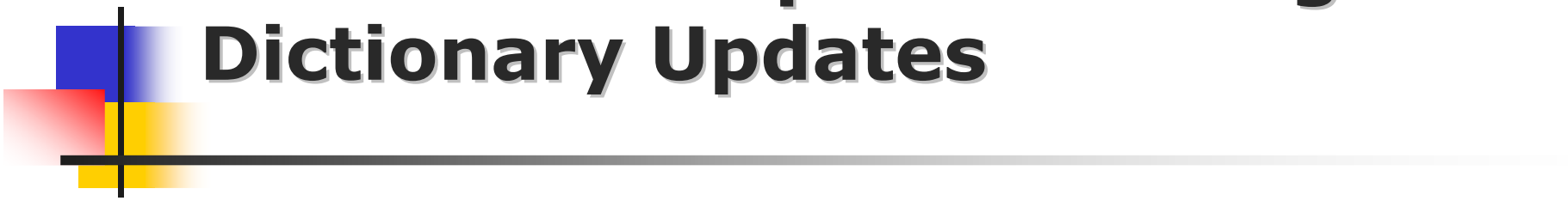

TMS: Case Studies of How Different Companies Manage Dictionary Updates

Sunil G. Singh
DBMS Consulting
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Tutorial 05

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Assumptions and Scope

- Assumption
  - The audience is familiar with TMS and its basic functionality.
- Scope
  - An overview of each scenario is provided with only minimal discussion of code for TMS update procedures.
  - These scenarios are used primarily for WHODrug and MedDRA, which have quarterly and semi-annual updates, respectively.
  - The focus is on methods for Dictionary Updating, which are in production use at actual TMS customer sites.

Disclaimer

- Not intended to be an all inclusive list of scenarios
  - No one, including Oracle, can possible know all of the uses of TMS at all customer sites.
  - Apologies if an in-use production scenario of TMS updating used at a TMS customer site has been omitted.
- Generalized scenarios which exist in at least one TMS customer in production
  - No specific customer names are provided for confidentiality protection reasons.

Dictionary Updating Case Studies

- Case Study overview of how companies handle dictionary updating
- Six (6) production in-use scenarios were identified.
- This does not mean these are the only solutions in production use, but these are the cases of which awareness was available at the time of this presentation.

Overview: Production In-Use Scenarios

TMS customers:

1. Do not update the dictionary in TMS, but instead modify existing studies to use new initial loaded TMS dictionaries.
2. Perform only base dictionary updates and do not use virtual dictionaries.
3. Perform base dictionary updates and also use virtual dictionaries.
4. Use a "continuous" virtual dictionary by not starting with a base dictionary but an initial virtual dictionary for TMS updates.
5. Leverage initial loading scripts instead of creating updating scripts (with and without 3rd party tools).
6. With a single instance OC/TMS/AERS integration, leverage the "latest" domain and Virtual Dictionary structures for Oracle AERS to drive updates for OC/TMS integrated studies.

Table of Scenarios In-Use

Scenario	Number of Cases	Type of Customers
1. New Initially Loaded Dictionaries with existing study modification	2	CROs, Medical Device
2. Base Dictionary Update only, no virtual dictionary in use	3	Large Pharma, Large biotech, CROs
3. Base Dictionary Update with Virtual Dictionary use	6	Large Pharma, Large biotech, CROs, Medical Device
4. Continuous Virtual Dictionary Updating	1	CRO
5. Initial Loading Scripts without separate Update scripts	2	Large pharma, CRO
6. OC/TMS/AERS integrated environment with AERS updates	1	Large pharma

Common Issues When Performing Updates

- Several issues are common to dictionary updates and can be assessed in conjunction with each update scenario:
  - How are terms declassified/reclassified during the update process?
  - What types of impact reports are required?
  - Should predict tables in a current production environment be used for impact reporting, or does an update need to occur in a separate environment to generate impact reporting?
  - Is a separately developed updating script required?

How Are Terms Declassified / Reclassified During Updates?

- Declassification of VTAs which would be associated to:
  - Non-current LLTs in MedDRA
  - Non-existent LLTs in MedDRA
  - Non-existent SYN/PN in WHODrug
- Reclassification of VTs which exactly match:
  - New LLTs for MedDRA
  - New PNs and SYNs for WHODrug
- These types of reclassifications and declassifications can have a potentially significant impact on existing OC studies using TMS, which makes the concept and content of impact reporting more important to in-progress studies in OC.

What Types of MedDRA Impact Reports Are Required?

