Consulting Canadians on the Regulation of Self-Care Products in Canada: A Response

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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

This document is a response to the call for submissions for the public consultation on the new regulatory framework by the Non-Prescription and Natural Health Products Directorate (NNHPD) released September 7th, 2016. The outline of this proposal can be found here: http://healthycanadians.gc.ca/health-system-systeme-sante/consultations/selfcare-autosoins/document-eng.php.

This document was prepared by an expert panel concerned about the proper use of evidence in the regulation of NHPs. We have focused on NHPs but our concerns can be extrapolated to non-prescription and cosmetic products who make similar claims. Bad Science Watch has a commitment to advocate for the use of good science in public policy and looks forward for the updating of the current regulations, which we have criticized heavily in the past.

Recommendations follow every question found in the document above, with citations at the end of the document. A summary of our recommendations can be found in the conclusion.

Review

1. ***The category that best describes your perspective is:***

Consumer/Public Interest Group

2. ***What do you think of the risk-based approach for self-care products proposed in this document?***

A risk-based classification system is required, but requires more explicit classification criteria than is discussed in the consultation. With less regulation, companies with products that fit more than one category (for example, toothpaste), could potentially categorize a product to be within the lower risk category while promoting health claims through off-label sources.

The standard must explicitly prohibit off-label advertising or marketing of a product by the company or their surrogate that contravenes the license of the product, a practice that may be more widespread currently than realized by Health Canada (HC) (Ashar et al., 2003, Morris and Avorn, 2003). Off-label advertising includes articles in industry magazines, or in the online or popular press espousing the use of the product either in a paid advertorial or editorial style. More robust classification criteria would allow evaluation of marketing materials by both the consumer and the Inspectorate, and make very clear to the marketer what is allowed and disallowed under the regulations.

Recommendations:

1. That HC include in the regulations explicit rules for allowed and prohibited consumer communications both on and off of the label, given the product's risk stratification and evaluated claims.

2. That HC be given sufficient human and fiscal resources to adequately review and if necessary enforce consumer communications.

3. What do you think about Health Canada's proposal to group self-care products according to the above-mentioned levels of risk, i.e., risk-based grouping?

The risk based approach, as outlined in the proposal, is founded on the ability to reliably categorize products into groups based on level of risk. However, the basis for which products are categorized is not explicitly defined in the proposal. It is crucial that a set of criteria for defining precisely how grouping will occur is put into place. Without such criteria, a risk-based approach becomes biased in favour of the product and therefore useless as a consumer safety tool.

The proposal states that "Many self-care products have a long history of use and have been shown to be safe under specific conditions. Therefore, these products do not need much oversight by Health Canada before they go to market." This statement implies that the only criteria for a self-care product to be placed in the *Lower Risk Self Care Products* category is "a long history of use". It is implied that no investigation into current scientific literature would be necessary to allow inclusion into this category. It also assumes that manufacturers are accountable to quality assurance and good manufacturing processes, and safety standards.

Classifying self-care products by risk level is a meaningful step only if products are not arbitrarily grandfathered based on existing functional monograph claims, and if there is sufficient pre-and post-authorization surveillance to ensure that products are compliant with safety and efficacy claims on the product label, in-store marketing and internet website. This requires vetting of all claims for all categories prior to market release/authorization.

Recommendations:

1. That upon adoption of the new regulation, all currently licensed products undergo a license review to ensure that they are stratified to a level according to their actual risk.

2. That risk-stratification include evaluation of the inherent safety of the product, not just the claims made by the manufacturer or the lack thereof.

3. That HC advise the Government of Canada to change the law to include NHPs in the most recent update to the Food and Drugs Act that, among other things, made mandatory the reporting of adverse events by health-care professionals to HC.

4. That HC institute post-authorization surveillance of all approved NHPs for both license compliance, and quality.

4. How would the risk-based grouping impact your decision-making and your purchases of these products?

This grouping would to allow consumers and their health care professionals to make a risk-based decision only if one could be assured that the low and moderate risk products were in fact evaluated on the basis of sound scientific information.

Regretfully, some of the monographs created by HC in the past few years are weak, and not based on sound scientific evidence. HC maintains that product claims must meet set requirements (i.e. diagnostic, treatment, cure, or prevention claims). However, there is a concern that general claims which only speak to a function may be accepted; such as the claim used as an example in the consultation document that states that the functional claim "a source of omega-3" would be acceptable. However, at what risk level would these claims be acceptable?

