Health Canada Santé Canada

Guidance Document

Post-Drug Identification Number (DIN) Changes

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Canada

Health Canada is responsible for helping Canadians maintain and improve their health. It ensures that high-quality health services are accessible, and works to reduce health risks.

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Linge directrice - Changements ultérieurs à l'attribution d'identifications numériques de drogues (DIN)

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Document change log

Version	Replaces
Post-Drug Identification Number (DIN) Changes Guidance Document	Post-Drug Identification Number (DIN) Changes Guidance Document
Date: December 19, 2013	Date: December 29, 2009

Change	Nature of and/or Reason for Change
1) December 19, 2013 Some revisions throughout the document.	Changes were made to the document to reflect an amendment to the Food and Drug Regulations that replaced Schedule F with Prescription Drug List.
2) March 17, 2017	Administrative changes were made to remove the requirement to provide a "Drug Submission Fee Application Form" for applications that do not require fees and to provide a contact to obtain the Drug Product Information Form.
3) October 5, 2018	Administrative changes were made to remove the Post DIN Change #25 – Private Label Line Extension – to be in line with the Guidance Document: Questions and Answers: Plain Language Labelling Regulations for Non-Prescription Drugs
4) April 18, 2019	Administrative changes were made to change "Submission and Information Policy Division (SIPD)" to "Office of Submissions and Intellectual Property (OSIP)"
5) August 2, 2022	Policy Change to the performance standards of Post-DIN Changes (PDCs) for human prescription pharmaceuticals and those administered or obtained through a health professional Administrative changes were made to: • replace names and dates of guidance documents with the most recent version • add new guidance documents not previously included • change the Therapeutic Product Directorate (TPD) to the Pharmaceutical Drugs Directorate (PDD)

Foreword

Guidance documents are meant to provide assistance to industry and health care professionals on how to comply with governing statutes and regulations. Guidance documents also provide assistance to staff on how Health Canada mandates and objectives should be implemented in a manner that is fair, consistent, and effective.

Guidance documents are administrative instruments not having force of law and, as such, allow for flexibility in approach. Alternate approaches to the principles and practices described in this document may be acceptable provided they are supported by adequate justification. Alternate approaches should be discussed in advance with the relevant programme area to avoid the possible finding that applicable statutory or regulatory requirements have not been met.

As a corollary to the above, it is equally important to note that Health Canada reserves the right to request information or material, or define conditions not specifically described in this document, in order to allow the Department to adequately assess the safety, efficacy, or quality of a therapeutic product. Health Canada is committed to ensuring that such requests are justifiable and that decisions are clearly documented.

This document should be read in conjunction with the accompanying notice and the relevant sections of other applicable Guidance documents.

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1. Introduction

All drugs subject to the Food and Drug Regulations (henceforth Regulations) are required to gain premarket authorization prior to issuance of a Drug Identification Number (DIN). After gaining authorization to market a drug through provision of information under C.01.014.1 (see appendix I) and through adherence to the requirements of the Regulations as a whole, a sponsor may for various reasons wish to make changes to the drug or the information associated with the drug. For those drugs regulated under Part C, Division 1 of the Regulations (for example [i.e.] drugs that do not fall under the definition of New Drug in Section C.08.001) and which are not eligible to receive a Notice of Compliance (NOC), the sponsor must comply with Section C.01.014.4 when undertaking any changes.

The guidance is intended to advise both internal and external stakeholders regarding the filing requirements for post market changes and the data recommendations to support those changes.

1.1 Policy objectives

As per Part C, Section C.01.014.4 of the Regulations, Health Canada must be notified whenever there is a change in "the subject matter of the information" previously provided for a drug to obtain a DIN under Section C.01.014.1(2). Health Canada has the responsibility to assess the change with respect to its impact on the safety, efficacy, and quality of the drug to ensure that the benefit of the drug continues to outweigh its risks. Further, in keeping with Section 9 (1) of the Food and Drugs Act (FDA), Health Canada has the responsibility to verify the character and merit of the amended drug product.

An updated interpretation of Section C.01.014.4 of the Regulations is provided by guidance with recommendations on the process for filing changes and the data considered necessary to support these changes.

1.2 Policy statement

Health Canada recognizes that:

a. any change to a drug may impact the safety, efficacy or quality of that drug and;

b. any change to the information associated with a drug (i.e. labels) may impact the safe and effective use of that drug.

To enable Health Canada to manage these risks:

a. a change to a drug, that has received a DIN and is not a New Drug, must be reported according to one of the following overarching categories: DIN Application or Notification (30 day) based on the criteria and conditions indicated in this guidance and;

b. data to support a proposed change, as recommended in this guidance, should be submitted to Health Canada.

1.3 Scope and application

This guidance applies to drugs regulated under Part C, Division 1 of the Regulations that have received a DIN pursuant to Section C.01.014.2. This includes pharmaceuticals for human and veterinary use, as well as disinfectant drugs, but excludes biologics and radiopharmaceuticals.

This guidance does not apply to changes to drugs that have received a NOC in accordance with Division 8 of the Regulations. For these changes, please refer to the Post-NOC Changes guidance documents.

1.4 Background

Sponsors of drugs regulated by Part C, Division 1 of the Regulations are required to file an application for a DIN under Section C.01.014.1. In addition to the information outlined in C.01.014.1, a sponsor is required to comply with all applicable Acts and Regulations when making an application for a DIN. Health Canada realized that the Regulations did not provide sufficient detail with respect to the information necessary to conduct a scientific evaluation of the safety, efficacy and quality of a drug prior to market authorization. The guidance Preparation of Drug Identification Number Submissions was published in 1995 to provide further clarification. This document provided additional detail with respect to the process and data considered necessary for initial filings, however, remained silent with respect to data recommendations and process for changes to an authorized drug.

After several years of ongoing and resource-intensive communication with sponsors, it had become increasingly evident that there was a need for clarification of the process and data recommended for filing changes to drugs regulated under Division 1 of the Regulations. This guidance will inform stakeholders of how they can fulfill the obligations outlined under the existing Regulations. The guidance will also provide a consistent approach, building upon existing practices amongst the Pharmaceutical Drugs Directorate (PDD), the Natural and Non-prescription Health Products Directorate (NNHPD) and the Veterinary Drugs Directorate (VDD).

2. Acronyms

DIN
Drug Identification Number

DINA
Drug Identification Number Application

DINA LS
Labelling Standard Drug Identification Number Application

DIND
Disinfectant Drug Identification Number Application

DINF
Category IV Monograph Drug Identification Number Application

HECS
Healthy Environments and Consumer Safety Branch

NNHPD
Natural and Non-prescription Health Products Directorate

NOC
Notice of Compliance

OSIP

Office of Submissions and Intellectual Property

PDC-prescription
Post-authorization Division 1 Change for prescription pharmaceuticals and those administered or obtained through a health professional

PDC-non-prescription

Post-authorization Division 1 Change for non-prescription pharmaceuticals

PDC-Disinfectant

Post-authorization Division 1 Change for disinfectant pharmaceuticals

PMRA
Pest Management Regulatory Agency

PDD

Pharmaceutical Drugs Directorate

SKMD
Submission and Knowledge Management Division

VDD
Veterinary Drugs Directorate

VDIN
Veterinary Drug Identification Number Application

VPDC
Veterinary Post-authorization Division 1 Change

3. Guidance for implementation

This section describes the reporting categories for making changes to authorized Division 1 drugs, as per Section C.01.014.4 of the Regulations, and then outlines the options and requirements for filing within each category. See Section 4 for further details on the recommended supporting documentation and filing process for specific changes for all reporting categories.

3.1 Reporting categories

A brief description of the reporting categories is provided below.

Health Canada recognizes that the Regulations require either the filing of a new DIN application or a notification for changes to authorized Division 1 drugs. However, in some instances the guidance strongly recommends that a DIN application be filed to seek regulatory authorization due to the inherent risk associated with the proposed changes. It is in the sponsor's best interest to ensure that all changes, regardless of the notification process outlined under C.01.014.4, are in compliance with Health Canada's requirements prior to sale. Health Canada will assess the proposed change and may request the filing of a New Drug Submission (NDS) if the change is deemed to fall within the definition of New Drug as stated in Section C.08.001 of the Regulations.

