Health Canada Santé Canada

Canada

Regulatory Operations and Regions Branch – Drug Establishment Licensing

CAPRA Education Day

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YOUR HEALTH AND SAFETY... OUR PRIORITY.

Today's Presentation

- Regulatory Operations and Regions Branch (RORB) – "Snapshot"
- Establishment Licensing
  - Workload and Performance
  - Application Management Policy
- NERBY
- Active Pharmaceutical Ingredients (API)

Part 1

RORB “SNAPSHOT”

Overview

- The new Regulatory Operations and Regions Branch (RORB) was launched on April 4, 2016 and brings together the Inspectorate of the Health Products and Food Branch (HPFB) and the Regions and Programs Bureau.

- Uniting regional frontline inspectors with Inspectorate staff in one branch allows for greater efficiency, consistency and coordination of national compliance and enforcement activities.

Organizational Chart

- RORB is divided into 3 national clusters: horizontal clusters, delivery clusters, and program clusters.

- The Health Product Compliance Directorate (HPCD) is a program cluster and is responsible for Drug Establishment Licensing, Good Manufacturing Practices, Compliance Verification and Investigations, Risk Intelligence and Good Pharmacovigilance.

- HPCD is led by a Director General. The Directorate includes 2 divisions:
  - Health Product Inspection and Licensing Division (HPIL);
  - Health Product Compliance and Risk Management Division (HPCRM).

