A Day in the Life of a Regulatory Project Manager at Heath Canada

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Regulatory Project Management Division
Office of Performance Planning and Review Services
Therapeutic Products Directorate
Health Products and Food Branch
Health Canada



Canada

Presentation Content

- Regulatory Project Management Division (RPMD) in context
- Main RPM Roles and Responsibilities
- Other RPM Roles and Responsibilities
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- Meetings!!! (Submission-specific)
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- Challenges
- Challenges – How sponsors can help!
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- New Initiatives




Regulatory Project Management Division (RPMD)

Health Products and Food Branch

11 Offices and Bureaus

Therapeutic Products Directorate

BCANS, BMORS, BGIVD, BPS

Office of Planning, Performance and Review Services

Regulatory Project Management Division (RPMD)

Bureau Support

Manager

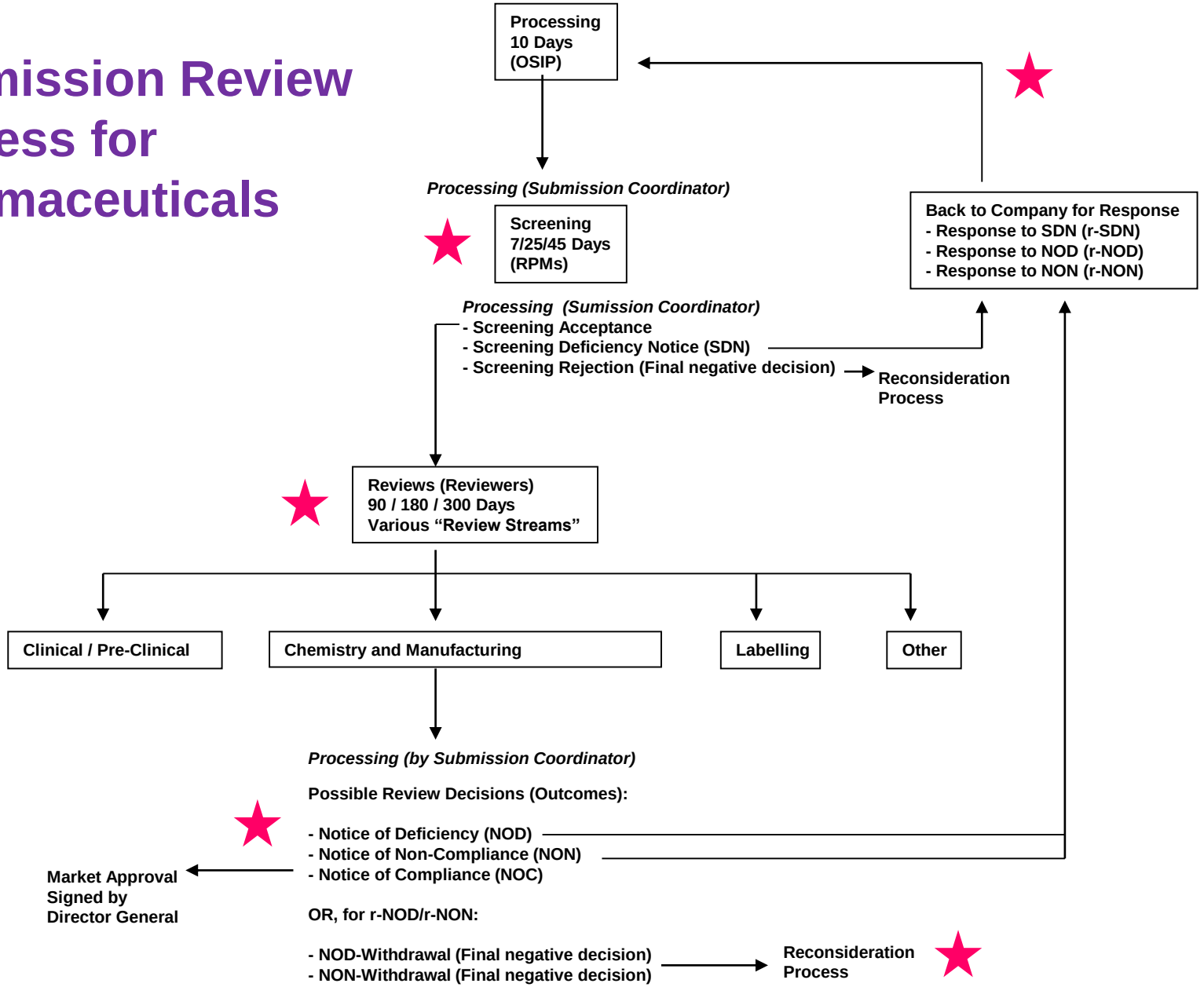
Senior Regulatory Project Managers

Submission Coordinators

Regulatory Project Managers (RPMs)

