Health Canada Santé Canada

Therapeutic Products Directorate

Health Products and Food Branch

Direction des produits thérapeutiques

Direction générale des produits de santé et des aliments




Post-DIN Changes

CAPRA
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Canada

Topics to Cover

- New draft guidance
- Regulations governing changes to a Division 1 drug
- Reporting categories
- Filing Process
- Examples of Changes

Changes to Authorized Division 1 Drugs

Draft *Post-DIN Changes* Guidance document

Scope:

Pharmaceutical and veterinary drugs regulated by Division 1, and not subject to Division 8

Drivers for guidance development:

- Increased request for clarity from industry
- Internal inconsistencies in approach
- Need for more current interpretation of *Food and Drug Regulations (FDR)*

Similar in format to Post-NOC guidance documents

Based on existing *FDR*

FDR: C.01.014(1)

The *FDR* state 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.

FDR: C.01.014(2)

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.

FDR: C.01.014(4)

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;

(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.

New Drugs

- C.08.001 of the *FDR* defines a New Drug as:
  - "(a) a drug that contains or consists of a substance, whether as an inactive or inactive ingredient, carrier, coating, excipient, menstrual 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 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."

  – New Drug changes are subject to the *Post-NOC Changes* guidance documents.

Reporting Categories

A) DIN Application

…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):

- name of the manufacturer
- pharmaceutical form
- route of administration (except disinfectants)
- the premises for use (only disinfectants)
- quantitative list of the medicinal ingredients
- brand name

Reporting Categories

B) Notification

…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):

- whether the drug is for human, veterinary or disinfection use
- the name and quantity of each colouring ingredient
- indication
- dosage
- DIN holder address (and Canadian distributor if DIN holder is non-Canadian)

Reporting Categories

- Other Changes Affecting Terms of Market Authorization
  - name and address of any individual, firm, partnership or corporation, other than DIN holder/CDN distributor
  - the written text of all labels and package inserts to be used in connection with the drug and of any further prescribing information
  - the name and position of the person who signed the application and the date of signature
  - formulation changes
  - packaging changes

Filing Process

A. Notification which does not necessitate assessment
   - Document to SIPD/SKMD within 30 days

B. Notification which does necessitate assessment
   - Post-authorization Division1 Change (PDC)

C. Administrative DIN submission
   - Product and/or manufacturer name change

D. Amended DIN Application
   - DINF, DINA (L/S), DINA (form), DINA (form + supporting data)

PDC

- 30 day target date
- No fees
- Required to be filed within 30 days of making the change
  - Strongly recommended to be done prior to implementing the change
- Receipt of either a NOL or NSN upon completion of assessment

Documentation

All filed changes require the following basic documentation package:

i. A signed and dated covering letter on company letterhead that includes:
   a. the type of submission ;
   b. a narrative of the change(s) and a brief rationale for the change(s);
   c. a listing of all drug products affected by the change(s);
   d. a reference to the control number (for human use drugs) or DSTS number (for vet drugs) for the original/subsequent DIN Application; and
   e. when applicable, a description of the type of supporting data provided.

ii. A sample of all proposed labels; and

iii. The completed and signed documents:
   a. Drug Submission Application Form (HC/SC 3011) for each product in question;
   b. Drug Submission Fee Application Form; and
   c. Submission Certification Form.

Documentation

- Additional supporting documentation depends on the type of change

Examples of Changes

Snapshot of a guidance table:

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

Description of Change	Conditions to be Fulfilled	Supporting Data	Filing Process
Change in name of the manufacturer for a human drug or a disinfectant drug; or change in name of the manufacturer or importer for a veterinary drug	1	1	C
Conditions			
1. The recommendations outlined in the policy entitled *Changes to Manufacturer Name and/or Product name (2001-01-03)* are met.			
Supporting Data			
1. Common Information for Notifications and DIN Applications (as outlined in 4.1).			

Examples of Changes

Example 1: C.01.014(4), change to (a)-(f):

C.01.014.1(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:

Excerpt from table:

Addition, deletion or change, including quantity, to the medicinal ingredients of the product:

A. DIN application if:
-ingredient has been previously authorized
-no affect on scheduling status

B. New Drug if:
-ingredient has not been previously authorized
-results in a scheduling status change

Examples of Changes

Example 2: C.01.014(4), change to (g)-(k):

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

Excerpt from table:

I. Addition of a colourant:

A. PDC Notification if:
-colourant is listed in C.01.040

B. New Drug if:
-colourant is not listed in C.01.040

II. Remove or change amount of a colourant: PDC Notification

Examples of Changes

Example 3: Change to terms of market authorization [C.01.014(4), change to (l)-(n); other regulatory premarket requirements]:

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

Excerpt from table:

I. Revisions to the authorized signing authority for the drug submission originally listed on the HC/SC 3011 form

A. If the submission is complete and DIN issued:
Not required to file

B. If the submission is in progress
Notify SIPD/SKMD and Review Bureau immediately

II. The name of the contact for the DIN ownership, regulatory contact and/or billing contact changes.

A. If the submission is complete and DIN issued:
Notify SIPD/SKMD within 30 days

B. If the submission is in progress
Notify SIPD/SKMD and Review Bureau immediately

Examples of Changes

Example 4: Change to terms of market authorization [C.01.014(4), change to (l)-(n); other regulatory premarket requirements]:

C.01.014(2)(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;

Excerpt from table:

Revision of storage conditions

A. Not required to file if:

-product is OTC OR is not sterile OR storage was not reviewed as part of terms of market authorization

B. PDC Notification if:

-product is for vet use, is prescription, is sterile, or storage was reviewed as part of terms of market authorization

-revision is within comparable range (i.e. from “store at room temp” to “store between 15-25 °C”

C. DIN Application if:

-product is for vet use, is prescription, is sterile, or storage was reviewed as part of terms of market authorization

-revision is not within a comparable range (i.e. from “store at room temp” to “keep frozen”

Next Steps

Early Fall 2008:

60 day external consultation

Go to: http://www.hc-sc.gc.ca/dhp-mps/prodpharma/applic-demande/guide-ld/draft_change_din_ebauche-eng.php

Late Fall 2008:

Review of comments

Winter 2009

Implementation of Guidance

Questions?

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