Part 2

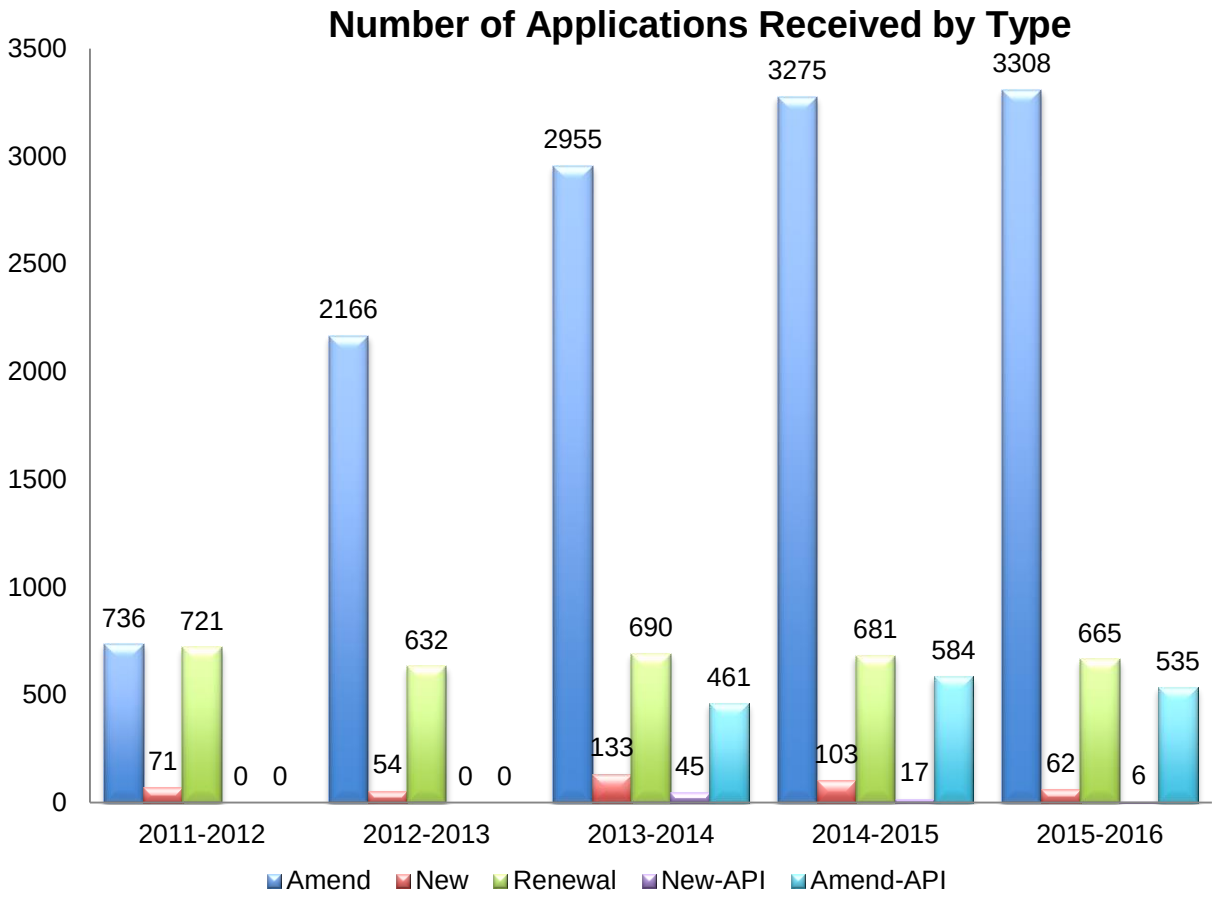
ESTABLISHMENT LICENSING

Workload Changes

300% workload increase in 4 years

Amendments stabilised in last 2 years

~ 550 API amendments per year is new workload

