Literature Review

# Multiplex PCR Respiratory Panel in Indonesia: A Narrative Review

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## Abstract

Acute Respiratory infections (ARIs) remain a major cause of illness and death worldwide. Conventional diagnostic methods are often slow or have limited sensitivity. Multiplex (Polymerase Chain Reaction) PCR respiratory panels allow rapid detection of multiple respiratory pathogens from a single specimen and are increasingly available in Indonesia. This review summarizes the respiratory panels available in Indonesia and discusses their potential clinical use. A narrative review was conducted using literature from PubMed, manufacturer technical documents, and the Indonesian Ministry of Health medical device registry. Information on pathogen coverage, diagnostic performance, specimen requirements, and clinical applications was reviewed. There are six respiratory panel platforms currently available in Indonesia: VITRO Respiratory Flow Chip Kit, BioFire FilmArray Respiratory Panel 2.1 Plus, BioFire FilmArray Pneumonia Panel Plus, QIAstat-Dx Respiratory SARS-CoV-2 Panel, ALLPLEX Respiratory Panel, and COBAS Respiratory Flex. Most platforms focus on respiratory viruses and atypical bacteria using nasopharyngeal/oropharyngeal specimens, whereas BioFire FilmArray Pneumonia Panel Plus is designed for lower respiratory tract infections and additionally detects common bacterial pathogens, antimicrobial resistance genes, and provides semi-quantitative results. BioFire, QIAstat-Dx, and COBAS offer highly automated sample-to-answer workflows with minimal hands-on time, whereas VITRO and ALLPLEX require more manual processing but provide greater flexibility through open systems. Despite these advantages, implementation remains challenged by high costs and limited access in Indonesia. Six multiplex PCR respiratory panel platforms are available in Indonesia, each with different diagnostic characteristics and potential clinical applications. No single platform is optimal for all situations. Therefore, test selection should be tailored to the clinical setting, laboratory capacity, and available resources. Appropriate implementation may improve respiratory pathogen diagnosis and antimicrobial stewardship, although local evidence regarding clinical impact and cost-effectiveness is still needed.

**Keywords:** acute respiratory infections, antimicrobial stewardship, molecular diagnostics, multiplex PCR, respiratory panel

## INTRODUCTION

Acute respiratory infections (ARIs) are one of the leading causes of morbidity and mortality globally, particularly in vulnerable populations such as children under five years of age and elderly individuals with comorbidities. Beyond clinical impact, ARIs also cause a substantial economic burden due to treatment costs and indirect costs from lost work productivity.[1,2]

In Indonesia, ARIs are the primary cause of under-five mortality, accounting for 22.3% of all under-five deaths. This figure represents the highest rate among Association of Southeast Asian Nations (ASEAN) countries, demonstrating the need for better management.[3] Although data on ARI-related mortality in Indonesia's elderly population remain limited, global data show that 56% of ARI deaths in the adult age group occur in individuals aged 60 years or older.[4]

The most common cause of ARIs is viral infection. Approximately 80% of ARI cases in children are caused by various viruses such as Respiratory syncytial virus (RSV), Metapneumovirus, Influenza, Parainfluenza, Rhinovirus, and SARS-CoV-2.[5] Nevertheless, bacteria also constitute an important cause of ARIs.

Epidemiological data from China indicate that 22.8% of ARI cases are caused by bacteria, with the highest number of cases in children, followed by the elderly. The most frequently detected bacterial pathogens include *Streptococcus pneumoniae* at 29.9%, followed by *Mycoplasma pneumoniae* and *Haemophilus influenzae*. Bacterial and viral coinfection also occurs in as many as 23.3% of cases.[6] The clinical presentation of ARIs often overlaps between viral and bacterial etiologies, making symptom-based diagnosis alone difficult to differentiate the causative etiology, resulting in inappropriate antibiotic use or delays in antiviral administration.[1]

The main challenge in ARI management is the limitation of conventional diagnostic methods that often cannot provide fast and accurate results. Culture methods, although considered the gold standard, require significant time. Additionally, pathogens such as viruses and atypical bacteria require specialized culture methods that are not done routinely.[7] Meanwhile, rapid examinations such as antigen detection tests have varied or low sensitivity.[8,9] As a consequence, physicians often provide broad-spectrum empirical antibiotic therapy that is unnecessary, contributing to antimicrobial resistance and increased treatment costs.[7]

