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Regulatory Data Submission and CDISC Compliance: Sponsor and Vendor Collaboration Best Practices

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ABSTRACT

Submission of Electronic Data requires compliance to CDISC and evolving regulatory agency data standard requirements (e.g, FDA and PMDA). Close collaboration and partnership between sponsors and vendors throughout the data collection and analysis process is critical to ensure that data/submission packages efficiently meet requirements. Pinnacle 21 is widely used for data validation as well as for the creation and/or validation of define documents. Standards specified by FDA/PMDA can be pre-loaded in P21 to generate submission documents and validate datasets and define packages. Alnylam has been using P21 Enterprise to ensure compliance between internal programming and data management departments, and has expanded access to this platform/process to our data management vendors to centrally load data, generate defines, run validation, document data and mapping issues and collaborate to reconcile all issues. In this paper, we will discuss our experience in using a common platform to review/ensure Data Submission compliance with our vendors, the challenges and benefits of using a common platform to review data and submission issues as well as our recommendations for best practices between the sponsor and vendors.

INTRODUCTION

Following submission standards and resolving issues in data and submission documents is often a challenge, especially when part of the work is outsourced. Vendors may use different tools or methods to upload and share data/updates with the sponsor. The review process and communication between the sponsor and vendor can be more efficient using a common platform. Pinnacle 21 Enterprise (P21E) facilitates this purpose of using a common platform to share data and submission documents as well as early detection of issues and their easy resolution with effective manner of communication. But the process of sharing a common platform between the sponsor and vendor has its benefits and challenges. We will discuss these details along with the best practices according to our experience.

P21 ENTERPRISE

P21E is a web-based platform that provides a range of tools and options for managing clinical trial data. Some of its key features include:

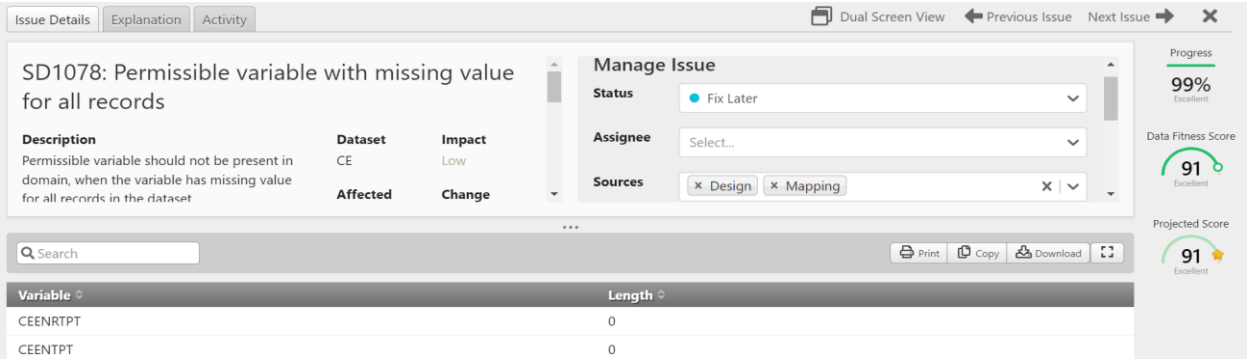
- Homepage: The homepage gives users access to all the studies and data packages they have permission to view.
- Overview: The Overview section provides a summary of the issues and submission documents related to a particular study. It also shows detailed issues identified during the review and/or validation of the datasets.
- Datasets and Data Report: This section allows users to navigate to issues in each dataset and view overall data reports.
- Define: The Define section allows users to update specifications for all tabs in the define file, such as variable, VLM, codelist, and issues, as needed. Users can also compare updated versions with older versions and revert to older versions if necessary.
- Reviewer's Guide: This section provides a standard version of the cSDRG (Clinical Study Data Reviewer Guide) that can be downloaded and updated according to study requirements.
- Validation Data: The Validation Data section allows users to select the intended zipped data package and run validation against the uploaded define and data.
- Metadata: The Metadata section allows users to view standards, terminologies, issue metadata, and compare specifications.
- Analytics: The Analytics section shows users the top unresolved issues affecting the data package.