3.1.1 Drug Identification Number (DIN) application

Section C.01.014 .4 of the Regulations states that:

If the information referred to in subsection C.01.014.1(2) in respect of a drug is no longer correct owing to a change in the subject matter of the information,

(a) in the case of a change in the subject matter of any of the information referred to in paragraphs C.01.014.1(2)(a) to (f)

(i) that occurs prior to the sale of the drug, a new application shall be made, or

(ii) that occurs after the sale of the drug, no further sale of the drug shall be made until a new application for a drug identification number in respect of that drug is made and a number is assigned;

The changes included in this reporting category shall be filed, along with the recommended supporting data, to Health Canada as a DIN Application. Any change that requires a DIN application to be filed may not be

implemented prior to the review of the supporting data by Health Canada and confirmation that this data is acceptable in support of the change. If acceptable, a new DIN may be issued or an active DIN may be retained for the changed drug and a No Objection Letter issued.

Appendices II and III provide a brief outline of the various DIN submission types for pharmaceuticals for human and veterinary drugs respectively.

3.1.2 Notification (30 day)

Section C.01.014 .4 of the Regulations states that:

If the information referred to in subsection C.01.014.1(2) in respect of a drug is no longer correct owing to a change in the subject matter of the information,

(b) in the case of a change in the subject matter of any of the information referred to in paragraphs C.01.014.1(2)(g) to (k)

> (i) that occurs prior to the sale of the drug, the particulars of the change shall be submitted with the return of the document referred to in section C.01.014.3, or
>
> (ii) that occurs after the sale of the drug, the person to whom the drug identification number in respect of that drug was issued shall, within 30 days of the change, inform the Director of the change.

The changes included in this reporting category should be filed, along with the recommended supporting data (see Section 4), to Health Canada as a notification, within 30 days of the change being implemented as defined in the Regulations. Health Canada may upon receipt of the notification: update its records, uphold the change, request that the change be undone, or request that a DIN application be filed to support the change.

Although the sponsor is allowed to submit these notifications within 30 days of making the change, it is strongly recommended that notification be provided to Health Canada prior to the sale of the drug to enable a risk assessment of the change, and thus, better ensure the safety, efficacy and quality of the drug.

3.2 Filing process

A brief description of the filing process for changes is provided below. For changes where it is indicated that no filing is necessary, the sponsor should maintain a record of the change in accordance with Division 2 of the Regulations and ensure that this information is made available to Health Canada if it is requested at any time.

Should a sponsor wish to make multiple changes to their product, the change should be filed in keeping with the most stringent filing process associated with the changes overall. Sponsors should ensure that the documentation for each change complies with the requirements of the corresponding section of the guidance. All proposed changes to the product should be disclosed in the cover letter or the post market change may be subject to refusal.

A sponsor may provide, at any time, information to Health Canada for changes that are not outlined in the recommendations of this guidance.

OSIP/SKMD will target to have all information and material sent to the reviewing Bureau/Centre within 10 calendar days.

3.2.1 Filing process for notifications

Notifications also referred to as Post-Authorization Division 1 Changes (PDCs) are separated into three (3) different classes: PDC-prescription, PDC-non-prescription, and PDC-disinfectant. When the filing of a Notification (PDC) as required in the tables found in Section 4.2, it is applicable to all classes of PDCs.

A. Notifications which do not necessitate assessment (OSIP or SKMD Notification):

The sponsor is requested to file the change with the recommended supporting documentation by written notification to either OSIP for human drugs, or SKMD for veterinary drugs within 30 days of making the proposed change.

B. Notifications that do necessitate assessment (Post-Authorization Division 1 Change, PDC/VPDC):

The intention of this process is to assess changes that may not necessarily entail the submission of scientific data and is used to triage enquiries to determine the appropriate filing process for the change. A PDC-non-prescription/PDC-disinfectant/VPDC has a target date of 30 days screening. Prescription pharmaceuticals have a 25-day screening and a 120-day review for Safety- PDCs and a 25-day screening and a 90-day review for Quality PDCs. There are currently no cost recovery fees for any PDCs.

Changes for all the PDC classes must be filed within 30 days of making the proposed change as per section C.01.014.4. However, sponsors should ensure compliance prior to making the change and submit any pertinent supporting data as outlined in the following tables under Section 4.2 and/or as per the applicable Health Canada guidance.

Health Canada will assess the proposed change. If the change is deemed acceptable, a No Objection Letter will be sent to the sponsor. If the change is deemed to fall outside the scope of a notification, Health Canada may request the re-filing of a full submission through the issuance of a Not Satisfactory Notice (NSN). Please note that if an NSN has been issued, the sponsor should refile a new PDC-prescription/PDC-non-prescription/PDC-disinfectant/VPDC or other submission to effectuate the authorization of any new revisions or changes.

The formalization of this process will allow workload tracking and introduces performance targets to ensure that prompt feedback is provided to stakeholders.

3.2.2 Filing process for Drug Identification Number (DIN) applications

C. Filing an Administrative DINA submission:

Reference should be made to Health Canada's Guidance Document: Administrative Processing of Submissions and Applications Involving Human or Disinfectant Drugs (https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/administrative-processing-human-disinfectant-drugs-2019/document.html).

D. Filing a DIN Application to support a change (DINF, DINA, DIND, VDIN):

This process captures changes that require further evaluation prior to implementation. The appropriate submission type depends on the nature of the change and the terms of original market authorization for the product. Should the sponsor wish to retain the original DIN this request should be made in the cover letter and will be considered at the time of evaluation. If the changes are acceptable a new DIN will be issued or, if no new DIN is required, then a No Objection Letter will be issued. If the changes are not acceptable, then the sponsor would be issued a notice to this effect.

3.3 Filing information

3.3.1 Related guidances for filing

Information regarding general submission requirements, contact information, and target performance standards may be found in the following Health Canada guidance documents: Guidance Document: Management of Drug Submissions and Applications for drugs for human use and disinfectants, and Veterinary drugs – Management of Regulatory Submissions Guidance (https://www.canada.ca/en/health-canada/services/drugs-health-products/veterinary-drugs/legislation-guidelines/guidance-documents/management-regulatory-submissions.html).

3.3.2 Other related guidances

This guidance document should be read in conjunction with other associated Health Canada policies and guidance documents including, but not limited to[i]:

- Guidance Document: Administrative Processing of Submissions and Applications Involving Human or Disinfectant Drugs
- Guidance Document for Industry - Review of Drug Brand Names
- Frequently Asked Questions - Guidance Document for Industry - Review of Drug Brand Names
- Guidance documents on disinfectants: Summary Preparation of Drug Identification Number Submissions
- Questions and Answers: Plain Language Labelling Regulations for Prescription Drugs document
- Guidance Document: Questions and Answers: Plain Language Labelling Regulations for Non-prescription Drugs

3.3.3 Pre-submission enquiries

The listing of changes in this guidance document is not considered to be exhaustive. Sponsors are advised to contact Health Canada, in writing, if clarification is required on the classification of a proposed change or if the sponsor wishes to discuss product specific data requirements. Verbal enquiries should be followed-up in writing by the sponsor.

4. Documentation

4.1 Common information for notifications and DIN applications

The following should be included for all Notifications (i.e., PDCs) and DIN Applications except where otherwise specified in Section 4.2.1:

i. A signed and dated cover letter on company letterhead that includes:
   a. the type of submission (Notification or DIN Application);
   b. a narrative of the change(s) and a brief rationale for the change(s);
   c. a listing of all drug products, including the DIN(s), which are affected by the change(s);
   d. reference to the Dossier ID and control number, or a CR file number where a control number is not available, for the original DIN Application and any subsequent submissions relevant to the present change; and
   e. when applicable (see Section 4.2.1), a description of the supporting data provided.

ii. A sample of all proposed labels[ii]; and

iii. The completed and signed documents:
   a. Applicable Regulatory Enrolment Process (REP) forms Drug Submission Application Form (HC/SC 3011) for each product in question, or, proof of authorization in the case of concomitant/cross promoted products regulated by other divisions of Health Canada (Medical Devices Directorate, Natural and Non-prescription Health Products Directorate, etc.) [see Section 4.2.1: C.01.014.1(2)(m) and 4.2.2(2)] ;
   b. Drug Submission Fee Application Form[iii] - replaced by the REP:RT (regulatory transaction) form – (fees)
   c. Drug Identification Number (DIN) Submission Certification Form
   d. Labels and Packages Certification Form (prescription or non-prescription accordingly)
   e. Administrative Changes – Certification Form for Human and/or Disinfectant Drug Submissions and Applications (where applicable)
   f. Third Party Authorization form (where applicable)

4.2 Specific information

In addition to the above common information, recommendations are provided in Section 4.2.1, with respect to the applicable conditions, supporting data, and filing process for specific changes as outlined in the Regulations. All changes are numbered to facilitate referencing.

