P55 PNEUMONIA APPLICATION
The Unyvero P55 Pneumonia Application combines adequate detection of pathogens and antibiotic resistances to aid diagnosing pneumonia. A single test handles one patient sample analyzing 40 DNA targets and delivers reliable results within 4 hours. This approach facilitates a confident treatment decision at an earlier stage in the cycle of care.
The diagnosis and treatment of infections as it is today is imprecise and fraught with problems. Results from sample cultures usually take 2 days or longer. Clinicians must almost always begin treatment before results are available. In addition, antibiotic resistances compound the difficulty of therapy selection. They have risen steadily in the last several decades also due to inadequate antibiotic treatment.

Clinical studies have demonstrated that adequate initial antibiotic treatment for most severe acute infections significantly improves medical outcome. In addition, appropriate and early antibiotic selection will limit the risk of increasing antibiotic resistance in the population as a whole.

Pneumonia is a severe, life-threatening high incidence acute infection of the lower respiratory tract (LRT), which results from various causes, most commonly bacteria or viruses. It is a fast progressing disease with mortality rates up to 30% and an average hospital stay of 11 to 14 days associated with high treatment costs.

The American Thoracic Society/Infectious Diseases Society of America (ATS/IDSA) guidelines distinguish the following types of pneumonia:

- **Community-acquired Pneumonia (CAP)** is acquired in the community without a history of medical intervention. Often caused by viruses, they usually follow a mild course, however 25% of CAP need hospitalization (hCAP).

- **Hospital-acquired (or nosocomial) Pneumonia (HAP)** is a pneumonia that occurs 48 hours or more after admission and did not appear to be incubating at the time of admission.

- **Ventilator-associated Pneumonia (VAP)** is a type of HAP that develops more than 48 to 72 hours after endotracheal intubation.

- **Healthcare-associated Pneumonia (HCAP)** is defined as pneumonia that occurs in a nonhospitalized patient with extensive healthcare contact.

Studies have demonstrated, that the medical outcome of hCAP and HAP including VAP would certainly benefit from faster diagnostics.
Antibiotic resistant bacteria have become an everyday occurrence and problem in hospitals across the world. Misuse of antibiotics may cause patients to become colonized or infected with antibiotic resistant bacteria, such as methicillin-resistant Staphylococcus aureus (MRSA), vancomycin-resistant Enterococci (VRE) and highly-resistant Gram-negative bacilli.

The emergence, selection and spread of resistant bacteria is a threat to patient safety in hospitals because:
- infections with antibiotic resistant bacteria result in increased morbidity, mortality, and length of hospital stay.
- antibiotic resistance frequently leads to a delay in appropriate antibiotic therapy.
- inappropriate or delayed antibiotic therapy in patients with severe infections is associated with worse patient outcomes and sometimes death.
- patients who are hospitalized have a high probability of receiving an antibiotic and 50% of all antibiotic use in hospitals can be inappropriate.
- misuse of antibiotics in hospitals is one of the main factors that drive the development of antibiotic resistance.
PNEUMONIA ASSAY

AN IDEAL PNEUMONIA ASSAY SHOULD COVER 90% OF PATHOGENS CAUSING HOSPITALIZED PNEUMONIA

**PNEUMONIA CAUSING PATHOGENS**

- Staphylococcus aureus
- Streptococcus pneumoniae
- Pseudomonas aeruginosa
- Enterobacteriaceae
- Klebsiella pneumoniae
- Enterococcus spp.
- Escherichia coli
- Stenotrophomonas maltophilia
- Staphylococcus saprophyticus
- Chlamydia pneumoniae
- Actinobacillus pleumoniae
- Mycoplasma pneumoniae
- Legionella pneumophila
- Moraxella catarrhalis
- Haemophilus influenzae
- Pneumocystis jirovecii
- Mycoplasma pneumoniae
- Serratia marcescens
- Legionella pneumophila
- Moraxella catarrhalis
- Haemophilus influenzae
- Pneumocystis jirovecii
- Mycoplasma pneumoniae

**RISK: ANTIBIOTIC RESISTANCE**

**IMPORANT GENETIC RESISTANCE MARKERS**

- beta-lactamase
- beta-lactamase
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**PNEUMONIA TREATMENT GUIDELINES**

- Clindamycin
- Augmentin
- Cefuroxime
- Clindamycin
- Augmentin
- Cefuroxime
- Clindamycin
- Augmentin
- Cefuroxime
- Clindamycin

