Regulatory Essentials – February 20, 2019

Health Updates

Sunscreen Pilot Expansion

Health Canada is now reviewing sunscreen pilot extension applications to allow for modified options for identification and confirmatory testing in Canada of drug sunscreen products imported from various countries over and above the United States only.

Please let us know if you:

- have applied under the pilot expansion as of today,
- plan on applying under the expansion or,
- do not plan on applying under the expansion.

by sending us a quick email at regulatory@cosmeticsalliance.ca to let us know!

CA continues our work with Health Canada to further expand the pilot to include other low-risk product categories. If you have any questions, please reach out to your CA regulatory team at regulatory@cosmeticsalliance.ca.

DEL Bulletin – EN

DEL Bulletin – FR

Expanded Sunscreen Pilot Application Form – EN

Expanded Sunscreen Pilot Application Form – FR

Expanded Sunscreen Pilot Table – EN

Expanded Sunscreen Pilot Table - FR

Stakeholder Info Session – EN

Stakeholder Infor Session - FR

Validation Rules for Regulatory Transactions Provided to Health Canada in the "non-eCTD electronic-only" format

Health Canada is publishing a set of validation rules for regulatory activities in the "non-eCTD electronic-only" format. These rules build on the information provided in the Guidance Document: Preparation of Regulatory Activities in "Non-eCTD Electronic-Only" format and will assist sponsors in preparing their regulatory transactions for filing to Health Canada.

It is important for sponsors to ensure that the validation rules are followed accurately in order to avoid encountering validation errors. Although they may be updated in the future, Health Canada is currently validating regulatory transactions in "non-eCTD electronic-only" format using the rules listed in the table below. Stakeholders are encouraged to use a commercially available tool to validate their regulatory transactions in "non-eCTD electronic-only" format, prior to filing them to Health Canada.

Although the profile may be updated without further notice, as of March 30, 2019, Health Canada will be validating regulatory transactions in non-eCTD format using version 4.4 of the "non-eCTD electronic-only" validation rules.

Should you have any questions regarding the content of the notice, please contact hc.ereview.sc@canada.ca.

Health Canada "Non-eCTD Electronic-Only" Validation Rules version 4.4

ID #	Rule Name	Rule Description	Severity
A – GENERAL			
A01	Empty Folders	This rule is configured to detect empty folders (folders without any files or subfolders) in the transaction structure. **TIP**: All empty folders must be deleted before submitting the transaction to Health Canada.	Error
A03a	File Size	This rule is configured to verify the size of the files. A warning will be generated for PDF files between 150 MB and 200 MB. A warning will be generated for other file types (excluding SAS XPT) between 100 MB and 200MB. **Revised** **TIP**: Check the size of each file before submitting to ensure it does not exceed the maximum limits.	Warning
A03b	File Size	This rule is configured to verify the size of the transaction. An error will be generated for PDF files greater than 200 MB, SAS XPT files greater than 1GB and other files greater than 200MB. **TIP**: Check the size of each file before submitting to ensure it does not exceed the maximum limits.	Error
A08	File types	This rule is configured to verify if the file extensions are valid. The acceptable file extensions are: .pdf, .doc, .docx, .xls, .xlsx, .wpd, .ppt, .pptx, .dat, .inf, .txt, .jpg, .png, .gif, .svg, .wav, .mp3, .mp4, .wmv, .jpeg, .tiff, .tif, .bmp, .sas, .xpt, .xml*. **Revised** *Applies only to regulatory transaction (hcreprt*.xml), product information (hcreppi*.xml) and application information (hcrepaim*.xml) files provided as part of the Regulatory Enrolment Process (REP). **TIP**: • Ensure that the file types for your documents are accepted before submitting. • File extensions written in uppercase letters are not accepted. • Do not change the file extension manually.	Error
A09	Corrupt and password protected WORD documents	Word document will be reported as corrupted or password protected if one or more of the following situations occur: 1. Document is corrupt or unreadable 2. Document has password protection	Error