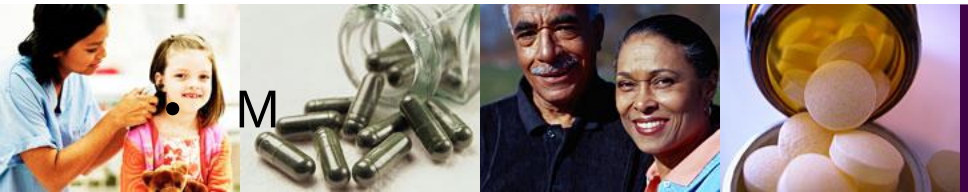



Submission Review Process for Pharmaceuticals



Main RPM Roles and Responsibilities

- Screening: Screening of drug submissions to ensure compliance with regulatory, legal, fee and policy requirements.
- Project Management: Managing the full life cycle of a drug submission: coordination, monitoring, tracking of progress.
- Communication: Provision of regulatory advice and guidance to the pharmaceutical industry, senior management and colleagues on the preparation and the evaluation of drug submissions.
- File auditing / data integrity: Conducting audits of drug submission files to ensure proper documentation and completeness.



Other RPM Roles and Responsibilities

- Participating in internal RPMD working groups (Best Practices, POWM, SAP).
- Participating in other working groups: HPFB, TPD.
- Some working groups are long-standing, others are formed prior to and during the implementation of new initiatives.
- Examples, ongoing: TPD's Good Review Practices Working Group (GRP WG), TPD's Morale and Recognition Committee (TPD MR).
- GRP WG: Meets every 2 months for two hours – a few hours of prep work before and after and sometimes in between meetings as needed.
- TPD MR: Meets once a month - a few hours of prep work before and after.
- Examples, new initiatives: Plain Language Labeling working group, Risk Management Plan working group.
- RPMs/SRPMs are heavily involved in the operational side of most new initiatives.
- General inquiries – not specific to a division or product – received through the RPMD generic email account (rotation).




Meetings!!! (Repeating)

- **Weekly debriefs** within each RPMD subgroup / team (ex: RPMD-BMORS). *Hint*: usually every Thursday afternoon.
  - ➢ Purpose: Debrief on what was discussed at RPMD-MC; new initiatives, process changes, TPD updates / issues.
- **Monday 'Breakout' meetings** within each RPMD subgroup.
  - ➢ Purpose: Discuss review decisions and screening due that week and any urgent issues.
- **Monthly or biweekly meetings with the Bureau Director**: Discussion of status of all submissions, issues, Bureau work assignment, upcoming submissions, screening, meetings.
- **Biweekly bilats with BPS** (clinical Bureaus only): Discussion of status / issues for all submissions with a BPS review stream.
- **Monthly bilat with MHPD**: Status for submissions with a MHPD review stream and discussion of ongoing signal assessments.
- **Division meetings** (ex: MMDD, OD): Workload / issues.
- **Clinical Division Manager – RPM bilats**: Workload / issues.




Meetings!!! (Submission-specific)

- Pre-submission meetings (one to two per month).
- Submission kick-off and progress meetings.
- Teleconferences during review with submission sponsors.
- Pre-Response to NON and NOD meetings (get fit in as needed).
- Special Advisory Committee meetings.
- Reconsideration preparatory meetings.




Typical Day

Percent time spent on:

- Screening: 1/4
- Managing submissions: 1/4
- Communicating with sponsors: 1/4
- File audit: 1/ 4




Screening

Submissions are screened for the following:

- Compliance with regulatory and policy requirements and cost recovery fee structures
- To identify deficiencies early in the process so the submission is “ready for review” and ensure consistent application of submission requirements
- To confirm appropriate submission type filed
- “Scoping out” the submission for planning purposes
- To summarize submission contents to RPMD, Division Manager and reviewers.