How to use the Tables in 4.2

The information summarized in the tables provides recommendations for the conditions and supporting data for each change:

In cases where some or all of the conditions or supporting data may apply, the document identifies these recommendations as "potentially" applying. For example, in table C.01.014.1(2)(b), a new DIN application may be required if there is an addition or change to the dosage form where the new dosage form has been previously authorized in Canada. Other conditions may be applicable such as if the change to dosage form raises concerns about the sterility of the drug, and/or the change in dosage form introduces materials where a Bovine spongiform encephalopathy/transmissible spongiform encephalopathy (BSE/TSE) risk assessment is needed and/or the change to dosage form affects the release parameters (dissolution, duration, onset, etc.) of the drug. If certain conditions do not apply, then the corresponding supporting data will not be necessary.

4.2.1 Changes to information captured by C.01.014.1(2) of the Regulations

4.2.1.1 Changes outlined in C.01.014.1(2)(a)-(f)

The following filing processes and supporting data are required in order to ensure that the proposed changes are consistent with the intent of the Act and Regulations:

C.01.014.1 (2)(a) the name of the manufacturer of the drug as it will appear on the label

Change #	Description of Change	Conditions	Supporting Data	Filing Process
1	Change in name of the manufacturer for a human, veterinary or a disinfectant drug	1	1	Admin Drug Identification Number Application
Conditions				
1. The recommendations outlined in the Guidance Document: Administrative Processing of Submissions and Applications Involving Human or Disinfectant Drugs are met.				
Supporting Data				
1. Common Information for Notifications and Drug Identification Number Applications (as outlined in 4.1).				

C.01.014.1(2)(b) the pharmaceutical form in which the drug is to be sold

Change #	Description of Change	Conditions	Supporting Data	Filing Process
2	Removal of an authorized dosage form	not applicable	1	Office of Submissions and Intellectual Property / Submission and Knowledge Management Division Notification
3	Addition or change to the dosage form of the drug	1 (and potentially 2, 3, and/or 4)	2 (and potentially 3,4, and/or 5)	Drug Identification Application
		5	6	New Drug
		6	not applicable	Not required to file

Conditions

1. The dosage form is previously authorized for the product type under Division 1 in Canada (for example [e.g.] - Sponsor has cough and cold capsules on the market and wishes to add a cough and cold syrup to their product line. The syrup dosage form has been previously authorized in Canada for cough and cold products).
2. The change to dosage form raises concerns about the sterility of the drug.
3. The change in dosage form introduces materials where a Bovine spongiform encephalopathy/transmissible spongiform encephalopathy (BSE/TSE) risk assessment is needed.
4. The change to dosage form affects the release parameters (dissolution, duration, onset, etc.) of the drug as described under C.01.012 of the Regulations.
5. The dosage form is not previously authorized for the specified product type under Division 1 in Canada (for example [e.g.] - sponsor for human drug has an acne treatment cream on the market and seeks to add an acne wipe to their product line. For veterinary drugs, sponsor has an approved acetylsalicylic acid (ASA) bolus and seek to add an ASA oral solution to their product line. No Division 1 products with these dosage forms and product types exist in Canada. This product falls within the definition of a New Drug in section C.08.001 of the Regulations).
6. The change only affects the appearance and does not involve a change in functionality of the dosage form (e.g. - addition of a film coating for aesthetic purposes only).

Supporting Data

1. A signed and dated cover letter on company letterhead with a description of the change.
2. Common Information for Notifications and Drug Identification Number (DIN) Applications (as outlined in 4.1).
3. If condition 2 applies, file supporting chemistry data according to the recommendations outlined in Quality Guidance: Applications for Drug Identification Numbers (DINAs) for Pharmaceuticals.
4. If condition 3 applies, file Animal Tissue form and/or data outlined in section P.4 of Quality Guidance: Applications for Drug Identification Numbers (DINAs) for Pharmaceuticals.
5. If condition 4 applies, file supporting chemistry data as per the recommendations outlined in Quality Guidance: Applications for Drug Identification Numbers (DINAs) for Pharmaceuticals and the clinical or comparative bioavailability data according to the guidance documents available on the Health Canada Web site: Bioavailability and Bioequivalence.

6. New Drug Requirements: Consult the guidance documents, Preparation of New Drug Submissions in CTD format and the Guidance Document: Management of Drug Submissions and Applications. For veterinary drugs, Guidance for Industry Preparation of Veterinary New Drug Submissions and Veterinary drugs - Management of regulatory submissions guidance: Overview.

C.01.014.1(2)(c) in the case of any drug other than a drug described in paragraph (d), the recommended route of administration

Change #	Description of Change	Conditions	Supporting Data	Filing Process
4	Removal of an authorized route of administration	1	1	Office of Submissions and Intellectual Property / Submission and Knowledge Management Division Notification
		2	2	Post-authorization Division 1 Change / Veterinary Post-authorization Division 1 Change
5	Addition or change to the authorized route of administration	3	2	Drug Identification Number Application
		4, 5, 6, or 7	2 and (3, 4, or 5)	Drug Identification Number Application
		8	6	New Drug

Conditions

1. The change does not result in the modification of labels for other routes of administration, which continue to be marketed.
2. The change results in the modification of labels for other routes of administration which continue to be marketed (for example [e.g.] - If a product is labelled for both otic and ophthalmic use and the otic route of administration is being withdrawn).
3. The route of administration is previously authorized for the specified product type under a Category IV Monograph or Labelling Standard.
4. The route of administration is previously authorized for the specified product type under Division 1 in Canada but is not captured under a Category IV Monograph or Labelling Standard (for example, [e.g.] - a sponsor has an antibiotic product for human use on the market currently applied as an otic preparation and wishes to add an ophthalmic indication. An ophthalmic route of administration for the antibiotic ingredient has been previously authorized in Canada).
5. The change to route of administration raises concerns about the sterility of the drug.
6. The change in route of administration introduces materials where a Bovine spongiform encephalopathy/transmissible spongiform encephalopathy (BSE/TSE) risk assessment is needed.
7. The change to route of administration raises concerns about absorption or delivery of the drug.
8. The route of administration is not previously authorized for the specified product type under Division 1 in Canada (for example, [e.g.] - sponsor has acetaminophen oral tablets on the market and wishes to declare on the label that the product can be used as a suppository. Acetaminophen via the rectal route

of administration is listed on the New Drug list and meets the definition of a New Drug in section C.08.001 of the Regulations).
Supporting Data
1. A signed and dated cover letter on company letterhead with a description of the change. 2. Common Information for Notifications and Drug Identification Number (DIN) Applications (as outlined in 4.1). 3. If condition 5 applies, file supporting chemistry data according to the recommendations outlined in Quality Guidance: Applications for Drug Identification Numbers (DINAs) for Pharmaceuticals. 4. If condition 6 applies, file Animal Tissue form and/or data outlined in section P.4 of Quality Guidance: Applications for Drug Identification Numbers (DINAs) for Pharmaceuticals. 5. If condition 7 applies, file supporting chemistry data as per the recommendations outlined in Quality Guidance: Applications for Drug Identification Numbers (DINAs) for Pharmaceuticals and the clinical, comparative bioavailability data, or waiver according to the guidance documents available on the Health Canada Web site: Bioavailability and Bioequivalence. 6. New Drug Requirements: Consult the guidance documents, Preparation of New Drug Submissions in CTD format, and Management of Drug Submissions and Applications. For veterinary drugs, Guidance for Industry Preparation of Veterinary New Drug Submissions and Veterinary drugs - Management of regulatory submissions guidance: Overview

C.01.014.1(2)(d) in the case of a drug for disinfection in premises, the types of premises for which its use is recommended

Change #	Description of Change	Conditions	Supporting Data	Filing Process
6	Addition, removal or change to the recommended premises for a disinfectant drug	1	1	Refer to Guidance Document: Disinfectant Drugs
Conditions				
1. The drug is for use on hard surfaces.				
Supporting Data				
1. File according to the recommendations outlined in the Guidance document on Disinfectants: Summary.				