ID #	Rule Name	Rule Description	Severity
		3. Document references an attached template located via http or https Note: This rule applies only to Word version 2007 or later (.docx). **New**	
B - PDF ANALYSIS			
B01	Corrupt or unreadable PDF documents	This rule is configured to detect corrupt or unreadable PDF files within the transaction. An Error will be generated if the document: 1. Cannot be opened because it is damaged or the encryption is too strong. 2. Appears to have zero number of pages. 3. Appears to be an application form, but the form content cannot be read. An example of situation number (3) could be a document appearing to have one page only and the page contains the text phrase “Please wait… If this message is not eventually replaced by the proper contents of the document, your PDF viewer may not be able to display this type of document.”	Error
B24	PDF Protection	**Revised** This rule is configured to detect if the PDF documents are password protected. An error will be generated if there is a password. **TIP**: Before submitting to Health Canada, ensure PDF documents are not password protected.	Error
B25	PDF version checking	This rule is configured to verify that if the PDF document versions are valid. The acceptable PDF versions are 1.4, 1.5, 1.6, and 1.7. **TIP:** Ensure the PDF documents are created using the acceptable PDF versions.	Warning
B32	PDF Protection: Owner password	Finds all documents with an owner password set, excluding forms regardless of their location in the folder structure. **Revised** **TIP**: Ensure that “No Security” is selected for the “Security Method” displayed in “File”, “Properties” and then, “Security”.	Warning
B36	Bookmarks - multi action	This rule is configured to detect all bookmarks with multiple actions assigned to them. **TIP**: Ensure that all bookmarks have only one action assigned to it. This action should open the destination page. These settings should be verified in the bookmark properties.	Error
B40	PDF documents with attachments are not allowed	This rule is configured to detect attachments and portfolio documents found in PDF documents. **TIP**: Ensure that the PDF document does not include attachments or portfolio documents.	Error

ID #	Rule Name	Rule Description	Severity
B44	PDF documents with more than 10 pages must have bookmarks	This rule is configured to verify if PDF documents greater than 10 pages have bookmarks. Excluded from this check are: literature references in sections 3.3, 4.3, and 5.4; and Health Canada application e-forms.	Warning
B45	PDF Protection – Printing	Finds all documents where printing is not allowed. **New**	Error
B46	PDF Protection – Content Copying	Finds all documents where copying is not allowed. **New**	Error
B47	PDF Content restrictions	This rule checks for pdf files that contain JavaScript, dynamic content (e.g., audio, video or special effects), or 3D content. **New**	Error
C - REFERENCED FILES			
C05	Naming Syntax	This rule is configured to verify that the maximum path length including the first level folder of the regulatory transaction must not exceed 200 characters. The file names must not exceed a maximum of 64 characters, including the file extension. **Revised** **TIP**: File path length character count starts at the application folder and includes the file name.	Error
		I: Regulatory Enrolment Process* New	
		***ONLY for users of the Regulatory Enrolment Process (REP)**	
I01	Corrupt xml file	An XML file will be reported as corrupt if the file cannot be opened because the file is damaged.	Error

Mandatory Use of the Electronic Common Technical Document (eCTD) Format

The eCTD format for regulatory activities allows Health Canada to move towards a common submission intake process, standardize and improve its business processes and tools, and align its regulatory requirements with those of other international regulatory authorities. Health Canada has been accepting regulatory activities in eCTD format since 2004. As of December 2018, 93 percent of regulatory activities under Part C, Division 8 of the Food and Drug Regulations, for human drugs, have been provided in this format.

The purpose of this updated notice is to communicate Health Canada's intention to expand the scope of regulatory activity types where filing in eCTD format is a mandatory requirement. The current and intended regulatory activity types (as per section 1.3 of the Guidance Document, Preparation of Drug Regulatory Activities in eCTD Format), where filing in eCTD format is a mandatory requirement, are summarized by effective date below:

Regulatory Activity Types Required in Mandatory eCTD Format by Date

January 1, 2018	**Division 8 (for Human Drugs only)** • New Drug Submission (NDS) • Supplement to a New Drug Submission (SNDS)

- Abbreviated New Drug Submission (ANDS)
- Supplement to an Abbreviated New Drug Submission (SANDS)

Remainder of Division 8 (for Human Drugs only)