A Screening Report is generated **summarizing the submission contents**, **identifying required review streams** as well as **flagging potential issues** for the review areas.




- **The screening report contains the following:**
  - General information (name, active ingredient, strength, etc.)
  - Reason for filing
  - **International status**
  - Relevant / related submissions currently in review
  - Identifies the RPM, Clinical Manager and other review team members
  - **Sponsor contact information**
  - Pre-submission meeting information and location of associated documents
  - Brief summary of pivotal studies / other submitted studies
  - Brief summary of non-pivotal clinical trials and non-clinical contents
  - Highlights key bioequivalence studies
  - **Identifies the required review streams**
  - Identifies whether a Prescription Drug List recommendation is required and highlights any other regulatory implications / issues
  - **Highlights potential submission issues and notes, by review stream, and documents internal consultation during screening**
  - **Includes screening communication with sponsor and SDN comments**

Screening

Health Canada Santé Canada ****This report may contain 3rd party information****

NDS/SNDS Screening Report
(Including response to NON/NOD/SDN)

Brand/Proprietary Name of Drug Product		
Proper, Common or Non-proprietary Name of Drug Substance (supplied as)		
Manufacturer / Sponsor		
Therapeutic Classification		
Dosage Form(s) and Strength(s)		
Route(s) of Administration		
Submission Type/Control Number		
Dossier ID/dB Sequence Number(s)		
Proposed and/or Currently Approved Indications		
Reason for Supplement		
Foreign Regulatory Status		
Relevant submissions currently in review		

Submission Issues to Flag	
Regulatory	
Quality	
Non-Clinical	
Clinical	
DBE	
Labelling	
Brand Name Assessment	
MHPD	

Regulatory Information
Sponsor Contact Info: Name and Title: Phone: Fax: E-mail:
Project Team Members: Team Leader/Quality Manager: Clinical Manager: DBE Manager: Regulatory Project Manager:

<BRANDNAME> 1 <Ctrl# > NDS/SNDS Screening Report
Last modified: 2 June 2016

- Can take from 30 minutes (‘simple’ NC) to 15 hours or more (complicated NDS-NAS) to complete.
- From 2 to 30 pages in length.
- Screening reports and all related correspondence with sponsors (screening clarifaxes) and internal correspondence (emails) are uploaded to docuBridge.




Managing Submissions

- Tracking of submission progress for all review streams.
- Scheduling of submission kick-off and progress meetings.
- Providing submission-related regulatory advice to colleagues during review.
- Making sure necessary regulatory steps happen during review (PDL request, pediatric extension review template, toxicological consults, etc.).
- Keeping databases updated (DSTS, SAP).
- Keep sponsors informed of review progress (SSUF).
- Maintain division tracking sheets.

	BMORS Workload Tracking Sheet		2016-06-02											
Division	Product, Sponsor & Control Number	Type, Class & Timeline	TPD Target Date	Clinical Target Date	Foreign Status (filed / approved / review available)	Reviewer(s)	Meetings (Scheduled/Held)	Review Streams	Label Review	PLL	Label Review Requirements	Clarifaxes	Reason for Filing	BILAT COMMENTS




Communicating with sponsors

- By phone or email.
- Providing pre-submission and filing advice.
- Often have to coordinate with various review groups for the provision of this advice (NDQD, DBE, Clinical Manager and reviewers) = can require time.
- Ensure consistency in advice provided within RPMD (consult with other RPMs, SRPMs, RPMD Management Committee and Manager) = can require time.
- Providing Submission Status Update Forms (SSUFs).
- Holding regular and scheduled submission update phone meetings with sponsors.




File audits

File auditing of drug submission review documentation to ensure proper documentation and completeness.

