Blue Ribbon Panel Discussion Points

Proposed HLGT and HLT Hierarchical Changes to Improve MedDRA’s Ability to Support Data Analysis
(Examples are based on MedDRA Version 9.1)

1. INTRODUCTION

In 2004, the MSSO received feedback from the MedDRA user community regarding the terminology hierarchy groupings, such as the ambiguity of “NEC” naming, the confusion of multi-axial HLTs in the cumulative data output, the possible alternative secondary groupings for congenital PTs to aid data analysis, and the difficulties in analyzing signs and symptoms (e.g., diarrhea, rash)¹.

In early 2005, in response to subscribers’ requests, the MSSO conducted a feasibility study on MedDRA hierarchy structure modifications to improve its utility in supporting statistical analysis and reporting². The existing MedDRA rules and conventions, such as primary SOC allocation, were reviewed in this context. The following are the areas involved and proposals made by the MSSO:

- Proposal 1: Review “NEC” HLTs and HLGTs (Note: “NEC” stands for “not elsewhere classified,” only HLTs and HLGTs in MedDRA may contain “NEC” as part of the term text.)
  - Explore alternative namings for clearer indication of their content
  - Review large sized HLT groupings for possible reduction of the number of subordinate PTs by building subgroupings
- Proposal 2: Group PTs representing congenital disorders and their acquired counterparts to the same HLT where applicable
- Proposal 3: Allow multi-axiality of SOC Investigations
- Proposal 4: Allow multi-axiality of SOC Social circumstances
- Proposal 5: Eliminate multi-axial HLTs (meaning an HLT shows in more than one SOC) in cumulative data outputs when only the primary paths are displayed
- Proposal 6: Change primary SOC for post procedural terms. Should it be SOC Injury, poisoning and procedural complications or should it be the site of manifestation SOC?
- Proposal 7: Consider whether hyper- and hypo- metabolic disorders should be under the same HLT in SOC Metabolism and nutrition disorders

Based on feedback from the user community, the MedDRA Management Board directed the MSSO to implement proposal 2 and 7 in Version 9.0. Proposal 6 was rejected by the Board based on subscriber comments. The remaining proposals were deferred to this Blue Ribbon Panel for discussion.
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Therefore, the focus of this BRP is as follows:

- Review “NEC” HLTs and HLG Ts
  - Explore alternative namings for clearer indication of their content
  - Review large sized HLT groupings for possible reduction of the number of subordinate PTs by building subgroupings

- Allow multi-axiality of SOC *Investigations*

- Allow multi-axiality of SOC *Social circumstances*

- Eliminate multi-axial HLTs (meaning an HLT shows in one than SOC) in cumulative data outputs when only the primary path is displayed
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2. POTENTIAL MEDDRA HIERARCHY MODIFICATIONS

Note to Readers:

The term “disorder SOCs” used in this document refers to MedDRA SOCs that classify diseases, such as SOC Metabolism and nutrition disorders. The term is used to differentiate from MedDRA “supporting SOCs” such as SOC Investigations, SOC Social circumstances, and SOC Surgical and medical procedures.

The term “anatomical SOCs” used in this document refers to a subgroup of MedDRA disorder SOCs. Each anatomical SOC classifies diseases of a specific anatomical body system, such as SOC Cardiac disorders, SOC Gastrointestinal disorders, SOC Hepatobiliary disorders, etc. The term is used to differentiate these from disorder SOCs that are based on etiology, such as SOC Congenital, familial and genetic disorders, SOC Neoplasms benign, malignant and unspecified (incl cysts and polyps), and SOC Infections and infestations.

2.1 REVIEW “NEC” HLTS AND HLGTS

2.1.1 Issues with “NEC” HLTs and HLGTs

There are two issues regarding “NEC” HLT and HLGT groupings:

- The acronym “NEC” is not intuitive. It does not reflect the grouped subordinate concepts explicitly.

- Oversized “NEC” HLTs:
  
  The MSSO has received feedback from subscribers that analyzing HLTs with a large number of subordinate PTs proves challenging at times. An MSSO survey, which was conducted during the time of the feasibility study, indicated that subscribers generally understood that certain groupings at the HLT and HLGT levels are large because of the nature of the MedDRA terminology.

