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The 2016 Canadian Product Monograph Guidance

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YOUR HEALTH AND SAFETY... OUR PRIORITY.

Outline

1. Key Messages
2. Product Monograph Parts I & II Project Background
3. Key Areas of Analysis
4. Side-by-Side Comparison (2004 versus 2016)
5. Implementation Strategy, Timeline
6. Next Steps

Key Messages

- Revisions to Parts I and II of the Product Monograph (PM) Guidance are now final and will be posted this Fall under a brand new 2016 PM Guidance
  - The Guidance, in its entirety, has been updated with plain language elements to all 3 Parts now, along with many necessary ‘science’ updates
- Several changes made to Parts I and II, since the consultation, all minor in nature - albeit one:
  - Text regarding use of comparator efficacy data has been scaled back

Product Monograph Parts I and II – Project Background

- The Canadian Product Monograph is considered part of the drug product label; defined by Guidance as:
  - A factual, scientific document on the drug product that, devoid of promotional material, describes the properties, claims, indications, and conditions of use for the drug, and that contains any other information that may be required for optimal, safe, and effective use of the drug
- Became a three-part module with the 2004 Product Monograph Guidance:
  - Part I: Health Professional Information
  - Part II: Scientific Information
  - Part III: Consumer Information
- Prepared by sponsor as part of a drug submission under Part C, Division 8 (New Drugs) of the *Food and Drug Regulations*

Product Monograph Parts I and II – Project Background (cont'd)

- Part I (Health Professional Information) and Part II (Scientific Information) of the Product Monograph and the associated guidance document came under review as part of the policy work associated with the Plain Language Labelling (PLL) initiative
- Opportunity to address much needed 'science' updates as well as plain language
- Considered completion of the PM Guidance work since plain language revisions already made to Part III: Patient Medication Information (released June 1, 2014)

Product Monograph Parts I and II – Project Background (cont'd)

- Pre-consultations: 2013
  - Internal surveys across the review community of Health Products and Food Branch (HPFB)
  - External web survey and face-to-face meetings with stakeholder groups
  - Paediatric Expert Advisory Committee (PEAC) engagement
  - Pharmaceutical Advertising Advisory Board (PAAB) discussions
  - Pharmaceutical Safety and Efficacy Workshops
- Product Monograph Working Group (WG) convened: October 2013
  - Subsequent formation of sub-working groups for specific topics and issue analyses for each
  - International scans

Product Monograph Parts I and II – Project Background (cont'd)

- External Consultation
  - 75 days - December 19, 2014 to March 4, 2015
  - 27 different stakeholder groups participated: health professionals, industry, consumer/patient groups, and academia
  - Approximately 500 comments were received
- Analysis of consultation results
  - Sub-working groups reassessed recommendations, worked with larger WG; subject matter experts consulted across the Branch
- Implementation Planning
  - Alignment with broadened scope of Part III: Patient Medication Information
  - Implementation period extended to 6 months after release and first phase to last 2 years minimum

What Topics/Areas Received the Most Analysis?

- Pediatric data
- Pharmacology
- Toxicology
- Adverse drug reactions (ADRs)
- Comparative efficacy data
- The References section
- Plain language improvements
  - Making critical information easier to find and read
- General editorial improvements
  - e.g. Table of Contents and Templates re-coded

Pediatric Data

- Why did we look at this?
  - Identified as a priority internally and with external stakeholders, including the Pediatric Expert Advisory Committee (PEAC)
  - In the absence of pediatric labelling claims, clear guidance is needed on the data to be included and its placement. Prescribers need to be properly informed of safety information when making the decision to prescribe off-label to a child
- What went out for consultation?
  - Clearer language, new standard statements
  - Emphasize differences in risk profile between children and adults
  - Add a reference to the International Council for Harmonisation (ICH) E11 categorization for pediatric populations and recognize the importance of identifying other criteria (e.g. weight) in the absence of a specified age range
  - A new Clinical Trial Adverse Reactions for Pediatrics section to include brief information on observed clinical trial ADRs in the absence of an HC authorized pediatric indication
- What changed since consultation?
  - Some difficulty understanding standard statements; these were modified slightly and reorganised
  - A positive statement was added (for instances where HC does authorize a pediatric indication)

