



Canadian Approach to Regulation of OINDP



Caroline Vanneste
Health Canada
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Presentation Overview

- **Canadian regulatory framework**
- **HC-EU guideline development**
- **Highlights of HC-EU guideline**
- **Canadian-specific guidance**
 - **Generic Products**
 - **Information for Consumers and Health Care Professionals (Labelling)**

Canadian Regulatory Framework

- **Current regulations broadly outline requirements for pharmaceuticals**
- **Both the USP and Ph. Eur. are recognized in Canadian regulations**
- **Most information is provided in guidelines**
- **Health Canada is an official ICH observer and adopts all ICH guidelines**

HC-EU Guideline Development (1)

- **December 2003: Health Canada draft guideline issued for comment**
- **May 2004: Health Canada and the European Union (EMA's Quality Working Party) begin collaboration on a joint guideline**

HC-EU Guideline Development (2)

- **Drafting team:**
 - **Marjolein Weda (RIVM), EU Lead, and Diana van Riet-Nales (RIVM), QWP Rapporteur**
 - **Caroline Vanneste, HC Lead and QWP Co-Rapporteur**
 - **Keith McDonald, Fiona Mortimer, Joseph Lim (MHRA), Randy Duhaime, Robin Zhang, Gary Condran (HC)**
- **January 2005: Health Canada – European Union draft guideline issued for comment**

HC-EU Guideline Development (3)

- **October 2005: Quality Working Party meeting with industry to discuss proposed changes to guideline**
- **April 2006: Release of finalized guideline at <http://www.hc-sc.gc.ca> and <http://www.emea.europa.eu>**
- **October 2006: Health Canada – European Union guideline comes into effect in both regions**

Highlights of HC-EU Guideline (1)

- **Describes quality aspects of inhalation and nasal products**
 - **pressurised metered dose inhalers, dry powder inhalers, products for nebulisation, non-pressurised metered dose inhalers**
 - **pressurised metered dose nasal sprays, nasal powders, nasal drops, nasal sprays**
 - **liquid inhalation anaesthetics and nasal ointments, creams and gels are excluded**

Highlights of HC-EU Guideline (2)

- **Addresses new marketing authorisation applications (for innovative and generic products)**
- **Does not specifically address clinical trial materials or changes to existing products**
- **Developed for products containing drug substances of synthetic or semi-synthetic origins**

Highlights of HC-EU Guideline (3)

- **Incorporates U.S. and European pharmacopoeial requirements where applicable**
 - **content uniformity (uniformity of dosage units) and delivered dose uniformity limits**
 - **microbial, preservative, and sterility testing**

Highlights of HC-EU Guideline (4)

- **Emphasizes characterization (of the drug substance-drug product-device) via pharmaceutical development tests**
 - **e.g., particle / droplet size distribution, (re-)priming and cleaning requirements, low temperature performance, performance after temperature cycling**
- **Ensures “quality by design”, with less emphasis on end product testing**

Highlights of HC-EU Guideline (5)

- **Addresses region-specific generic, labelling, and delivery system aspects**
 - **Appendix I: Generic Products**
 - **Appendix II: Information for Consumers and Health Care Professionals**
 - **Appendix III: Devices, Spacers and Holding Chambers (European Union only)**

Canadian Guidance: Generics (1)

- **Extensive *in vitro* comparative testing against Canadian Reference Product, including**
 - **Formulation (qualitatively the same and quantitatively within $\pm 10\%$ of the amount of the excipient in the CRP)**
 - **Physicochemical properties of the drug substance and drug product (e.g., particle size, crystal structure, viscosity, hygroscopicity within $\pm 10\%$ where feasible)**

Canadian Guidance: Generics (2)

- **Extensive *in vitro* comparative testing against Canadian Reference Product, including**
 - **Delivery device attributes (physical attributes and operating characteristics)**
 - **Delivery characteristics (delivered dose uniformity, content uniformity / uniformity of dosage units, particle / droplet size distribution, drug delivery rate and total drug delivered)**

Canadian Guidance: Generics (3)

- **Differences from the Canadian Reference Product should be scientifically justified, addressing the potential impact on**
 - **Deposition and absorption characteristics**
 - **Patient compliance**
 - **Underdosing / overdosing**

Canadian Guidance: Labelling (1)

- **Declaration of strength**
 - Use of ex-actuator or target delivery amount is encouraged for all types of products
 - Target should be consistent with the results for batches used in *in vivo* (pivotal clinical and/or comparative) studies
 - Line extension and generic product labelling should be consistent with innovator product

Canadian Guidance: Labelling (2)

- **Dosage and administration**
 - Information on the effect of flow rate on performance
 - Information on the effect of a spacer or holding chamber on performance
 - Information on the nebuliser system(s) and settings used in *in vivo* (pivotal clinical and/or comparative) studies

Canadian Guidance: Labelling (3)

- **Instructions for the consumer**
 - **Shaking**
 - **Initial and re-priming of the container**
 - **Cleaning**
 - **Low temperature use**
 - **Spacer / holding chamber use**
 - **The need to count number of doses used**
 - **General care of the product**

The End...of Part I

- **European perspective to follow**
- **Thank you for your attention**
caroline_vanneste@hc-sc.gc.ca
Therapeutic Products Directorate,
Health Canada