# BioFire® FilmArray® Pneumonia *plus* Panel Performance Evaluation: A Multicenter, International Collaborative Study

CHRISTINE C GINOCCHIO[1,2], CAROLINA GARCIA-M[2], BARBARA MAUERHOFER[2], CORY RINDLISBACHER[1] AND THE EMEA EVALUATION PROGRAM COLLABORATIVE
[1]. BIOFIRE DIAGNOSTICS, SALT LAKE CITY, UT, USA; [2]. BIOMERIEUX, BIOMÉRIEUX, MARCY L'ETOILE, FRANCE

## IDWeek 2020: 907872

## BACKGROUND

Identification of pathogens causing community acquired, heath-care and ventilator associated pneumonia can be problematic. The BioFire® Pneumonia *Plus* (PN*plus*) Panel detects 15 bacteria (with semi-quantification), three atypical bacteria, eight viral classes and seven antibiotic resistance markers directly from sputum-like specimens (induced or expectorated sputum; endotracheal aspirates), and bronchoalveolar lavage (BAL)-like specimens with results in about one hour. This multinational study evaluated performance of BioFire PN*plus* Panel as compared to standard of care (SOC) testing.

**Bacteria**
**Semi – Quantitative Log Bins**
*Acinetobacter calcoaceticus-baumannii*
Complex*^^
*Enterobacter cloacae* complex*^+
*Escherichia coli*^
*Klebsiella pneumoniae* group*^+
*Klebsiella aerogenes*
*Klebsiella oxytoca*^+
*Haemophilus influenzae*
*Moraxella catarrhalis*
*Proteus spp.*^+
*Pseudomonas aeruginosa*^^
*Serratia marcescens*^+
*Staphylococcus aureus*
*Streptococcus pneumoniae*
*Streptococcus pyogenes*
*Streptococcus agalactiae*

**Atypical Bacteria**
**Qualitative**
*Legionella pneumophila*
*Mycoplasma pneumoniae*
*Chlamydia pneumoniae*

**Viruses**
Influenza A (H1, 09H1, H3)
Influenza B
Adenovirus
Coronavirus (OC43, NL63, HKU1, 229E)
Parainfluenza virus (1, 2, 3, 4)
Respiratory syncytial virus (A, B)
Human Rhinovirus/Enterovirus
Human Metapneumovirus

OUS: includes MERS CoV

**Resistance Markers**
**Qualitative**
**Methicillin resistance**
*mecA/mecC* and MREJ

**ESBL**
CTX-M*

**Carbapenemases**
KPC^
NDM^
VIM^
IMP^
Oxa-48-like+

*, ^, +: Denote when resistance marker would be reported based on pathogen detection
Resistance markers cannot be directly linked to a specific pathogen

## MATERIALS AND METHODS

In total, 52 laboratories from 13 countries (Europe and Israel) compared BioFire PN*plus* Panel results to SOC results. SOC tests varied by site and included various combinations of Gram stain, culture, urinary antigen, molecular assays, and direct fluorescent antibody assays. 2,463 samples (1,237 sputum-like and 1,226 BAL-like) were evaluated. Values were applied to BioFire PN*plus* Panel semi-quantification results (bin results in copies/ml) (1=not detected (<10^3.5); 2=10^4; 3=10^5; 4=10^6; and 5=≥10^7) and compared to three algorithms of standardized SOC reporting (rare, few, moderate, numerous, 1+, 2+, 3+, 4+, quantitative culture etc.) to assess quantification correlation. All BioFire PN*plus* Panel and SOC results were considered true positive.