Overall, P21E is a comprehensive platform that streamlines the management and submission of clinical trial data along with sponsor and vendor collaboration.

ISSUES

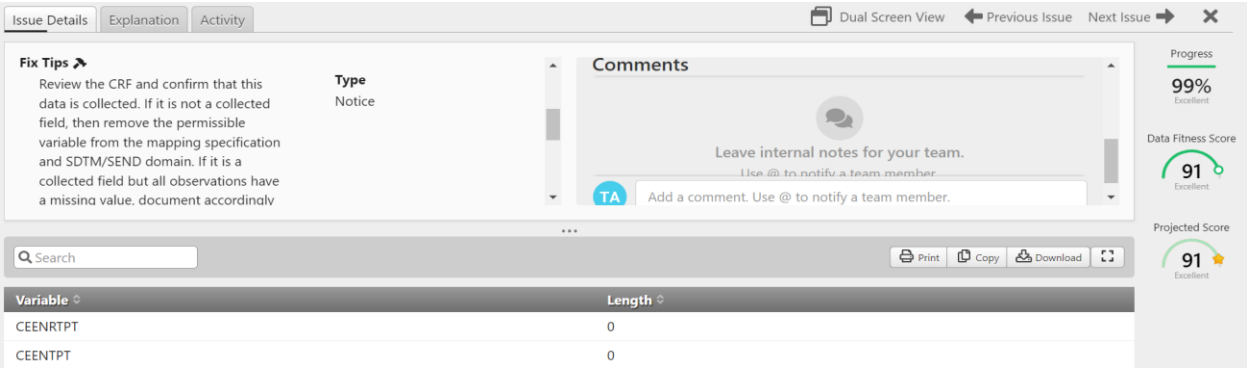
A key benefit of using the P21E as a common platform is having an up to date snapshot of the data issues and define issues summary that the entire team can reference, including selecting an appropriate action option (e.g., close, resolve later, keep open etc.) for each issue identified, along with an explanation, comment and targeted assignment and communication between team members.

For example, in P21E display below, users can indicate status (e.g, Open/Fix Now/Fix Later/Closed) per the drop down in the right-hand panel. In the “Assignee” section, users can select a team member’s name and tag them – they will be notified instantly that an issue needs to be addressed. Sources drop down gives options as Data/Mapping/Process/Design etc. to further clarify the issue:

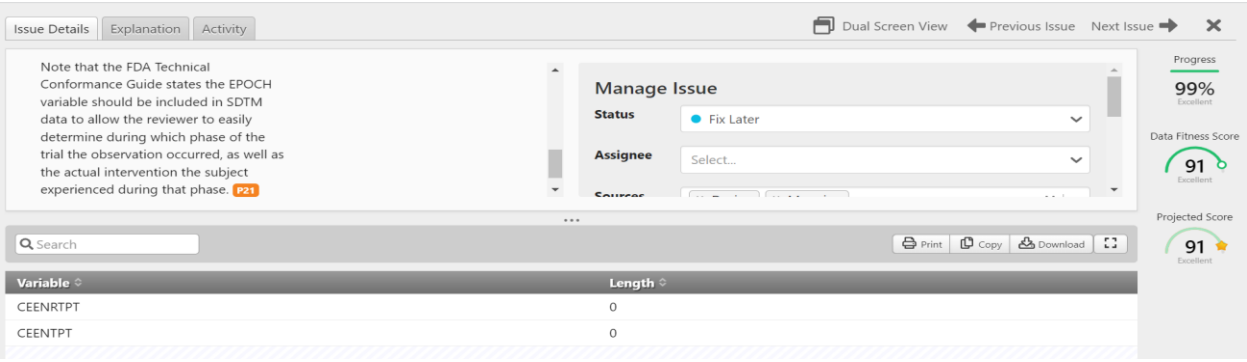


Display 1. Issue Details

Scrolling down in the “Issue Detail” section, P21E provides Fix Tips on the left hand side and comment section in the right hand side where the team member responsible for the type of concern (e.g., mapping/programming/data) can be tagged:

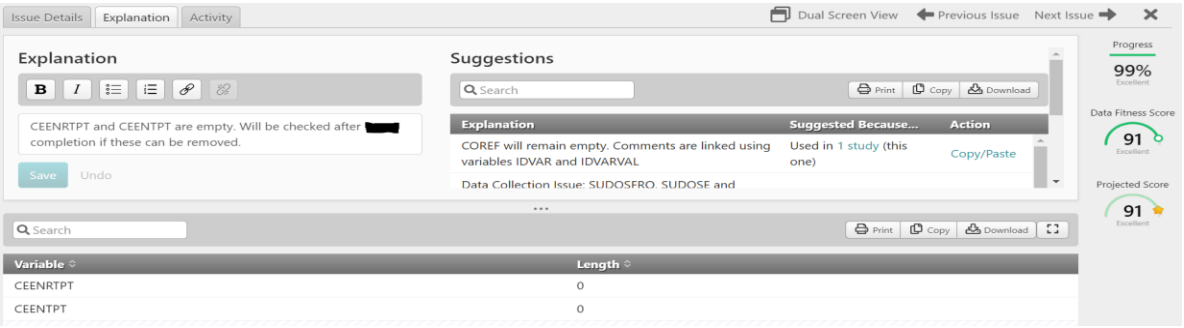


Display 2. Fix Tips suggested



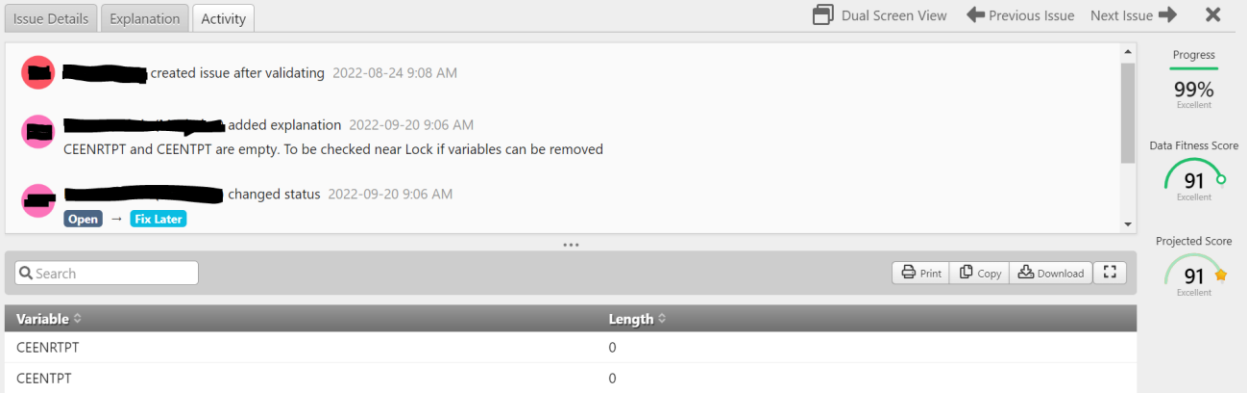
Display 3. Further drop down in the Fix Tips

The “Explanation” tab displays the explanation added by the team member:



Display 4. Explanation tab under the selected issue

The P21E Activity tab shows when a user detected an issue after validation, assigned a team member and the assignee’s response and change of status of the issue:



Display 5. Activity tab under the selected issue

PROCESS – CHALLENGES AND BENEFITS

The following summarizes Alnylam’s perceived benefits, challenges, and opportunities to improve the data review process by using the P21E common platform for identifying and resolving data issues, how we approached this as a process/collaboration platform, and lessons learned from our engagement with our vendors.

