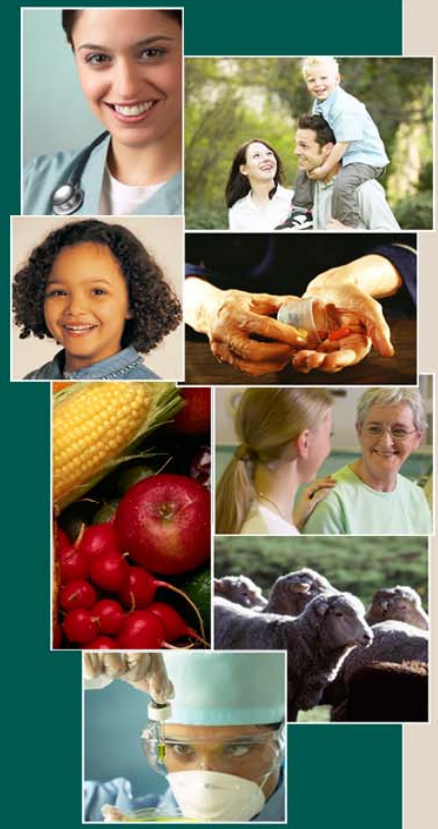
Health Products and Food Branch

Your Health and Safety - Our Priority



Post-Notice of Compliance (NOC) Changes:

Quality – Biologics for human use

Presentation to CAPRA

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Canada

Outline

- Guidance for biologics superceded by the Post-NOC Changes guidance
- Overview of New Guidance
  - Content and structure
  - Change in filing requirement (examples)
- Next Steps

Policies and Guidances for Biologics that will be superceded

- *Extension of Expiration Dates (1991)*
- *Changes to Marketed New Drug Products policy (1994)*
- *Changes in Product-Specific Facility Information (revised in 2004)*

Policies and Guidances for Biologicals that will be superceded

- *Extension of Expiration Dates (1991)*
  - If the approved shelf life is ≥ 24 months, any extension → Annual Notification
    - Considering that no changes were made to the packaging in direct contact with the drug or the drug's storage conditions
    - The extension was based on stability data generated on at least three regular production batches
  - If the approved shelf life is ≤ 24 months; any extension → Notifiable Change

Policies and Guidances for Biologicals that will be superceded

- *Changes to Marketed New Drug Products (1994)*
  - reflected “the regulatory amendments to C.08.003 proposed in Schedule 733”.
  - introduced to “reduce the number of instances where a S/NDS must be filed, and to provide an updated interpretation of the requirements of C.08.003.”
  - Defines 4 levels of change based on the potential impact on safety and efficacy
    - placed Notifiable Changes within the tiered structure

Policies and Guidances for Biologicals that will be superceded

- *Changes in Product-Specific Facility Information (revised in 2004*)
  - Provides guidance to the biological drug industry on making changes to a facility in which an approved drug product is being fabricated
  - Based upon experience gained by BGTD, the guidance was revised in 2004
  - Industry request for more examples

Overview of New Guidance

- Quality Document for Biologics
  - follows ICH CTD progression
  - resulting from extensive consultations with the Blood, Vaccine and Biotherapeutics Divisions
    - Reassess the level of change for any post-NOC changes and establish the required supporting information
    - Examine practices by other regulatory agencies

Result?

- Decrease in the filing requirement for several post-NOC changes:
  - Many changes that required the filing of S/NDS or NC may now be submitted as NC or Annual Notification, respectively
  - Somes conditions must be met
- Clear and comprehensive guidance could lead to better quality submissions and decrease the amount of correspondence between sponsor/regulator

Overview of New Guidance

(a) the *conditions to be fulfilled* for a given change to be classified as a either a Level I, II, or III change. If the conditions outlined for a given change are not fulfilled, the change is automatically considered the next higher level of change. For example, if the conditions recommended for a Level II - Notifiable Change are not fulfilled, the change is considered a Level I - Supplement. Similarly, if the conditions recommended for a Level I - Supplement are not fulfilled, the change would warrant the filing of an NDS or an ANDS3;

(b) the *supporting data* for a given change, either to be submitted to Health Canada and/or maintained by the sponsor. Where applicable, the corresponding modules of the Common Technical Document (CTD) for the supporting data have been identified in brackets;

(c) the *reporting category* (e.g., Supplement, Notifiable Change or Annual Notification).