## BACTERIA DETECTED BY BIOFIRE PNplus PANEL VS SOC (ALL SAMPLES)

**Figure 1:** 3,262 bacteria included in the BioFire PN*plus* were detected by at least one method. The BioFire PN*plus* Panel identified 3,125 (95.77%) bacteria compared to 1,861 (57.05%) for SOC (p=<0.0001).
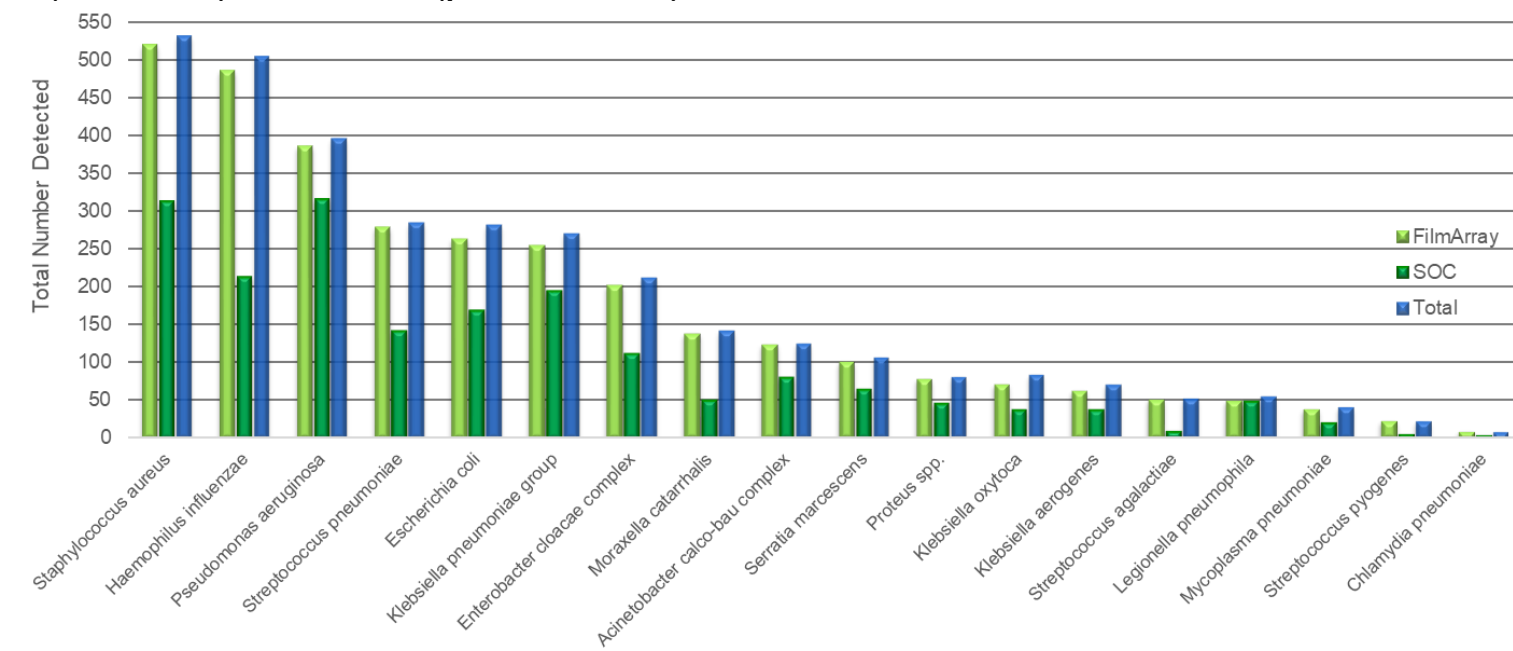


## TABLE 1: PATHOGENS* DETECTED PER SAMPLE BY BIOFIRE PNplus PANEL VS SOC

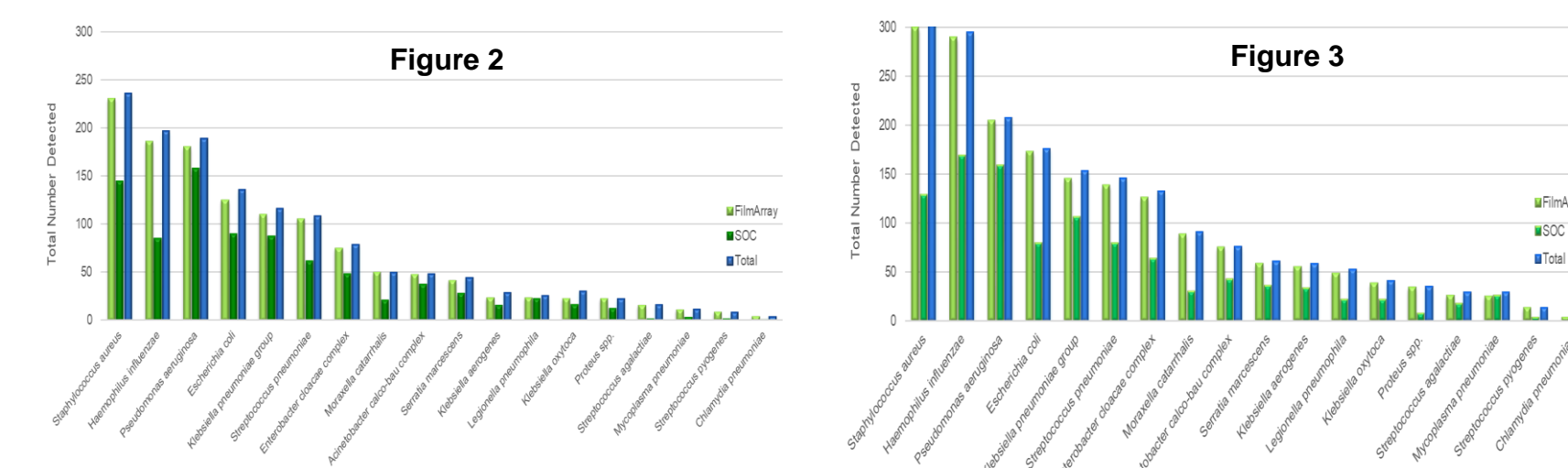Table 1: *Bacteria and viruses included in the BioFire PN*plus* Panel