June 1, 2019

- Extraordinary Use New Drug Submission (EU NDS)
- Extraordinary Use Supplement to a New Drug Submission (EU SNDS)
- Supplement to a New Drug Submission-Confirmatory (SNDS-C)
- Notifiable Change (NC)
- Request for Priority Review Status for NDS or SNDS
- Yearly Biologic Product Report (YBPR)
- Periodic Safety Update Report - Confirmatory (PSUR-C) or Periodic Benefit Risk Evaluation Report - Confirmatory (PBRER-C) when provided to TPD, BGTD or NNHPD - submitted to support the fulfilment of a Notice of Compliance with Conditions (NOC/c).
- Pre-Submission Meeting Information (MPNDS, MPSNDS, MPDIN, or MPNC)
- Undefined Regulatory Activity (UDRA)
- Development Safety Update Report (DSUR) when provided as a **standalone** regulatory activity to Therapeutic Products Directorate (TPD), Biologics and Genetic Therapies Directorate (BGTD) or Natural and Non-prescription Health Products Directorate (NNHPD).
- Post NOC - Level III Changes Form
- Including
    - Administrative regulatory activities (i.e. NDS, ANDS),
    - Labelling ONLY regulatory activities

Post-market Vigilance Data (Human Drugs only)

June 1, 2019

- Periodic Safety Update Report (PSUR) or Periodic Benefit Risk Evaluation Report (PBRER) when provided to the Marketed Health Products Directorate (MHPD)
- Risk Management Plan (RMP), when provided to MHPD
- Other Post-market Vigilance data (Undefined Data Post-market Vigilance (UDPV)) requested by MHPD
    - Risk communication document (e.g., Dear Health Care Professional Letter, dissemination lists, Proposed Dissemination Strategy) should be sent to the Office of Submissions and Intellectual Property (OSIP) with an electronic convenience copy being provided directly to MHPD via email
    - Post-market Surveillance (e.g., Issue-related Summary Reports, Council For International Organizations Of Medical Sciences (CIOMS), Line Listings, Registry Reports, Clinical Study Reports, or Patient Exposure Data)
    - Benefit Risk Assessment
    - Response to MHPD Requests for Additional Information
    - Notification of Change in benefit-risk profile (under sections C.01.018(3) and (4) of the Food and Drug Regulations)
    - Meetings regarding post marketing issues with MHPD

Division 1

September 1, 2019

(to be confirmed)

- Application for Drug Identification Number (DINA)
- Application for Drug Identification Number - Biologic (DINB)
- Post-Authorization Division 1 Change (PDC)
- Post-Authorization Division 1 Change - Biologics (PDC-B)
- Post-DIN Notification (for DINA only)

Master Files

- New Type I Master Files - Drug Substance
- New Type II Master Files - Container Closure Systems and Components
- New Type III Master Files - Excipients
- New Type IV Master Files - Drug Product

It should be noted that, once an eCTD formatted regulatory activity has been filed by a Sponsor for one of the above regulatory activity types listed above, all subsequent transactions are also mandatory in that format. Any individual product exemptions from the mandatory eCTD format requirement will continue to be considered by Health Canada on a case by case basis. These requests should be submitted as per the template below:

To: hc.ereview.sc@canada.ca.

Subject: Mandatory eCTD Format - Exemption

Email body:

- Company name:
- Product name:
- Regulatory activity type:
- Anticipated date of filing:
- Rationale for the exemption:

Filing in eCTD format is not mandatory, but recommended, for the following regulatory activity types:

- Clinical Trial Applications (eCTD CTA pilot only),
- UDRA: Notification of Discontinued Sale (DIN cancellation) and Notification of interruption of sale
- Non-Prescription Human Drugs* regulated under Division 1 of the Food and Drug Regulations (i.e ., DINA (over the counter products only), DIND, DINF, PDC and, Post DIN Notifications)

Regulatory activity types for the following product lines currently remain out of scope for filing in eCTD format; they must be filed in "non-eCTD electronic-only" format:

- Medical Devices
- Veterinary Drugs

Regulatory transactions in eCTD format should be prepared as prescribed in the Guidance Document – Preparation of Regulatory Activities in eCTD Format, and must be sent via the Common Electronic Submissions Gateway, when applicable. Refer to the Frequently Asked Questions – Common Electronic Submission Gateway (CESG FAQ), and the Notice - Mandatory Requirements for using the Common Electronic Submissions Gateway (CESG) documents for requirements and further guidance on using the CESG.

