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Reducing the Risk of Harm due to Medication Incidents An Integral Component of Health Canada's Product Vigilance Framework

Product Vigilance Workshop
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Canada 

Globe & Mail – June 12, 2002

Wrong injection causes death

BY GRAEME SMITH

A drug used to execute death-row prisoners was mistakenly injected into an elderly woman, whose death in a Peterborough, Ont., hospital will be examined in a coroner's inquest.

Bonita Porter, Ontario's deputy chief coroner of inquests, announced yesterday that a jury will look at why Frances Marie Tanner, 84, died at the Peterborough Regional Health Centre on Jan. 21.

The cause of Ms. Tanner's death is already known: Somebody injected a dose of potassium chloride into her vein. Small quantities of the drug can cure potassium deficiencies, but larger amounts are poisonous.

At least three other Canadians have died after receiving the same drug, sometimes from nurses who thought it was a different medicine.

Some doctors blame these accidents on manufacturers who sell potassium chloride in plastic ampoules and vials that closely resemble containers of sterile water, saline solution, and other harmless solutions.

Others say hospitals need stricter controls over potentially deadly substances. Ontario's chief coroner sent a memo to hospitals last year specifically warning them that potassium chloride has been wrongly

Litany of errors

Incidents involving potassium chloride in Canada:

- 1 Potassium chloride (KCl) was administered via direct IV when the intended action was to flush an intravenous line with diluted sodium chloride. **Result: Patient died.**
- 2 KCl concentrate was used to reconstitute a drug for parenteral administration when the intended diluent was sterile water. **Result: Error was noted before administration.**
- 3 KCl concentrate was administered as a bolus injection – an injection given in high quantity, all at once – by a health-care professional who was unaware that KCl concentrate cannot be given as a bolus but must be diluted in a minibag and given as an infusion. **Result: Patient died.**
- 4 A one-litre IV solution was prepared with potassium chloride and although it was administered at a very low rate, the incident was felt to be a near miss because of the potential for accidental overdose. **Result: Error was noted during administration.**
- 5 IV solutions containing KCl were administered as a fluid replacement in a patient requiring several litres of fluid in a short time frame. **Result: Hyperkalemia, patient died.**
- 6 Frances Marie Tanner, 84, received an intravenous injection of potassium chloride at the Peterborough Regional Health Centre on Jan. 21, 2002. **Result: Patient died.**

SOURCE: INSTITUTE FOR SAFE MEDICATION PRACTICES REPORT, MAY, 2002 IMAGE: PHOTODISC

administered in the past.

After the latest death, however, the coroner's office decided it was time to emphasize the danger.

"It was felt that an inquest might be the best way to get the information out," Dr. Porter said.

The medical community knows surprisingly little about its own errors. A newsletter published last month by the Institute for Safe Medication Practices Canada recorded five cases in which patients

were accidentally given potassium chloride; three died, and two were considered "near misses."

More cases could exist, said the institute's president, physician David U. While many hospitals have removed potassium chloride from nursing stations, he said, some doctors still demand to have it on hand, particularly in intensive-care units. And the drug manufacturers have a financial interest in maintaining their products' un-

iform packaging.

"The companies have just one assembly line, so they all look the same," he said. "It's an accident waiting to happen."

Researchers have suggested that perhaps 5,000 to 10,000 Canadians die because of medical error in hospitals every year.

The estimate is extrapolated from just one American study, however. A Canadian study was launched last month.



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- Small size and poor readability of information
- Similar appearing labels and names
- Mix-ups between these medications given to women in labour can be fatal for babies

Brethine



Methergine



Naming: Product Line Extensions



Squeaky clean Silken tests positive

What's the difference between Benadryl and Benadryl Decongestant? For Silken Laumann, it's a gold medal and a tarnished reputation. The rower says she mistakenly took the second type, which contains the banned stimulant pseudoephedrine, to fight a cold at the 1995 Pan Am Games in Argentina. When her drug test comes back positive, Laumann and her quadruple sculls teammates are stripped of their gold medals. Three days later, she tells her side of the story to CBC Radio's *The Inside Track*.

Laumann thinks she was treated harshly: nobody claims she did it intentionally, nor do they think it helped her performance.



Objectives

- Demonstrate how the health product's Name, Package and Label* (NPL) issues are contributing to serious patient harm in the Canadian health care system.
- Describe the current status regarding Health Canada's involvement in the prevention and management of health product name, package and label issues
- Propose the features of a proactive Health Canada program for the prevention and management of product name, label and package issues.

* Label refers to the label on or affixed to an immediate container of a drug.



What is a Medication Incident?