  Based on our analysis using 50 subordinate PTs as the dividing line (arbitrary), there are 46 HLTs containing more than 50 PTs:

  - 31 out of 46 HLTs are in SOC Investigations. A large number of PTs within an HLT in SOC Investigations is common because each term for an investigation in this SOC is accompanied by several terms for the qualitative results of that test. For example, PT Blood glucose is accompanied by another six PTs for test results of normal (PT Blood glucose normal), abnormal (PT Blood glucose abnormal), etc.

  - 15 other HLTs involve the following non-SOC Investigations
    
    o SOC General disorders and administration site conditions
    
    o SOC Infections and infestations
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- SOC Injury, poisoning and procedural complications
- SOC Neoplasms benign, malignant and unspecified (incl cysts and polyps)
- SOC Nervous system disorders
- SOC Surgical and medical procedures

2.1.2 Implementation Options

- “NEC” naming: Replace “NEC” with a more meaningful name if subordinate PTs are relatively “pure” in concept, for example:
  - Rename HLT Heart failures NEC to HLT Heart failures, laterality unspecified

![Figure 2-1. Current HLTs linked to HLGT Heart failures](image)

- Rename HLT Headaches NEC to HLT Non-migraine headaches

![Figure 2-2. Current HLTs linked to HLGT Headaches](image)

It is also proposed that “NEC” will not be eliminated from MedDRA because a miscellaneous grouping is needed at the HLT and HLGT level per the original pragmatic design of MedDRA. Therefore, this proposal is intended to be applied wherever it is appropriate.

- Large HLT groupings: Eight of 15 non-SOC Investigations HLTs are “NEC” HLTs (Table 2-1). It is possible to review and identify new and specific sub-groupings from these “NEC” HLTs to reduce their current size per the proposal outlined above.

<table>
<thead>
<tr>
<th>Count of PTs</th>
<th>HLT</th>
<th>HLGT</th>
<th>SOC</th>
</tr>
</thead>
<tbody>
<tr>
<td>172</td>
<td>Therapeutic procedures NEC</td>
<td>Therapeutic procedures and supportive care NEC</td>
<td>Surgical and medical procedures</td>
</tr>
<tr>
<td>123</td>
<td>Bacterial infections NEC</td>
<td>Bacterial infectious disorders</td>
<td>Infections and infestations</td>
</tr>
</tbody>
</table>
**Blue Ribbon Panel Discussion Points**

<table>
<thead>
<tr>
<th>Count of PTs</th>
<th>HLT</th>
<th>HLGT</th>
<th>SOC</th>
</tr>
</thead>
<tbody>
<tr>
<td>102</td>
<td>Injection and infusion site reactions</td>
<td>Administration site reactions</td>
<td>General disorders and administration site conditions</td>
</tr>
<tr>
<td>75</td>
<td>Infections NEC</td>
<td>Infections - pathogen class unspecified</td>
<td>Infections and infestations</td>
</tr>
<tr>
<td>74</td>
<td>Viral infections NEC</td>
<td>Viral infectious disorders</td>
<td>Infections and infestations</td>
</tr>
<tr>
<td>73</td>
<td>Non-site specific procedural complications</td>
<td>Procedural and device related injuries and complications NEC</td>
<td>Injury, poisoning and procedural complications</td>
</tr>
<tr>
<td>70</td>
<td>General signs and symptoms NEC</td>
<td>General system disorders NEC</td>
<td>General disorders and administration site conditions</td>
</tr>
<tr>
<td>69</td>
<td>Fungal infections NEC</td>
<td>Fungal infectious disorders</td>
<td>Infections and infestations</td>
</tr>
<tr>
<td>61</td>
<td>Prophylactic procedures NEC</td>
<td>Therapeutic procedures and supportive care NEC</td>
<td>Surgical and medical procedures</td>
</tr>
<tr>
<td>61</td>
<td>Metastases to specified sites</td>
<td>Metastases</td>
<td>Neoplasms benign, malignant and unspecified (incl cysts and polyps)</td>
</tr>
<tr>
<td>59</td>
<td>Implant and catheter site reactions</td>
<td>Administration site reactions</td>
<td>General disorders and administration site conditions</td>
</tr>
<tr>
<td>55</td>
<td>Central nervous system haemorrhages and cerebrovascular accidents</td>
<td>Central nervous system vascular disorders</td>
<td>Nervous system disorders</td>
</tr>
<tr>
<td>55</td>
<td>Therapeutic and nontherapeutic responses</td>
<td>Therapeutic and nontherapeutic effects (excl toxicity)</td>
<td>General disorders and administration site conditions</td>
</tr>
<tr>
<td>53</td>
<td>Application and instillation site reactions</td>
<td>Administration site reactions</td>
<td>General disorders and administration site conditions</td>
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<tr>
<td>50</td>
<td>Non-site specific injuries NEC</td>
<td>Injuries NEC</td>
<td>Injury, poisoning and procedural complications</td>
</tr>
</tbody>
</table>

