

# Medical Dictionary for Regulatory Activities (MedDRA) Upgrade in National Cancer Institute (NCI) Cancer Central Clinical Database (C3D) Studies



The National Cancer Institute (NCI) Cancer Therapy Evaluation Program (CTEP) updates its MedDRA codes once a year in compliance with the ICH (International Conference on Harmonization) guidance. The July 2007 update affected CTEP's lists of values for Common Toxicity Criteria (CTCv2.0), Common Terminology Criteria for Adverse Events (CTCAEv3.0), Simplified Disease Classification (SDCv1.0), and Legacy Disease Codes. NCI's Cancer Centralized Clinical Database (C3D) had over 100 active studies at that time, among which 25 reported to the Clinical Data Update System (CDUS/CDS) and 26 reported to the Clinical Trials Monitoring Service (CTMS). The CTMS/CDUS reporting studies had to be updated to utilize the new codes. CTEP no longer accepted the old codes as of July 1, 2007.

## What's MedDRA?

MedDRA defines itself as "a pragmatic, clinically validated medical terminology with an emphasis on ease-of-use data entry, retrieval, analysis, and display, with a suitable balance between sensitivity and specificity, within the regulatory environment." \* This definition precisely describes its role serving as terminology resource for the all phases of the discovery and development of new drugs or medical devices, and MedDRA improves the efficiency and effectiveness during this process.

\*: "MedDRA FAQs" from meddransso.com website

## Purpose of Using MedDRA

- To report adverse event data from clinical trials, as well as post-marketing and pharmacovigilance. 1
- To facilitate identification of common data sets for evaluation of clinical and safety information. 2
- To facilitate consistent retrieval of specific cases or medical conditions from a database. 3
- To facilitate electronic data interchange of clinical safety information. 4
- To improve consistency in comparing and understanding "safety signal" and aggregated clinical data. 5

1: "MedDRA FAQs" from meddransso.com website

2,3,4,5: "MedDRA Term Selections: Points to Consider" Release 3.8

## MedDRA Use in C3D

C3D is the Clinical Trials Database for the Cancer Biomedical Informatics Grid (caBIG™) initiative. Oracle Clinical serves as the foundation of C3D by supporting clinical trial definition, data capture, multiple site reporting, data definition and usage standardization. In C3D, MedDRA is collected indirectly in several template forms, including Adverse Events, Baseline Symptoms, Enrollment, Prior Therapy Supplement, etc. Since MedDRA is updated annually, updating MedDRA in C3D studies is an important activity.

Unlike Oracle's Thesaurus Management System (TMS), C3D studies are using Thesaurus DVGs to enforce implementation of consistent terminology and allow selection of entries from the Thesaurus. Code list and values are managed by CTEP.

MedDRA Term	Status	Approved	Secondary Term	Code	Source	Terminology	Level
ITC_000100	Yes	Exp. 2/04	ICD-992	GL2BL	Med/94-Primary Pat	Lowest Level Term	
PLAZOTIP_PAIN	Yes	Baseline	IC00000	ME000AB	Med/94-Primary Pat	Preferred Term	
BACK_PAIN	Yes	Baseline	IC00000	ME000AB	Med/94-Primary Pat	Preferred Term	
RECOGNIZED_PAIN	Yes	Adverse/SA	IC00000	ME000AB	Med/94-Primary Pat	Lowest Level Term	

TMS

## MedDRA Update Impact in C3D Studies

In C3D eCRFs, Term is an enterable field, and the associated Code is used to submit to the reporting agencies. Code is a non-displayed field and is derived through a derivation procedure from the Term entered.

### 1. Impact on CDUS/CDS Reporting Studies

- Baseline Abnormalities: changes of CTC List of Values
- Adverse Events and Late Adverse Events: changes of CTC List of Values
- Patients: changes of SDC (Simplified Disease Codes) List of Values

CDUS/CDS submission requires quarterly cumulative data. All data submitted from previous quarters must be submitted in subsequent quarters. Submissions may contain new data as well as updates to previous submitted data. NCI C3D Data Extract Utility is the tool to extract data from C3D in the format required by the data submission guideline.

4.3.11. ADVERSE\_EVENTS TABLE

Each record associated with the ADVERSE\_EVENTS Table shall consist of the following information:

Protocol_ID	Protocol(255)
Patient_ID	Patient(250)
Center_ID	Number(9)
AE_Type_Code	Number(9)
AE_Group_Code	Number(9)
AE_Onset_Sympt	Timestamp(100)
AE_Attribution_Code	Number(1)
AER_End	Variant(1)

A sample record associated with the ADVERSE\_EVENTS Table will appear as follows:

```

*ADVERSE_EVENTS*"Protocol_ID"%"Patient_ID"%"Center_ID"%"AE_Type_Code"%"AE_Group_Code"%"AE_Onset_Sympt"%"AE_Attribution_Code"%"AER_End"
    
```

Source: CDUS Instructions and Guidelines, Version 3.0, Release 3. July 20, 2005

C3D Data Extract Utility

### 2. Impact on CTMS Reporting Studies

- Baseline Symptom (BS): changes of CTC List of Values
- Adverse Event (TX and LA): changes of CTC List of Values
- Enrollment (EN): changes of SDC List of Values

CTMS submission, contracted through Theredex, is an incremental bi-weekly process. Both deleted records and updated records generated after last submission must be submitted. Theredex does not want to see records caused by MedDRA code changes. The agreed-upon process is:

- Extract data before database change. This minus the last extract should be the pure data change which will be sent to Theredex.
- Apply changes in database.
- Execute related procedures. Do another extraction, which will generate records caused by code change. Do not submit these files to Theredex; use them as the baseline for the next extraction.

## Proposed Approaches

During 2006 MedDRA 9 upgrade, different implementation/database change approaches were presented:

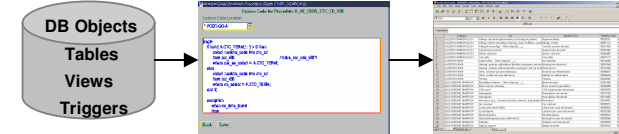
- Populating MedDRA code into a new column.
- Updating table columns "in place", i.e., implementing the latest MedDRA code by updating the MEDDRA\_CODE column, and adding a column for the previous version to provide the continuity and historical cross-checks. After thorough analysis and discussion of pros and cons by all parties, the decision was to go with approach B. Starting from MedDRA 9, all subsequent MedDRA upgrades will follow the same approach.

## Testing Plan

- Identify appropriate database environment and studies to do testing. In this case, we use development database.
- Make sure table structures and data are same in both production and testing database. This can be done through table import including data.
- Apply changes in database.
  - Enter data into form, for example AE, patient 1. Then check current view. Since derivation procedure is set to "ON-LINE/DCM", CDUS CTC Code is derived immediately upon data save.
  - Run update table script.
  - Execute derivation procedure, then check current view, CDUS CTC Code changed to the updated MedDRA 10 code.
  - Enter data into AE form for patient 2. Enter same value into the CTC\_TERM field. Make sure DVG is working fine.
  - Check data in current view, CDUS CTC Code get derived correctly.

## MedDRA Update Processes

- Change the table underlying the Thesaurus DVGs.
- Execute Derivation Procedures in Oracle Clinical.
- Auto-refresh the Oracle Discoverer Workbooks used for reporting/QC.



## C3D Local Adopter Support

After running the MedDRA update in our main production environment, we provided database update scripts to local replica sites, working with them to apply changes in their instances.

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