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November 17, 2003

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TO: ASSOCIATIONS

I am pleased to inform you that a revised version of the document "*Drug Good Manufacturing Practices (GMP) and Establishment Licencing (EL) Enforcement Directive"* is now available on the Health Products and Food Branch Inspectorate Website at:

www.hc-sc.gc.ca/hpfb-dgpsa/inspectorate

This document replaces the previous version published in January 1998 and will become effective January 1st, 2004.

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Original signed by
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Jean Lambert
Director General

Health Canada
Health Products and Food Branch

Health Products and Food Branch Inspectorate

DRUG GOOD MANUFACTURING PRACTICES (GMP) AND ESTABLISHMENT LICENSING (EL) ENFORCEMENT DIRECTIVE

Supersedes:
January 1st, 1998

Date issued:
December 1st, 2003

Date of implementation:
January 1st, 2004

Ce document est aussi disponible en français.

TABLE OF CONTENTS

1. PURPOSE

The purpose of this document is to ensure the uniform, efficient, and effective enforcement of the requirement for all Canadian drug establishments[1], and any foreign drug establishments providing drug products to the Canadian market, to comply with Division 2 of Part C of the *Food and Drug Regulations*[2] (*FDR*) and to the requirements for Canadian drug establishments to hold an establishment licence (EL) to fabricate, package, label, distribute, import, wholesale, or test a drug in Canada.

This document is also intended to increase transparency by providing the industry with a clear description of the Inspectorate's role in applying the Drug Good Manufacturing Practices (GMP) and EL regulatory scheme and the internal steps followed when a proposal to suspend an establishment licence is contested.

2. BACKGROUND

2.1 General

The mandate of the HPFB is to take an integrated approach to the management of the risks and benefits to health related to health products and food by: minimizing health risk factors to Canadians while maximizing the safety of the regulatory system for health products and food; and, promoting conditions that enable Canadians to make healthy choices and providing information so that they can make informed decisions about their

[1]Includes establishments not subject to EL requirements as per C.01A.002 (d).

[2]C.R.C., c. 870, as amended. Also referred to as the "Good Manufacturing Practices" (GMP) Regulations".

health. To this end, the HPFB created a branch-level Inspectorate which works to ensure the compliance with and enforcement of federal legislation that sets standards for quality, health and safety, conditions for sale and the prevention of fraud and diversion from legitimate uses.

The Inspectorate is responsible for branch-wide compliance and enforcement activities, and provides an opportunity to achieve consistency of approach across the spectrum of regulated products. Using risk management principles and employing the best science available, appropriate standards are applied to regulated products and activities in order to maximize safety while balancing the availability and quality of the products.

2.2 Drug GMP Requirements

Drug GMP is that part of quality assurance which ensures that drugs are consistently produced and controlled to the quality standards appropriate to their intended use as required by the marketing authorization.

The Drug GMP requirements under Division 2 Part C of the FDR apply to all drug establishments that fabricate, package, label, distribute, import, wholesale, or test a drug and to which Division 1A (EL requirements) applies. Establishments exempted under Section C.01A.002 (d) are also required to comply with Drug GMPs. Compliance with Drug GMP requirements is assessed by conducting inspections of these establishments pursuant to the powers provided in s. 23 of the *Food and Drugs Act (FDA)* and complemented by corresponding with regulatees or making specific inquiries. As described in the next section, these inspections and the determination of compliance with Drug GMP requirements are the basis for the issuance of ELs to domestic sites.

2.3 EL Requirements

Important regulatory changes were introduced on January 1st, 1998 to provide for an EL framework under Division 1A of Part C of the *FDR* and to extend Division 2 to apply uniform GMPs for all drugs.

These EL requirements apply to all Canadian drug establishments except those exempted under *FDR* s. C.01A.002. Natural Health Products (NHP) establishments have been so exempted by paragraph (d) of that section. Despite this exemption to EL, *FDR* s. C.02.003 requires NHP manufacturers and importers to meet GMP requirements set on in Division 2 of the *FDR*

NHP will continue to be so exempted from EL requirements until S. C.01A.002 (d) is repealed, if the manufacturer chooses to retain its DIN during the transition period. This

transition will run until the issuance of an NHP site licence or December 31, 2005 whichever comes first; see sections 3 and 113 of the *Natural Health Product Regulations*.[3]

It should also be noted that an establishment which performs the tests specified in Division 2 must hold a licence as a testing facility. Although licenced fabricators, packagers/labellers, distributors (who holds a DIN), and/or importers who have their own testing laboratory, are not required to hold a licence which specifies testing laboratory, the testing is listed on the EL, thus providing more information on all the activities being carried out at a particular site. Wholesalers are not addressed in the exclusion since there are no product or material testing requirements for wholesalers.