Discontinuation of Acknowledgement Letters for Regulatory Activities Received by Health Canada

To modernize and align internal processes, Health Canada is proposing to discontinue the issuance of letters of Acknowledgement of Information Received ("acknowledgement letters").

Effective April 1, 2019, Health Canada is proposing to no longer send acknowledgement letters for the following regulatory activity types that fall under Part C, Division 1 and Division 8 of the Food and Drug Regulations:

- Abbreviated Extraordinary Use New Drug Submission (AEUNDS)
- Abbreviated New Drug Submission (ANDS)
- Application for a Drug Identification Number (DINA)
- Application for a DIN - Biological product (DINB)
- Application for a DIN - Disinfectant product (DIN-D)
- Application for a DIN - Category IV product (DIN-F)
- Development Safety Update Report (DSUR)
- Extraordinary Use New Drug Submission (EUNDS)
- Supplement to an Extraordinary Use New Drug Submission (EU SNDS)
- Supplement to an Extraordinary Use Abbreviated New Drug Submission (EU SANDS)
- Notifiable Change (NC)
- New Drug Submission (NDS)
- Periodic Benefit Risk Evaluation Report - Conditional (PBRER-C)
- Periodic Benefit Risk Evaluation Report - Pharmacovigilance (PBRER-PV)
- Post-authorization Division 1 Change (PDC)
- Post-authorization Division 1 Change - Biologics (PDC-B)
- Periodic Safety Update Report - Conditional (PSUR-C)
- Periodic Safety Update Report Pharmacovigilance (PSUR-PV)
- Risk Management Plan - Pharmacovigilance (RMP-PV)
- Supplement to an Abbreviated New Drug Submission (SANDS)
- Supplement to a New Drug Submission (SNDS)
- Supplement to a New Drug Submission - Conditional (SNDS-C)
- Undefined Pharmacovigilance (UD-PV)

Information currently found on acknowledgement letters can be obtained from the Drug Submission Tracking System – Industry Access (DSTS-IA). Sponsors are encouraged to rely on the DSTS-IA to view the following details of their submissions:

- tombstone submission information, i.e. control number ("submission number"), submission type, submission class, Lead Bureau/Office, date of filing (also known as "CR date"), dossier ID
- drug product information, i.e. product name, manufacturer, country, active ingredient
- status history information, i.e. submission status, status date and target date
- review history information, i.e. review details including review type, division, status of the review (i.e. pending, active, completed) and status dates
- document history, i.e. documents issued and received, including dates

For information regarding DSTS-IA, or for account set up, please contact the Office of Submission and Intellectual Property by sending an e-mail to: hc.client.information.sc@canada.ca

Please note that this change will not impact those submissions or supplements that require a certification as per the Patented Medicines (Notice of Compliance) Regulations, these

regulatory activities will continue to receive a letter of Acknowledgement and Certification of Information Received once they are deemed administratively complete.

Should you have comments on the proposed changes outlined in this Notice please provide your feedback to Health Canada, within 30 days of the publication of this Notice via e-mail: hc.eReview.sc@canada.ca.

IFRA 49th Amendment: Consultation on IFRA Standard Setting Process and the Guidance for the use of IFRA Standards

The consultation on the draft Standards as part of the IFRA 49th Amendment will be launched in the coming weeks. Details will be shared at a later stage and CA will notify members. This consultation is planned to last 4 months.

In the meantime, IFRA is opening today a consultation on (1) the IFRA Standard Setting Process and (2) the Guidance for the use of IFRA Standards. This consultation will be open until the closing of the consultation on the 49th Amendment and will therefore last more than 4 months.

The purpose of this consultation is to ensure that IFRA members, members of national associations members of IFRA, but also their customers and customer associations, have a chance to review and comment on both such documents and also to allow users of the IFRA Standards to get familiar with the new IFRA product categorization that will be applied with the 49th Amendment.

