

Implementation of MedDRA within Global Drug Safety

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Conversion Strategy

Conversion Strategy

- ◆ Business needs
- ◆ Scope of the project
- ◆ MedDRA conversion strategy
- ◆ Implementation strategy

Business Needs

- ◆ Drug Safety integration following AstraZeneca merger
- ◆ Implementation of global safety database (Clintrace)
 - 7 legacy systems
 - 6 R&D sites + 2 marketing companies
 - 4 medical dictionaries
- ◆ Adoption of ICH standards

Scope of the Conversion Project

- ◆ Adverse events, indications and relevant medical history terms from all AZ safety databases
- ◆ Code verbatim (or equivalent) to LLT
- ◆ Produce a coding guidelines document
- ◆ Establish a training plan for Global Drug Safety
- ◆ Develop MedDRA maintenance strategy
- ◆ Provide support and knowledge acquired to the clinical function

Scope of the data and timelines

- ◆ Supplied AE (unique) terms (57,000+)
- ◆ Indication and Medical History terms (73,000+)
- ◆ Timelines:
 - start mid - December 1999
 - complete April 2000

The Conversion Team

- ◆ Establish a ‘working’ team:
 - representatives of both former companies and sites
 - multidisciplinary team (Drug Safety and Clinical)
 - Drug Safety physician to provide medical advice and perform QA
- ◆ Effective communication within team: weekly teleconferences plus face to face meetings

Coding

- ◆ Consider former coding when appropriate
- ◆ No changes to verbatim text during conversion
- ◆ Develop legacy data coding guidelines
- ◆ Selection of appropriate coding tool
- ◆ Methods for resolving coding issues
- ◆ Consider the possibility of outsourcing some of the coding: indications/history

Implementation Strategy

- ◆ Adopt MedDRA at each R&D site following implementation of Clintrace
- ◆ Timeline: July 2000 to December 2000
- ◆ Legacy coding to form basis for a synonym table
- ◆ Use of auto-coder from safety database application

Training

- ◆ Training at each site prior to conversion
- ◆ Three levels of training:
 - 1) Overview
 - 2) Coding
 - 3) Advanced
- ◆ External training experts used
- ◆ Long term development training plan to establish site experts for MedDRA ('Train the Trainer')

Maintenance

- ◆ Adopt a central contact point with MSSO
- ◆ Database maintenance to focus on LLTs
- ◆ Process for dealing with non-current terms
- ◆ Maintain conversion matrix throughout implementation process
- ◆ Quarterly updates to be utilised
- ◆ Develop long term strategy for requesting new terms

Conversion Process

Conversion to MedDRA

- ◆ Who did it?
- ◆ How did we do it?
- ◆ What guidelines were used?
- ◆ How was existing data handled?
- ◆ What were the challenges?

Conversion Team

- ◆ Team comprised representatives from:
 - Global Drug Safety
 - other Global Clinical Development skills centres
- ◆ Sub-team of Clintrace Implementation team
- ◆ Drug Safety physician (provide QA and medical support)

Overview

- ◆ Used auto-coding software to code direct matches (approx. 12% of terms)
- ◆ All remaining adverse event terms manually coded by team of 14 coders
 - assisted by removal of range of ‘stop’ words (e.g. numbers, punctuation, etc): enabled simple matching of another 25% terms against LLTs

Conversion Process

- ◆ Gathered all unique supplied terms from AZ sites
- ◆ Divided up by SOC and distributed according to expertise within team
- ◆ Communicated weekly as a team by teleconference
- ◆ Several face to face meetings held
- ◆ Recorded difficult decisions
- ◆ Decisions taken by consensus
- ◆ Submitted new terms to the MSSO
- ◆ Outsourced Medical History and Indication terms
- ◆ Submitted coding for medical review and validation

Rules and guidelines

- ◆ Coding guidelines developed to assist term selection
- ◆ Initially specific to adverse events
- ◆ Created coding guidelines for future application

How did we handle existing data?

- ◆ Former coding retained (referred to as necessary)
- ◆ No changes to verbatim text

Strategies to help

- ◆ Gather all the unique terms to be coded - you do not want to code the same term more than once
- ◆ Sort the terms by System Organ Class and Preferred Term according to the current dictionary - coding a set of similar terms together is quicker and improves consistency
- ◆ Pick one version of MedDRA to code against and keep with it until the work is done
- ◆ Distribute the terms amongst your team according to their expertise
- ◆ Make medical advice readily available

- ◆ Consider out-sourcing less critical data
- ◆ Record difficult decisions and incorporate these into training/coding guidelines - communicate these to other coders for their benefit
- ◆ Submit new term requests to the MSSO as needed
- ◆ Peer review everything
- ◆ Decide on a validation process - what is an acceptable error rate in 57,000 terms?
- ◆ Validate, sign off and celebrate!

Alternative strategies for recoding existing data

What terms should you code?

