Health Canada Santé Canada

Draft Guidance Document

Regulatory requirements for Drug Identification Numbers (DINs)

This guidance document is being distributed for comment purposes only.

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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.

Également disponible en français sous le titre :
Exigences réglementaires associées à une identification numérique de drogue (DIN)

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Document change log

Date	Change	Location (section, paragraph)	Nature of and/or reason for change
January 25, 2019	This guidance document consolidates the following policies and guidance documents: •Guidance Document: Cancellation of a Drug Identification Number (DIN) and Notification of Discontinuation of Sales •Issuance of Drug Identification Numbers for New Drugs •Notice: Instructions for filing Drug Notification Forms (DNF) and Supporting Documents Provided in Electronic Format •Assignment of Drug Identification Numbers (DINs) According to Product Name •Notice – Revision of the Procedure on the issuance of Drug Identification Numbers (DINs) for Unit Dosage Pre-filled Syringes	Global change	To make it easier to find information relating to DINs by consolidating a number of policies and guidance document into a single document.
January 25, 2019	Addition of the following wording: "(available for immediate use via hospital and retail pharmacies [i.e., the drug is physically on pharmacy shelves]), "	6.4, paragraph 4	To provide clarification on the concept of availability of a drug on the Canadian market

Foreword

Guidance documents are meant to provide assistance to industry and health care professionals on how to comply with governing statutes and Food and Drug 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 program 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 drug. Health Canada is committed to ensuring that such requests are justifiable and that decisions are clearly documented.

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1. Introduction

When Health Canada authorizes a drug to be marketed in Canada, a Drug Identification Number (DIN) is issued to the manufacturer and printed on the package labels. A DIN indicates that the evaluation of the drug determined that it met the relevant requirements of the Food and Drug Act and its regulations and the drug has a favourable risk/benefit profile. Manufacturers of prescription and non-prescription drugs must obtain a DIN before they are marketed in Canada. Market authorization of a drug may require the additional issuance of a Notice of Compliance (NOC).

The DIN assigned to a drug is unique and serves as a tool to help in the post-market activities of products on the market, such as product identification and verification by health care professionals, recall of products, inspections, and quality monitoring. While the authorization of a drug includes the issuance of a DIN to the manufacturer, the DIN is the property of Health Canada.

2. Purpose

This guidance document provides:

1. assistance on the interpretation of the regulatory requirements associated with a DIN
2. guidance to manufacturers on their obligation to accurately report to Health Canada the following notifications for a change of drug status within the required timelines:
    - Market notification
    - 12 months without sale notification
    - Discontinuation of sales notification

3. Scope

This guidance document applies to all drugs that have been issued a DIN (i.e., human and veterinary drugs, biologics, disinfectants, and radiopharmaceuticals). This document is limited to changes that impact the status of a DIN. This guidance covers the following activities:

- DIN issuance by Health Canada to the manufacturer
- Issuance of a revised Drug Notification Form by Health Canada to the manufacturer
- Filing of market notifications by the manufacturer to Health Canada
- Filing of 12 months without sale notifications by the manufacturer to Health Canada
- Filing of discontinuation of sale notifications by the manufacturer to Health Canada

This document does not cover the following:

- Filing requirements and management of drug submissions and applications
- Reporting of adverse drug reactions
- Reporting of potential or real drug shortages on the third party drug shortages website
- User fees and fees for the right to sell drugs
- Establishment licensing

- Products that have not been issued a DIN (i.e. medical devices, natural health products, veterinary health products, pest control products, cosmetics, and experimental treatments for human and animals, and cannabis for medical purposes regulated under Part 14 of the Cannabis Regulations)
- Annual drug notification process

4. Policy objectives

The policy objectives that guide the regulatory authority for activities relating to DIN issuance and reporting to Health Canada include:

- To protect the health and safety of Canadians from the sale of unsafe, and/or unauthorized drugs
- To provide Canadians with timely, reliable and accurate information on the availability of drugs in Canada

5. Definitions

Annual Drug Notification Form (ADNF)

Form intended to assist manufacturers in complying with section C.01.014.5 of the Food and Drug Regulations, which requires that every manufacturer of a drug confirms annually before October 1st that all information previously supplied with regard to that drug is correct.

- For more information on the ADNF, consult the Guidance Document – Fees for the Right to Sell Drugs (https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/fees/guidance-document-fees-right-sell-drugs.html).

Discontinue
When the manufacturer permanently stops the sale of the drug.

Discontinuation Date
If a manufacturer is marketing a drug and decides to permanently discontinue its sale, the date of the discontinuation is the date of the last sale by the manufacturer.

If a manufacturer has temporarily stopped marketing a drug and then subsequently decides to permanently discontinue its sale at a later date, the discontinuation date is the date on which the decision to permanently discontinue the sale was made.

Drug, as defined Section 2 of the Food and Drugs Act
Includes any substance or mixture of substances manufactured, sold or represented for use in:

a) the diagnosis, treatment, mitigation or prevention of a disease, disorder, abnormal physical state, or its symptoms, in human beings or animals,
b) restoring, correcting or modifying organic functions in human beings or animals, or
c) disinfection in premises in which food is manufactured, prepared or kept.

Drug Identification Number (DIN)
A computer-generated 8 digit number assigned by Health Canada to a drug upon market authorization under subsection C.01.014.2 (1) of the Food and Drugs Regulations.

