Disclaimer

I will generally be talking about potential scenarios and options in the industry rather than specific Vertex operational activities. Although I may mention some specific examples of my company's practices from time to time, this should be seen as a disclaimer that the views expressed are my own based on industry experience.

There are two types of people in this world:
1) Those who can extrapolate from incomplete data
Considerations & Limitations for Splitting

• Paper vs Electronic
  – Paper studies may allow for ‘Obvious corrections’ (agreed with the PI)
  – EDC studies require query and update

• Technology
  – Coding systems may allow for different options
  – Integrated DataBase & Coding Systems may be limited
  – Off the shelf systems vs In-house tools
  – Safety DB vs Clinical DB

• Phase of study – Clinical Trial vs Post-Marketing
  – Options to query may be limited in Post-Marketing & Spontaneous reporting
  – Different term handling conventions may apply (e.g. Phase I may be paper based trials vs later phase EDC)

• Other Data Fields
  – If Paper CRF - Copy down dates / severity etc.?
  – Responsibility of site to ensure data is correct.
The EU Industry MedDRA UG surveyed the user community in 2014 and the results (from 156 respondents) are highlighted above.
Verbatim:
‘Cholelithiasis, Myocardial Infarct’

Query:
“Please review and update to ensure only one medical concept is recorded per line or provide a single unifying diagnosis that collectively represents these events in accordance with eCRF Completion Guidelines.”

Result:
2 new codable Verbatim of ‘Cholelithiasis’ and ‘Myocardial Infarct’
Verbatim:
‘Grazed knee due to fall’

Action:
Term clearly requires a split but not necessarily a query to ensure both elements can be coded.

Result:
Same Verbatim but 2 different ‘Modified fields’ that can be coded:

V: Grazed knee due to fall        Mod: Grazed Knee        Code: Abrasion

V: Grazed knee due to fall        Mod: Fall              Code: Fall

NOTE: Ensure the context is clear in the modified field if appropriate for coding purposes (e.g. Traumatic blindness from the verbatim ‘Blindness due to fall’)
Use Parentheses

Verbatim:
‘Vomiting and diarrhoea’

Action:
Query to split but request specific data entry with parenthesis to enable coding of different elements in the term.

Query:
“Please enter a single underlying diagnosis or split as
1. Vomiting (and diarrhoea) and 2. (Vomiting and) diarrhoea”

Result:
2 new Verbatim created:
V: Vomiting (and diarrhoea) Code: Vomiting
V: (Vomiting and) diarrhoea Code: Diarrhoea

Or the query may lead to a single diagnosis verbatim being entered in place of the symptoms: e.g. if the response was ‘Food Poisoning’
Don’t Split – Link instead

Verbatim:
‘Influenza, runny nose, headache’

Action:
When all elements of a reported record may require coding (e.g. Diagnosis and it’s related symptoms). In the Safety DB there could be a ‘Primary’ code and then secondary ‘linked’ codes.

Query:
Not Required

Result:
Single Verbatim with multiple linked codes
Primary Code: Influenza
Secondary Code: Runny nose
Secondary Code: Headache
Other??

- These are just some different ways of splitting terms that I have come across over the years.
- Are there any other practices out there?
Summary

• No Regulatory Mandate of HOW to manage Term Splitting
• Must be GCP Compliant
  – Auditable
  – Investigator approval (where appropriate)
• Documentation is key
  – Term Handling / Coding Plan / Coding Conventions
  – Obvious Corrections Document
Term Specification for MedDRA coding in clinical studies

Carol-Ann Wilson
Purpose of Term Specification Rules

- Good quality data input is a pre-requisite for accurate coding
  - ‘Trash foot’, ‘Posterior not visible’, ‘Could not get out of bed’
- The Term Specification Rules were developed
  - To support Investigator’s training and data verification and clarification processes in clinical studies
    - These rules intend to provide guidance to Investigator’s and support CRAs, Study Managers and Data Managers. They should not restrict reporting practices of Investigators.
  - To avoid need for clarification of medical terms (queries) that cause problems during the coding process with MedDRA
  - They can also be provided to personnel in Pharmacovigilance to support term extraction from unstructured case information
Examples for Term Specification Rules

1. **Specify** each Adverse Event precisely providing the relevant medical information in a concise wording, avoid irrelevant details

**Examples:**

- Bone fractures: add site and etiology/cause
- Bleedings: provide the localization; specify details of menstrual irregularities, if applicable
- Cramps: add localization like e.g. calf cramps, intestinal cramping or uterine cramps
- Infections: provide localization and infectious agent, if available
- Local “lesions”: do not report as “lesion” only, specify as malignant neoplasm, metastases, ulcer, etc
- Administration site conditions: specify type of administration site and the specific event as e.g. injection site swelling
Examples for Term Specification Rules

2. Use medical terminology instead of popular descriptions

**Examples:**

- Not: ‘Bumps on face’ or ‘Facial blemishes’
- Report: ‘Acne on face’
- Not: ‘Angina’
- Not: ‘Sensitive skin’
- Report: ‘Skin allergy’, ‘Skin irritability’ or ‘Hyperesthesia’
- Not: ‘Sores’
- Report: ‘Pain’, ‘Ulcer’, ‘Wound’ etc and provide localization
3. Prefer diagnoses over symptoms:

- **Report a diagnosis** (final or provisional), whenever available. Report related signs and symptoms separately, if medically relevant.

