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WHITE PAPER PURPOSE AND SCOPE

- PHUSE WP061 published in December 2021 based on discussions within the Safety Analytics Working Group at the 2020 PHUSE CSS Conference
- Provide recommendations and justification for listings to include/exclude in eCTD CSR Sections 14 and 16 and regulatory submissions
- Provide example alternatives to static listings
- Scope
 - Phase 2-4 clinical trials and regulatory submissions
 - Focus mainly on Section 16 general study data listings

RECOMMENDATIONS

- Stop routinely producing complete data listings for CSRs and regulatory filings
 - Regulatory guidance from EMA requires only two participant data listings (protocol deviations and serious AEs)
 - FDA, PMDA (Japan) and NMPA (China) all receive clinical study data in electronic format and have their own tools for reviewing data, and EMA is starting to investigate data review tools
- Consult with applicable regulatory agencies about the need for listings before automatically producing them
- Adopt interactive data review tools for internal use



DEFINITIONS

- **Static listing** – A listing that is created without any interactive features, to be viewed in its entirety on one or more pages
 - Example: RTF or PDF file displaying data collected for a study
- **Interactive listing** – A listing that allows point-and-click technology and/or scroll bars to view the data
 - Examples: data visualization tools that allow a user to combine data from different sources, filter on specific conditions, and sort and drill down through multiple levels; spreadsheets containing downloads of study data for internal use

DATA INTEGRITY

- Maintaining the integrity of source datasets, when using interactive displays within the review tool, is critically important
- Incorporate validation procedures into company policy, ensuring traceability and restriction of access only to users who are authorized to see the data
- Prevent modification of source data via review tools
- Establish policy to restrict exporting of processed data or reports created by review tools

STATIC LISTING DRAWBACKS

- Inefficient to review, especially when they are hundreds of pages long
- Challenging to string separate pieces of data together when working with multiple listings
- Any listings required for further data exploration (e.g., subsetting, drilling down, individual profiling) need additional statistical programming, and are not readily produced by the user/reviewer



IMPACT ON INTERNAL PROCESSES

- Reference datasets instead of listings for internal QC and validation of any internal tools and ensure that the datasets are accessible
- Include the data cutoff date in references
- Reference participant-level datasets in in-text tables with a footnote
- Develop processes for writing narratives for patients meeting specific criteria that pull directly from study data or can be based on interactive visualizations
- Provide internal operational listings (investigator information, randomization, study lot numbers) directly from internal operations groups as supplemental files or static listings, if required

MAIN DRIVERS

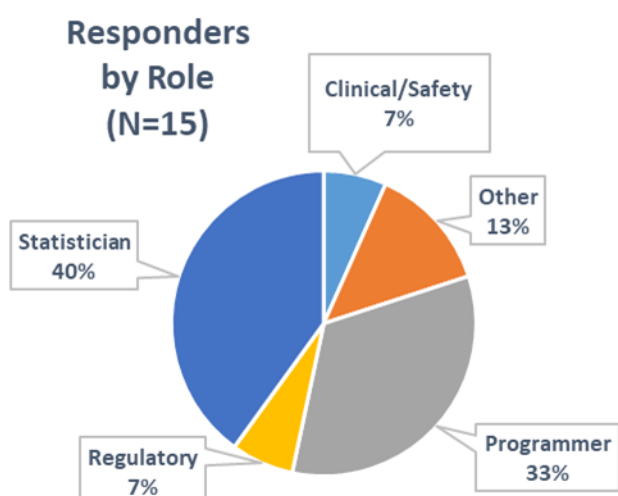
- ICH Guidelines outline recommended data displays
- Interpreted by many companies as a requirement that all collected data be displayed somewhere on a listing
- However, ICH Guidelines were published before widespread use of interactive data review tools, both internally and by regulatory agencies, and before submission of electronic study data to regulatory agencies
- Programming nicely formatted, "publication-ready" listings is time-consuming and tedious
- Can be burdensome to locate specific information in static listings

VERIFICATION / VALIDATION

- Cover verification process for any information generated from data review tools and incorporated into publications, decision-making or regulatory documents in company policy
- If listings generated interactively from a data review tool are used as a reference when writing a CSR or other submission documents, need to consider how the tool should be validated according to FDA principles on software validation and requirements for computerized systems used in clinical investigations

ADDITIONAL CONSIDERATIONS

- Some sponsors have already deviated from the full list of CSR listings specified in ICH Guidelines without negative repercussions
- Informal survey of sponsors at the 2020 PHUSE CSS Conference identified a small set of commonly-produced listings considered helpful for reviewing study data



SUMMARY

- Minimizing dependence on static data listings will require a concerted and sustained multi-disciplinary effort
- Cross-functional advocates for interactive data review tools in internal company departments will be needed, including from Medical Writing, Clinical, and Safety
- Some sponsors have successfully reduced the number of static listings generated for both internal purposes and regulatory submissions to a small number (<10)
- Submission of study data in standard format, plus wider adoption of interactive data review tools, enables reduction/elimination of complete sets of routine study "data dump" listings

ACKNOWLEDGEMENTS

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FOR MORE INFORMATION

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