It identifies each drug under the Food and Drug Regulations, sold in a dosage form in Canada, and is located on the package label of prescription and non-prescription drugs that have been evaluated and authorized for sale in Canada.

A DIN uniquely identifies the following characteristics:

- Product Name
- Manufacturer Name
- Active Ingredient(s)
- Strength of Active Ingredient(s)
- Dosage Form
- Route(s) of Administration
- Species (for veterinary drugs only)

Drug Notification Form (DNF)
Form issued by Health Canada in accordance with section C.01.014.2 (1) of the Food and Drug Regulations that contains the DIN assigned for a drug, as well as some of the information included in the drug submission.

In accordance with section C.01.014.3 of the Food and Drug Regulations, the manufacturer must, within 30 days after the day on which the drug is first sold, date and sign the completed DNF and return it to Health Canada with a statement it that the information it contains is correct and with an indication of the date of that first sale.

Expiration Date of Drug in Dosage Form
Means the earlier of:

- the last date a drug would maintain its labelled potency, purity and physical characteristics, or
- the date after which the manufacturer recommends that the drug not be used

The expiration date should be expressed at a minimum as a year and a month.

Label
Includes:

- Labels affixed to the container or packaging of the drug
- Any separate package inserts
- Prescribing Information
- Fact sheets
- Consumer information/patient medication information (i.e., patient leaflets)
- Patient diaries,
- Product Monograph, or
- Other material containing information specific to the drug

Package labels generated by the manufacturer may be included in the packaging or supplied to the consumer at the time of dispensing.

Lot Number
Any combination of letters, figures, or both, which can be used to trace a drug being manufactured and/or in distribution.

Manufacturer
The person, including an association or partnership, who under their own name, or under a trade, design or word mark, trade name or other name, word or mark controlled by them, markets a drug. This is the person or company, to which the DIN is issued. For the purpose of this guidance document, manufacturer may include an agent authorized to act on their behalf.

Market Notification
Notification sent by the manufacturer to Health Canada to report the date of first sale pursuant to section C.01.014.3 of the Food and Drug Regulations.

New Drug, as defined in Part C, Division 8, of the Food and Drug Regulations
Means a drug, other than a veterinary health product,

a) 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) 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) 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.

Notice of Compliance
A notice issued under section C.08.004 or C.08.004.01 of the Food and Drug Regulations to a manufacturer following the satisfactory review of a drug submission for a New Drug.

Private Label
Label of an authorized non-prescription drug sold under the name of a retail store that is neither the manufacturer nor the fabricator of the drug.

6. Guidance for implementation

6.1 DIN issuance

Once a drug has been authorized for sale in Canada, Health Canada issues a DIN under Part C, Division 1 of the Food and Drug Regulations which permits the manufacturer to market the

drug in Canada. For drugs that meet the definition of a new drug under Part C, Division 8 of the Food and Drug Regulations, the drug is required to have a Notice of Compliance (NOC) in addition to a DIN in order to be authorized for sale in Canada.

Prior to June 13, 2018, Schedule C drugs (radiopharmaceuticals) received only an NOC and no DIN. Since the amendments to the Food and Drug Regulations that came into force on June 13, 2018, manufacturers of previously authorized Schedule C drugs have been required to submit an application for a DIN.

- For more information on the issuance of DINs for Schedule C Drugs, refer to the Guidance Document: Drug Identification Numbers for Schedule C Drugs (Radiopharmaceuticals and Kits) (https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/drug-identification-numbers-schedulec.html).

The DIN is issued in the form of a Drug Notification Form (DNF). The DNF contains, in addition to the DIN, information that is specific to the drug as it has been authorized by Health Canada. DNFs are sent by email directly to the manufacturer by Health Canada.

6.1.1 The timing of DIN issuance

6.1.1.1 New DINs

For manufacturers seeking authorization for a drug for human use under Part C, Division 8 of the Food and Drug Regulations, the DIN is issued prior to issuance of the NOC, when all relevant review streams are completed so that labelling material can be prepared in advance.

For manufacturers seeking authorization for a drug for veterinary use under Part C, Division 8 of the Food and Drug Regulations, the DIN is issued to the manufacturer when the NOC is granted.

For manufacturers seeking authorization under Part C, Division 1 of the Food and Drug Regulations for drugs for human or veterinary use, no NOC is granted. The DIN, in the form of a DNF, represents the market authorization.

6.1.1.2 Revised Drug Notification Form

Any change to one or more of the drug characteristics as listed in the definition of a DIN (refer to section 5) must be authorized before the DNF can be revised. A submission or application seeking authorization for the proposed changes must be filed.

As a result, for subsequent changes to a drug authorized for human or veterinary use under Part C, Division 8, the revised DNF with the same sequence of numbers as the original DIN is issued to the manufacturer after the NOC is granted. If the authorization is granted, Health Canada will issue either issue a new DNF with a new DIN or a revised DNF with the original DIN (same sequence of numbers).

For subsequent changes to a drug for human or veterinary use authorized under Part C, Division 1 of the Food and Drug Regulations, a revised DNF with the same sequence of numbers as the original DIN may be issued to the manufacturer. The DNF represents the market authorization, since no NOC is granted for these drugs.

The Table 1 below shows the specific changes to characteristics of a drug that would require either the issuance a new DIN or a revised DNF.

