



Adenovirus C Prevalence in BAL and Sputum Specimens

Introduction

In June 2021, BioFire Diagnostics issued a Medical Device Correction (FSCA 5183) due to an increased risk of false negative Adenovirus results using BioFire® FilmArray® Pneumonia Panel (Part No: RFIT-ASY-0144 and RFIT-ASY-0145) and BioFire® FilmArray® Pneumonia Panel *plus* (Part No: RFIT-ASY-0142 and RFIT-ASY-0143) within 6 months of expiration.

These potential Adenovirus false negatives are due to a 10-100x reduction in sensitivity, specifically for adenovirus species C, when using BioFire Pneumonia Panel/Pneumonia Panel *plus* kits within 6 months of expiration. This results in an estimated change in LoD (limit of detection) for adenovirus C from 7.5E+03 copies/mL to 7.5E+04 – 7.5E+05 copies/mL.

- The test performance is **NOT** impacted if kits are more than 6 months from expiration date.
- Performance for other adenovirus species (e.g. A, B, D, E, F, and G) is **NOT** affected.
- The adenovirus assays on all other BioFire® Respiratory Panels are **NOT** affected.

BioFire advises customers using a BioFire Pneumonia Panel/Pneumonia Panel *plus* kit that is within 6 months of expiration to confirm all negative Adenovirus results from patients suspected of adenovirus C infection via another method prior to reporting the result (e.g. retest specimens with a BioFire Pneumonia or Pneumonia Panel *plus* that is greater than 6 months from expiration or consider results from testing a nasopharyngeal swab with a different BioFire respiratory panel such as the BioFire® Respiratory Panel 2.1 (RP2.1) or BioFire® Respiratory Panel 2.1 *plus* (RP2.1*plus*)), or alternatively, that the BioFire Pneumonia Panel/Pneumonia Panel *plus* Adenovirus negative result should not be reported.

In response to this communication, customers have asked for guidance on the prevalence of (or expected values for) adenovirus C among patients tested with the BioFire Pneumonia Panel/Pneumonia Panel *plus* tests. The purpose of this technical note is to provide a summary of information that may be useful to answer this question.

Adenovirus Prevalence

Adenoviruses are double-stranded DNA viruses most commonly associated with self-limiting respiratory, gastrointestinal, and conjunctival disease, but infections can lead to severe disseminated illness in immunocompromised patients. There are seven species (A through G) and 52 distinct serotypes. Most human adenovirus circulate globally, but predominant types and species differ between countries or geographic regions, and they change over time.¹⁻³

Adenovirus species A, B, C, and F are associated with disseminated disease in immunocompromised patients,⁴ with a strong predominance of species C (reviewed in Lion et al.³). According to a US CDC surveillance study the most commonly reported adenovirus species in the US from 2003–2016 were B, C, and E.¹ This surveillance study monitored many specimen types, but the most commonly reported specimen type was respiratory specimens (82.0% of specimens) and species C was the most commonly reported species (41% overall), followed by species



B (40% overall) during the 13-year period. Surveillance data from other countries/regions (reviewed by Lynch et al.^{5,6}) indicates similar prevalence of adenovirus B, C, and E in respiratory infections around the world.

A prospective clinical evaluation of the BioFire Pneumonia Panel/Pneumonia Panel *plus* was conducted from October 2016 to July 2017 at eight US sites⁷ to generate performance data for the product Instructions for Use. Performance of the BioFire Pneumonia Panel/Pneumonia Panel *plus* Adenovirus assay result was determined by comparison to two independent PCR assays that included sequence analysis: one assay targeted the *pol* gene (encoding DNA polymerase) and the other assay targeted the *penton* gene (encoding a major capsid protein). A review of this sequence data reveals the species of adenovirus that were observed in the study. Table 1 and Table 2 below are modifications of the Expected Values tables (Table 7 to Table 12 in the product Instructions for Use) that are expanded to include the adenovirus species information. In this study, the overall prevalence of adenovirus was 0.9% (8/845) in BAL and 1.6% (13/834) in sputum, and the most common species of adenovirus in both specimen types was B (5 and 7 in BAL and sputum, respectively), followed by C (2 and 6 in BAL and sputum, respectively). One BAL specimen had adenovirus species F. No other adenovirus species were observed.