As a solution to these limitations, molecular diagnostic technology has evolved toward a syndromic panel approach based on multiplex Polymerase Chain Reaction (PCR). This syndromic panel enables detection of various pathogen targets, both viruses and bacteria, from one clinical specimen in a single workflow. Unlike conventional PCR, which targets a single pathogen, respiratory panels offer an approach with shorter turnaround time.[2]

Implementation of multiplex PCR respiratory panels in clinical practice is expected to provide a significant positive impact on patient outcomes and hospital efficiency. Evidence shows that the use of these panels is associated with reduced length of hospital stay because patients can be discharged earlier after viral etiology is confirmed and serious bacterial infection can be excluded. Furthermore, rapid and specific etiologic diagnosis facilitates better antimicrobial stewardship implementation through reduced unnecessary antibiotic administration.[2,10]

Several multiplex PCR respiratory panel platforms are currently available in Indonesia, each with different pathogen coverage, analytical performance, and specimen requirements.[11] However, information regarding these platforms is often dispersed across individual studies, technical documents, and manufacturer data, making it difficult for clinicians and laboratory professionals to select the most appropriate test for specific clinical settings.

Therefore, this narrative review aims to provide an overview of multiplex PCR respiratory panels available in Indonesia, compare their diagnostic characteristics, and discuss their clinical applications, advantages, limitations, and implementation challenges.

## METHODS

This narrative review was conducted to summarize multiplex PCR respiratory panel platforms available in Indonesia and their clinical applications in the diagnosis of acute respiratory infections. Literature searches were performed using the PubMed database from January 2010 to January 2026. The search strategy used the following terms: ("multiplex PCR" OR "respiratory panel" OR "syndromic testing" OR "pneumonia panel") AND ("respiratory tract infection" OR "acute respiratory infection" OR pneumonia).

Original research articles, systematic reviews, and meta-analyses describing the principles, performance characteristics, pathogen coverage, specimen requirements, and clinical utility of multiplex PCR respiratory panels were included. Studies unrelated to respiratory pathogen detection, non-human studies, duplicate publications, and publications without accessible full-text manuscripts were excluded.

Additional information regarding the availability of respiratory panel platforms in Indonesia was manually searched from the Indonesian Ministry of Health medical device registry, while technical specifications and performance data were also manually obtained from publicly available manufacturer documentation, including instructions for use (IFU) and product technical materials when peer-reviewed evidence was limited.

## BASIC CONCEPTS OF RESPIRATORY PANELS

A respiratory panel is a diagnostic test for detecting and identifying various respiratory infection pathogens (viruses

and bacteria). This test uses the multiplex PCR method, which is a modification of conventional PCR that enables simultaneous amplification of multiple deoxyribonucleic acid (DNA)/ribonucleic acid (RNA) targets in a single reaction. Unlike singleplex PCR, which has one target per reaction, multiplex PCR uses several pairs of primers and probes designed for several different targets in one reaction.[12]

The PCR process begins with DNA/RNA extraction from clinical specimens. Because the majority of respiratory viruses have RNA genomes, reverse transcription is necessary, where the reverse transcriptase enzyme converts RNA into complementary DNA (cDNA), allowing it to be amplified by DNA polymerase. Next, the master mix is prepared, containing Taq polymerase, deoxynucleotide triphosphates (dNTPs), buffer, and primers ready for the amplification process.[13]

The amplification process is then performed in a thermocycler with repeated cycles, usually 30-40 times. The cycle begins with denaturation at 95°C, where double-stranded DNA separates into single-stranded DNA; followed by annealing at 50-60°C, where primers bind to complementary target DNA/cDNA; and extension at 72°C, where Taq polymerase synthesizes, producing amplicons.[13]

After the series of cycles is complete, the amplicons are then analyzed using various methods. Amplicons can be detected in real-time with fluorescence using the TaqMan probe system. When Taq polymerase synthesizes, the probe is cleaved and releases a reporter that emits fluorescence. Another alternative is SYBR Green, a fluorescent dye that binds to double-stranded DNA.[14]

