Health Canada / Santé Canada

Working with ICH Quality Guidelines - the Canadian Perspective

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Outline

- Introduction – Health Canada in the global regulatory world.
- ICH Quality guidelines - Canadian Perspective.
- Examples from ICH guidelines.
- Challenges with companies from non-ICH regions.
- Conclusions.

Health Canada in the Global Regulatory World

- Close ties with US-FDA, EMEA, EDQM, USP, and WHO.
- Mutual Recognition Agreement (GMP) with European Union member states, Switzerland, Iceland, Liechtenstein, Norway & Australia.
- Participates in EDQM's Certificate of Suitability review process for API and recognizes the certificate.
- *Observer* status, and active participation in ICH guidelines development. ICH guidelines have been implemented by Health Canada and the Canadian industry.

Health Canada's Role in Bridging ICH and non-ICH Regions and Countries

ICH Guidelines

- Based on scientific expertise, years of experience and elaborate consultation.
- Adopting ICH guidelines makes good scientific and business sense.
- Industries can use ICH guidelines to do a self assessment and get quicker regulatory approvals .

Health Canada

- Canadian sponsors have adopted ICH guidelines. These sponsors have ties with companies both in ICH and non-ICH countries.
- HC reviewers participate regularly in WHO's pre-qualification program.
- HC has MOU with non-ICH countries, including China. HC conducts workshops on quality topics, invites scientists, etc.

MOU: Memorandum of understanding

THREE KEY ATTRIBUTES OF DRUG PRODUCTS

SAFETY

MOST IMPORTANT ATTRIBUTE

EFFICACY

QUALITY

CAN BE ASCERTAINED IN EVERY BATCH BEFORE MARKETING

IF THE QUALITY STANDARD IS APPROPRIATE, AND MET IN EACH BATCH, SAFETY AND EFFICACY COULD BE ASSUMED

Four Categories of ICH Topics

SAFETY → *In vitro* and *in vivo* pre-clinical studies (Carcinogenicity, Genotoxicity etc.)

EFFICACY → Clinical studies in humans (Dose Response Studies, Good Clinical Practices, etc.)

QUALITY → Chemical and Pharmaceutical Quality (Purity, Stability, Development, GMP, etc.) ✓

MULTI-DISCIPLINARY → Cross-cutting topics which do not fit into the above categories (Common Technical Document etc.)

Pharmaceutical Quality
Canadian Expectations

- The Canadian public expects the same quality and performance from both innovator & generic products.
- All products have to meet the standards set by the Food and Drugs Act and Regulations. Additional guidance on pharmaceutical quality is provided in Health Canada's guidance documents and the ICH guidelines.
- 50% of prescription drugs are generics. The generic industry also follows the ICH guidelines.

Pharmaceutical Quality
Global Expectations

- Canada's generic drug industry generates 20% of its sales volume by exporting pharmaceuticals to 120 countries. Use of the ICH guidelines has a positive impact in being a global player.
- WHO gets drug applications from different countries. Quality expectations at WHO (an ICH observer) is also based on the ICH quality guidelines.
- Increasing number of companies in the ICH-regions get their drug substances and products from Asia (China and India).

Challenges with Outsourcing

- Outsourcing is a huge opportunity for growth and also a big responsibility.
- Only the top quality companies will survive in the outsourcing market.
- Following the ICH quality guidelines is not only an expectation, but also the right thing to do!
- These guidelines are available free of cost at www.ich.org. To demonstrate their usefulness, a few examples are described in the following slides.

Example 1: ICH Q3 – Impurities

Demonstrates the clarity in expectations

Q3A(R): Drug Substances, Q3B(R): Drug Products, Q3C: Residual solvents

Q3A(R2)

Maximum Daily Dose[1]	Reporting Threshold[2,3]	Identification Threshold[3]	Qualification Threshold[3]
≤ 2g/day	0.05%	0.10% or 1.0 mg per day intake (whichever is lower)	0.15% or 1.0 mg per day intake (whichever is lower)
> 2g/day	0.03%	0.05%	0.05%

[1] The amount of drug substance administered per day

[2] Higher reporting thresholds should be scientifically justified

[3] Lower thresholds can be appropriate if the impurity is unusually toxic

Reference: http://www.ich.org/LOB/media/MEDIA422.pdf

Example 2: ICH Q2 - Analytical Method Validation

Conveys the expectations in detail

Type of analytical procedure Characteristics	Identification	Testing for Impurities Quantit.	Testing for Impurities Limit	Assay -dissolution -content/potency
Accuracy	-	+	-	+
Precision	-	+ (1)	-	+
Repeatability	-	+	+	+ (1)
Interim. Precision	+	- (3)	+	+
Specificity (2)	-	+	-	-
Detection Limit	-	+	-	-
Quantitation Limit	-	+	-	+
Linearity	-	+	-	+
Range				

- signifies that this characteristic is not normally evaluated

+ signifies that this characteristic is normally evaluated

(1) where reproducibility has been performed, intermediate precision is not required

(2) lack of specificity of one procedure could be compensated by supporting analytical procedure(s)

(3) may be needed in some cases

Analytical Method Validation (Cont'd)

- An accurate analytical method is vital for product development, manufacturing, and management of quality throughout the product lifecycle.
- Laboratory errors complicate and compromise clinical trials.
- Finding out major deficiencies in the analytical method late in the lifecycle (e.g., during regulatory assessment) could jeopardize the entire drug submission!

Example 3: ICH Q1A (R2): Stability Testing

Conveys data requirements to allow planning

2.1.7.1. General case

Study	Storage condition	Minimum time period covered by data at submission
Long term*	25°C ± 2°C/60% RH ± 5% RH or 30°C ± 2°C/65% RH ± 5% RH	12 months
Intermediate**	30°C ± 2°C/65% RH ± 5% RH	6 months
Accelerated	40°C ± 2°C/75% RH ± 5% RH	6 months

*It is up to the applicant to decide whether long term stability studies are performed at 25 ± 2°C/60% RH ± 5% RH or 30°C ± 2°C/65% RH ± 5% RH.

- Stability data support formulation, process, storage recommendation, shelf life & labelling.
- Discovering deficiency in stability during regulatory review is generally too late!

Challenges (Cont'd)

- Challenges with outsourced companies:
  - Balancing risk and benefit – recent incidents have raised many questions on the appropriate choice and control of outsourced facilities.
  - Knowledge sharing and transfer between the sponsor and contract company.
  - Having the outsourced company commit to quality standards desired by the sponsor.

Conclusions

- The ICH guidelines on pharmaceutical quality are based on sound scientific principles and provide a solid framework for developing, manufacturing and controlling drug substances and products.
- Experiences in the ICH regions and Canada show that all drugs, including generics, need to follow the ICH quality guidelines to ensure the products are of high quality, safe and efficacious.
- Outsourced companies are expected to follow ICH quality guidelines to meet global quality expectations.

Thank you

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