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## **Versioning Clinical Trials: Taking a 'full' approach**

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## Questions to Consider

- *Do I need to upgrade my database?*
- *What is 'full versioning'?*
- *Where do I start?*
- *How big is the task?*
- *What is the impact on my data?*
- *How should I communicate the changes?*
- *What are the benefits or drawbacks?*

## Do I need to upgrade my database?

*There are no regulations governing use of MedDRA for Clinical Trials in any ICH region*

*but,*

*SUSARS in Europe need to be submitted in the current or last version of MedDRA*

*and,*

*MedDRA is mandatory for all electronic safety reporting*

*so,*

*It makes sense to use the same dictionary for both safety and clinical trials*

# What is 'full versioning'?



*Option 6: Recode the trial data for all trials on a project on an ongoing basis with the most recent version of MedDRA*

*(Based on MSSO Recommendations for MedDRA Implementation and Versioning for Clinical Trials)*

- *Dictionary Management at Roche:*
  - *One copy of MedDRA stored centrally*
  - *One verbatim term pool of previously coded terms*
  - *MedDRA LLTs + Verbatim term pool = Roche 'Corporate Thesaurus'*
  - *This 'Corporate Thesaurus' is used by all Clinical trials & Drug Safety*
  - *MedDRA version used in 'Corporate Thesaurus' is updated twice a year*
- *Examples shared today relate to upgrades performed 11.0 – 11.1 & 11.1 – 12.0*

## Where do I start ... Preparation?

- *Estimate the resources required to upgrade – staff and time frame*
- *Assess the types of changes*
  - *MSSO “What’s new?” document & webinar*
  - *Focus attention on priority areas*
- *Consider your portfolio*
- *Identify the changes you have requested*
- *Review company guidelines & implications of changes*
- *Document your planned strategy*
- *Communicate any relevant changes*



# Where do I start ... Process?

## Top down approach

1. *Relink non-current terms & verbatims*
2. *Take each new LLT & define the concept*
3. *Search the database using Boolean search criteria for verbatims to bring over*
4. *Review 'siblings' of verbatims chosen to move*
5. *Move all selected verbatims*
6. *Review search criteria & terms moved*



# Top-down vs bottom-up approach to dictionary updates



# Where do I start ... People?

## Versioning is an important task

- *Not a mechanical activity*
- *Requires thinking beyond the terms*
- *Has an impact on guidelines & similar terms*



### Consider:

*Where is it handled - Insourced vs outsourced?*

*Do you assign it to designated coder(s) or share it among staff?*

*Provide reference resources & explanations/training*

**Medical review is critical**

## How big is the task ... Results ?

- *60 day period allowed for versioning – when do you start?*
  - *Include time to assess, plan & document*
  - *Allow time for review at end*
- *Estimate time needed based on average mins needed per new LLT*
  - *E.g. 10 mins x 500 new LLTs = 83 hours*
    - *Version 12.0 – 538 new LLTs versioned\**
    - *Version 11.1 – 404 new LLTs versioned\**
    - *Version 11.0 – 450 new LLTs versioned\**
    - *Version 10.1 – 422 new LLTs versioned\**

*\* (Excludes British vs US spellings, Acronyms & lexical variants)*



# What is the impact... on the dictionary?

**Version 11.1 upgrade - Corporate Thesaurus = 546,780 terms**

- *Additions to MedDRA*
  - *LLTs – 452 (incl. PT)*
  - *PTs – 200*
  - *Non-current LLTs - 3*
- *Verbatims manually moved to new terms – 1,246 (0.2% CorpThes)*
- *Changes to MedDRA hierarchy*
  - *15 PTs changed SOC*
  - *41 LLT changed SOC*
  - *336 LLT changed PT*
- *Verbatims automatically moved with hierarchy – 2,667 (0.5% CorpThes)*
- *Total number of changes in the Corporate Thesaurus – 3,913 (0.7% CorpThes)*
- *Significant changes (change in SOC or PT) – 2,393 (61% of changes made)*