Pharmacology

- Why did we look at this?
  - Stakeholders told us of difficulties with retrieval of information due to (1) separation of the pharmacology information into two different areas, and (2) length and level of detail in Part II
  - It is sometimes difficult to determine where to put information
- What went out for consultation?
  - Move all pharmacology information into one section under Part I (i.e,. remove Detailed Pharmacology from Part II), and limit the amount of animal data that is presented to most relevant (e.g. safety only), where human studies are lacking or deficient or the information helps the healthcare professional with interpretation of toxicity or mode of action
  - Improve organization of pharmacology information under Part I with additional headings or bullets where needed (e.g., additional subheadings for electrocardiogram intervals)
- What changed since consultation?
  - A few words edited for clarity

Toxicology

- Why did we look at this?
  - Toxicology section has been criticized for its length, often with numerous tables
  - Question whether extensive data is useful or relevant for health care professionals
- What went out for consultation?
  - Change title to Non-clinical Toxicology
  - Move any human tolerance studies to Part I
  - Limit animal data to important findings only
  - Provide significant additional instructions to explain what to include
  - Discourage use of tables
- What changed since consultation?
  - Minimal text edits made for clarity

Adverse Reactions

- Why did we look at this?
  - Stakeholders identified lack of clarity around:
    - Definition of ‘adverse events’ vs. ‘adverse reactions’
    - Threshold requirements for adverse reaction data
    - Placement of information
- What went out for consultation?
  - New sections and text to provide clearer instruction, including definitions, criteria for inclusion
  - Flexibility with regard to threshold requirements
  - Addition of Department position outlined in 2010 notice regarding practice of reassessing causality of previously reported adverse events
  - Clarification of HC expectations on both pre-market and post-market adverse reaction data
- What changed since consultation?
  - Additional text added to explain flexibility around threshold requirements
  - Comparator statement revised
  - Numerous text revisions without changing intent

Comparator Data

- Why did we look at this?
  - Inconsistent approaches to the inclusion of comparator data and comparator claims in the Product Monograph, which can impact advertising and decisions by provincial and territorial formularies; growing challenge for Therapeutic Products Directorate
- What went out for consultation?
  - Description of conditions under which the inclusion of comparator data is permitted
  - Provide direction to avoid the use of words or phrases that lack a commonly understood meaning, are not easily defined, are vague, misleading, or promotional in tone (e.g., unique, convenient)
- What changed since consultation?
  - Description of conditions under which the inclusion of comparator data is permitted has been made less stringent
  - Statement for not permitting comparator data under Indications section has been removed
  - Proposed definition of pivotal trials removed from Glossary

References Section

- Why did we look at this?
  - Identified as an issue by internal and external stakeholders with respect to usefulness and length
- What went out for consultation?
  - Remove References section; only include references as a footnote in very select cases, and only when requested by HC in the relevant section of the Product Monograph (e.g. those impacted by class labelling, safety data requested references)
  - Create new section “Supporting Product Monographs” for listing authorized HC Product Monographs that were supportive in the development of the Product Monograph (e.g., for certain generic drug products, subsequent market entry drug products or combination products)
  - Where there are no supporting Product Monographs, this section is removed
- What changed since consultation?
  - Text added to provide an example of format to be used (e.g., how to list supporting Product Monographs)
  - Referencing to follow Uniform Requirements for Manuscripts from the International Committee of Medical Journal Editors (e.g., changed from Vancouver style)

General Plain Language Improvements

- Why did we look at this?
  - Parts I and II had not yet been assessed from a plain language perspective, stakeholder comments supported the need to do so especially with respect to organization of information and the ability (or lack thereof) to find critical information
- What went out for consultation?
  - Better cross-referencing between sections rather than duplication of data
  - More standardized text
  - New Recent Major Label Changes section
  - Addition of sub-headings to the Table of Contents; numbering of sections
  - Streamlining of certain sections (limiting information or removing)
  - Change of location of some sections (e.g. Dosage and Administration)
- What changed since consultation?
  - Text added for clarity and examples of how to list recent major changes included
  - Some re-ordering of information within sections (e.g., Dosage and Administration, Clinical Trials section)

