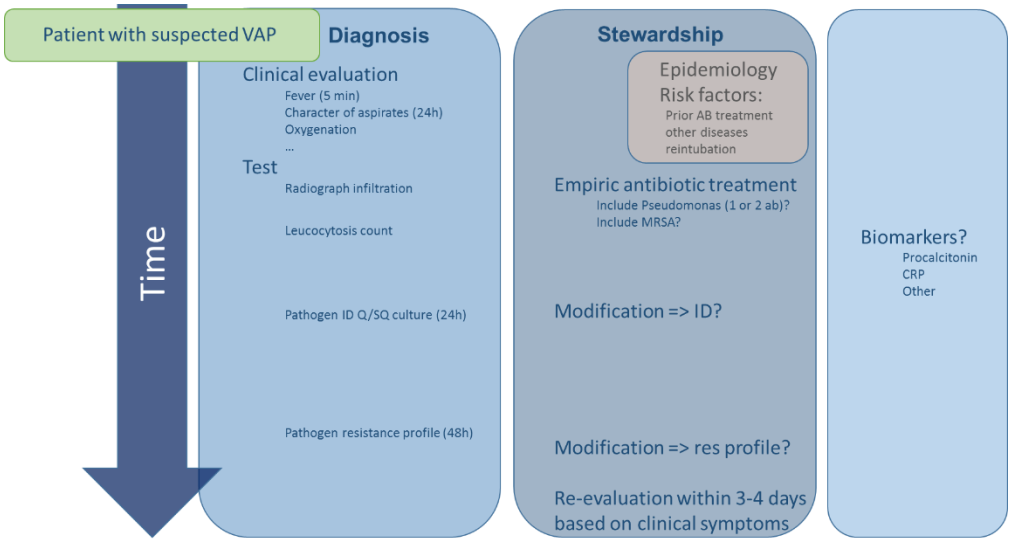


Figure 1: Current clinical decision tree for VAP

After the literature review, we defined a new clinical decision tree, where a diagnostic test will improve the clinical diagnostic pathway of VAP (Figure 2). The diagnostic test will have an important impact on the decision tree where the pathogen identification and resistance profile will be determined sooner compared to the current clinical decision tree. This data was presented during a break out session in the kick-off meeting in Brussel, all partners provided their input on this topic.

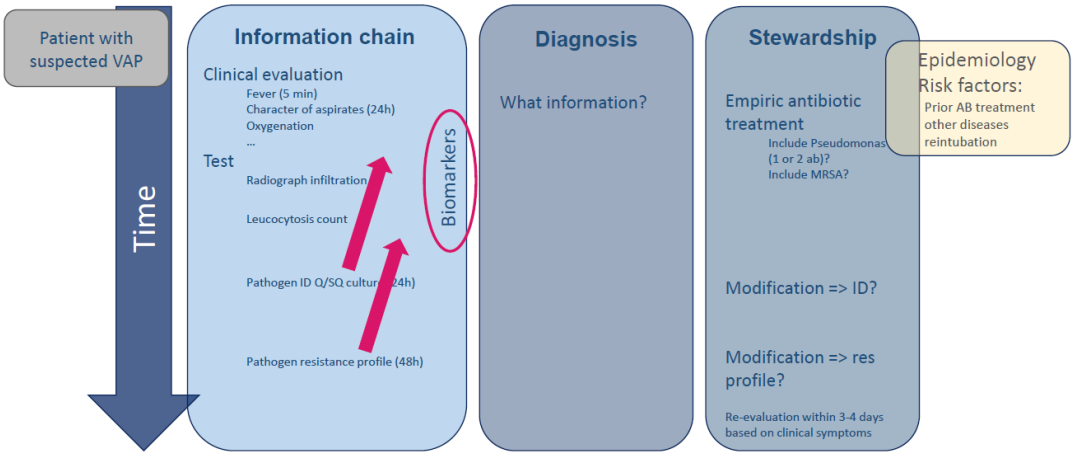


Figure 2: New clinical decision tree for VAP

The user requirement specifications are shown in figure 3. Input from previous projects was taken into account as for example the IMI funded European project RAPP-ID (Rapid Point - of -Care test Platforms for Infectious Diseases) in which experts from pharma and clinicians helped to develop product specifications for a POCT test. These data were implemented in this step of the EURIPHI project. The technical specifications were split into different levels; global, hospital, instrument. These data were presented during a break out session in the kick-off meeting in Brussel, all partners provided their input on this topic.

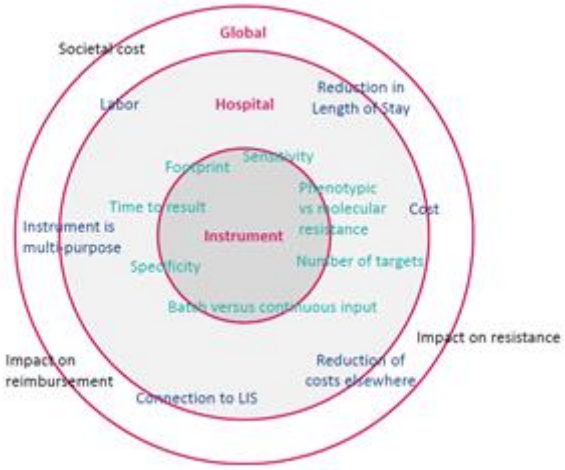


Figure 3: User requirement specifications

Algorithms

To define the ideal and minimum acceptable product specifications for rapid diagnostic tests the two algorithms were being considered. The first algorithm focuses on antibiotic stewardship of VAP by early detection of the presence of pathogens and their antibiotic resistance/susceptibility patterns. Such early detection might allow to alter treatment or de-escalation strategies and can thus impact on mortality and morbidity rates, the length of stay and overall costs and reduce the development of antibiotic resistance. The second algorithm considers a diagnostic test that would allow prevention strategies, reduce pathogen transmission and avoid VAP infections. These strategies were presented during a meeting in Antwerp with the WP4 partners (12/2/2019).

Algorithm 1: stewardship

We have witnessed the emergence of new diagnostic tools over the last few years that might allow to promptly initial antibiotic therapy or rapid de-escalation after the initial dose. These diagnostic tools are capable of guiding antibiotic treatment, particularly in the case of broad-spectrum antibiotics in Intensive Care Units. Current recommendations for management of VAP in patients at risk of multi-drug resistant pathogens call for prompt broad-spectrum empirical treatment, including dual Gram-negative coverage. This recommendation is supported by consistent findings that delayed appropriate antibiotic therapy in multi-drug resistant pneumonia is associated with increased mortality. However, the definition of "patients at risk for multi-drug resistant pathogens" is very broad and results in massive overtreatment with broad-spectrum antibiotics. Kett et al showed that adherence to empirical treatment of these patients was associated with increased mortality [28]. A potential explanation for this increased mortality was the antibiotic-specific toxic effects of colistin, aminoglycosides and fluoroquinolones. ATS-IDSA guidelines recommend that the broad-spectrum empirical treatment is de-escalated when possible, based on clinical response and microbiological data. The goal of de-escalation is to limit the emergence of resistance and to reduce mortality.

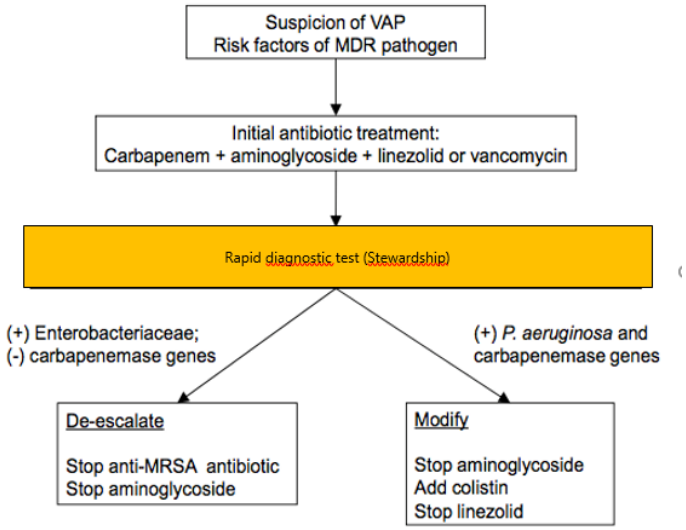


Figure 4: An example of an algorithm for a stewardship approach.

Algorithm 2: prevention

Prior colonization with potential pathogens plays a significant role in the development of VAP. Apart from current prevention strategies such as better mouth hygiene, the minimization of the duration of mechanical ventilation or the minimization of the risk of aspiration of oropharyngeal pathogens, a rapid diagnostic test might help to identify patients at risk and enable prevention strategies targeting the involved pathogens. The target of such a diagnostic test would be all patients in ICU, even before they show clinical signs of pneumonia. One such potential preventive strategy could be the use of monoclonal antibodies (mAbs), not necessarily aimed at killing the bacteria, which has been done for decades with antibiotics, but rather by targeting specific virulence factors, reducing the onset of disease and helping to improve the patient outcome. Currently, such mAbs are being developed for *S. aureus* and *P. aeruginosa*, opening the door for applying new screening tools identifying these organisms.