It is Health Canada position that drugs presently subject to the drug EL framework (e.g. not exempted by C.01A.002 (d) which nonetheless fall within the scope of the new NHP Regulations) will remain subject to the drug EL requirements only until the day on which their NHP site licence is issued or December 31, 2005, whichever comes first.

In addition to the Establishment Licence under Division 1A of the *FDR*, fabricators, packagers/labellers, testers, distributors, importers and wholesalers of narcotics or controlled drugs, must hold a valid licence or have applied for a licence under the *Narcotic Control Regulations*[4] or Part G of the *FDR*, or under the Controlled Drugs and Substances Act. This licence is issued by the Office of Controlled Substances, Healthy Environments and Consumer Safety Branch, Health Canada.

An establishment wishing to obtain an EL must demonstrate that applicable requirements for Drug GMP have been met. To demonstrate Drug GMP compliance, the establishment will need to provide evidence that its buildings, equipment and proposed practices and procedures meet the applicable requirements of Divisions 2 to 4 of the *FDR*, ie. the establishment must have been inspected by the Inspectorate and have been subsequently found to comply with Drug GMP requirements and consequently been assigned a C

[3] Section 3 of the *NHP Regulations*:-Except where otherwise indicated in these Regulations, the provisions of *Food and Drug Regulations* do not apply to Natural Health Products
Section 113 of the *NHP Regulations*. - (1) A person who, before January 1, 2004, manufactures, packages, labels or import for sale a drug to which these Regulations apply may continue to conduct these activity in respect of that drug without complying with the requirements of Parts 2 and 3, until the earlier of
(a) the day on which that person's application for a site licence to conduct that activity in respect of the drug is disposed of or withdrawn, and
(b) December 31, 2005
(2) A person who conducts an activity under subsection (1) shall conduct that activity in accordance with the requirements of the Food and Drug Regulations.

[4] C.R.C., c. 1041, as amended

rating[5]. For foreign sites, they must demonstrate Drug GMP compliance by submitting inspection reports as described in the policy document entitled *Conditions for Acceptance of Foreign Inspections Reports for listing foreign sites on Canadian Establishment Licences*. These report are assessed to determine Drug GMP Compliance.

3. SCOPE

This policy applies to all persons subjected to the Drug GMP requirements outlined in Division 2 of Part C of the *FDR* including manufacturers of drugs for clinical trials and those subjected to the EL requirements outlined in Division 1A of Part C of the *FDR*.

4. DEFINITIONS

Terms used in this document have the same meaning as in the *Food and Drugs Act*[6] (*FDA*) and Regulations *(FDR)*. However, the following terms are defined for the purposes of this policy:

Class monograph: A document prepared by Health Canada that:

(a) lists the types and strengths of medicinal ingredients that may be contained in drugs of a specified class; and
(b) sets out labelling and other requirements that apply to those drugs.

Drug: Under the *FDA*, a drug 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 or abnormal physical state, or its symptoms, in human beings or animal;
(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.

[5]Ratings are classified according to the Inspectorate document entitled "GUI 0023 - *Risk Classification of GMP Observations*". There are two possible inspection ratings:
C = recommended for the continuation or issuance of the EL
NC = not recommended for the continuation or issuance of the LE.
Inspection ratings pertaining to establishments meeting the criteria of Section C.01A.002(d) are defined as conforming (**C**), or not conforming (**NC**) with the Drug GMP requirements.

[6]R.S. 1985, c. F-27, as amended.

Under Division 1A and Division 2 of Part C of the *FDR*, a drug means drug in dosage form (C.01A.001(2)), or a drug that is a bulk process intermediate that can be used in the preparation of a drug listed in Schedule C or D to the *FDA* that is of biological origin. It does not include a dilute drug premix, a medicated feed as defined section 2 of the Feeds Regulations, 1983, a drug that is used only for the purposes of an experimental study in accordance with a certificate issued under section C.08.015 or a drug listed in Schedule H to the *FDA*.

Establishment: Includes fabricators, packagers/labelers, distributors, importers, wholesalers and testing laboratories of biologicals, blood and blood components, pharmaceuticals, vaccines and radiopharmaceuticals.