**PREREQUISITES**

- SHOULD WORK WITH VARIOUS NATIVE SAMPLES
- NEEDS SAMPLE PREPARATION WITH HIGH DNA YIELD
- ALLOWS MULTIPLE PCR OF UP TO 100 ANALYSES
- REQUIRES HIGHLY SPECIFIC DETECTION

**SPUTUM, LAVAGE (BAL), TRACHEAL ASPIRATE**

- ~ 4 – 5 H

**COVERAGE**

- Detects 90% of infectious disease causing pathogens and clinically most relevant antibiotic resistances

**DIVERSITY**

- Enables testing of clinically relevant, different native sample types

**SPEED**

- Delivers clinically relevant answers in time
DNA purification
PCr set-up
Multiplex PCR with array detection

1. Unyvero T1 sample tube for preparation of the patient sample, pre-filled with specific lysis reagents.
2. Unyvero T1 sample tube cap seals the Unyvero Sample Tube and contains proteinase K and an internal control gene for quality control.
3. Unyvero M1 master mix tube with reagents for DNA amplification.

Therefore, the closed Unyvero Cartridge is equipped with integrated reagent containers, a DNA purification column, eight PCr chambers and an according number of arrays. The cartridge is pre-filled with buffers for DNA clean-up, reagents and fluorescence-labeled primers for PCR amplification, respectively for array hybridization of the PCR product.

UNIQUE SOLUTION TAILORED TO CLINICAL NEEDS:
- Comprehensive, disease-oriented test panels not on or easy to operate platforms, requiring neither the special infrastructure of a laboratory environment nor specially trained personnel.
- Translates a complex laboratory process into an easy to use format. The analytical process requires only addition of the unprocessed patient sample and enzymes for DNA amplification.
- Generates complete diagnostic information in ~4–5 hours, without any further operator interaction.

PREREQUISITES FOR AN IDEAL PNEUMONIA ASSAY:
> COVERAGE
> DIVERSITY
> SPEED

SOLUtion – UnYvero P55
PNEUMONIA APPLICATION

UNIQUExe UNYVERO P55 PNEUMONIA CARTRIDGE ALLOWS THE DETECTION OF 40 ANALYTES AND INTEGRATES:
- DNA purification,
- PCr set-up,
- multiplex endpoint PCr and
- amplicon detection by array hybridization.

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UNIQUE SOLUTION TAILORED TO CLINICAL NEEDS:
- Comprehensive, disease-oriented test panels not on or easy to operate platforms, requiring neither the special infrastructure of a laboratory environment nor specially trained personnel.
- Translates a complex laboratory process into an easy to use format. The analytical process requires only addition of the unprocessed patient sample and enzymes for DNA amplification.
- Generates complete diagnostic information in ~4–5 hours, without any further operator interaction.
In Pneumonia, the early detection of pathogens and antibiotic resistances is key to improving clinical outcome. The Unyvero System uniquely addresses the analysis of antibiotic resistance markers simultaneously with the pathogen detection.

The Unyvero Pneumonia panel of microorganisms and resistance gene markers is designed based on feedback of clinical experts and international, as well as national treatment guidelines.*

The panel is primarily designed to capture patients at risks for pathogens causing severe, difficult to treat forms of pneumonia e.g. Pseudomonas aeruginosa, pathogens carrying antibiotic resistance and where patients may need isolation (Klebsiella, Acinetobacter)

In addition, for the panel composition pathogen incidences have been taken into account, thus it includes those microorganisms showing an incidence of above 5%. The panel is completed by adding difficult to diagnose pathogens (e.g. Legionella pneumophila) with lower incidence, but with a rather high clinical impact.

THE CURATIS UNYVERO PNEUMONIA PANEL TARGETS THE FOLLOWING ANTIMICROBIAL CLASSES BY ANALYZING 19 GENETIC MARKERS

> β-lactam-resistance
> Macrolide-resistance
> Fluoroquinolone resistance
> Carbapenem resistance

as clinically most relevant in pneumonia causing pathogens.

Curetis’ proprietary and universal sample preparation technology prepares DNA from any native clinical sample type without losing time for preculturing. Curetis’ technology efficiently extracts DNA from different microorganisms (gram-positive and gram-negative bacteria, fungi and other intracellular organisms) even in complex samples like highly viscous sputa or in samples contaminated with blood.