Decision Package Content Checklist Drug name: _____

___NOC ___NON ___NOD ___Withdrawal Control #: _____

Item	Points to check	Done
Screening	• Screening Report(s) is/are signed and dated, and on docuBridge	
	• Has information been identified in Screening Report that should not be released? (*i.e.* 3rd party info)	☐ Yes ☐ No
	• Acceptance Letters is signed and dated on docuBridge	
Clinical Review	• Nonclinical Review is on docuBridge	☐ Yes ☐ N/A
	• Clinical Review is on docuBridge	☐ Yes ☐ N/A
	• External Review is on docuBridge	☐ Yes ☐ N/A
	• Clin Manager Memo and all referenced reviews are on docuBridge	
	• Clin Manager Memo clearly identifies the date and location (docuBridge sequence or email receipt date) of the approved PM	
	• All review reports authorised for release in Manager's Memo	
	• Has information been identified that should not be released?	☐ Yes ☐ No
	• Confirm Use of Foreign Review method is specified in Manager Memo	
	• Approved PM signed & dated by Reviewer(s) on docuBridge (BCANS and BMORS)	
	• Ctrl # and Date of Preparation or Revision (if applicable) on PM	
	• Confirm whether the pediatric data protection extension form is required to be completed (OSIP)	
	• If yes, ensure that review is on docuBridge and OSIP is notified	
	• Prescription Drug List Recommendation is completed, on docuBridge	
	• If an SBD is required, ensure that Technical Writer is aware that reviews are completed	
Quality Review	• Manager Cover Memo is on docuBridge	
	• Manager has signed off on portion of Labelling (*i.e.* Chemistry information)	
	• All Review Reports referenced in Manager's Memo are signed and dated, on docuBridge	
	• Text for Executive Summary has been identified in the memo	
	• Has information been identified that should not be released in the manager's memo?	☐ Yes ☐ No
	• Any follow-up notes/items identified for other divisions?	☐ Yes ☐ No
	• Ensure tox consults, if applicable, have been uploaded to docuBridge	
	• Verify that the final CPID-CE has been uploaded to docuBridge	
	• Verify the Ctrl # and Dossier ID on CPID	
	• Confirm that the date on CPID matches the date of the NDQD Manager Memo	
Label Review	• Final review report (including Brand name review, if applicable) signed by the Reviewer and Manager is on docuBridge	
	• Interim review report (including initial mock-up label review and review of LASA package, if applicable) is on docuBridge	
	• Verify that the date and location (docuBridge sequence or email receipt date) of the approved PM are clearly identified within the report	
	• Final approved PM and labels signed and dated by reviewer, on docuBridge	
	• Verify that DIN(s)/DNF uploaded to docuBridge, if applicable	
Other review	• Verify whether there were any other review streams (*i.e.* Biostats, QT, MHPD, DBE, OSIP)	
	• If yes, confirm that all review reports and/or memos are on docuBridge	
docuBridge and I:\drive	• Delete any documents shared with an external reviewer on docuBridge through "Document for Consultation"	
	• Final CPID saved on I:\DPD, if applicable	
	• Approved copy of the PM saved on I:\SUBMISS and docuBridge, if applicable	
	• Verify that all annotations are removed from approved clean version of PM and that it is not marked as draft	
	• Verify that notification email to Sponsor of Approved PM version has been uploaded to docuBridge	
DSTS	***Submissions Module***	
	• Verify all information for accuracy against DPD, DNF, NOC and HC/SC 3011	
	• Verify fee field for accuracy	
	• Status is "Review 1" or "Review 2", as applicable	
	• If applicable, ensure that the "pediatric" box is checked	
	• If there are any admin submissions currently in house or recently approved, verify that information on decision package is still correct (i.e. manufacturer name)	
	Reviews Module	
	• Ensure INITIAL LABEL REVIEW stream was included as applicable	
	• Ensure that the status of all required review streams is "completed", as applicable (Reminder for PLL: Was there an administrative update within a labelling only submission, and if yes, was OSIP consulted?)	
	• If NON/NOD issued, status of all review streams listed as "inactive"	
	• Confirm correct Use of Foreign Review method(s) entered	