GMP: means Drug Good Manufacturing Practices - Part C, Division 2 of the *FDR* and the interpretive guidelines**.**

HPFB: Health Products and Food Branch

Inspection: General monitoring activities to assess the industry's compliance with the Food and Drug Act and Regulations in accordance with established policies and procedures.

Inspector: A person designated as an Inspector under the *FDA* and authorised to conduct inspections of regulated establishments (Inspectorate Compliance Officer).

Inspectorate: Health Products and Food Branch Inspectorate

5. POLICY STATEMENT

An establishment, whether or not it is subject to the Drugs EL requirements, may be found to be non-compliant with Drug GMP requirements. In addition to being non-compliant with Drug GMPs, an establishment whose activities are covered under the Drugs EL Regulations, may not be in possession of a valid EL for the activities it conducts or wishes to conduct, for the following reasons:

- the establishment has not applied for an EL;
- the establishment has not renewed their EL by December 31st;
- the establishment has applied for, but was refused a licence due to a non-compliant (NC) inspection rating;
- the establishment has applied for a licence but certain foreign sites have not been approved for inclusion on the EL;

- the establishment has applied for an EL amendment or gave notice of a major change, but this request was denied;
- the establishment EL's terms and conditions have been amended or new terms and conditions have been imposed; or
- the establishment's EL has been suspended.

Consistent with the Inspectorate's *Compliance and Enforcement Policy* (POL-0001), appropriate enforcement actions will be considered in these situations, as the Inspectorate will not permit establishments to conduct regulated drug related activities without compliance with Drug GMP and/or EL requirements. These enforcement actions will be coordinated with any other violation discovered, such as Drug Identification Number (DIN) violations. Non-compliance with any other EL regulatory requirement, such as failure to apply for amendments, and failure to notify regarding changes made or proposed, may also result in enforcement action being taken.

Although the Inspectorate will work with drug establishments to help bring their operations into Drug GMP compliance, it will not tolerate chronic non-compliance with the regulations, which are meant to ensure that the health of the consumer is protected through quality and safety standards being met. Appropriate enforcement action must be considered in such situations to prevent further distribution of potentially unsafe drug products.

5.1 Non-Compliance with Drug GMP Requirements

Whether or not a drug establishment requires an EL, all must comply with Drug GMP requirements. Establishments that are found non-compliant with these requirements must take the necessary and timely corrective action to bring their operations into compliance. These firms must provide evidence of their commitment to comply with the Drug GMP requirements and submit a written plan of corrective action. Compliance is normally achieved following a cooperative approach between the regulated party and the Inspectorate; however, when this is not possible, or when the regulated party is unable to correct non-conformities, a number of enforcement options may be used to respond to non-compliance with Drug GMP requirements.

(a) Drug Establishments not Subject to EL Requirements

Enforcement action will normally be taken following a "Stepped Approach" (see section 6.2.4 "Stepped Enforcement Approach" for more details) following an evaluation by the Inspectorate to determine the most appropriate enforcement action(s) to be taken. This determination will consider the various circumstances of each case and will take into account, along with other applicable information, a number of factors as identified in the

Compliance and Enforcement Policy.

(b) Drug Establishments Subject to EL Requirements

Establishments subject to EL requirements must also comply with Drug GMP requirements, however, the EL regulations provide the Inspectorate with additional measures to deal with non-compliance such as:

- Refusal to Issue or Amend EL;
- Amendment of Terms and Conditions of EL; and
- Suspension of EL

The Inspectorate may, in addition to using these measures, use any of the other enforcement actions identified in the *Compliance and Enforcement Policy*.

5.2 Non-Compliance with Drugs EL Requirements

The Minister may suspend an establishment licence without giving the licensee an opportunity to be heard if it is necessary to do so to prevent injury to the health of the consumer, by giving the licensee a notice in writing that states the reason for the suspension. (C.01A.017(1)). All other situations will be handled according to the following:

(a) No application for an EL or no renewal by December 31 was submitted

Subject to paragraphs (I) and (ii), where an establishment is known to be conducting licensable drug-related activities and is required to hold an EL but has not applied for an EL, the Inspectorate will request, in writing, that the establishment suspend, within 15 calendar days of receipt of the notice, all licensable activities until they have received an EL.

(i) Establishments that have not applied for an EL but have been inspected and are in compliance with the Drug GMP regulations (‘C’ rating), including establishments which have submitted acceptable action plans or commitments to comply, will be permitted to complete any production that is in process, any importation in transit, and sell any stock on hand, during the 15 calendar days period following receipt of the notice.