Table 1 - Issuance of new DIN versus revised DNF with the same sequence of numbers as original DIN

Change in Characteristic	New DIN	**Revised DNF** with the same sequence of numbers as original DIN
Product Name		✓
Manufacturer Name		✓
Active Ingredient(s)	✓	
Strength of Active Ingredient(s)	✓	
Dosage Form	✓	
Route(s) of Administration	✓	✓*
Species (for veterinary drugs only)		✓

* Change in use areas for disinfectants; additional routes

6.1.2 Assignment of DIN according to product name

A product name for a drug is proposed by the manufacturer so that it may market and advertise that drug. Health Canada reviews each product name as part of a drug submission or an application before a drug is authorized for sale in Canada.

- For information on the assessment of brand names for drug for human use, refer to:
  - Guidance Document for Industry - Review of Drug Brand Names (https://www.canada.ca/en/health-canada/services/drugs-health-products/reports-publications/medeffect-canada/guidance-document-industry-review-drug-brand-names.html)
  - Frequently Asked Questions - Guidance Document for Industry - Review of Drug Brand Names (https://www.canada.ca/en/health-canada/services/drugs-health-products/reports-publications/medeffect-canada/frequently-asked-questions-guidance-document-industry-review-drug-brand-names.html).

If a manufacturer wishes to market an authorized drug (i.e., a drug that already has been assigned a DIN) under two or more product names, a separate DIN will be assigned for each additional unique product name.

- For more information on the filing of a submission for an additional product name for drugs for human use, refer to the Frequently Asked Questions - Guidance Document for Industry - Review of Drug Brand Names (https://www.canada.ca/en/health-

canada/services/drugs-health-products/reports-publications/medeffect-canada/frequently-asked-questions-guidance-document-industry-review-drug-brand-names.html)

- For information on the filing of a submission for an additional product name for veterinary drugs, contact the Veterinary Drugs Directorate at hc.vdd.skmd.so-dgps.dmv.cp.sc@canada.ca.

A new DIN will not be issued if a manufacturer wishes to market an authorized non-prescription drug with retail specific branding, also known as private label (refer to section 5 for the definition of private label), provided that the product name is the same.

An example of two products that would have the same DIN is provided in Table 2 below.

Table 2 - Assignment of DINs for two drugs that have different retail branding

DIN	ZZZZZZZZ	ZZZZZZZZ
Product Name	Omeprazole	Omeprazole
Manufacturer Name	Drug Company	Drug Company
Retailer	Drug Store1	Drug Store2

Changes to an authorized label to include or modify retail specific branding elements (e.g., graphics, colour, and font, etc.) require a review and authorization by Health Canada before they can be introduced on the market. As a result, a Submission and Information Policy Division (SIPD) Notification will no longer be accepted for private labels.

- For information on how to submit additional labels for an authorized drug non-prescription drug for human use, refer to section 5.9 of the Guidance Document: Questions and Answers: Plain Language Labelling Food and Drug Regulations for Non-prescription Drugs (https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/guidance-document-questions-answers-plain-language-labelling-regulations-non-prescription-drugs-contact-lens-disinfectants.html).

6.1.3 Issuance of multiple DINs to address safety issues

To support Health Canada's ongoing effort to prevent potentially serious dosing errors, Health Canada may issue separate DINs for the same concentration but different dose volumes under specific conditions, such as where the entire package represents one dose. This may apply to pre-filled pens and auto-injectors of differing dose volumes.

Authorized New Drug Submissions and DIN Applications involving unit dose pre-filled syringes of the same concentration but offered in syringes of different total volumes will result in the issuance of separate DINs for each of the available total volumes. For example, a product with a strength of 10mg/ml that comes in a unit dose of 1ml in a prefilled syringe and also a unit dose of 2ml would be assigned two DINs. Health Canada will deal with already marketed drugs on a case-by-case basis.

Future refinements to this policy may be necessary as a result of experience gained.

6.2 Drug statuses and the Drug Product Database

Once the DIN and/or the NOC are/is issued to the manufacturer, Health Canada publishes information associated with the drug, including the DIN and the status of the drug on the Drug Product Database (DPD). The status of a drug in the DPD is indicative of the availability of the drug on the Canadian market. The manufacturer is required by the Food and Drug Regulations to inform Health Canada of a change in the status of a drug.

Figure 1 - displays the different statuses that may be assigned to a drug in the DPD. It shows the general order from left to right of how the drug status may change over time.

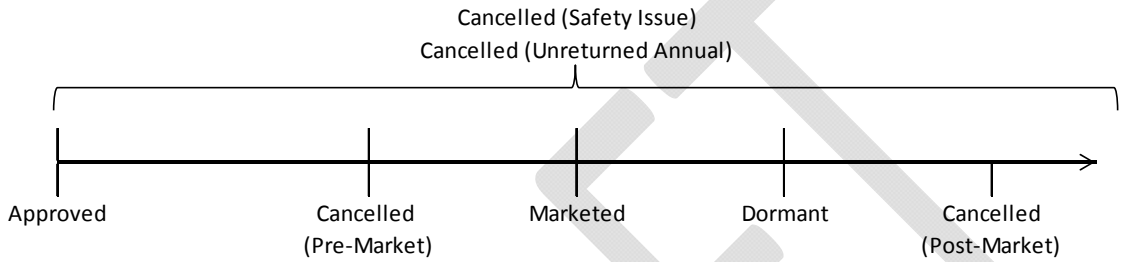

Figure 1: Possible statuses in general chronological order that may be associated with a drug and that may appear in the DPD

Description of Figure 1: Possible statuses in chronological order that may be associated with a drug and that may appear in the Online DPD

Figure 1 displays 5 statuses in chronological order. From left to right: Approved, Cancelled (Pre-Market), Marketed, Dormant, and Discontinued (Post-Market). The statuses Cancelled (Safety Issue) and Cancelled (Unreturned Annual) appear over the top of the chronology to indicate that either of these two events may occur at any time after a DIN has been issued.