C01.014.1(2)(e) a quantitative list of the medicinal ingredients contained in the drug by their proper names or, if they have no proper names, by their common names

Change #	Description of Change	Conditions	Supporting Data	Filing Process
7	Addition, deletion or change, including quantity, to the medicinal ingredients of the product	1 (and potentially 3,4, and/or 6)	1,2 (and potentially 3,4)	Drug Identification Number Application
		2 (and potentially 3)	5 (and potentially 3)	New Drug

8	Change in the chemical form of the medicinal ingredient[iv]	1, 5 or 6	1,2	Drug Identification Number Application
		2	5	New Drug
9	Revision to labelling or rate of medicinal ingredient delivery	7	1,2	Post-authorization Division 1 Change / Veterinary Post-authorization Division 1 Change
		8	1,2	Drug Identification Number Application[v]
10	Revision to the pharmacopeial standard	9	not applicable	Not required to file
		10	1	Post-authorization Division 1 Change / Veterinary Post-authorization Division 1 Change

Conditions

1. The change in or form of the medicinal ingredient is previously authorized for the specified product type under Division 1 in Canada (for example, [e.g] - sponsor has a sunscreen product which contains avobenzone, octinoxate and oxybenzone. The sponsor wishes to add an additional ingredient titanium dioxide. There are other products on the market with this combination for this product type).
2. The change in or form of the medicinal ingredient causes the product to meet the definition of New Drug as per C.08.001 (for example, [e.g.] - the sponsor wishes to add the ingredient, diethylamino hydroxybenzoyl hexyl benzoate, to their sunscreen product which contains avobenzone, octinoxate and oxybenzone. Products containing the medicinal ingredient, diethylamino hydroxybenzoyl hexyl benzoate, have never been marketed either alone or in combination with other medicinal ingredients in Canada. As such, this change would make the product a New Drug.)
3. The change in the medicinal ingredient is impacted by the Prescription Drug List (for example, [e.g.] - an increase in the amount of benzoyl peroxide in the product to greater than 5% becomes a prescription product).
4. The medicinal ingredient is derived from animal sources where a Bovine spongiform encephalopathy/transmissible spongiform encephalopathy (BSE/TSE) risk assessment is needed.
5. The change in medicinal ingredient meets the definition of an identical medicinal ingredient as described in the interim policy Updated Notice: Interim Policy on Health Canada's Interpretation of Medicinal Ingredient and Assessment of Identical Medicinal Ingredient. Similar conditions apply for veterinary drugs.
6. The change in medicinal ingredient does not meet the definition of an identical medicinal ingredient as described in the interim policy Updated Notice: Interim Policy on Health Canada's Interpretation of Medicinal Ingredient and Assessment of Identical Medicinal Ingredient. Similar conditions apply for veterinary drugs. Further, the change does not meet the criteria for a New Drug. For example, in an allergy medication diphenhydramine citrate is changed to diphenhydramine hydrochloride. Both ingredients have been previously authorized for this category of product.
7. The change does not affect the actual final delivered quantities (dose) of the medicinal ingredient, but is an alternate and equivalent declaration of amount delivered or present in the drug (for example, [e.g.] - a transdermal patch which has “X milligram” (mg) of medicinal ingredient revises the labels to also declare the delivery rate as “Ymg/hour”, but both were authorized for that drug product).

8. The change does not affect the actual final delivered quantity (dose) of the medicinal ingredient nor the pharmaceutical form of the drug. It does, however, change the delivery rate (for example, [e.g.] - a transdermal patch previously delivered Xmg/hour or X mg/square inch to give X mg overall dose, but now delivers Ymg/hour or Ymg/square inch to give Xmg overall dose). 9. The pharmacopeial standard used at time of original market authorization will be maintained but the standard itself has been revised (for example, [e.g.] - authorized as United States Pharmacopeia (USP) grade, but USP revises the standard). 10. The pharmacopeial standard has been changed (for example, [e.g.] - from British Pharmacopeia (BP) to USP).
Supporting Data
1. Common Information for Notifications and Drug Identification Number (DIN) Applications (as outlined in 4.1). 2. Scientific rationale for the proposed change. 3. If condition 3 applies, the sponsor must ensure they meet prescription status requirements (for example, labelling). 4. If condition 4 applies, file Animal Tissue form and/or data outlined in section P.4 of Quality Guidance: Applications for Drug Identification Numbers (DINAs) for Pharmaceuticals. 5. New Drug Requirements: Consult the guidance documents, Preparation of New Drug Submissions in CTD format, and Management of Drug Submissions and Applications. For veterinary drugs, Guidance for Industry Preparation of Veterinary New Drug Submissions, and Veterinary drugs - Management of regulatory submissions guidance: Overview.

C.01.014.1(2)(f) the brand name under which the drug is to be sold

Change #	Description of Change	Conditions	Supporting Data	Filing Process
11	Addition, deletion or revision of part or all of the brand name (as per Drug Identification Number notification form) or alteration of the presentation of the brand name in any way or form	1	not applicable	Not required to file[vi]
		2,3	1	Admin Drug Identification Number Application

Conditions
1. For a human, disinfectant, or veterinary drug, a change to the colour or font size of the brand name originally listed on the HC/SC 3011 form / REP forms. 2. For a human, disinfectant, or veterinary drug, any change to the brand name originally listed on the HC/SC 3011 form / REP forms, other than those listed under Condition #1. 3. The recommendations according to the guidance document entitled Administrative Processing of Submissions and Applications Involving Human or Disinfectant Drugs (https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/administrative-processing-human-disinfectant-drugs-2019/document.html) are met.
Supporting Data
1. Common Information for Notifications and Drug Identification Number Applications (as outlined in 4.1).

4.2.1.2 Changes outlined in C.01.014.1(2)(g)-(k)

The following filing processes and supporting data are strongly recommended in order to ensure that the proposed changes are consistent with the intent of the Act and Regulations:

C.01.014.1(2)(g) whether the drug is for human use, veterinary use or disinfection in premises

Change #	Description of Change	Conditions	Supporting Data	Filing Process
12	Addition, removal or change in the intended user (or species for veterinary use) of the drug	1	1,2	Drug Identification Number Application
		2	3	New Drug
Conditions				
1. The change in intended user (or species) of the drug is previously authorized for the specified product type under Division 1 in Canada. 2. The change in intended user (or species) of the drug is not previously authorized for the specified product type under Division 1 in Canada and meets the definition of a new drug under C.08.001 of the Regulations.				
Supporting Data				
1. Common Information for Notifications and Drug Identification Number Applications (as outlined in 4.1). 2. Recommendations may vary depending on the proposed use/ user. Contact the appropriate Directorate/ Bureau for pre-submission enquiries. 3. New Drug Requirements: Consult the guidance documents, Preparation of New Drug Submissions in CTD format and Management of Drug Submissions and Applications. For veterinary drugs, Guidance for Industry Preparation of Veterinary New Drug Submissions and Guidance for Industry Management of Regulatory Submissions.				

C.01.014.1(2)(h) the name and quantity of each colouring ingredient that is not a medicinal ingredient

Change #	Description of Change	Conditions	Supporting Data	Filing Process
13	Removal or decrease in amount of a colourant	1	1	Office of Submissions and Intellectual Property / Submission and Knowledge Management Division Notification
14	Addition or increase in amount of a colourant	1	2	Post-authorization Division 1 Change / Veterinary Post-authorization Division 1 Change
		2	3	New Drug[vii]

Conditions
1. The colourant is listed in the Regulations under C.01.040.2 2. The colourant is not listed in the Regulations under C.01.040.2
Supporting Data
1. A signed and dated cover letter on company letterhead with a description of the change. 2. Common Information for Notifications and Drug Identification Number Applications (as outlined in 4.1). 3. New Drug Requirements: Consult the guidance documents, Preparation of New Drug Submissions in CTD format and Management of Drug Submissions and Applications. For veterinary drugs, Guidance for Industry Preparation of Veterinary New Drug Submissions and Veterinary drugs - Management of regulatory submissions guidance: Overview.

