December 10, 2010

Notice

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Submissions Seeking Changes to the Product Monograph Sections: (a) Clinical Trial Adverse Drug Reactions (3.5.2 - 3.5.3) and; (b) Post-Market Adverse Drug Reactions (3.5.5)[1]

This Notice clarifies the Health Products and Food Branch's (HPFB) position on the acceptability of certain changes to the Clinical Trial Adverse Drug Reactions Sections (3.5.2 - 3.5.3) and the Post-Market Adverse Drug Reactions Section (3.5.5) of a pharmaceutical and biologic drug Product Monograph.

The HPFB has received Supplementary New Drug Submissions (SNDSs) containing algorithms that detail the method used to examine the causality between a previously reported adverse event (AE) and the drug product, in order to support conversion of AEs to Adverse Drug Reactions (ADRs). Some of these submissions have also requested changes to the treatment-emergent adverse event (TEAE) tables, such as:

- removing an AE that was observed during clinical trials, based on the rationale there was low reporting of this event post-market; or,
- not including a TEAE observed in new clinical trials, based on the rationale the event has not been observed post-market in previously approved patient populations.

HPFB will no longer accept these types of changes to the Clinical Trial Adverse Drug Reactions Sections (3.5.2 - 3.5.3) and Post-Market Adverse Drug Reactions Section (3.5.5) of a drug Product Monograph. Where a submission is filed seeking only the types of changes described above, the submission will not be accepted to review. Where a submission is filed seeking various types of changes, the Sponsor will be asked to withdraw those changes described above, through a Screening Deficiency Notice (SDN).

The Product Monograph constitutes part of a drug's product label and contains the necessary information to support the drug's optimal, safe and effective use. HPFB believes that acceptance of the changes being sought by such submissions can lead to inconsistent drug product labelling, and may contribute to health care professional and patient confusion. To date, there is no universally accepted method for causality assessment of ADRs and recent reviews of causality assessment methods have outlined problems in testing for reproducibility and validity. In the absence of a universally accepted method for causality assessment, the Branch will no longer accept the types of changes to a drug Product Monograph described above.

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[1] *Guidance for Industry: Product Monograph*, October 1, 2004

Questions regarding this notice should be directed to:

Bureau of Policy, Science and International Programs
Therapeutic Products Directorate
Health Products and Food Branch
Health Canada
1600 Scott Street
Holland Cross, Tower B
2nd Floor, Address Locator 3102C1
Ottawa, Ontario
K1A 0K9

Fax: 613-941-1812
E-mail: Policy_Bureau_Enquiries@hc-sc.gc.ca