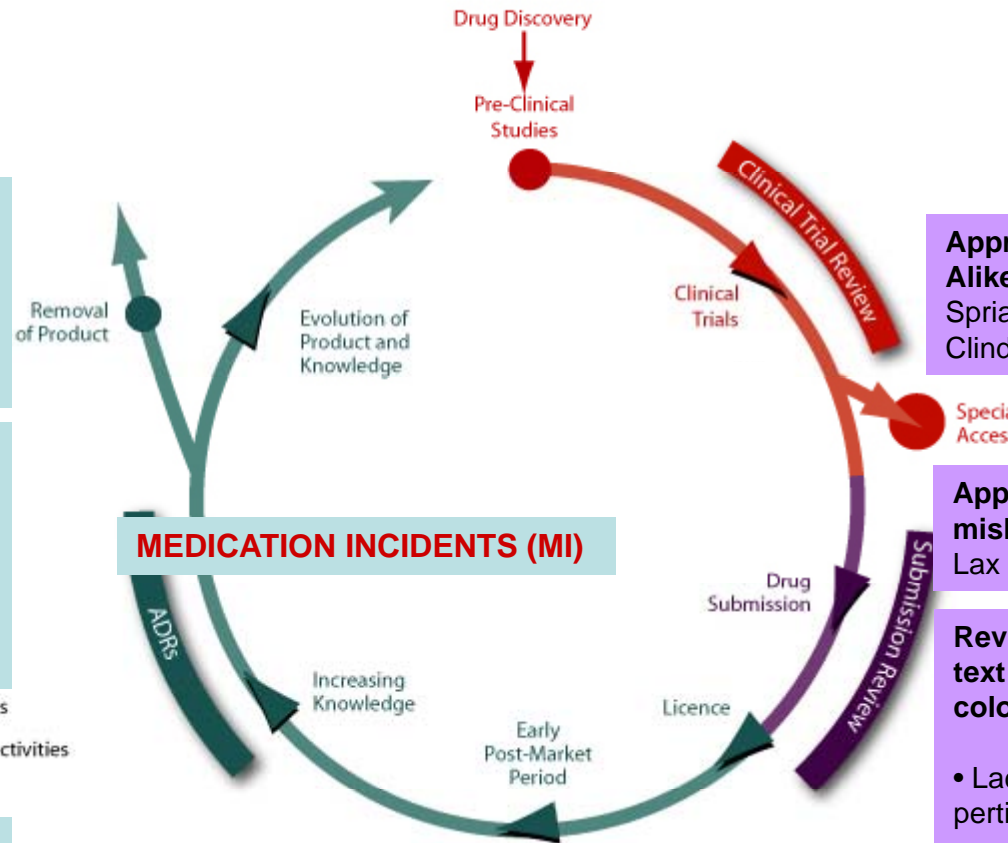
- Any **preventable** event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the healthcare professional, patient, or consumer.
- Medication incidents due to a health product's name, package & label affect the **real world safety** of health products and are implicated in one quarter of all medical errors that result in death (approximately 2,000 – 7,000 deaths each year*).
- Responsibility for medication incidents relating to a health product's **name, package and label** fall under Federal jurisdiction (*Food and Drugs Act*).

* Baker GR, Norton PG, Flintoft B, et al. The Canadian Adverse Events Study: the incidence of adverse events among hospital patients in Canada. CMAJ 2004;170(11):1678-86.



Sharing responsibility for safe medication use

Current Point-in-Time Process



A landmark Canadian Study (Baker & Norton) estimated that 9,000 to 27,000 Canadians die each year due to medical errors. Almost one quarter of these are due to medication incidents.

Prevention of look-alike/sound-alike medication names is the first on the list of nine solutions unveiled by WHO (1997) to prevent health care errors that harm millions of people daily throughout the world.

Industry Activities
Health Canada Activities

One of ten adults report receiving the wrong drug or dose according to CIHI.

Approval of Look-Alike/Sound-Alike health product names:
Spriafil/Sprycel, Zyban/Zytram, Clindets/Clindesse etc.

Approval of potentially misleading names:
Lax A Day; CTP30 etc.

Review and approval of written text of label vs. approval of full-colour label mock-up:

- Similar appearing labels or packages of different products
- Lack of differentiation between drug products that have similar names
- Lack of prominent placement of pertinent information
- Small size and poor readability of printed information
- Use of abbreviations or trailing/preceding zeros on labels
- Poorly designed or cluttered labels (designed for marketing vs. practice conditions)



- Similar appearing packages of different products
- Mix-ups between KCl and other products can be fatal



Look-Alike/Sound-Alike Health Product Names



Celebrex vs Cerebyx



International Scan

- Medication NPL is recognized as a significant contributing factor of MI worldwide and has become a global concern.
- The occurrence of medication incidents is repetitive in nature; an incident occurring in one area is likely to repeat itself in another.
- Regulatory agencies are moving forward with looking at ways in reducing medication incidents including having divisions that specifically deal with the prevention and analysis of MI from a real world perspective.



