STRAND DIAGNOSTICS
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DNA Testing Confirms Presence of Sampling Fraud in Infectious Disease Study

BACKGROUND

A large, global pharmaceutical company was conducting an infectious disease study overseas. Investigators had become suspicious of fraudulent specimen collection due to multiple instances wherein specimens identified as coming from distinct individuals appeared to be from a common donor. To definitively establish whether or not fraud had occurred, the company ordered DNA Specimen Provenance Assignment (DSPA) testing to determine how many unique individuals' genetic profiles were present among the suspicious specimens.

MATERIALS AND METHODS:

Suspicious blood samples from the study were submitted to Strand for DNA Specimen Provenance Assignment ("DSPA") testing. DSPA employs Short Tandem Repeat ("STR") analysis originally developed by the forensics community and often referred to as "genetic fingerprinting." The technique examines a panel of 16 microsatellite markers representing highly variable loci on the human genome. The collective STR profiles from these loci constitute a genetic "fingerprint" which can uniquely identify an individual with precision exceeding 99.99%.

RESULTS:

Of the 42 blood samples submitted for DNA testing only 18 unique individuals' profiles were present, confirming that the actual subject population was much smaller than the fraudulently inflated population reported by the enrollment site. Had this irregularity gone undetected, the integrity of the study might have been significantly compromised. Early identification of the fraud enabled the study sponsor to exclude these samples from the data set and take corrective action to preserve the validity and integrity of study results. Had the problem not been identified, study results may have led to invalid conclusions with significant financial and clinical ramifications.

It is important to note that suspicion of fraudulent activity was only raised in this case due to investigators' astute observation of common chemical traits unique to the specific trial protocol, which implied that allegedly disparate samples were from a common donor. In the vast majority of trial settings, routine lab testing would not have detected such patterns. The sampling error would have been completely unknown to the investigators, leading to incorrect study conclusions of potentially drastic consequence.

CONCLUSIONS:

It is well known that complications involving specimen transposition and contamination are inherent across all clinical settings, impacting as many as 3% of cases in tissue histopathology specifically.[1] Specimen handling in the research and clinical trial context carries these same risks, plus the added risk of fraudulent activity related to data representation and/or specimen acquisition. Whether the root cause is intrinsic handling errors or deliberate fraud, these complications are typically impossible to detect other than through DSPA testing. This case presents one representative example of the fraud risk which pervades clinical trials, but has historically been tolerated by the research community given the lack of available methods to identify and mitigate this risk. However, recent advances in the

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availability of cost effective and timely DSPA testing protocols available mean that investigators now have a viable tool to completely eliminate specimen provenance ambiguity from the research paradigm. Prospective DSPA testing through the **know error® system** is quickly becoming the new standard of care for diagnosing patients with cancer in a variety of specialty areas, as the imprecision inherent in those testing cycles is no longer considered acceptable by physicians who now demand identity verification before rendering treatment to patients. For precisely the same reasons and more (fraud risk), investigators and regulators should consider study results achieved without DSPA testing to be potentially suspect.

The average cost to obtain approval for a major pharmaceutical compound exceeds $4 billion, and in some cases can be well over $11 billion. A single clinical trial can cost as much as $100 million, with many trials required in order to yield a single approved drug.[2] Considering the magnitude of societal benefit and financial investment which hinges upon the accuracy of study data, the potential implications of compromised data due to undetected specimen provenance complications cannot be overstated. Multi-billion dollar decisions with the potential to impact millions of lives demand data which embody the highest degree of accuracy and integrity available to science. Investigators should consider that the modest marginal cost of adding prospective DNA testing via the **know error® system** to a study protocol is readily justified given the ramifications of an invalid study conclusion resulting from preventable specimen provenance complications including fraud.

1. Pfeifer JD, Zehnbauer B, Payton J. The changing spectrum of DNA-based specimen provenance testing in surgical pathology. *Am J Clin Pathol.* 2011;135:132-138.

2. Herper M. The truly staggering cost of inventing new drugs. Forbes.com. www.forbes.com/sites/matthewherper/2012/02/10/the-truly-staggering-cost-of-inventing-new-drugs/. Published February 2, 2012. Accessed June 21, 2012.