1. IFRA Standard Setting Process

A summary of the IFRA Standard Setting Process is included in Chapter 2 of the Guidance for the use of IFRA Standards (Att. 01 below). A more complete description of this process is available to companies active in the formulation or use of fragrance materials upon request (please send your request to cgonzalez@ifraorg.org).

2. Guidance for the use of IFRA Standards

IFRA has gathered all information related to the use of Standards in a single document for your convenience. This “Guidance” document combines the following documents that were previously available individually:
- Introduction to the IFRA Standards (Chapter 1);
- the IFRA-RIFM QRA information booklet and
- the Standard Operating Procedure for the implementation timelines of Amendments to the IFRA Standards.

In addition, it also contains information that is new to the IFRA 49th Amendment:
- A description of the procedure for setting IFRA Standards (Chapter 2).
- How risk assessments for various toxicological endpoints is performed and its consequences for setting IFRA Standards (Chapters 3, 4, 5), including a detailed description of the IFRA Categories (Chapter 6).
- Frequently Asked Questions about the application of IFRA Standards (Chapter 7).

The draft Guidance for the use of IFRA Standards is attached to this email (Att. 01).

Your feedback is an essential part of the process for setting the IFRA Standards. CA encourages members that are members of IFRA to participate in the consultation on the IFRA Standard Setting Process and the Guidance for the use of the IFRA Standards. Please send in your comments by filling out Att.02 below and send it to cgonzalez@ifraorg.org.

Att.01 – Consultation Document
Att. 02 – Feedback Template

Proposed New Regulatory Activity Types for Transactions Filed to the MHPD

Health Canada is proposing a set of new regulatory activity (RA) types to be used in lieu of the Undefined Data Post-Market Vigilance (UD-PV) regulatory activity, filed to the Marketed Health Products Directorate (MHPD). The objective of this notice is to provide awareness of this proposal and obtain feedback from stakeholders if they have any concerns.

Currently, the UD-PV regulatory activity type is being used for a variety of regulatory transactions filed to MHPD. In order to process these regulatory transactions more efficiently, Health Canada is proposing to assign defined regulatory activity types to more accurately reflect the information contained within the transactions. The proposed RA types are presented in the table below. With each proposed RA type, a list of possible transaction (sequence) descriptions has also been developed to further identify the information contained in the regulatory transaction.

Current RA type	Proposed RA types	Transaction (Sequence) Descriptions
Undefined Data Post market Vigilance (UD-PV)	Post-Authorization commitments - Post market Vigilance (PA-PV)	• Post Marketing Surveillance • Minutes of meeting, mmm.dd, yyyy • Notification of change in benefit-risk profile • Response to email Request dated mmm.dd, yyyy • Response to MHPD Request dated mmm.dd, yyyy
	Post-Authorization Act and Regulations - Post market Vigilance (REG-PV)	• Response to MHPD request for Benefit-Risk Analysis, C.01.013, C.01.014 • Response to Terms and Conditions commitment C.01.014.21 • Foreign Safety Action Notification C.01.050 • Response to MHPD Test and Studies Order - Act 21.32 • Response to MHPD Reassessment Order - Act 21.31
	Issue Related Summary Report (IRSR-PV)	• Response to MHPD request of Issue Related Safety Request dated mmm.dd, yyyy
	Risk Communication – Post market Vigilance (RC-PV)	• Risk communication document • Dissemination list

Patient Safety/ Advertising Ad-Hoc Post market requests (PSA-PV)	• Response to MHPD for Patient Safety Information (Medication error) dated mmm.dd, yyyy • Response to Advertising complaint request for information dated mmm.dd, yyyy

Health Canada intends to begin accepting these new regulatory activity types, in lieu of UD-PV, effective May 1, 2019 for regulatory transactions in both electronic Common Technical Document (eCTD) and non-eCTD formats.

As per requirements in the Canadian Module 1 schema version 2.2, Regulatory activities filed in eCTD format must continue to use UD-PV as the RA type when building their transactions, however, the sponsor must indicate the specific regulatory activity type (PA-PV, REG-PV, IRSR-PV, RC-PV or PSA –PV) and transaction description in their enclosed cover letter.