(ii) Establishments that have not applied for an EL and are not in compliance with the Drug GMP regulations (‘NC’ rating), will not be permitted to engage in any licensable activity until they meet licensing requirements

and are issued an EL.

Any establishment that does not comply with licence application requirements within 15 calendar days of receipt of this notice, but continues to conduct licensable activities, is subject to immediate enforcement action.

(b) Application for an EL was received but licence was refused

Where an establishment has applied for a licence but the Minister refuses to issue the licence, in whole or in part, the Inspectorate's Director General, on behalf of the Minister, will notify the applicant, in writing, of the reason for the refusal and will give the applicant an opportunity to be heard. The applicant must suspend those activities, categories or dosage form classes for which the licence was refused, until EL requirements are met. Failure to comply with this notice within 15 calendar days of receipt of the notice will result in immediate enforcement action. This delay could be shortened based on risk evaluation.

(C) Application for an EL was received but certain foreign sites have not been approved for inclusion on the EL

Where an establishment applies for a licence as an "importer" but the Minister refuses to include a specified foreign site on that licence, the Inspectorate's Director General, on behalf of the Minister, will issue a notice advising the establishment not to import drug products from that site until that site has been approved and included on the licence and will give the applicant an opportunity to be heard. Failure to comply with this notice within 15 calendar days of receipt of the notice will result in action being taken to prevent products from being imported from unapproved foreign sites.

(d) Application for an EL amendment or notice of a major change was made, but was denied

Once licences have been issued, where an establishment has applied for a licence amendment or has given notice of a reportable change, and where this request has been denied, the Inspectorate's Director General, on behalf of the Minister, will issue a notice advising that the establishment is not to engage in the licensable or reportable change requested, and will give the establishment an opportunity to be heard with respect to refusal of amendments. Failure to comply with this notice within 15 calendar days of receipt of the notice will result in immediate enforcement action.

(e) EL's Terms and Conditions have been Imposed or Amended

Where a licence has been issued and subsequently amended by the Inspectorate's Director General, on behalf of the Minister, the establishment must comply with the new or amended terms and conditions. The Inspectorate's Director General will provide the establishment, in writing, with at least 15 calendar days notice of the reasons for the amendment and the date on which the notice becomes effective. Failure to comply with the terms and conditions will result in immediate enforcement action.

(f) EL has been suspended

Where a licence has been suspended by the Inspectorate's Director General, on behalf of the Minister, the establishment must suspend all licensable activities as of the effective suspension date until the EL in question has been reinstated pursuant to s. C.01A.018 of the *FDR* or another EL has been issued. Failure to comply with the final suspension notice will result in immediate enforcement action.

6. RESPONSIBILITIES/PROCEDURES

6.1 RESPONSIBILITIES

The implementation of this policy is the responsibility of the staff of the Inspectorate.

In general, Inspectors are responsible for:

- inspecting domestic drug establishments for Drug GMP compliance and making EL recommendations;
- monitoring regulatory compliance; and
- recommending and taking enforcement action.

In general, Managers of the Operational Centres are responsible for:

- if required, signing the letter confirming the NC rating
- representing the Inspectorate during the meeting with the Regional Director.

In general, Regional Directors are responsible for:

- chairing meetings to resolve issues related to non-compliance with Drug GMPs; and
- gathering facts and recommending to the HPFB Assistant Deputy Minister (ADM) the rating for the establishment.

In general, the Inspectorate's National Coordination Centre is responsible for:

- evaluating Drug GMP compliance of foreign drug establishments and making EL recommendations;
- recommending enforcement action where appropriate; and
- coordinating compliance activities.

In general, the Inspectorate's Director General is responsible for:

- issuing ELs;
- and
- issuing notices of refusal to issue or amend a licence, and notices to suspend a licence.

In general, the HPFB Assistant Deputy Minister is responsible for:

- taking final decisions on the rating of an establishment or the suspension of the licence in case of contestation.

6.2 PROCEDURES

6.2.1 Assignment of NC Inspection Ratings (see Appendix A)

In case of issuance of a NC inspection report, the Inspector will provide the management of the establishment with a letter and draft Inspection Report informing the establishment that the results may lead to enforcement action(s) being taken, including the suspension of its EL. The establishment will also be informed that the report will be submitted to an internal review group for quality assurance purposes and that as a consequence, the rating will either be confirmed or changed. Confirmation of the rating will be communicated to the establishment in a maximum of 45 calendar days, from the date the draft inspection report was provided to the establishment. However, establishments are encouraged to address the NC concerns immediately. During that period, measures other than EL suspension may also be taken to mitigate the risk. The final report will identify the deficiencies observed, if any, corrective actions to be taken by the establishment and the time within which the action(s) must be taken.

