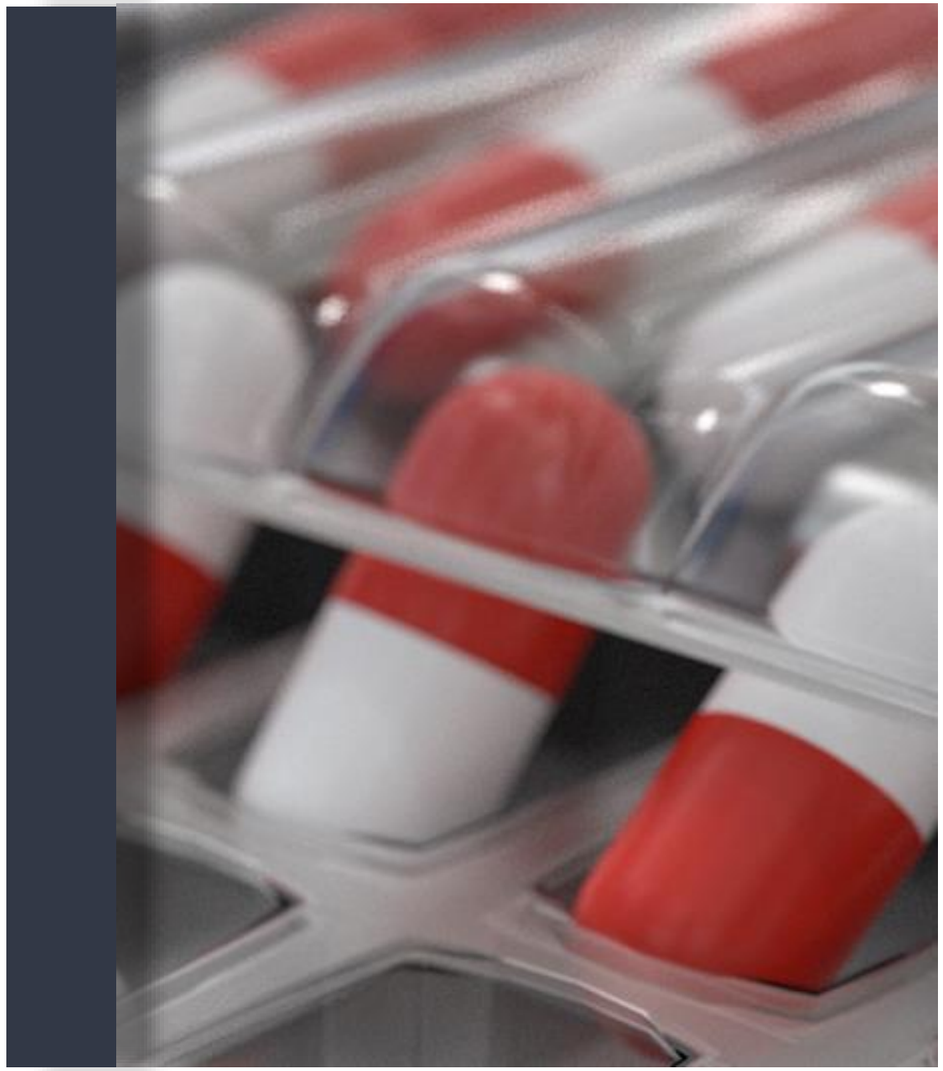
Canadian Generic Pharmaceutical Association

Nitrosamine Task Force
– 2024 –

Martin Ehlert, Nitrosamine Task Force



AGENDA

1. CGPA's Nitrosamine Task Force
2. Unique challenges for the generic sector
3. Industry perspective on progress
4. Priorities for further action

TASK FORCE **MEMBERS AND STAFF**

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Commitment to Quality

Defending patient access to safe products

CGPA members are committed to ensuring the medicines they manufacture, and market are safe, effective, high quality and do not contain potentially mutagenic nitrosamines in harmful amounts.

UNIQUE CHALLENGES FOR THE GENERIC SECTOR

- Large, Diverse Supplier Base
- Larger Number of Products
- Analytical Constraints
- Impact of Remediation

BUSINESS IMPACT

All factors potentially impact product approval timelines, continuity of product supply and patient access.

Recap 6 YEARS OF PROGRESS

IN THE BEGINNING (2018)	CURRENT STATE OF PLAY (2024)
Precautionary approach	Incorporating evolving science
Health Canada is more conservative than EMA and FDA	Health Canada guidance mostly aligned with EMA.
Government working groups excluded industry.	CGPA increased bilateral engagement with Health Canada and stakeholders. New forums created to share research.
No role for ICH to drive international harmonization.	ICH now engaged and generic experts involved.
Default limits practically impossible to achieve, jeopardizing industry and supply sustainability.	Default limits more reasonable for most products. Significantly fewer products require remediation, but challenges remain managing the costs and number of products to remediate.
Lack of predictability and delays when proposing more reasonable evidence-based limits.	Improved transparency and predictability with more reasonable default limits.