- Most TMS customers are concerned with the impact of an update on the existing OC studies using TMS. Some of the most common types of impact reports for MedDRA (assuming LLT coding level) include:
  - Listings of VTs by study which were classified to a LLT and will be declassified since the LLT no longer exists or is no longer current;
  - Listings of VTs which were once classified to a LLT, but are now reclassified to a different LLT, since the VT now exactly matches a newly added (or newly current) LLT term;
  - Listings of VTs which code to a LLT which now has a different derivable path, that is, the Primary Path now returns a different PT, HLT, HLGT or SOC for a given LLT, showing the previous and current derivable level terms.

What Types of WHODrug Impact Reports Are Required?

- Some of the most common types of impact reports for WHODrug (assuming SYN/PN group coding level) include:
  - Listings of VTs by study which were classified to either a SYN (Synonym/Brand Name) or PN (Preferred Name/Generic) and will be declassified since the SYN or PN no longer exists;
  - Listings of VTs which were once classified to a to either a SYN or PN, but are now reclassified to a different SYN or PN, since the VT now exactly matches a newly added SYN or PN term;
  - Listings of VTs which code to a SYN or PN which now have a different derivable path, that is, either the derived PN is different, or the default ATC code is different (assuming a Primary Link of some kind is used);
  - A Listing which shows cases where a VT was coded to SYN which is now promoted to PN and conversely, a VT was coded to a PN which is now demoted to a SYN, since VTs code to a group level of SYN or PN.

Should Predict Tables Be Used?

- Should predict tables in a current production environment be used for impact reporting, or does an update need to occur in a separate environment to generate impact reporting?
  - Using predict tables to generate impact reports is not mutually exclusive of using a production refresh environment to generate impact reports.
  - If a refreshed copy of production is used for impact reporting, it does NOT necessarily mean that the reporting could not have been done in the production environment using PREDICT tables.

What Environment Should Be Used?

- Many of the larger TMS customers use a method of generating impact reports from a refreshed copy of their current production environment. This implies:
  - An infrastructure exists with sufficient space to generate this copy of production (usually from on-line or off-line backups);
  - Technical resources exist to perform the production refresh process correctly.
- In situations where the impact reporting is NOT based on TMS Predict tables, then a production refresh environment is REQUIRED for impact reporting to understand the impact of TMS update BEFORE it occurs in production.

Is a Developed Update Script Required?

- There are some publicly downloadable update scripts for MedDRA Primary Path and WHODrug B2 with alphabetical Primary Links for ATCs from Metalink, but these scripts are not supported by Oracle OLS support.
- Most TMS customers develop their own update scripts (either internally or with external consulting help).

Why Do TMS Customers Develop Update Scripts Internally?

- The following factors drive TMS customers to develop their own TMS update scripts, even though there is a time and resource cost associated with this process:
  - Any customization to the MedDRA or WHODrug dictionary structure, such as not using the Primary Path in MedDRA, using PT level classification level in MedDRA, using a split dictionary in WHODrug, etc...;
  - Corporate requirements for having internally developed code use specific coding standards;
  - Validation requirements for TMS updates. Since this is a repeating process which can affect production data, many companies want to have more control over the update cycle, which in turn implies having control of the source code which performs the TMS update.

No Update Script Required for Scenario 1 & 4

- Note that Scenario 1 (New initially loaded TMS dictionaries with existing study modification does not require any update script.
- Note that Scenario 4 (Initial loading Scripts with comparison to existing TMS terms) if a 3rd party tool is purchased.

Table of Scenarios and Implications on Impact Reporting

Scenario	Predict Table reporting possible?	Production Refresh environment used?	Requires separate Update Script?
1. New Initially Loaded Dictionaries with existing study modification	NO	YES	NO
2. Base Dictionary Update only, no virtual dictionary in use	YES	YES, by larger TMS customers	YES
3. Base Dictionary Update with Virtual Dictionary use	YES	YES, by larger TMS customers	YES
4. Continuous Virtual Dictionary Updating	YES	YES	YES
5. Initial Loading Scripts without separate Update scripts	YES	NO, but it is technically possible	NO if 3rd party tools are used to existing TMS terms
6. OC/TMS/AERS integrated environment with AERS updates used for OC/TMS	Not Currently	YES	YES, but supplied as part of AERS. Supported by Oracle OLS

Scenario 1 Populating existing VT terms into new Parent Questions in OC: Concept and Usage

- Concept
  - Since TMS customers know how to load dictionaries initially, separately load each new version of MedDRA and WHODrug as done initially.
  - Modify the existing studies to use this newly loaded dictionary by adding a Parent Question and related Question Set Questions associated with this new dictionary to the existing DCM.
  - Copy the existing data to this new Parent Question.
  - This method usually requires a test in a production refreshed environment first. However, it can be performed directly in production because if it fails, there is no impact to the data and coding which was already occurring/in process.
- Usage
  - Used in companies with a small number of OC coded studies in TMS.
  - CROs who want maximum flexibility in Dictionary loading.