Table 2-1. Non-SOC Investigations HLTs (All SOCs represent the primary SOC allocation)

**Question #1 to Panel:**

Should the MSSO implement these changes?

If so, which SOC(s) should take the priority in implementing this action?

Note that the MSSO has referenced FDA data on the frequency of reported adverse events by SOC; these are presented in Table Appendix A-1. Should the MSSO use these data to determine the priority order of SOCs to be addressed?

Is a maximum of 50 PTs linked to a single HLT appropriate?
2.2 ALLOW MUTI-AXIALITY OF SOC *Investigations*

2.2.1 Issue With the Multi-axiality of SOC *Investigations*

Based on current MedDRA rules, SOC *Investigations* is currently non-multi-axial. In other words, the terms within SOC *Investigations* (e.g., laboratory findings, physiologic testing findings, radiologic findings, etc.) do not have multi-axial links to the potentially corresponding diagnoses terms in the disorder SOCs. For example, PT *Platelet count decreased* (SOC *Investigations*) has no axial link to PT *Thrombocytopenia* in SOC *Blood and lymphatic system disorders*.

2.2.2 Implementation Options

- SOC *Investigations* could remain non-multi-axial for the following reasons:
  - Many investigation results are contributing factors in assisting clinical diagnosis and do not directly lead to the diagnosis.
  - The ICH M1 Expert Working Group (EWG), which constructed MedDRA on behalf of ICH had discussions regarding possible SOC *Investigations* secondary linkages. The outcome was to leave it non-multi-axial because there is not always a direct relationship between a particular investigation result and a diagnosis. For example, elevated serum potassium could be due to exogenous sources of potassium, associated with acidosis, or due to kidney disease.
  - Investigation results are frequently non-specific. For example, an elevated transaminase (AST/ALT) could be interpreted as either a level of enzyme that has risen but is still within normal range; or it may indicate possible hepatocellular injury caused by diverse etiologies represented by terms in SOC *Hepatobiliary disorders* (e.g., alcohol, chronic viral hepatitis, autoimmune hepatitis, hepatic steatosis); or it may be elevated in conditions represented by terms in other SOCs such as myocardial infarction (SOC *Cardiac disorders*). As a result, attempting to add secondary links for investigation results to the related diagnostic HLTs in other SOCs could potentially lead to a large number of secondary links to a test result. This could cause conflict with the MedDRA placement rule that obligates a PT to have only one HLT link per SOC. Also, unlimited numbers of secondary links for certain laboratory terms might complicate data presentation and analysis, especially when using a secondary SOC analysis.

- Add secondary links to certain investigation results
  - All investigation PTs are primarily linked to SOC *Investigations*
  - Allow secondary links to apply to certain PTs in SOC *Investigations*
  - Be conservative by applying specifically defined criteria:
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- Investigation results that could only represent the specific disease or diagnosis would be linked to the corresponding disorder SOCs. For example, PT *HIV antigen positive* (investigation result) would be linked together with PT *HIV infection* (diagnosis).