- ◆ AEs only?
- ◆ AEs plus drug indication terms?
- ◆ AEs plus drug indication terms plus medical history?

- ◆ AZ solution: code all

How should terms be coded?

- ◆ Raw text - the ‘verbatim term’?
- ◆ Keywords?
- ◆ Preferred terms/codes from existing dictionary?
- ◆ COSTART coding symbol?

The more specific the level chosen the more accurate the coding will be

BUT

Greater accuracy = More work

Re-coding based on previous codes effectively preserves the existing data

BUT

As new data are added terms may go to a different LLT or even PT

- ◆ Say current dictionary has:
 - PT1
 - synonym1
 - synonym2
 -
 -
 - synonym8
- ◆ MedDRA may code synonyms 1- 8 to different PTs - thus old and new cases will have different MedDRA codes

- ◆ In AstraZeneca, we recoded the ‘as reported’ term wherever possible
- ◆ Some of the legacy data did not support this (only the code was available)
- ◆ Some medical history text was free text (never keyworded) and was left uncoded
- ◆ **Recoding from the lowest level stored on the database is strongly recommended**

What about previously uncoded data?

For example: medical history terms not coded in current system

- ◆ Now that MedDRA is available are you going to start coding these? (Yes!)
- ◆ If the terms can be easily broken out into text which can be coded (e.g. text separated by semi-colons) then do it - you will never have a better opportunity

Can I use re-coded data to help with future coding?

- ◆ If you have a really good auto-encoder keep it!
- ◆ AstraZeneca have incorporated 32,000 terms (excludes all LLTs and ‘one off’ terms) into a ‘synonym’ list checked by our auto-encoder. This helps with consistent coding

What elements of MedDRA do I need to store with the case data?

- ◆ Factors to consider
 - all the information will be stored in dictionary tables
 - searching/output is usually performed at a higher level than LLT
 - E2B requirements
 - E2C (PSUR) requirements
- ◆ AstraZeneca have concluded that it is best to store just the LLT code and the MedDRA version used to code the case with the case data
- ◆ The LLT text, PT text and Primary SOC are displayed to the user

What is the impact of new releases of MedDRA?

- ◆ If the LLT code only is stored with the case data then the impact is minimal
- ◆ If higher levels are stored then some higher level codes may change
- ◆ Provision of new codes (especially PTs) may allow better coding of existing terms

Automated labelling and MedDRA - can it be done?

- ◆ Both Astra and Zeneca had automated ‘listedness’ based on preferred terms (in their old dictionaries)
- ◆ Advantages:
 - guarantee of consistency
 - if held separately from the case, with dates, allows the E2C requirement ‘the company core data sheet in effect at the beginning of the period covered by the report should be used as the reference’ to be met
- ◆ Disadvantages
 - prevents different assessments for the same term in different cases based on the conditions prevailing in a particular case
 - cannot cope with concepts such as ‘mild’ and ‘transient’
 - MedDRA does not differentiate drug interactions

Challenges

- ◆ Tight deadlines imposed
- ◆ High degree of accuracy
- ◆ Company integration taking place
- ◆ Sites work in different ways
- ◆ No dedicated physician or IT support at some of the smaller R&D sites

Project Status

- ◆ Conversion and validation of legacy AE terms: completed
- ◆ Conversion/validation Medical History and Indication legacy terms: completed
- ◆ Training for Global Drug Safety: completed

Project Status (cont'd)

- ◆ Coding guidelines developed:
 - for legacy data conversion
 - for new users of MedDRA
- ◆ Database conversions using MedDRA 3.1
- ◆ Support for Global Clinical as they embark on conversion of clinical data to MedDRA

Lessons Learned

Lessons learned

- ◆ Do not underestimate the enormity of the task - MedDRA has a learning curve and complexity
- ◆ Make sure management understand the issues and the enormity of the task
- ◆ Do not underestimate differences in standards and practices between the R&D sites (particularly in a newly merged company)
- ◆ Set a deadline and stick to it.
- ◆ Give your conversion team sufficient time to do the job properly

Lessons learned

- ◆ Spread the work amongst as many experienced people as you can - it will help them learn MedDRA
- ◆ Prepare good coding guidelines before data conversion
- ◆ People can only stand so much recoding each day
- ◆ Be prepared to consider outsourcing some of the work
- ◆ Share your results but be ready to agree to disagree!
- ◆ If you start with Drug Safety then the knowledge gained can be transferred to Clinical

Training

- ◆ MedDRA is different from any dictionary you have used before
- ◆ Invest in training!
 - it is probably necessary to go external - where will the skills come from in-house?
- ◆ Coders need to be trained: there are approx. 11,000 PTs to choose from
- ◆ Those who search and analyse the data also need to be trained

MedDRA Conversion

- ◆ **M** - mind-blowing
- ◆ **e** - exhausting
- ◆ **d** - daunting
- ◆ **D** - done
- ◆ **R** - reviewed
- ◆ **A** - achieved