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How to Reduce Labelling Clarification Requests

Presentation to CAPRA
by the Natural and Non-prescription Health Products Directorate (NNHPD)

Tuesday June 17, 2025

YOUR HEALTH AND SAFETY... OUR PRIORITY.

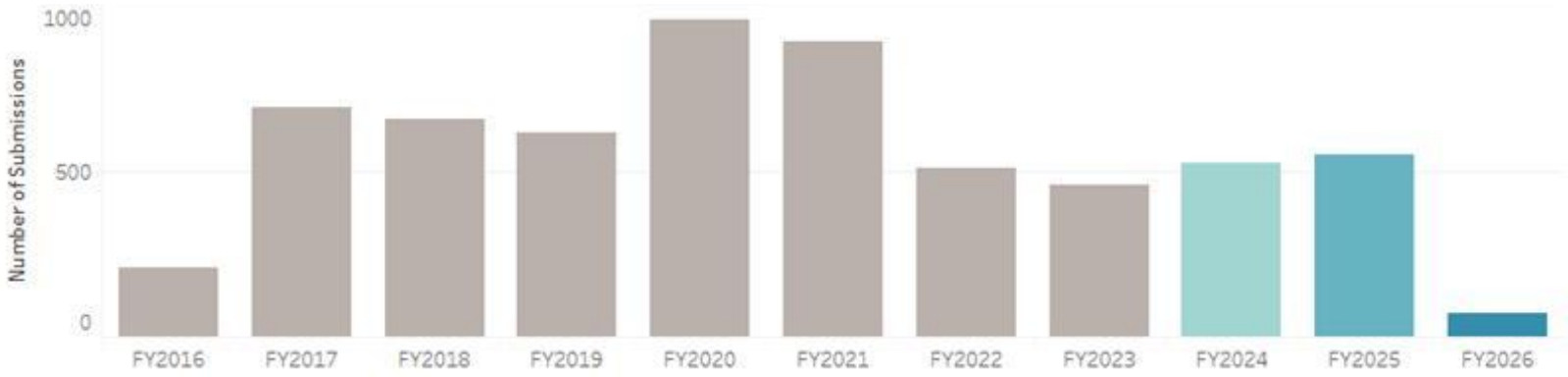
Presentation Outline

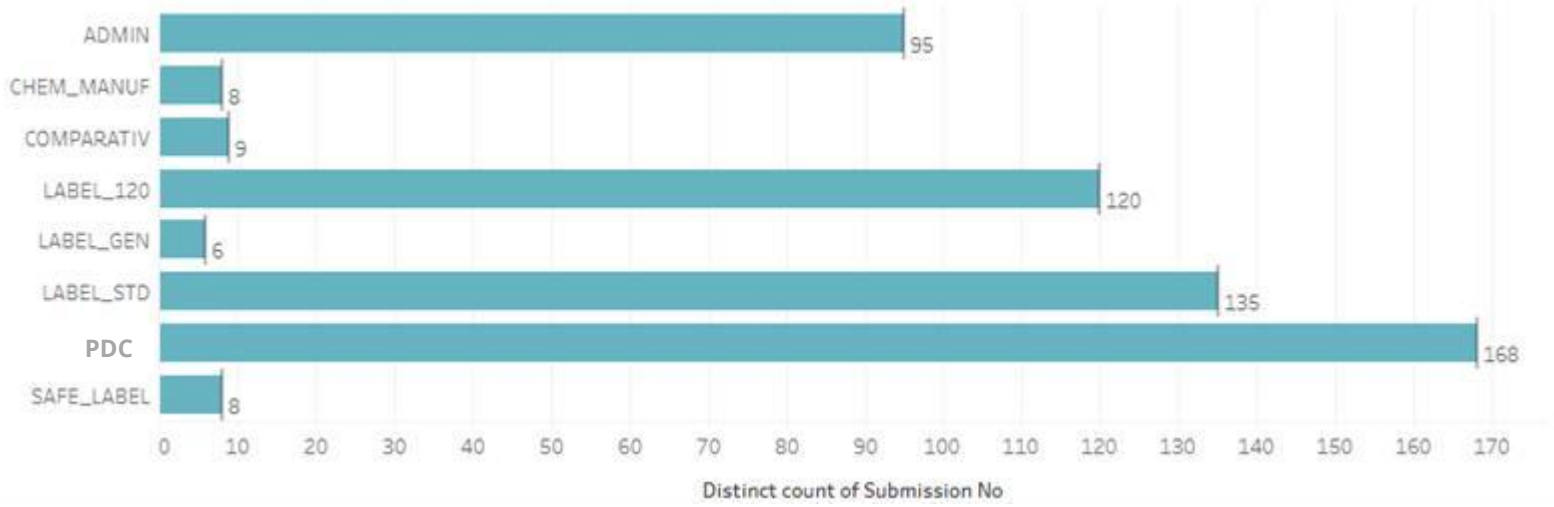
- Update on Submissions
  - Volumes
  - Performance