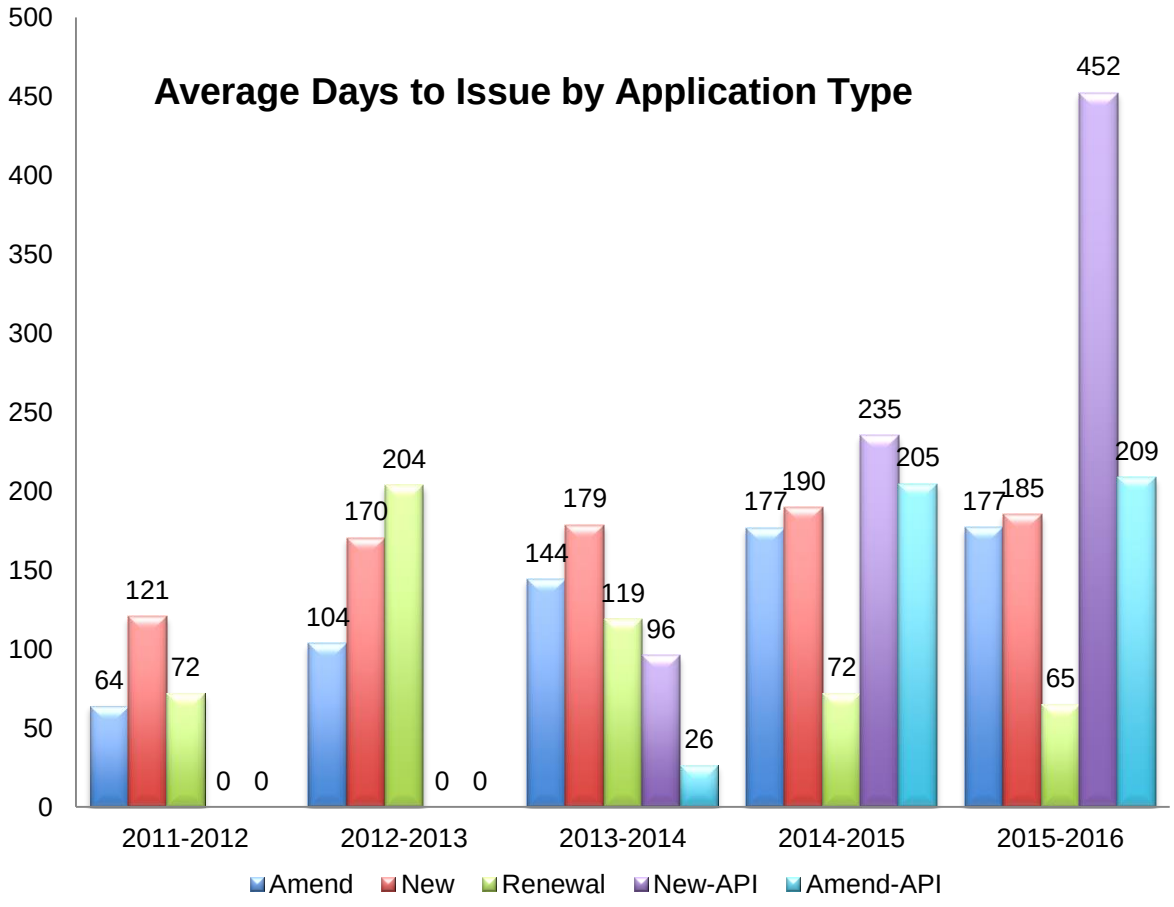


Average Performance

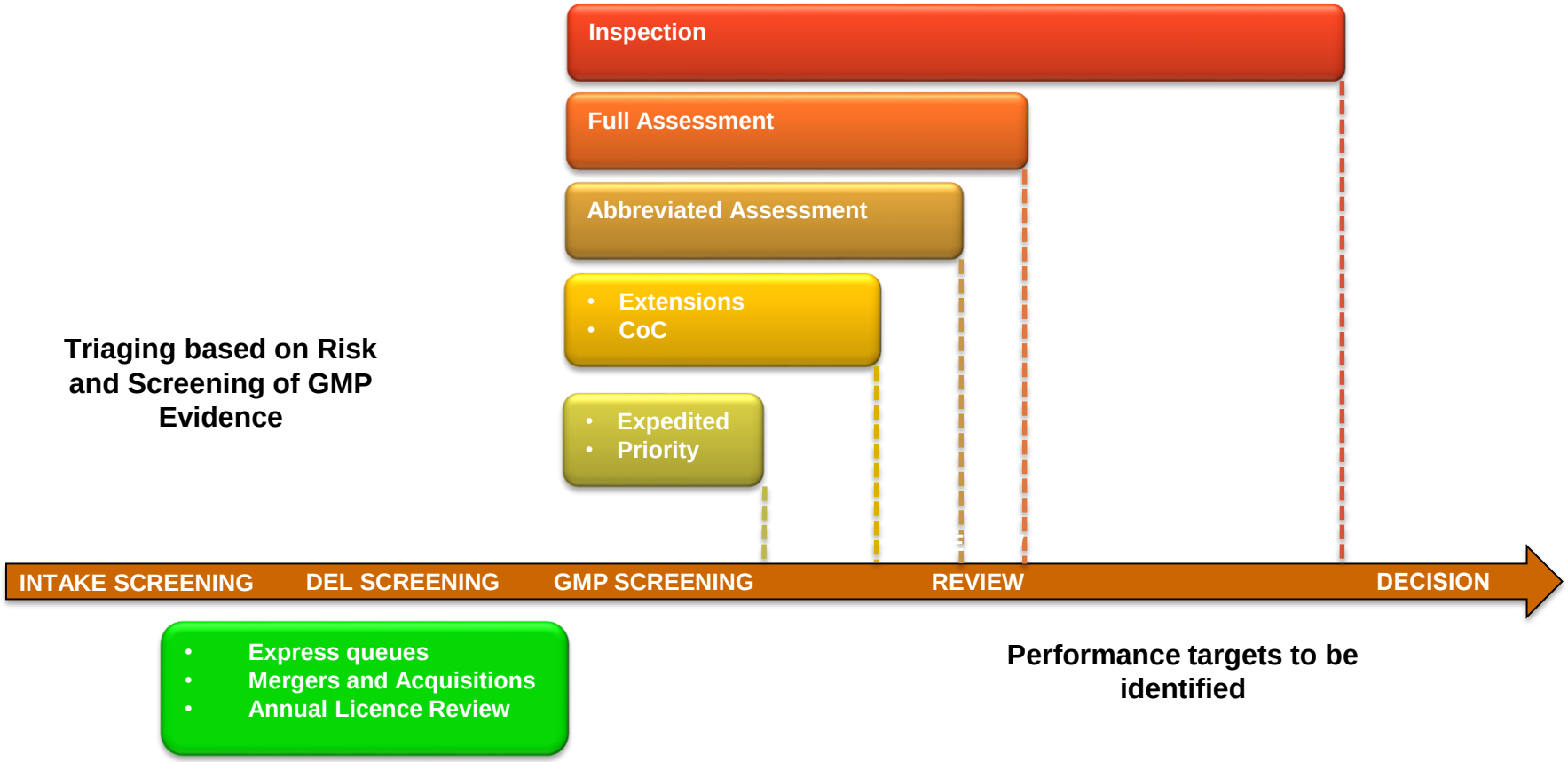
Same or shorter time to make decision compared to 2014-2015:

- **Amendments**
- **New**
- **Annual Licence Renewal (ALR)**

API implementation of inspections and licensing is complete



Drug Establishment Licence (DEL) Applications Approach (Launched in 2015)



Express Queues

- cancellations
- contact and company updates
- addition of warehouses
- removals/deletions

Mergers and Acquisitions

- **Step 1:** Request a pre-submission meeting to DEL_questions@hc-sc.gc.ca with the following:
  - Date of acquisition or merger
  - DEL # and letter impacted in the transaction
  - Details of the new entity
  - The list of foreign buildings to be transferred, if applicable.

- **Step 2:** Meet with HC

- **Step 3:** HC evaluates the request and confirms next steps

- **Step 4:** Applicants submit FRM-0033s and Table A for the amendments as per HC's advice

Expedited and Priority Reviews

- **Expedited reviews**
  - medically necessary with no alternative
  - Request the form **Template for determination of medical necessity of a drug product (FRM-0378)**
  - Complete the form and send it ahead of, or with, your application.

- **TPD priority reviews**
  - Include evidence of the priority review accepted by TPD and the name of the RPM for the submission

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GMP Evidence is a COC

- Send an application only to :
  - Add a new foreign building
  - change the dosage forms, activities or categories
  - Remove the foreign building (at any time, not just ALR)

- Expiry dates:
  - Do not send an application to update the expiry date.
  - Foreign buildings relying on CoCs will no longer be assigned expiry dates.
  - The changes will appear on licences over the year.
  - Importation is permitted if the building is listed on the DEL so long as HC has not communicated otherwise (such as a request to stop sale, recall, etc).
  - These buildings will remain on the DEL unless HC is informed that the building no longer holds a valid authorization issued by the MRA partner or it is necessary to respond to a risk.

Extensions

- Extension requests can be made 90 days in advance of the NERBY/expiry date listed on the DEL.
- Extension requests need to be specific to each foreign building
  - accompanied by an application form (section 5 of FRM-0033 for each foreign building).
- Establishments submit an application with all the required evidence. If the inspection report is not available, a detailed rationale of the reasons why an extension should be provided must be included.
  - The rationale must explain why the report is not available, when it will be available and who is/will be the inspecting authority.

- Applicants should not submit an extension request if the application is complete and is under review. If the review has exceeded 200 days, they are encouraged to contact us and request an update.

- Requests for on-site inspection should be submitted ahead of the NERBY date and ensure that the importer has enough time to find alternate evidence in the event that Health Canada is not able to do an on-site inspection.

Abbreviated Assessments

- Mutual Recognition Agreement (MRA) inspection reports
- U.S. Food and Drug Administration (U.S. FDA) Establishment Inspection Report (EIR) with no 483.

Latest Business Improvements:
Licensing and Issuance

Implemented:

- No backlogs for issuance once the licence is signed (7 to 10 days).
- Foreign Building Supplements to DELs are issued instead of full Foreign Building Annexes.
- Faster issuance of DELs upon completion of foreign site GMP evidence assessment.
- New DEL numbers (new IT system).
- API licences from the coming into force have been issued.
- API Annexes are issued with importer DELs.

Ongoing implementation:

- Queuing by application type – reporting and setting targets.
- Changes to expiry dates.