Last updated on 19 May 2016

Decision Package Content Checklist Drug name: _____

___NOC ___NON ___NOD ___Withdrawal Control #: _____

Item	Points to check	Done
	• Ensure file audit start and completion dates have been entered	
	Documents Module	
	• Ensure correct docs added from Updated Safety Information chart in Clin Manager's Memo (SNDS only)	
	• Confirm correct document(s) added to reflect use of foreign reviews	
	• For NDS, if French PM was committed to be provided 15 days after acceptance, was it tracked in DSTS by OSIP (document for "Second-language labels Pre-Approval")	
SAP-PS	• All necessary SAP Project fields are populated and verified for accuracy	
	• Ensure SBD WBS2 element is added, if required	
Positive Decision Package/ *e-notice*	• Correct version of fee form included and verified for accuracy, and initialed and dated in submission (if the fees need to be revised, ensure that a Note to File RE: Cost Recovery is added to the file (duplicate to OSIP))	
	• Ensure the **NOC form** is included and verified for accuracy: ◦ Correct submission type template has been used (i.e. NDS vs SNDS, NOC vs NOC/c) ◦ Sponsor name and address (as per Box E of HC3011 and the DPD) ◦ Dossier ID and Control Number ◦ Brand Name and medicinal ingredient (including "supplied as", if applicable) against the DPD, HC3011, and approved PM ◦ DIN(s) (if new DINs are issued or for submission with admin component) ◦ Route(s) of Administration ◦ Dosage form(s) ◦ Strength(s) ◦ Reason for supplement (if applicable) ◦ Enclosures (i.e. PM and/or CPID, if applicable)	Edited? Yes / No
	• **DIN Notification Form(s)** included and verified for accuracy (i.e., API (supplied as, if applicable)), DIN(s) in DPD and DSTS, route, form, strength, sponsor contact information) on docuBridge and on *e-notice*	
	• Correct CPID-CE and PM included (if applicable)	
	• PDF of 1st page of the CPID and 1st page/last page of PM included (if applicable)	
	• Ensure that the IP check tag has been correctly applied. IP check is required for NOC, NOC/c, Revised NOC and Revised NOC/c	
	• For NAS, ensure Prescription Drug List (PDL) Recommendation and Prescription Drug List Notice of Amendment included for approval	
	• For NAS, ensure Note to DG indicates PDL documents are included in package for approval	
	• If PDL addition(s)/revision(s) are required, ensure that the PDL tag has been correctly applied.	
	• Sponsor contact info in Sec. 3.0 "Fax package" in *e-notice* matches Box E of the HC3011 form	
Negative Decision Package/ *e-notice*	• Ensure the **NOD, NON** or **Withdrawal** Letter is included and the following information within has been verified for accuracy: ◦ Correct decision type template has been used (i.e. NOD, NON, NOD-W or NON-W) ◦ Sponsor contact information (as per Box B of 3011) ◦ Dossier ID and Control Number ◦ Brand Name and medicinal ingredient (including "supplied as", if applicable) against HC3011 and DPD ◦ NOD/NON/Withdrawal comments make sense and match the Manager's Memo	Edited? Yes / No
	• Sponsor contact info in Sec. 3.0 "Fax package" in *e-notice* matches Box B of the HC3011 form	
All Decision Package / *e-notice*	• Ensure that the Fee form tag has been correctly applied. Fee Form Tag is required for NOC, NOC/c, Revised NOC, Revised NOC/c, NOD/W and NON/W	
	• Ensure all review reports have been included within the e-notice	
	• Executive Summary is included and verified for accuracy on *e-notice*	Edited? Yes / No
	• Other? Describe:	

