Health Canada Santé Canada

Filing Post-NOC Submissions to the BGTD

Stephanie Priest
Acting Manager
Submission Management Division
Centre for Policy and Regulatory Affairs
Biologics and Genetic Therapies Directorate
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Health Products and Food Branch
Direction générale des produits de santé et des aliments

Overview

- Post-NOC requirements for Biologics
- Lot release program
- Filing post-market changes for marketed Biologics
  - Changes to Marketed New Drugs Policy
  - Changes to Product-Specific Facility Information Guidance
- Tips for filing multiple changes

Post-NOC Requirements for Biologics

- Drug Identification Number (DIN) Notification within 30 days of first sale pursuant to C.01.014.4
- Lot release evaluation group obligations
- Annual DIN notification, includes list of Level 3 changes
- Filing post-market changes (SNDSs, NCs, DINBs)

Post-NOC Letter

- Issued by the Submission Management Division of BGTD following the issuance of the NOC

- Confirms:
  - Expiry dating
  - Lot evaluation group assigned
  - Requirements for lot evaluation group

Lot Release Program

- C.04.015

"Upon written request from the Director, a manufacturer shall submit protocols or tests with any samples of any lots of any drug prior to its being sold"

- Routine testing of all vaccine lots
- Targeted testing of other products

Lot Release Program

- Refer to the policy, "Review/Testing/Approval of Biologic Drug Lots"

- Rationalized, risk-based approach to product testing
  - Based on the assessment of several factors, BGTD establishes a risk profile for each product and assigns it one of four review/testing/approval categories.

Evaluation Groups

- Group 1
  - Pre-market samples: Clinical Trial materials and consistency samples
- Group 2
  - Post-approval: targeted lot testing, review and approval

Evaluation Groups *continued*

- Group 3
  - Post-approval: Protocol Review and Approval
- Group 4
  - Notification

Changing Evaluation Groups

- A company may request a change to the lot group for their drug
  - include a rationale
  - request addressed to the Director of BREC
- The Directorate may decide to change the lot group for a drug based upon the product history

Requirements for filing post-market changes for marketed biologics

Changes to Marketed New Drugs Policy, 1994

- 4 levels of change based on the significance of the change and the potential impact on the safety and efficacy of the product

Why are changes to biologics often assessed as higher impact than pharmaceuticals?

Nature of Biologic Drugs

- Not always well characterized
- Active ingredients are large and complex molecules
- The consistency, safety, efficacy and stability of biologics, especially vaccines, are dependent on clearly defining and adhering to the approved manufacturing processes
- Increased risk of the introduction of adventitious agents

Level 1 Changes

- Highest impact
- Requires a Supplemental New Drug Submission
- Examples of Biologic changes classified as level 1
  - Site change for drug substance or drug product manufacturing
  - Conversion of production and related areas from single to multiple product manufacturing

Level 2 Changes

- Medium impact
- Requires a Notifiable Change Submission (target default=90 days)
- Examples of Biologic changes classified as level 2
  - Change in product contact equipment used in a critical step to equipment having different specifications from the approved equipment

Level 3 Changes

- Minimal impact

- Notification required with the Annual DIN notification

Level 4 Changes

- No impact

- Record of change to be kept on premises

Changes to Product-Specific Facility Information Guideline, 1999

Background

- Prior to January 1, 1998, for biologic drugs not subject to Division 8, the provisions of C04.012 required the submission of information on changes to the premises in which a drug is fabricated be submitted in the form of a Licence Amendment.

Background *continued*

- With the implementation of the Establishment Licensing Framework on January 1, 1998, Section C04.012 was revoked.

  License amendment submissions became Biological DIN applications (since the Canadian Biological License no longer existed).