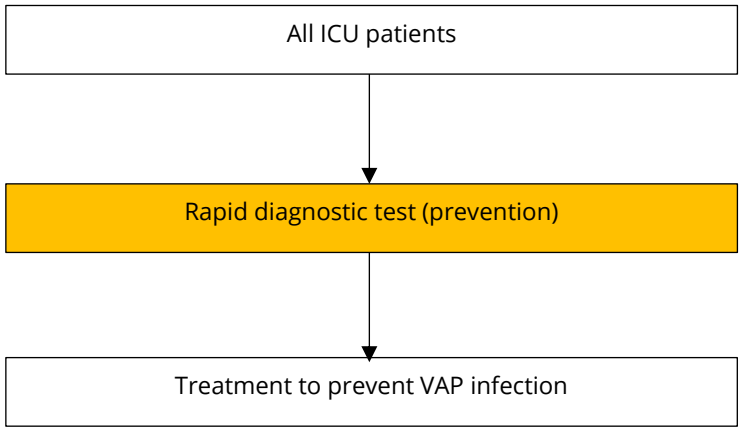


Figure 5: An example of an algorithm of a diagnostic test for the prevention of VAP and transmission of pathogens.

3. Results and Analysis

Scoring of the technical specifications' questionnaire

The aim of this questionnaire developed by the UAntwerp partner was to identify the technical specifications needed for a rapid diagnostic test for microbiological detection of pathogens causing VAP. The target audience for this questionnaire included seven renowned VAP experts proposed by the European Respiratory Society (ERS). Two algorithms were considered and scored by these experts. Briefly, the first algorithm focused on antibiotic stewardship of VAP by early detection of the presence of pathogens and their antibiotic resistance/susceptibility patterns. Such early detection allows to alter treatment or de-escalation strategies and can thus impact on mortality, morbidity, the length of stay, overall costs and the development of antibiotic resistance. The second algorithm considered a diagnostic test that would allow prevention strategies, reduce pathogen transmission rates and prevent development of VAP. We identified the technical specifications of the diagnostic test by analyzing the questionnaire results, allowing us to allocate weight factors to the various value associated outcomes and the underlying technical specifications, and bridging clinical significance to value. The goal of this questionnaire was to define (i) the importance of the technical specifications, and (ii) the ideal and minimum acceptable product specifications for rapid diagnostic tests that might fit these two algorithms. The technical specifications were split according to the different outcomes and levels. Detailed information about the questionnaire can be found in table 2 and attachment 1-2.

Table 2: Specifications of the questionnaires

Pathways	**Stewardship**	**Detection of colonisation**
Number of questions	87	60
Minimum time to fill in	17 min	12 min
Average time to fill in	28 min	18 min
Maximum time to fill in	57 min	26 min
Program	Qualtrics	Qualtrics

Stewardship pathway

Based on the descriptive analyses, the technical specifications at the patient level were scored as the most important (Figure 6). The top 10 included 7 specs at the patient level, such as time to result, sensitivity, specificity, list of pathogens and resistance genes, type of sample and the culture method of the sample (Quantitative versus qualitative). All specs were having a score higher than 2.7/3, indicating the high importance ranked by the VAP experts. Also, the reduction of prescribing (global spec) and selective pressure (global spec), the reproducibility (device specs) and positive predicted value (PPV; device specs) were considered important (scores >2.7). On the other hand, the costs (hospital level) were scored as less important, of which the waste and footprint were the least important (score: 1.9).

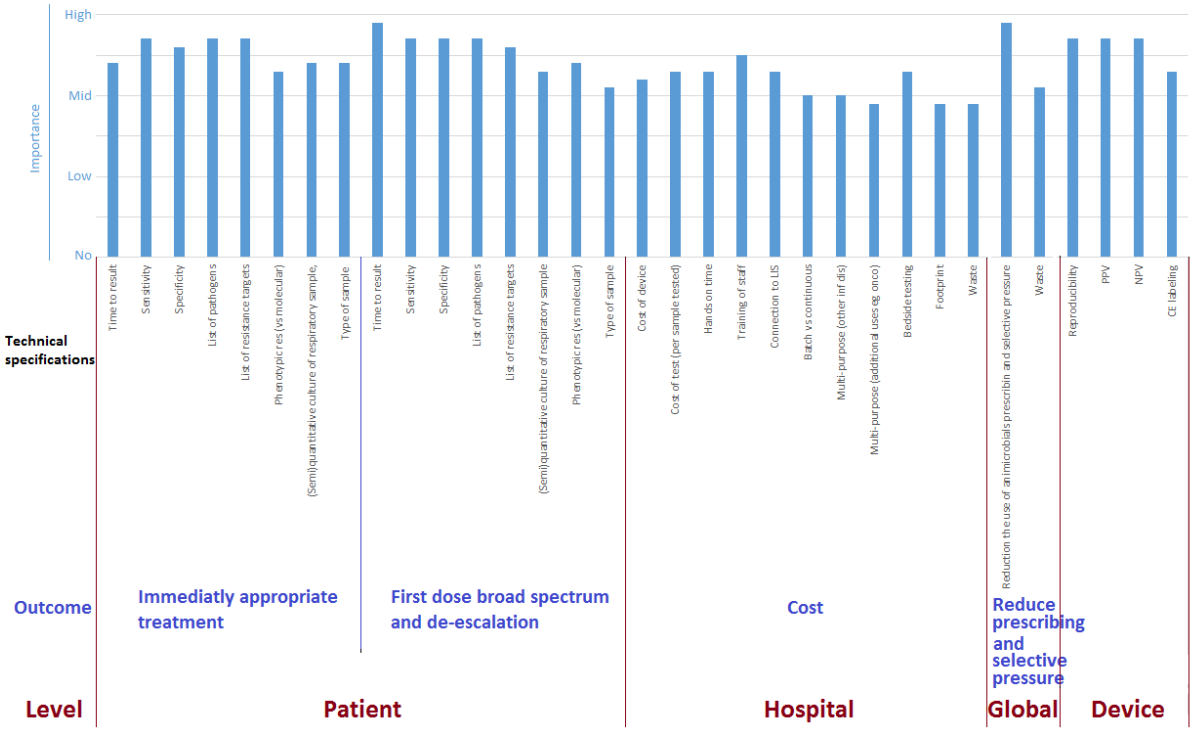


Figure 6: Importance of technical specification in the stewardship pathway

For analyzing the product specifications, we have chosen to identify the minimum and ideal product specifications.

Patient level

At the patient level, the outcomes were divided into (1) immediately appropriate treatment and (2) first dose of a broad spectrum antibiotic followed by de-escalation. Both results will be discussed.
For the data, the time to result (speed of the test itself) one of the important specifications, should be ideally as soon as possible (Figure 7). The VAP experts preferred to receive the results within 15 minutes (n=5). Although this is not a realistic technical specification for the moment, the majority of the responses (n=4) also suggested that the time to result can be more than 8 hours. As the opinions of the respondents were divided, we concluded that the exact duration of the assay is not the most crucial yet. Other VAP experts believed that it should be available within 3-4 hours (n=3-4). A rapid test that can rule in or out infection, diagnose a syndrome (sepsis, pneumonia), or identify a specific pathogen or resistance determinant should be targeted as this will improve patient care and reduce healthcare costs [29].

The sensitivity of the assay should be more than 50 % according to all respondents, 43% (n=3) of the responses targeted a minimum sensitivity of 80% for both outcomes. Ideally, the sensitivity should be more than 95%. In line, the ideal specificity should be more than 95%, whereas 43% of the VAP experts agreed with a minimal specificity of 70% in case of the "first dose broad spectrum" and 2 respondents targeted a 60% specificity, respectively. Therefore, it is best to target a rapid diagnostic test with high sensitivity and specificity[1].

According to all responses the ideal list of pathogens should include the ESKAPE pathogens (*Enterococcus faecium*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, and Enterobacter species) and *E. coli*. These bacteria are common causes of life-threatening infections amongst critically ill and immunocompromised patients and regularly characterized by high antibiotic resistance [30]. The reference techniques used to identify the bacteria remain the Gram stain and semi-quantitative conventional culture from direct respiratory samples, followed by bacterial identification using MALDI-TOF (matrix-assisted laser desorption/ionisation time-of-flight mass spectrometry) and susceptibility testing [1]. Different opinions were observed for the list including a minimum of pathogens. For the outcome

'immediately treatment', 4 respondents believed that targeting *P. aeruginosa* was sufficient. Also, 3 respondents believed that viruses should be included.

Rapid identification of antibiotic resistant pathogens is central to timely isolation of patients. The VAP experts also indicated that a minimum number of resistance genes should be included, although two persons did not agree and indicated that it is not required for this assay. No consensus could be reached on the selection of the resistance genes. The details can be found in the figure below.

Ideally the pathogen detection in a respiratory sample should be done by a quantitative assay. A minimal is the detection by a qualitative assay. Almost all respondents (n=5) agreed that the assay should be able to analyze BAL in the ideal setting. On the other hand, the minimal sample requirements are throat and sputum samples. Detailed results can be found in figure 7.

Figure 7: Minimal and ideal scoring per technical specification. (A) for the prompt administration of the appropriate treatment (B) for the first dose of the broad spectrum antibiotics followed by de-escalation.