Part I: Health Professional Information – Main Sections

- **2004**
  - Summary Product Information
  - Indications and Clinical Use
  - Contraindications
  - Serious Warnings and Precautions Box
  - Warnings and Precautions
  - Adverse Reactions
  - Drug Interactions
  - Dosage and Administration
  - Overdosage
  - Action and Clinical Pharmacology
  - Storage and Stability
  - Special Handling Instructions
  - Dosage Forms, Composition and Packaging

- **2016**
  - Indications
  - Contraindications
  - Serious Warnings and Precautions Box
  - Dosage and Administration
  - Overdosage
  - Dosage Forms, Strengths, Composition and Packaging
  - Warnings and Precautions
  - Adverse Reactions
  - Drug Interactions
  - Action and Clinical Pharmacology
  - Storage, Stability and Disposal
  - Special Handling Instructions

Part II: Scientific Information – Main Sections

- **2004**
  - Pharmaceutical Information
  - Clinical Trials
  - Detailed Pharmacology
  - Microbiology
  - Toxicology
  - References

- **2016**
- Pharmaceutical Information
- Clinical Trials
- Microbiology
- Non-clinical Toxicology
- Supporting Product Monographs

2004

1 INTRODUCTION
2 PREPARING A STANDARD PRODUCT MONOGRAPH
- 2.1 General Instructions
- 2.2 Style Guide
- 2.3 Title Page
- 2.4 Table of Contents

3 **PART I: HEALTH PROFESSIONAL INFORMATION**
- 3.1 Summary Product Information
- 3.2 Indications and Clinical Use
- 3.3 Contraindications
- 3.4 Warnings and Precautions
  - Serious Warnings and Precautions Box
  - Specific Subheadings
- 3.5 Adverse Drug Reactions
  - Adverse Drug Reaction Overview
  - Clinical Trial Adverse Drug Reactions
  - Less Common Clinical Trial Adverse Drug Reactions
  - Abnormal Hematologic and Clinical Chemistry Findings
  - Post-Market Adverse Drug Reactions
- 3.6 Drug Interactions
- 3.7 Dosage and Administration
- 3.8 Overdosage
- 3.9 Action and Clinical Pharmacology
- 3.10 Storage and Stability
- 3.11 Special Handling Instructions
- 3.12 Dosage Forms, Composition and Packaging

4 **PART II: SCIENTIFIC INFORMATION**
- 4.1 Pharmaceutical Information
- 4.2 Clinical Trials
- 4.3 Detailed Pharmacology
- 4.4 Microbiology
- 4.5 Toxicology
- 4.6 References

5 **PART III: PATIENT MEDICATION INFORMATION**
6 GLOSSARY
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2016

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- 2.4 Recent Major Label Changes
- 2.5 Table of Contents

3 **PART I: HEALTH PROFESSIONAL INFORMATION**
- 3.1 Indications
- 3.2 Contraindications
- 3.3 Serious Warnings and Precautions Box location
- 3.4 Dosage and Administration
- 3.5 Overdosage
- 3.6 Dosage Forms, Strengths, Composition and Packaging
- 3.7 Warnings and Precautions
  - Serious Warnings and Precautions Box
  - Specific Subheadings
- 3.8 Adverse Reactions
  - Definitions and Terminology
  - General Information
  - Adverse Reaction Overview
  - Clinical Trial Adverse Reactions
  - Less Common Clinical Trial Adverse Reactions
  - Abnormal Laboratory Findings…
  - Clinical Trial Adverse Reactions (Pediatrics)
  - Post-Market Adverse Reactions
- 3.9 Drug Interactions
- 3.10 Action and Clinical Pharmacology
- 3.11 Storage, Stability and Disposal
- 3.12 Special Handling Instructions

4 **PART II: SCIENTIFIC INFORMATION**
- 4.1 Pharmaceutical Information
- 4.2 Clinical Trials
- 4.3 Microbiology
- 4.4 Non-clinical Toxicology
- 4.5 Supporting Product Monographs

