Expert Answers to Community Questions – March 2021

On 26th March 2021 a team of experts from Industry, CDISC and FDA came together to discuss the topic of 'Data Integration and Submission Challenges'. You can find the recording on the PHUSE Archive.

The panel actively sourced questions prior to the event from the SDTM/ADaM Implementation FAQ project, as well as a 'call out' to our community members who were given the opportunity to submit questions ahead of the event. In addition, on the day questions came in via the Q&A chat from the audience. Many questions were answered 'live' so we encourage you to listen back to the recording, but those that the panel didn't have time to address have been curated and captured below.

The following blog shares highlights of the event and additional links.

Questions	Team Response
What's FDA preference? Integrating ADaM from individual ADaM seems a good option if ADaM at study level were well "curated". But still would it be a plus for FDA having one single source with data from all studies contributing for example to an ISS? i.e. iSDTM.	From individual ADaM to integrated ADaM is a good option and is recommended. However, there are multiple approaches discussed during the EAtCQ event which the Sponsor can consider. Sponsors should discuss ISS content and approach during the pre BLA or pre NDA meeting with their review division.
Are there any initiatives taken to align the data standard requirements (versions) across different regulatory authorities?	There is no formal initiative to use the same data standards requirements across the different authorities.
We have a couple of situations where FDA have asked us to provide integrated SDTM - do different divisions have different expectations?	It's not uncommon for different divisions to have different expectations when it comes to how the standard data is integrated. The language is continually updated in the Study Technical Conformance Guide to further establish a consistent request and requirements across the divisions. This will evolve based on industry approaches and existing code, and each individual divisions have adopted and grown accustomed to over time.
What is the input from FDA representatives on submitting ADaM programs only or submit both (ADaM & TFL's programs)?	We require from SDTM to ADaM and then other requests will be based on division.
What is the strategy to be followed for submitting aCRF for ISS studies?	There is no expectation to have an aCRF for ISS. The data is collected for the individual study and so the aCRF at the study level is what is expected.
What about an oncology compound that continues to submit for each unique indication /tumour type. We re-use the same studies in our ISS again and again.	The approach of adding newer studies to the existing ISS is valid.
For integrated SDTM and ADaM datasets used for ISS/ISE, is there a need to run the SDTM /ADaM conformance validation checks on the datasets, in the same way we do at study level?	Yes. Even though conformance or validation rules does not exist from CDISC and FDA for integrated data, it is necessary to ensure the data/metadata is compliance just like individual study. Of course, some of the validation checks may not apply for integrated data. The upcoming iADRG and iCSDRG template do have provision to provide conformance issue summary just like ADRG and cSDRG template.
Integrating legacy studies (started prior to December 2016) and studies in SDTM format directly into an iSDTM (eg., we skip conversion at study level, we do it directly in the pool), provided that is fully traceable (documented), it's an acceptable option provided that this is discussed upfront (we did with a couple of projects where we had to pool several old legacy studies).	The sponsor may be required to integrate studies that have been completed using different versions of the SDTM IG or may have legacy data in a non-standard format. Older studies may have been finalised suing custom SDTM domains that, in later versions of the SDTM standards, have become standard SDTM domains. This would require some amount of harmonisation activity to take place. The Sponsor should determine whether to implement this legacy data conversion in individual studies, as intermediate datasets used in the integrated SDTM dataset generation, or within the code to generate the integrated SDTM dataset itself. Please refer to the White Paper for further details. (See section 3.2).

If individual study SDTMs are up-versioned /harmonised (but not integrated) and then used to create ADaM integration, what should be submitted to fulfil the traceability requirements?. All the original study SDTMs/SDPs in addition to the set of up-versioned SDTMs/SDPs for each study used for the ADaM integration.	For traceability purposes, we do recommend that the Sponsor submits the up-versioned /harmonised SDTMs from the individual studies if they are used for integrated ADaM. If those up-versioned SDTMs are stacked/integrated to generate iSDTM, then our recommendation would be to submit iSDTM only. We strong recommend to document this in the Study Data Standardisation Plan (SDSP) and discuss ISS content and approach during the Type C or pre BLA/pre NDA meeting with their review division.
For new studies, we have ADaM datasets and for the legacy studies we have SDTM and so we were hoping to use combination of ADaM and SDTM as a source to generate integrated ADaM. What is your recommendation?	This scenario is not common. We strongly recommend to document this in the Study Data Standardisation Plan (SDSP) and discuss ISS content and approach during the Type C or pre BLA/pre NDA meeting with their review division.
For Integrated SDTM, how to populate trial design datasets?	The recommendation is not to integrate the trial design domains. Please reference the White Paper for further details.