International Scan (Cont'd)

- TGA, Australia
 - Can mandate a sponsor to change an existing health product NPL when patient safety issues arise.
 - Subsection 3(5) of the *Act* covers Look-Alike/Sound-Alike issues as well as product line extensions containing additional or different therapeutically active ingredients
- MHRA, UK
 - For any change in the label, a mock-up of the proposed label, and examples of all packing components have to be submitted to the MHRA
- EMEA:
 - Mock-ups and specimens for the packaging and label prior to marketing



International Scan (Cont'd)

- EMEA

- *Volume 9A of The Rules Governing Medicinal Products in the European Union: Guidelines on Pharmacovigilance for Medicinal Products for Human Use*
 - Risk Minimization Activities “MAH to address potential for medication errors and state how this has been reduced in the final design of the pharmaceutical form, product information, packaging etc.”
 - Potential for Medication Errors “Routinely consider the likelihood of medication errors, taking into account the naming, presentation, instructions for use etc.”
 - Risk-Benefit Assessment – Take into account the potential for medication errors
- Guideline on Risk Management Systems for Medicinal Products for Human Use (4.7.1) and Annex C Template for EU Risk Management Plan
 - Routinely consider the likelihood of medication errors



International Scan (Cont'd)

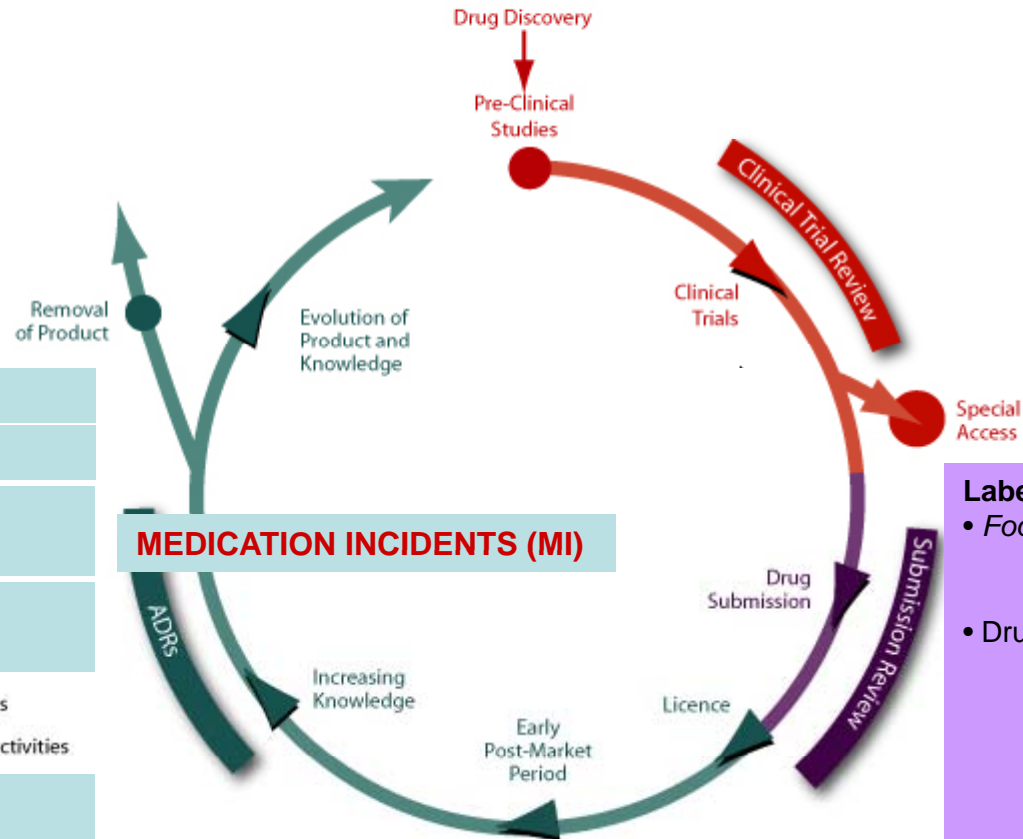
- FDA, US

- 21 CFR 201.10(c)(5) *“Designation of a drug or ingredient by a proprietary name that, because of similarity in spelling or pronunciation, may be confused with the proprietary name or the established name of a different drug or ingredient”*
- Under the re-authorization of the Prescription User Fee Act (PDUFA IV) signed into law on September 27, 2007, FDA stated it would use user fees to implement various measures to reduce medication errors related to LA/SA names, unclear label abbreviations, acronyms, dose designations, and error-prone label and package design.