Additionally, functional claims may be interpreted as inverse prevention claims. For example, a preparation marketed as "maintaining healthy bones" could be inferred as a product that prevents the deterioration of healthy bones. In other words, perhaps functional, diagnostic, treatment, cure, and prevention claims are not easily distinguishable.

An example of where an existing monograph may lead to a confounding of the proposed new framework is the HC monograph on Marigold Extracts (randomly selected by us). Two separate genera are linked to the common name "marigold" and this could possibly lead to confusion. The HC monograph is specific for *Tagetes erecta* (Family: *Asteraceae*). This is not to be confused with *Calendula* (*Calendula officinalis*) which was found as a monograph under a search for "Marigold Extract" in the Natural Medicines Comprehensive Database (NMCD) (Therapeutic Research Faculty, 2013).

The indications in the HC monograph are: "Antioxidant for the maintenance of eye health"; and "Provides antioxidant for the maintenance of eye health". According to the consultation document these indications meet the definition of a general function, hence these products may receive a *Low Risk* classification. These indications are not listed in either the Tagetes or Calendula NMCD monographs. Into which risk group would the "Marigold Extract" products be grandfathered, on the basis of this HC monograph? As a comparison, the NMCD Tagetes monograph states:

> "Safety: LIKELY SAFE ...when used orally in amounts commonly found in foods. Tagetes has Generally Recognized as Safe (GRAS) status in the US (4912) . There is insufficient reliable information available about the safety of tagetes used in amounts greater than those found in foods. PREGNANCY AND LACTATION: Insufficient reliable information available; avoid amounts greater than those commonly found in foods." (Therapeutic Research Faculty, 2013).

Another concern with the Tagetes HC monograph is that key references in the general section fail to support the claim as listed above. They include: Blakely et al. (2003), a study conducted in female rats; Dwyer et al. (2001), a publication on atherosclerosis; Miranda et al. (2006) on diabetic retinopathy (published in Spanish which limits the ability of most to evaluate the scientific integrity); and Bone and Landrum (2006) on human serum lutein and macular pigment optical density. None of these directly address the maintenance of eye health claims and are largely irrelevant.

There is also the risk of allergic reactions. The risk revision process would be compromised if this product with a generalized indication is grandfathered. Will a new risk categorization be undertaken along with revision of existing product monographs? If not, HC has then wasted our time and effort in providing a meaningful critique.

Most troubling in the HC monograph is in the sections: *Duration of use*, *Caution(s) and Warning(s)*, and *Contraindications*. In these sections, the phrase "No statement required" suggests that there is complete long term safety with these products, but no evidence is offered or required to substantiate these claims. It is generally accepted that if a product has pharmacological properties, there can be a risk for an interaction or adverse event.

As illustrated with this example, safety and efficacy based upon historical traditional use may not reflect the commercially available finished product, risks associated with interactions with other health care products, or possible allergen exposure. As noted in the consultation document, use of some products may delay the individual from seeking the appropriate health care for their condition as evidenced in the case where a child died as a consequence (Graveland, 2016).

Recommendations:

1. General and/or functional claims for self-care products must be stringently assessed and considered in the context of scientific evidence.

2. HC monographs need to be reviewed to ensure that they meet sufficient scientific scrutiny that allows for a sound risk to benefit assessment for all patient populations. This includes stringent allergy warnings.

5. ***What are your thoughts on the proposal to require scientific data to support a health claim? If you do not support, please explain why.***

Health claims should of course be supported by scientific evidence. What else would a science-based regulatory body otherwise allow? An example of concern is homeopathic products that have been allowed to make specific health claims on the basis of "traditional use" despite having no scientific plausibility for efficacy and relying on generally very poorly designed (i.e., often small and/or not properly blinded) clinical research studies (Linde and Melchart, 1998, Shang et al., 2005). Traditional use should be abolished and an objective threshold of research quality and/or quantity should be included in the proposal to better define how products are able to prove efficacy prior to approval.