Hospital level

The relative costs and outcomes of diagnostic testing must be considered when the decision to implement these rapid tests should include cost-effectiveness [1]. Ideally, the device should be free of charge or leased as part of a user contract. The maximum price of the machine was set at 100,000 euros (n=5). The cost per test should be ideally less than 20 euros (n=5). Whereas the maximum should be 200 euros.
Well trained staff are needed as they should ensure proper quality assurance, being capable of interpreting the results, and having troubleshooting abilities [29]. The maximum training of the staff should be 3 days (n=4). Some respondents also indicated that it should include self-learning (n=2). A short Turnaround time (TAT) is considered an important function for treatable infections and a favourable attribute of any automated system in a clinical setting [31]. The respondents targeted a maximum preparation time of 15 minutes. Two respondents indicated that the test should not include any sample preparation and 2 other respondents agreed that one sample preparation step was sufficient.

All respondents (n=6) believed that a connection to LIS, bedside testing, as well as multipurpose are necessary. Devices that are multipurpose, capable of detecting other infections, or applicable in other fields (e.g. Oncology) will increase the testing capacity and the efficiency, and help bridging the laboratory-clinical interface.

Figure 8: Minimal and ideal scoring per technical specification for the hospital level.

Global level

All VAP experts believed that reducing the use of antimicrobial prescribing and selective pressure or a first dose of broad spectrum antibiotic(s) followed by de-escalation should be the main outcomes of the rapid diagnostic test. Also on a global level, the VAP experts believed that waste should comply with environmental regulations.

Device level

The reproducibility should be ideally 95% or more, and having the CE labeling. Also, the positive predicted value and negative predicted value should be as high as possible, preferable more than 95%.

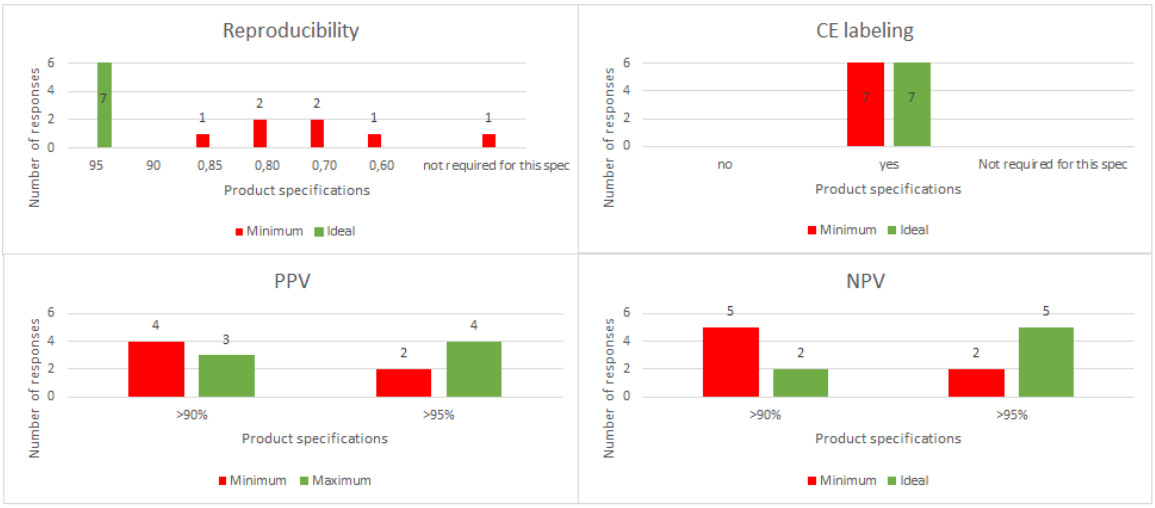


Figure 9: Minimal and ideal scoring per technical specification for the device level.

Detection of colonization pathway

When comparing the importance of the specification between the two pathways, the detection of colonization was scored with lower importance compared to the stewardship pathway.

For the detection of colonization, the focus of importance was also different. Here the focus was on the hospital technical specifications, having 5 specs in the top 10 of importance. The cost of the test, identification of pathogens, the cost of the device, LIS connection were receiving high scores (>2.4/3). Also, the reproducibility, CE labeling and actionable thresholds, all device specs, were scored as high (>2.4). Finally, the sensitivity and identification of disease were also in the top 10 of importance (>2.2).

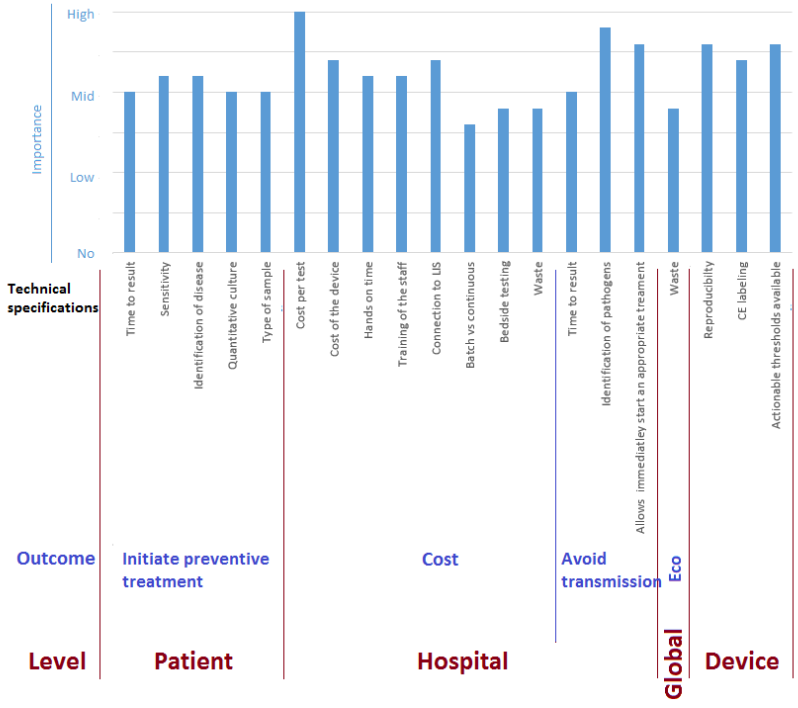


Figure 10: Importance of technical specification in the colonization pathway

For the prevention pathway the technical specification results were in line with the stewardship pathway. A few differences were observed. First, the VAP experts preferred to have rapid diagnostic tests which provide a time to result of maximum 8 hours, where in the previous pathway more than 8 hours was allowed. Here the sensitivity and specificity should be more than 85% and 90%, respectively. These are also more strict compared to the stewardship pathway. This rapid diagnostic test should also be able to differentiate the bacterial from viral load and if possible to differentiate the MRSA from MSSA and to detect *P. aeruginosa*. The

rest of the data was in line with the colonization pathway. A detailed overview can be found attached (attachment 3).

Rapid diagnostic tests for VAP

Since the introduction of rapid diagnostic tests, the number of tests available on the market has grown rapidly. Timely diagnosis will result in quickly and accurate treatment, which will improve patient mortality and morbidity [3]. Additionally, rapid diagnosis may decrease the length of stay and improve antibiotic stewardship. So far, we identified 11 commercially available molecular-based technologies for rapid identification of causative organisms of VAP, including FilmArray® system (BioFire Diagnostics), Xpert® MRSA NxG (Cepheid), GeneOhm™ MRSA (BD Diagnostics), BD MAX™ System (BD Diagnostic), Cobas® MRSA/SA test (Roche), ELITe MGB® kits and panels (ELITechGroup Solutions), Pheno™ Test BC (Accelerate Diagnostics), Unyvero™ Hospitalized Pneumonia (HPN) Cartridge (Curetis), respiFISH® Masterpanel (Miacom Diagnostics) and Panther Fusion® MRSA (Hologic). Additionally, new tests are under development, like LabDisk (SinDiag).

The FilmArray® is a small, fully-automated multiplex PCR device that includes nucleic acid extraction, an initial reverse transcription step and multiplex nested PCR, followed by a melting curve analysis [4]. The FilmArray® Respiratory Panel (FilmArray RP) and the FilmArray® Pneumonia Panel (FilmArrayPP) are both FDA-cleared and CE IVD-marked starting from respiratory samples. The FilmArray RP is able to detect 17 viral and 3 atypical respiratory organisms in a closed system that requires 5 min of hands-on time and 45 min of instrumentation time, while the FilmArray PP is able to detect 7 clinically relevant antimicrobial resistance genes in addition to 8 viral and 18 bacterial pathogens, 15 of them in a semi-quantitative way, in 60 minutes. Both panels can be run on FilmArray® 2.0 or Torch instruments, which allow to analyze up to 8 or 12 samples at the same time, respectively.

The Xpert® MRSA NxG assay is a fully-automated, FDA-cleared and CE IVD-marked nucleic acid amplification test for the detection of MRSA from both rayon nasal swabs and ESwab specimens [5]. This sample-to-answer assay requires only a few minutes hands-on time and takes about 1-2 h to produce results on a random-access platform. Depending on the instrument 1, 2, 4 or 16 samples can be run in parallel.

The GeneOhm™ MRSA assay is a multiplex PCR for the MRSA detection and is a FDA-cleared and CE IVD-marked qualitative in-vitro test for direct detection of MRSA from nasal swabs [6]. It detects the Staphylococcal chromosomal cassettes mec (SCCmec) (carrying the *mecA* gene) and a *Staphylococcus aureus (S. aureus)* specific sequence located within the orfX gene, allowing discrimination between methicillin-resistant *S. aureus* (MRSA) and methicillin-resistant coagulase-negative staphylococci. Samples require a 10 minutes lysis step before loading into the SmartCycler® instrument, which allows to process 16, 32, 48, 64, 80, or 96 samples at the same time.

