

Conversion of Legacy Data from Topical Corticosteroid Clinical Studies to SDTM Format

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Introduction

- Corticosteroids constitute an important class of compounds across many indications primarily based on their anti-inflammatory or immunosuppressive properties.
- Topical corticosteroids are indicated for the treatment of corticosteroid-responsive dermatoses based on successful outcomes in clinical trials on psoriasis and atopic dermatitis.
- There are levels of potency of topical corticosteroids based on their vasoconstriction effect, which has been believed to be related to clinical efficacy.
- Comparison of topical corticosteroids across potencies would be facilitated by conversion of legacy data for clinical trials involving topical corticosteroids.
- Clinical trials on topical corticosteroids would also offer an opportunity to view the relevance of SDTM in data presentation for topical dermatologic product studies.

Objective

- The objective of the current project is the conversion of legacy data from clinical trials on topical corticosteroids into SDTM format, by taking previously submitted topical corticosteroid clinical data and transforming them into CDISC’s SDTM format.

Having a standardized format for all submitted data increases the ability to compare across studies/products for better data analysis and highlights what significant information current submissions may be lacking.

Methods

- Conversion was done using SAS programming to rename and reformat existing variables in previously submitted datasets.
- Validation of the SDTM datasets established was by OpenCDISC.

Materials

- Clinical data from 5 topical corticosteroids representing 6 applications were studied.

–Steroid 1: super-high potency	– 6 trials
–Steroid 2: lower mid-strength potency	– 4 trials
–Steroid 3: lower mid-strength potency	– 3 trials
–Steroid 4: high potency	– 16 trials
–Steroid 5: super-high potency	– 8 trials
Total of	– 37 clinical trials, including efficacy studies, PK studies, HPA axis studies, and dermal safety studies

There were a total of 484 datasets studied among the 37 studies.

Results

- Legacy clinical data from the submitted datasets were successfully converted into CDISC’s SDTM format for all the applications studied.
- Define.xml files were also successfully created.
- Observed deficiencies in the legacy datasets affecting conversion include, but are not limited to the following:
 - CRF annotation incomplete or misleading
 - Lacking essential information, e.g., country where study took place, investigation site ID, TESTCD, etc.

Results (Continued)

- Observed deficiencies in the legacy datasets affecting conversion (cont’d):
 - Terminology issues, e.g, non-standard terminology, or outdated versions of dictionaries
 - Problematic reference issues, e.g., referencing SEQ while the reference variable is character.
 - Invalid event dates, e.g., start date after end date
 - Subjects in dataset domains but excluded in DM domain, e.g., screen failures
- Outstanding issues with respect to topical corticosteroid data conversion include:
 - (1) multiple treatment arms within a single subject
 - (2) location for treatment history and
 - (3) difficulty in quantifying exposure.

These are issues that may not be unique to topical corticosteroid studies, but common among topical dermatologic product clinical trial data. These issues are also relevant to the development of therapeutic standards for topical dermatologic products.

Multiple Treatment Arms within an Individual Subject

- Topical dermatologic product studies may involve simultaneous application of different drugs, doses, or dosage forms on the skin of each subject.
- This is typically the case in dermal safety studies with application of test drug doses, and positive/negative controls.
- Some studies may also involve procedures such as irradiation to skin in addition to test drug.
- However, ARM and ARMCD variables in the DM domain will allow only one value per subject.

Treatment History

- Treatment history information in the legacy clinical data on topical corticosteroid trials are difficult to find.
- Using the annotated CRFs from submitted materials, this information is sometimes traced to a non-standard domain. However, the data may also appear under EX or CM but more often under SUPPQUAL domains.
- When converted to SDTM, we also found that there is not a pertinent domain for the location of treatment history data.

Quantifying Exposure

- With respect to drug exposure, the amount of topical drug administered depends on the severity and size of the skin condition. This variability does not allow consistent description of dosage as a variable in the standard datasets.
- Measurement of drug administered is rarely accurate for each individual dosing when a topical drug is applied to skin, and so is its recording in the standard datasets, e.g.,
 - Dosing with descriptors such as “thin film”, “liberally” etc. cannot be accommodated as a numerical variable.
- The term “application” as a dosing unit is not standard.

Conclusions

- This project has prepared data for better safety and efficacy analysis; the clinical data converted to standard format will be helpful for comparative effectiveness of topical corticosteroids across potencies as defined by the vasoconstriction assay.
- This project has helped to discover potential issues to be considered for therapeutic standards projects for topical products.
- This project has made it possible to develop a proposal to further adapt SDTM to encompass the challenges of topical medication data.