Revision to the Notice of Compliance with Conditions Policy and Guidance Documents

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Canada

Outline

- NOC/c Background
- NOC/c Revision Project
- Concepts for ANDS/SANDS submission under NOC/c
- Concepts for other revisions to the guidance document
- Next Steps




NOC/c Policy Background

A Notice of Compliance with conditions (NOC/c) is an authorization to market a drug (i.e. an NOC) with the condition that the sponsor undertake additional clinical studies to verify the clinical benefit

For consideration under the NOC/c Policy the drug must demonstrate:

- Promising clinical benefit;
- Be of high quality;
- Possess an acceptable safety profile based on a benefit/risk assessment.

No overriding safety concerns in order for the authorization to proceed.




NOC/c Policy Background

The objective of the Notice of Compliance with Conditions policy is to:

(a) provide access to promising new drugs for patients suffering from serious, life-threatening or severely debilitating diseases or conditions for which no drug is presently marketed in Canada or for which a significant increase in efficacy or a significant decrease in risk is demonstrated in relation to an existing drug marketed in Canada;

(b) create mechanisms for the appropriate completion of confirmatory trials to verify the clinical benefit of a drug authorized under this policy; and

(c) ensure transparency of the conditions associated with the market authorization.




NOC/c Policy Background

NOC/c Monitoring:

- Provide the results of confirmatory trials and other ongoing trials;
- Notification of specific areas of concerns (within 15 days)
- Adverse Drug Reaction Reporting;
- Post-market surveillance – Period Safety Update Reports (PSUR-c's).




NOC/c Policy Background

NOC/c Enforcement:

Regulatory options:

- Revocation of DINs, suspension of NOC (C.01.013, C.08.006)
- ADR reporting, and unusual failures of efficacy (C.01.016, C.08.008)

Non Regulatory Options:

- Changes to product labelling
- Restrictions for prescribing information
- Re-assessment/amendment of conditions
- Enhanced/active post-market surveillance




NOC/c Policy Background

NOC/c Policy Application:

- NDS/SNDS submissions only;
- Health Canada did not envisaged the acceptance of ANDS submissions into review that referenced a Canadian Reference Product (CRP) with NOC/c indications;
- it was viewed that confirmatory trials would be completed for the innovative product prior to patent expiration and entry of generic drugs on the market.




NOC/c Revisions Project

Issue:

The *NOC/c Policy and Guidance* do not address the situation when ANDS submissions reference a CRP which has been issued an NOC under the NOC/c policy and where the conditions have not yet been fulfilled.

Project Objective:

- Address the immediate gaps in the current policy
- Ensure that solutions are operationally feasible and consistently implemented:
  - processing of current ANDSs is aligned with the policy direction
  - issues arising from ANDSs are considered in the other policy and operational components




Proposed NOC/c Revisions:

1. Eligibility For ANDS submissions:

Current: ANDS eligibility criteria are not addressed in the Policy

Proposed: In circumstances where an ANDS or SANDS submission references a CRP with unfulfilled NOC/c conditions, the second-entry drug submission shall:

a) contain all the information and material to comply with the requirements of sections C.08.002.1 and C.08.005.1, pursuant to section C.08.004 of the *Food and Drug Regulations*; and

b) pursuant to section C.08.002.1(3)(d) of the *Food and Drug Regulations*, the ANDS or SANDS sponsor will be requested to provide similar undertakings to those provided by the CRP's sponsor prior to the approval of the ANDS or SANDS.




Eligibility For ANDS submissions (cont'd):

Rationale: Criteria based on the policy direction posted and detailed in the Notices.

Prior to authorization, undertakings for ANDS or SANDS submissions will, at minimum, include:

- enhanced post-market surveillance and reporting for the purposes of monitoring the safety of the drug product;
- a Product Monograph, Consumer Information Section and labelling that clearly highlights the conditions under which the drug product is authorized. The sponsor may also be requested to undertake to comply with restrictions imposed by Health Canada on the advertisement and/or distribution of the drug; and
- preparation of educational material including Dear Health Care Professional Letters for distribution to health care practitioners, and the Consumer Information Section for distribution to patients/caregivers.




Eligibility For ANDS submissions (cont'd):

- The sponsor may also be requested to undertake in writing to design, carry out and report on confirmatory trials to verify the clinical benefit of the drug. However, ANDS sponsor will not automatically be requested to complete the confirmatory trials.

- The necessity to conduct confirmatory trials by ANDS sponsors will be decided on a case-by-case basis through an appropriate clinical bureau evaluation.