Table 1. Expected Value (As Determined by BioFire Pneumonia Panel/Pneumonia Panel *plus*) Summary for BAL Specimens, Stratified by Age, for the BioFire Pneumonia Panel/Pneumonia Panel *plus* Prospective Clinical Evaluation (October 2016 to July 2017)

BAL												
Overall												
Adenovirus Result	Total (N=845) ^{a,b}		≤5 (N=23)		6-17 (N=27)		18-34 (N=70)		35-65 (N=469)		>65 (N=255)	
	#	EV	#	EV	#	EV	#	EV	#	EV	#	EV
Adenovirus (<i>all</i>)	8	0.9%	1	4.3%	0	0%	1	1.4%	5	1.1%	1	0.4%
Adenovirus B	5	0.6%	0	0%	0	0%	0	0%	4	0.9%	1	0.4%
Adenovirus C	2	0.2%	1	4.3%	0	0%	1	1.4%	0	0%	0	0%
Adenovirus F	1	0.1%	0	0%	0	0%	0	0%	1	0.2%	0	0%

^a One of the 846 enrolled BAL specimens was excluded for Adenovirus comparator result

^b Age unknown for one BAL specimen

Table 2. Expected Value (As Determined by BioFire Pneumonia Panel/Pneumonia Panel *plus*) Summary for Sputum Specimens, Stratified by Age for the BioFire Pneumonia Panel/Pneumonia Panel *plus* Prospective Clinical Evaluation (October 2016 to July 2017)

Sputum												
Overall												
Adenovirus Result	Total (N=834) ^a		≤5 (N=137)		6-17 (N=107)		18-34 (N=86)		35-65 (N=284)		>65 (N=220)	
	#	EV	#	EV	#	EV	#	EV	#	EV	#	EV
Adenovirus (<i>all</i>)	13	1.6%	3	2.2%	2	1.9%	1	1.2%	5	1.8%	2	0.9%
Adenovirus B	7	0.8%	1	0.7%	2	1.9%	1	1.2%	2	0.7%	1	0.5%
Adenovirus C	6	0.7%	2	1.5%	0	0%	0	0%	3	1.1%	1	0.5%

^a Two of the 836 enrolled Sputum specimens were excluded for Adenovirus comparator result

Conclusions

- BioFire has identified an increased risk of false negative Adenovirus results using BioFire Pneumonia Panel/Pneumonia Panel *plus* within 6 months of expiration.



- These potential Adenovirus false negative results are due to a 10-100x reduction in sensitivity, specifically for adenovirus species C when using all BioFire Pneumonia Panel kits within 6 months of expiration.
- The test performance is **NOT** impacted if kits are more than 6 months from expiration date.
- Immunocompromised persons are at risk for disseminated disease and severe illness when infected with adenovirus C.
- Globally, studies suggest that adenovirus B, C and E are the most common adenovirus species reported in respiratory infections.
- The overall prevalence of adenovirus in the BioFire Pneumonia Panel/Pneumonia Panel *plus* clinical evaluation was 0.9% (8/845) in BAL and 1.6% (13/834) in sputum; the prevalence of adenovirus species C was 0.2% (2/845) in BAL and 0.7% (6/834) in sputum. Adenovirus species C represented 25% (2/8) of adenovirus observed in BAL and 46% (6/13) of adenovirus observed in sputum.

Additional Information

BioFire® Syndromic Trends (Trend; <https://syndromictrends.com/>) is a website displaying trends for various pathogens using anonymized, aggregated data generated in real time by participating BioFire customers.⁸ At the time of his writing, the Trend website displays data from US sites for BioFire® FilmArray® Respiratory Panel, BioFire® FilmArray® Respiratory Panel 2 (RP2), and BioFire RP2.1, which include assays for detection of adenovirus from nasopharyngeal swab specimens. Therefore, Trend may be a resource for monitoring real-time adenovirus prevalence in the US population.

References

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Technical Support Contact Information

BioFire is dedicated to providing the best customer support available. If you have any questions or concerns about this process, please contact the BioFire Technical Support team for assistance.

BioFire Technical Support
Email: support@biofiredx.com
Phone: +1-801-736-6354, select Option 5