We also argue that a requirement be set that a majority of documentation allowed to support health claims be peer-reviewed: Peer-review has been set as the international requirement for assessing validity of statements and experimental hypotheses, and as such this minimum standard should also apply to the use of scientific evidence as it applies here (Voight, 2012).

Additionally, the use of scientific evidence is vital so that health providers are informed and able to discuss the safe use of health care products with patients. As an additional example, in one study health care providers were consulted about the use of echinacea - a commonly used NHP - during pregnancy. Many suggested the product is safe and unlikely to be a concern, though studies do not exist to support these claims (Gallo et al., 2000).

The mandate of the Health Protection and Foods Branch can only be accomplished by use of a rigorous scientific approach.

6. ***If you do not support, please explain why.***

It must be emphasized that it may not be possible to rely solely on some published literature where the source of funding has not been established or conflicts of interest are not divulged. As well, studies that utilize improperly standardized products and/or substances along with adequate controls such as outlined in a US NIH guidance documents (NICCH, 2011) cannot be relied upon to render a clear picture.

Even more, publication bias as seen in the Tagetes monograph above where the findings have been extrapolated beyond the limitations of the study show a poor evidentiary standard. Therefore, we suggest that the scientific data be used to investigate and support claims only in the case where the literature meets a high standard of transparency and review. In vitro studies with animal-sourced

cells or tissues, or animal studies would have a lower evidentiary weight than studies with human tissues or clinical studies.

Recommendation:

1. There should be a clear hierarchy of evidence and a standard below which scientific studies should not be relied upon as evidence to affirm a claim made by a manufacturer.

7. ***Health Canada is exploring ways to provide Canadians with information that can assist them in making choices about self-care products, including the use of a disclaimer on product labels to identify claims that are not reviewed by the Department. What do you think about this approach? Would this type of information be helpful to you as a consumer?***

Such disclaimers should be required to be prominently displayed on the package and not relegated to the fine print. Otherwise, non-reviewed or non-approved products could be virtually indistinguishable from approved products particularly in the context of being sold next to other more strictly regulated and approved products such as pharmaceuticals. The average consumer may not be able to differentiate between HC approved products or pharmaceuticals and NHPs in similar packaging and making similar claims when these products are sold next to each other, as is often the case today.

Additionally, we suggest that information about known interactions and contraindications be listed on the label and in product monographs. This is critical as one Canadian study noted that a majority of NHP users were taking other medications (health products) simultaneously, and interactions between NHPS and other medications was found to be common (Singh and Levine, 2007).

Recommendation:

1. Any labels that warn the consumer that the product has not been tested for efficacy by HC should be prominently displayed on the front of the box so as to make the product distinguishable from a comparable tested product.

8. ***Do you think that a product identifier (i.e., a number on the product) is necessary to help consumers identify a product in the event that they wish to report an issue with the product?***

All products must have a product identifier. This is the only way that HC would be able to track products consistently with post-market surveillance. The inspectorate will need to be able to compare the claims, if any, made by the manufacturer or distributor about that product to the

claims allowed in the license or registration of that product. As well, a license number will make it easier to identify a product in a marketplace where many brands exist with the same or similar ingredients.

Recommendation:

1. All products regulated by the NNHPD should have a unique license or registration number associated with it.

9. Do you feel confident that the proposed safety oversight approach will allow you to continue accessing good quality, safe and effective products?

No.

10. If no, what are your concerns?

The proposed compliance monitoring, as written, is vague. It is stated that "as the potential risk of a product increases, HC would apply more oversight to it". In considering this question, we have the following concerns that are not stated:

I. How will products be monitored?
II. How often will it be monitored?
III. What action would be taken for non-compliance?
IV. How many violations and at what severity would be allowed before a product or company is banned or recalled?
V. What steps would be required to come into compliance if found non-compliant?
VI. How would these processes would be communicated to the public?

In considering oversight powers, off-label use must be considered, and is not discussed in this consultation. Off-label use of self-care products may place the product in a higher risk category (unknown to the consumer), and have adverse effects.

For example, one patient with oral cancer used rosehip oil, an NHP, as treatment, though a doctor had recommended surgery. The cancer progressed under this treatment regime and the patient passed away as a result (Blackwell, 2015). Accordingly, we suggest that off-label/non-regulated uses of NHPs be considered in the design of a comprehensive regulatory process.