C.01.014.1(2)(i) the use or purpose for which the drug is recommended

Change #	Description of Change	Conditions	Supporting Data	Filing Process
15	Removing a therapeutic claim, indication, or condition of use (including removal of patient categories, claims about duration, onset of action, sterility etc.)	1	1,2	Post-authorization Division 1 Change / Veterinary Post-authorization Division 1 Change
16	Adding or revising a therapeutic claim, indication, or condition of use (including revisions to patient category, duration or onset of action, sterility etc.)	2	1, 2	Post-authorization Division 1 Change / Veterinary Post-authorization Division 1 Change
		3	1, 2 (and potentially 3)	Drug Identification Number Application
		4	4	New Drug
17	Addition of non-therapeutic claims[viii]	5 and/or 6	not applicable	Not required to file
		7	1 and (potentially 2 and/or 3)	Post-authorization Division 1 Change / Veterinary Post-authorization Division 1 Change
18	Addition of a graphic, picture, symbol or logo that makes an implied claim (for example, sunburn protectant puts pictures of Deoxyribonucleic acid (DNA) on label; addition of heart or joint graphics to analgesic labels, etc.)[ix]	2 or 3	1	Post-authorization Division 1 Change / Veterinary Post-authorization Division 1 Change

Conditions
1. There are no safety issues instigating or related to the removal of the claim. 2. The claim, direct or implied, is listed as an acceptable statement in the most current Category IV monograph or Labelling standard and the therapeutic class is not being modified (for example [e.g.] - An antiseptic skin cleanser wishes to add the additional claim "for personal hand hygiene to help prevent the spread of certain bacteria". This is an acceptable claim under the Antiseptic Skin Cleansers monograph). 3. The claim, direct or implied, is not an acceptable statement in a Category IV monograph or Labelling standard and/or the therapeutic class is modified. However, the claim for that product category and/or the therapeutic class of the drug has been previously reviewed and authorized by Health Canada for the product category in question and does not cause the product to meet the definition of a New Drug under C.08.001 of the Regulations (for example, [e.g.] - change in claim- adding photostability claims for a sunburn protectant; change in therapeutic class - diphenhydramine can be used as a sleep aid, antitussive or an antihistamine). 4. The change in claim(s) or change in the therapeutic class causes the product to meet the definition of a New Drug under C.08.001 of the Regulations. 5. The non-therapeutic claims highlight only existing flavours, fragrances or colour already authorized previously for this drug product.[x] 6. The non-therapeutic claims are taken **verbatim** from the Guidelines for Cosmetic Advertising and Labelling. The claim also meets the requirements of other Authorities (Healthy Environments and Consumer Safety, Pest Management Regulatory Agency, Natural and Non-prescription Health Products Directorate, etc.) 7. All other changes other than 5 and 6.
Supporting Data
1. Common Information for Notifications and Drug Identification Number (DIN) Applications (as outlined in 4.1). 2. Rationale or justification of the proposed change 3. Data provided may include chemistry, clinical, and/or comparative data to support the proposed change(s). Please consult the Quality Guidance: Applications for Drug Identification Numbers (DINAs) for Pharmaceuticals and the guidance documents regarding bioequivalence/bioavailability studies available on the Health Canada Web site: Bioavailability and Bioequivalence. 4. New Drug Requirements: Consult the guidance documents including Preparation of New Drug Submissions in CTD format, and Management of Drug Submissions and Applications. For veterinary drugs, Guidance for Industry Preparation of Veterinary New Drug Submissions and Veterinary drugs - Management of regulatory submissions guidance: Overview.

C.01.014.1(2)(j) the recommended dosage of the drug

Change #	Description of Change	Conditions	Supporting Data	Filing Process
19	Revisions to the dosage frequency, daily dose, the dose amount, the duration of dosing	1 or 2	1, 2	Post-authorization Division 1 Change / Veterinary Post-authorization Division 1 Change
		3	1 and (potentially 2 and/or 3)	Drug Identification Number Application
		4	4	New Drug
20	Change to withdrawal instructions for veterinary drugs	2	1,5	Drug Identification Number Application

Conditions

1. The proposed changes to the dosage recommendations are in compliance with the dosing criteria in the Category IV monograph or Labelling standard.
2. The proposed changes to the dosage recommendations are not in compliance with the criteria in the Category IV monograph or Labelling standard, but have been previously reviewed and authorized by Health Canada for that product category as a Division 1 product.
3. The proposed changes to the dosage recommendations are not in compliance with the dosing criteria in a Category IV monograph or Labelling standard, have not been previously reviewed and authorized by Health Canada for that product category, but do not meet the definition of a New Drug under C.08.001 of the Regulations ((for example, [e.g.] - the total daily dose remains the same, but the dosing schedule is changed).
4. The dose is not acceptable under a Category IV monograph or Labelling standard, or has not been previously reviewed and authorized by Health Canada for that product category, and meets the definition of a New Drug under C.08.001 of the Regulations.

Supporting Data

1. Common Information for Notifications and Drug Identification Number (DIN) Applications (as outlined in 4.1).
2. Rationale or justification of the proposed change.
3. Submission of supporting data which may include clinical data depending on the type of claim being made.
4. New Drug Requirements: Consult the guidance documents including Preparation of New Drug Submissions in CTD format, and Management of Drug Submissions and Applications. For veterinary drugs, Guidance for Industry Preparation of Veterinary New Drug Submissions and Veterinary drugs - Management of regulatory submissions guidance: Overview.
5. Submission of a complete residue depletion study done in the intended species and with the same dosage and route of administration. In a case where there is more than one route of administration, a particular route must be specified.

C.01.014.1(2)(k) the address of the manufacturer referred to in paragraph (a) and where the address is outside the country, the name and address of the importer of the drug

Change #	Description of Change	Conditions	Supporting Data	Filing Process
21	Any change to the physical location of the manufacturer and/or Canadian importer of the product listed on the original HC/SC 3011 form / REP forms[xi]	1	1,2	Office of Submissions and Intellectual Property / Submission and Knowledge Management Division Notification
22	Any change in the name of the Canadian importer of the product listed on the original HC/SC 3011 / REP forms	1	1,2	Office of Submissions and Intellectual Property / Submission and Knowledge Management Division Notification

Conditions

1. No other changes to the manufacturer other than the address (for example, Manufacturer X moves from Richmond Hill to Markham, Ontario); or to the importer other than name and/or address and the change in address does not affect the conditions set out in C.01.004.1.

Supporting Data

1. A signed and dated cover letter on company letterhead with a description of the change.
2. Confirmation of which products (identify the Drug Identification Number, and Dossier ID, for submissions under review, refer to the Dossier ID and control number. In both scenarios, include all establishment licences which are affected by the change.

4.2.1.3 Changes outlined in C.01.014.1(2)(l)-(n)

The following filing processes and supporting data are strongly recommended in order to ensure that the proposed changes are consistent with the intent of the Act and Regulations:

C.01.014.1(2)(1) the name and address of any individual, firm, partnership or corporation other than the names and addresses referred to in paragraphs (a) and (k), that will appear on the label of the drug[xii]

Change #	Description of Change	Conditions	Supporting Data	Filing Process
23	Addition of a buy-out company or cross marketing for other companies	1, 2, 3	1,2	Office of Submissions and Intellectual Property / Submission and Knowledge Management Division Notification
24	Addition of contact information for ingredient suppliers (for example, for questions about ingredient X, contact Company X)			
25	REPEALED (see Document Change Log for more information)			

Conditions
1. The change in address does not affect the conditions set out in C.01.004.1 of the Regulations 2. The change does not affect the ownership of the Drug Identification Number (DIN), (for example, DIN is owned by Company X. Company X is acquired by Company Y, but the DIN owner does not change. Sponsor adds the statement "manufactured by Company X, a subdivision of company Y") 3. For any reference to other companies other than the DIN owner on the labelling, only the company or store name is added. No product specific information or inappropriate references to other products are allowed. Please refer to the Guidance Document: Regulatory Requirements for Drug Identification Numbers (DINs)
Supporting Data
1. A signed and dated cover letter on company letterhead with a description of the change. 2. Written documentation from the non-Drug Identification Number owner acknowledging acceptance of the use of their company information in this manner. 3. Revised labels.