Part 4

NERBY

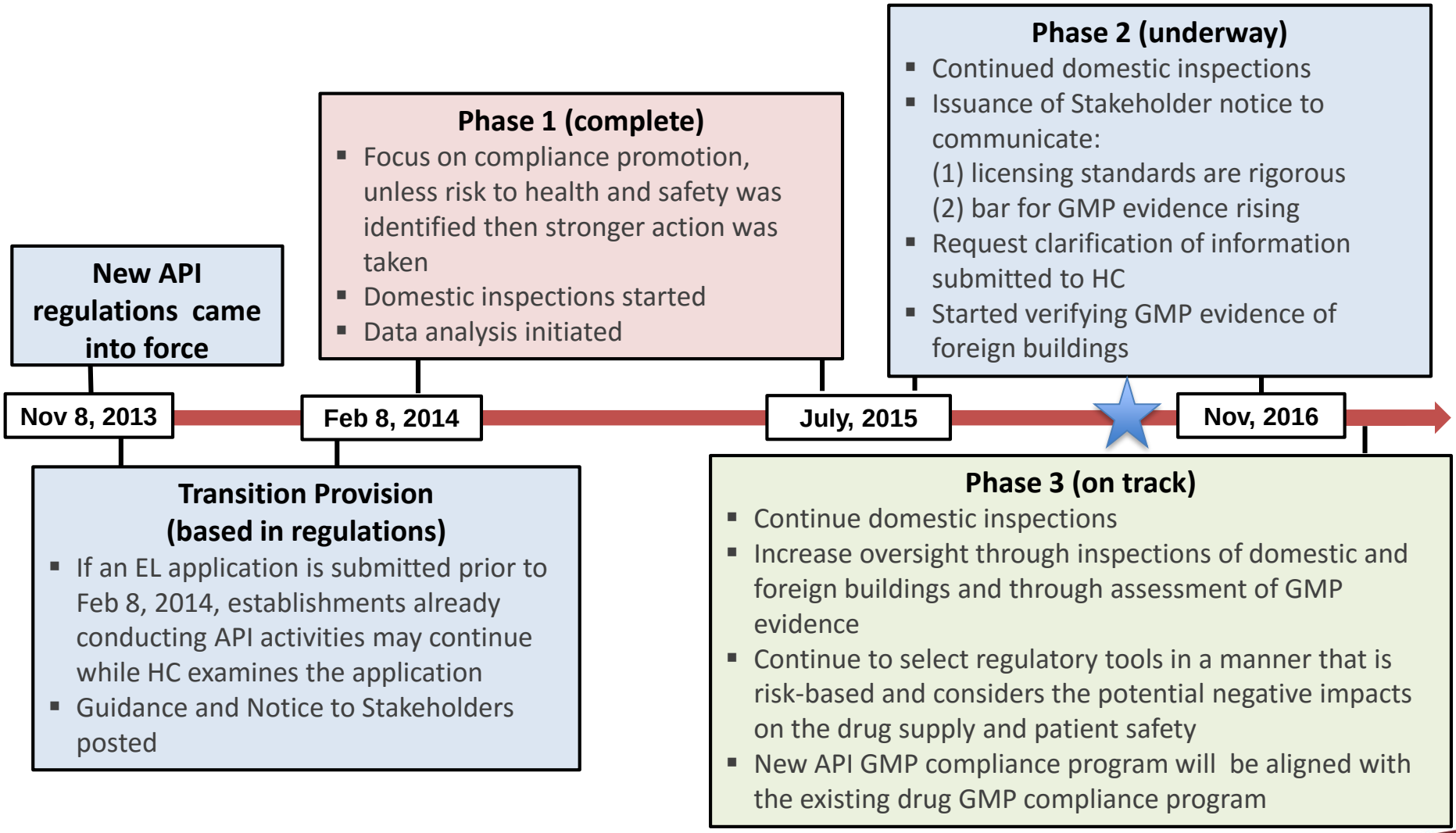
NERBY (coming soon)

- New Evidence Required By Date
- Importers submit evidence by the NERBY date indicated on their licence instead of 250 before the expiry date.
- If a complete application is received, the building will remain listed on the DEL during the review of the application.
- During the review of the application, importation will be permitted in accordance with the DEL and terms and conditions.
- A DEL Bulletin will be issued to announce the implementation date of the new practice.
- Licence will be issued over time.

