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EDITORIAL

Why is There a Problem with Data Integrity?

Data Integrity—it sounds so simple. Data should have integrity; we should be able to trust data.

However, for some reason the integrity of data is a problem. The recent examples relate to testing results for production of pharmaceuticals. So right now it is a "GMP" problem. Perhaps the larger question, though, is that integrity of data is an even larger problem than GMPs.

In the GLPs (Good Laboratory Practices), responsibility for the integrity of data is identified for the:

- Study Director (21 CFR 58.33)

- Quality Assurance Unit (21 CFR 58.35)

- Computer Systems (21 CFR 58.62)

- SOP Evaluation (21 CFR 58.81)

Among others to assure that data is handled properly with integrity and quality. Further, FDA investigators are instructed in the GLP manual to conduct a data audit to ensure that data are attributable, legible, contemporaneous, original and accurate. Representative samples of raw data are audited against the final report. A representative number of animals from selected groups are traced from receipt through final histopathological examination.

The reason for this level of requirements and scrutiny for the GLPs was due to a crisis in data integrity in this area. A notable problem is what I will call the "Lazarus" Animals, where an animal that is part of a GLP study is having data recorded regularly as part of the study. At some point, the animal dies and data recordings stop, and only an animal with the same identification number for the study begins to contribute data later in the study. Irregularities were found at the Industrial Bio-Test Laboratory by the U.S. FDA in 1976 that included these problems contribute to the finding that a "Lazarus" animal is not only an affront to data integrity, but to scientific procedure. Does this happen many times? No—The vast majority of studies are conducted by scientists with good ethics, but unfortunately there have been enough instances for the problem to result in changes to the regulations.

Might there have been a similar problem in GCPs (Good Clinical Practices)?

In the GCPs, there is a process that applies to the drug, device, and veterinary medicine regulations where a clinical investigator will be "disqualified" by the U.S. FDA when it has been found that they have "submitted to the sponsor false information in any required report" (21 CFR 312.70, for CDER).

Here a notable problem is what I will call "Alphabet Soup" patients. Clinical investigators are paid for each patient they enroll and follow in a clinical study. In a few cases, a patient is enrolled in the study—we'll call the patient "ABC" because the initials are usually the only identifier provided to the clinical study sponsor. However, sometime later, as other patients are enrolled, a patient is enrolled whose initials are "BCA" then later becomes a patient whose initials are "CAB." The patient data on these patients is remarkably similar. These are the "Alphabet Soup" patients—really the same patient with duplicated records and whose initials are scrambled. Such duplications are not only an affront to data integrity, but a fraud. Examples exist dating back to 1963. (2) Does this happen many times? No—again the vast majority of studies are conducted by healthcare professionals with good ethics, but there have been enough instances for the problem to result in changes to the regulations.

Coming back to GMPs, every major pharmaceutical/biopharmaceutical company conducts GLP studies and GCP studies, and produces product under the GMPs (or they are responsible for contractors who perform the work for them?). Therefore, it would behoove us to take a step back and look at data integrity in a more holistic manner, understanding it is not just a GMP problem confronting us now.

A way to address data integrity holistically is to assure that the culture of quality in the organization is healthy. If it is not, then the culture needs to change. It might sound old, but it still rings true: Quality is

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everyone's job, not just the role of the members of the Quality Unit. When I led a production group, I wanted to imbue the image of the patient who would be taking the product onto the employees so they would have a quality perspective. For the younger people, I would say, "Make every dose as if your mother was going to take it." To reinforce the point, I would continue by saying, "And it's your mother we are speaking about, not your mother-in-law." For older employees, to make that quality connection, I suggest that the dose might be for a grandson or niece. The scenario is realistic; we were making products used as adjuncts to anesthesia.

The point is, for data integrity to be assured then everyone responsible for the data needs to be part of the quality culture. If those people could identify with the patient, the commitment to quality would likely follow. Merck & Co. posts pictures of infants born to employees receiving their RotaTeq™ oral vaccine. PDA has patients speak of their personal experiences at the annual meetings. These are a start, but it is crucial that every employee, technician, clerk, and analyst has the opportunity to connect with the patients to have them understand the importance of what they do and the impact that a failure to maintain data integrity might have.

1. Foster, Doug; "Industrial Bio-Test Lab's Dirty Research," Oakland Tribune, December 6, 1983. Retrieved from the Center for Investigative Reporting May 9, 2017.

2. Onofrietti, Tony; "Case Studies in Research Misconduct," The University of Utah, Presentation made at the University of Alabama (Huntsville) September 15, 2011. Retrieved from Google search May 9, 2011.

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