- Key Messages and Best Practices for Non-Prescription Drug Submissions
  - Labelling Team
  - Clinical Team
  - Quality Team

- Contact

Non-prescription Drug Submission Volume – FY 2025*

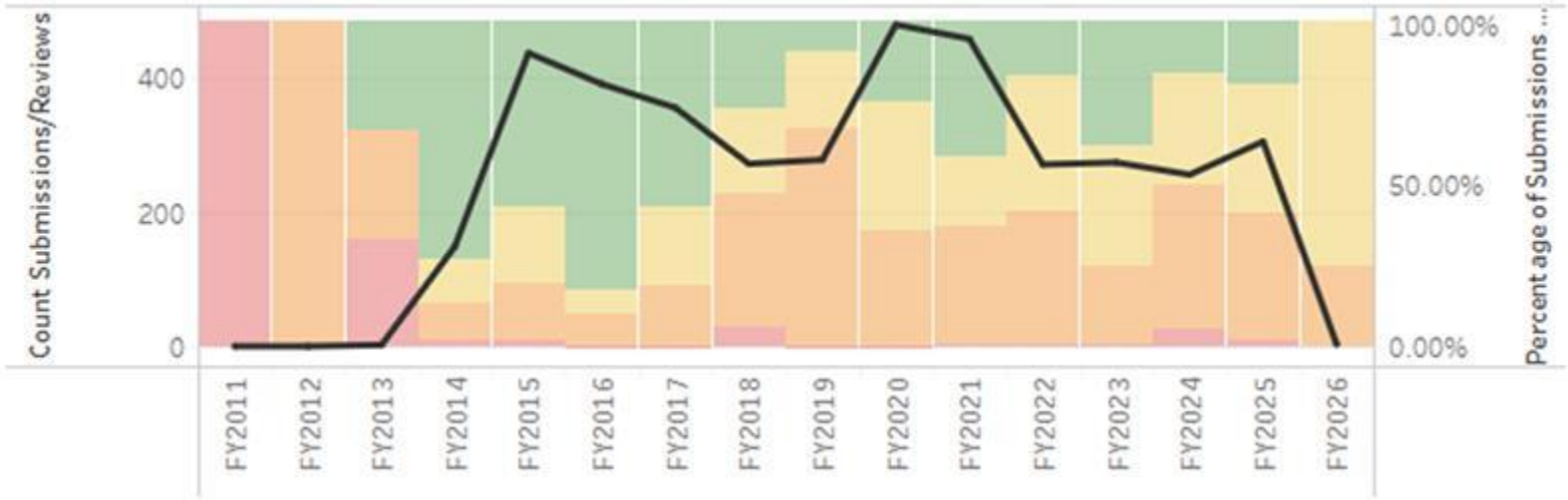




*April 2024 to March 2025

Non-prescription Drug Submission Performance*

Cost-Recovered Submissions:

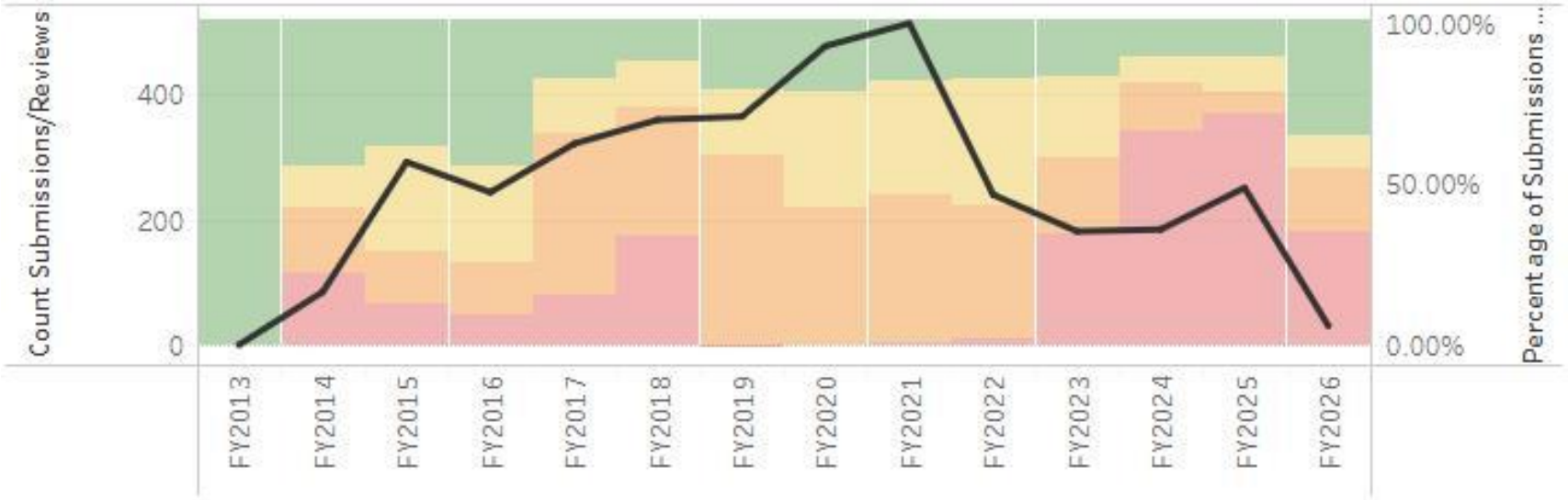


Over the Target Date	Less than 3 Days Before Target Date	Less than 10 Days Before Target Date	More than 11 Days Before Target Date
7 2.17%	134 41.61%	121 37.58%	60 18.63%

*April 2023 to March 2024

Non-prescription Drug Submission Performance*

Non Cost-Recovered Submissions:



Over the Target Date	Less than 3 Days Before Target Date	Less than 10 Days Before Target Date	More than 11 Days Before Target Date
179 71.31%	17 6.77%	27 10.76%	28 11.16%

*April 2023 to March 2024

Common Errors & Best Practices for Screening

Common Deficiencies	Best Practices
• Missing/Incomplete/Blank Forms	• Ensure all necessary forms are complete, signed, and dated • Ensure 'Product Name' is consistent across all documentation
• Labels and Packages Certification Form for wrong schedule of drugs (i.e. Prescription Drugs)	• Ensure to submit the Labels and Packages Certification Form for Non-prescription Drugs, even if no labelling changes proposed
• Inaccurate/Inconsistent list of ingredients in the REP-PI form	• Update NMI list as appropriate • Ensure consistency of ingredients between REP-PI, consumer-facing information and labelling, and applicable documentation • On the REP-PI, the "Calculated as base" field for each active ingredient should accurately confirm whether or not the active ingredient is supplied as a salt or base as well as how the strength is calculated

Common Errors & Best Practices for Screening

Common Deficiencies	Best Practices
• Incorrect contact information in the REP-RT form	• Ensure contact information in the REP-RT form matches the Third Party Authorization form submitted
• Incorrect Regulatory Activity Lead selection on REP-RT form	• For all non-prescription and disinfectant submissions to NNHPD, the correct 'Regulatory Activity Lead' option: Consumer Health Products
• Inconsistency in packaging formats listed in REP-PI form vs. listed in labelling material	• The packaging formats listed in the REP-PI form must match the PM/PI/mock-up labels, as appropriate

For any technical information regarding filling and submitting the REP forms, please contact hc.ereview.sc@canada.ca.

Common Errors & Best Practices for General Review

Common Deficiencies	Best Practices
• NMIs listed on labelling and/or Brand Name without qualification	• NMIs must be qualified with a non-therapeutic purpose. Sponsors can refer to the Guidelines for the Nonprescription and Cosmetic Industry Regarding Non-therapeutic Advertising and Labelling Claims.
• CDFT content is not appropriately translated using PLL	• CDFT translations (English and French) are available in the Guidance Document: Drug Facts Table for Non-prescription Drugs.
• Clarification Request not adequately responded to	• If sponsors disagree with clarification points and wish to provide a rationale, this approach should be discussed with the reviewer prior to sending the response.