# What is the impact... on the dictionary?

**Version 12.0 upgrade - Corporate Thesaurus = 573,301 terms**

- *Additions to MedDRA*
  - *LLTs – 572*
  - *PTs – 285*
  - *Non-current LLTs - 7*
- *Verbatims manually moved to new terms – 902 (0.2% CorpThes)*
- *Changes to MedDRA hierarchy*
  - *20 PTs changed SOC*
  - *77 LLT changed SOC*
  - *243 LLT changed PT*
- *Verbatims automatically moved with hierarchy – 1,926 (0.3% CorpThes)*
- *Total number of changes in the Corporate Thesaurus – 2,828 (0.5% CorpThes)*

# What is the impact... on a study?

## Comparison reports highlight changes between versions

- *Types of changes*
  - *New term additions require manual relinking*
  - *Changes in the hierarchy cause terms to move automatically*
- *Medical significance*
  - *Changes add accuracy & specificity to coding*
  - *Changes are more medically significant if the PT and/or SOC change*

**If terms have been reported clearly and coded out of context, when the study is updated to a later version, the data does not change - it might just look different**

# What is the impact... on a study?

*Study 1: 800 patients*

*Approx. 2500 events coded*

P	Verbatim	MedDRA 111 Preferred Term	MedDRA 111 System Organ Class	MedDRA 110 Preferred Term	MedDRA 110 System Organ Class
P	AURICLE INFECTION RIGHT (DUE TO STING INJECT)	INFECTED BITES	INFECTIONS AND INFESTATIONS	INFECTED INSECT BITE	INFECTIONS AND INFESTATIONS
P	BREAST PLASTIC SURGERY	MAMMOPLASTY	SURGICAL AND MEDICAL PROCEDURES	BREAST COSMETIC SURGERY	SURGICAL AND MEDICAL PROCEDURES
P	COLON DIVERTICULOSIS DISEASE	DIVERTICULUM INTESTINAL	GASTROINTESTINAL DISORDERS	DIVERTICULUM	GASTROINTESTINAL DISORDERS
P	EX-SMOKER	EX-TOBACCO USER	SOCIAL CIRCUMSTANCES	EX-SMOKER	SOCIAL CIRCUMSTANCES
P	EX-SMOKER (TEN CIGARETTES)	EX-TOBACCO USER	SOCIAL CIRCUMSTANCES	EX-SMOKER	SOCIAL CIRCUMSTANCES
P	EX-SMOKER (5 CIGARETTE 1 DAY)	EX-TOBACCO USER	SOCIAL CIRCUMSTANCES	EX-SMOKER	SOCIAL CIRCUMSTANCES
P	LEFT EYE VISUAL DEFICIT (MODERATE)	VISUAL IMPAIRMENT	EYE DISORDERS	VISUAL DISTURBANCE	EYE DISORDERS
P	LEFT VENOUS INSUFFICIENCY (MILD)	VENOUS INSUFFICIENCY	VASCULAR DISORDERS	VENOUS STASIS	VASCULAR DISORDERS
P	MILD VENOUS INSUFFICIENCY	VENOUS INSUFFICIENCY	VASCULAR DISORDERS	VENOUS STASIS	VASCULAR DISORDERS
P	MODERATE VENOUS INSUFFICIENCY	VENOUS INSUFFICIENCY	VASCULAR DISORDERS	VENOUS STASIS	VASCULAR DISORDERS
P	PERIPHERAL VENOUS INSUFFICIENCY	VENOUS INSUFFICIENCY	VASCULAR DISORDERS	VENOUS STASIS	VASCULAR DISORDERS
B	RIGHT HAND TENDON SHEATH CYST	SYNOVIAL CYST	MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS	CYST	GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS
P	SMOKER	TOBACCO USER	SOCIAL CIRCUMSTANCES	SMOKER	SOCIAL CIRCUMSTANCES
P	TWINGE PAIN IN LUMBAR SPINE	BONE PAIN	MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS	BACK PAIN	MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS
P	VENOUS INSUFFICIENCY	VENOUS INSUFFICIENCY	VASCULAR DISORDERS	VENOUS STASIS	VASCULAR DISORDERS
P	VISUAL IMPAIRMENT	VISUAL IMPAIRMENT	EYE DISORDERS	VISUAL DISTURBANCE	EYE DISORDERS