If the NC rating is changed to a C rating, the establishment will be informed in writing that the rating was changed. If applicable, the letter will identify the deficiencies, any action to be taken and the time within which the corrective action(s) must be taken. If the recommendation is to maintain the NC rating, the Inspector and/or Operational Manager will communicate with the establishment to inform them of the intent to maintain the NC

rating and will provide the establishment with an opportunity to meet with them.

The meeting will provide both parties an opportunity to discuss the draft Inspection Report, the corrective actions that should be taken to bring the establishment into compliance, time periods within which these should be taken, and possible terms and conditions or amendments to terms and conditions that could be imposed on the EL to prevent enforcement actions.

Following the meeting, the Operational Manager and Inspector will provide the establishment with the final Inspection Report and a letter confirming the NC rating, reiterating deficiencies and if any, the actions to be taken within 15 days. If no action can be taken within 15 days, the letter may identify possible terms and conditions or amendments to terms and conditions on the EL. The letter will also indicate that, unless the corrective actions are taken within 15 days, terms and conditions accepted, or an Intent to Contest is filed, enforcement actions will be taken [7].

6.2.2 Establishment's Response to Letter Confirming NC Rating

a) Establishment responds within 15 days that they have taken corrective actions

A re-inspection will be conducted by the Inspector to confirm that appropriate corrective actions have been taken. This re-inspection will be normally limited to one day. If the corrective actions are confirmed, the Inspector will issue a new Inspection Report with a C rating. If the inspection reveals that the corrective actions have not been taken, first notice of intent to initiate enforcement action will be issued, by certified mail, by the Inspector to the establishment outlining the offence and action to be taken by the firm. In the case of an establishment that possesses an EL, a proposal to suspend the EL will be forwarded to the Inspectorate's Director General.

b) Establishment responds that they will not take corrective actions and they don't intend to contest

A first notice of intent to initiate enforcement action will be made by the Inspector. In the case of an establishment that possesses an EL, a proposal to suspend the EL will be forwarded to the Inspectorate's Director General.

c) Establishment responds that they will not take corrective actions and they intend to contest

[7] In the case of an EL, a proposal to suspend the EL will be made to the Inspectorate's Director General.

No notice of intent to initiate enforcement action will be given, unless a risk to the health of consumers exists (refer to 6.2.3). In the case of an establishment that possesses an EL, no proposal to suspend the EL will be forwarded to the Inspectorate's Director General. The establishment will be required to forward a letter of Intent to Contest to the Regional Director where the site is located. Please refer to section 5 (Policy Statement).

d) In the case of an establishment that possesses an EL, the establishment responds that they accept terms and conditions

A re-inspection will be conducted to confirm that the establishment respects the new terms and conditions imposed on the EL. These terms and conditions will be related to prevent injury to the health of the consumer. If the inspection reveals that the new terms and conditions are respected, the Inspectorate's Director General will send a letter to the establishment to confirm the issuance of a new EL with the terms and conditions.

6.2.3 Situations where an immediate risk to the health of consumers exist

It should be noted that where it is necessary to do so to prevent injury to the health of consumers, immediate enforcement action such as product seizure, request for a recall of the product or products may be taken. In the case of an EL, a proposal to suspend an EL under section C.01A.017 of the *FDR* may be made to the Inspectorate's Director General at any time. The Operational Manager and Inspector may also, following the meeting with the establishment, when they are faced with a situation where no satisfying corrective actions are possible (for example, when there is evidence of record falsification or concealment) immediately recommend that a proposal to suspend the Establishment Licence under section C.01A.016 of the FDR be made to the Inspectorate's Director General.

6.2.4 Stepped Enforcement Approach based on the risk to the health of consumers

Notwithstanding the content of this Section 6.2.4, should any serious health risk be identified during the course of implementing enforcement action, more severe and immediate measures may be taken to ensure that no potentially hazardous products continue to be sold. Additional measures, such as recall or injunction, may be necessary to remove violative products from the market and prevent further distribution.

The first notice of intent to initiate enforcement action will be issued, by certified mail, by an Inspector to the establishment outlining the offence, enforcement action contemplated, and action to be taken. Notices issued by the Inspectorate's Director General, relative to refusal to issue a licence or refusal to amend a licence are also considered to be first level notices.