Scenario 1 Populating existing VT terms into new Parent Questions in OC: Advantages and Disadvantages

- Primary Advantages
  - Does not require separate update scripts
  - Minimal impact to production studies if update fails
- Primary Disadvantages
  - Predictive Impact reporting not possible
  - How is data copied into the new Parent Question in OC?
- Scenario 1, to populate existing VT terms into new Parent Questions in OC, is generally accomplished with the following three techniques:
  - Technique 1: Population of new TMS Parent Questions through Derivation Procedures
  - Technique 2: Use Mass Changes in combination with New Parent Questions for the TMS Dictionary which are added to the DCM Question (study-specific) level (Technique 1)
  - Technique 3: Use BDL Method in combination with existing DX views

Technique 1: Populate New TMS Parent Questions Via Derivation Procedures

- A new question can be introduced at the DCM Question level (within a specific study) which is the Parent Question associated with the new TMS Dictionary for which Data should now be coded. It can be set to be not displayed to alleviate the need to regenerate the DCM layouts.
- Note: In TMS 4.5.2, a GLIB parent question CAN be derivable, but in all previous TMS versions 4.0.x - 4.5.1, the DCM question TMS parent question can be made derivable.
- A derivation procedure can be written which simply assigns the response value from the existing question to the TMS Parent Question.
- Executing the Derivation Procedure in Single Procedure Execution mode will cause the existing data to be populated at the next Batch Validation, for ALL patients in the study.

Technique 1: Populate New TMS Parent Questions Via Derivation Procedures (2)

- Custom code is also required to mark the patient which is associated with the existing question as modified
  - Update PATIENT_DM_TRACKING in TMS 4.0.x
  - Update CLINICAL_STUDY_STATES LAST_TMS_DERIVATION_TS in TMS 4.5
- At the 2nd Batch Validation, the Derived Parent Question associated with the TMS Dictionary is populated and TMS Coding can continue as normal.
- Note: In TMS 4.5.2 and higher, only 1 batch validation is required in this method, as RXC.TMS_OCL_DERV is called at the START and at the END of Batch Validation.
- No changed to the actual DCM Layout are required and Data Entry continues in the existing (legacy) collected questions.

Technique 2: Use Mass Changes with Technique 1

- Use Mass Changes in combination with New Parent Questions for the TMS Dictionary which are added to the DCM Question (study-specific) level (Technique 1)
  - A Mass change is used to copy the existing (legacy) question data to the new TMS Parent Question in the DCM.
  - Entry and display of existing (legacy) Questions is disabled.
  - Requires regeneration of existing DCM layouts.
  - Large Mass Changes should be performed in smaller increments to verify successful completion.

Technique 3: Use BDL Method with Existing DX Views

- Since the existing (legacy) question presumably has data which is available in the Oracle and SAS Data Extract (DX) Views, this data can be queried by a variety of tools.
- By using either SQL Queries or SAS programs, the source data (term data) can be queried with the DX View data and formatted to exactly match a Batch Data Load format in OC.
  - Note: This process is greatly facilitated in some companies by 3rd party data loading tools, which can directly generate the BDL file from a DX view and change it match the new Parent question without developing SQL scripts or SAS code.
- Batch Data Load can then be used to re-load the data into the Parent question for the new TMS Dictionary.
- Entry and display of existing (legacy) Questions is usually disabled

Scenario 2 Base Dictionary Update Only, No Virtual Dictionary In Use: Concept

- Use a separately developed update script for comparing the new dictionary data to the existing VTs and TMS dictionary terms.
- Develop queries which compare either TMS_DICT_CONTENTS.DICT_CONTENT_CODE or TMS_DICT_CONTENTS.DICT_CONTENT_ALT_CODE to the existing Dictionary Terms. These queries are passed into TMS API TMS_LOAD_DICTIONARY.MIGRATETERMS and TMS API TMS_LOAD_DICTIONARY.MIGRATERELATIONS.
- Reclassification/Declassification also performed using TMS APIs TMS_USER_CLASSIFICATION.AUTOCREATEVTA and TMS_USER_RECLASSIFICATION.UNDOVTA
- Impact reports either generated from TMS_PREDICT_CONTENTS/RELATIONS table before activation, or from logging tables generated during the load.