Eligibility For ANDS submissions cont'd:

Consideration will be given to:

- the status of the original confirmatory trial(s);
- the potential to affect subject recruitment in both the original and subsequent confirmatory trials;
- potential competition for the same and possibly limited human and material research resources needed to conduct the trial; and
- ethical considerations for requesting a duplicative trial.

Health Canada's goal in these considerations is to avoid unnecessary delay of the completion of confirmatory trials and possibly undermining the objective of the NOC/c policy 'to create mechanisms for the appropriate completion of confirmatory trials to verify the clinical benefit of a drug'.




Proposed NOC/c Revisions:

2. Annual Progress Reports for Confirmatory Trials:

Current: "Sponsors may be required to submit to Health Canada reports on the progress of confirmatory studies."

Proposed: Sponsors will be required to submit to Health Canada on an annual basis status reports on the progress of ongoing confirmatory studies until the studies are completed.

Progress report template similar to US FDA's annual Post-Market Requirements Progress Report.

The template will include the commitment summary, the current status of the trial (confirmatory study pending, ongoing, delayed, terminated, or submitted), and details explaining the status and subsequent action taken.




Proposed NOC/c Revisions:

Annual Progress Reports for Confirmatory Trials (cont'd):

Rationale:

The manufacturer to provide this information annually, previously HC may have required a progress report to be submitted.

Addresses some of the critique for the NOC/c Policy and Guidance.

Template consistent with similar reports/processes in other regulatory jurisdictions.

Annual report can be used to identify issues earlier and allow opportunities for LOU amendments.



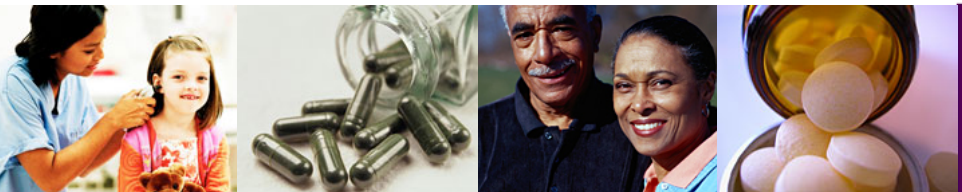

Proposed NOC/c Revisions:

3. Post-Market Surveillance Reporting

Current: “Provision of PSUR-'C's on a semi-annual basis until such time as conditions associated with market authorization are removed, is a commitment required of the sponsors at the time the Letter of Undertaking is drafted.”

Proposed: Sponsor will inform Health Canada in writing of the conclusions from the analysis of their annual summary report (PSUR-c). This document should indicated whether or not there is a 'significant change in the risk-benefit profile of the drug relating to its safe use'. HC can request the annual summary report or an interim report, the report will be requested to be in the Periodic Safety Update Report (PSUR) format.

Same requirement for NDS and ANDS submissions.



Proposed NOC/c Revisions:

Post-Market Surveillance Reporting (cont'd)

Rationale: Consistent with the branch Adverse Drug Reaction reporting based on MHPD's regulatory amendment published in CG I (June 13, 2009).

Consistent with NOC/c policy objective to confirm clinical benefit/efficacy; drugs approved under the NOC/c policy must have an acceptable safety profile.

The manufacturer will notify HC when a change is detected and opportunity for HC to request PSUR-c when warranted.

Documentation to be submitted to Health Canada can be based on part 9.0 Overall Safety Summary of the Periodic Safety Update Report (PSUR).




Proposed NOC/c Revisions:

4. Labelling, Educational and Marketing materials:

Current: "Fact Sheet" is the lay-language patient educational document, no DHPL template for ANDS, no linkage to HC NOC/c webpages.

Proposed: Replace the "Fact Sheet" with Consumer Information Section.

Add URL links for the NOC/c webpage to the NOC/c PM cover page box.

Created standard templates for NDS and ANDS DHPLs.




Proposed NOC/c Revisions:

Labelling, Educational and Marketing materials (cont'd):

Rationale:

Consumer Information Section is the comprehensive lay language document. Did not exist when NOC/c Policy was implemented.

Replacing the Fact Sheet with the Consumer Information Section will decrease the work for both reviewers and industry.

Standard templates for NDS and ANDS DHPL will decrease workload and be in a consistent format for the end user.

URLs links on the PM cover page will 'connect' the end user to the QN, DHPLs, and Consumer Information Sections and make the information more transparent.




Next Steps

- Draft revision will be posted on Health Canada's website for a 60 day consultation period
- Anticipated posting period is April, 2010

Contact Information:

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