Post-Notice of Compliance (NOC) Changes – Quality

Pharmaceuticals

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Canada

Outline

- Risk Management
- Development of Appendix 1
- Default Implementation
- Notifiable Change Backlog




Risk Management

- Risk = Probability X Consequence
- Classification based upon an assessment of the risk associated with the change
- Each classification level represents a “range” of risks




Development of Quality Appendix 1

- Determination of risks by Health Canada experts
- All consultation comments were considered
- Attempted to minimize supporting documentation to that considered necessary




Default Implementation

- NCs accepted before September 30, 2009 may be implemented after 90 days by sponsor
- NCs accepted after September 30, 2009 should not be implemented prior to receipt of No Objection Letter (NOL)
- BPS was notified of approximately 130 changes implemented in 2009 by “default”




Notifiable Change Backlog - Situation

- Approximately 300 Quality NCs in current queue at Bureau of Pharmaceutical Sciences
- Most will not be reviewed before 90 day target




Notifiable Change Backlog – Current Measures

- Additional resources assigned
- Existing NCs in queue now classed as Level 3 removed (approximately 10%)
- Streamlining of review for “less complicated” NCs (approximately 50%)




Notifiable Change Backlog – Outlook

- Current measures will likely not succeed in eliminating the NC backlog
- Sponsors are anticipated to continue to implement changes without prior approval
- Alternative approaches need to be realized




Future Revisions to Post-NOC Changes

- Review every 2 years as per *Good Guidance Practices*
- Review would consider any stakeholder comments received during this period
- Certain revisions such as for consistency and typographic errors can be made without consultation
- Extensive revisions that include changes to approach in risk classification would require external consultation
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Questions – How to use the tables

27. Replacement or addition of a drug product manufacturer / manufacturing site, involving:

b. production of an immediate release product (e.g., tablet, capsule, liquids, sterile liquids, semi-solids)

For an Notifiable Change (Level 2) the following conditions apply:

1.No change in the **Batch Formula**, Description of **Manufacturing Process** , Equipment Class and Process **Controls**, Controls of Critical Steps and Intermediates, or Drug Product **Specifications**.

2.No change in the **container closure system**.

Would still be a Notifiable Change if any other associated changes are Level 2 or 3.

Check any corresponding change examples:

17. Change in the **composition** of an immediate release solid oral dosage form (other than colours, flavours)

29. Change in the drug product **manufacturing process**

30. Change in the **controls** (in-process tests and/or acceptance criteria) applied during the manufacturing process or on intermediates

35. Change in the **specification** for the drug product tests and acceptance criteria, involving:

37. Replacement or addition of a primary **container closure system**....

...and so on.




Questions - DMFs for Level 3 Changes

When a Drug Master File/Letter of Access is required in support of a Level 3 change this information should be filed separately with SIPD- DMF Unit and not included with the Annual Notification.

The DMF may be reviewed as part of the auditing of Level 3 changes.




Questions- Content in DMF

2. Replacement or addition of a manufacturing site and/or manufacturer involving:

a. production of the starting material, intermediate, or drug substance

For an Annual Notification (Level 3) one of the conditions that applies is:

2.No change in the route of synthesis, physical characteristics, and impurity profile of the drug substance (that is [i.e.] no new impurity above 0.10%, no change in the approved total impurity limit and residual solvents within ICH limits).

Can a sponsor file this change as a Level 3 if the information to answer condition 2 is contained in a DMF?

No. The drug submission sponsor must have sufficient information available to allow the condition to be assessed.




Questions – Executed or Blank Manufacturing Documents

Executed manufacturing documentation should be provided as indicated in the Post-NOC Changes guidance.

Generally speaking, blanks should not be required as it is expected that the executed documents will represent the proposed change.




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