C.01.014.1(2)(m) the written text of all labels and package inserts to be used in connection with the drug and product monograph

Change #	Description of Change	Conditions	Supporting Data	Filing Process
26	Additions or revisions to the adequate directions for use (that is, warnings, precautions, adverse event information etc.)	1	1,2,3	Post-authorization Division 1 Change / Veterinary Post-authorization Division 1 Change
27	Removal of adequate directions for use	1,2	1,2	Post-authorization Division 1 Change / Veterinary Post-authorization Division 1 Change
		1,3	1,2,3	Drug Identification Number Application
28	Revision to storage conditions	1 and (4 or 5)	not applicable	Not required to file[xiii]
		1,6 or 7	1,2,3	Drug Identification Number Application
29	Revision to shelf-life	1,4 and/or 8	not applicable	Not required to file[13]
		1,6	1,2	Veterinary Post-authorization Division 1 Change
		1,9	1,2,3	Drug Identification Number Application

30	Change in references for the Product Monograph	1,10	1,2,3	Post-authorization Division 1 Change / Veterinary Post-authorization Division 1 Change
		1,11	1,2,3	Drug Identification Number Application
31	Change to the Universal Product Code (UPC) code, item or lot number	1	not applicable	Not required to file
32	Change to the information layout on the label or packaging	1,12	not applicable	Not required to file
		1,13	1,2	Post-authorization Division 1 Change / Veterinary Post-authorization Division 1 Change
33	Cross promotion of other products	1,14,15	not applicable	Not required to file
		1,14,16	1,2,4	Post-authorization Division 1 Change / Veterinary Post-authorization Division 1 Change [xiv]
		1,14,17	1,2,4 and potentially 5	Post-authorization Division 1 Change / Veterinary Post-authorization Division 1 Change [15]
34	Change to any other text not captured in sections C.01.014.1(2)(a) to (l) and the above	1	1,2 and potentially 3 or 5	Post-authorization Division 1 Change / Veterinary Post-authorization Division 1 Change

Conditions

1. The change(s) to the information are not otherwise captured in (a)-(l).
2. The change does not involve the removal of safety information (for example, [e.g.] - for a sunburn protectant the directions state “wash face, towel dry and apply prior to sun exposure”. Removing the directions “wash face and towel dry”). Alternatively, the change involves the removal of safety information required by international jurisdictions but not Health Canada.
3. The change involves the removal of safety information (for example, [e.g.] - warnings, precautions, adverse event information, etc.)
4. The product is a non-prescription drug for human use **or** is not sterile **or** is not a modified release product **or** is not a transdermal patch drug **or** is a product in which no stability data had been reviewed as part of the original or subsequent submissions.
5. The revisions to the storage conditions are within a comparable range (for example [e.g.] - “store at

room temperature" to "store between 15-25°C"). The product is a prescription drug, **or** is sterile, **or** modified release **or** a transdermal patch drug **or** is a product in which stability had been reviewed as part of the original or subsequent submissions.

6. The product is for veterinary use.
7. The revisions to the storage conditions are not within a comparable range (for example, [e.g.] - "Store at room temperature" to "Keep frozen"). The product is a prescription drug, **or** is sterile, **or** modified release **or** a transdermal patch drug**, or** is a product in which stability had been reviewed as part of the original or subsequent submissions.
8. The product meets similar conditions outlined in the Guidance document: Post-Notice of Compliance (NOC) Changes: Framework Document (Pharmaceutical, biologic and radiopharmaceutical drugs for human use only).
9. The product does not meet condition #8, **and** is a prescription drug for human use **or** is sterile **or** modified release **or** a transdermal patch drug **or** is a product in which stability had been reviewed as part of the original or subsequent submissions.
10. Any addition that does not affect any other text in the label or does not explicitly or implicitly expand the claims, including indications for use (for example [e.g.] - changing a publication listed as "in press" to a published listing).
11. Any addition that does affect any other text in the label or may explicitly or implicitly expand the claims, including indications for use [see also 4.2.1: C.01.014.1 (2)(i)].
12. The content of the text has not been changed, any reordering of information complies with the requirements of the Regulations, and/or a novel label format (for example, [e.g.] - accordion label, butterfly label, peel back label etc.) has not been introduced.
13. The content of the text has not been changed and a novel label format (e.g. - accordion label, butterfly label, peel back label etc.) has been introduced.
14. The other product[xv] must be in compliance with all applicable Acts or Regulations (for example, [e.g.] - if the other product is a cosmetic, it is compliant with the requirements of the Cosmetic Regulations).
15. The other product is completely unrelated to the current product (for example, [e.g.] - in terms of indication, route of administration, concomitant usage etc.) and/or is a general statement which does not identify a specific product (e.g. - try our other brand X products). The other product must also not impact the safety, efficacy or quality of the drug product.
16. The other product is not intended for concomitant use and does not treat the same indication, but may have potential implications on safety or efficacy. (for example, [e.g.] - a night time moisturizer containing alpha-hydroxy acid promoted on the label of a sunscreen product can result in the necessity of additional safety warnings on the drug product label).
17. The other product is intended for concomitant use or to treat the same indication, or has additional safety implications for consideration.[xvi]

Supporting Data

1. Common Information for Notifications and Drug Identification Number (DIN) Applications (as outlined in 4.1).
2. Rationale or justification of the proposed change.
3. Submission of supporting data which may include, but is not limited to: safety information (periodic safety update reports, adverse event information, post-market data) chemistry, clinical data.
4. If condition 15 or 16 are fulfilled, information on the other product should be provided (e.g. - ingredients, dosage form, dose, intended use, labels etc.).
5. New Drug Requirements: For human drugs consult the guidance documents including Preparation of New Drug Submissions in CTD format, and Management of Drug Submissions and Applications. For veterinary drugs, consult the guidance documents Guidance for Industry Preparation of Veterinary

New Drug Submissions and Veterinary drugs - Management of regulatory submissions guidance: Overview.

C.01.014.1(2)(n) the name and position of the person who signed the application and the date of signature

Change #	Description of Change	Conditions	Supporting Data	Filing Process
35	Revisions to the authorized signing authority for the drug submission originally listed on the HC/SC 3011 form / REP forms	1	not applicable	Not required to file
		2	not applicable	Notify Review Bureau and Office of Submissions and Intellectual Property / Submission and Knowledge Management Division Notification immediately
36	The name of the contact for the Drug Identification Number ownership, regulatory contact and/or billing contact changes	1	not applicable	Notify Office of Submissions and Intellectual Property / Submission and Knowledge Management Division Notification within 30 days[xvii]
		2	not applicable	Notify Review Bureau and Office of Submissions and Intellectual Property / Submission and Knowledge Management Division Notification immediately

Conditions

1. The change occurs post-authorization of the product/submission.
2. The change occurs during an active submission.

4.2.2 Other Changes Related to the Drug Authorization

The Regulations referred to in this Guidance are not exhaustive. Other regulatory requirements for labelling a drug must also be met by the sponsor of a DIN product prior to Health Canada granting market authorization. The following recommendations for filing processes and supporting data with respect to changes affecting the safety, efficacy and quality of the authorized drug product not otherwise captured in C.01.014 are made with the intent to ensure compliance with the Regulations as a whole.

4.2.2.1 Change to the formulation (Subject to C.01.036-038, 040, 064, 066 and 067)

Change #	Description of Change	Conditions	Supporting Data	Filing Process
37	Addition, revision, or removal of a non-medicinal ingredient	1	not applicable	Not required to file.
		2	1	Office of Submissions and Intellectual Property / Submission and Knowledge Management Division Notification
		3 and (4 or 5)		
		6	2,3	Post-authorization Division 1 Change / Veterinary Post-authorization Division 1 Change
		7	2, 3 and potentially 4	Drug Identification Number Application
38	Revision to an ingredient using nanomaterials	8	not applicable	Seek a pre-submission meeting[xviii]

Conditions

1. The non-medicinal ingredients were not reviewed as part of the original drug submission application, nor submitted afterwards at any time.
2. The non-medicinal ingredients were submitted as part of an information gathering project (for example [e.g.] - Bovine spongiform encephalopathy/transmissible spongiform encephalopathy (BSE/TSE), phthalates, Drug Product Information Forms).
3. The change in the quantity of the ingredient does not exceed established limits in guidances or the Regulations (for example [e.g.] - an increase in the amount of methylisothiazolinone as a preservative greater than 0.01% is prohibited).
4. The quantity of the ingredients in the formulation previously authorized for the drug product has been altered, but no non-medicinal ingredients have been removed or added.
5. The change results in the removal of an authorized variant in flavour or fragrance (for example [e.g.] - lip balm product line removes mint flavour variant, but keeps lemon and cherry lip balms). Alternatively, there is no change in the labelled flavour or fragrance, however, the non-medicinal ingredients contributing to the flavour or fragrance have been varied (for example [e.g.] - product is labelled as “floral” scent, perfume changes from “rose” to “lilac”).
6. The change results in an addition or change in quantity of a flavour or fragrance, and all other parameters are identical to the authorized product. See the Guidance Document: Regulatory Requirements for Drug Identification Numbers (DINs).[xix]
7. The authorization was dependent on the original product formulation, including non-medicinal ingredients (for example [e.g.] - separate Drug Identification Numbers (DINs) were issued for a preservative versus preservative-free formulation; separate DINs were issued for a sucrose-free versus sucrose containing formulation; the change concerns ingredients sourced from animal tissue, etc.) **or** the change is to an ingredient sourced from animal tissue.
8. The revision to a medicinal or nonmedicinal ingredient affects whether the product incorporates nanomaterials (including micronized sunscreen ingredients).

