22nd October 2012

Project Officer
Office of Complementary Medicine
Therapeutic Goods Administration
PO Box 100
WODEN ACT 2606

Dear Sir/Madam

RE: Comment on *Evidence Required to Support Indications for Listed Medicines (excluding sunscreens and disinfectants)*

Thank you for the opportunity to provide comment on the Therapeutic Goods Administration second consultation round on for the *Evidence Required to Support Indications for Listed Medicines (excluding sunscreens and disinfectants).*

Sanofi strongly supports the key recommendations and transitional arrangements as identified within the ASMI response to the TGA, including the modifications made to version 2 of the guideline document.

Our company representatives were involved in the development of the industry proposal and fully support comments made within the detailed analysis of the proposed guideline presented by ASMI.

We acknowledge the change that occurred from the previous round; however we still have some areas of concern outlined below.

- If implemented, the changes outlined in the document would have significant material impact on our business, and this impact is not understood by the TGA. Especially when you considered the possible implications to sponsors from coded indication changes occurring practically simultaneously.
- Sanofi acknowledges that other parts of the complementary medicines industry, as the TGA itself has already expressed, have exploited the ambiguity and/or lack of enforcement in the current system. Sanofi agrees that reform is necessary, however in the TGA's attempt to address these issues, the TGA has **over compensated** when drafting the proposed new Levels of Evidence guidelines. The unintended consequence will create a significant and unnecessary burden on Sanofi. Given our track record, Sanofi believes it should not be unfairly penalised in this manner as the TGA looks to address certain anomalies within the system.
- Sanofi fully supports the creation of a "level playing field". We suggest that a step by step approach to reforms, including a major focus on increased enforcement of existing regulations, will achieve the TGA's desired outcome.
- We agree with the TGA's overall intent to assure that complementary medicine sponsors hold the appropriate level of evidence to support claims made, but sections of the current document goes too far beyond what is required to achieve this. The overarching principles of effective regulation should ensure that any controls in place are proportional to the level of risk.
- Strong innovation is a key feature of the complementary medicine industry. The changes proposed may create a disincentive for sponsors to explore innovative new products. This may result in consumers seeking new products from overseas via the internet, which will steadily erode the Australian based industry, and put consumers at a public health risk of obtaining unknown ingredients from unregulated manufacturing sites.

Concerns consistent with ASMI response highlighted as major concerns to Sanofi:

1. **Revised Section A**
   It was industry's understanding that the Part A section of the produced document would have legislation underpinning, thus based on this it was revised to remove repetition from Part B the guidance document of 'how to' . The legislative entry should refer to the principles of the evidence requirements (Part A) and these should be clear and concise as possible.
2. **Sources of Established Evidence (SEEs)**
   TGA has acknowledged the acceptability of evidence draw from established sources provided that that these are in the list of resources recognised by the TGA. **However**, the list of accepted references while improved excludes a large number of sources put forward by industry, and there does not appear to be any mechanism to add other high-quality resources to this list.
3. **Nutrients and Nutrient Supplementation**
   The draft guideline includes a substantial increase to the percentage of RDI, adequate intake or nutrient reference value for vitamins/minerals/nutrients, from 25% to at least 50% in relation to statements supporting supplementation. This proposed change would have an unsubstantiated and unjustified impact on existing products in industry. We recommend that requirements of the current guideline are maintained to assist consistency and transparency. Suggested wording below:

   a) Health benefits: Statements relating to supplementation with vitamins, minerals or other essential nutrients (e.g. 'a source of calcium') imply a health benefit (i.e. the maintenance of good health). Health benefit claims are only permitted on products if the recommended daily dose of the product provides at least 25 % of the Australian Recommended Dietary Intake (RDI), Adequate Intake (AI) or nutrient reference value for that vitamin, mineral or nutrient.
   Claims should not refer to the presence of vitamins, minerals or nutrients (e.g. 'contains Zinc') unless they are present in the recommended daily dose of the product to at least the level of 10% of the RDI, AI or nutrient reference value for that vitamin, mineral or nutrient, unless there is evidence to support a therapeutic effect below this level.
   b) Prevention or treatment of a nutrient deficiency: If the indication refers to prevention or treatment of a nutrient **/ dietary** deficiency, the nutrient must provide at least 100 percent of the RDI, AI or nutrient reference value for the relevant nutrient.
   c) Specific Indications: Where vitamins, minerals or other nutrients are the subject of other indications, the dose must be consistent with the evidence to support the indication.
   Where available, Australian RDI, AI or nutrient reference values published by NHMRC are to be used. If there is no Australian RDI, AI or nutrient reference value for a vitamin, mineral or other nutrient, a nationally accepted RDI, dietary reference intake or equivalent nutrient reference value of another country may be used.
4. **Unreachable standards for Evidence Report**
   A number of the requirements for a review of scientific evidence are difficult or impossible to satisfy many requirements such as power calculations, clinically significant are not uniformly used and such requirements will have the effect of disqualifying a large body of previously acceptable evidence.
   In particular, the requirement to mathematically calculate the clinical significance of every relevant study, even when this has not been reported in the research paper, is unreasonable. For no apparent reason, the template demands the addition of a numerical d-value, itself theoretical, untested and rarely provided by researchers. However, the sponsor who calculates power or d-values, as recommended in the guideline, could then be accused of altering the data. This is inappropriate for low risk medicines and should not be required.

5. **Ineffective response**: Without increased and effective enforcement activity, the proposal will have little or no effect on existing non-compliant sponsors. In contrast, it will have a major adverse impact on our company as we already comply with the current guidelines and these proposed changes will result in an unnecessary cost and resource burden.
6. **Context:** We are aware that the TGA is working on a number of reforms affecting complementary medicines, including the Coded Indications project, labelling, transparency and advertising. This second draft evidence guideline in isolation of these critical components of the full reform package is considered difficult to assess the real-world impact of the full package.
7. **Disproportional:** The Council of Australian Governments (COAG) principles state that government action should be proportional to the issue being addressed. The requirements laid out in the evidence report section of this document appear to be equivalent to or higher than those for a registered over-the-counter medicine, yet applied to listed medicines which may carry only listable indications and claims. We consider them inappropriate for listed medicines which are low-risk by definition.
8. **Clarity:** The overall readability of the document is not user friendly and contains many occurrences of repeated/confusing information from preceding sections.
9. **Straightforward**: Requirements should be clearly spelt out and not added in as examples only.
10. **Advisory Statements**: There is no place for advisory statements in a guideline for evidence.