Scenario 2 Base Dictionary Update Only, No Virtual Dictionary In Use: Usage

- Large companies who wish to enforce harmonization of in-use dictionaries across all study groups
- CROs who have sponsor requirements for most current dictionary

Scenario 2 Base Dictionary Update Only, No Virtual Dictionary In Use : Advantages and Disadvantages

- Advantages
  - Can provide most current dictionary use across an entire environment
  - Option for predictive impact reporting using TMS PREDICT tables or Production refresh environment can be used
- Disadvantages
  - Requires a separate set of developed, tested and validated update scripts. These scripts will require modification if the vendors' source data structure changes, such as replacement of SSCs with SMQs in MedDRA
  - Can not provide a previous version of a dictionary in the environment if required
  - Many technical nuances required in the comparison of current VTs and Dictionary Terms to vendor source data.

Scenario 3 Base Dictionary Update with Virtual Dictionary Use: Concept

- Use a separately developed update script for comparing the new dictionary data to the existing VTs and TMS dictionary terms.
- Develop queries which compare either TMS_DICT_CONTENTS.DICT_CONTENT_CODE or TMS_DICT_CONTENTS.DICT_CONTENT_ALT_CODE to the existing Dictionary Terms. These queries are passed into TMS API TMS_LOAD_DICTIONARY.MIGRATETERMS and TMS API TMS_LOAD_DICTIONARY.MIGRATERELATIONS.
- Reclassification/Declassification also performed using TMS APIs TMS_USER_CLASSIFICATION.AUTOCREATEVTA and TMS_USER_RECLASSIFICATION.UNDOVTA

Scenario 3 Base Dictionary Update with Virtual Dictionary Use: Concept (2)

- Impact reports either generated from TMS_PREDICT_CONTENTS/RELATIONS table before activation, or from logging tables generated during the load.
- Create Virtual Dictionary domains for EACH TMS Domain in Use, and perform the update in the SAME calendar day as the Virtual Dictionary is created.
  - **Note:** This limitation exists because the Virtual Dictionary creation does not include a dynamic timestamp, it is always 12:00:00 on the for the date of the Virtual Dictionary cutoff timestamp.

Scenario 3 Base Dictionary Update with Virtual Dictionary Use: Usage

- Large companies who wish to have varying levels of visible data in different study groups
- Companies who have Oracle AERS and Oracle OC in the same instance
- CROs who have sponsor requirements for any version of a dictionary at point in time of a study
- Most commonly used TMS Updating technique by larger TMS customers

Scenario 3 Base Dictionary Update with Virtual Dictionary Use: Advantages and Disadvantages

- Advantages
  - Can provide any version of dictionary for use with a specific study or Program/Project combination
  - Separate Virtual Dictionary Domains can propagate domain-specific coding across various version of the dictionary
  - Option for predictive impact reporting using TMS PREDICT tables or Production refresh environment can be used
- Disadvantages
  - Requires a separate set of developed, tested and validated update scripts. These scripts will require modification if the vendors' source data structure changes, such as replacement of SSCs with SMQs in MedDRA
  - Must be performed and completed in the same calendar day
  - Many technical nuisances required in the comparison of current VTs and Dictionary Terms to vendor source data.
  - Many technical nuisances when using multiple TMS dictionary domains and Virtual Dictionary Domains

Scenario 4 Continuous Virtual Dictionary Updating: Concept

- Do not perform a base dictionary load. Instead, make the very first load of the dictionary a Virtual Dictionary update
- Use a separately developed update script for comparing the new dictionary data to the existing VTs and TMS dictionary terms.
- Develop queries which compare either TMS_DICT_CONTENTS.DICT_CONTENT_CODE or TMS_DICT_CONTENTS.DICT_CONTENT_ALT_CODE to the existing Dictionary Terms. These queries are passed into TMS API TMS_LOAD_DICTIONARY.MIGRATETERMS and TMS API TMS_LOAD_DICTIONARY.MIGRATERELATIONS.
- Reclassification/Declassification also performed using TMS APIs TMS_USER_CLASSIFICATION.AUTOCREATEVTA and TMS_USER_RECLASSIFICATION.UNDOVTA
- Impact reports either generated from TMS_PREDICT_CONTENTS/RELATIONS table before activation, or from logging tables generated during the load.

Scenario 4 Continuous Virtual Dictionary Updating: Usage

- Currently one CRO will present "TMS Virtual Dictionaries in CRO Environment" specifically on this method during the TMS Breakout session Monday, 18 September 2006 2:00 – 3:30 pm.

