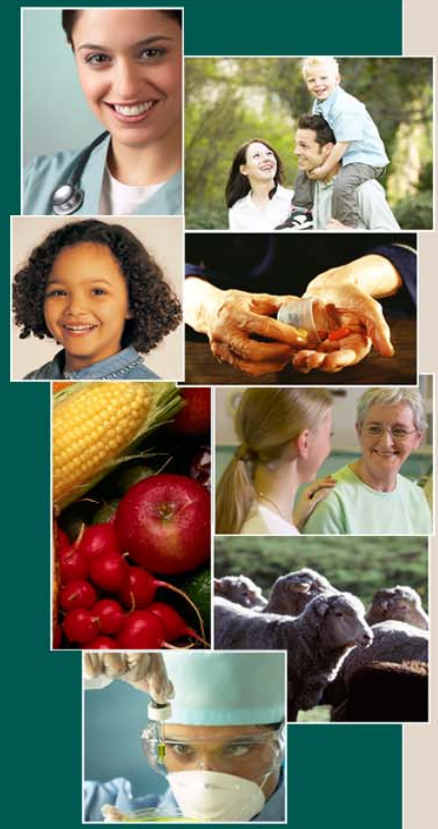
Health Products and Food Branch

Your Health and Safety - Our Priority



Post-Notice of Compliance (NOC) Changes:

Safety and Efficacy

Presentation to CAPRA
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Safety and Efficacy:
Overview of Presentation

- Current Guidance
- Key Elements of Proposed Guidance
- Issue re Implementation of New Criteria

- Note: focus in presentation is on human drugs, (vs vet drugs*, biologics)

Safety and Efficacy:
Outline of Presentation

- **Existing Guidance** (or Where we are coming from)
  = "Changes to Marketed New Drug Products" Policy (1994) (Applies to human drugs)
- **Key Elements of Proposed Guidance:**
  1) New criteria by which to categorize proposed changes to label
  2) Clarity regarding required supporting information
- **Issue re Implementation of New Criteria:**
  In order for new Criteria to fit with existing Regs, new Process structure required, but…..

Existing Guidance

- Changes to Marketed New Drug Products (1994)
  - a) **Criteria for Level II vs Level I, in terms of labelling:**

    Primarily by the type of information / PM* section affected:

    NC = overdosage, side effects, warnings, precautions, contra-indications (provided no indirect claims), references

    SNDS = claims; dosage; route of administration; (whether implicitly or explicitly)

Existing Guidance

- Changes to Marketed New Drug Products (1994)

  b) <u>re Guidance on Supporting Information:</u>

  Reader referred to “Management of Drug Submissions” Policy…..

  But that document is about process, thus guidance in it is limited to:

  “Health Canada expects original information and material to contain the requisite information for the type of submission”

Key Elements of Proposal

For Safety and Efficacy:

- Revised criteria by which to categorize changes to drugs or drug products ie explicitly based on risk management principles

- Provision of more comprehensive guidance as to information required in support of change

Key Elements: New Criteria

- Overview of New Criteria by which to categorize labelling changes

  Shorter review Timeframe = Changes with the potential to improve the management of risk to the exposed patient population **= Level II (NC)**
  (for vet drugs: when human exposure affected)

vs

  Longer review Timeframe = Changes with the potential to increase the risk associated with the use of, or increase exposure to, the drug
  = Level I (SNDS)
  (for vet drugs: when new target species)

Key Elements: New Criteria

(Level II) Notifiable Change:

Any change that has the potential to improve the management of risk to the population presently indicated for use of, or in any other way exposed to, the drug. This includes but may not be limited to:

a) The identification of subgroups, or conditions of use, for which the benefit to risk ratio of the drug has the potential to be less favourable;

b) The addition of any adverse reactions; and

c) The addition or strengthening of risk management measures that are currently available to the population using it, or in any other way exposed to the drug

Key Elements: New Criteria

(Level I) Supplemental NDS

Any change that has the potential to increase the risk associated with the use of, or increase the exposure to, that drug. This includes but may not be limited to the following:

a) The addition of any claims, including indications or use, explicit or implicit, or changes to the current claims, that have the potential to increase exposure levels of the current population and/or expose in any other way, a new population to the drug.

b) The deletion or reduction of risk management measures, that are available to the population using, or in any other way exposed to, the drug

c) The addition of data, other than that related to adverse reactions, which does not result in any other changes to the information provided to the Health Care Professional or consumer, or other* (eg farmer)

Key Elements: New Criteria

Examples Chart in Appendix A: Section by Section of the PM

Each section of the PM: **Category**

Type of Change:

Addition	Type of Addition	SNDS or NC?
Deletion	Type of Deletion	SNDS or NC?
Other (eg reworded or otherwise altered)		

Hierarchy of Risk Management (RM) Measures:

- No text at all on the safety issue
- Text re “non-target species” data
- Line listing in ADVERSE EVENTS *
- Text in alphabetized PRECAUTIONS
- Text in upfront section of WARNINGS *,
  or Indications or Dosage and Administration
- Boxed Warning / Boxed cautions*
- Contraindications
- Patient Registration program *
- Patient monitoring program

↓

= ↑ **RM**

Key Elements: Supporting Information

- Part of the intent is to minimize time spent by reviewers requesting and waiting for information that provides essential context

- The more complete the initial submission, the fewer delays, as the entire picture is needed for optimal regulatory decision-making.

Key Elements: Supporting Information

“ Common to Level I (SNDS) and Level II (NC)” :

includes:

- supporting data (studies, AE reporting etc), plus any pertinent on-going studies, epidemiological data
- most recent core data sheet, and PSURS
- any communications to health professionals
- copies of most recent FDA, EU labelling, and all regulatory exchanges related to the issue eg review reports, feedback on draft labelling etc
- sponsor rationales for proposed changes

Implementation Issue:

- **Level II:** Any change that has the potential to improve the management of risk associated with the use of the drug….

- **Level I:** Any change that has the potential to increase the risk associated with the use of, or increase the exposure to, that drug…

- Clearly, both Level II and Level I criteria involve changes that are “significantly different”

Implementation Issue:

- Under Current Regulations:

  Division 8: C.08.003 - "*if any of the matters specified….are significantly different*…."
    - Significant changes require a supplement to the New Drug Submission
- Both Level I and II changes fit SNDS status of "significantly different"
- But the existing "process" structure requires major changes to support two levels of SNDS
- More efficient to address this change during the overhaul that will anyway be required with the pending Reg changes (ie PLP)

Implementation Issue:

- Therefore:

  Phase 1 = Use existing process structure of SNDS and NC, but with revised criteria (ie interim or bridging period, prior to PLP revision to Regs)

- Phase 2 = Use new framework for revised criteria (ie new Regulations, and consequential new process structure)

Thank You

Contact Information:

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