The description of each status is summarized below:

- **Approved**: refers to a DIN that has been authorized for sale in Canada but has not yet been marketed in Canada. The DIN is considered active.
- **Cancelled Pre-Market**: refers to a DIN that is cancelled before it was ever marketed in Canada. The DIN is no longer considered active.
- **Marketed**: refers to a DIN that is currently being sold in Canada. The DIN is considered active.
- **Dormant**: refers to a DIN that was previously marketed in Canada but for which there have been no sales for a period of at least 12 consecutive months. The DIN is considered active as the drug is still authorized for sale in Canada and could be marketed again.
- **Cancelled Post-Market**: refers to a DIN that is cancelled further to the discontinuation of the sale by the manufacturer. The DIN is no longer considered active.

Cancelled (Safety Issue): refers to a DIN that is cancelled under the following paragraphs of the Food and Drug Regulations. In all cases, the DIN is no longer considered active.

- Paragraph C.01.014.6 (2) (b) of the Food and Drug Regulations due to failure to provide evidence regarding the safety and effectiveness of a drug, under section C.01.013 of the Food and Drug Regulations
- Paragraph C.01.014.6 (2) (b) of the Food and Drug Regulations following the suspension of a Notice of Compliance under section C.08.006
- Paragraph C.01.014.6 (3) (a) of the Food and Drug Regulations following the failure to comply with the order issued under section 21.31 of the Food and Drugs Act to conduct an assessment and provide the results
- Paragraph C.01.014.6 (3) (b) of the Food and Drug Regulations following the examination of the results of an assessment provided in response to an order issued under section 21.31 of the Food and Drugs Act

- **Cancelled (Unreturned Annual)**: refers to a DIN that is cancelled due to failure to provide the Annual Drug Notification Form pursuant to paragraph C.01.014.6 (2) (a) of the Food and Drug Regulations. The DIN is no longer considered active.

6.3 Market notification

As per section C.01.014.3 of the Food and Drug Regulations, the manufacturer has the obligation to notify Health Canada when it first sells a drug that has been issued a DIN. A manufacturer must submit a completed DNF to Health Canada within 30 days of first selling the drug. The DNF must be filled out, signed, and dated. All pages of the DNF must be returned to Health Canada.

If a manufacturer has been issued a revised DNF (refer to section 6.1.1.2 for more information on revised DNF), it must notify Health Canada when it begins to market the drug with the authorized change. A manufacturer must submit a completed DNF to Health Canada within 30 day of selling the drug with new changes. The DNF must be filled out, signed, and dated. All pages of the DNF must be returned to Health Canada.

6.3.1 Completing the market notification

A market notification consists of:

- A cover letter
- A completed and signed DNF
- Labelling material, when applicable (see Table 3)

The DPD will only be updated to show the status as Marketed when a market notification is received and deemed accurate and complete.

The sections below outline for the manufacturer:

- how to accurately complete the DNF
- under which circumstances labelling material should be submitted

6.3.1.1 Part I of the Drug Notification Form

Part I of the DNF shows information currently contained in the DPD. It is the responsibility of the manufacturer to verify the information on the DNF when it is received. If any inconsistency is found in the contact information (i.e., mailing address, contact, telephone number, fax number, email address) for the DIN holder; agent; or, listed importer(s), the manufacturer

should cross out the incorrect information and fill in the appropriate space with the correct information.

Changes to the company name of the DIN holder; brand name; dosage form; route of administration; active ingredient(s); strength(s); and species (for veterinary drugs only) cannot be made on the DNF. Instead, the manufacturer must file a new application or submission.

6.3.1.2 Part II of the Drug Notification Form

Part II of the DNF contains information provided by the manufacturer as part of the market notification.

The following information must be provided in Part II:

- Date the drug was first sold in Canada following:
  - the initial authorization
  - the authorization of a change and for which a revised DNF was issued; or
  - a period of at least 12 consecutive months of no sales and for which a 12 months without sale notification was submitted to Health Canada
- Authorized official (title, signature):
  - Any person designated by the manufacturer to act on behalf of the manufacturer
- Date:
  - Date the DNF was completed and signed

6.3.1.3 Providing labels with market notification

Under certain circumstances, labelling material is required as part of the market notification.

In 2014, the publication of the Regulations Amending to the Food and Drug Regulations (Labelling, Packaging and Brand Names of Drugs for Human Use) (Plain Language Labelling Regulations) repealed the requirements in the Food and Drug Regulations to submit copies of marketed labels after a drug is available for sale.

As a result, to determine if a copy of the marketed labels should be submitted with a market notification for a drug, as per the Plain Language Labelling Food and Drug Regulations, refer to Table 3.