Melting curve analysis is then performed after amplification is complete by gradually increasing the temperature. Double-stranded amplicons will denature at their specific temperature (melting temperature, Tm), which depends on the length and guanine-cytosine (GC) composition of the amplicon.[15] Another method is probe hybridization, where formed amplicons will hybridize with specific probes.[16]

Target selection is a fundamental step in molecular PCR assay development because it directly determines the specificity, sensitivity, and resistance of the assay to genetic changes. The ideal target genes must be conserved, specific to the species, strain, or variant, and have sufficient copy numbers to maintain high sensitivity.[17]

In variant detection, such as SARS-CoV-2, the target is often characteristic mutations or single nucleotide polymorphisms (SNPs) rarely found in other variants, thus capable of accurately differentiating variants. However, for routine diagnostic purposes, conserved and low-mutation genes are the targets used.[17]

Besides specificity and stability, the number of target copies plays an important role in determining test sensitivity. Targets with high copy numbers, including tandem repeat elements or repetitive sequences,

can increase detection opportunities, especially in samples with low or degraded nucleic acid levels, reflected in better limit of detection (LoD). Primer and probe design is then optimized to support these target characteristics, considering thermodynamic parameters and in silico specificity testing. In addition to identification, some panels also detect resistance genes.[18]

## RESPIRATORY PANELS IN INDONESIA

Several commercial respiratory panels are available and have distribution permits in Indonesia, namely VITRO Respiratory Flow Chip Kit, BioFire FilmArray Respiratory Panel 2.1 Plus, BioFire FilmArray® Pneumonia Panel Plus (FA-PP), QIAstat-Dx Respiratory SARS-CoV-2 Panel, ALLPLEX™ Respiratory Panel, and COBAS® Respiratory Flex.[11] All six panels use multiplex PCR as the basic examination method, with differences in amplification result detection methods, pathogen coverage, sensitivity, specificity, LoD, cost, and the types of specimens that can be used.

### VITRO Respiratory Flow Chip Kit

This kit uses multiplex PCR with reverse hybridization on a membrane through three main stages in its process. First, the amplification stage involves simultaneous amplification of multiple RNA and DNA targets using specific primers designed for each respiratory pathogen. Amplification occurs in one PCR reaction with optimal thermal cycling to produce different amplicons for each target. Second, the biotinylation stage, where amplicons resulting from PCR undergo biotinylation to prepare for subsequent detection. The biotin attached to these amplicons enables binding to streptavidin in the detection stage.[19]

The process continues with hybridization and immunoenzymatic detection stages. At this stage, biotinylated amplicons are hybridized with complementary DNA probes attached to the membrane. This membrane contains specific DNA probe spots for each pathogen. After hybridization, the membrane is incubated with Streptavidin-Alkaline Phosphatase (Strep-AP), which binds to the amplicon biotin. Then, chromogen (substrate for alkaline phosphatase) is added, producing a colorimetric reaction that generates a blue-purple color at positive hybridization sites. Color intensity is directly proportional to the amount of target amplicon formed. Result interpretation is then performed using the HybriSpot device.[19]

The VITRO Respiratory Flow Chip Kit detects a total of 13 pathogens, including viruses and bacteria causing acute respiratory infections. Detected viruses include Influenza A and B, Adenovirus, Bocavirus, Coronavirus (including SARS-CoV-2), Human metapneumovirus (hMPV), Parainfluenza virus, RSV, Enterovirus, and Rhinovirus. For bacteria, this kit detects *Bordetella pertussis, Bordetella parapertussis*, and *Mycoplasma pneumoniae*. Probes for hybridization control, mix, and human cells are also

included in this kit. Specimen types that can be used for this examination are bronchoalveolar lavage (BAL), aspirate, or nasopharyngeal swab.[19]

In a previous study, Li et al reported limits of detection ranging from 20 to 200 copies per reaction, with sensitivities of 87.5–100% and specificities close to 100% for the respiratory viruses included in their two-tube multiplex RT-PCR assay.[20] Similarly, validation data from the manufacturer for the Respiratory Flow Chip Kit showed a limit of detection of 10–500 copies per reaction, depending on the target pathogen.[19]