Part 3

ACTIVE PHARMACEUTICAL INGREDIENTS

API Phased Approach



Active Pharmaceutical Ingredients

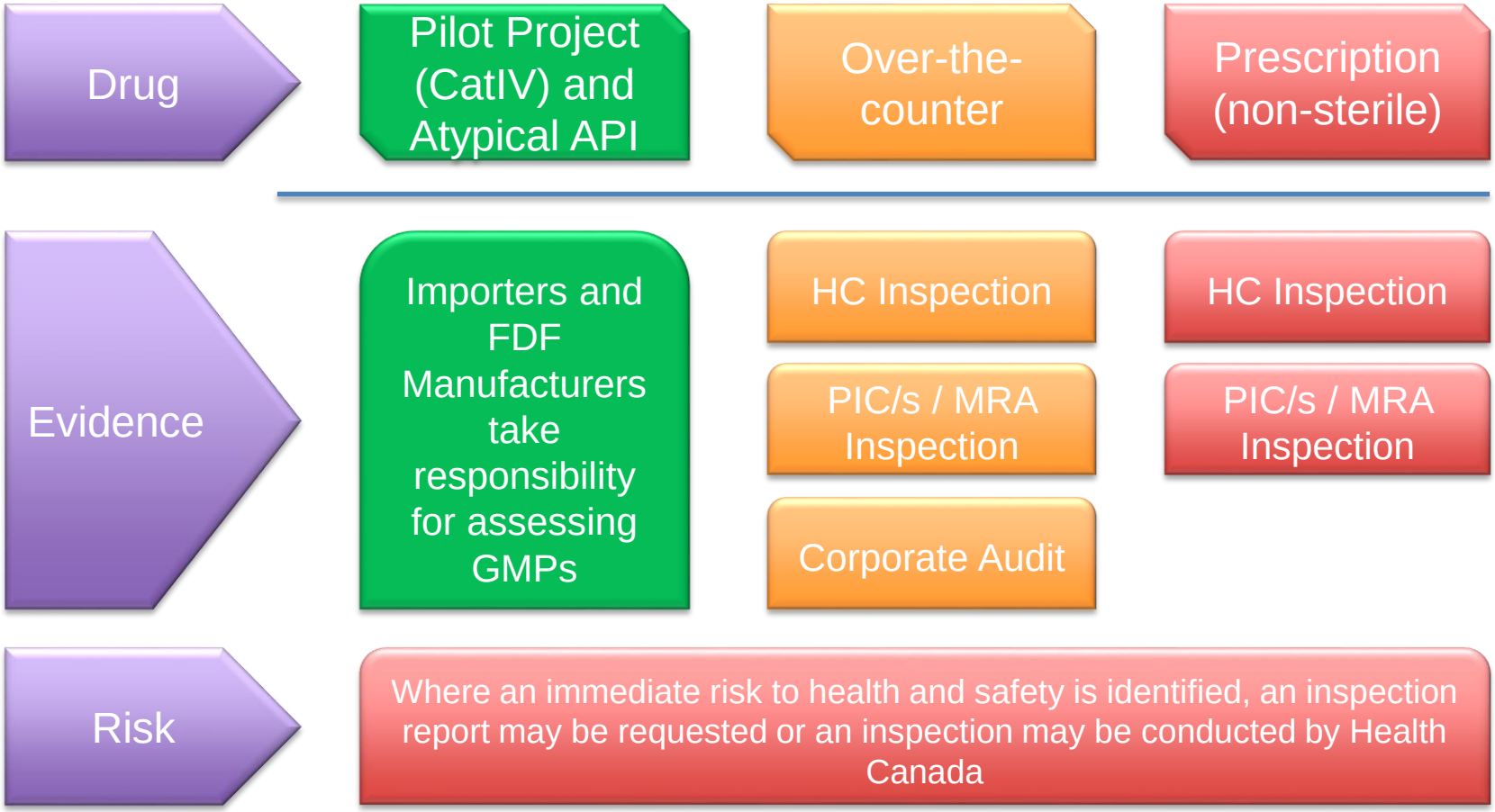
Implemented:

- Improved Table A forms and instructions.
- Screening of API information in Table A.
- Acknowledgement within 20 business days of complete Table A applications.
- No importation until acknowledgement is issued.
- Outlined levels of evidence that will be accepted (Notices and Guidance)
- Started verifying evidence (clarification of evidence, upon inspection of importer, paper assessment), and guidance on Quality Agreements.