Where an establishment does not comply with the requirements of the first notice, within 15 calendar days of receipt of that notice, a second notice will be issued by certified mail, by the Inspectorate Operational Manager, requesting the establishment to stop sale of all drug products subject to the action and to suspend all specified licensable activities, until the establishment complies with Drug GMP and EL requirements. A Notice of licence suspension, issued by the Inspectorate's Director General, is also defined as a second notice.

Where no satisfactory response is received within 15 calendar days of receipt of the second notice and where there is evidence of continuing non-conformance, Inspectors will take all measures necessary to protect the health of consumers. Where applicable, the National Coordination Centre will also issue an alert to Canada Customs and Revenue Agency to refuse further importations.

In the case of a foreign site, a first notice will be sent by the Inspector in the National Coordination Centre (NCC) and failure to respond to that notice within 45 days will result in a notice issued by the Inspectorate's Director General advising the importer that the foreign site will be removed from the EL.

Where an establishment wishes to discontinue distribution of drug products in question, forfeiture, export, or other options may be proposed by the establishment to dispose of products in question. Such requests would be evaluated according to existing policies and procedures and according to any enforcement action in progress.

Where the products are to be exported to a country with which Canada has a Mutual Recognition Agreement (MRA), a Memorandum of Understanding (MOU) or that is a member of the Pharmaceutical Inspection Co-operation Scheme (PIC/S), the foreign authority will be informed by the Inspectorate. Where no such agreements are in place, the Inspectorate will make every efforts to inform the foreign regulatory authority of the status of the exported products.

6.2.5. Steps followed when a proposal to suspend an establishment licence is contested (see Appendix B)

The management of the establishment wishing to contest a decision confirming a NC rating is required to submit a letter of Intent to Contest to the Regional Director where the establishment's site is located. See Appendix C.

Within 15 calendar days of submitting a letter of Intent to Contest, the management of the establishment must file a comprehensive document with the Regional Director explaining their position and containing full supporting information in relation to the

decision being contested. Should the establishment wish to meet with the Regional Director, this should be indicated when filing the comprehensive document. The purpose of this meeting will be to provide the establishment with an opportunity to reiterate the major aspects of their contest as stated in their comprehensive document and to provide the establishment an opportunity to ensure the Regional Director is aware of the salient points of the establishment's position. There will not be a debate of the issues at this meeting. The Inspector and Operational Manager responsible for the original decision may attend this meeting.

The Regional Director's recommendation will be based only on the information and material upon which the original decision was taken. Any new information referenced or contained in the comprehensive document will result in its return to the establishment.

The Regional Director is responsible for reviewing all of the relevant documents and submissions and issuing a recommendation and report to the HPFB ADM regarding the contest. A copy of this recommendation will also be sent to the establishment. Within 20 calendar days from the filing of the comprehensive document or from the date of the meeting if one is requested, the Regional Director will make one of the following recommendations to the HPFB ADM :

- Recommendation that the NC rating be maintained;
- Recommendation that the NC rating be changed to a C rating;
- Recommendation that the NC rating be changed to a C rating with Terms and Conditions as identified in the original decision imposed on the EL.

The Regional Director's recommendation will be provided to the HPFB ADM in a package of information, that will include, in addition to the Regional Director's report, the following documents:

- Inspectorate Compliance Officer's Inspection Report;
- Internal Review Group's Report;
- Letter from Operational Manager and Inspector to establishment confirming NC rating;
- Comprehensive document filed by establishment;
- Minutes of Meetings; and
- Any other correspondence sent to or received from the establishment.

At the latest 5 days after the receipt of the Regional Director's recommendation, the establishment can submit in writing comments to the HPFB ADM. Within 15 calendar days of the receipt of the Regional Director's recommendation the HPFB ADM will consider the recommendations and inform the establishment of its final decision. The

HPFB ADM's decision will be one of the following:

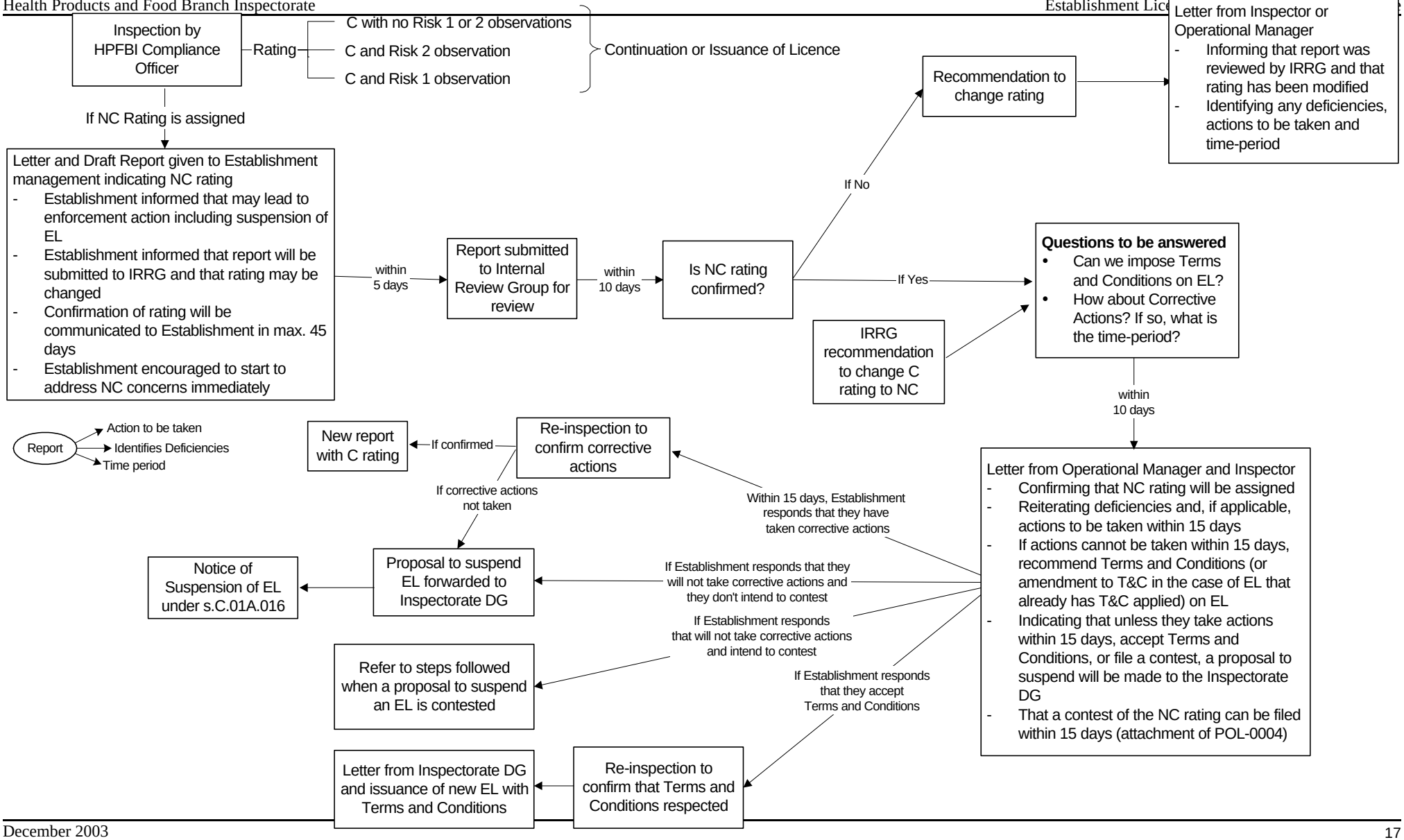
- Maintain the NC rating;
- Change the NC rating to a C rating;
- NC rating changed to C rating with Terms and Conditions imposed on the EL.

If the HPFB ADM's decision is to maintain the NC rating, a Notice of Suspension of the EL under section C.01A.016 of the FDR will be sent to the establishment, by the Inspectorate Director General, within 15 calendar days of the final decision. In this case, if a Certificate of Compliance was previously issued to a country with which Canada as a Mutual Recognition Agreement (MRA), the Certificate of Compliance will be cancelled by the Inspectorate and the foreign authority will be informed.