Table 3 - When to provide marketed labels for a market notification

	Date that the regulatory activity (e.g. NDS, DINA) was filed and authorized by Health Canada		
Drug Type	Before June 13, 2015	Between June 13, 2015 and June 13, 2017	After June 13, 2017
Prescription	Yes	No	No
Administered or obtained through a health care	Yes	No	No

professional (Ethical)			
Non Prescription	Yes	Yes	No
Disinfectant	Yes	Yes	Yes
Veterinary (Prescription and Non-Prescription)	Yes	No	No

6.4 Twelve months without sale notification - dormant status

After a drug has been marketed, it is possible that there may be periods where the manufacturer has not sold the drug. If any of these periods reaches 12 consecutive months, the manufacturer is obligated under section C.01.014.71 and subparagraph C.01.014.5(1)(a)(ii) of Food and Drug Regulations to report the period of no sales to Health Canada. The timing of reporting a period of 12 months without a sale is outlined below in sections 6.4.1 and 6.4.2.

After a complete notification is received and processed, Health Canada updates the status of the drug in the DPD to "Dormant". A drug that is deemed Dormant is still authorized for sale in Canada.

A manufacturer is required to report when 12 months have elapsed without a sale of its drug to Health Canada when the following conditions are met:

- the drug has received an NOC and/or a DIN
- the drug has been marketed; and
- the drug has not been sold on the Canadian market for a period of 12 consecutive months

In the case of a drug with no sales due to low market demand (e.g. small patient populations), if the manufacturer maintains an inventory of the drug, and the drug is still available for purchase on the Canadian market (available for immediate use via hospital and retail pharmacies [i.e., the drug is physically on pharmacy shelves]), the manufacturer is still required to report the DIN as Dormant as per section C.01.014.71 and subparagraph C.01.014.5(1)(a)(ii) of the Food and Drug Regulations. The manufacturer however has the opportunity to indicate the situation when they notify Health Canada.

However, in such circumstances, Health Canada may choose to keep the status of the DIN as marketed in the DPD in order to avoid unintended impact on treatment plans. If there are some sales, there is no obligation to notify under section C.01.014.71 or subparagraph C.01.014.5(1)(a)(ii) of the Food and Drug Regulations.

6.4.1 Reporting 12 months without sale within 30 days

Manufacturers of all drugs are encouraged to report 12 months without sale within 30 days as this will allow Health Canada as well as patients, health care practitioners, and other health care stakeholders to have a clear and up to date picture of which drugs are available on the Canadian market.

However, manufacturers of the following drug types for human use are required under section C.01.014.71 of the Food and Drug Regulations to submit a notification to Health Canada within 30 calendar days after a period of 12 consecutive months that a drug has not been sold on the Canadian market by the manufacturer:

- Drugs included in Schedules I, II, III, IV or V to the Controlled Drugs and Substances Act (http://laws-lois.justice.gc.ca/eng/acts/C-38.8/)
- Prescription drugs (https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/prescription-drug-list/list.html)
- Drugs listed in Schedules D and C to the Act (http://laws.justice.gc.ca/eng/acts/F-27/)
- Drugs that may be sold without a prescription, but are administered only under a practitioner's supervision (e.g., hemodialysis solutions, pre-filled syringes with epinephrine for severe allergic reactions, magnetic resonance imaging (MRI) contrast agents, insulins and vaccines), also known as ethical products

The 12 months without sale notification from the manufacturer should be in writing on company letterhead and signed by an authorized official. It should be sent electronically as per section 6.9 below.

The DPD will be only updated to show the status as “Dormant” when a 12 month without sale notification is received and deemed accurate and complete.

6.4.2 Reporting 12 months without sale for all drugs on the Annual Drug Notification form

For all marketed drugs, which have been issued a DIN under subsection C.01.014.2(1) of the Food and Drug Regulations, the manufacturer must indicate, on the Annual Drug Notification Form (ADNF), whether the drug is dormant at the time of filing.

Instructions on how to complete and submit the ADNF are included with the ADNF package sent to the manufacturer in June of each year by Health Canada.

Once the ADNF is received by Health Canada, the status of the drug will be updated on the DPD to “Dormant”. The status of “Dormant” will be assigned as of the signature date included on the ADNF.

6.4.3 Recommencing sale after being dormant

If the manufacturer restarts the sale of a drug that was previously reported as "Dormant", the manufacturer must submit, within 30 days after re-starting sale of the drug, a signed and dated DNF. The date that the sale was restarted should be listed on the DNF. The manufacturer should not use the date that the drug was initially marketed. Marketed labels for a drug that is subsequently marketed are not required with the DNF.

6.5 Notification of discontinuation of sale

The manufacturer must submit the notification of discontinuation of sale within 30 days after the sale of the drug was discontinued as per section C.01.014.7 of the Food and Drug Regulations. Health Canada cancels the DIN further to the receipt of the notification as per paragraph C.01.014.6 (1) (a) of the Food and Drug Regulations. The manufacturer remains subject to several obligations for its drug distributed prior to the cancellation of the DIN until the expiration of the last lot distributed or the longest time period referred to in the Food and

Drug Regulations. Refer to section 6.7 for more information on required activities following the cancellation of DIN.

The DPD will only be updated to show the status as “Cancelled” when a notification of discontinuation of sales is received and deemed accurate and complete. The discontinuation date provided in the letter will be added to the DPD. If the discontinuation date is not included in the letter, the date of the letter will be used.