## What is the impact... on guidelines?

*Guidelines and versioning are interdependent*

- Guidelines determine how terms are reviewed and potentially re-linked*
- MedDRA changes can highlight need for new or revised guidelines*

*Examples in 12.0*

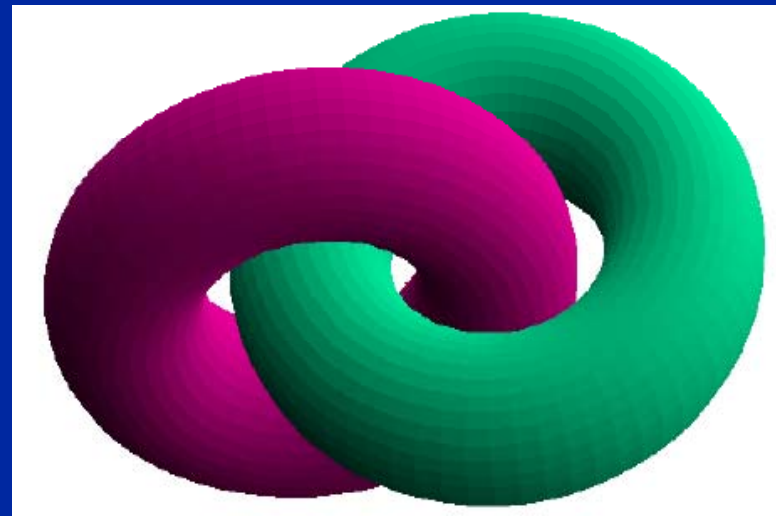
*Colour vision change*

*Eye prosthesis insertion*

*Upper abdominal tenderness*

*Anorectal varices*

*Vulvovaginal condyloma*



## How should I communicate ... internally?

- *Corporate Mindset*
  - *Upgrades occur at the same time each year*
  - *Avoid database locks at time of upgrade*
  - *SMOs are updated by MSSO so need less work ad-hoc queries*
- *Advance notice to study teams*
  - *Provide a 60 day warning – around release date in March & September*
  - *Send MSSO detailed version reports to study Science teams*
- *Post upgrade communication*
  - *Post a general notice that upgrade has been performed*
  - *Distribute individual study reports detailing changes*

## How should I communicate ... externally?

- *Clinical Study Reports, Interim Assessments and Follow-up reports*
  - *Current version is always used*
  - *Version number is included in document and as footnote on data listings*
  - *No need to explain coding differences due to MedDRA versioning*
- *Integrated Safety Summaries*
  - *A verbatim term pool allows updated summary tabulations*
  - *General comment is included to state that data have been updated*
  - *If a particular area of focus is affected, specific explanation is added*
- *Annual Safety Summaries*
  - *Current version is always used*
  - *MedDRA version number is specified*
  - *No year-on-year comparison is needed*

## What are the benefits of 'full versioning'?

- *Specificity – Additions to MedDRA of new medical concepts & investigations*
- *Accuracy – Improves signal detection*
- *Consistency – 6 monthly review of verbatims in database*
- *Quality control – Opportunity to review ongoing coding & guidelines*
- *Closer SAE reconciliation – Both Clinical & Safety are using same version*
- *Merge & comparison of data – In-house meta-analyses & comparison by regulators*
- *Guidelines & definitions – Remain current and aligned to data needs*
- *Staff knowledge – Familiarity with MedDRA, guidelines & product data*

## What are the drawbacks to 'full versioning'?

- *Workload – Intense period of work for coders & medical reviewer*
- *IT requirements – Top down approach relies on sophisticated search tools*
- *'Corporate Thesaurus' – Needs centralised data repository linked to coding tool*
- *Outsourced studies – Need to centralise for use in Integrated Safety Summaries*
- *Ad hoc queries – Need to review and add relevant new terms*
- *Changes in appearance of data – Frustration for medical reviewers*
- *Communication – Need for company wide reassurance that impact is low*



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