Please send comments regarding this advanced notice to hc.ereview.sc@canada.ca

Drug Submission Performance Quarterly Reports (October – December 2018)

The Drug Submission Review Performance Reports provide detailed metrics about the timeliness of pre-market drug review process against performance service standards. The quarterly report compares five consecutive quarters from October – December 2017 to October – December 2018. The reports are broken down by operational areas. The Therapeutic Product Directorate (TPD) report summarizes performance metrics for pharmaceuticals. The Biologics and Genetic Therapies Directorate (BGTD) report summarizes performance metrics for biologics. The Natural and Non-prescription Health Products Directorate (NNHPD) report summarizes performance metrics for non-prescription (over-the-counter) and disinfectant drugs. Within each report, statistics are provided by submission type and show the number received, the number in workload, the number of decisions and the number of approvals.

BGTD – EN

NNHPD – EN

TPD – EN

Environment Updates

Final Screening Assessment Published for Aliphatic Diesters Group

The Final Screening Assessment for the Aliphatic Diesters Group was published. A notice of intent to apply the Significant New Activity (SNAc) provisions of the Canadian Environmental Protection Act, 1999 to hexanedioic acid, diisodecyl ester was also published for a 60-day public comment period ending on April 10, 2019. It was concluded that DID does not meet any of the criteria set out under section 64 of CEPA. Please take the time to review and submit comments for the SNAc before the deadline.

The Final Screening Assessment for the Benzoates Group

The Final Screening Assessment for Benzoates Group was published in the Canada Gazette Part 1 on February 9, 2019. Below is a table of the substances assessed. It is concluded that the substances in the Benozates Group do not meet any of criteria set out under Section 64 of CEPA.

Substances in the Benzoates Group

CAS RN footnote 8	***Domestic Substances List* name**	**Common name**
93-58-3	Benzoic acid, methyl ester	Methyl benzoate
93-89-0 table 1 note a	Benzoic acid, ethyl ester	Ethyl benzoate
120-50-3 table 1 note a	Benzoic acid, 2-methylpropyl ester	Isobutyl benzoate
120-55-8	Ethanol, 2,2′-oxybis-, dibenzoate	Diethylene glycol dibenzoate
136-60-7	Benzoic acid, butyl ester	Butyl benzoate
614-33-5	1,2,3-Propanetriol, tribenzoate	Tribenzoin
8024-05-3 table 1 note b	Oils, tuberose	Tuberose oil
27138-31-4	Propanol, oxybis-, dibenzoate	Dipropylene glycol dibenzoate
68052-23-3	1,3-Pentanediol, 2,2,4-trimethyl-, dibenzoate	Trimethylpentanediyl dibenzoate

Final Screening Assessment released for the Trimellitates Group

The Final Screening Assessment for the Trimellitates Group was published on February 16, 2019 in the Canada Gazette Part 1. There were three substances on the Trimellitates Group that was assessed which were 1,2,4-Benzenetricaboxylic acid, tris(2-ethyhexyl)ester (TEHT) CAR RN: 3319-31-1, 1,2,4- Benzenetricarboxylic acid, mixed branced tridecyl and isodecyl esters (BTOT) CAS RN: 70225-05-7 and 1,2,4- Benzenetricarboxylic acid, tritridecyl ester (TTDT) CAS RN 94109-09-8. It is concluded that TEHT, BTIT and TTDT do not meet any of the criteria set out under section 64 of CEPA.

Publication of the New Substances Risk Assessment Summaries

The new risk assessment summaries are now available on the New Substances Program website. The Standing Committee on the Canadian Environmental Protection Act, Environment and Climate Change Canada and Health Canada are publishing summaries of risk assessment reports for chemicals and polymers, animate products of biotechnology, as well as notifications where control measures are applied (including Significant New Activities, Ministerial Conditions, and Ministerial Prohibitions). This initiative provides the public an opportunity to learn more about the risk assessments of new substances that are being manufactured and/or imported into Canada. These summaries are part of the CMPs transparency agenda which CA has

advocated for through our engagement at the CEPA ICG and at the CMP Stakeholder Advisory Council (SAC). The Government of Canada has committed to releasing these publications on a regular basis.