**Example:**

- ‘Commotio cerebri with blackout and retrograde amnesia’
  - Report:
    1. Commotio cerebri
    2. Blackout
    3. Retrograde amnesia

- **If no diagnosis is available, report the individual signs and symptoms as separate Adverse Events**

**Example:**

- ‘Knee pain and knee edema’
  - Report:
    1. Knee pain
    2. Knee edema
Examples for Term Specification Rules

4. Avoid the terms “due to” or “secondary to”
   Relationship to medical history or previous Adverse Event could be reported in the comment field. If two new causally related diagnoses have to be documented, record them separately.

Examples:

😊 Not: ‘Renal colic due to renal stone’
😊 Report: ‘Renal Colic’ (and in addition ‘Renal stone’ if not already reported as AE or in Medical history)
😊 Not: ‘Hyperglycemia due to diabetes’
😊 Report: ‘Hyperglycemia’ (and in addition ‘Diabetes’ if not already reported as AE or in Medical history)
😊 Not: ‘Sepsis secondary to cholecystitis’
😊 Report: ‘Cholecystitis’ and ‘Biliary Sepsis’
😊 Not: ‘Hematoma due to animal bite’
😊 Report: ‘Animal bite’ and ‘Traumatic hematoma’
Examples for Term Specification Rules

5. **Report changes in laboratory values/ investigational results instead of numerical values**
   Do not qualify as abnormal when “increased” or “decreased” is applicable. Also specify the body fluid.

**Examples:**

- ☹️ Not: ‘Blood glucose 150 mg/dl’

- 😊 Report: ‘Blood glucose increased’

- ☹️ Not: ‘Protein increased’

- 😊 Report: ’Increased protein in cerebrospinal fluid’, ’Urinary protein Increased” or ’Serum total protein increased’
6. When reporting changes of conditions reported in medical history or as a previous Adverse Event, add descriptors like “Relapse”, “Progression”, “Exacerbation” etc.

Examples:
- Report:
  - ‘Relapse of multiple sclerosis’
  - ‘Exacerbation of pre-existing asthma’
  - etc.

7. If a medical reason is available, do not report outcomes like hospitalization, surgical interventions or death as an Adverse Event. Specify if hospitalization or surgery is elective for pre-existing, unchanged conditions.

Examples:
- Not: ‘Hospitalization’
- Report: ‘Hospitalization for investigation of acute abdominal pain’
- Not: ‘Surgery’
- Report: ‘Elective surgery for pre-existing cataract’
Examples for Term Specification Rules

8. Do not use abbreviations and unusual special characters

Examples:

- ☹ Not: ‘CHF’
- ☀ Report: ‘Congestive heart failure’ or ‘Chronic heart failure’
- ☹ Not: ‘Decreased BS’
- ☀ Report: ‘Decreased blood sugar’, ‘Decreased breathing sounds’ or ‘Decreased bowel sounds’
- ☹ Not: ‘Pain extr’
- ☀ Report: ‘Pain in extremity’ or ‘Pain extreme’
- ☹ Not: ! ? & @ + ; : “” <> etc.
Thank you!
Coding Guidelines in Clinical Safety

Christina Winter
16 April 2015
Data entry guidelines

Case Handling Procedural Manual
- More than MedDRA: covers all data fields
- Safety database includes Clinical SAEs, Post marketing and Spontaneous reports
- Includes coding principles that are not in ICH MedDRA
  Term Selection: Points to Consider (PtC) document
- Cross refers to PtC

Spontaneous coding guidelines
- Based on ICH PtC
- States GSK choice when PtC has more than one option
Clinical SAEs

- Code events on SAE form
- Do not code signs/symptoms in narrative. Query site for other potential serious events in narrative

Post-marketing Surveillance
(e.g. Patient support programmes)

- Code reported adverse reactions (ADR) and associated signs and symptoms
- When surgical procedures/treatments are reported as events, query reporter for ADR that led to the procedure
Procedural Manual (2)

Spontaneous cases

- Surgical procedures not coded
  - described in narrative

- Multiple episodes of same event are coded once
  - to avoid recurrence of same PT
  - details described in narrative

- Incidental events (not the subject of the report)
  - code as concurrent conditions or medical history
  - if in doubt, code as AE
Training and Quality Assurance

Trainee:
- All cases checked by trainer/manager
- Periodic checking by line manager

Later quality assurance:
- Safety physician available for advice
- Selected cases reviewed (e.g. twice a week) by safety evaluation risk management group (SERM, including physicians) – feedback on coding, follow up queries etc
- Periodic (e.g. monthly) safety signal detection – screens more cases for product
- Common errors gathered for refresher training
EXAMPLES of CODING CHALLENGES
Post marketing - example

- **SAE “Recurrence on left shoulder excision”**
  - Detailed medical records not available at time of SAE report
  - Patient had been readmitted
  - Oncology product
    - Assume cancer recurrence?
    - Wound infection recurrence?
    - Surgical wound dehiscence?

- QUERY sent to reporter
Spontaneous case - example

- “cat walking across her chest” *Animal scratch*
- “mammogram and ultrasound.. they did see an abnormality, but the patient said it could be bruising from her 19 pound cat walking across her chest” *Contusion (?? Mammogram /Scan abnormal)*
- “each injection was painful for a while afterwards... Patient would swear that square needles were used and she did not know why it burned so much while it was being injected” *Injection site pain* (did not code *Device issue* for square needles)
- “held the phone for so long in one hand, that she could not move her fingers” *Stiff fingers*
Medication errors - example

May need more than one code

- “Prescribed half a tablet daily”
- “Prescribed 1.5 tablets daily”
  - Drug dose prescribing error
  - Tablet split incorrectly

- “used asthma inhaler when empty”
  - Device use error
  - Underdose or Missed dose?
Thank You