- If the drug has never been marketed (i.e., “Approved” status in the DPD), the status of the drug will be updated on the DPD to “Cancelled (Pre-Market)”.
- If the drug was marketed or previously marketed (i.e., “Marketed” or “Dormant” status in the DPD), the status of the drug on the DPD will be updated to “Cancelled (Post-Market)”. The expiry date of the last lot distributed in Canada, the lot number, and the DIN cancellation date must be provided by the manufacturer and will be posted on the DPD.

Health Canada will send confirmation to the manufacturer and/or a designated representative that the DIN cancellation has been processed.

Drugs can only be cross-referenced to other already authorized drugs if their DINs are not cancelled. In addition, for drugs that have entered into a licensing agreement under the administrative pathway, following the cancellation of a DIN by a licensor, associated licensees should refer to section 2.5.4.1 of the Guidance Document Administrative Processing of Submissions and Applications: Human or Disinfectant Drugs (https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/guidance-administrative-processing-human-disinfectant-drugs.html) to understand the impact on their respective DINs.

6.5.1 Discontinuing after being dormant

After notifying Health Canada of the 12 month period without a sale, a manufacturer may decide that it will not resume marketing of the drug on the Canadian market again. In cases where the DIN has been listed as “Dormant”, the date of discontinuation should fall on any day after the date the drug became dormant.

6.6 DIN cancellation

There are many reasons that Health Canada can initiate the cancellation of a DIN. These reasons are outlined in section C.01.014.6 of the Food and Drug Regulations.

6.6.1 Cancellation due to safety issue

6.6.1.1 Cancellation due to concerns regarding safety and efficacy - C.01.014.6 (2) (b) of the Food and Drug Regulations

The cancellation of the DIN may be initiated by Health Canada when a manufacturer fails to provide Health Canada with sufficient evidence regarding the safety and efficacy of the drug for its recommended use.

Following the determination that a DIN cancellation is warranted, Health Canada will subsequently update the status of the drug on the DPD. The new status of the DIN, “Cancelled (Safety Issue)”, will be reflected on the DPD.

6.6.1.2 Cancellation following the suspension of a Notice of Compliance- C.01.014.6 (2) (c) of the Food and Drug Regulations

As outlined by paragraph C.08.002 (1) (c) of the Food and Drug Regulations, no person can market a drug with a suspended NOC. This prohibition on sale applies to the manufacturers and to all other parties such as wholesalers, retailers, pharmacists and medical practitioners and is effective on the date the NOC is suspended.

Following the suspension of the NOC, Health Canada may cancel the DIN in accordance with paragraph C.01.014.6 (2) (c) of the Food and Drug Regulations.

Further to the decision to cancel the DIN, Health Canada will subsequently update the status of the drug on the DPD. The new status of the DIN, “Cancelled (Safety Issue)”, will be reflected on the DPD. The NOC Database will be updated to indicate that the NOC has been suspended.

6.6.1.3 Cancellation following the failure to comply with the order to conduct an assessment and provide the results - C.01.014.6 (3) (a) of the Food and Drug Regulations

To enable Health Canada to regulate a drug more efficiently and effectively, Health Canada has the authority to order the manufacturer to conduct assessments, compile information, conduct tests or studies or monitoring of experience in respect of the drug and provide Health Canada with the results under section 21.31 of the Food and Drugs Act.

- For more information on Health Canada's authority to require assessment under section 21.31 of the Food and Drugs Act and authority to require test, studies, etc., refer to the following: Amendments to the Food and Drugs Act: Guide to New Authorities (power to require and disclose information, power to order a label change and power to order a recall) (https://www.canada.ca/en/health-canada/services/drugs-health-products/legislation-guidelines/amendments-food-drugs-act-guide-new-authorities-power-require-disclose-information-power-order-label-change-power-order-recall.html).

If the manufacturer fails to comply with the order under section 21.31 of the Food and Drug Act to provide the requested information, Health Canada may cancel the DIN in accordance with paragraph C.01.014.6 (3)(a) of the Food and Drug Regulations.

Further to the decision to cancel the DIN, Health Canada will subsequently update the status of the drug on the DPD. The status of the DIN, "Cancelled (Safety Issue)”, will be reflected on the DPD.

6.6.1.4 Cancellation following the examination of the results of an assessment - C.01.014.6 (3) (b) of the Food and Drug Regulations

If following the assessment of the information provided in response to an order under section 21.31 of the Food and Drug Act (as described in section 6.5.1.3), it is determined that the risks to injury or health outweigh the benefits, Health Canada may cancel the DIN in accordance with paragraph C.01.014.6 (3)(b) of the Food and Drug Regulations.

Further to the decision to cancel the DIN, Health Canada will subsequently update the status of the drug on the DPD. The status of the DIN, "Cancelled (Safety Issue)", will be reflected on the DPD.

6.6.2 Cancellation due to failure to provide annual drug notification - C.01.014.6 (2) (a) of the Food and Drug Regulations

Every year manufacturers must provide a signed copy of their Annual Drug Notification Form (ADNF) to Health Canada. The ADNF serves as an attestation that all the information previously provided by the manufacturer with respect to the drug is correct, and provides any related updates to Health Canada.

Each year before the 1st day of October, Health Canada will contact all manufacturers who have failed to return a signed copy of their ADNF to remind them of their regulatory obligations.