Benefits:

- Easy upload of data in timely manner using P21E between Alnylam and the data vendor.
- Generation of submission documents per the regulatory submission standards: define can be created from different sources including - (1) data, (2) Excel specifications, (3) previously created define, (4) merging new define to an existing specification or define.
- Validation of data and define documents within the common platform meant no need to spend time on extensive SAS macros or programs to generate the define, detect and fix define issues as programmers did in the past.
- Generation of Reviewer’s Guide from a standard template.
- Easy selection and links to validation standards.
- Able to upload and update different versions of dictionaries as required.
- Able to compare different versions of specifications and define documents.
- Merging multiple define documents and specifications generated from different sources into one in just a few minutes instead of programmers spending significant effort regenerating an entirely new specification with new datasets to create the merged define.
- Detection of issues through P21E reduces the time required to detect all the issues by validation through programming or visual check as soon as data arrives.

- Easy communication between the sponsor and vendor, and between different departments within the same organization – P21E allows to tag certain team members and share comments so that the issue can be communicated with and addressed by the intended person responsible for it, e.g. data management or programming or vendor.
- Reduction of the number of emails or copying issues into trackers with the possibility of losing or overwriting comments.
- Effective documentation of issues, assignments and updates of the status/resolution captured readily within P21E.
- Resolution of issues at early stage following early detection.

Sharing a common CDISC/Data Issue Compliance (e.g. P21E) platform between the Sponsor and Vendor – Best Practices:

- The sponsor needs to discuss with the vendor about the process / expectations early on, where/how to use the platform and which team members will receive access from the vendor.
- Align on cadence of data transfer/dates by when new data will be loaded (e.g., every month) as well as timeframe for review.
- Identify project specific SMEs on both the vendor and sponsor side in case team members need support and/or they have issues or queries which require faster resolution. Identifying vendor (SME) partners also helps to train/advocate for use of the platform with their team.
- Sponsor will define user roles, load the dictionary versions; ensure communication within the Vendor team. The sponsor must be prepared to answer questions and resolve issues and ensure everything is validated.
- It is beneficial on the Sponsor/Vendor side to also train the data management team to use common platform to load data and related documents, review and communicate with the vendor team. This reduces need to track/capture and close issues in multiple files/formats.
- It is important to train the team members from the vendor side on the platform and expected process. This may need multiple meetings if the vendor is using P21E for the first time.
- Sponsor will review the data and submission documents loaded or generated by the vendor and share comments with the vendor.
- The sponsor needs to partner with the vendor teams to ensure they are able to use the primary tool to load data and identify/resolve compliance issues, vs using their own tools to review and create the define and then loading the resulting data and define back into P21E – in the latter case, the sponsor may not be able to view the current version if vendor has already made any update in their tool. This may create confusion – we provide lessons learned to mitigate this experience:
    - We re-checked our comments on the initial transfer and matched those with the next transfer where vendor had responded that the issues were fixed.
    - Where there were discrepancies in issues being corrected, we set up direct contact / meeting to discuss the process in detail.
    - It is important that the review from the sponsor is done as soon as possible following the transfer as well as understanding the vendor's process, especially if they use their own tools/platforms to create the define. This will require the sponsor to work with the vendor to ensure that all P21E issues are resolved through the entire process.
    - Use of the P21E tool as a common platform also identifies issues early in controlled terminology decision-making. For example, there were a few instances where inconsistency in a unit used for exposure data and controlled terminologies in some datasets were detected. Based on our discussion of potential risks and inconsistencies with submission standards, our vendor was requested to change the unit and controlled terminologies for the data. P21E helped us detect such inconsistency at a very early stage and both the sponsor and vendor received enough time for the review, discussion and resolution.

CONCLUSION

Using a common platform (in this case P21E) is useful to facilitate data and submission document sharing, faster communication among internal teams and between the sponsor and vendor, validation and resolution of issues. With the use of a platform following the best practices, the process of regulatory submission following the submission standards from the beginning to the end can be highly efficient.

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