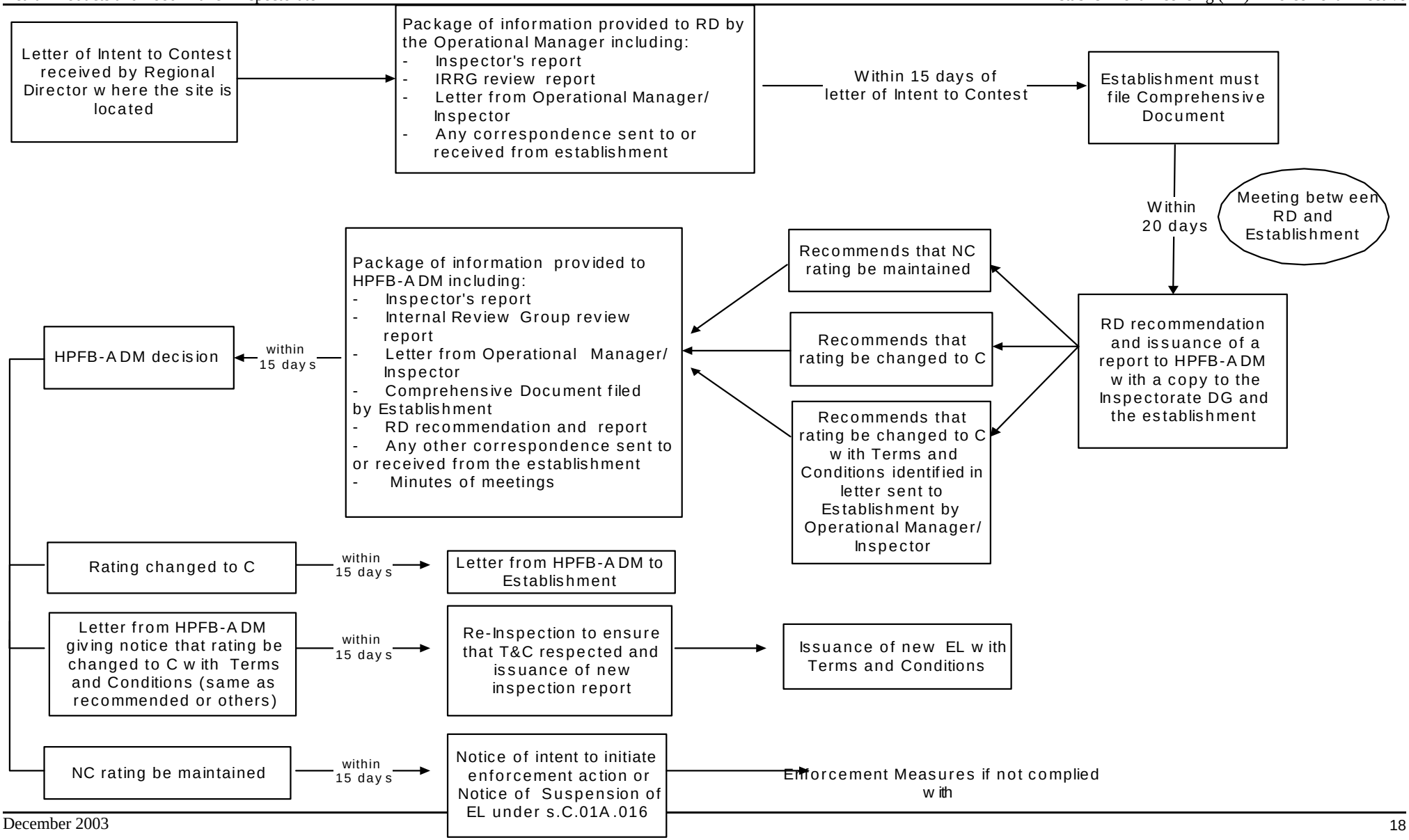
7. APPROVAL/EFFECTIVE DATE

This Drug Good Manufacturing Practices and Establishment Licensing Enforcement Directive was approved on October 27, 2003 by the Inspectorate Management Committee and is effective as of January 1st, 2004.

Appendix A. Steps in the Attribution of Inspection Ratings and Suspension of an EL under s. C.01A.016



Appendix B. Steps followed when a proposal to suspend an Establishment Licence is contested



Appendix C

List of Regional Directors offices

ATLANTIC REGION
Suite 1625
1505 Barrington Street
Halifax, Nova Scotia, B3J 3Y6

T 902-426-2161
F 902-426-7108

QUEBEC REGION
1001 West St-Laurent Blvd
Longueuil, Québec, J4K 1C7

T 450-646-1353
F 450-928-4455

ONTARIO AND NUNAVUT REGION
2301 Midland Avenue
Scarborough, Ontario, M1P 4R7

T 416-973-1475
F 416-954-4582

MANITOBA AND SASKATCHEWAN REGION
510 Lagimodière Blvd
Winnipeg, Manitoba, R2J 3Y1

T 204-983-3004
F 204-983-2363

BRITISH-COLOMBIA AND YUKON REGION
3155 Willingdon Green
Burnaby, British-Columbia, V5G 4P2

T 604-666-3704
F 604-666-1398