CPIM, June 15, 2022

Use of DP in the regulated nonclinical environment

Information to Plcc steering committee

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On behalf of BigPicture WP5

Foreword

Background

While many companies have already undertaken efforts to transition to digital pathology in the regulated GLP environment, the regulatory framework and expectations are not completely laid out.

Collaborating with health authorities in order to precise areas of uncertainty will allow for an accelerated transition and access to the advantages linked to digital pathology

Expected outcome

Regulatory: better defining expectations and providing opinions on means to achieve these will encourage companies to invest in this transition with limited regulatory risks, and will speed-up the successful development of digital pathology in the nonclinical area

R&D: digital pathology in the GLP environment offers advantages in terms of speed and accuracy, reduces the need and risks around specimen shipments, and opens the way to get immediate access to historical data and increase accuracy of diagnoses. Looking forward, this first step will pave the way for artificial intelligence developments in that field.

Regulatory background applicable to Toxicologic Pathology

- Differences between clinical and nonclinical pathology
- GLP categorization of the different WSI components: notions of specimens / raw data / faithful reproduction (faithful replica)

- (1) Use of DP in the context of informal consultations
- (2) Use of digitized slides in a way that they become essential to the generation of raw data and thus reconstruction of the study report
- Primary evaluation vs peer review

- General (technical) requirements for WSI
- WSI system GLP validation recommendations

- Storage and archiving

Discussion items for the CPIM discussion

- Whole slide imaging systems do not need to be approved/cleared as a medical device for GLP-compliant nonclinical use. Instead, an institutional 'fit for purpose' validation can be performed as published in the toxicologic pathology field.
- Should WSI, when generated by a validated system, be categorized as a faithful replica of the glass slide and be used to prepare and modify the pathology report to support regulatory decision making?
- Copies of WSI generated by softwares and the risk of loss due to compression or transformation of the original WSI into a proprietary format are acceptable as long as the end-to-end evaluation has demonstrated that a faithful representation of the originator glass slide can still be observed on the screen following subsequent image formats
- Fit for purpose validation can be achieved by running a non-inferiority/concordance study in the institution, as an inter-laboratorial approach, or as a study performed by the vendor
- Formal GLP documentation is not necessary when used for contemporaneous peer review or informal consultation
- If the end-to-end evaluation has demonstrated that a faithful representation of the originator glass slide can be observed on the screen after retrieving data from archives, there is no need to archive previous intermediate images generated in different format for viewing, mining or other purposes
- Is "on premise" (physically amenable to inspection) archiving required?

Inclusion of attendees in a listen-only mode

- Option for a limited number of BigPicture EFPIA partners
- Option for a limited number of interested PIcc members

=> These are being proposed to the FDA meeting manager.

Back-up slides

Background and objectives of the consortium

As part of establishing a regulatory dialogue, BigPicture conducted a review of the current regulatory standards within the GLP environment for whole slide image and AI use in nonclinical studies.

This review highlighted unclear areas that would benefit from deeper discussions with HAs.

Objectives:

- *anticipate regulatory requirements applicable to the Bigpicture beneficiaries*
- *share perspective re: nonclinical data collection, management and use*
- *secure implementation of Digital Pathology across the industry*
- *disseminate best practices*
- *favor further regulatory acceptance*

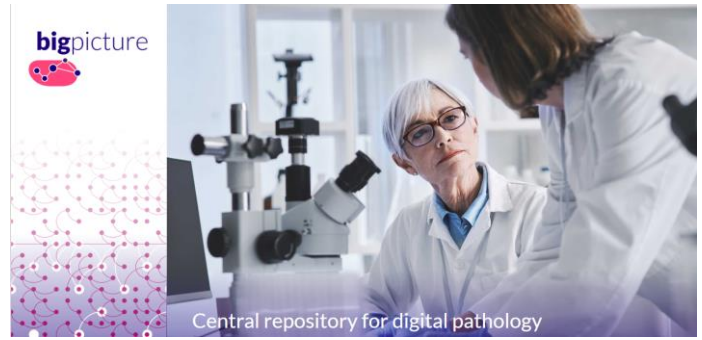
Potential outcome:

- *White Paper?*

Overview of IMI BigPicture consortium

innovative medicines initiative

IMI2-18 Central repository of digital pathology slides to support the development of artificial intelligence tools



Budget € 70 M — 6 years

Infrastructure 4.5 PBytes (WP2)

Data digital slides (WP3)

- 2 Mio non-clinical = Tox — in-kind
- 1 Mio clinical = largest collection ever (oncological and non-oncol.)

Tools access, analysis, models (WP4)

Regulations acceptance, usage sharing (WP5)

- EMA, FDA

Sustainability platform (WP6)