The use of Digital Pathology for GLP compliant Primary Pathology Evaluation and Peer Review

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GLP implications for WSI use

• No specific regulatory guidance on WSI use for GLP studies
• 2020 OECD update to GLP FAQs did not preclude the use of digitised histopathology slides in GLP studies
  • WSI should be a ‘faithful replica’ of the original slide
  • Evaluation of WSI should be ‘equivalent’ to glass slides
  • The concept of digitised ‘slide integrity’ and the need for validation of all laboratory instruments (scanners) and IT systems used through the entire workflow
  • Only WSI that contribute to raw data need archiving
  • The usual principles that underpin GLP are followed
What do WSI represent in GLP?

**Specimens**
- Specimen means any material derived from a test system (animal) for examination or analysis
- Specimens are archived

**WSI files**
- Don’t meet the definition of specimens
- Don’t meet the definition of raw data
- Not considered ‘true copies’ of slides
- ‘Faithful representation of a glass slide’

Broad consensus that only WSI that contribute to raw data generation require archiving
OECD FAQ - Equivalence and Faithful Replica

**Faithful replica**

- The WSI as a ‘copy’ of the glass slide
- Acceptable Colour, Resolution, Focus
- Must include ‘Human Readable’ data from the original slide label and ability to see all tissues present on the original slide
- All of the above features adequately maintained throughout the workflow = ‘digitised slide integrity’

**Equivalence**

- Software and hardware that produces an ‘equivalent’ experience as a microscope
- Emphasis on functionality?
- How much functionality is equivalent?
Validation of the Digital Pathology Workflow

- Workflow uses Leica and Deciphex digital pathology platforms
- Study pathologist evaluates WSI from CRL server using Leica based platform
- Images encrypted at CRL by Deciphex platform and uploaded to Patholytix cloud
- Peer review pathologist downloads the images and reviews using the Deciphex platform
GLP Validation

• No specific guidance for GLP Validation – follow established process at each GLP footprint
  • Quality assurance audit of vendor/s
  • Where the workflow is split between CRO/Sponsor: Quality assurance audit of each parties approach
  • Process map for all components of workflow
  • Define use case and user requirements
  • Validation plan
  • User acceptance testing
  • Validation report
• Higher degree of risk for primary histopathology evaluation using WSI that contributes to raw data
Learning from the validation process

• Pathologists need to be able to explain the unique nuances of WSI to validation team members (IT, QA)
  • *These nuances often dictate the key risks and mitigation strategies*

• Close cooperation and trust required when WSI workflow split between CRO and Sponsor

• Provision for SOP driven image quality control checks as part of study conduct

• An experienced pathologist is the best judge of WSI faithful reproduction and equivalence – precedent set by a lack of validation protocols for light microscopes
Thank you.
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