

Legacy Data from Topical Corticosteroid Clinical Trials: Issues in SDTM Conversion



Lillian Qiu and Hon-Sum Ko

DDDP, ODE3, CDER, FDA, Silver Spring, MD 20993



Introduction

- Topical corticosteroids are widely used to treat inflammatory skin conditions such as atopic dermatitis and psoriasis based on their anti-inflammatory or immunosuppressive properties.
- Successful treatment depends on an accurate diagnosis and consideration of the steroid's delivery vehicle, potency, frequency of application, duration of treatment, and side effects.
- Topical corticosteroids' potency levels are based on their vasoconstriction effect.
- Comparison of topical corticosteroids across potencies would be facilitated by CDISC SDTM conversion of legacy data from topical corticosteroid clinical trials.
- Legacy data conversion would also be helpful to discover potential issues to be considered for therapeutic standards projects for topical corticosteroid products.

Objective

- The objective of the current project is to convert legacy data from previously submitted topical corticosteroid clinical trials into CDISC SDTM format, and to discover potential issues to be considered for therapeutic standards projects for topical corticosteroid clinical trials and highlight what significant information current submissions may be lacking.

Methods

- Employing SAS programming to rename and reformat non-standardized variables in previous submitted clinical datasets, according to an updated CDISC SDTM Implementation Guide (version 3.2).
- Validation of the converted SDTM datasets was performed by OpenCDISC software.

Materials

- Legacy data from 9 topical corticosteroid applications containing a total of 50 trials and 572 datasets were converted into SDTM, including efficacy studies, HPA axis studies, and dermal safety studies. Information on the products and their studies is shown in Table 1.

Table 1. Topical Corticosteroid Clinical Trials for CDISC SDTM Conversion

	Steroid 1	Steroid 2	Steroid 3	Steroid 4	Steroid 5	Steroid 6	Steroid 7	Steroid 8	Steroid 9
Total Trials	4	2	4	3	16	8	8	2	3
Potency Class	super-high	super-high	lower mid-strength	lower mid-strength	upper mid-strength	super-high	super-high	mild	super-high

Results

- Legacy clinical data from the submissions were successfully converted into CDISC's SDTM format.
- Observed deficiencies in the legacy datasets affecting conversion include, but are not limited to the following:
 - Terminology issues, e.g., non-standard terminology applied among concomitant medicine dosage units, i.e. the term "application" as a dosing unit is not standard.
 - Lacking essential information, e.g., (a) for DAORRES, 'Dispensing amount' and 'Return amount' are not available, and (b) for IETESTCD, unavailable inclusion or exclusion criterion information, etc.
 - Incomplete or misleading CRF annotation.
 - Certain subject evaluation values being inconsistent with the defined evaluation levels in CRF.
- Some issues with respect to topical corticosteroid data conversion have been resolved, including:
 - 1) Multiple Treatment Arms within a Single Subject
 - Topical dermatologic products might be applied on each subject's skin simultaneously with different drugs, doses, or dosage forms.
 - This is common in dermal safety studies.
 - Possible solution is to accommodate all treatments for each subject under the variable ARM in DM domain; that could translate into multiple records for the variable EXTRT in EX domain.

Results (Continued)

- 2) Difficulty to Capture Subject Multiple Baseline Evaluation Results
 - Subject skin baseline evaluation often was performed by a series of solicited standard tests during screen visit.
 - During the evaluation, severity of skin condition and size of the affected body surface area, etc. were recorded. Subject morphology records also were reported during the following visits.
 - Employing MO (Morphology) domain is suitable to capture this information. The finding in original units is acceptable in the MO domain, e.g., percentage of BSA (body surface area affected), etc
 - 3) Lacking Standard Variables for Certain Data in the Medical History Case Report Form
 - There are no variables in MH domain for the frequency of administrated substance in subject medical history, e.g. alcohol use frequency, etc.
 - SU (Substance Use) domain can be created to accommodate this information.
- There are also outstanding issues with respect to topical corticosteroid data conversion that have not been resolved, including:
- 1) Difficulty in Quantifying Treatment Exposure
 - Treatment dosage depends on severity and size of the skin condition, and accurate measurement is rarely obtainable
 - This variability among dosage and units does not allow consistent description of dosage and units as standard variables in the EX domain.
 - 2) Subject Demographic for Skin Type Evaluation and Treatment Location
 - Basic evaluation of subject's skin type is often required for dermatological product clinical trials before the study is performed.
 - Different parts of body are often applied with the study product for each subject.
 - There is a lack of specific dermatology-related variables in the standard model and deciding which variables fit best into the related standardized terminology. For instance, there are no skin type variables in SDTM Demographics domain.
 - 3) Lacking Standard Variables for Certain Data in the Medical History Case Report Form
 - For certain skin disorder studies, the history of the specific skin problem is often documented in the case report form at baseline.
 - There may be insufficient information to translate into standardized variables of MH domain, e.g., 'visible flexural involvement', etc.

- Many of the above issues may not be unique to topical corticosteroid trials, but common among topical dermatologic product clinical trial data.

Conclusions

- Conversion of legacy data from topical corticosteroid clinical trials met with a variety of data issues pertaining to deficiencies, errors, and difficulties in fitting into the standard model.
- Some of these issues can be resolved with the current model, while there are also issues more unique to dermatologic product clinical trials that require additional considerations.
- Experience gained in conversion may be helpful in the consideration of therapeutic area standards for dermatologic conditions.

Acknowledgements

This project was funded by the US Food and Drug Administration through Oak Ridge Associated Universities and Oak Ridge Institute for Science and Education. The findings and conclusions in this project have not been formally disseminated by the Food and Drug Administration and should not be construed to represent any agency determination or policy.

Contacts

Aijun (Lillian) Qiu, M.S.
ORISE Fellow
FDA/CDER/ODE III
Phone: (301) 796 0637
aijun.qiu@fda.hhs.gov

Hon-Sum Ko, MD
Medical Officer
FDA/CDER/ODE III
Phone: (301) 796 3827
HonSum.Ko@fda.hhs.gov