NHPD Consultation Submission
On
The Compendium of Monographs

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Bad Science Watch

Bad Science Watch is an independent Canadian consumer protection organization dedicated to promoting good science in public policy.

The following was prepared by volunteers and represents what we believe to be an honest, fair, and science-based evaluation. We are an independent body that is funded by private donations and we do not represent any corporate interests.

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Introduction

On behalf of Canadian consumers and our supporters we would like to submit for your review our comments regarding the *Revised Draft Guidance Document for the Compendium of Monographs*. Our primary concerns and comments focus on the how the document deals with issues of risk management and issues of off label use.

The Natural Health Products Directorate (NHPD) prepares and makes available compendium monographs that manufacturers can use in the Product Licence Application process. Licence applications that solely cite Compendium monographs in support of their safety and efficacy claims can expect an expedited licensing process under section 6. (1) of the *Natural Health Products Regulations*. The process is efficient for both manufacturers seeking licensing and the Natural Health Products Directorate since no further evaluation of safety and efficacy is required.

There are currently a wide variety of monographs available for use by applicants in the compendial stream. The monograph topics range from popular herbal ingredients such as Echinacea and St. Johns Wort to product categories such as homeopathy and traditional Chinese medicine. A product that receives a NPN or DIN-HM under the compendial application stream is not distinguishable from products licensed under the non-compendial stream to the consumer. All products licensed by the NHPD, regardless of the application process used are deemed “safe, effective, and of high quality” when used according to the information on the label and are intended for over the counter selection and use. For products licensed under the compendial stream, the information available to the consumer via the label is largely dependent on evidence provided and vetted by the Natural Health Products Directorate itself.

Issues of Risk Management

While the toxicity of many NHPs is generally viewed by the public as lower in comparison to pharmaceuticals (Ipsos Reid Public Policy, 2011), it should be noted that even substances with relatively low toxicity can have serious side effects(Ersnt, 1997). This is especially true for some individuals with inherent predispositions (Hanna , 2006). NHP’s are generally perceived by the public as carrying little to no risk compared with comparable over the counter medications and this pre-existing belief may drive consumers to misunderstand or ignore risk information as presented on the label (Krewski et al, 2006). All Compendium monographs should account for this reality via the use of clear, easy to understand risk information based on high quality, scientific evidence and should avoid risk statements that are based on lower quality traditional sources or anecdotal information. In the absence of a reliable evidentiary basis for risk statements, a statement that reflects this should be required by the Compendium monograph.

Further, and contrary to the perception of consumers that NHPs are safe, recent work has found that NHPs available in Canada can contain levels of toxic element contamination above preferred daily endpoints or serious contamination and/or adulteration (Genuis et al, 2012)(Newmaster et al, 2013).The use of the Compendial approval process may speed up approvals at the expense of ongoing quality assurance and product testing. The NHPD must consider the downstream risks inherent in the use of Compendial approval, given the known problems with toxic contamination of many NHPs and the inadequacy of the current regulatory regime.

There are some NHP ingredients and products that are known for their potential drug interactions, such as Saint John's Wort; one Canadian study found potential drug-NHP interactions in 28% of people surveyed (Singh and Levine, 2007). It is not clear whether the NHPD in constructing Compendium monographs assesses risk information with a preference for high quality scientific sources. Indeed it may be the case that for certain ingredients a lack of high quality information exists upon which reliable risk statements and warnings can be made. Relying on traditional or anecdotal sources for risk assessment and label statements exposes consumers to more risk than they would otherwise anticipate according to their pre-existing beliefs about NHPs in general and the information on the product label. Consumers can be expected to act on reliance of the information vetted by Health Canada on the label.

In many cases, the evidence that forms the basis of the recommended use or purpose of Compendium monographs may be of lower quality than that required for over the counter or prescription pharmaceutical products (Walji and Wiktorowicz, 2013). In these circumstances, the lack of efficacy or outright non-efficacy is the risk management issue that the Compendium fails to address appropriately. Risk cannot be viewed narrowly as encompassing only direct risk to the consumer, such as those arising out of interactions between NHPs and prescription products. There are indirect risks associated with delayed or inappropriate treatment that may not be appropriately considered by a consumer contemplating the use of an NHP (Davis et al, 2006). The preparation of Compendium monographs should therefore use an expansive view of the concept of risk and risk management.

There are several vitamin and mineral Compendiums in use that may require special attention by the NHPD in the compilation and evaluation of their risk information. Prior to the enactment of the Natural Health Products Regulations vitamins and minerals were regulated differently and carried a DIN on their label. Many consumers are familiar with these products and may not be aware of the change in regulatory status or that there has been a change in the way that the risks of these products are managed and assessed. The relaxation of standards for these NHPs may mean that consumers are unaware that these products may be more susceptible to contamination and/or recall than they were previously.

Finally, concerns arise over the granting of applicants latitude when making statements about the use or purpose, directions of use, duration of use and risk information of products. Although the guidance document is clear that application may "alter the wording, but not the intent" of these statements, the sheer variety of possible statements and variations on them makes it difficult to conclude that consumers would interpret what they read on the label in the same way. Words connote different meanings to different people. Considering the fact that applications in the Compendial stream enjoy a faster path to licensing, it would seem reasonable to require applicants to use the exact wording in the monographs, especially since review of the statements is not necessarily automatic.

Off-Label Use

The Natural Health Products Directorate currently licenses natural health products as "safe, effective, and of high quality". The license, by definition, refers to the intended use as indicated in the product's license application, and the Natural Health Products Regulations place limitations on the language that can be used in product labeling, marketing and advertising. However, via natural health media such as television shows, magazines and websites, claims for these products proliferate outside the purview of that NHPD (Government of Canada, 2007) Natural health products approved for sale by Health Canada are being indirectly marketed for off-label use, and practitioners are able to prescribe with no regard to the original license. Consumers do not base their decision making solely on Health Canada vetted information available on the label. There is no indication that the construction of any Compendium monograph takes this into account.

Careful monitoring of the marketing practices surrounding natural health products is essential to ensure that these products are being used as per their approved licensed monographs. Off-label use of NHPs effectively circumvents Health Canada's approval system and undermines assurances to the public that the products are safe and effective. The licensing process and the realities of alternative medical practice means that interested parties have nearly free reign to promote the dubious health benefits of these products. When practitioners and promoters are responsible for making off label claims there is no incentive for manufacturers or retailers to correct them. Indeed, some of these products would fail on the market but for off label promotion and use. Without close scrutiny of the real-world application of natural health products, both pre-market and post-market, this situation will continue. Currently, Health Canada's public assurances of safety and efficacy are undermined.

We urge Health Canada to acknowledge that the indication being applied for by the manufacturer often does not reflect how the product is being used in the marketplace. We hope that steps can be taken to minimize this practice and improve the efficacy of the licensing process as a whole. For products applying for licensure in the compendial stream this could take the form of a requirement that labels clearly list the indications that are not approved. For the composition of Compendium monographs this

would entail a direct investigation of how the products is marketed and used, compared to the evidence base.

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