The Max™ StaphSR assay (https://moleculardiagnostics.bd.com/bd-max-system/) performed on the BD Max™ system (BD Diagnostic Systems) is an FDA-cleared molecular test for detection of *S. aureus* or MRSA DNA from nasal swabs collected from patients at risk due to nasal colonization. This fully-automated PCR-based test can provide results for up to 24 samples in approximately 2.5 h.

The fully-automated cobas® MRSA/SA Test is performed on the cobas® 4800 System and uses a single nasal swab specimen to detect both MRSA and SA targets in a single sample run to deliver the results in 2.5 hours, allowing the analysis of up to 94 samples in the same run. https://diagnostics.roche.com/global/en/products/-params/cobas-mrsa-sa-test.html.

The Labdisk is a centrifugal microfluidics and nested PCR based device able to detect MRSA from nasal samples. It is fully-automated and also allows the detection of other antimicrobial resistance genes. Results are obtained within 30 minutes [7]. However, this instrument is not commercially available yet.

ELITe MGB® Kit is a triplex PCR assay designed for the detection and differentiation of *S. aureus* and MRSA DNAs within 2.5 hours [8]. The assay is performed in the ELITe InGenius® instrument, which combines extraction, amplification and result interpretation for up to 12 samples in parallel.

The Accelerate Pheno™ system combines accurate and timely identification and antimicrobial susceptibility testing (AST) into one instrument starting from blood culture [9]. The system can detect gram positive and negative bacteria (including *S. aureus*) within 90 minutes and AST results in approximately 7 hours, but only one sample can be analyzed per run. The Accelerate Pheno™ system uses an automated sample preparation and bacterial immobilization method to enable microscopy-based, single-cell analysis for ID and AST.

The Unyvero™ HPN cartridge allows to analyze a total of 48 genetic markers from a respiratory sample within 4-5 hours, including main bacterial pathogens and antimicrobial resistance genes. This system enables targeted syndromic treatment in the first few critical hours of infection [10]. Samples need to undergo lysis Unyvero™ T4 Lysator prior to be transferred to the cartridge and the instrument, whose capacity is 2 cartridges.

The respiFISH® HAP Master Panel combines the classical FISH technology with fluorescently labeled DNA molecular beacons as probes, known as the beacon-based FISH (bbFISH) technology [11]. The panel is able to detect 12 Gram-negative and Gram-positive pathogens within 30 min (including processing of the sample) and has been approved for CE IVD.

The Panther Fusion® MRSA assay accurately detects and differentiates *S. aureus* and MRSA DNA from nasal samples (https://pantherfusion.com/). The Panther Fusion® runs PCR based on transcription-mediated amplification (TMA) which includes ready to use, unit-dose lyophilized reagents. Results are displayed within 2.5 hours for up to 120 samples.

Overall, all tests reported here are providing qualitative results, except the FilmArray® and Pheno™ Test BC that are also able to provide quantitative results. Importantly, all assays have less than 10 minutes hands on time, and should be performed by trained staff. This means that all tests should preferentially be used in a lab environment and not at the point-of-care (e.g. at the ICU), except the LabDisk, which is not currently commercially available.

4. Conclusion

The clinical diagnosis of VAP is currently based on clinical signs and symptoms, including a new infiltrate on the chest X-ray. A rapid diagnostic test may potentially improve the clinical pathways associated with VAP. Therefore, we first identified the current guidelines, including the USA and European guidelines. Next, we were able to identify the demand side from a clinical perspective which can be matched with the currently available innovative diagnostics. As it was impossible to use one clinical decision tree for both prevention and treatment of VAP, two algorithms were identified. Based on these pathways the outcomes for the diagnostic test were set up. The user specifications were defined and matched with technical specifications of potential innovative diagnostic solutions, and the minimum and optimal criteria are being scored by VAP experts. The goal of this questionnaire was to define (i) the importance of the technical specifications, and (ii) the ideal and minimum acceptable product specifications for rapid diagnostic tests that might fit these two algorithms. Detailed information about the questionnaire can be found in the result section. So far, we identified 11 commercially available molecular-based technologies for rapid identification of causative organisms of VAP, including FilmArray® system (BioFire Diagnostics), Xpert® MRSA NxG (Cepheid), GeneOhm™ MRSA (BD Diagnostics), BD MAX™ System (BD Diagnostic), Cobas® MRSA/SA test (Roche), ELITe MGB® kits and panels (ELITechGroup Solutions), Pheno™ Test BC (Accelerate Diagnostics), Unyvero™ Hospitalized Pneumonia (HPN) Cartridge (Curetis), respiFISH® Masterpanel (Miacom Diagnostics) and Panther Fusion® MRSA (Hologic). Additionally, new tests are under development, like LabDisk (SinDiag).

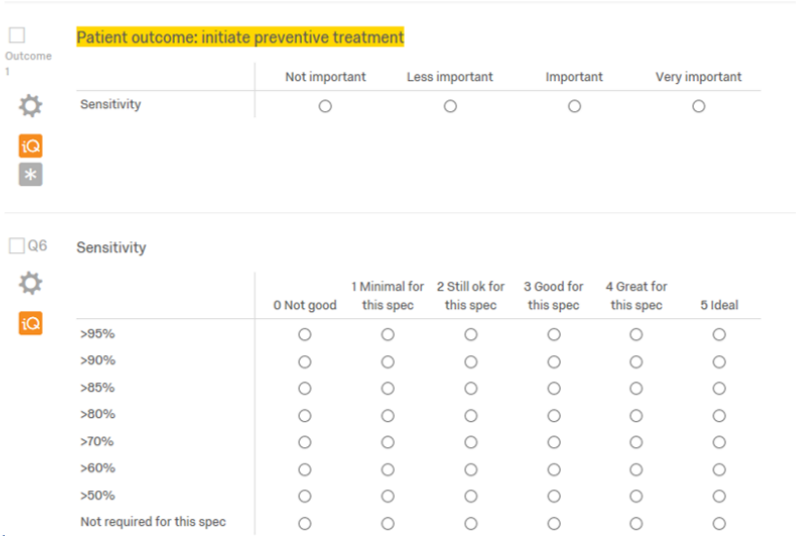
5. Annex

Attachments

Attachment 1: Overview of the outcome and specifications questionned by the UA questionnaire

1. **Stewardship**
   - Patient
     - Allows to immediately start appropriate treatment — Time to result, sensitivity, specificity, list of pathogens, list of resistance targets, phenotypical vs molecular, quantitative vs qualitative, type of sample
     - First dose broad spectrum antibiotic(s) and de-escalation — Time to result, sensitivity, specificity, list of pathogens, list of resistance targets, phenotypical vs molecular, quantitative vs qualitative, type of sample
   - Hospital
     - Cost — Waste, footprint, multi-purpose (other inf. Diseases, others), bedside testing, batch vs continuous, connection to LIS, training of staff, hands on time, cost of device, cost per test
   - Global
     - Reduction of the antimicrobial prescribing and selective pressure — Reduction of the use of anitmicrobials and selective pressure, first dose broad AB and de-escalation
     - Ecological — Waste
   - Device — Reproducibility, CE labeling, Actionable thresholds available
2. **Detection of colonisation**
   - Patient
     - Allows to initiate preventive treatment — Type of sample, Qualitative vs quantitative, pathogen identification, disease identification, specificity, sensitivity, time to result
   - Hospital
     - Cost — Waste, Bedside testing, batch vs continuous, connection to LIS, training of staff, hands on time, cost of device, cost per test
     - Avoidance of transmission — Time to result, identification of pathogens
   - Global
     - Reduction the use of animicrobials prescribing and selective pressure — Allows to immediately start an appropriate treatment
     - Ecological — Waste
   - Device — Reproducibility, CE labeling, Actionable thresholds available

Attachment 2: Examples of questions in Qualtrics



Attachment 3: Detailed results of the product specifications for the stewardship pathway and colonization pathway

Overview survey:

OVERVIEW SURVEY		
Contact person	**Stewardship survey**	**Detection of colonisation survey**
Prof. Ignacio Martin-Loeches	X	x
Prof. Jean-Francois Timsit	X	
Prof. Murali Shyamsundar	X	x
Prof. Miquel Ferrer Monreal	X	x
Prof. Charles-Edouard Luyt and Jean Chastre	X	X
Prof. Antionio Torres	X	x
Prof. Tobias Welte	X	X
France	X	x
bioMérieux	X	
Parc Tauli	X	

Stewardship ERS:

Scoring Card STEWARDSHIP											
Level	**Outcomes**	**Specs**	**Score (0 3)**	**Scoring within the specs (0-5)**							**Comments**
		time to result		<15 min	<30min	<1 uur	<2u	<4u	<8u	>8u	Not required for this spec	Alles ok
		Dublin (Martin Loeches)	2	2	2	4	4	4	5	2	0	
		Paris (Timsit)	2	5	4	4	2	1	0	0	0	
		Belfast (Shyamsundar)	3	5	4	4	2	1	0	0	0	
		Barcelona (miquel)	3	5	5	5	5	4	3	1	0	
		Paris (Chastre)	3	5	5	5	4	4	2	1	0	
		barcelona (Torres)	3	4	4	5	4	4	3	2	0	
		Welte	1	5	4	3	2	1	0	0	0	
		AVERAGE	2,4	4,4	4,0	4,3	3,3	2,7	1,9	0,9	0,0	
		Minimum		0,0	0,0	0,0	0,0	2,0	0,0	4,0		
		Ideal		5,0					1,0			
		sensitivity		>95%	>90%	>85%	>80%	>70%	>60%	>50%	Not required for this spec	
		Dublin	3	5	4	4	3	3	2	2	0	
		Paris (Timsit)	3	4	4	3	2	1	0	0	0	
		Belfast	3	5	5	4	2	0	0	0	0	
		Barcelona (miquel)	3	5	5	3	2	1	1	0	0	
		Paris (Chastre)	3	5	4	3	1	0	0	0	0	
		barcelona (Torres)	3	5	4	4	4	2	1	0	0	
		Welte	1	5	3	2	1	0	0	0	0	
		AVERAGE	2,7	4,9	4,1	3,3	2,1	1,0	0,6	0,3	0,0	
							3,0	1,0	2,0	1,0		
				6,0	1,0							
		specificity		>95%	>90%	>85%	>80%	>70%	>60%	>50%	Not required for this spec	
		Dublin	3	5	4	4	3	2	2	2	0	
		Paris (Timsit)	2	4	2	2	2	1	0	0	0	
		Belfast	2	5	5	3	3	0	0	0	0	
		Barcelona (miquel)	3	5	5	4	4	2	0	0	0	
		Paris (Chastre)	2	5	4	4	3	2	1	0	0	
		barcelona (Torres)	3	4	4	4	3	2	1	0	0	
		Welte	3	5	3	1	0	0	0	0	0	
		AVERAGE	2,6	4,7	3,9	3,1	2,6	1,3	0,6	0,3	0,0	
						1,0	1,0	2,0	2,0	1,0		
				5,0	2,0							
		list of pathogens		ESKAPE pathogens + E. coli	Only Pseudomonas	only S. aureus	Fungi	Virusses	Not required for this spec		(*ESKAPE: Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa, and Enterobacter species)	Could you please specify the ideal panel?
		Dublin	3	5	3	2	0	0	0		AmpC/ESBL/CPE	
		Paris (Timsit)	3	1	1	0	0	1	0		Gram neg EB and A PCR PAN enterobacteria pyo steno spaph aureus strp pneumo hemophilus influenza and other resp viruses	
		Belfast	2	5	1	1	0	0	0		ESKAPE+E.COLI. Crittically ill patientss increasingly have previous healtcare exposure and so any diagnostic assay should have the ability to detect both community acquired as well as healthcare associated microorganisms	

Scoring Card STEWARDSHIP												
Level	Outcomes	Specs	Score (0-3)	Scoring within the specs (0-5)								Comments
	allows to immediatelty start appropriate treatment	Barcelona (miquel)	3	5	1	0	3	3	0		ESKAPE, other enterobacteriaceae, s. pneumonia, H. influenza, virusses	
		Paris (Chastre)	3	5	3	1	1	1	0		E.coli, S. pneumonia, Heamophilus pulus ESKAPE (Except E. faecium)	
		barcelona (Torres)	3	5	3	3	4	4	0			
		Welte	2	4	1	0	3	3	0		Enterobacteriacae + non fermenters + s. aureus+ aspergillus + influenza/RSV/CMV	
		AVERAGE	2,7	4,3	1,9	1,0	1,6	1,7	0,0	#DIV/0!	#DIV/0!	
				1,0	4,0	2,0	2,0	3,0				
				5,0								
		list of resistance targets		not required to start immediate treatment	MRSA	Carbapenem-Resistant Enterobacteriacea e	Carbapenem-Resistant *Acinetobacter* baumanii	Carbapenem-Resistant P. aerugino sa				
		Dublin	3	0	3	3	2	3				
		Paris (Timsit)	3	0	3	3	3	2				
		Belfast	2	3	3	3	0	3				
		Barcelona (miquel)	3	5	5	5	5	5				
		Paris (Chastre)	3	0	3	3	3	3				
		barcelona (Torres)	3	0	3	3	3	3				
		Welte	2	0	5	5	5	5				
		AVERAGE	2,7	1,1	3,6	3,6	3,0	3,4	#DIV/0!	#DIV/0!	#DIV/0!	
							1,0	1,0				
				1,0	2,0	2,0	2,0	2,0				
		phenotypic res (vs molecular)		Phenotypic	molecular	Not required for this spec						
		Dublin	3	5	5	0						
		Paris (Timsit)	2	5	4	0						
		Belfast	2	4	4	0						
		Barcelona (miquel)	1	2	2	2						
		Paris (Chastre)	3	5	4	0						
		barcelona (Torres)	3	5	4	0						
		Welte	2	2	5	0						
		AVERAGE	2,3	4,0	4,0	0,3	#DIV/0!	#DIV/0!	#DIV/0!	#DIV/0!	#DIV/0!	
				2,0	3,0	1,0						
				4,0	1,0							
		(semi)quantitative Culture of respiratory sample,		Qualitative	Semi-quantitative	Quantitative	Not required for this spec					
		Dublin	3	3	3	5	0					
		Paris (Timsit)	3	0	1	3	0					
		Belfast	2	5	5	4	0					
		Barcelona (miquel)	2	0	2	5	0					
		Paris (Chastre)	3	1	2	5	0					
		barcelona (Torres)	3	2	UNK	4	0					
		barcelona (Torres)	3	2	UNK	4	0					
		Welte	1	3	4	5	0					
		AVERAGE	2,4	2,0	2,8	4,4	0,0	#DIV/0!	#DIV/0!	#DIV/0!	#DIV/0!	
				3,0	3,0	1,0						
				1,0	1,0	5,0						
		type of sample		BAL	ETA	Sputum	Throat swab	Not required for this spec				
		Dublin	3	5	4	3	0	0				
		Paris (Timsit)	2	4	3	2	2	0				
		Belfast	3	2	4	4	4	0			In the event of a polymicrobial culture result, the ability to discrriminat coloniser vs causative microbe for infection is	
		Barcelona (miquel)	2	5	4	2	1	0			blood culture	
patient		Paris (Chastre)	3	5	3	UNK	0	0				
		barcelona (Torres)	3	5	4	3	1	0			MIC can be very important in some cases	
		Welte	1	3	2	2	1	0			blood culture	
		AVERAGE	2,4	4,1	3,4	2,7	1,3	0,0	#DIV/0!	#DIV/0!	#DIV/0!	
				1,0		2,0	4,0					
				6,0								
		time to result		<15 min	<30min	<1 uur	<2u	<4u	<8u	>8u	Not required for this spec	
		Dublin	3	3	3	4	4	4	5	3	0	
		Paris (Timsit)	3	4	4	4	4	4	4	4	0	
		Belfast	2	5	5	5	5	3	1	1	0	
		Barcelona (miquel)	3	5	5	5	5	4	1	0	0	
		Paris (Chastre)	3	5	5	5	4	3	2	0	0	
		barcelona (Torres)	3	4	4	4	4	3	UNK	2	0	
		Welte	3	5	4	3	2	1	1	0	0	
		AVERAGE	2,9	4,4	4,3	4,3	4,0	3,1	2,3	1,4	0,0	
									3,0	4,0		
				4,0		1,0						
		sensitivity		>95%	>90%	>85%	>80%	>70%	>60%	>50%	Not required for this spec	
		Dublin	3	5	4	3	3	2	2	1	0	
		Paris (Timsit)	2	4	4	2	2	1	0	0	0	
		Belfast	3	5	5	4	4	0	0	0	0	
		Barcelona (miquel)	3	5	5	5	4	2	0	0	0	
		Paris (Chastre)	3	5	5	3	2	0	0	0	0	
		barcelona (Torres)	3	4	4	4	3	2	1	0	0	
		Welte	2	5	3	UNK	1	0	0	0	0	
		AVERAGE	2,7	4,7	4,3	3,5	2,7	1,0	0,4	0,1	0,0	
				5,0			3,0	2,0	1,0	1,0		
		specificity		>95%	>90%	>85%	>80%	>70%	>60%	>50%	Not required for this spec	
		Dublin	2	5	4	4	3	3	2	2	0	
		Paris (Timsit)	3	5	4	3	2	1	0	0	0	
		Belfast	3	5	5	3	3	0	0	0	0	
		Barcelona (miquel)	3	5	5	5	3	2	0	0	0	
		Paris (Chastre)	2	5	5	4	3	2	0	0	0	
		barcelona (Torres)	3	5	4	4	4	2	1	0	0	
		Welte	3	5	3	1	0	0	0	0	0	
		AVERAGE	2,7	5,0	4,3	3,4	2,6	1,4	0,4	0,3	0,0	