Common Errors & Best Practices for General Review

Common Deficiencies	Best Practices
• CDFT not included on product labelling	• Regulatory Requirement as per Section C.01.004.02 (1)
• Revised labels no longer comply with PLL Regulations	• Ensure all revisions continue to meet PLL requirements, as set out in the FDR, please see Guidance: Document: LRND for further details
• Sending a response to SDN/Clarification Request directly to the person who sent the email	• Responses to SDNs need to be sent through the Common Electronic Submissions Gateway, as per standard process.
• Cover letters and REP PI form templates have been recycled and often contain errors; or it is indicated in the cover letter that a change was made, but it is not reflected on the mock-up.	• Before filing a submission or responding to clarification/SDN points, please perform an internal review of the mock-ups and supporting documentation.

Common Errors Found During PLL Review

Principal Display Panel

- Proper Name not immediately before or after Brand Name, and/or in a font size less than half of the Brand Name

Other Panels

- Font size of Manufacturer Name and Address must be 6 point

Canadian Drug Facts Table (CDFT)

- Ensure the correct level of flexibilities is applied:
  - If using 2 Branding Panels (PDPs), only Level I flexibilities may be implemented. i.e., use of condensed font is **not** permitted
  - If using 1 PDP, all levels of flexibilities may be implemented
  - Self-care Category 1 drug products have access to flexibilities listed in Table 5 of the LRND
- Pay attention to font size of CDFT content
- Use Rules, not hairlines, to separate different sections of the CDFT

Common Errors & Best Practices for PDC submissions

Common Deficiencies	Best Practices
• Requested revisions are not outlined in the cover letter. • E.g. "Revisions to artwork" is unacceptable.	• Clearly specify the changes captured in the PDC in the cover letter. • Include annotated mock-up labels in PDC submission
• PDP text is not consistent across all private brands	• Claims should be consistent across all private brands. PDP text should be identical across all private brands. • E.g. "10 hours of relief" vs. "Long-lasting"…pick one or the other
• Product Monograph mentioned on the product labelling, usually under heading "**Other information**"	• Drug products under the PDC stream will not have a PM, and so, reference to a PM should not be made
• "**Uses**" text removed from PDP during artwork revisions	• Moving "**Uses**" text from the CDFT to the PDP is a flexibility; ensure not to remove this required text during PDP revisions

Common Errors & Best Practices for Admin submissions

Common Deficiencies	Best Practices
• Labels included in Admin sub attested to PLL compliance, but were found to be not compliant with PLL	• Ensure labels are PLL compliant (use of a standard CDFT, or a submission was already filed for a CDFT with flexibilities or innovative label). • If not, file a submission for PLL compliance, prior to submitting an Admin sub
• Requesting Brand Name changes under Admin stream	• Must file a DIN application for Brand Name changes
• Changes being made are outside the scope of an Admin submission	Administrative Submissions are only for the following changes: • Manufacturer Name Change • Change in Product Ownership • Merger/ Buy-out • Labelling Update (to match Licensor) • Chemistry and Manufacturing Update (to match Licensor) • Licensing Agreement between two manufacturers

Best Practices for Division 8 Submissions

Annotated Product Monograph/Prescribing Information:

1. The annotated PM/PI should always be based on the currently authorized PM/PI available on the Drug Product Database (DPD) at the time of filing. If level III/minor changes were made since the last PM update, these should be annotated as well with a note or comment confirming that the conditions for a level III change have been met (where applicable).
2. For generic drugs with a Canadian Reference Product (CRP) or labelling reference: an annotated PM against the currently authorized CRP or labelling reference PM is also required.
3. In the event that multiple submissions affecting the PM/PI are filed concurrently, the changes proposed in each concurrent submission are to be kept separate. Upon authorization of one submission, the sponsor can voluntarily submit the updated PM/PI and labelling as applicable to the other submission(s) currently in review without a Clarification Request being issued. If not, Health Canada will issue a Clarification Request to update the labelling accordingly.
4. For the package insert, if the text is based on a section of the PM/PI (such as the Patient Medication Information), an annotated insert is not necessary as the annotated PM/PI is sufficient.

