Post-Notice of Compliance (NOC) Changes

CAPRA Symposium

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Canada

Outline

- Overview of Post-NOC Changes Guidances
- Highlight the Major Changes
- Screening Experience Since Implementation
- Questions




Post-NOC Changes Project

- First draft – March 16, 2007
- Second draft – December 5, 2008
- Finalized Guidances posted on Health Canada website with effective date of September 30, 2009.




Post-NOC Changes Guidances

- Framework Document that provides overarching authorities, general description of the proposed reporting categories, drug submission filing and contact information
- Safety and Efficacy Guidance Document
- Quality Guidance Document
  - Appendix Tables
    - 1- Pharmaceuticals (TPD and VDD)
    - 2 - Veterinary Drugs – NEW (supplementary to Appendix 1)
    - 3 - Biologics
    - 4 - Radiopharmaceuticals




Post-NOC Changes Guidances

Scope and Application:

- changes to new drugs that have received an NOC pursuant to section C.08.004 of the *Food and Drug Regulations*
- pharmaceuticals, biologics, and radiopharmaceuticals for human use
- pharmaceutical, radiopharmaceutical and certain biotechnological products for veterinary use
- applies to those submissions for which a NOC has been recommended but issuance of the NOC has been placed on hold




Post-NOC Changes Guidances – cont'd

Oversight Required prior to implementation:

Level I (300 days*) –Safety and Efficacy & Quality

Level II (90 days) Safety and Efficacy & Quality

Level II (120 days) Safety and Efficacy

Oversight **not** required prior to implementation:

Level III - Annual Notification

Level IV - No notification req'd –Quality only




Post-NOC Changes Guidances – cont'd

Guidance documents supersedes:

- *New Drug: Sufficient Time* policy (1991)
- *Extension of Expiration Dates* (1991)
- *Changes to Marketed New Drug Products* policy (1994)
- *Stability Requirements for Changes to Marketed New Drugs* (1994)
- *Changes in Product-Specific Facility Information* (revised in 2004)
- *New Drug: Sufficient Time* Notice (2005)
- *Changes in Product Colours and Markings* (2005)




Highlight the Major Changes

Major changes:

- replaced the default date with a target date for Level II (90 day) change;
- addition of Level II (120 day) change with target date;
- retention of the Level IV change category -Quality sub-components only;
- new Appendix for Veterinary drugs (Appendix 2);
- electronic Level III form developed;
- CPID and PM not required to be submitted for Level III changes.




Screening Comments - Organization and Completeness of Submissions

Cover Letter

Safety and Efficacy changes -clearly indicate whether Level II (90 day or 120 day) or clarification request will be sent

Quality changes

- clearly indicate what changes are being filed referencing the corresponding section of the Guidance (i.e. change #);
- clearly indicate which relevant conditions have been met;
- clearly indicate whether all supporting data have been provided and ensure the data or rationale for absence is appropriately organized as per CTD format and location in submission (e.g. description of batches located under P.5.4).




Screening Comments - Organization and Completeness of Submissions

- SDN is sent by TPD if supporting data is not provided in the corresponding CTD section of the submission or clarification is required of its location;
- distinguish the NC from any other highlighted text (e.g. Level III change or Level IV);
- identify each NC if multiple changes are being proposed or if one NC change stems from another change (e.g. a revision to test specification where a new site of manufacture is being proposed)
- supporting data submitted “where applicable” (e.g. inner/outer labels only if affected by the change)




Screening Comments – Appropriate Classification of Quality Changes

- changes are not accurately classified with the conditions to be fulfilled

  (e.g. addition of a drug substance manufacturing site involving production of starting material, intermediate, or drug substance can Level I, Level II or Level III depending on condition to be fulfilled)




Example of Quality NC Screening Clarification

Notifiable Change for Brand Name (common name), Control No. #######

In accordance with section 2.2.3.3 of the Post-NOC Changes Framework Document and section 3.1 of the Post-NOC Changes Quality Document, the following information should be clearly indicated in your submission. *To facilitate the screening process, please indicate this information in your cover letter for future filings.*

1. Please state the nature of the change(s) being filed and the corresponding section of the guidance document.

2. Please indicate whether all relevant conditions have been met to qualify as a level II change as outlined in that section of the guidance.

3. It should be clearly indicated whether all supporting data listed in that section of the guidance has been included in the submission and organized as per CTD for Quality (Chemistry and Manufacturing). If any supporting data is not provided as outlined, a rationale explaining the reason should be listed.

To facilitate screening and review, you may wish to consider using a tabular format in your cover letter, as suggested below:

Description of Change	Conditions to be Fulfilled	Conditions Fulfilled	Supporting Data Required	Supporting Data Provided	Location in Submission

4. For situations where multiple changes are being proposed, or a level II change stems from another change (for example, a revision to test specification where a new site of manufacture is being proposed), each NC change should be clearly identified, as above.

In order for your submission to be acceptable for review, a complete response must be received within **XX** days of the date of this **facsimile/email.**




Screening Comments – GMP Compliance

Notice (January 22, 2010) Submission Filing Requirements - Good Manufacturing Practices (GMP)/Establishment Licences (EL)

For drug submission purposes, "evidence of GMP compliance" would include a:

- Valid Health Canada EL, or
- Current GMP compliance rating issued by the HPFB Inspectorate (TPD) or rationale for omission (BGTD)

This requirement is be applicable to all (NDSs), (ANDSs), (SNDSs), (SANDSs), (NCs) submitted for review to TPD/BGTD. Manufacturers need to have a satisfactory rating for their site for the particular dosage form.




Screening Comments – GMP Compliance – cont'd

- Note: GMP required for testing (drug substance release) for the drug product manufacturer whether or not the substance is sterile;
- refer to table - Summary of Good Manufacturing Practices (GMP) Requirements for Drug Submission Purposes




Screening Comments – Revision in Final Quality Guidance (Appendix 1 – Pharmaceuticals)

Since the release of these documents via email on September 30, 2009, the following corrections have been made to the Post-NOC Changes Quality document:

1) Appendix 1 - corrections in the supporting data requirements for changes #2b and #27d,
2) Appendix 6 - addition of "core" weight to the title of the table.

The final version posted on the Health Canada website has been corrected.




Screening Comments – cont'd

- For Clinical Changes (NC or SNDS):
  - PSURs should only be provided if they support a PM change, otherwise, submit all PSURs to MHPD in future;
  - If possible, Company Core Data Sheets (CCDS) should be provided to facilitate review;
- For Quality Changes (NC or SNDS):
  - signed and dated specifications are required.




Screening Comments – cont'd

Pre-submission enquires

(Section 2.2.2 of the Framework guidance)

- classification of a proposed change
- supporting documentation

Contact information

- *Guidance for Industry: Management of Drug Submission (Human drugs)*
- *Guidance for Industry: Management of Regulatory Submissions (Veterinary drugs)*




General Comments

Submissions submitted prior to Sept.30, 2009:

- where a Level II change has been submitted to Health Canada for which the review has not commenced, sponsors may request withdrawal of that submission if it is now classified as a Level III change. Sponsors should provide a written request to the appropriate review bureau;
- notify Health Canada that you have implemented NCs which have passed the 90 day default date.




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.




QUESTIONS

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Thank You

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