No cross-reactivity was observed during specificity testing using high concentrations of genetic material from all pathogens included in the panel. Evaluation using clinical samples showed sensitivities ranging from 70.8% to 100% and specificities from 98.4% to 100%, while repeatability testing demonstrated concordant results across six replicate analyses for all targets.[19]

**BioFire FilmArray Respiratory Panel 2.1 Plus (RP2.1)**

This is a molecular diagnostic test based on nested multiplex PCR integrated in a single automated cartridge. The process begins with sample lysis through mechanical agitation combined with chemical lysis. After lysis, nucleic acids are extracted and purified using magnetic beads. For RNA targets, reverse transcription is performed to convert RNA into amplifiable cDNA.[21]

Amplification then proceeds in two nested PCR stages: the first PCR stage is multiplex PCR, while the second PCR stage is a singleplex PCR reaction with primers distributed in wells for amplification of previously obtained PCR products. Amplicon detection is obtained by melting curve analysis. The system software automatically performs analysis. All of this work is done automatically in the FilmArray machine.[21]

This device is designed to detect 23 respiratory pathogens. Detected viral pathogens include six types of Coronaviruses*:* Coronavirus HKU1, NL63, 229E, OC43, Middle East Respiratory Syndrome Coronavirus (MERS-CoV), and SARS-CoV-2. For influenza, the panel detects Influenza A in general form and its specific subtypes, namely H1, H3, and H1-2009, plus Influenza B.[21]

The panel also includes four types of Parainfluenza virus (types 1, 2, 3, and 4) and detection for other viruses such as Adenovirus, hMPV, Rhinovirus/Enterovirus, and RSV. Bacterial pathogens include four clinically important atypical respiratory bacterial species, namely *B. parapertussis, B. pertussis*, *Chlamydia pneumoniae,* and *Mycoplasma pneumoniae*.[21]

This kit is specifically designed to analyze nasopharyngeal swab specimens. Specimens are stored at 4°C and must be processed as soon as possible after collection to maintain pathogen viability. For long-term storage, specimens can be stored at -80°C.[21]

Overall analytical performance is very good, with sensitivity of 97.1% and

specificity of 99.3% when evaluated against reference methods or clinical case definitions. However, these figures vary depending on the specific pathogen detected and specimen condition.[21]

### BioFire FilmArray® Pneumonia Panel Plus (FA-PP)

This is a molecular diagnostic device from BioFire that uses the same method as the FilmArray Respiratory Panel 2.1 Plus. The difference is that this device has different pathogen detection coverage. This device can detect and identify 9 types of viruses, 18 bacteria (including three atypical pneumonia bacteria), and 7 antimicrobial resistance genes (See Table 1).[22]

The detection results for bacteria from this test are also reported semi-quantitatively in different logarithmic multiples ($10^4$-$\geq10^7$ copies per milliliter). Three atypical bacteria (*C. pneumoniae, L. pneumophila,* and *M. pneumoniae*) are reported qualitatively, as are nine respiratory viruses. Resistance genes are only reported when the relevant carrier bacteria are also detected in the specimen.[23]

This device can process various types of lower respiratory specimens. In a multicenter study in France, 90.1% of bacteria detected at $\geq10^6$ DNA copies/mL showed significant growth in culture, with quantitative agreement reaching 100% at $\geq10^7$. The proportion of isolates above culture threshold increased from ~20-40% at $10^4$, ~45-65% at $10^5$, ~75-85% at $10^6$, to ~90-100% at $\geq10^7$, especially in ICU VAP/vHAP patients. Most studies support a cutoff of $\geq10^6$ (especially $\geq10^7$) for typical respiratory pathogens in optimal samples and strong clinical context indicating significant infection, while $10^4$-$10^5$ is more likely colonization.[24,25]