  - Rationale:
    - Since many investigation results assist in clinical diagnosis, only those investigation results that represent the disease or diagnosis will be secondarily linked from SOC *Investigations* to the same HLT where the diagnostic term is linked. This criterion is proposed to avoid uncontrollable secondary links to an investigation result.
    - Example 1: PT *HIV antibody positive* would be secondarily linked to HLT *Retroviral infections* and HLT *Acquired immunodeficiency syndromes* where PT *HIV infection* is grouped, but PT *HIV antibody negative* and PT *HIV antibody* would not be linked. Similarly, PT *Hepatitis B antigen positive* will be secondarily linked to HLT *Hepatic viral infections* and HLT *Hepatitis viral infections*, but PT *Hepatitis B antibody* would not be.
    - Example 2: PT *Protein urine present* would be secondarily linked to HLT *Urinary abnormalities* where PT *Proteinuria* is grouped.

  - Pros:
    - Allows easy retrieval of diagnosis and test results representing the diagnosis from the same HLT in the disorder SOCs

  - Cons:
    - Indirect (non-specific) or contributing investigation results would still need to be retrieved separately from SOC *Investigations*.
    - A large number of PTs could be linked to an HLT. For example, in Figure 2-3, the number of PTs linked to HLT *Hepatic viral infections* is increased from 19 to 42 to include hepatitis related antibody and antigen investigation results.
    - That multi-axiality would not be applied to all investigation results leads to some degree of inconsistency. Based on this conservative approach, liver function test terms such as PT *Alanine aminotransferase increased* and PT *Aspartate aminotransferase increased* would not be linked despite being relevant diagnostic test results.
    - Although this approach groups the investigation results and the diagnosis under the same HLT, it does not provide direct associations between the associated PT concepts. As shown in Figure 2-3, PT *Hepatitis B antigen* positive is linked under HLT *Hepatic viral infections* in SOC *Hepatobiliary disorders*. But one still needs to associate this investigation result to an associated
diagnosis such as PT *Congenital hepatitis B infection* or PT *Hepatitis B*.

![Diagram of HLT and HLGT hierarchical changes](image)

**Figure 2-3.** PTs subordinate to HLT *Hepatic viral infections* before and after the investigation results are linked

**Question #2 to the Panel:**

BRP – Proposed HLGT and HLT Hierarchical Changes to Improve MedDRA’s Ability to Support Data Analysis

04 October 2006

MSSO-DI-6274-1.0.0
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Should SOC *Investigations* be left as is or made multi-axial?

If yes to the multi-axial option, does the Panel support the MSSO’s proposed criteria for creating secondary links for investigation results?

If neither approach is ideal, should the MSSO consider a non-conventional proposal to solve this issue (see section 2.2.3)?

2.2.3 The Concept Property – “Is a diagnostic test for”
Would it be helpful to MedDRA users if a property attribute relationship is created outside of the MedDRA hierarchy to connect the associated concepts? A “property attribute relationship” refers a relation or linkage in addition to hierarchy that helps to define the concept of interest.

For investigation results, this property attribute would be called “Is a diagnostic test for” as suggested by Corneliu Henegar, *et al.*³ For example, both PT Alanine aminotransferase increased and PT Aspartate aminotransferase increased would have the “Is a diagnostic test for” relationship with the diagnosis term PT *Hepatitis A*.

2.2.3.1 “attrib.asc” File
The “Is a diagnostic test for” relationship could be implemented in an additional ascii file called “attrib.asc”. Having this property in a file separate and external to the 14 “traditional” MedDRA ascii files assures that the current MedDRA hierarchy groupings and distributed ascii files (Figure 2-4) are not impacted; in other words, a user can opt not to use the “attrib.asc” files. The resulting list of distributed MedDRA ascii files is shown in Figure 2-4, and the “attrib.asc” file format is shown in Figure 2-5.
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### BRP – Proposed HLGT and HLT Hierarchical Changes to Improve MedDRA’s Ability to Support Data Analysis

04 October 2006

MSSO-DI-6274-1.0.0

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<th>Type</th>
<th>Date Modified</th>
</tr>
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<td>ASC File</td>
<td>10/3/2006 2:10 PM</td>
</tr>
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</tbody>
</table>