- “Drug Facts” label required for OTC drugs



Current Point-in-Time Process



Look-Alike health product names

Sound-Alike health product names

Lack of prominent placement of pertinent information

Small size and poor readability of printed information

Industry Activities
Health Canada Activities

Use of abbreviations or trailing/preceding zeros on labels

Poorly designed or cluttered labels (designed for marketing vs. practice conditions)

MEDICATION INCIDENTS (MI)

Lack of differentiation between drug products that have similar names

Similar appearing labels or packages of different products

Label Submission Review

- Food and Drug Regulations:
 - C.01.004 – C.01.006, C.01.014.1, C.08.002
- Drug Name Submission Review:
 - 27 reviews received since 2007
 - Submission moves ahead without name review
 - Approvals of CTP30, Zyban/Zytram, Spriafil/Sprycel
- Label Review
 - Review of written text



Poorly Designed Labels



Insufficient prominence given to route of administration

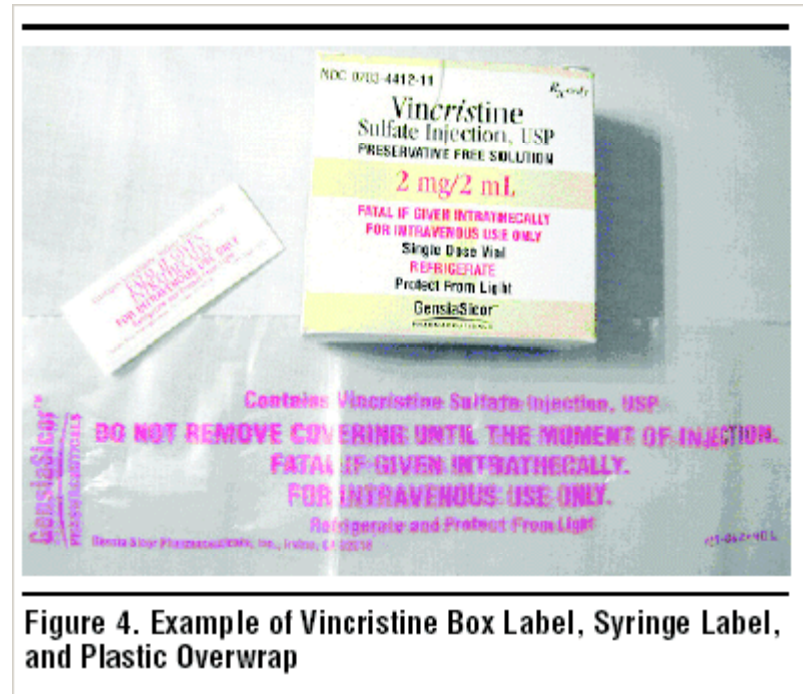
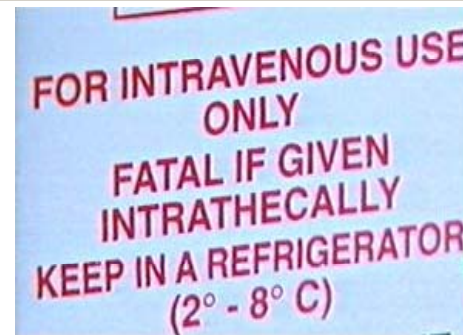


Figure 4. Example of Vincristine Box Label, Syringe Label, and Plastic Overwrap



- Similar appearing labels of different products
- Inadequate warnings about proper drug use
- Administration of a neuromuscular blocking agent to a non-intubated patient would cause paralysis of respiratory muscles and death.