One of Curetis’ core competencies is the design of reliable bio-assays in self-contained cartridges for enabling sensitive multiplex testing. The required multiplex grade is achieved by combining the unmatched sample preparation and PCR technology with a proprietary detection array. Endpoint-PCR can deliver higher multiplex grades than most other amplification methods and in that respect holds clear advantages over e.g. real-time PCR.

The array has been optimized for hybridization times of a few minutes compared to standard arrays. To enhance specificity, the dissociation kinetics of the array hybridization are automatically assessed.

In addition with each patient sample, an artificial gene is simultaneously processed as internal process control. The control verifies all PCR steps, as well as the array hybridization.

<table>
<thead>
<tr>
<th>Sample Types</th>
<th>Sample Quality</th>
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<tbody>
<tr>
<td>&gt; sputum</td>
<td>&gt; liquid</td>
</tr>
<tr>
<td>&gt; lavage (BAL)</td>
<td>&gt; viscous</td>
</tr>
<tr>
<td>&gt; tracheal aspirate</td>
<td>&gt; contaminated with...</td>
</tr>
<tr>
<td></td>
<td>- cells</td>
</tr>
<tr>
<td></td>
<td>- blood</td>
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</tbody>
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**BECAUSE OF ITS UNIVERSAL APPLICABILITY**
THE CURETIS TECHNOLOGY CAN USE A SINGLE PROTOCOL FOR SAMPLE PREPARATION FOR MANY DIFFERENT SAMPLE TYPES IN ANY CLINICAL APPLICATION.
The intuitive simple workflow is consistent across all clinical applications and sample types, thus drastically reducing invalid tests due to operator errors.

**STEP 1**
TRANSFER OF SAMPLES AND LYSIS

**~ 60 seconds:**
1. The patient sample is transferred to the Unyvero Sample Tube, then sealed in with the Unyvero Sample Tube Cap and lysed for 30 minutes in the Unyvero Lysator.

**STEP 2**
ASSEMBLING THE UNYVERO CARTRIDGE

**~ 30 seconds:**
2. After 30 minutes, the Unyvero Sample Tube can be removed from the Lysator and inserted together with the Unyvero Master-Mix Tube into the corresponding Unyvero Cartridge.

**STEP 3**
SCANNING AND INSERTING THE UNYVERO CARTRIDGE

**~ 20 seconds:**
3. The cartridge is now scanned and inserted into the Unyvero Analyzer. Up to two cartridges per analyzer can be analyzed simultaneously.

**STEP 4**
FOUR TO FIVE-HOUR ANALYSIS PROCESS

**It takes just a few minutes for subsequent analysis of the results:**
4. The Unyvero analysis now runs for four to five hours. The results are then displayed on the screen or can be exported as a PDF.

THE UNYVERO SOLUTION FEATURES A "SAMPLE TO ANSWERS" APPROACH AND CONSISTS OF:

- the Unyvero L4 Lysator for sample lysis
- the application specific Unyvero Cartridge
- the Unyvero A50 Analyzer handling the Unyvero Cartridge
- the Unyvero C8 Cockpit for intuitive user interaction
- and the optional Unyvero Server Software for integration into the hospital’s information systems

The Unyvero System translates a complex laboratory process into an easy-to-use format. The analytical process requires merely the addition of the unprocessed patient sample and enzymes for DNA amplification. All other reagents are preloaded into a self-contained, contamination safe cartridge. After the patient sample and the master mix are inserted into the cartridge, the cartridge is loaded into the analyzer and processed fully automatically. The Unyvero System generates complete diagnostic information in 4 – 5 hours, without any further operator interaction.
UNYVERO
AT A GLANCE

THE UNYVERO SOLUTION

> detects broad panels of pathogens and antibiotic resistances from a single sample in one run

> enables testing of many clinically relevant native samples

> delivers clinically relevant information in ~ 4 – 5 hours, to aid an informed therapy decision as early as possible

> enables point of need testing

> provides high productivity through
  - minimizing operator time to a few minutes with full walk-away automation based on a simple and consistent workflow for any clinical application
  - low implementation requirements and low total cost of ownership, as no staff with molecular biology skills nor special infrastructure is needed
  - configurations that meet individual customer needs, satisfying any throughput demands
  - optimizing the routine hospital workflow by sophisticated information management