Figure 2-4. MedDRA ascii files (including attrib.asc)

```
10001551: Is a diagnostic test for 10019719
10003481: Is a diagnostic test for 10019719
10005207: Is a diagnostic test for 10019719
10059570: Is a diagnostic test for 10019719
10005364: Is a diagnostic test for 10019719
10019725: Is a diagnostic test for 10019719
10059751: Is a diagnostic test for 10019719
10057398: Is a diagnostic test for 10019719
10001551: Is a diagnostic test for 10009208
10001565: Is a diagnostic test for 10009208
10003481: Is a diagnostic test for 10009208
10005287: Is a diagnostic test for 10009208
10003481: Is a diagnostic test for 10028596
10005474: Is a diagnostic test for 10028596
10005630: Is a diagnostic test for 10028596
10014391: Is a diagnostic test for 10028596
10014392: Is a diagnostic test for 10028596
10014395: Is a diagnostic test for 10028596
10023625: Is a diagnostic test for 10028596
10059268: Is a diagnostic test for 10028596
10058267: Is a diagnostic test for 10028596
10053269: Is a diagnostic test for 10028596
```

Figure 2-5. attrib.asc file format

#### 2.2.3.2 Utilities of the Attribute File

The “attrib.asc” file provides the connection between diagnosis and diagnostic test results within MedDRA. This attribute feature not only provides the list of diagnostic tests associated with a particular diagnosis (Figure 2-6, top), but also
provides the list of diagnoses related to a certain investigation result (Figure 2-6, bottom).

<table>
<thead>
<tr>
<th>Test result</th>
<th>Relationship</th>
<th>Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alanine aminotransferase increased</td>
<td>Is a diagnostic test for</td>
<td>Hepatitis A</td>
</tr>
<tr>
<td>Aspartate aminotransferase increased</td>
<td>Is a diagnostic test for</td>
<td>Hepatitis A</td>
</tr>
<tr>
<td>Blood albumin decreased</td>
<td>Is a diagnostic test for</td>
<td>Hepatitis A</td>
</tr>
<tr>
<td>Blood alkaline phosphatase increased</td>
<td>Is a diagnostic test for</td>
<td>Hepatitis A</td>
</tr>
<tr>
<td>Blood bilirubin increased</td>
<td>Is a diagnostic test for</td>
<td>Hepatitis A</td>
</tr>
<tr>
<td>Hepatitis A antibody positive</td>
<td>Is a diagnostic test for</td>
<td>Hepatitis A</td>
</tr>
<tr>
<td>Hepatitis A antigen positive</td>
<td>Is a diagnostic test for</td>
<td>Hepatitis A</td>
</tr>
<tr>
<td>Hepatitis A positive</td>
<td>Is a diagnostic test for</td>
<td>Hepatitis A</td>
</tr>
<tr>
<td>Alanine aminotransferase increased</td>
<td>Is a diagnostic test for</td>
<td>Cirrhosis alcoholic</td>
</tr>
<tr>
<td>Albumin globulin ratio decreased</td>
<td>Is a diagnostic test for</td>
<td>Cirrhosis alcoholic</td>
</tr>
<tr>
<td>Aspartate aminotransferase increased</td>
<td>Is a diagnostic test for</td>
<td>Cirrhosis alcoholic</td>
</tr>
<tr>
<td>Blood albumin decreased</td>
<td>Is a diagnostic test for</td>
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</tr>
<tr>
<td>Aspartate aminotransferase increased</td>
<td>Is a diagnostic test for</td>
<td>Myocardial infarction</td>
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<tr>
<td>Blood creatine phosphokinase MB increased</td>
<td>Is a diagnostic test for</td>
<td>Myocardial infarction</td>
</tr>
<tr>
<td>Blood lactate dehydrogenase increased</td>
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<tr>
<td>Electrocardiogram ST segment elevation</td>
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</tr>
<tr>
<td>Electrocardiogram T wave inversion</td>
<td>Is a diagnostic test for</td>
<td>Myocardial infarction</td>
</tr>
<tr>
<td>Myoglobin blood increased</td>
<td>Is a diagnostic test for</td>
<td>Myocardial infarction</td>
</tr>
<tr>
<td>Troponin T increased</td>
<td>Is a diagnostic test for</td>
<td>Myocardial infarction</td>
</tr>
<tr>
<td>Troponin T increased</td>
<td>Is a diagnostic test for</td>
<td>Myocardial infarction</td>
</tr>
</tbody>
</table>