Table 1. Pathogen Coverage of Commercial Multiplex Respiratory PCR Panels Available in Indonesia[19,21,22,26–28]

| Pathogen | VITRO | RP2.1 | FA-PP | QIAstat | ALLPLEX | COBAS |
|---|---|---|---|---|---|---|
| Influenza viruses | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |
| RSV | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |
| Adenovirus | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |
| Coronaviruses | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |
| Rhinovirus/Enterovirus | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |
| hMPV | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |
| Parainfluenza viruses | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |
| *Bordetella spp.* | ✓ | ✓ | – | ✓ | ✓ | – |
| *Mycoplasma pneumoniae* | ✓ | ✓ | ✓ | ✓ | ✓ | – |
| *Chlamydia pneumoniae* | – | ✓ | ✓ | ✓ | ✓ | – |
| *Legionella pneumophila* | – | – | ✓ | ✓ | ✓ | – |
| Typical bacterial pathogens | – | – | ✓* | – | ✓** | – |
| Resistance genes | – | – | ✓ | – | – | – |

Note: *including *A. baumannii* complex, *E. cloacae* complex, *E. coli, H. influenzae*, *Klebsiella spp.*, *M. catarrhalis, Proteus spp., P. aeruginosa, S. marcescens, S. aureus, S. agalactiae, S. pneumoniae, S. pyogenes.* Typical bacterial targets are reported semi-quantitatively ($10^4$–$\geq10^7$ copies/mL); **H. influenzae* and *S. pneumoniae*

The diagnostic performance of this kit is quite good compared to culture, which is the standard of care. This device has high sensitivity, approximately 89.6-100%, with specificity ranging approximately 83-99%.[22,23,29–31] This kit often detects more pathogens than culture, especially in patients who have received antibiotics or fastidious pathogens such as *S. pneumoniae, S. pyogenes, M. catarrhalis,* and *H. influenzae*.[23]

The main strength of this diagnostic device is its consistently high negative predictive value (NPV) of 96-99.7%, so it can be trusted to rule out bacterial infection, allowing de-escalation or discontinuation of antibiotics if this test and culture results are negative.[23] The main limitation of FA-PP is that it does not detect bacteria outside the panel. Therefore, culture is still needed, especially in cases with high clinical suspicion or negative FA-PP results.[30]

**QIAstat-Dx Respiratory SARS-CoV-2 Panel**

This is a cartridge-based multiplex RT-PCR test that runs on the QIAstat-Dx platform. This panel integrates SARS-CoV-2 targets into the QIAstat respiratory panel which detects pathogens including Adenovirus, Bocavirus, 4 seasonal coronaviruses (229E, NL63, OC43, HKU1), hMPV, Rhinovirus/Enterovirus, Influenza A (including subtypes H1, H1N1/2009, H3) and Influenza B, Parainfluenza 1-4, RSV, and atypical bacteria (such as *M. pneumoniae, C. pneumoniae, B. pertussis,* and *L. Pneumophila*). The recommended specimen for this device is a combined nasopharyngeal and oropharyngeal swab transported in molecular media.[32,33]

In a multicenter evaluation of 445 samples, the original QIAstat Respiratory panel showed positive percent agreement (PPA) of 98.0% and negative percent agreement (NPA) of 99.8% compared to the FilmArray and Seegene Allplex reference methods.[32] The limit of detection for SARS-CoV-2 is 500 copies/mL, while other pathogens show a wide LoD range, from 0.01 $TCID_{50}$/mL for hMPV to 33,000 copies/mL for bocavirus.[26]

**ALLPLEX™ Respiratory Panel**

This is a one-step multiplex real-time RT-PCR-based test developed by Seegene for simultaneous detection of pathogens causing respiratory tract infections. The distinguishing technology is Multiple Detection Temperature, an innovation that enables detection of multiple targets in a single fluorescence channel without requiring melting curve analysis.[27]

The process begins with automatic nucleic acid extraction using the Seegene NIMBUS platform, followed by real-time PCR amplification in reaction tubes that already contain all reagents. Total analysis time from sample input to final results is 4 to 4.5 hours, with hands-on time of only about 15 minutes for a batch of 24 samples when using the complete automated system.[27]