| | Total Positive N | 1 Analyte N (%) | 2 Analytes N (%) | 3 Analytes N (%) | 4 Analytes N (%) | 5 Analytes N (%) | 6+ Analytes N (%) |
|---|---|---|---|---|---|---|---|
| BioFire PNplus | 1875 | 848 (45.22) | 536 (28.59) | 275 (14.67) | 130 (6.93) | 60 (3.20) | 26 (1.39) |
| SOC | 1380 | 904 (65.51) | 370 (26.81) | 85 (6.16) | 15 (1.09) | 4 (0.29) | 2 (0.14) |

Average number of pathogens* per positive sample: BioFire PN*plus* Panel = 1.99; SOC = 1.44

## BACTERIA DETECTED BY BIOFIRE PNplus PANEL VS SOC BY SAMPLE TYPE

**Figure 2: BAL-like samples:** 1,358 bacteria included on BioFire PN*plus* Panel were detected by at least one method. The BioFire PN*plus* Panel identified 1,288 (94.35%) bacteria compared to 841 (61.93%) for SOC (p=<0.0001).

**Figure 3: Sputum-like samples:** 1,904 bacteria included on BioFire PN*plus* Panel were detected by at least one method. The BioFire PN*plus* Panel identified 1,836 (96.43%) bacteria compared to 1020 (53.57%) for SOC (p=<0.0001).




**BAL-like Samples:** Average number of bacteria/viruses* per positive sample: PN*plus* Panel =1.8; SOC =1.44
**Sputum-like Samples:** Average number of bacteria/viruses* per positive sample: PN*plus* Panel =2.15; SOC = 1.48

*Bacteria and viruses included in BioFire PN*plus* Panel

## TABLE 2: COMPARISON OF BIOFIRE PNplus PANEL VS SOC SEMI-QUANTIFICATION

Semi-quantification results for BioFire PN*plus* Panel and SOC bacteria were compared for 1,297 matched detections.

| | Total N | PNplus = SOC Value (%) | PNplus 1 lg > SOC (%) | PNplus 2 lg > SOC (%) | PNplus 3 lg > SOC (%) | PNplus 4 lg > SOC (%) | SOC 1 lg > PNplus (%) | SOC 2 lg > (%) | SOC 3 lg > PNplus > FA |
|---|---|---|---|---|---|---|---|---|---|
| All Samples | 1297 | 329 (25.37) | 477 (36.78) | 282 (21.74) | 123 (9.48) | 20 (1.54%) | 53 (4.09) | 8 (0.62) | 5 (0.39) |
| Total % | | 25.37 | | 58.52 | | 11.03 | | 5.91 | |
| Total % | | | | 69.55 | | | | | |
| BAL-Like Samples | 645 | 125 (19.38) | 213 (33.02) | 189 (29.30) | 74 (11.47) | 16 (2.48) | 24 (3.72) | 1 (0.16) | 3 (0.49) |
| | | | | 62.32 | | 13.95 | | | |
| Total % | | 19.38 | | 76.28 | | | | 4.34 | |
| Sputum-like Samples | 652 | 204 (31.29) | 264 (40.49) | 93 (14.26) | 49 (7.52) | 4 (0.61) | 29 (4.45) | 7 (1.07) | 2 (0.31) |
| Total % | | 31.92 | | 54.75 | | 8.13 | | 5.83 | |
| Total % | | | | 62.88 | | | | | |

Lg = log₁₀; For the majority of samples (69.55%) BioFire PN*plus* Panel quantified bacteria higher than SOC methods. 25.4% of samples were reported with comparable quantification between BioFire PN*plus* and SOC and only 5.9% were quantified higher by SOC than BioFire PN*plus* Panel.

## TABLE 3: DETECTION OF MSSA/MRSA BY BIOFIRE PNplus PANEL VS SOC

| | Total + (%) | No FA+ (%) | No SOC (%) | No SOC+/FA+ No (%) | No SOC-/FA+ No (%) | No SOC+/FA- No (%) |
|---|---|---|---|---|---|---|
| *Staphylococcus aureus* (Total) | 531 | 521 (98.12) | 313 (58.95) | 303 (57.06) | 218 (41.05) | 10 (1.88) |
| *Staphylococcus aureus* (MSSA) | | 412[a] | 269[b] | 234 | 178 | 11 |
| *Staphylococcus aureus* (MRSA) | | 106[b] | 47[a] | 45 | 59 | 0 |