The use of maintenance claims as well can be inferred to be a prevention claims, (e.g. for the maintenance of strong bones can be inferred to mean to prevent pathological bone loss) so these should be evaluated for evidence in support of these claims.

As well, some NHPs having been found in scientific research to contain undisclosed medicinal and/or non-medicinal substances, adulterants such as allergens, micro-organisms, and heavy metals such as lead (Genius et al., 2010, Newmaster et al., 2013, Ruparel and Lockwood, 2011, Zhang et al., 2013). Some adulterations may interfere with clinical or laboratory tests (Therapeutic Research Faculty, 2013). Any of these violations could have potentially lethal consequences. Therefore, safety monitoring of all NHPs should be treated with sufficient oversight to reflect such serious potential consequences.

Recommendations:

1. Apply the same quality assurance oversight that is required for pharmaceutical drugs. This would require a change in legislation to update the current low standard for the requirements of quality testing for NHPs.
2. When considering the approval of a new NNHP the off-label or common use of the product must be taken into account when assigned the product a risk level. If the common use is a high risk, the product should be placed in the high risk category.
3. Any plan for post-market surveillance and compliance oversight must be well-funded, specific, effective, and transparent.

11. Do you believe that additional powers to change labels, require a recall and new penalties would help address safety issues and discourage companies from breaking the law?

These oversight powers by HC would certainly help to address safety issues. As it stands currently, the onus is placed on manufacturers who clearly have a vested interest in continued sale of their product to remove an ineffective from the market or recall unsafe products. As such, the decision by a manufacturer to recall a product exists with an extraordinary amount of implicit bias. In matters of public safety, it is absolutely imperative that an objective party, such as HC, is involved in revoking market authorization or recalling unsafe products. The penalties should be based on total sales and need to be high enough to deter violations rather than appear as a "marketing licence fee" for companies. However, a proper monitoring system would at least detect violations and address issues as they occur in order to protect consumers. We made these recommendations to the House of Commons Standing Committee on Health during the deliberations of the Protecting Canadians from Unsafe Drugs Act (aka Vanessa's Law) in 2014. The risks of not including NHPs in this law

were outlined in our submission available at: http://www.badsciencewatch.ca/wp-content/uploads/2014/05/BSW-Vanessas-Law-2014-Brief-to-Standing-Committee-on-Health.pdf . Our recommendations were ignored in favour of lobbying by the makers and sellers of these products, and today NHPs remain the only product that cannot be mandatorily recalled by the government. This is shameful and should be rectified.

Clear evidence has been provided that sufficient quality control processes are not in place in the manufacturing of NHPs. When herbal products from a variety of companies were tested, it was found that most of the products contained ingredients not listed on the label (Newmaster et al., 2013). It was found that some of these adulterants are associated with known health risks. In another study, NHPs were found to be contaminated with toxic elements such as mercury, cadmium, lead, arsenic, or aluminum (Genuis et al., 2012). Furthermore, it was found that several common vitamins were associated with toxicities and adverse effects and had known drug interactions. This study demonstrated that NHPs assumed to be safe may in fact pose safety concerns (Rogovik et al., 2010).

These studies indicate that some companies which manufacture NHPs may have little interest in public safety. This as well as the fact that NHPs may in fact pose real health risks, further underscores the need for enhanced HC oversight and recall powers.

Another concern is that the perceived low risk products will not be adequately monitored and that some moderate risk products will be evaluated on the basis of faulty monographs. We have identified several problems in the public consultations on monographs we have participated in the past, and an evidence review of the existing monographs would be prudent.

In addition, HC has limited resources and therefore inadequate monitoring will be undertaken until after an incident. Most consumers would not be able to distinguish the risk level or recognize that the absence of a unique identifier designating a low risk group unless it was clearly stated on the label; in this case the legal onus rests with HC. All the evidence shows that NHPs in the low level risk grouping have a reasonable chance of being non-compliant with regards to quality/safety. Vulnerable individuals would be at increased risk from non-compliant products or products which may interact with pharmaceutical products given under the care of a trained healthcare professional or affect clinical testing. The risk-based grouping must also take into consideration the disease/condition and the risk of treatment failure. A moderate risk product used for a high risk disease/condition would not be acceptable.