If, by the 1st of October, the ADNF has not been received by Health Canada, as per section C.01.014.5 of the Food and Drug Regulations, Health Canada may initiate the cancellation of the DIN(s). A written final notice will be provided to the manufacturer to inform them that their DIN(s) will be cancelled in accordance with paragraph C.01.014.6 (2) (a) of the Food and Drug Regulations and that it can no longer market the drug as per C.01.014 (1) of the Food and Drug Regulations.

Health Canada will subsequently update the status of the drug on the DPD to "Cancelled (Unreturned Annual)".

6.6.4 Cancellation as product is not a drug - C.01.014.6 (1) (c) of the Food and Drug Regulations

The cancellation of the DIN is initiated by Health Canada when it is determined that the product is not a drug under the Food and Drug Regulations.

In this situation, Health Canada will explain to the manufacturer in writing that the product is being reclassified and will no longer be regulated as a drug under the Food and Drug Regulations.

Health Canada will provide the manufacturer with the date on which the drug status will be changed and the DIN(s) cancelled. If applicable, information will be provided on the relevant regulations the product will be subject to in order for the product to be marketed in Canada.

Following the reclassification of the product, Health Canada will cancel the DIN and remove the product from the DPD.

6.7 Required activities following the cancellation of a Drug Identification Number

When a DIN is cancelled under section C.01.014.6 of the Food and Drug Regulations, no further sales may be made by the manufacturer since C.01.014 (1) of the Food and Drug Regulations prohibits a manufacturer from marketing a drug without a DIN.

To not create undue burden on industry, Health Canada may allow other parties in the downstream chain of distribution such as wholesalers, retailers, pharmacists and medical practitioners to continue to market or distribute the remaining drug after the DIN is cancelled, if:

- the expiry date of the lot has not passed, and
- the cancellation of the DIN was not due to health or safety reasons

If the DIN is cancelled, the drug can no longer be commercially imported into Canada.

If Health Canada becomes aware of any risk or non-compliance with respect to a drug with a cancelled DIN, Health Canada will take appropriate actions to mitigate the risk in accordance with the Compliance and Enforcement Policy (POL-0001).

The following scenarios are provided to illustrate some of the required activities that should be undertaken by a manufacturer following a DIN cancellation. Manufacturers should consult the regulations for the full details on their obligations.

Scenario 1: Safety updates to product monograph

Even if the DIN has been cancelled, the manufacturer should continue to file the appropriate submission(s) in order to incorporate additions or other changes to the Product Monograph related to safety (particularly with respect to contraindications, warnings and precautions, or adverse reactions) that may be necessary, as a result of newly available information, until all the lots of the drug that exist on the market have expired.

Scenario 2: Adverse reaction reporting

The requirements for manufacturers to maintain records of adverse drug reactions as per section C.01.020 of the Food and Drug Regulations, and for wholesalers and distributors to keep records as per section C.02.022 of the Food and Drug Regulations are still applicable after the DIN has been cancelled. Although the manufacturer is not obliged to report any new cases of adverse reactions received following the drug discontinuation, Health Canada strongly encourages the reporting of all serious adverse reactions and may request the provision of this information. Additional information on these reporting requirements for drugs for human use can be found in the Reporting Adverse Reactions to Marketed Health Products - Guidance Document for Industry (https://www.canada.ca/en/health-canada/services/drugs-health-products/reports-publications/medeffect-canada/reporting-adverse-reactions-marketed-health-products-guidance-industry.html).

Scenario 3: Sale, record keeping and reporting

A manufacturer discontinues the sale of a drug on February 28th and informs Health Canada on the same day. Health Canada cancels the DIN. However, the drug is currently on the market and the expiry date of the last lot is December 30th.

Wholesalers, retailers, pharmacists and medical practitioners may continue to market or distribute the drug until December 30th, if there were lots of the drug which were already in their possession before the DIN was cancelled. However, an importer cannot continue to import a drug with a cancelled DIN for commercial use.

The wholesalers, distributors and importers are still responsible for all the record keeping requirements of the Food and Drug Regulations, including C.02.022 of the Food and Drug Regulations, for all the lots of the drug that existed on the market, including the ones after the DIN was cancelled (i.e., between February 28th and December 30th). Under section C.02.022 of

the Food and Drug Regulations, records shall be retained for 1 year after the expiration date of the last lot unless the establishment license specifies some other period.

Scenario 4: Labelling update

In the case where a manufacturer cancels a DIN associated with a particular strength of a drug (e.g., Drug X, 10 mg) while maintaining the DINs associated with other strengths of the same drug (e.g. Drug X, 20 mg, 40 mg, 80 mg), the manufacturer is required to file a submission to remove the information related to the cancelled DIN from the labelling (i.e., product monograph, package insert, prescribing information, etc.) after the expiry of all the lots of the drug available on the market.

6.8 Reissuance of a DIN by Health Canada

Under specific circumstances, Health Canada may reissue the same sequence of numbers as the original DIN for the same drug after it has been cancelled.

The manufacturer must contact the Office of Submissions and Intellectual Property (OSIP) in order to determine the requirements for an application or submission to market the drug again.

The request should be sent by email to the OSIP at HC.DIN.SC@canada.ca using the template in Appendix A.

The information received from the manufacturer will be forwarded to the appropriate review bureau to determine what type of submission, if any, (e.g., S(A)NDS, DIN(A)(B)(F)PDC) should be filed in order to reissue the same sequence of numbers as the original DIN associated to the drug. The applicable submission fee, if any, and review timelines will apply.