Scoring Card STEWARDSHIP												
Level	Outcomes	Specs	Score (0-3)	Scoring within the specs (0-5)								Comments
				7,0		1,0	1,0	3,0	1,0	1,0		
		list of pathogens		ESKAPE pathogens + E. coli	Only Pseudomonas	only MRSA	Fungi	Virusses	Not required for this spec			Could you please specify the ideal panel?
		Dublin	2	4	4	4	3	0	0			
		Paris (Timsit)	3	0	1	0	0	0	0			
		Belfast	3	5	1	1	1	1	0			
		Barcelona (miquel)	3	5	0	0	3	3	1		ESKAPE, other enterobacteriaceae, s. pneumonia, H. influenza, virusses	
		Paris (Chastre)	3	5	2	2	0	0	0		E.coli, S. pneumonia, Heamophilus pulus ESKAPE (Except E. faecium)	
		barcelona (Torres)	3	5	3	3	4	3	0		PES Pathogens, Pseudomonas MDR/XDR, Enterobacteriaceae ESBL and carbapenem resistant, Acinetobacter XDR	
		Welte	2	3	0	0	3	2	0		Enterobacteriacae+ S aureus+ aspergillus+ some viruses	
		AVERAGE	2,7	3,9	1,6	1,4	2,0	1,3	0,1	#DIV/0!	#DIV/0!	
					2,0	2,0	2,0	3,0	1,0			
				4,0								
	first dose broad spectrum antibiotic(s) and de-escalation	list of resistance targets		not required to start immediate treatment	MRSA	Carbapenem-Resistant Enterobacteriaceae	Carbapenem-Resistant *Acinetobacter baumanii*	Carbapenem-Resistant P. aeruginosa				
		Dublin	2	4	4	4	2	0				
		Paris (Timsit)	2	0	1	2	2	2				
		Belfast	3	2	4	4	4	4				
		Barcelona (miquel)	3	0	5	5	5	5				
		Paris (Chastre)	3	0	4	4	4	4				
		barcelona (Torres)	3	0	5	5	5	5				
		Welte	2	3	3	4	4	4				
		AVERAGE	2,6	1,3	3,7	4,0	3,7	3,4	#DIV/0!	#DIV/0!	#DIV/0!	
		(semi)quantitative Culture of respiratory sample		Qualitative	Semi-quantitative	Quantitative	Not required for this spec					
		Dublin	2	1	3	5	0					
		Paris (Timsit)	2	1	3	5	0					
		Belfast	3	3	5	4	0					
		Barcelona (miquel)	2	1	4	5	0					
		Paris (Chastre)	3	0	4	5	0					
		barcelona (Torres)	2	3	4	4	0					
		Welte										
		AVERAGE	2,3	1,5	3,8	4,7	0,0	#DIV/0!	#DIV/0!	#DIV/0!	#DIV/0!	
				4,0								
					1,0	4,0						
		phenotypic res (vs molecular)		Phenotypic	molecular	Not required for this spec						
		Dublin	3	4	5	0						
		Paris (Timsit)	2	4	3	3						
		Belfast	3	4	4	0						
		Barcelona (miquel)	1	1	1	1						
		Paris (Chastre)	3	5	4	0						
		barcelona (Torres)	3	5	4	0						
		Welte	2	2	5	0						
		AVERAGE	2,4	3,6	3,7	0,6	#DIV/0!	#DIV/0!	#DIV/0!	#DIV/0!	#DIV/0!	
				4,0	5,0	2,0						
				1,0	2,0							
		type of sample		BAL	ETA	Sputum	Throat	Not required for this spec				
		Dublin	2	5	4	2	0	0				
		Paris (Timsit)	2	4	4	3	2	1				
		Belfast	3	2	4	4	4	0				
		Barcelona (miquel)	2	5	4	3	1	0	Blood culture			
		Paris (Chastre)	3	5	3	UNK	0	0				
		barcelona (Torres)	2	5	4	2	1	0				
		Welte	1	3	2	2	1	0	Blood culture			
		AVERAGE	2,1	4,1	3,6	2,7	1,3	0,1	#DIV/0!	#DIV/0!	#DIV/0!	
		others										Not required for this spec
				1,0		2,0	3,0	1,0				
				6,0								
		Cost of device		<10,0000,00 euro	<50,000 euro	<20,000 euro	<10,000 euro	Free of leased as part of a per use contract	Not required for this spec			
		Dublin	2	4	5	3	3	0	0			
		Paris (Timsit)	2	2	3	4	4	5	0			
		Belfast	3	3	4	5	5	5	0			
		Barcelona (miquel)	2	1	2	3	5	5	0			
		Paris (Chastre)	2	0	0	2	4	5	0			
		barcelona (Torres)	2	3	3	4	5	5	0			
		Welte	UNK	2	3	4	5	3	0			
		AVERAGE	2,2	2,1	2,9	3,6	4,4	4,0	0,0	#DIV/0!	#DIV/0!	
				5,0		1,0	1,0					
					1,0		1,0	5,0				
		Cost of test (per sample tested)		<200 euro	<150 euro	<100 euro	<70 euro	<40 euro	<20 euro	Not required for this spec		
		Dublin	2	4	5	4	3	2	0	0		
		Paris (Timsit)	2	4	3	3	2	1	1	0		
		Belfast	2	0	0	1	1	3	5	0		

Scoring Card STEWARDSHIP											
Level	Outcomes	Specs	Score (0-3)	Scoring within the specs (0-5)							Comments
		Barcelona (miquel)	2	0	1	3	5	5	5	0	
		Paris (Chastre)	3	0	2	3	5	5	5	0	
		barcelona (Torres)	3	2	2	2	2	4	5	0	
		Welte	UNK	1	2	3	4	5	5	0	
		AVERAGE	2,3	1,6	2,1	2,7	3,1	3,6	3,7	0,0	#DIV/0!
				2,0	2,0	1,0		1,0	1,0		
				1,0	1,0				5,0		
		hands on time		15 min. Preparation maximum	10 min. Preparation maximum	5 min. Preparation maximu	1 preparation step maximu	No sample preparation	Not required for this spec		
		Dublin	2	5	5	4	3	0	0		
		Paris (Timsit)	2	1	2	2	2	2	2		
		Belfast	3	2	3	4	5	5	0		
		Barcelona (miquel)	3	4	5	5	4	0	0		
		Paris (Chastre)	2	4	4	5	5	5	0		
		barcelona (Torres)	2	4	4	5	4	5	0		
		Welte	2	1	2	4	3	5	0		
		AVERAGE	2,3	3,0	3,6	4,1	3,7	3,1	0,3	#DIV/0!	#DIV/0!
				6,0			1,0				
				1,0		1,0	1,0	2,0			
		training of staff		max. 3 days training	max 2 days training	max 1 day training	no training, self learning	Not required for this spec			
		Dublin	2	0	0	5	4	0			
		Paris (Timsit)	2	4	4	2	2	2			
		Belfast	3	0	1	2	5	0			
		Barcelona (miquel)	3	1	2	5	4	1			
		Paris (Chastre)	2	2	2	3	5	0			
		barcelona (Torres)	3	3	3	4	3	0			
		Welte	UNK	1	3	4	3	0			
		AVERAGE	2,5	1,6	2,1	3,6	3,7	0,4	#DIV/0!	#DIV/0!	#DIV/0!
				4,0	1,0		2,0				
					1,0	3,0	2,0				
		Connection to LIS		no	yes	Not required for this spec					
		Dublin	2	0	5	0					
		Paris (Timsit)	1	0	5	0					
		Belfast	3	0	5	0					
		Barcelona (miquel)	2	0	0	5					
		Paris (Chastre)	3	0	5	0					
		barcelona (Torres)	3	0	5	0					
		Welte	2	0	5	0					
		AVERAGE	2,3	0,0	4,3	0,7	#DIV/0!	#DIV/0!	#DIV/0!	#DIV/0!	#DIV/0!
					6,0	1,0					
					6,0						
		batch vs continuous		batch	continous	Not required for this spec					
		Dublin	2	3	5	3					
		[illegible]	[illegible]	[illegible]	[illegible]	[illegible]					
hospital	Cost	Paris (Timsit)	2	3	3	3					
		Belfast	3	0	5	0					
		Barcelona (miquel)	2	4	1	0					
		Paris (Chastre)	1	4	5	0					
		barcelona (Torres)	3	5	4	0					
		Welte	1	2	3	0					
		AVERAGE	2,0	3,0	3,7	0,9	#DIV/0!	#DIV/0!	#DIV/0!	#DIV/0!	#DIV/0!
				2,0	2,0	2,0					
				1,0	2,0						
		Multi-purpose (other inf dis)		no	yes	Not required for this spec					
		Dublin	3	0	5	0					
		Paris (Timsit)	2	0	5	0					
		Belfast	0	0	0	5					
		Barcelona (miquel)	2	0	5	0					
		Paris (Chastre)	2	0	5	0					
		barcelona (Torres)	3	0	5	0					
		Welte	2	0	5	0					
		AVERAGE	2,0	0,0	4,3	0,7	#DIV/0!	#DIV/0!	#DIV/0!	#DIV/0!	#DIV/0!
					6,0	1,0					
					6,0	1,0					
		Multi-purpose (additional uses eg onco)		no	yes	Not required for this spec					
		Dublin	2	0	5	0					
		Paris (Timsit)	2	0	5	0					
		Belfast	0	0	0	5					
		Barcelona (miquel)	2	0	5	0					
		Paris (Chastre)	2	0	5	0					
		barcelona (Torres)	3	0	5	0					
		Welte	2	0	5	0					
		AVERAGE	1,9	0,0	4,3	0,7	#DIV/0!	#DIV/0!	#DIV/0!	#DIV/0!	#DIV/0!
					6,0	1,0					
					6,0	1,0					
		Bedside testing		no	yes	Not required for this spec					
		Dublin	2	0	5	0					
		Paris (Timsit)	2	0	5	0					
		Belfast	2	0	5	0					
		Barcelona (miquel)	2	0	5	0					
		Paris (Chastre)	2	0	5	0					
		barcelona (Torres)	3	0	5	0					
		Welte	3	0	5	0					
		AVERAGE	2,3	0,0	5,0	0,0	#DIV/0!	#DIV/0!	#DIV/0!	#DIV/0!	#DIV/0!
					7,0						
					7,0						
		footprint		1m²	0,5m²	handhel					
		Dublin	2	4	5	0					
		Paris (Timsit)	2	3	3	2					
		Belfast	2	3	5	0					