Figure 2-6. Utilities of “Is a diagnostic test for” relationship
2.3  ALLOW MULTI-AXIALITY OF SOC Social circumstances

2.3.1 Issue With Multi-axiality of SOC Social circumstances

The purpose of SOC Social circumstances is for encoding patient social history or background. It provides a grouping for social factors that may give insight into personal issues that could have an effect on the event being reported. The MedDRA Introductory Guide states that “SOC Social circumstances contains information about the person, not the adverse event. As an example, terms such as PT Drug addict and PT Death of spouse are found in this SOC, whereas their respective disorder terms such as LLT Drug addiction and PT Death are found in SOC Psychiatric disorders and SOC General disorders and administration site conditions, respectively.” However, “some terms currently contained within this SOC are the only option for capturing certain ADR/AEs.” – “MedDRA Term Selection: Points to Consider” Release 3.6, section 3.17

Some terms linked to HLT Drug and chemical abuse in SOC Social circumstances are closely related to a corresponding relevant psychologic condition. For example:

- Drug “abuser” and “abuse” related terms are in SOC Social circumstances (Figure 2-4)
- Drug “dependence” related terms are in SOC Psychiatric disorders (Figure 2-4)

Depending on the wording in the ADR/AE report, the coded MedDRA term could be in SOC Social circumstances if the wording is “drug abuse” or in SOC Psychiatric disorders if the wording is “drug dependence.” This makes analysis difficult. On this issue, the guidelines from “MedDRA Term Selection: Points to Consider” Release 3.6 states in section 3.17 that “This SOC contains terms that are similar to terms in the disorder SOCs. Users should be aware of the impact that use of these terms will have on data retrieval, data analysis, and reporting.”
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### Proposed HLGT and HLT Hierarchical Changes to Improve MedDRA's Ability to Support Data Analysis

1. **Drug abuser**
   - Addicted to amphetamines
   - Addicted to cocaine
   - Addicted to drugs
   - Addicted to heroin
   - Amphetamine or related acting sympathomimetic abuse
   - Amphetamine or related acting sympathomimetic abuse, continuous use
   - Amphetamine or related acting sympathomimetic abuse, episodic use
   - Amphetamine or related acting sympathomimetic abuse, in remission
   - Amphetamine or related acting sympathomimetic abuse, unspecified use

2. **Analgesic abuse**
   - Antidepressant type abuse
   - Antidepressant use, continuous use
   - Antidepressant use, episodic use
   - Antidepressant use, in remission
   - Antidepressant use, unspecified use

3. **Barbiturate abuse**
   - Barbiturate and similarly acting sedative or hypnotic abuse
   - Barbiturate and similarly acting sedative or hypnotic abuse, continuous use
   - Barbiturate and similarly acting sedative or hypnotic abuse, episodic use
   - Barbiturate and similarly acting sedative or hypnotic abuse, in remission
   - Barbiturate and similarly acting sedative or hypnotic abuse, unspecified use

4. **Caffeine abuse**
   - Cannabis abuse, continuous use
   - Cannabis abuse, episodic use
   - Cannabis abuse, in remission
   - Cannabis abuse, unspecified use

5. **Cocaine abuse**
   - Cocaine abuse, continuous use
   - Cocaine abuse, episodic use
   - Cocaine abuse, in remission
   - Cocaine abuse, unspecified use

6. **Drug abuse**
   - Drug abuse in remission

7. **Drug abuse NOS**
   - Drug abuser
   - Drug abuser NOS
   - Drug abuser NOS
   - Drug abuse