At the discretion of Health Canada, DIN(s) may be re-issued without the filing of a submission and at no cost if the manufacturer can attest that there has been no change to the drug or its label since the cancellation of the DIN.

The drug for which the manufacturer is seeking a DIN reissuance is subject to all current regulatory requirements, which may include a look-alike sound-alike (LASA) brand name assessment. If a potential LASA issue arises, the drug for which the manufacturer is seeking a DIN reissuance may require a change to its brand name. Refer to Guidance Document for Industry - Review of Drug Brand Names (https://www.canada.ca/en/health-canada/services/drugs-health-products/reports-publications/medeffect-canada/guidance-document-industry-review-drug-brand-names.html) for more information on brand name assessments.

If the information provided by the manufacturer is acceptable, a DNF with the same sequence of number as the original DIN will be sent to the manufacturer. The status of the DIN in the DPD will be updated to Approved. The manufacturer will be required to notify Health Canada once the product is marketed as per section C.01.014.3 of the Food and Drug Regulations. Refer to section 6.3 above for more information on market notification.

6.9 Commercial exportation

When a manufacturer stops the sale of a drug for consumption in Canada but continues to market and export the drug, the exportation with or without invoking section 37 of the Act will determine whether the sale of the drug is considered to be discontinued in Canada.

- For more information on section 37 of the Food and Drugs Act, consult the document Intention to Invoke Section 37 of the Canada Food and Drugs Act for Products Being Exported (https://www.canada.ca/en/health-canada/services/drugs-health-products/compliance-enforcement/establishment-licences/intention-invoke-section-37-canada-food-drugs-act-products-being-exported.html).

6.9.1 Exportation without invoking Section 37

To export a drug without invoking section 37 of the Food and Drugs Act, manufacturers require, among other things, to hold a DIN and/or NOC, since these types of commercial exportations are usually considered sales in Canada.

In this case, the exported drug is not considered to be discontinued and manufacturers are not required to send a notification of discontinuation of sale to Health Canada. The product will continue to appear in the DPD with the status “Marketed” and the manufacturer remains subject to post-market obligations.

6.9.2 Exportation under Section 37

If the sale of a drug which was destined for consumption in Canada is stopped, but the manufacturer continues to export under section 37 of the Food and Drugs Act, the drug is considered discontinued in Canada.

In this case, manufacturers will be required to send a notification of discontinuation of sale to Health Canada. Once Health Canada receives the notification and deems it accurate and complete, Health Canada will updated the DPD to show the status as Cancelled (Post-Market).

6.10 Submitting notifications to Health Canada

For Health Canada to be able to process notifications received from manufacturers in a timely manner, all required documents must be provided, completed accurately, and submitted in the proper format.

6.10.1 Document requirements

Table 4 - Document requirements for notifications and requests for DIN reissuance submitted to Health Canada

Activity	DNF	Label
Market Notification	Required	Refer to Table 3
12 Months without Sale Notification	Not required	Not required
Discontinuation of Sale Notification	Not required	Not required

Request for DIN reissuance	Not required	Not required

When submitting a notification or a DIN reissuance request to Health Canada, the manufacturer must provide all required documents and information (see Table 4 for required documents). If the provided documents are incomplete or the required information in missing or incorrect, the notification will be placed on hold. Once Health Canada has received all required information and documents, the notification will be processed.

A confirmation email will be sent to the manufacturer once the processing of the notification or DIN reissuance request has been completed. No confirmation email is sent following the processing of a market notification. The manufacturer can confirm the status change by consulting the DPD.

6.10.2 Format and filing instructions

Market notifications, discontinuation of sale notifications, 12 months without sale notifications and requests for DIN reissuance must all be sent electronically. Duplicate copies must not be sent in paper format as Health Canada no longer accepts hard copies. As with other drug submission related information submitted electronically, any information received after 5:00 pm Eastern Standard Time, on a weekend, or on a statutory holiday will be considered received on the next business day.

Documents related to submissions filed in eCTD format must be prepared and filed as per the Guidance Document: Preparation of Drug Regulatory Activities in Electronic Common Technical Document Format (https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/ectd/preparation-drug-submissions-electronic-common-technical-document.html).

Documents related to submissions filed in non-eCTD electronic-only format must be prepared and filed as per the Updated – Guidance Document: Preparation of Regulatory Activities in the "Non-eCTD Electronic-Only" Format (https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/common-technical-document/updated-guidance-document-preparation-regulatory-activities-non-ectd-electronic-only-format.html).

Appendix A Template email – Request for DIN reissuance

To: HC.DIN.SC@canada.ca

Subject: Request for DIN reissuance for [Product Name – DIN XXXXXXXX]

Dear Sir or Madam:

I am requesting that Health Canada reissue DIN XXXXXXXX for [Product Name].

The following information is provided to assist Health Canada in determining whether the filing of a submission or application is needed to reissue the DIN(s).

1. Were there any changes in formulation since the discontinuation of the drug? Y/N
2. Were there any manufacturing changes since the discontinuation of the drug? Y/N
3. Is the product available in other jurisdiction(s) (e.g., United States Food and Drug Administration)? Y/N
4. Were there any labelling changes since the discontinuation of the drug? Y/N
5. Have there been any unexpected adverse events reported domestically or internationally? Y/N
6. Why was the DIN discontinued?

I certify that the information provided is true and accurate.

Yours sincerely,
[Authorized signature]