

PP12 - A Machine-Readable Structure for Generating Nonclinical Study Protocols



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Abstract:

The PHUSE nonclinical scripts team is exploring concepts for an electronic nonclinical protocol. The desire is to define a data model that describes a protocol that can be shared between tools for protocol planning and output as an approvable protocol document. This would need to include structured and unstructured elements of the protocol including the study design, animal model, planned dosing and scheduled endpoints to be measured. Existing initiatives are summarized, a data model is being proposed and a proof of concept is being planned.

Goals - A data model that:

- Describes a protocol
- Shareable between tools for study execution
- Output as an approvable protocol document.

Content/scope of information

- Structured:
- Study design, animal model
 - Planned dosing/exposure/challenge agents
 - Schedule of planned measurements
- Unstructured elements (narrative):
- Objective of study
 - Animal model decisions basis
 - Statistical analysis planned
 - Dosing escalation decisions

Rendering into files, possibilities include:

- XPT – as in SDTMIG and SENDIG – a flat structure
- XML – as in dataset.xml, a hierarchical / tree
- JSON – as in dataset json, flat or hierarchical / tree

Proposed use the SEND data structures

- Trial domains
 - * Trial Summary - Add narratives on study design decisions, statistical planning
 - * Arms, Sets, Elements - Planned dosing, groups
- Animal domains
 - * Demographics – Animal numbering, ages
 - * Subject characteristics – If required in planning
 - * Disposition – Planning sacrifices by trial sets
- Exposure domain
 - * Planned dosing by trial sets
- Finding domains
 - * Body weights - schedule
 - * Laboratory - tests and schedule
 - * Macro/Micro pathology - tissues/organs
 - * other finding domains – schedule, tests

Other Existing initiatives

- BioCelerate Study template** – document output
- Digital Data Flow** – system and API model
- Open Study Builder** – Concentrating on Clinical
- CDISC PRM** – relationship model only

Next steps

- Proof of concept planning
- Considerations for
 - Amendments and version control
 - Narrative parts including formatting
- Discussions with stakeholders (Pharmas, CROs, regulatory agencies)
- Discussions with standards body (CDISC)

Figure 1 – Protocol generated from model

The purpose of this study is to evaluate the toxicity [and determine toxicokinetics] of the test item/article, [TRT], when administered [PDOSFRQ], [ROUTE], [SPECIES], [DOSDUR] (e.g. once daily by oral gavage to rats for at least 4 weeks)], and to provide data to support the use of [TRT] in humans.		The purpose of this study is to evaluate the toxicity [and determine toxicokinetics] of the test item/article, MyDrug, when administered ONCE, INTRAVENOUS, RAT, P29D (e.g. once daily by oral gavage to rats for at least 4 weeks)], and to provide data to support the use of MyDrug in humans.	
2. Proposed Study Schedule		2. Proposed Study Schedule	
Schedule detail may vary based on study/sponsor/CRO needs. The black text in brackets may be included for studies requiring SEND.		Schedule detail may vary based on study/sponsor/CRO needs. The black text in brackets may be included for studies requiring SEND.	
Experimental Start Date (date of first data collection):	[EXPSTDTC]	Experimental Start Date (date of first data collection):	2019-08-03
Dosing Start Date:	[DOSSTDTC]	Dosing Start Date:	2019-08-03
Dosing End Date:	[DOSENDTC]	Dosing End Date:	2019-09-01
Experimental Completion Date (date of last data collected):	[EXPENDTC]	Experimental Completion Date (date of last data collected):	2019-09-01
Audited Draft Report Date:	[DATE]		