



OECD Principles of GLP: What is Working and What Needs Work

CT. Viswanathan, Ph.D.

U.S. Food and Drug Administration
Silver Spring, Maryland USA
ct.viswanathan@fda.hhs.gov



- Starting Point

- Regulatory agencies assess nonclinical safety data first to understand human safety.



- Data quality is key
 - For the protection of human subject safety, assessments must be made with robust and reliable safety data.



- OECD Principles of GLP
 - Facilitates data quality and integrity
 - A good foundation and infrastructure in place
 - Result of exceptional teamwork



- What is working well ?

Many Areas are....



- Robust consensus document for multi-site study conduct
 - addressed a defined trend in study conduct
 - recognized increased complexity of study design and management, risk to study integrity
 - established the need for clear lines of communication between all involved parties



- Are there opportunities for optimization?
 - Considerations
 - Inspectional cases



- Case 1: Reprotoxicity studies found unusually low incidence of spontaneous variations, malformations
 - In both control and treated animals
 - Concern regarding observational sensitivity
 - Abnormality rate reported to FDA 0.15%
 - Published, spontaneous abnormality rate 4.3-7.2%



- Inspection found
 - Study personnel with less training than counterparts at other facilities
 - No explanation for low reported rate of thoracic and abdominal abnormalities reported



- More than 100 studies unreliable for review purposes
 - If no inspection, having accepted numerous flawed studies, how are the safety assessments valid in preparing for human exposure?
- What could be done to assure appropriate controls and prevent multiple applications from being rejected?



- Case 2: Findings and conclusions of expert pathologist not documented
- Inspection found
 - Signed and dated histopathology report not archived



- Conclusions of the expert scientists involved with the study can significantly affect assessment of human safety.
- What could be done to maintain the transparency of expert scientist contributions?



- Case 3: No confirmation that the intended dose was the actual dose administered
 - Dosing formulation testing for concentration, uniformity, and stability can be further strengthened
 - Test article characterization data not obtained from sponsor
 - Dose formulation concentration reported separately by sponsor; not provided to study director for evaluation



- Study directors sometimes lack the results necessary for a meaningful assessment of study outcomes.
 - Without assuring the actual dose, how can conclusions be drawn regarding toxicity, or the lack thereof, at a given dose?
- What could be done to highlight the central role of the study director and emphasize the criticality of dosing formulation results?



- In conclusion
 - Accountability is critical to generating robust data and reliable study outcomes.
 - Optimizing the existing GLP infrastructure, where necessary, can be worthwhile.
 - Opportunities to optimize data quality and integrity are welcome advancements.