- Predict future use by many companies if this conceptual functionality is not incorporated into TMS 4.6.x base product.

Scenario 4 Continuous Virtual Dictionary Updating: Advantages and Disadvantages

- Advantages
  - Can provide any version of dictionary for use with a specific study or Program/Project combination
  - Separate Virtual Dictionary Domains can propagate domain-specific coding across various version of the dictionary
  - Option for predictive impact reporting using TMS PREDICT tables or Production refresh environment can be used
  - Alleviates technical nuisances when using multiple TMS dictionary domains and Virtual Dictionary Domains
- Disadvantages
  - Requires a separate set of developed, tested and validated update scripts. These scripts will require modification if the vendors' source data structure changes, such as replacement of SSCs with SMQs in MedDRA
  - Must be performed and completed in the same calendar day

Scenario 5 Initial Loading Scripts Without Separate Update Scripts: Concept

- Instead of developing an new update script, perform the initial load of the dictionary again.
- While the data for the dictionary is in the TMS_PREDICT_CONTENTS/RELATIONS table, perform a comparison agains the existing VT and TMS Dictionary Term data
- Generate a set of API calls to the TMS_LOAD_DICTIONARY.MIGRATETERMS/MIGRATERELATIONS API.
- Delete the initial loaded data, and execute the generate set of API calls
- Reclassification/Declassification also performed using TMS APIs TMS_USER_CLASSIFICATION.AUTOCREATEVTA and TMS_USER_RECLASSIFICATION.UNDOVTA
- Impact reports either generated from TMS_PREDICT_CONTENTS/RELATIONS table before activation
- Performed by a TMS Dictionary Updater tool.

Scenario 5 Initial Loading Scripts Without Separate Update Scripts : Usage

- Smaller TMS customers and CROs who want a single method for updating all dictionaries, usually customers with many custom TMS dictionaries
- Any TMS customer who wants to have another 3rd party software provider responsible for the code used in the TMS dictionary update process for all TMS dictionaries, not specialized code for each dictionary

Scenario 5 Initial Loading Scripts Without Separate Update Scripts: Advantages and Disadvantages

- Advantages
  - Using this approach, one update script will work for all dictionaries
  - If a 3rd party tool is used, then there is a single tool used to perform all updates, with an external vendor responsible for maintenance of the TMS dictionary updating code
- Disadvantages
  - Not a supported method by Oracle OLS Support
  - Requires a separate validation of a 3rd party tool; or, Requires a single set of developed, tested and validated update scripts which may require modification if the vendors' source data structure changes, such as replacement of SSCs with SMQs in MedDRA

Scenario 6 OC/TMS/AERS integrated environment with AERS updates used for OC/TMS: Concept and Usage

- Concept
  - Using the documented process included with Oracle AERS, perform the dictionary updates are required for MedDRA and WHODrug in AERS.
  - This process is actually very similar to Scenario 4:Base Dictionary Update with Virtual Dictionary use
- Usage
  - Only TMS customers with a single integrated OC/TMS/AERS environment, who use AERS coding for all OC studies.

Scenario 6 OC/TMS/AERS integrated environment with AERS updates used for OC/TMS: Advantages and Disadvantages

- Advantages
  - This is the only set of TMS Update scripts and procedures which Oracle OLS is required to support for licensed Oracle AERS customers.
  - No cost of development or maintenance for update scripts or procedures. Oracle OLS must provide functional, working scripts for all supported and integrated versions of AERS and TMS.
- Disadvantages
  - All OC coding must use AERS "Latest" domain coding and corresponding virtual dictionary domains.
  - No OC-specific TMS Domains would be available in the base dictionary or virtual dictionaries.
  - Some additional time is required working with OLS support to fix issues as they arise with new versions of MedDRA and/or WHODrug and/or TMS, and especially if loading very old versions of MedDRA and WHODrug into TMS-integrated AERS.

Additional Comments

- Other methods for performing dictionary updating will be possible with TMS 4.6. They are not included here since this version is not in production.
- It is not clear what the impact of filter dictionary functionality will be on existing TMS dictionary update scripts.
- TMS DSI functionality might also be useful in the future in facilitating some types of TMS dictionary updates, and could be theoretically be used in Scenario 1 for re-populating new Parent Questions in OC.

Question and Answers

All follow-up questions, please contact:

Sunil G. Singh
singh@clinicalserver.com
+1-860-983-5848
+1-888-463-4751
+91-98-181-34-017

Stephan Kromov
skromov@clinicalserver.com
+1-215-353-0811

Dr. Letian Liu
lliu@clinicalserver.com
+86-134-0212-4879