STANDING OUR GROUND FOR YOUR DATA QUALITY

Nasal Secretion ECP Assay Validation

Eosinophil cationic protein (ECP) is a biomarker sometimes used to assess levels of inflammation or allergic response in various body tissues. It may be used as a screening or effectiveness marker in clinical trials such as those for asthma or other immune-mediated inflammatory diseases. Assays for ECP can be done on a variety of sample types. Since ECP assays are not common enough to be run in-house at Covance Central Laboratory Services (CLS), these assays are sent to an external laboratory. On one occasion, a clinical trial sponsor requested that we use a specific laboratory to perform ECP assays on nasal secretions. The Covance Expanded Laboratory Management Solutions (ELMS) team uncovered problems with the validation and some of the subsequent trial data, and then worked closely with the sponsor and external laboratory to ensure any data reported would be valid and stand up to regulatory scrutiny as part of an FDA submission.

Understanding the Challenge

- The referral laboratory utilized a kit that had been validated for a sample type different from the nasal secretions collected in this trial
- The new specimen type necessitated a complete revalidation of the assay to ensure data quality and consistency; however, initially this was only partially done
- As a consequence, positive/negative criteria were not properly validated and the lower limit of quantitation (LLOQ) was improperly validated; as a result, a significant amount of data were returned to us with values below the LLOQ, meaning those data points were obviously invalid and would be a red flag for any regulatory review
- Sponsor scientists, who do not routinely oversee external clinical laboratory validations, did not immediately understand the challenges this presented and were unaware of the threat this situation posed to their drug development program

Resourceful Review Preserves Data Integrity

The Covance global ELMS team comprises approximately twenty staff members dedicated to ensuring that testing conducted outside of Covance is performed according to specifications and meets the stringent regulatory scrutiny applicable to clinical trial testing. Covance CLS operates according to the ISO 15189:2012 standard and has already obtained this accreditation for several of our laboratories. Part of this standard includes a high level of operational oversight of external laboratories to ensure that assays are properly validated and data returned to us are consistent with such validations.

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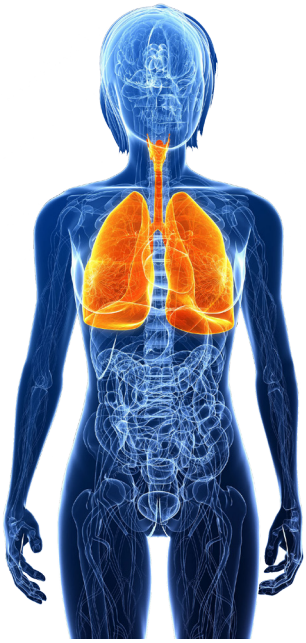
Upon reviewing the external laboratory's validation report, we identified that the validation was insufficient to accommodate change of sample type, that data were in some cases below the LLOQ and the data lacked proper positive/negative results. The clinical scientific team initially wanted us to just pass through the data from the external laboratory, including the invalid data points that were below the LLOQ, despite the problems we had found. Working with the sponsor's Quality Assurance team, we educated the sponsor's scientific team on what was necessary for data compliance and ensured that no compromised data would be included in the clinical trial data package. The sponsor was able to proceed to data lock by using only those data points that were valid, which we were able to include in our database and provide as part of the trial database.

This example clearly demonstrates the value that ELMS brings to studies where external laboratories are used. Under the prior model, Covance would have simply sent samples to the laboratory and passed the data back to the sponsor, without oversight of the validation or the data that came from the laboratory. The clinical trial data package would not have survived regulatory scrutiny and the entire clinical trial may have been invalidated.

Managing external laboratories is a time-consuming process, and is difficult to do part-time by sponsor clinical trial scientists, biomarker scientists or program managers. There are strong economies of scale that come into play when the external laboratories are managed full-time by the central laboratory attached to the study. The identification and resolution of the problem with this assay's data involved not only the ELMS team, but also the dedicated contributions of our laboratory immunology director and associate director, senior director of medical affairs, our quality assurance staff and the project management staff handling the study. Had the problem not been uncovered, not only would the sponsor be at risk of having to re-run the trial—at considerable expense—but also the delay in advancing the drug candidate to its next milestone may have been enough to undermine the entire program.



Working with Covance, you can rest assured that all of your testing will be performed to the highest standard, no matter where the testing occurs.

Learn more about how ELMS can help you reduce your external lab management costs at **www.covance.com/elms**

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