5 **PART III: PATIENT MEDICATION INFORMATION**
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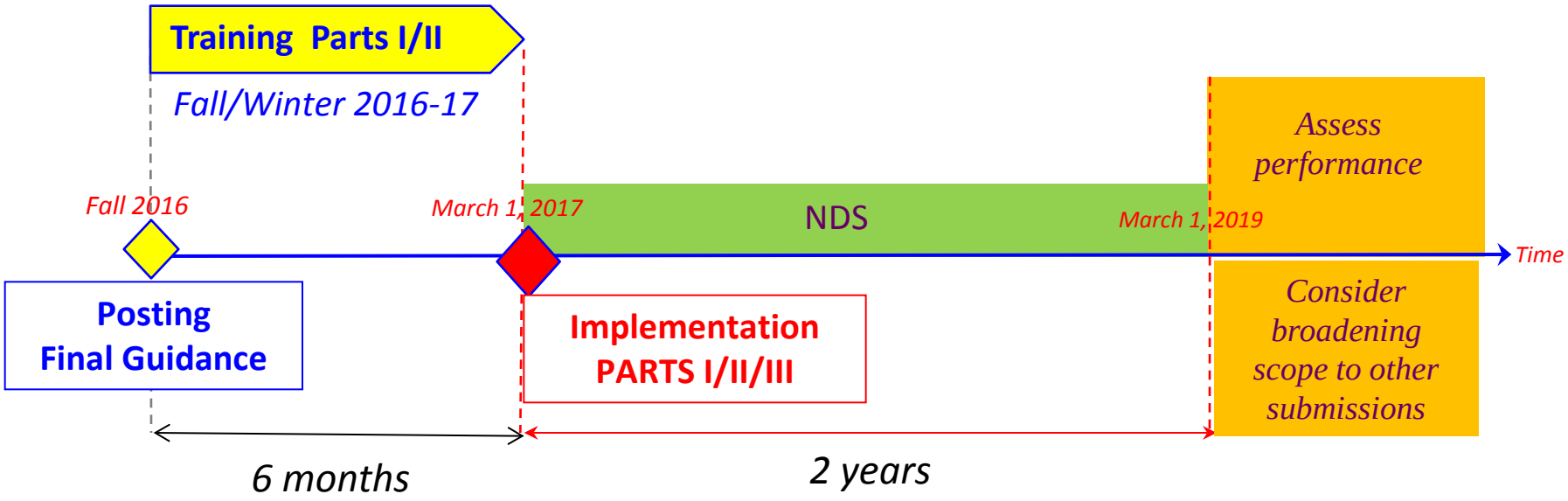
Implementation Strategy

- Posting target: Fall 2016
- Implementation target: March 1, 2017 all New Drug Submissions (NDS) will use the new 2016 PM Guidance (with new Parts I, II, III)
  - All biologics, radiopharmaceuticals and **prescription** pharmaceutical products
  - All subsequent submissions of a product already filed in the new format, are also required to file in the new format
  - Where a corresponding innovator PM is in the new format, all Abbreviated New Drug Submissions (ANDSs) and Supplements to Abbreviated New Drug Submissions (SANDSs) must file in new format
- Reviewer training (e.g., classroom) prior to implementation as well as industry training (e.g., webinar)
- Assess the implementation after a minimum 2 year period

Implementation Timeline



Next Steps

- Fall 2016: Training program development
- Fall 2016: Webposting of:
    - PM Guidance
    - 5 new Templates
    - Notice to Industry (explaining implementation)
- Fall-Winter 2016-17: HPFB review areas & industry training sessions
- March 2017: Targeted adoption of 2016 PM Guidance for NDS

Thank You!

Product Monograph Weblinks:

Product Monograph Project page:
http://www.hc-sc.gc.ca/dhp-mps/prodpharma/applic-demande/guide-ld/monograph/index-eng.php

Product Monograph Guidance 2004 & Templates
http://www.hc-sc.gc.ca/dhp-mps/prodpharma/applic-demande/guide-ld/monograph/pm_mp_2010-eng.php

Product Monograph Guidance 2014 & Templates (new Patient Medication Information)
http://www.hc-sc.gc.ca/dhp-mps/prodpharma/applic-demande/guide-ld/monograph/pm_mp_2013-eng.php

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