This device can detect and identify 26 respiratory pathogen targets divided into four separate panels, allowing flexible use according to clinical needs. Panel 1

includes Influenza—with subtype differentiation of Influenza A H1, H1pdm09, and H3, as well as Influenza B—along with RSV types A and B. Panel 2 detects Adenovirus, Enterovirus, Parainfluenza viruses 1-4, and hMPV. This panel is important for diagnosis of respiratory infections in pediatric and immunocompromised populations.[27]

Panel 3 focuses on pathogens whose importance is increasing, including Bocavirus, Rhinovirus, and endemic coronaviruses (229E, NL63, OC43). Panel 4 targets seven bacteria causing pneumonia and atypical respiratory infections: *M. pneumoniae, C. pneumoniae, L. pneumophila, H. influenzae, S. pneumoniae, B. pertussis,* and *B. parapertussis*.[27]

The primary recommended specimen is a nasopharyngeal swab. Additionally, this panel can process nasopharyngeal aspirate, which is preferred in pediatric populations because it is easier to collect. For severe pneumonia cases or lower respiratory tract infection investigations, this panel can also analyze BAL and sputum samples (Panel 4 specifically for sputum). Samples can be collected in various standard transport media commonly used in clinical laboratories.[27]

The majority of viruses have LoD at 10-100 copies/reaction. Parainfluenza virus type 1 shows relatively low LoD at 10 copies/reaction, but type 4 requires higher concentration (1,000 copies/reaction). hMPV also shows lower analytical sensitivity with LoD of 1,000 copies/reaction compared to other viruses.[27]

Multicenter studies involving >400 clinical samples show sensitivity of 82.8% to 100%, with most viruses reaching 95% or higher compared to comparison methods. Specificity ranges from 94.1% to 100% across all target pathogens, with the majority reaching 99-100%.[34]

**COBAS® Respiratory Flex**

This is a multiplex PCR-based panel that runs on the COBAS platform. The fundamentally distinguishing technology is Temperature-Assisted Generation of Signal (TAGS), an innovation that enables detection of multiple targets per fluorescence channel through temperature-dependent signal activation.[35]

In its implementation, this system captures fluorescence signals from five standard channels and three temperature channels during each PCR cycle, enabling differentiation of up to three targets per fluorescence channel. The process begins with fully automated nucleic acid extraction using magnetic glass particles, followed by amplification and detection with specific fluorescent-labeled probes.[35]

This panel includes Influenza A and B with subtype differentiation capability for influenza A (H1N1, H3N2); RSV; SARS-CoV-2 with targets on ORF1a and ORF1ab genes; Adenovirus with species B, C, and E coverage; hMPV; Rhinovirus and Enterovirus; four human endemic coronaviruses (229E, HKU1, NL63, OC43); and Parainfluenza virus types 1, 2, 3, and 4. This device is specifically designed for nasopharyngeal swab specimens collected

using standard techniques and immediately placed in 3 mL of viral transport medium (VTM).[35]

According to manufacturer clinical validation data involving 1,306 nasopharyngeal swab specimens compared to FDA-cleared reference methods, COBAS® Respiratory Flex showed good clinical performance across the majority of targets. Sensitivity reached 100% for Influenza A, Influenza B, Adenovirus, Parainfluenza types 1 and 2. SARS-CoV-2 reached 98.4% (95% CI=94.4-99.6%), while RSV showed 96.0%, hMPV 96.3%, Parainfluenza types 3 and 4 at 95.8% and 97.4%, respectively. Lowest performance was seen in Rhinovirus/enterovirus at 83.9%. Specificity was consistently high, above 97% for all targets.[35]

## COMPARISON OF AVAILABLE PLATFORMS

The main characteristics, advantages, limitations, and operational requirements of multiplex respiratory diagnostic platforms currently available in Indonesia are summarized in Table 2. These differences in pathogen coverage, specimen requirements, degree of automation, instrument requirements, and diagnostic capabilities have important implications for test selection and clinical implementation, which are discussed in the following section.