Change in filing requirement - Examples

Change to a drug substance manufacturing facility, involving:	
Description of change	**Reporting category**
1. Addition of product(s) to an approved multi-product manufacturing area.	Annual Notification
Conditions	
1. The addition of product does not involve changes to the validated cleaning and change-over procedures. 2. The addition of product does not involve additional containment requirements.	

Change in filing requirement - Examples

Change to the cell bank	
Description of change	**Reporting category**
1. Generation of a new Master Cell Bank (MCB)	Notifiable Change
Conditions	
1. The new MCB is generated from a pre-approved Master or Working Cell Bank.	

Change in filing requirement - Examples

Change to the cell bank (cont'd)	
Description of change	**Reporting category**
1. Generation of a new Working Cell Bank (WCB) or a new Working Seed Bank (WSB)	Annual Notification
Conditions	
1. The new cell/seed bank is generated from a pre-approved MCB/MSB. 2 The new cell/seed bank is at the pre-approved passage level. 3. The new cell/seed bank is released according to a pre-approved protocol.	

Change in filing requirement - Examples

Change in a **facility** involved in the manufacture of a drug substance, such as	
Description of change	**Reporting Category**
1. relocation of equipment to another room at the same site ➔ ***conditions 1-3***	Annual Notification
2. modification to a non-critical manufacturing area (e.g., construction of a new warehouse on the site) ➔ ***conditions 2-3***	Annual Notification
3. change in the location of steps in the production process ➔ ***condition 1***	Annual Notification

Change in filing requirement - Examples

Change in a **facility** involved in the manufacture of a drug substance, (cont'd)
Conditions
1. The change in the location of steps has no impact on the risk of contamination or cross-contamination. 2. The modification has no direct product impact. 3. Re-qualification of the equipment follows the original qualification protocol, if applicable.

Change in filing requirement - Examples

Change in **equipment** involved in the manufacture of a drug substance, such as	
Description of change	**Reporting Category**
1. equipment change for an identical/ equivalent equipment	Annual Notification
Conditions	
1. Re-qualification of the equipment follows the original qualification protocol.	

Change in filing requirement - Examples

Change in a **facility** involved in the manufacture of a drug product, such as	
Description of change	**Reporting Category**
1. conversion of production and related area(s) from campaign to concurrent for multiple product manufacturing areas ➔ ***condition 1***	Notifiable Change
2. introduction of new product into an approved multi-product formulation/ filling suite ➔ ***conditions 2-3***	Annual Notification

Change in filing requirement - Examples

Change in a **facility** involved in the manufacture of a drug product, (cont'd)
Conditions
1. The manufacturing process is a closed process. 2. The newly introduced product has the same therapeutic classification. 3. The maximum allowable carry-over is not affected by the introduction of the new product.

Change in filing requirement - Examples

Description of change	**Reporting Category**
1. Qualification of a reference standard	Notifiable Change
2. Subsequent qualification of a reference standard ➔ ***conditions 1-2***	Annual Notification
Conditions	
1. Qualification of the reference standard is performed according to the approved protocol (i.e. no deviation from the approved protocol)	
2. The reference standard is not for a bacterial or a viral vaccine or <u>for a product in lot release Group 2</u>	

Next Steps

- Consider stakeholder feedback in finalization of guidance (Summer 2007)
- Implementation plan (Finalize by Summer 2007)
- Posting of Final versions of Guidance (Anticipated Fall 2007)
- Effective date (Early 2008)

Thank You

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Question???