Can MedDRA be used for labelling? Should it?

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What is the purpose of safety data in product labelling?

- Primary users - prescribers / dispensers
- Secondary users - sponsors, regulators, patients, lawyers
- Benefit vs. risk - patient well-being
- Selection of optimal therapy
  - Comparison of one therapy vs. another
  - Comparison of therapy vs. no therapy
Applicable regulations

• “... a summary of the essential scientific information needed for the safe and effective use of the drug.”
  – 21 CFR §201.57(a) FDA

• “the information supplied to users should provide a high degree of consumer protection, in order that medicinal products may be used correctly on the basis of full and comprehensible information”
  – Directive 92/27 EEC
CIOMS-III
Purpose of Core Safety Information

• “Core Safety Information should be … designed to provide doctors and other healthcare professionals with the most relevant information possible to assist in the selection and use of a medicine”

• “its focus must be the essential … safety information that will permit the intelligent choice and optimum use of a medicinal product by the practicing physician or other health-care provider anywhere in the world”
Purpose of Core Safety Information

- “core safety information (CSI)… should serve as the clinical-safety reference information for the manufacturer”
How does current safety labelling measure up?

- The adverse events section in current package inserts is “a disaster” that contains “a mishmash of things” rather than a

- “useful document for the practicing health practitioner,” containing information that would be “needed at the bedside ... to use the drug appropriately.”
  - Murray Lumpkin, FDA

  - “The Pink Sheet” 18 April 1994
Conflicting purposes

• Medical guide for prescribers / dispensers
  – Benefit - risk balance

• Legal “contract” between sponsors and regulators for promotion / expedited reporting
Will MedDRA enhance or exacerbate current safety labelling practices?
MedDRA in EU Guidelines

• Draft SmPC Guidelines: “If MedDRA is used, ADRs should be based on LLTs or PTs”
  – Industry concern over premature mandate with no basis in experience
  – Regulators intended to allow flexibility and specificity in the SmPC
  – Response to Industry being being drafted
MedDRA - pros

• Harmonised international terminology
  – International comparability between products
• Designers envisaged use for labelling (esp. safety)
MedDRA - cons

- Primarily a tool for data analysis
  - LLTs designed for data entry (synonyms)
  - Hierarchy designed to retrieve and display medically meaningful groupings of PTs
    - Signal generation
    - Medical analysis / evaluation

- No advantage to standardized terminology without agreed “good coding practices”
- Not consistent with normal clinical practice
<table>
<thead>
<tr>
<th>MedDRA PT</th>
<th>MedDRA HLT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pancreatitis acute</td>
<td>Pancreatitis (all forms)</td>
</tr>
<tr>
<td>Pancreatitis acute on chronic</td>
<td></td>
</tr>
<tr>
<td>Pancreatitis chronic</td>
<td></td>
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<tr>
<td>Pancreatitis haemorrhagic</td>
<td></td>
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<tr>
<td>Pancreatitis necrotising</td>
<td></td>
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<tr>
<td>Pancreatitis mumps</td>
<td></td>
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<tr>
<td>Pancreatitis NOS</td>
<td></td>
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<tr>
<td>Pancreatitis relapsing</td>
<td></td>
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<tr>
<td>Pancreatitis</td>
<td></td>
</tr>
</tbody>
</table>
## MedDRA Specificity

<table>
<thead>
<tr>
<th>Abdominal pain</th>
<th>Abdominal pain lower</th>
<th>Abdominal pain upper</th>
<th>Abdominal pain NOS</th>
<th>Abdominal tenderness</th>
<th>Acute abdomen</th>
<th>Gastrointestinal pain NOS</th>
<th>Infantile colic</th>
<th>Oesophageal pain</th>
<th>Ulcer type pain</th>
<th>GI &amp; abdominal pain</th>
</tr>
</thead>
</table>

Other MedDRA issues / options

• Reporter term “disconnection”
  – e.g. thrombocytopenia vs. platelets decreased
    • no link in hierarchy
• Possible use of existing Special Search Categories (SSCs)
• ? Develop SSCs specific for labelling use
Proposal

• Three-tier label
  – Manufacturer / regulator (promotion, expectedness based on MedDRA PTs)
  – Prescriber (salient features, natural medical language, clear benefit-risk description)
  – Patient (lay terms)
Conclusions

- Wide experience with MedDRA in safety data communication needed before specific commitment to other uses
- Opportunity to improve the “prescriber-friendliness” of medicinal product labelling