Table 2. Comparison of the currently available respiratory panels in Indonesia

| Platform | Technology | Specimen | Automation/ Ease of Use | Instrument Requirement | Advantages | Limitations |
|---|---|---|---|---|---|---|
| VITRO[19] | Multiplex PCR followed by reverse hybridization and membrane-based detection | NP swab, aspirate, BAL | Requires manual hands-on nucleic acid extraction, PCR amplification, and membrane hybridization | Conventional thermocycler and HybriSpot reader | Suitable for batch testing; broad pathogen detection | Requires dedicated hybridization/reading system and more hands-on time |
| RP2.1[20] | Fully automated nested multiplex PCR with melting curve analysis | NP swab | Fully integrated automated sample-to-answer workflow | BioFire FilmArray instrument | Rapid turnaround time; minimal hands-on time | Closed system with dedicated instrumentation |
| FA-PP[22] | Fully automated nested multiplex PCR with melting curve analysis | BAL, ETA, sputum, and other lower respiratory specimens | Fully integrated automated sample-to-answer workflow | BioFire FilmArray instrument | Rapid turnaround time; extensive bacterial coverage with AMR gene detection and semi-quantitative reporting | Limited to lower respiratory specimens and panel targets. Closed system with dedicated instrumentation |
| QIAstat[26] | Cartridge-based multiplex RT-PCR | Combined NP/OP swab | Fully integrated automated sample-to-answer workflow | QIAstat-Dx Analyzer | Rapid and standardized workflow with minimal hands-on time | Closed system with dedicated instrumentation |

Continue Table 2. Comparison of the currently available respiratory panels in Indonesia

| Platform | Technology | Specimen | Automation/ Ease of Use | Instrument Requirement | Advantages | Limitations |
|---|---|---|---|---|---|---|
| ALLPLEX[27] | Multiplex real-time RT-PCR (MuDT™ technology) | NP swab, NPA, BAL, sputum | Open-platform workflow, allowing flexible integration with manual or automated workflows | Compatible with multiple real-time PCR platforms | Flexible testing strategy; suitable for higher throughput laboratories | Full pathogen coverage requires multiple panel reactions |
| COBAS[28] | Multiplex real-time PCR using TAGS technology | NP swab | Automated extraction, amplification, detection, and result analysis on the COBAS platform | COBAS platform | Highly automated, high-throughput workflow | Dedicated platform and limited coverage |

Note: PCR=polymerase chain reaction; NP=nasopharyngeal; BAL=bronchoalveolar lavage; ETA=endotracheal aspirate; OP=oropharyngeal swab

## OPTIMAL SPECIMEN TYPES

Specimen selection for respiratory panel testing is based on the tropism and primary replication sites of these pathogens. In general, for respiratory viral pathogens and atypical bacteria, nasopharyngeal swabs are the optimal specimen. Conversely, for typical pneumonia bacteria, BAL/tracheal aspirate/sputum are the specimens of choice.[36] For *Legionella*, sputum has better sensitivity compared to nasopharyngeal swabs.[37]

In clinical cases with lower respiratory tract infection, sputum can also be used for atypical bacterial pathogens, except for *B. pertussis* due to its tropism for upper respiratory ciliated epithelium. Collected specimens should ideally be sent to the laboratory using VTM within 2 hours at room temperature or within 24 hours at 2-8°C.[38]

## ADVANTAGES AND LIMITATIONS OF RESPIRATORY PANELS

Multiplex PCR-based respiratory panels have several advantages. This test shows 30-50% higher sensitivity compared to traditional methods, with the capability to simultaneously detect up to 26 respiratory pathogens in one reaction.[39] Fast turnaround time brings significant clinical impact, including reduced antibiotic administration and shorter hospital stays.[2,40] This test also excels in detecting viruses and bacteria that cannot or are difficult to detect in routine culture examinations.[41]

On the other hand, this test has limitations such as the inability to differentiate viable pathogens from non-viable pathogens or asymptomatic carriers and prolonged viral shedding. Some pathogens that play a role in respiratory tract infections, such as *Stenotrophomonas* and *Aspergillus,* are also not included in these panels.[42] Although there have been studies showing cost-effectiveness in using this test, the initial cost of purchasing equipment and reagents is still high. To date, there have also been no cost analysis studies conducted in Indonesia.[43]