Before



After

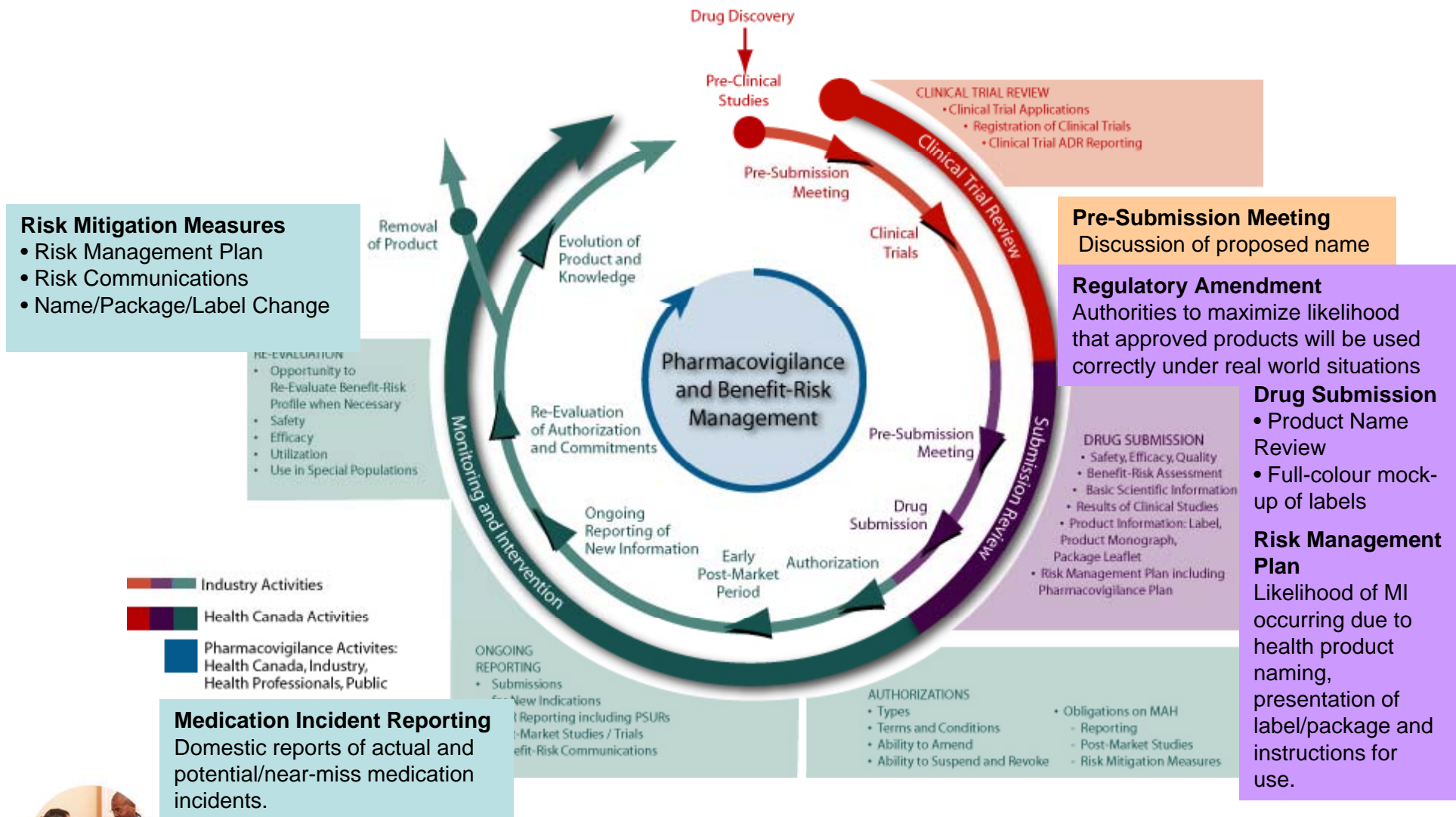


Why changes are needed?

- Medication incidents are preventable.
 - There are known causes of medication incidents that can be prevented prior to the product going out onto the market.
- Current Canadian regulatory requirements do not take into account how the product will be used by the end-user.
 - Authorities needed to maximize the likelihood that approved products will be used correctly under real world situations.
- ISMP Canada has pushed for voluntary changes to NPL following product marketing but uptake is varied.
 - Ensure compliance of stakeholders.



Progressive Licensing Model



Risk Mitigation Measures

- Risk Management Plan
- Risk Communications
- Name/Package/Label Change

RE-EVALUATION

- Opportunity to Re-Evaluate Benefit-Risk Profile when Necessary
- Safety
- Efficacy
- Utilization
- Use in Special Populations

Legend:

- Industry Activities
- Health Canada Activities
- Pharmacovigilance Activities: Health Canada, Industry, Health Professionals, Public

Medication Incident Reporting
Domestic reports of actual and potential/near-miss medication incidents.

Pre-Submission Meeting
Discussion of proposed name

Regulatory Amendment
Authorities to maximize likelihood that approved products will be used correctly under real world situations

Drug Submission

- Product Name Review
- Full-colour mock-up of labels

Risk Management Plan
Likelihood of MI occurring due to health product naming, presentation of label/package and instructions for use.



Thank you!