Scoring Card STEWARDSHIP											
Level	Outcomes	Specs	Score (0-3)	Scoring within the specs (0-5)							Comments
		Barcelona (miquel)	2	1	4	0					
		Paris (Chastre)	1	4	5	0					
		barcelona (Torres)	2	4	5	0					
		Welte	2	4	2	0					
		AVERAGE	1,9	3,3	4,1	0,3	#DIV/0!	#DIV/0!	#DIV/0!	#DIV/0!	#DIV/0!
				5,0	1,0	1,0					
				1,0	5,0						
		waste		no plastic	comply with enviromental regulations	Not required for this spec					
		Dublin	1	2	2	2					
		Paris (Timsit)	2	1	1	1					
		Belfast	3	4	4	0					
		Barcelona (miquel)	2	4	5	0					
		Paris (Chastre)	2	5	5	0					
		barcelona (Torres)	2	4	5	0	Consider the cost of many samples at each time				
		Welte	1	2	3	0					
		AVERAGE	1,9	3,1	3,6	0,4	#DIV/0!	#DIV/0!	#DIV/0!	#DIV/0!	#DIV/0!
		others									
				3,0	1,0	2,0					
					6,0						
		reduction the use of animicrobials prescribin and selective pressure		no	yes	Not required for this spec					
		Dublin	3	0	5	0					
		Paris (Timsit)	3	0	5	0					
		Belfast	3	0	5	0					
	reduction the use of antimicrobials prescribing and selective pressure	Barcelona (miquel)	3	0	5	0					
		Paris (Chastre)	3	0	5	0					
		barcelona (Torres)	3	0	5	0					
		Welte	2	0	5	0					
		AVERAGE	2,9	0,0	5,0	0,0	#DIV/0!	#DIV/0!	#DIV/0!	#DIV/0!	#DIV/0!
					7,0						
					7,0						
		first dose broad spectrum antibiotic(s) and de-escalation		no	yes	Not required for this spec					
		Dublin	2	0	5	0					
		Paris (Timsit)	2	0	5	0					
		Belfast	3	0	5	0					
		Barcelona (miquel)	3	0	5	0					
		Paris (Chastre)	3	0	5	0					
		barcelona (Torres)	3	0	5	0					
		Welte	2	0	5	0					
global		AVERAGE	2,6	0,0	5,0	0,0	#DIV/0!	#DIV/0!	#DIV/0!	#DIV/0!	#DIV/0!
					7,0						
					7,0						
	ecological	waste		no plastic	comply with enviromental regulations	Not required for this spec					
		Dublin	1	2	2	2					
		Paris (Timsit)	2	1	1	1					
		Belfast	3	4	4	0	Applicability to low and middle income countries where cost will be an important factor for uptake				
		Barcelona (miquel)	3	4	5	0					
		Paris (Chastre)	3	4	4	0					
		barcelona (Torres)	2	4	5	0					
		Welte	1	2	3	0					
		AVERAGE	2,1	3,0	3,4	0,4	#DIV/0!	#DIV/0!	#DIV/0!	#DIV/0!	#DIV/0!
		others									
				3,0	2,0	2,0					
				2,0	4,0						
		reproducibility		95	90	85%	80%	70%	60%	50%	not required for this spec
		Dublin	3	5	4	4	3	2	0	0	0
		Paris (Timsit)	2	4	3	3	2	2	2	1	1
		Belfast	3	5	5	4	4	0	0	0	0
		Barcelona (miquel)	3	5	5	4	2	1	0	0	0
		Paris (Chastre)	3	5	4	3	2	0	0	0	0
		barcelona (Torres)	3	5	5	4	4	2	1	0	0
		Welte	2	5	3	1	0	0	0	0	0
		AVERAGE	2,7	4,9	4,1	3,3	2,4	1,0	0,4	0,1	0,1
						1,0	2,0	2,0	1,0		1,0
				7,0							
		ppv (Positive predictive value)		>90%	>95%						
		Dublin	3	5	3						
		Paris (Timsit)	2	3	3						
		Belfast	3	4	5						
		Barcelona (miquel)	3	4	5						
		Paris (Chastre)	3	5	5						
		barcelona (Torres)	3	4	5						
		Welte	2	2	4						
		AVERAGE	2,7	3,9	4,3	#DIV/0!	#DIV/0!	#DIV/0!	#DIV/0!	#DIV/0!	#DIV/0!
				4,0	2,0						
				3,0	4,0						
device		npv (Negative predictive value)		>90%	>95%						
		Dublin	3	5	3						
		Paris (Timsit)	1	4	2						
		Belfast	3	4	5						
		Barcelona (miquel)	3	4	5						
		Paris (Chastre)	3	4	5						

Scoring Card STEWARDSHIP												
Level	Outcomes	Specs	Score (0-3)	Scoring within the specs (0-5)								Comments
		barcelona (Torres)	3	4	5							
		Welte	3	1	4							
		AVERAGE	2,7	3,7	4,1	#DIV/0!	#DIV/0!	#DIV/0!	#DIV/0!	#DIV/0!	#DIV/0!	
				5,0	2,0							
				2,0	5,0							
		CE labeling		no	yes	Not required for this spec						
		Dublin	3	0	5	0						
		Paris (Timsit)	2	0	5	0						
		Belfast	3	0	5	0						
		Barcelona (miquel)	ND	0	5	0						
		Paris (Chastre)	3	0	5	0						
		barcelona (Torres)	2	0	5	0						
		Welte	1	0	5	0						
		AVERAGE	2,3	0,0	5,0	0,0	#DIV/0!	#DIV/0!	#DIV/0!	#DIV/0!	#DIV/0!	
					7,0							
					7,0							

Prevention:

Detection of colonisation Scoring Card												
Level	Outcomes	Specs	Score (1-4)	Scoring within the specs (0-5)								Comments
		time to result		<15 mi	<30mi	<1 uu	<2u	<4u	<8u	>8u	Not requ for this s	
		Dublin	2	3	3	3	3	3	5	0	0	
		Paris (Timsit)										
		Belfast	1	4	4	4	4	4	4	2	0	
		Barcelona (miquel)										
		Paris (Chastre)	3	5	5	5	5	4	3	1	0	
		barcelona (Torres)	2	2	2	2	2	2	5	2	0	
		Welte (Hannover)	2	5	4	3	2	1	1	0	0	
		time to result	2	3,8	3,6	3,4	3,2	2,8	3,6	1	0	
		sensitivity		>95%	>90%	>85%	>80%	>70%	>60%	>50%	Not required for this spec	
		Dublin	2	5	4	3	2	2	0	0	0	
		Paris (Timsit)										
		Belfast	1	5	5	4	4	2	0	0	0	
		Barcelona (miquel)										
		Paris (Chastre)	3	5	5	4	3	2	1	1	0	
		barcelona (Torres)	3	5	4	4	3	2	1	0	0	
		Welte (Hannover)	2	5	3	2	1	0	0	0	0	
		sensitivity	2,2	5	4,2	3,4	2,6	1,6	0,4	0,2	0	
		specificity		>95%	>90%	>85%	>80%	>70%	>60%	>50%	Not required for this spec	
		Dublin	3	5	4	3	3	3	0	0	1	
		Paris (Timsit)										
		Belfast	2	5	4	4	3	0	0	0	0	
		Barcelona (miquel)										
		Paris (Chastre)	2	5	5	5	4	3	2	1	0	
		barcelona (Torres)	3	5	4	3	2	1	0	0	0	
		Welte (Hannover)	3	5	3	1	0	0	0	0	0	
		specificity	2,6	5	4	3,2	2,4	1,4	0,4	0,2	0,2	
		Identification of disease		differentiates	identifies bact	idenifies viral	Not required for this spec					
		Dublin	2	4	5	4	0					
		Paris (Timsit)										
		Belfast	2	5	4	4	0					
		Barcelona (miquel)										
		Paris (Chastre)	2	5	5	5	0					
patient	allows to initiate preventive treatment	barcelona (Torres)	3	5	4	4	0					
		Welte (Hannover)	2	4	5	3	0					
		Identification of disease	2,2	4,6	4,6	4	0	#DIV/0!	#DIV/0!	#DIV/0!	#DIV/0!	
		Identification of pathogen		S. Aureus	MRSA/ MSSA	P. Aeruginosa	Not required for this spec					
		Dublin	3	4	5	5	0					
		Paris (Timsit)										
		Belfast	3	4	5	4	0					
		Barcelona (miquel)										
		Paris (Chastre)	3	5	5	5	0					
		barcelona (Torres)	3	3	5	5	0					
		Welte (Hannover)	2	3	4	4	0					
		Identification of pathogen	2,8	3,8	4,8	4,6	0	#DIV/0!	#DIV/0!	#DIV/0!	#DIV/0!	
		quantitative Culture of respiratory sample		Qualitative	Semi-quantitative	Quantitative	Not required for this spec					
		Dublin	2	2	2	5	0					
		Paris (Timsit)										

