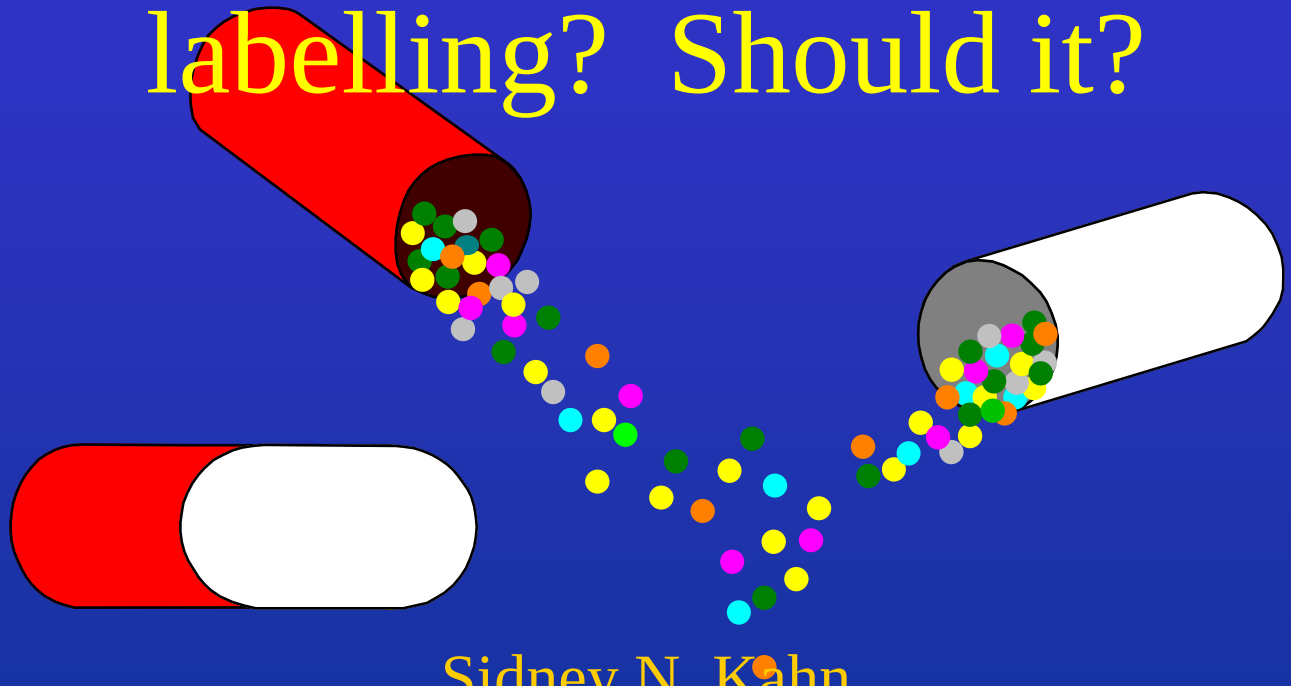
Can MedDRA be used for labelling? Should it?



Sidney N. Kahn
Worldwide Safety & Surveillance
Bristol-Myers Squibb

DIA Annual Meeting, June 1999

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"

CIOMS-III
Purpose of Core Safety Information

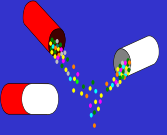
- “core safety information (CSI)... should serve as the clinical-safety reference information for the manufacturer”

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 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

MedDRA Specificity

	MedDRA PT	MedDRA HLT
Pancreatitis	Pancreatitis acute Pancreatitis acute on chronic Pancreatitis chronic Pancreatitis haemorrhagic Pancreatitis necrotising Pancreatitis mumps Pancreatitis NOS Pancreatitis relapsing	Pancreatitis (all forms)

MedDRA Specificity

	MedDRA PT	MedDRA HLT
Abdominal pain	Abdominal pain lower	GI & abdominal pain
	Abdominal pain upper	
	Abdominal pain NOS	
	Abdominal tenderness	
	Acute abdomen	
	Gastrointestinal pain NOS	
	Infantile colic	
	Oesophageal pain	
	Ulcer type pain	

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