Best Practices for Division 8 Submissions

Product Monograph: Recent Major Label Changes (RMLC) Table

- Ensure the RMLC table and their corresponding vertical lines to identify the new safety updates in the Product Monograph are up to date. As indicated in the *Guidance Document: Product Monograph*:

  "All recent major label changes made during the last 24 months should also be indicated within the body of the product monograph where they occur, with a vertical line on the left margin of the page of the new or modified text, to alert the reader to the new information."

- All recent major label changes must remain listed for at least 24 months after the date the label change was authorized.
- After the 24-month period, the update can be removed from the RMLC table in the next filing.

Common Errors & Best Practices: Clinical Perspective

Common Deficiencies	Best Practices
• The sequence numbers do not match the title headings specified in the 2024 PM format in the Table of Contents / content of the PM	• The Guidance Document: Product Monograph (2024) should be used for direction around appropriate format / content.
• The **4.5 Missed Dose** section (i.e., actions to be taken in the event a patient misses a dose) is often missed during PM Part I migrations, since it may not have been included previously.	• Where applicable, this section (**4.5 Missed Dose** section) must be introduced in the proposed PM, based on the Guidance Document: Product Monograph (2024)
• During Migration to the master template, information from **Detailed pharmacology** section of the 2016 PM format is often incorrectly migrated to **10.2 Pharmacodynamics** and **10.3 Pharmacokinetics** section of the 2024 PM format, especially information about the *Animal pharmacology*.	• Ensure that all information from the **Detailed pharmacology** section of the 2016 PM format is accurately placed under **10.2 Pharmacodynamics** and **10.3 Pharmacokinetics** section. Each of these subsections may include a separate Animal Pharmacology section pertaining to pharmacodynamics or pharmacokinetics.

Common Errors & Best Practices: Clinical Perspective

Common Deficiencies	Best Practices
• During Migration to the master template, errors in values and/or units are often noted in the Bioavailability tables in Part II.	• Ensure that all information (units and values) are migrated accurately from the previously approved PM. Any new information in these tables must be supported by evidence / data.
• Rationale not provided to support the proposed changes to Product Monograph revisions. Company Core Data Sheets (CCDS) are sometimes omitted during a safety update.	• All safety updates must be supported by CCDS, clinical overview and the relevant literature references.
• No evidence to support the pediatric indications that are extrapolated from the adult population.	• All pediatric claims must be supported by data.
• No data provided to support every claim on product labels.	• This may lead to restricting those claims from being made in the labelling documents. Ideally, every claim should be supported with data
• Not engaging Health Canada early for complex submissions	• Request pre-submission/pre-application meetings

Common Errors & Best Practices: Quality Perspective

Common Deficiencies	Best Practices
• Specifications for related substances need to control all compendial impurities where applicable. This includes adequately validated analytical methods for all impurities.	• Verify availability of compendial requirements (BP, USP, Ph. Eur.) for drug substances and drug products. • Where compendial information is not applicable, process and degradation products should be controlled according to ICH Q3A/B. • Analytical methods especially for related substances in the drug product need to be suitable to quantify ALL relevant impurities as required.
• Comparative dissolution studies: Comparative dissolution profiles and calculations are not considered suitable.	• The dissolution method is product-specific and should be developed as such. Refer to Guidance Document: Use of a Foreign-sourced Reference Product as a Canadian Reference Product for f2 factor calculation.

Common Errors & Best Practices: Quality Perspective

Common Deficiencies	Best Practices
• Dissolution method development: - Lack of data to justify the choice of dissolution method.	• Provide studies to show the discriminatory power to detect moderate changes in manufacturing
• Incomplete Nitrosamine risk assessment	• Review HC's updated Guidance on Nitrosamines: Nitrosamine impurities in medications: Guidance • It provides a stepwise approach to nitrosamine assessment, including the Carcinogenic Potency Categorization Approach (CPCA) to calculate acceptable intake limits. • Checklist assessments of nitrosamines may not be acceptable if not all aspects (DS, excipients, manufacturing) are considered.
• Insufficient in-process control of critical manufacturing steps	• In-process controls must be consistent with pharmaceutical development studies and demonstrate suitable control throughout the formulation process.

Questions

Presentation-related Questions, Please Direct to:

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All Other Queries:

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