Ongoing/upcoming implementation:

- November 2016 – GMP Evidence for API foreign buildings listed on DEL API Annex
- Continue submitting the application (FRM-0033 and Table A) as you are now.
- HC will continue verifying the evidence, by request.

Nov. 2016 – Onward: Compliance & Enforcement



API – Do's and Don'ts

Do:

- Do use the most recent Table A from September 11, 2015. Failure to do so will result in an automatic deficiency notice, meaning the 20 day performance standard referred to in the Notice to Stakeholders of July 31, 2015, will no longer apply.

- Do respond to deficiency notices within 10 business days, as requested. All deficiencies should be addressed or the application may be rejected.

- Do contact DELU if you are unsure of what needs to be fixed on your Table A in response to a deficiency notice. This will reduce the chance of additional deficiency notices and delays.

- Do send applications in a more consolidated fashion (ie. send the least amount of amendments as possible); this will allow for more efficient processing of applications by DELU.

API – Do's and Don'ts

Do *(continued)*:

- Do enable macros each time you are modifying Table A and add to the table starting in row 7, below the orange bar. This will apply validation rules to your entries and minimize deficiency notices.

- Do provide a clear and detailed list identifying all changes to Table A in a cover letter and specify when no changes to Table A have been made and indicate the date of the last revised and comprehensive Table A submitted. This will reduce duplication of effort and improve processing time. (ie. no changes from Table A submitted on X date).

- Do send a comprehensive Table A listing both FDF and API with every application, as per the July 31, 2015, Notice to Stakeholders.

- Do use the pick lists for columns D (API name) and J (country).

API – Do's and Don'ts

Don't:

- Don't follow the instructions included in FRM-0033 for filling out Table A, since these refer to the old Table A. These will be updated with the next release of FRM-0033.

- Don't start importing newly added active pharmaceutical ingredients (APIs) until you have received an acknowledgement notice informing you that your Table A has been reviewed, and that you are able to import APIs. Importation can continue from buildings listed on your previously issued DEL API Annex unless otherwise informed by HC.

- Don't send in a Table A with "N/A" or "#" in required fields. This will result in a deficiency notice and the 20 day performance standard referred to in the Notice to Stakeholders of July 31, 2015, will no longer apply.

API – Do's and Don'ts

Don't *(continued):*

- Don't copy information from columns D (API name) and J (country) from old Table A and paste into new Table A. The API names have been standardized and will prevent multiple versions of the same API, and the countries are displayed in both English and French. Enter the information using row 7, below the orange bar.

- Don't submit Table A's directly to inspectors; only Table As sent with Section 5.1 of FRM-0033 directly to the Drug Establishment Licensing Unit (DELU) using the ELapplicationsLE@hc-sc.gc.ca account will be processed and acknowledged. You may cc. the Inspector on your application submitted.

- Don't respond to an acknowledgement notice with specific questions related to an application. Any questions following receipt of an acknowledgement notice should be sent to the DEL_questions_LEPPP@hc-sc.gc.ca account.

Next Steps

- Increase foreign on-site inspections.
- Fully implement changes to the foreign building evidence submission process.
- Publish revised guidance documents.
- Useful links related to health product inspection and licensing:
  - Drug and health product inspection database (DHPID): http://healthycanadians.gc.ca/drugs-products-medicaments-produits/inspecting-monitoring-inspection-controle/inspections/index-eng.php
  - Inspection Tracker: http://www.hc-sc.gc.ca/dhp-mps/pubs/compli-conform/tracker-suivi-eng.php
  - Provide you comments: http://www.hc-sc.gc.ca/home-accueil/rto-tor/index-eng.php

How Can You Help Us?

The quality of your application has an impact on timelines for processing.

- Read instructions and notices.
- Send complete applications.
- Send a complete rationale with any requests (priority, expedited, extensions)
- Send a complete rationale for incomplete applications.
- Ensure that FRM-0033 is completed and signed.
- Ensure that your contact person is up to date in our systems.
- Respond to Health Canada’s inquiry in a timely manner.
- Minimise status updates.

QUESTIONS?