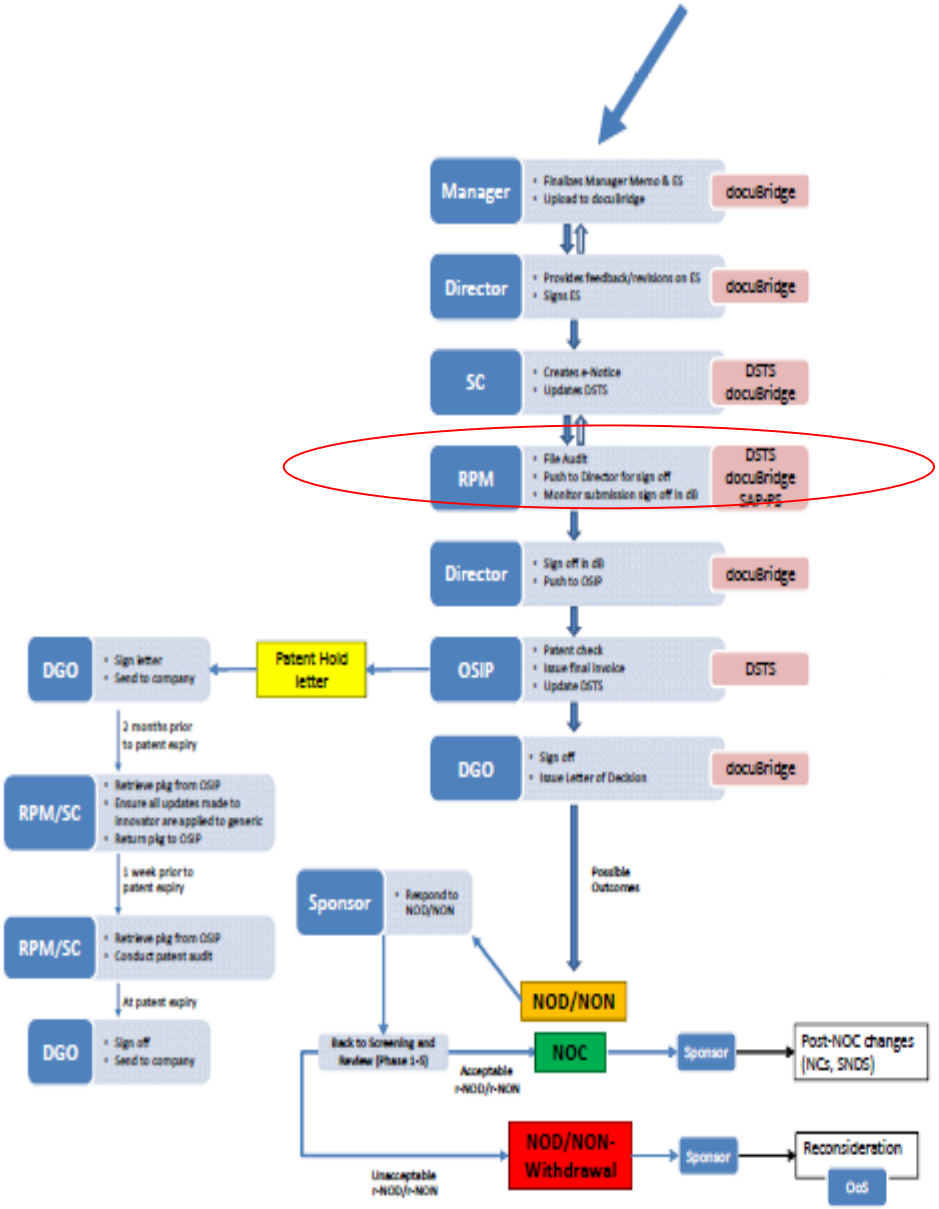
RPM: _____ Date: _____

Last updated on 19 May 2016

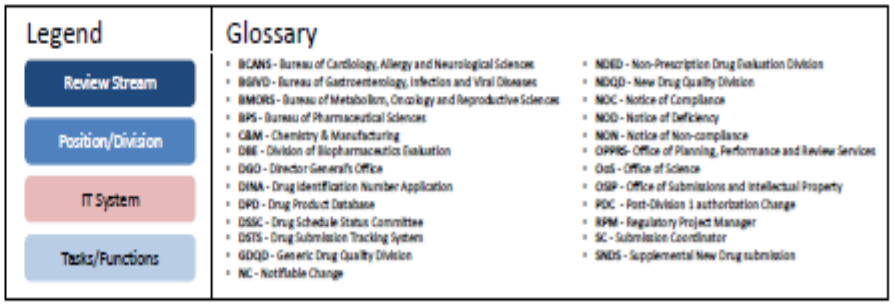



NDS/SNDS Finalization Process

The Decision Stage:



- **File audit**



File audits

SUMMARY TABLE OF ESTIMATED TIME RANGES FOR THE DECISION STAGE

PRIOR TO PACKAGE PREPARATION	
Total	114-139 min vs. 119-144 min
Total (Clinical Supplements only)	109-139 min vs. 118-144 min
Total (BPS only)	114-139 min vs. 115-144 min
PACKAGE PREPARATION	
Total	37-47 min
Total (Clinical Supplements only)	32-42 min
Total (BPS only)	37-47 min
FILE AUDIT OF POSITIVE AND NEGATIVE DECISIONS	
Total (Positive Decision)	154-194 min vs. 138-162 min
Total (Positive Decision - Clinical only)	154-194 min vs. 124-162 min
Total (Positive Decision - BPS only)	131-178 min vs. 115-147 min
Total (Negative Decision)	160-210 min vs. 130-178 min
Total (Negative Decision - Clinical only)	160-210 min vs. 130-178 min
Total (Negative Decision - BPS only)	137-234 min vs. 121-163 min
FOLLOWING DECISION'S APPROVAL	
Total (Positive Decision)	13-18 min vs. 12-17 min
Total (Positive Decision - Clinical only)	13-18 min vs. 12-17 min
Total (Positive Decision - BPS only)	8-13 min vs. 8-11 min
Total (Negative Decision)	13-18 min vs. 12-17 min
Total (Negative Decision - Clinical Only)	13-18 min vs. 12-17 min
Total (Negative Decision without DMF issues - BPS only)	8-13 min vs. 8-11 min
Total (Negative Decision with DMF issues - BPS only)	8-13 min vs. 13-17 min

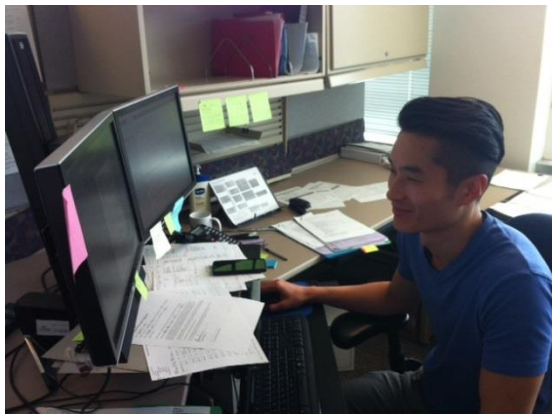
PRIOR TO PACKAGE PREPARATION + PACKAGE PREPARATION (SC tasks) = 2 ½ to 3 hours and 10 min

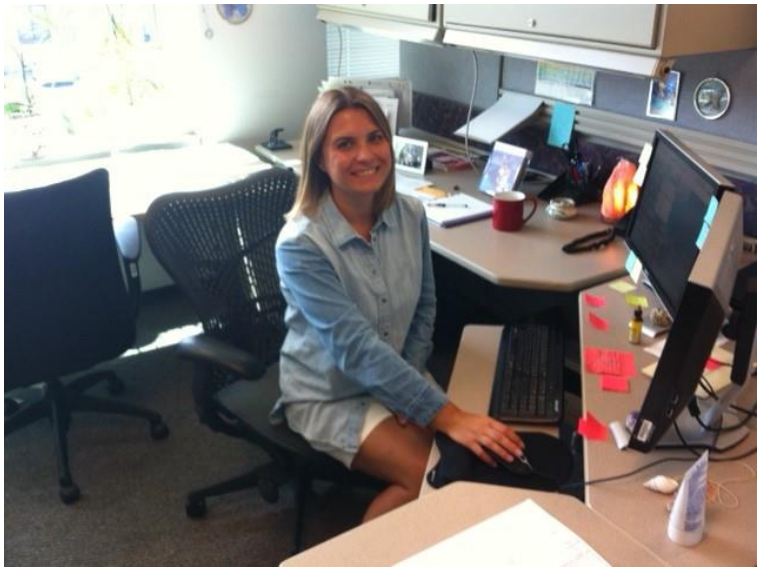
***Other considerations*:**

- **SCs have other decision packages to process, often there is a processing queue**
- **SCs also have other work to complete: NOLs, SALs, checking in submissions, provision of review reports, end-stage tasks after DGO sign-off, other DSTS updates…**




Where we spend most of our days …





Positive aspects of the job

- Varied, high-paced work (days go quickly!).
- Always learning.
- New / unexpected situations – exciting!
- Problem solving.
- Interesting cutting edge products.
- Positively impacting Canadians.
- Hard-working, positive team environment.
- Friendly work environment.
- See immediate impacts of the work you do; filling an unmet medical need, getting new and improved products to Canadians.




Challenges

- Constant change; Implementation of new initiatives and huge impact on work, ie. PLL.
- Heavy workload.
- Answering challenging regulatory questions and giving correct and consistent guidance to sponsors.
- Technological challenges – databases and document-management system (docuBridge) going down.
- Last minute time crunch at finalization / decision stage.
- Fitting in urgent and unexpected work within normal workload.
- Providing timely response to sponsors; our performance standard is to respond within 24 – 48 hours (initial response) – difficult during periods of peak workload.
- High volume of meetings / limited desk time.