Scope

Guidance applies to

- SNDSs
- NCs
- DINBs
- Records and Notices of Change
- Records of Change

For “old” biological drugs

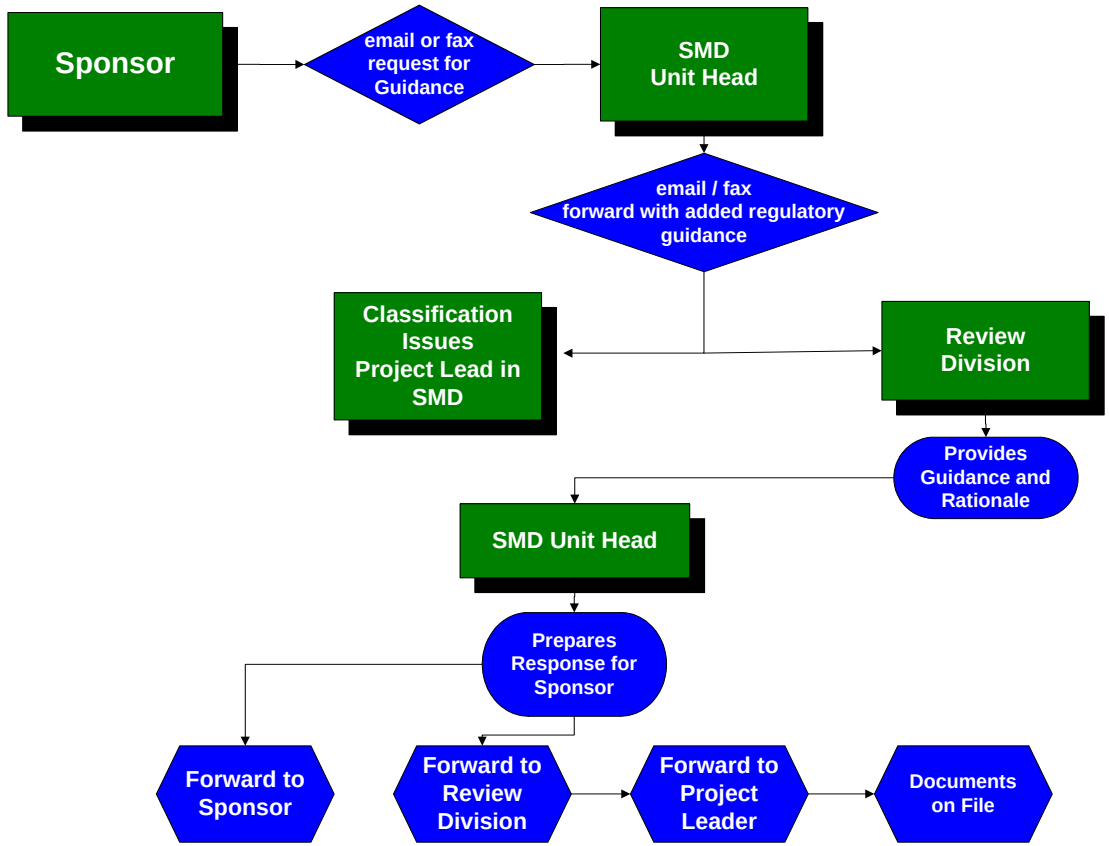
- Changes should be considered as equivalent to SNDSs or NCs
- Biological DIN application (change) should be filed
- Contact Submission Management Division for specific guidance on the requirements, format for DINB submissions

Changes to Product-Specific Facility Information

Based upon experience gained by BGTD since the posting of this guidance in March 1999, some examples in Sections 5c and 5d are being reassessed with respect to their impact upon the drug products. The final revised guidance document will include, as an addendum, additional examples for each category of change.

Post-Market Submission Classification

Process for Requesting Guidance



Tips for Filing Post-Market Submissions to BGTD

- For chemistry and manufacturing changes that affect more than one biologic drug (eg. Change in manufacturing for a component vaccine used in more than one multi-valent vaccine)
  - Submission required for each drug
  - Cover letter should state that change applies to more than one drug
  - Submissions should be filed together
  - Product-specific data may be required

TIPs for Filing Post-Market Submissions to BGTD *continued*

- When filing multiple NCs and SNDSs for the same drug
  - Once an approval is granted
    - Ensure that Product Monograph is updated for all related submissions in review
    - Ensure that the CPID is updated for all related submissions
  - Caution when filing NCs within SNDSs

What's Coming…

- Vaccine Barcoding project
  - Lead: Population and Public Health Branch (PPHB)

- BGTD/TPD Look-Alike Sound-Alike project
  - Lead: BGTD

References

- *Food and Drug Regulations*
- Management of Drug Submissions Guidance (MDSG), 2003
- Changes to Marketed New Drugs Policy, 1994
- Changes to Product Specific Facility Information, 1999
- Review/Testing/Approval of Biologic Drug Lots, draft 1996
- BGTD website:

http://www.hc-sc.gc.ca/hpfb-dgpsa/bgtd-dpbtg/

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Thank-you

Stephanie Priest
Acting Manager
Submission Management Division
Centre for Policy and Regulatory Affairs
Biologics and Genetic Therapies Directorate
Tel. 613-957-1488
Fax 613-957-0364

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