Overall, BioFire PN*plus* Panel detected more MSSA and MRSA than SOC. (+) = positive; (-) = negative
[a]Two samples reported to contain MRSA by SOC were reported to contain MSSA by BioFire PN*plus* Panel
[b]24 samples reported to contain just MSSA by SOC were reported to contain MRSA by BioFire PN*plus* Panel

## TABLE 4: DETECTION OF ATYPICAL PATHOGENS BY BIOFIRE PNplus PANEL VS SOC

| Pathogen | PNplus | SOC^ | Total Detected | % Detection PNplus | % Detection SOC | P Value |
|---|---|---|---|---|---|---|
| *Chlamydia pneumoniae* | 7 | 4 | 7 | 100% | 57.14 | 0.193 |
| *Legionella pneumophila* | 49 | 49 | 55 | 89.09 | 89.09 | 1.00 |
| *Mycoplasma pneumoniae* | 37 | 20 | 41 | 90.24 | 48.78 | 0.0001 |
| Overall Detection Rate | 93 | 73 | 103 | 90.29 | 70.87 | <0.0001 |

^Limited SOC site testing for typical pathogens: culture, molecular testing and/or urinary antigen

## TABLE 5: DETECTION OF VIRAL PATHOGENS* BY BIOFIRE PNplus PANEL VS SOC

| Pathogen | PNplus | SOC^ | Total Detected | % Detection PNplus | % Detection SOC |
|---|---|---|---|---|---|
| Adenovirus | 44 | 4 | 45 | 97.78 | 8.89 |
| Coronavirus | 51 | 6 | 52 | 98.08 | 11.54 |
| Metapneumovirus | 10 | 6 | 11 | 90.91 | 54.55 |
| Rhinovirus/Enterovirus | 365 | 60 | 368 | 99.18 | 16.30 |
| Influenza A | 44 | 25 | 45 | 97.78 | 55.56 |
| Influenza B | 2 | 2 | 2 | 100.00 | 100.00 |
| Parainfluenza Virus | 63 | 19 | 68 | 92.65 | 27.94 |
| Respiratory Syncytial Virus | 39 | 12 | 40 | 97.50 | 30.00 |
| Overall Detection Rate | 618 | 134 | 631 | 97.94 | 21.24 |

^Viruses on BioFire PN*plus* Panel only. Percent detection does not reflect direct comparison of testing by PN*plus* and SOC. SOC low detection rate was due to limited or no viral testing by clinical sites. There were 24 additional SOC viral detections reported for viruses not on BioFire PN*plus* Panel: 10 CMV; 5 EBV; 6 HSV; 2 HHV-6; 1 VZV

## TABLE 6: CONCORDANCE BETWEEN BIOFIRE PNplus PANEL AND SOC (ALL SAMPLES)

| Concordance | Number Total= 2463 | Percentage (%) |
|---|---|---|
| Overall concordance | 1209 | 49.10 |
| Overall concordant positive | 665 | 27.00 |
| Concordant bacteria | 601 | 24.40 |
| Concordant bacteria and virus | 25 | 1.02 |
| Concordant virus | 39 | 1.58 |
| Concordant negative for any pathogen | 412 | 16.73 |
| Concordant negative for FilmArray pathogens | 132 | 5.36 |
| Partial concordance | 651 | 26.43 |
| No concordance | 603 | 24.48 |

**Overall concordance:** PN*plus* Panel and SOC in agreement for positive and negative samples
**Concordant positive:** PN*plus* Panel and SOC in agreement for all pathogens detected
**Concordant bacteria:** PN*plus* Panel and SOC in agreement for all bacteria detected
**Concordant bacteria and virus:** PN*plus* Panel and SOC in agreement for all bacteria and viruses
**Concordant virus:** PN*plus* Panel and SOC in agreement for all viruses detected
**Concordant negative for any pathogen:** PN*plus* Panel and SOC both negative
**Concordant negative for PN*plus* Panel pathogens:** PN*plus* Panel and SOC negative for pathogens on PN*plus* Panel (other pathogens may have been detected by SOC)
**Partial concordance:** PN*plus* Panel and SOC in agreement for some pathogens detected
**No concordance:** PN*plus* Panel and SOC not in agreement

## SUMMARY OF RESULTS

1. Overall, and in both sample types, BioFire PN*plus* Panel detected more potential bacterial pathogens and at a higher concentration than SOC.
2. Detection of viral pathogens was significantly higher for BioFire PN*plus* Panel as the majority of samples were not tested for these pathogens as part of their SOC testing. This highlights a missed opportunity to provide a more comprehensive and accurate diagnosis through a syndromic solution.
3. The combined detection of the three atypical pathogens was higher for BioFire PN*plus* Panel than SOC. With the exception of *Legionella*, this difference was mainly due to a lack of SOC testing.
4. The rapid and comprehensive detection of the cause of LRTI and antimicrobial resistance markers could lead to rapid initiation of targeted therapy.