CASE STUDY

Improving spirometry data integrity: The collaborative role of AI-enabled signal detection and independent clinical review

A KEY QUESTION

How can a CRO support a biotech's AI-enabled anomaly detection and help enable clinical assessment, data verification and targeted risk mitigation?

KEYWORDS

Biotech, Phase III Global Clinical Trial, COPD Studies, Respiratory, Spirometry, Artificial Intelligence (AI) Analysis, Data Integrity, Independent Data Review

Fortrea was supporting a biotech sponsor in its Phase III global clinical trial for chronic obstructive pulmonary disease (COPD). With three studies, each enrolling more than 3,000 participants, the sponsor wanted to evaluate its initial spirometry study data by piloting a third-party AI tool.

The AI-supported analysis identified an unexpected concentration of spirometry curves that appeared inconsistent with physiologically credible testing. This initial review highlighted one U.S. site with potential technical errors and eligibility concerns across nine participants.

Given that the findings extended beyond what would typically be apparent from individual spirometry assessments, the sponsor requested independent reviews by both Fortrea and an independent respiratory quality-review vendor.

This case study shares how Fortrea:

1. **Engaged its internal medical and respiratory specialists** to interpret the pattern detected by the sponsor's third-party AI tool
2. **Performed a thorough medical review and clinical assessment** of the underlying clinical and source data across participants, sites and studies
3. **Took appropriate action** to mitigate risk, modify operations, protect endpoints and enhance data quality

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Understanding the challenge

Traditional spirometry quality control focuses primarily on the technical acceptability and repeatability of individual tests against protocol-defined requirements. It does not routinely assess patterns across participants, sites or studies.

The sponsor's AI-supported findings raised a broader set of challenges that went beyond a single test or site.

Some tests were considered acceptable through routine review, but cross-participant analysis revealed unusual patterns and limited variability.

An investigation was needed to determine whether the AI tool's findings could be explained by participant effort, coaching, technician technique or other legitimate factors. The sponsor also wanted to know if potential data integrity concerns warranted required escalation and broader study-level action.

Conducting an independent medical and respiratory review

The sponsor requested independent reviews by Fortrea and the independent respiratory quality-review vendor to provide an independent medical and respiratory assessment and help examine their shared concerns.

Concerns	Fortrea's plan
Eligibility and duplication	Examine the potential inclusion of ineligible participants or duplication of participants
Endpoint integrity	Review questionable spirometry measurements affecting endpoint analyses and identify potential sources of variability
Data reliability	Assess the reliability of assessments considered acceptable through standard quality check processes and determine whether the flagged findings were medically and clinically credible
Study validity	Determine the potential impact on study validity and confidence in the data
Scope of risk	Evaluate whether the concerns are isolated to spirometry or extended to other aspects of study conduct and decide if further investigation is needed

Fortrea's review incorporated spirometry data alongside relevant clinical information, including medical history, laboratory results, ECG findings, concomitant medications and spirometry records. Fortrea also conducted targeted site discussions, engaging site staff and principal investigators to explore potential explanations for the observed spirometry patterns.

The team reviewed the subjects and spirometry loops that were identified through the AI-supported analysis, including the associated standard quality checks and clinical data. They conducted within-subject and cross-subject comparisons and assessed patterns across sites and studies.

Key findings from the medical and respiratory assessment

Initially, Fortrea focused on one U.S. site and then expanded to more than eight sites, including sites participating across multiple studies. Eight out of the nine sites were from a single metropolitan area, a geographic clustering that reinforced the need for cross-site analysis.

Within this targeted, high-risk subset of sites, Fortrea found that:

- **121 of 273** measurements reviewed **(44%)** from **79** subjects were considered questionable
- **61 (22%)** measurement findings were suggestive of using a calibration syringe, a device used to check that a spirometer is measuring airflow correctly
- **14** subjects from the flagged sites were still enrolled and actively participating in the study despite uncertainty about whether they genuinely existed or had COPD

Both Fortrea and the respiratory quality-review vendor reached consistent conclusions: They identified measurements suggestive of calibration syringe use and determined that a substantial proportion of measurements at one site might not represent distinct participant assessments.

Implementing operational changes

The findings led to targeted operational actions and study oversight activities, including:

- **Strengthening site controls:** Recruitment or enrollment was paused at selected sites and sites were retrained as needed
- **Reinforcing participant verification:** Requests were made to confirm participant existence, review historical pulmonary function test records and check source documentation
- **Increasing site oversight:** Additional site investigations, CRA visits and direct observation of spirometry procedures and technician performance were carried out
- **Enhancing clinical corroboration:** The team reviewed medical history, informed consent forms, laboratory results and ECGs and expanded the review across additional sites and studies

These activities enabled the sponsor and study teams to move beyond anomaly detection to clinical assessment, source verification and targeted risk mitigation.

Recognizing the impact

273	79	121	61	8
Measurements evaluated	Subjects reviewed	Measurements flagged	Measurements associated with a calibration syringe	Sites flagged from the same metropolitan area

The investigations strengthened study oversight, helped address several challenges and offered:

- **Protected endpoint integrity:** Participant eligibility was investigated through clinical records and source documentation, while questionable spirometry was assessed for potential impact on efficacy analyses
- **Enhanced data quality:** Patterns that may not have been apparent through conventional review of individual tests were now investigated across participants, sites and studies
- **Delivered greater data confidence:** Independent medical review provided clinical corroboration of the signals identified through AI-supported analysis and helped guide appropriate operational responses

The investigation also demonstrated the complementary value of technology and clinical experience. AI provided an initial signal for investigation, while medical and respiratory specialists interpreted that signal in its clinical and operational context and implemented appropriate actions.

Looking ahead

Working closely with the sponsor, Fortrea highlighted the value of combining the sponsor's third-party AI-enabled surveillance with medical review. For future respiratory studies, a proactive strategy could incorporate:

- AI-supported surveillance of spirometry data followed by an assessment with medical monitors and respiratory vendor specialists
- Cross-participant and cross-site pattern analysis along with cross-study review of sites that participate in multiple studies
- Review of historical pulmonary function data where concerns arise and defined escalation pathways for unusual data patterns
- Targeted investigation and retraining based on identified risk signals

In this case, the combination of sponsor-led AI signal detection, independent CRO medical review, respiratory experience and targeted operational follow-up provided a framework for protecting endpoint integrity, strengthening study oversight and increasing confidence in the reliability of the sponsor's study data.

As AI continues to transform clinical trial oversight, independent clinical strengths remain critical to turning signals into informed action. Explore how Fortrea helps sponsors strengthen data integrity and protect endpoint integrity.

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