8. **Drug dependence**
   - Addiction any drug
   - Addiction to drugs
   - Addiction to drugs (excl drug psychosis)
   - Amphetamine and other psychostimulant dependence
   - Amphetamine and other psychostimulant dependence, continuous use
   - Amphetamine and other psychostimulant dependence, episodic use
   - Amphetamine and other psychostimulant dependence, in remission
   - Amphetamine and other psychostimulant dependence, unspecified use
   - Amylobarbital dependence
   - Barbiturate and similarly acting sedative or hypnotic dependence
   - Barbiturate and similarly acting sedative or hypnotic dependence, continuous use
   - Barbiturate and similarly acting sedative or hypnotic dependence, episodic use
   - Barbiturate and similarly acting sedative or hypnotic dependence, in remission
   - Barbiturate and similarly acting sedative or hypnotic dependence, unspecified use
   - Benzodiazepine dependent
   - Cannabis addiction
   - Cannabis dependence, continuous use
   - Cannabis dependence, episodic use
   - Cannabis dependence, in remission
   - Cannabis dependence, unspecified use
   - Cocaine addiction
   - Cocaine dependence
   - Cocaine dependence, continuous use
   - Cocaine dependence, episodic use
   - Cocaine dependence, in remission
   - Cocaine dependence, unspecified use
   - Combinations of drug dependence excluding morphine type drug
   - Combinations of drug dependence excluding opioid type drug
   - Combinations of drug dependence excluding opioid type drug, continuous use
   - Combinations of drug dependence excluding opioid type drug, episodic use
   - Combinations of drug dependence excluding opioid type drug, in remission
   - Combinations of drug dependence excluding opioid type drug, unspecified use
   - Combinations of opioid type drug with any other drug dependence
   - Combinations of opioid type drug with any other drug dependence, continuous use
   - Combinations of opioid type drug with any other drug dependence, episodic use
   - Combinations of opioid type drug with any other drug dependence, in remission
   - Combinations of opioid type drug with any other drug dependence, unspecified use
   - Dependence addictr
   - Dependence drug (NOS)

---

**Figure 2-7. “Abuse” and “Dependence” terms**

BRP – Proposed HLGT and HLT Hierarchical Changes to Improve MedDRA’s Ability to Support Data Analysis
04 October 2006
MSSO-DI-6274-1.0.0
2.3.2 Implementation Options

- Since the involved terms are isolated within a single HLT and movement of these terms would not drastically alter SOC *Social circumstances*, it is proposed to move the “abuse” terms from SOC *Social circumstances* to SOC *Psychiatric disorders*. This would resolve the current disconnection between the “abuse” terms in SOC *Social circumstances* and “dependence” terms in SOC *Psychiatric disorders*.

- If the move proposal is not agreeable, creating secondary links for SOC *Social circumstances* to connect “abuse” and “abuser” PTs to HLT *Substance-related disorders* in SOC *Psychiatric disorders* allows the concepts of “abuse” and “dependence” to be logically grouped and represented in SOC *Psychiatric disorders*.

Question #3 to the Panel:

Should “abuse” terms be moved to SOC *Psychiatric disorders*?

OR should SOC *Social circumstances* be made multi-axial?
2.4 ELIMINATE MULTI-AXIAL HLTS IN CUMULATIVE DATA OUTPUT

2.4.1 Issue With the Multi-axial HLTS in Cumulative Data Output

In the cumulative data output when only primary paths are displayed, a few HLTS appear in two different SOCs with different subordinate PTs.

As shown in Figure 2-5, the HLT groupings for “Skin neoplasms benign” in both SOC Neoplasms benign, malignant and unspecified (incl cysts and polyps) and SOC Skin and subcutaneous tissue disorders have the same number of PTs when both primary and secondary PTs are listed.

![Figure 2-8. PTs under HLT Skin neoplasms benign](image)

However, in the primary SOC view, only the “blue” PTs are listed under HLT Skin neoplasms benign. In this case, users are confused by why the same HLT name represents one PT in SOC Skin and subcutaneous tissue disorders and another set of PTs in SOC Neoplasms benign, malignant and unspecified (incl cysts and polyps).
2.4.2 Implementation Option

Eliminate multi-axiality of the involved HLTs by renaming the groupings. For example, regarding HLT *Skin neoplasms benign*:

- The HLGT and HLT names in SOC *Neoplasms benign, malignant and unspecified (incl cysts and polyps)* would remain unchanged
- The HLGT name in SOC *Skin and subcutaneous tissue disorders* would be changed to HLGT *Benign cutaneous neoplasms*
- The HLT name in SOC *Skin and subcutaneous tissue disorders* would be changed to HLT *Benign skin neoplasms*

When two HLTs contain the same PTs (primary and secondary), a “lexical variant” approach (e.g., “Skin neoplasms benign” vs. “Benign skin neoplasms” in the above example) would be used in their naming to indicate that these two grouping have the same scope. The “lexical variants” then allow for proper placement in MedDRA.