Level	Outcomes	Specs	Score (1-4)	Scoring within the specs (0-5)								Comments
		Belfast	2	4	4	4	0					
		Barcelona (miquel)										
		Paris (Chastre)	3	1	3	5	0					
		barcelona (Torres)	1	2	4	4	0					
		Welte (Hannover)	2	4	3	3	0					
		quantitative Culture of respiratory sample	2	2,6	3,2	4,2	0	#DIV/0!	#DIV/0!	#DIV/0!	#DIV/0!	
		type of sample		BAL	ETA	Sputum	Throat	Not required for this spec				
		Dublin	2	5	4	2	0	0		Time to most AB is 8h so faster than 8h is not needed		
		Paris (Timsit)										
		Belfast	2	2	4	4	4	0				
		Barcelona (miquel)										
		Paris (Chastre)	3	5	3	1	0	0				
		barcelona (Torres)	2	3	4	4	4	0				
		Welte (Hannover)	1	4	3	3	1	0				
		type of sample	2	3,8	3,6	2,8	1,8	0	#DIV/0!	#DIV/0!	#DIV/0!	
		others										
		Cost of test (per sample tested)		<200 euro	<150 euro	<100 euro	<70 euro	<40 euro	<20 euro	Not required for this spec		
		Dublin	3	4	4	5	4	0	0	0		
		Paris (Timsit)										
		Belfast	3	0	0	0	2	3	5	0		
		Barcelona (miquel)										
		Paris (Chastre)	3	1	2	3	4	5	5	0		
		barcelona (Torres)	3	0	0	0	0	2	3	0		
		Welte (Hannover)	UNK	1	2	3	4	5	5	0		
		Cost of test (per sample tested)	3	1,2	1,6	2,2	2,8	3	3,6	0	#DIV/0!	
		Cost of device		<100000,00 euro	<50000 euro	<20000 euro	<10000euro	Free or leased as part of a per use contract	Not required for this spec			
		Dublin	1	4	5	5	0	0	0			
		Paris (Timsit)										
		Belfast	3	2	3	4	4	4	0			
		Barcelona (miquel)										
		Paris (Chastre)	3	4	5	5	5	2	0			
		barcelona (Torres)	3	1	2	3	4	5	0			
		Welte (Hannover)	2	2	3	4	5	4	0			
		Cost of device	2,4	2,6	3,6	4,2	3,6	3	0	#DIV/0!	#DIV/0!	
		hands on time		15 min. Preparation maximum	10 min. Preparation maximum	5 min. Preparation maximum	1 preparation step maximum	No sample preparation	Not required for this spec			
		Dublin	2	3	5	3	3	0	0			
		Paris (Timsit)										
		Belfast	3	3	3	5	5	5	0			
		Barcelona (miquel)										
		Paris (Chastre)	2	3	3	5	5	5	0			
		barcelona (Torres)	2	3	5	5	3	5	0			
		Welte (Hannover)	2	0	3	3	5	3	0			
hospital	Cost	hands on time	2,2	2,4	3,8	4,2	4,2	3,6	0	#DIV/0!	#DIV/0!	
		training of staff		max. 3 days training	max 2 days training	max 1 day training	no training, self learning	Not required for this spec				
		Dublin	3	0	0	5	3	0				
		Paris (Timsit)										
		Belfast	2	0	0	3	5	0				
		Barcelona (miquel)										
		Paris (Chastre)	3	3	3	5	5	0				
		barcelona (Torres)	2	0	3	5	UNK	0				
		Welte (Hannover)	1	0	3	5	3	0				
		training of staff	2,2	0,6	1,8	4,6	4	0	#DIV/0!	#DIV/0!	#DIV/0!	
		Connection to LIS		no	yes	Not required for this spec						
		Dublin	2	0	5	0						
		Paris (Timsit)										
		Belfast	3	0	5	0						
		Barcelona (miquel)										
		Paris (Chastre)	3	0	5	0						
		barcelona (Torres)	2	0	5	0						
		Welte (Hannover)	2	0	5	0						
		Connection to LIS	2,4	0	5	0	#DIV/0!	#DIV/0!	#DIV/0!	#DIV/0!	#DIV/0!	
		batch vs continuous		batch	continuous	not required						
		Dublin	2	3	5	0						
		Paris (Timsit)										
		Belfast	1	5	3	0						
		Barcelona (miquel)										
		Paris (Chastre)	2	3	5	0						
		barcelona (Torres)	2	3	5	0						
		Welte (Hannover)	1	3	3	0						
		batch vs continuous	1,6	3,4	4,2	0	#DIV/0!	#DIV/0!	#DIV/0!	#DIV/0!	#DIV/0!	
		Bedside testing		no	yes	Not required for this spec						
		Dublin	2	0	5	0						
		Paris (Timsit)										
		Belfast	1	5	0	0						
		Barcelona (miquel)										
		Paris (Chastre)	2	0	5	0						
		barcelona (Torres)	2	0	5	0						
		Welte (Hannover)	2	0	5	0						
		Bedside testing	1,8	1	4	0	#DIV/0!	#DIV/0!	#DIV/0!	#DIV/0!	#DIV/0!	
		waste		no plastic	comply with enviromental regulations	Not required for this spec						
		Dublin	1	2	2	2						
		Paris (Timsit)										
		Belfast	3	5	4	0						
		Barcelona (miquel)										
		Paris (Chastre)	1	5	5	0						
		barcelona (Torres)	3	4	5	0						
		Welte (Hannover)	1	3	3	0						
		waste	1,8	3,8	3,8	0,4	#DIV/0!	#DIV/0!	#DIV/0!	#DIV/0!	#DIV/0!	

Level	Outcomes	Specs	Score (1-4)	Scoring within the specs (0-5)								Comments
		time to result		<15 min	<30min	<1 uur	<2u	<4u	<8u	>8u	Not required for this spec	
		Dublin	2	4	5	4	4	3	3	3	0	
		Paris (Timsit)										
		Belfast	1	4	4	4	4	4	4	2	0	
		Barcelona (miquel)										
		Paris (Chastre)	3	5	4	4	4	4	3	1	0	
		barcelona (Torres)	2	4	4	4	5	4	3	2	0	
		Welte (Hannover)	2	5	4	4	3	2	1	0		
	avoidance of transmission	time to result	2	4,4	4,2	4	4	3,4	2,8	1,6	0	
		Identification of pathogen(s)		ESKAPE pathogens + E. coli	Only Pseudomonas	only MRSA	Fungi	Virusses	Not required for this spec			
		Dublin	3	4	4	4	1	0	0			
		Paris (Timsit)										
		Belfast	3	5	2	2	2	2	0			
		Barcelona (miquel)										
		Paris (Chastre)	3	5	2	2	2	2	0			
		barcelona (Torres)	3	5	4	0	4	4	0			
		Welte (Hannover)	2	4	3	3	1	2	0			
		Identification of pathogen(s)	2,8	4,6	3	2,2	2	2	0	#DIV/0!	#DIV/0!	
		others										
		Allows to immediately start an appropriate treatment		no	yes	Not required for this spec						
	reduction the use of antimicrobials prescribing and selective pressure,	Dublin	2	0	5	0						
		Paris (Timsit)										
		Belfast	3	0	5	0						
		Barcelona (miquel)										
		Paris (Chastre)	3	0	5	0						
		barcelona (Torres)	3	0	5	0						
		Welte (Hannover)	2	0	5	0						
global		Allows to immediately start an appropriate treati	2,6	0	5	0	#DIV/0!	#DIV/0!	#DIV/0!	#DIV/0!	#DIV/0!	
		waste		no plastic	comply with enviromental regulations	Not required for this spec						
		Dublin	0	1	1	1						
		Paris (Timsit)										
		Belfast	3	5	4	0						
		Barcelona (miquel)										
		Paris (Chastre)	3	4	5	0						
		barcelona (Torres)	2	4	5	0						
		Welte (Hannover)	1	3	3	0						
	ecological	waste	1,8	3,4	3,6	0,2	#DIV/0!	#DIV/0!	#DIV/0!	#DIV/0!	#DIV/0!	
		reproducibility		>90%	100%							
		Dublin	3	3	5							
		Paris (Timsit)										
		Belfast	3	4	5							
		Barcelona (miquel)										
		Paris (Chastre)	3	3	5							
		barcelona (Torres)	2	5	5							
		Welte (Hannover)	2	3	5							
device		reproducibility	2,6	3,6	5	#DIV/0!	#DIV/0!	#DIV/0!	#DIV/0!	#DIV/0!	#DIV/0!	
		CE labeling		no	yes	Not required for this spec						
		Dublin	3	0	5	0						
		Paris (Timsit)										
		Belfast	3	0	5	0						
		Barcelona (miquel)										
		Paris (Chastre)	3	0	5	0						
		barcelona (Torres)	2	0	5	0						
		Welte (Hannover)	1	0	5	0						
		CE labeling	2,4	0	5	0	#DIV/0!	#DIV/0!	#DIV/0!	#DIV/0!	#DIV/0!	
		Actionable thresholds available		no	yes	Not required for this spec						
		Dublin	3	5	0	0						
		Paris (Timsit)										
		Belfast	3	0	5	0						
		Barcelona (miquel)										
		Paris (Chastre)	2	0	5	0						
		barcelona (Torres)	3	5	0	0						
		Welte (Hannover)	2	0	5	0						
		Actionable thresholds available	2,6	2	3	0	#DIV/0!	#DIV/0!	#DIV/0!	#DIV/0!	#DIV/0!	
		others										

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