Supporting Data
1. A signed and dated cover letter on company letterhead with a description of the change along with a revised Drug Product Information Form (DPIF) (the form is available upon request from OSIP-BPPI@hc-sc.gc.ca). 2. Common Information for Notifications and Drug Identification Number (DIN) Applications (as outlined in 4.1). 3. Rationale or justification of the proposed change. 4. Submission of supporting data which may include chemistry, clinical, or comparative data depending on the type of claim being made. Please consult the Quality Guidance: Applications for Drug Identification Numbers (DINAs) for Pharmaceuticals and the guidance documents regarding bioequivalence/bioavailability studies available on the Health Canada Web site: Bioavailability and Bioequivalence.

4.2.2.2 Change to the packaging (Subject to A.01.016, C.01.004, C.01.065, 067, 069, 070, Division 2)

Change #	Description of Change	Conditions	Supporting Data	Filing Process
39	Any noticeable revision to the overall colour of the packaging	1	not applicable	Not required to file[xx]
40	Change to the type of label format used	2	1, 2	Post-authorization Division 1 Change / Veterinary Post-authorization Division 1 Change
41	Change to packaging type or size (that is, cartons, vials, child resistant packaging, etc.)	1, 3	not applicable	Not required to file[20]
		1, 4	1,2	Post-authorization Division 1 Change / Veterinary Post-authorization Division 1 Change
42	Co-packaging of products, kits (the products are sold together or packaged together as a unit (for example, shrink wrapped packages)[xxi]	5,6	not applicable	Not required to file
		5,7	1,2,3	Post-authorization Division 1 Change / Veterinary Post-authorization Division 1 Change [xxii]
		5,8,and/or 9	1,2,3,4	Drug Identification Number Application
		10	5	New Drug

Conditions
1. No other changes are made to the labels. 2. The content of the label is not changed however the format is revised: specifically a label is added, removed, or revised to alter consumer accessibility to information (for example [e.g.] - addition of an outer carton; change in label type from a flat label to an accordion panel) 3. The change is not subject to size, type and/or related ingredient restrictions in the Food and Drugs Act (FDA), Food and Drug Regulations (FDR), or other applicable regulations and guidances. 4. The change is subject to size, type and/or ingredient restrictions in the FDA, FDR, or other applicable regulations and guidances (for example, [e.g.] - child resistant packaging, limitation of quantity, risk management, etc.). 5. The other product must be in compliance with all applicable Acts or Regulations (for example [e.g.] - if the other product is a cosmetic, it must be compliant with the requirements of the Cosmetic Regulations) 6. The other product is either unrelated to the current product (for example, [e.g.] - in terms of indication, route of administration, concomitant usage etc.) and/or would not impact on safety, efficacy or quality of the drug product (for example, [e.g.] - packaging of a toothpaste and a toothbrush; packaging of a children's analgesic with stickers, inclusion of coupons). 7. The other product is not intended for concomitant use, but either treats the same indication, and/or still necessitates a safety assessment. 8. The other product is intended for concomitant use or to treat the same indication, or has additional safety or efficacy implications for consideration. 9. The copackaging of the product affects the prescription status (that is [i.e.] prescription or over-the-counter [OTC]) of the drug. 10. The drug product combination meets the definition of a New Drug under C.08.001 of the Regulations.
Supporting Data
1. Common Information for Notifications and Drug Identification Number (DIN) Applications (as outlined in 4.1). 2. Rationale or justification of the proposed change. 3. If conditions 6 or 7 are fulfilled, information on the other product should be provided (for example, [e.g.]- ingredients, dosage form, dose, intended use etc.). 4. Submission of revised labelling and potentially clinical data to ensure the safe and efficacious use of the two products together. If condition 8 applies, the sponsor must ensure they meet prescription drug requirements. 5. New Drug Requirements: Consult the guidance documents, including Preparation of New Drug Submissions in CTD format and Management of Drug Submissions and Applications. For veterinary drugs, Guidance for Industry Preparation of Veterinary New Drug Submissions and Veterinary drugs - Management of regulatory submissions guidance: Overview.

4.2.2.3 Change to a sterile drug (Subject to C.01.004, 032, 064, 065, 066, 067, 068, 069, 070, Division 2)

Change #	Description of Change	Conditions	Supporting Data	Filing Process
43	Change to the manufacturing of a sterile drug	1, 2 and (4 or 5)	1	Not required to file
		1, 3 and (4 or 5)	1	Drug Identification Number Application

Conditions

1. The change concerns a sterile drug product.
2. The reporting category of the change is not defined as Level I in the guidance document Post-Notice of Compliance Changes (Quality).
3. The reporting category of the change is defined as Level I in the guidance document Post-Notice of Compliance Changes (Quality).
4. The change concerns the tests and analytical procedures that control the sterility of the drug in dosage form.
5. The change concerns the sterilization process of the drug.

Supporting Data

1. As per the recommendations for supporting data in the guidance document Post-Notice of Compliance Changes (Quality).

4.2.2.4 Change to a modified release or transdermal patch drug (Subject to C.01.004, 012, 015, Division 2)

Change #	Description of Change	Conditions	Supporting Data	Filing Process
44	Change to the manufacturing of a controlled release drug	1, 2 and (4 or 5)	1	Not required to file
		1,3 and (4 or 5)	1	Drug Identification Number Application

Conditions

1. The change concerns a drug in final dosage form that has been formulated to provide control with respect to the site and rate of release of the drug other than immediate release (includes modified, controlled or sustained release and enteric coated) **or** is a transdermal patch.
2. The reporting category of the change is not defined as Level I in the guidance document Post-Notice of Compliance Changes (Quality).
3. The reporting category of the change is defined as Level I in the guidance document Post-Notice of Compliance Changes (Quality).
4. The change concerns the tests and analytical procedures that control the release rate of the drug in dosage form.
5. The change concerns any aspects of the manufacturing of the drug that is critical to the rate releasing mechanism of the drug in final dosage form.

Supporting Data

1. As per the recommendations for supporting data in the guidance document Post-Notice of Compliance Changes (Quality).

5. Effective date

This guidance document will come into effect on the same day as the online publication date. All changes from the effective date of the Post-DIN Changes guidance are expected to be reported as per the procedures detailed within. In the interim, established processes for filing changes outlined in Section C.01.014 of the Regulations should continue to be followed (for example, [e.g.] - changes to brand name, active ingredients, etc.).

For veterinary drug products, process recommendations for filing changes, as indicated in this guidance document, will come in effect once the Veterinary Drugs Directorate has officially published a guidance on the preparation of veterinary DIN (Division 1 drugs) submissions.

6. Appendices

Appendix I: Excerpt from Food and Drug Regulations

Section C.01.014.1 of the Regulations states that:

(1) A manufacturer of a drug, a person authorized by a manufacturer or, in the case of a drug to be imported into Canada, the importer of the drug may make an application for a drug identification number for that drug.