BUSINESS IMPACT

Investments can be better prioritized and streamlined.

PRIORITIES FOR ACTION

REDUCE SUPPLEMENT FILINGS

- Avoid unnecessary burden that does not provide substantive benefit

STREAMLINE TESTING

- Canadian-specific requests to confirm the absence of theoretical nitrosamines

TRANSPARENT AND PREDICTABLE PROCESS WHEN LIMITS ARE EXCEEDED

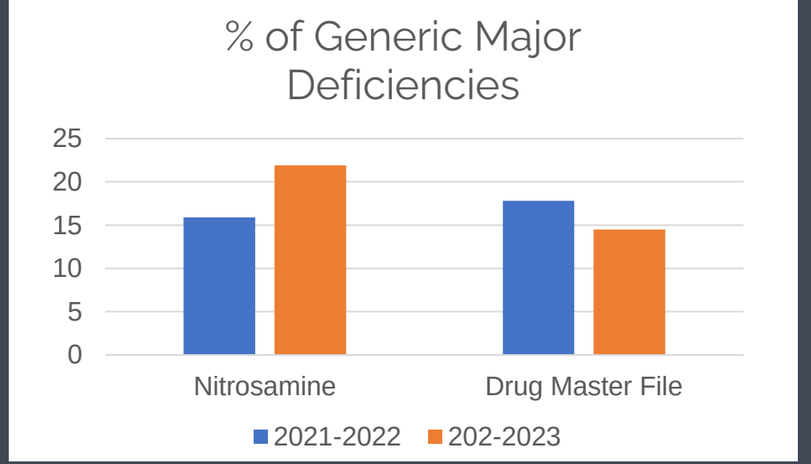
- Capacity challenges to manage risk assessments, extensive confirmatory testing and numerous investigations.

DRIVE LONGER-TERM HARMONIZATION

- Solidify international alignment built to date through a revision to internationally harmonized ICH M7 guidance

REDUCE SUPPLEMENT FILINGS

- Nitrosamine is one of the top reasons for receiving a negative review decision.
- Almost half of deficiencies received for Drug Master Files are nitrosamine related.



ISSUE

Need to avoid unnecessary administrative burden without any substantiative benefit..

Need to mitigate already strained pre-market review process.

CGPA PROPOSAL

Adding a published limit into specifications should be filed through a Notification.

Leverage Post-NOC Guidance to guide nitrosamine remediation filings, like the EU.

STREAMLINE TESTING

ISSUE

Health Canada reviewers continue to request testing to confirm the absence of theoretically possible, but unlikely NDSRIs.

CGPA PROPOSAL

Align with EMA and FDA and accept scientifically based justifications to waive testing based on modelling to de-risk certain NDSRIs.

BUSINESS IMPACT

Delays collective progress and diverts limited resources away from priority products.

TRANSPARENT & PREDICTABLE approach when limits are exceeded

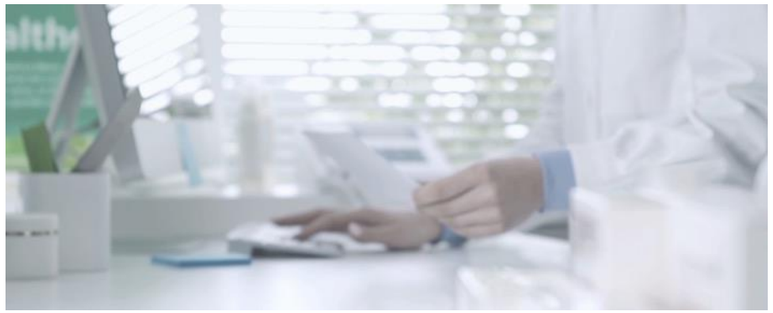
ISSUE

Health Canada urges sponsors to contact them prior to taking market action, so impact on drug supply to Canadians can be considered on a case-by-case approach.

EMA and FDA set out different approaches, each with drawbacks

CGPA PROPOSAL

Blends best of FDA & EMA approach to achieve transparency and predictability



1 CPCA Limits Exceeded?

- Apply **Default Temporary Limits** based on EMA Less-than-life time approach
- Valid for the duration of Step 3 deadline

2 Default Temporary Limits Exceeded?

- Contact Health Canada to propose **alternative temporary limit**, which is immediately published
- Valid for the duration of Step 3 deadline

Maintaining the drug supply for Canadians

DRIVE LONG-TERM HARMONIZATION

ISSUE

"Alignment" is not the same as "harmonization."

Harmonization simplifies requirements for globally managed projects, minimizes delays and allows limited resources to be streamlined.

ICH process takes years to develop/revise guidance that requires foundational alignment prior to begin.

CGPA PROPOSAL

Until ICH M7 is revised, Health Canada should continue to work with stakeholders and regulators to improve CPCA:

- Resolve inconsistencies
- Evolve limits based on science
- Adopt more realistic timing expectations

THANK YOU

#PrescriptionForCanada