## CLINICAL CONSIDERATIONS FOR RESPIRATORY PANEL SELECTION

The use of multiplex respiratory panels should be selective rather than routine, as these assays are associated with substantial costs. Current evidence suggests that respiratory panel testing provides the greatest clinical value when test results are likely to influence patient management, antimicrobial therapy, infection prevention measures, or hospital resource utilization.[2,44,45]

These tests may be particularly useful in hospitalized patients with severe acute respiratory infections, patients admitted to intensive care units, immunocompromised individuals, and those at increased risk of complications, such as young children, older adults, transplant recipients, patients receiving immunosuppressive therapy, and individuals with significant cardiopulmonary comorbidities.[2,44,45]

The choice of platform should be guided by the primary diagnostic objective. Broad respiratory panels are most useful in hospitalized or high-risk patients when identification of viral or atypical pathogens is likely to alter treatment decisions, isolation measures, or antimicrobial use. Examples include patients with severe acute respiratory infections of unclear etiology, respiratory outbreaks, or immunocompromised patients in whom a broad range of respiratory pathogens may be considered.

In contrast, pneumonia-focused panels may provide greater clinical value in patients with suspected bacterial lower respiratory tract infections, particularly severe hospital-acquired pneumonia, ventilator-associated pneumonia, or critically ill patients. Their extensive bacterial coverage, antimicrobial resistance gene detection, and semi-quantitative bacterial reporting may provide clinically relevant information beyond that offered by conventional respiratory panels.

## IMPLEMENTATION CONSIDERATIONS IN INDONESIA

Several factors support the implementation of multiplex respiratory panels in Indonesia. The expansion of molecular diagnostic capacity during the COVID-19 pandemic has increased the availability of PCR instruments, automated molecular platforms, and trained laboratory personnel in Indonesia.[46] In addition, growing awareness of antimicrobial stewardship and antimicrobial resistance may increase the clinical value of rapid respiratory pathogen identification.

However, molecular diagnostic capacity is still concentrated in major referral centers, and access may be limited in remote regions. The relatively high cost of respiratory panel testing may also limit widespread adoption, particularly in resource-constrained settings. In general, fully automated or cartridge-based respiratory panels tend to be more expensive than manual open-platform assays.

Based on informal inquiries to several clinical laboratories and hospitals in Indonesia, open-platform assays generally cost approximately IDR 1.5–3 million per test, whereas fully automated cartridge-based systems may cost approximately IDR 3–5 million per test. However, these estimates should be interpreted with caution because pricing varies substantially according to procurement agreements, testing volume, and institutional settings. Further studies evaluating the clinical utility and cost-effectiveness of respiratory panel testing in Indonesia are needed to support evidence-based implementation.

This review has several limitations. First, as a narrative review, it did not employ a systematic review methodology with formal study selection and quality assessment, which may introduce selection bias. Second, the respiratory panel platforms were compared using data from different types of studies involving different patient populations, specimen types, and reference methods. Therefore, the reported performance of each platform may not be directly comparable. Finally, most available evidence comes from studies outside Indonesia, while local data on the clinical utility, cost-effectiveness, and implementation of respiratory panel testing remain limited.

## CONCLUSION

Six respiratory panel platforms are currently available in Indonesia, including VITRO Respiratory Flow Chip Kit, BioFire FilmArray Respiratory Panel 2.1 Plus, BioFire FilmArray Pneumonia Panel Plus, QIAstat-Dx Respiratory SARS-CoV-2 Panel, ALLPLEX Respiratory Panel, and COBAS Respiratory Flex, each with different pathogen coverage, specimen requirements, workflow characteristics, and diagnostic capabilities. While broad respiratory panels are mainly designed for detecting respiratory viruses and atypical bacteria, pneumonia-focused panels provide more extensive bacterial coverage and antimicrobial resistance information for lower respiratory tract infections.

These platforms offer advantages in terms of diagnostic speed and sensitivity but remain limited by cost, incomplete pathogen coverage, and challenges in distinguishing active infection from colonization or prolonged pathogen shedding. Appropriate panel selection and result interpretation should consider the clinical context, specimen type, laboratory capacity, and available resources. Further studies are needed to evaluate the clinical impact and cost-effectiveness of respiratory panel implementation in Indonesia.

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