(2) An application under subsection (1) shall be made to the Director in writing and shall set out the following information:

(a) the name of the manufacturer of the drug as it will appear on the label;

(b) the pharmaceutical form in which the drug is to be sold;

(c) in the case of any drug other than a drug described in paragraph (d), the recommended route of administration;

(d) in the case of a drug for disinfection in premises, the types of premises for which its use is recommended;

(e) a quantitative list of the medicinal ingredients contained in the drug by their proper names or, if they have no proper names, by their common names;

(f) the brand name under which the drug is to be sold;

(g) whether the drug is for human use, veterinary use or disinfection in premises;

(h) the name and quantity of each colouring ingredient that is not a medicinal ingredient;

(i) the use or purpose for which the drug is recommended;

(j) the recommended dosage of the drug;

(k) the address of the manufacturer referred to in paragraph (a) and, where the address is outside the country, the name and address of the importer of the drug;

(l) the name and address of any individual, firm, partnership or corporation, other than the names and addresses referred to in paragraphs (a) and (k), that will appear on the label of the drug;

(m) the written text of all labels and package inserts to be used in connection with the drug and of any further prescribing information stated to be available on request; and

(n) the name and position of the person who signed the application and the date of signature.

(3) In the case of a new drug, a new drug submission or an abbreviated new drug submission filed pursuant to section C.08.002 or C.08.002.1 shall be regarded as an application for a drug identification number.

C.08.001 For the purposes of the Act and this Division, "new drug" means

(a) a drug that contains or consists of a substance, whether as an active or inactive ingredient, carrier, coating, excipient, menstruum or other component, that has not been sold as a drug in Canada for sufficient time and in sufficient quantity to establish in Canada the safety and effectiveness of that substance for use as a drug;

(b) a drug that is a combination of two or more drugs, with or without other ingredients, and that has not been sold in that combination or in the proportion in which those drugs are combined in that drug, for sufficient time and in sufficient quantity to establish in Canada the safety and effectiveness of that combination and proportion for use as a drug; or

(c) a drug, with respect to which the manufacturer prescribes, recommends, proposes or claims a use as a drug, or a condition of use as a drug, including dosage, route of administration, or duration of action and that has not been sold for that use or condition of use in Canada, for sufficient time and in sufficient quantity to establish in Canada the safety and effectiveness of that use or condition of use of that drug.

Appendix II: DIN submission types - pharmaceuticals for human use and disinfectant drugs

1. Administrative DINA

    Timeline: 45 days screening

    This type of DIN submission is for changes to product name and/or manufacturer name only. Any other change to the labelling falls outside the scope of this type.

2. Category IV DIN (DINF)

    Timeline: 60 days screening

    This is a DIN submission that is compliant with the criteria outlined in a Category IV monograph and does not necessitate the filing of supporting scientific data.

3. DINA Labelling Standard (DINA LS)

    Timeline: 60 days screening

    This is a DIN submission that is compliant with the criteria outlined in a Labelling Standard and does not necessitate the filing of supporting scientific data.

4. DINA

    Timeline: 45 days screening, 210 days review target

    These submissions require supporting data for safety, efficacy, and quality requirements) which require review.

5. DIND – disinfectant

    Timeline: 45 days screening, 210 days review target

    These submissions require supporting data for safety, efficacy and quality, which requires review.

6. PDC – prescription: Safety

    Timeline: 25 days screening, 120 days review

    These submissions require supporting data for safety and/or efficacy changes, which requires review.

7. PDC – prescription: Quality

    Timeline: 25 days screening, 90 days review

    These submissions require supporting data for quality changes, which requires review.

8. PDC – non-prescription:
    Timeline: 30 days screening

9. PDC – disinfectant:

    Timeline: 30 days screening

Appendix III: DIN submission types - pharmaceuticals for veterinary use

1. Administrative DINA

    Timeline: 14 days screening, 120 days review target

    This type of DIN submission is for changes to a drug product that do not need scientific assessment (for example, [e.g.] - change in brand name and/or manufacturer name). Any other change to the labelling falls outside the scope of this type.

2. VDIN

    Timeline: 14 days screening, 120 days review target

This is a type of submission for veterinary products that references one or more similar Division 1 product(s) previously authorized. In order to confirm that the product does not fall within the definition of a New Drug, the submitted product must be comparable to one or more drug products(s) previously approved under Division 1, in all of the following areas: active ingredients or combination of active ingredients (including salt, strengths(s), dosage form, conditions of use (indications(s), intended species, dosage(s), route(s) of administration, methods of reconstitution. A review will be conducted once the status (Div. 1 drug) is confirmed. Some additional information, such as a rationale, may be required as needed.

[i] Veterinary Drugs Directorate may refer to human guidance documents as applicable for veterinary drug submissions (for example, Animal tissue forms, Preparation of Drug Identification Number Submissions, Changes to Manufacturer's Name and/or Product Name).

[ii] To be included when the authorized labels are to be revised as a result of the change.

[iii] A Drug Submission Fee Application Form is only required when there is a fee associated to the application

[iv] The chemical form of the medicinal ingredient is as outlined in the guidance document Interpretation of Identical Medicinal Ingredient (2003) and does not refer to the pharmaceutical form.

[v] As per C.01.014.4, it is recognized that an amended DIN application for a change in delivery rate without a change to quantitative declaration of medicinal ingredient would not likely result in assignment of a new Drug Identification Number if there are no additional amendments to the authorization granted by Health Canada.

[vi] Sponsor are required to ensure that the change does not impact on legibility as per A.01.016 of the Regulations nor impact on consumer comprehension of the registered brand name (as per Section 9 (1) of the Act.

[vii] A regulatory amendment will also be required.

[viii] Non-therapeutic attributes of a drug product relate to its physical, sensory (colour, flavour, smell etc.) or market characteristics (market position, retail cost) to the impact on physical characteristics of the body organ (for example, cleansing/moisturizing effect, impact on texture, feel softness, beauty, smoothness and any other cosmetic performance claims) upon or in which it is used, to cosmetic-type characteristics and to other aspects such as presentation, but excluding any characteristics that relate to the classification of the product as a drug. Section 9(1) of the Food and Drug Act states that it is unacceptable to represent a drug in a manner that is false, misleading or likely to create an erroneous impression of the product.

[ix] Following assessment may be requested to file a new Drug Identification Number (DIN) application or a New Drug submission.

[x] Changes to colours, and flavours/fragrances and associated label changes are captured under "C.01.014.1(2)(h)" and "4.2.2.1 Change to the formulation", respectively.

[xi] All establishments that fabricate, package/label, test, import, distribute and/or wholesale a drug must comply with the Act and its Regulations which includes Good Manufacturing Practices (GMP) and Establishment Licence (EL) requirements. Guidance on EL and GMP can be found on Health Canada's Compliance and Enforcement Web site (http://www.hc-sc.gc.ca/dhp-mps/compli-conform/licences/index-eng.php).

[xii] This section does not apply to manufacturer (Drug Identification Number owner) names as this is captured under C.01.014(2)(a).

[xiii] It is the sponsor's responsibility to ensure that all stability data necessary to support the change in expiry date and/or storage conditions is in accordance with the guidance document the Good Manufacturing Practices Guidelines, 2002 Edition (GUI-0001) and kept on file for the Health Products and Food Branch Inspectorate.

[xiv] It may be determined from the information submitted through a Post-authorization Division 1 Change / Veterinary Post-authorization Division 1 Change (PDC/VPDC) that the sponsor still needs to file a new Drug Identification Number submission.

[xv] The "other product" can include, but is not limited to, cosmetics, medical devices, natural health products or other drugs.

[xvi] In cases where the other product is being recommended for concomitant use and/or is sold in conjunction with the product in question, it is possible the prescription drug status (i.e. prescription or Over the Counter [OTC]) and/or the assessment of the product as a New Drug or Old Drug may change (for example, benzoyl peroxide when sold in combination is prescription). The sponsor may be required to file a new DIN application or a New Drug Submission.

[xvii] It is strongly recommended that the sponsor notify the Office of Submissions and Intellectual Property and the Submission and Knowledge Management Division of changes immediately to ensure that the legal contact information is current.

[xviii] As the use of nanomaterials in drug products presents an unknown risk at the current time, it is recommended that sponsors seek out a pre-submission meeting to determine the filing recommendations for enacting such a change.

[xix] Flavours should be recognized by the Food and Drug Regulations. For example-[e.g.,] - almond extract is considered a recognized flavour under the Regulations pertaining to foods; however, vitamin C is not.

[xx] It is the sponsor's responsibility to ensure that the change does not impact legibility or layout of the labels.

[xxi] The unit should not be co-packaged in a manner that obscures the drug product information.

[xxii] It may be determined from the information submitted through a Post-authorization Division 1 Change / Veterinary Post-authorization Division 1 Change (PDC/VPDC) that the sponsor still needs to file a new Drug Identification Number (DIN) submission.