Question #4 to Panel:

Should this proposal (elimination of multi-axial HLTs by a renaming approach) be implemented?

If so, should multi-axiality be eliminated from all HLTs and HLGTs because the same problem could occur again as long as there are still multi-axial HLTs?
Blue Ribbon Panel Discussion Points

3. Reference


Appendix A  FDA FOI Data Analysis

Data from the first three quarters of 2005 FDA AERS data published through FOI (Freedom of Information) were used to generate the following frequency table.

<table>
<thead>
<tr>
<th>SOC Name</th>
<th>Count</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>General disorders and administration site conditions</td>
<td>186320</td>
<td>13.8%</td>
</tr>
<tr>
<td>Nervous system disorders</td>
<td>146170</td>
<td>10.8%</td>
</tr>
<tr>
<td>Investigations</td>
<td>130714</td>
<td>9.7%</td>
</tr>
<tr>
<td>Gastrointestinal disorders</td>
<td>112092</td>
<td>8.3%</td>
</tr>
<tr>
<td>Psychiatric disorders</td>
<td>89432</td>
<td>6.6%</td>
</tr>
<tr>
<td>Cardiac disorders</td>
<td>88039</td>
<td>6.5%</td>
</tr>
<tr>
<td>Injury, poisoning and procedural complications</td>
<td>69687</td>
<td>5.2%</td>
</tr>
<tr>
<td>Respiratory, thoracic and mediastinal disorders</td>
<td>68952</td>
<td>5.1%</td>
</tr>
<tr>
<td>Musculoskeletal and connective tissue disorders</td>
<td>63932</td>
<td>4.7%</td>
</tr>
<tr>
<td>Infections and infestations</td>
<td>61670</td>
<td>4.6%</td>
</tr>
<tr>
<td>Skin and subcutaneous tissue disorders</td>
<td>54287</td>
<td>4.0%</td>
</tr>
<tr>
<td>Vascular disorders</td>
<td>39553</td>
<td>2.9%</td>
</tr>
<tr>
<td>Metabolism and nutrition disorders</td>
<td>35108</td>
<td>2.6%</td>
</tr>
<tr>
<td>Renal and urinary disorders</td>
<td>29548</td>
<td>2.2%</td>
</tr>
<tr>
<td>Blood and lymphatic system disorders</td>
<td>28658</td>
<td>2.1%</td>
</tr>
<tr>
<td>Eye disorders</td>
<td>27053</td>
<td>2.0%</td>
</tr>
<tr>
<td>Neoplasms benign, malignant and unspecified (incl cysts and polyps)</td>
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</tr>
<tr>
<td>Hepatobiliary disorders</td>
<td>20265</td>
<td>1.5%</td>
</tr>
<tr>
<td>Surgical and medical procedures</td>
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<tr>
<td>Reproductive system and breast disorders</td>
<td>11620</td>
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</tr>
<tr>
<td>Immune system disorders</td>
<td>10411</td>
<td>0.8%</td>
</tr>
<tr>
<td>Social circumstances</td>
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</tr>
<tr>
<td>Pregnancy, puerperium and perinatal conditions</td>
<td>8085</td>
<td>0.6%</td>
</tr>
<tr>
<td>Ear and labyrinth disorders</td>
<td>6233</td>
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</tr>
<tr>
<td>Congenital, familial and genetic disorders</td>
<td>4913</td>
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</tr>
<tr>
<td>Endocrine disorders</td>
<td>3207</td>
<td>0.2%</td>
</tr>
</tbody>
</table>

Table Appendix A-1. The Frequency of SOCs Representing Reported Adverse Events

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