Challenges – How sponsors can help!

- Booking discussions for submission updates for larger files (NDS, SNDS) in advance.
- Sending questions prior to submission update / issue discussions over the phone.
- Giving advanced notice if multiple people are to be on a call.
- Requesting feedback / regulatory guidance early with the understanding that responses take time especially since RPMs often have to consult with many different groups before responding.
- Any additional questions posed at pre-submission meetings should be posed before the meeting to allow for internal discussion; if not possible, sponsors should understand that a final response might not be provided at the meeting – follow up often required – less efficient.




Challenges – How sponsors can help! … Cont.

- Filing foreign reviews and communication with other regulators (EU questions and responses) proactively and at any time whenever they become available. (*Do inform RPM first*).
- Filing foreign review attestation along with foreign review documents.
- Screening aides: clearly link DS batches to DP batches used in the pivotal clinical study.
- Proactively completing the Post-NOC Changes Quality Chart.
- Booking submission update phone meetings in advance; gives RPM time to gather information.
- Proactively checking in on submission status during review.



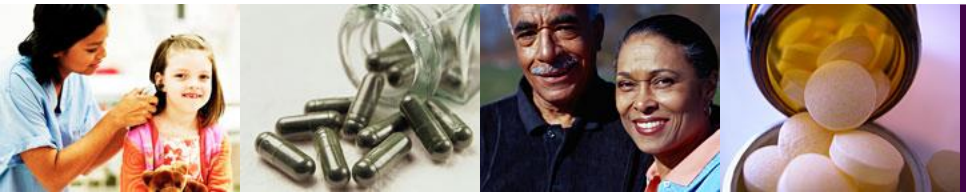

RPMD Working Group Achievements

- Process, Operations and Workload Management: Removal of pristine PM process.

- Best Practices:

  - Screening guide (129 page document).
  - Screening templates.
  - Common phrasing document (CFX and SDN comments).
  - File audit checklists.
  - Pre-submission meeting checklist (NEW).
  - DINA screening guide (NEW).
  - SOP: Joint reviews with MDB (COMING).
  - Screening decision checklist (COMING).

- *Above guides, templates, checklists and SOPs need constant maintenance*.



Screening Guide

Screening Guide

Table of Contents




New Initiatives

- Plain Language Labelling (PLL)!
- New database for GMP compliance ratings: from the Inspection Reporting System (IRS) to the Electronic Compliance and Enforcement System (eCES)
- Vanessa's Law and new advisement letter processes.
- Additional screening for potential sites with GMP concerns and / or data integrity issues.
- Use of EDQM certificate of suitability – goal: cut down on review time – additional validation steps at screening.
- Submission Status Update Forms (SSUFs).




SSUF

Health Canada / Santé Canada

Protected B, once completed

Please be advised that this document is being provided to support project planning. Any information referred to below is subject to change during the review of the submission.

Submission Status Update
Following Kick-Off/Progress Meeting

Date: _____

Brand Name		
Manufacturer/Sponsor		
Submission Type/Control Number		
TPD Target Date		

	Review Stream Status	Review Start Date	Potential Clarifax Date(s) (It is possible to receive clarifaxes at times other than those listed below)
Quality			
Non-Clinical			
Clinical			
Biopharmaceutical			
Brand Name Assessment			
Labelling			
Risk Management Plan			
Other			

<BRANDNAME> 1 <Ctrl#>

Potential Progress Meeting Dates	
Kick-Off Meeting	
Progress Meeting 1	
Progress Meeting 2	
Progress Meeting 3	
Progress Meeting 4	

General Comments

The intent of this section is to highlight specific elements discussed at a recent kick-off or progress meeting and should not be mistaken as a request for clarification. Should follow up be required, a separate request will be issued. Any information provided in response to this form will be treated as unsolicited. An absence of items at this time does not mean that other items will not be communicated in future iterations of this form or though other standard practices.

The following items have been identified at this time:

1-
2-
3-

<BRANDNAME> 2 <Ctrl#>




Thank you!

Questions?

Email me:
honorata.zurakowski@hc-sc.gc.ca