Legacy Data Conversion Issues for Topical Product Studies

Lillian Qiu and Hon-Sum Ko

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

Introduction

- Non-standardized legacy data are common in previous submissions from the pharmaceutical industry to regulatory authorities.
- We conducted legacy data conversion of topical corticosteroid clinical studies into SDTM to facilitate comparison of topical corticosteroids across topical corticosteroid potencies.
- We anticipated that there might be potential issues that could be applicable to therapeutic standards projects for topical drug products.

Objective

- To convert legacy data from previously submitted topical corticosteroid clinical trials into CDISC SDTM format.
- Discover potential issues to be considered for therapeutic standards projects and highlight what significant information current submissions may be lacking.

Methods

- We used 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).
- We created define file for each study with XML (Extensible Markup Language): listing and explaining all the SDTM domains used in the study, the variables included in each domain, and the controlled terminology used for the variables.
- We validated the converted SDTM datasets by OpenCDISC software.

Materials

- Legacy data from 10 topical corticosteroid applications containing a total of 59 trials and 732 datasets were converted into SDTM, including safety/efficacy studies, hypophalamic-pituitary-adrenal (HPA) axis studies, and dermal safety studies.

Results (Continued)

b) Issues concerning laboratory assessment results and reference ranges for LB domain, e.g.:
   - In HPA axis suppression studies, there were no lab results and reference ranges for pre-dose sample evaluations in some visits in the legacy datasets, while there were lab results available for post-dose sample evaluations. However, HPA suppression was determined by both pre-dose and post-dose sample levels.
   - Resolution is to accommodate the values of pre-dose from the clinical trial study report into a supplemental dataset with excel file. Then importing the values into SAS programming for LB domain conversion.
   - Assessments on the use of alcohol, tobacco, and drug occur before administration of topical products. Alcohol and tobacco usage are supposed to be in SU domain. However, the CRF rarely contains data to be placed in that domain, including substance dosage, form, frequency, etc., for SU domain conversion.
   - Because the patients were given urine drug tests, with test results being “Positive” or “Negative”, we captured substance assessment results in LB domain.
   - There was inconsistent information between response grades in the legacy dataset and defined response grades in define file, e.g.:
     - Response grades were used to evaluate signs of plaque psoriasis for the entire treatment area during the visits. In the define file, 5 grades, ‘1’, ‘2’, ‘3’, ‘4’, and ‘5’ were given for the response grades, which correspond to ‘None’, ‘Mild’, ‘Moderate’, ‘Severe’, and ‘Very Severe’. However, there were 9 response grades in the legacy dataset. In addition, there was no text description for the intermediate grades (1, 3, 5, and 7) in the CRF, i.e., midpoints between the defined grades (0, 2, 4, 6, and 8).
     - The ordinal descriptive response grades for signs of plaque induration/scaling, etc., are an example for topical product studies. The responses, 1, 3, 5 and 7, could not be converted with the standard responses.

Table 1. Topical Corticosteroid Clinical Trials for CDISC SDTM Conversion

<table>
<thead>
<tr>
<th>Steroid Drug</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
</tr>
</thead>
<tbody>
<tr>
<td>Potency Class</td>
<td>super-high</td>
<td>super-high</td>
<td>super-high</td>
<td>lower mid-strength</td>
<td>lower mid-strength</td>
<td>upper mid-strength</td>
<td>super-high</td>
<td>super-high</td>
<td>mild</td>
<td>super-high</td>
</tr>
</tbody>
</table>

Results (Continued)

- Legacy clinical data from the submissions were successfully converted into CDISC’s SDTM format. Example of sponsor datasets and SDTM datasets:

<table>
<thead>
<tr>
<th>DATASET</th>
<th>DESCRIPTION OF DATASET</th>
</tr>
</thead>
<tbody>
<tr>
<td>eaexpt</td>
<td>Adverse Event data for statistical analysis</td>
</tr>
<tr>
<td>eaexes</td>
<td>Adverse Events summary data</td>
</tr>
<tr>
<td>basetest</td>
<td>Baseline Test data</td>
</tr>
<tr>
<td>commhds</td>
<td>Concomitant medication summary data</td>
</tr>
<tr>
<td>commeds</td>
<td>Concomitant medication data</td>
</tr>
<tr>
<td>domxa</td>
<td>Demographics data</td>
</tr>
<tr>
<td>full</td>
<td>Follow-up data</td>
</tr>
<tr>
<td>medhis</td>
<td>Medical History data</td>
</tr>
<tr>
<td>pd</td>
<td>Protocol Deviation data</td>
</tr>
<tr>
<td>saeh</td>
<td>Study disposition data</td>
</tr>
<tr>
<td>smiz</td>
<td>Surgical History summary data</td>
</tr>
<tr>
<td>visits</td>
<td>Visit data</td>
</tr>
</tbody>
</table>

- Many of the issues observed during conversion 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.
- There are issues common to dermatological product clinical trials, some of which may require additional considerations, although many of them can be resolved within the current model.
- Experience gained in handling these conversion issues may be beneficial 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

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

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