Recommendations:

1. That NHPs be included in the changes that updated the Food and Drugs Act in Bill C-17, The Protecting Canadians from Unsafe Drugs Act, 2014.

12. If no, why not?

There are some ethical companies within industry, but there are also those who push the limits, or do not accept HC oversight, and thus put Canadians at risk with unsafe and/or ineffective products. An ethical industry should have no problems with HC having adequate powers and resources; particularly as some companies promote regulatory oversight as a marketing tool for their product(s). As well, there is a significant lobby led by the Canadian Health Food Association that is against these provisions and spreading misinformation about the banning of these products. Given this framework there is a balance to be struck between allowing a product that has a good safety profile to market with few restrictions and not allowing indefensible claims for the product's use.

13. Do you think the frequency of inspections of companies should vary depending on the risk category of the products these companies make?

The frequency of inspections of NHPs should be comparable to that of pharmaceutical companies. Companies that have a poor record should be subject to higher monitoring, even if their products are low risk. Products known to be adulterated with other herbals or related species should be subjected to enhanced surveillance. See our answer above re: quality assurance monitoring.

Recommendations:

1. The frequency of inspections should be similar to those of pharmaceutical companies, with increased scrutiny at plants with a history of quality violations.

14. Do you feel that the proposed Framework addresses any concerns you have with self-care products?

Many concerns are addressed, but there are also gaps.

15. What else could Health Canada include in the Framework to address your concerns?

A major concern is that products covered by an existing HC monograph should NOT be grandfathered when their claims are general or functional in nature. All product labels must be kept within a HC registry and be reviewed to ensure that no health claims are being made outside of their license.

The framework should ensure that all products for children be placed into the high risk category, with concomitant levels of evidence required for any claims made for the product.

All products should have a fee commensurate with their risk level so that adequate resources can be provided for approval and surveillance.

In section 5b in the sub-section detailing *Making Claims* there is a statement that "claims based on traditional systems of medicines" will be accepted; what does this mean, and is it an attempt to give homeopathic medicines an escape clause for making medical claims? Our concern is that many traditional preparations are being formulated and marketed as a non-traditional form and may then be used together with other health products for which there is minimal, if any, information on interactions and adverse events.

Recommendations:

1. No product based on a monograph and/or now making functional or general claims unsupported by evidence should be grandfathered.
2. All monographs should undergo a review to ensure that they have a high standard of scientific evidence.
3. Traditional use medications should be held to the same standard of evidence as all other products and not be allowed to make unsupportable claims.

Conclusion

Safety and Efficacy

All health products have risk, some more than others. Many traditional medicines are now being formulated in a non-traditional manner in capsules or tablets that have not been adequately evaluated for safety and efficacy, particularly in vulnerable populations along or when taken concomitantly with other health products. All claims should be regulated by a consistent science-based standard. As a minimum, all product labels should be reviewed by HC.

Quality Assurance

The QA standard should be applied to ALL products regardless of their risk-status. All producers should have the responsibility to put in place lab-based QA process and be subject to random mandatory inspections by the regulator (Newmaster et al., 2013, Genius et al., 2012).

The Inspectorate should have sufficient resources to conduct random QA testing of any product on the Canadian market.

Recall

NHPs remain the only product in Canada that does not have a mandatory recall. This is due to direct lobbying by the health food industry during the Vanessa's Law debate in 2014 that resulted in an explicit exemption of NHPs from the update to the FDA. Most products are safe when used as directed but HC must have sufficient authority to remove products which put Canadians at undue risk.

Labeling

If a product does not meet the minimum standard for evidence, it should not make any claim, and must contain a prominent label that says the product has not been tested for effectiveness and/or safety by HC. Marketing of the product cannot use claims of diagnosis, cure, treatment or prevention.

Health Freedom

Canadians have a right to self-medicate. Canadians also have the right to expect that products in our marketplace are safe and effective. Most consumers have a fundamental misunderstanding of these regulations - the regulations in this proposal are evaluating claims, not the underlying use of the NHP. If a company wants to market a product that is not on a restricted list due to safety concerns without clinical evidence of safety and efficacy, it could be brought in under the low risk category if there is some published literature under these guidelines. The only time that restrictions occur is if you want to make a medical claim, the problem being that an ambiguous generalized claim can be made which appears preventative or medical in nature.

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