

Complaint to TGA – GSK Centrum immunity references

Acknowledgements:

This complaint was drafted and submitted by Mr Ron Batagol; the reference list was searched by Mal Vickers (Monash MPH student) and checked by Assoc Prof Ken Harvey.

Product and Sponsor

Product name: Centrum Advance (and others)

Sponsor: GlaxoSmithKline Consumer Healthcare Australia Pty Ltd

Address: Locked Bag 3, Ermington, NSW, 2115 Australia

ARTG no: 193683

Product Ingredients: Multiple vitamins and minerals, see ARTG

Advertisement type:

Internet – Web site

Accessed on:

5 June 2020

Claims (screen shots appended):

‘SUPPORTING YOUR IMMUNITY’

There are a number of vitamins and minerals that help build immunity.

- **Vitamin C** - Low levels of the antioxidant vitamin C are associated with poor immune cell function and a lower immune response². Vitamin C has been shown to improve certain immune cell activities. People taking vitamin C supplements may experience the common cold less frequently⁵⁻⁶
- **Vitamin E** - is an antioxidant that has been shown to improve certain immune cell activities
- **β-Carotene** - Processed by the body to form vitamin A, but may have its own immune activity⁷
- **Selenium** - Improves certain immune cell activities including white blood cell reproduction, immune cell adherence and migration, and cytokine production⁸⁻⁹
- **Zinc** - Improves certain immune cell activities, including phagocytosis, natural killer cell activity, T- cell reproduction, and antibody production⁵⁻⁹.

References cited:

- ¹Harvard Medical School 2014, How To Boost Immune System
²Shaik Y, et al. J Nutr Food Sci. 2016;6(1):456-458;
³Sorice A, et al. Mini Rev Med Chem. 2014;14(5):444-452;
⁴Puertollano MA, et al. Curr Top Med Chem. 2011;11(14):1752-1766;
⁵Sasazuki S, et al. Eur J Clin Nutr. 2006;60(1):9-17; 5. Hemila H. Nutrition. 1996;12(11-12):804-809;
⁶Wu D, et al. J Leukoc Biol. 2008;84(4):900-914;
⁷1. Puertollano MA, et al. Curr Top Med Chem. 2011;11(14):1752-1766
⁸Takeda S, et al. Biosci Biotechnol Biochem. 2008;72(6):1595-1600
⁹Huang Z, et al. Antioxid Redox Signal. 2012;16(7):705-743;
¹⁰AARP 2020, Boost Your Immune System
*where dietary intake is inadequate

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Concerns:

This reference list provided by a major pharmaceutical company is appalling. The only references with title of the articles are 1 and 10. References 4 and 7 are duplicated. There is no reference within the text of the advertisement to reference 1, 3, and 4. There are two references numbered 5. The first of these reference (Sasazuki 2006), is listed as a reference for **Zinc** in the text of the advertisement but, in fact, this reference relates to **Vitamin C**, not Zinc. Finally, reference 10 is not an academic journal but is a commercial organisation which gives 'advice;' to its registered members.

It is alleged that these references breach the following sections of the Therapeutic Goods Advertising Code (No.2) 2018:¹

15	Scientific or clinical representations
15(2)(a)	Where an advertisement makes a scientific or clinical representation, any scientific or clinical terminology must be appropriate, clearly communicated and able to be readily understood by the audience to whom it is directed.
15(2)(b)	Any scientific or clinical representation must be consistent with the body of scientific or clinical evidence applicable to the advertised therapeutic goods.
15(3)(a)	Where an advertisement contains a citation to scientific or clinical literature, either explicitly or impliedly, any research results must identify the researcher and financial sponsor of the research, where the advertiser knows, or ought reasonably to have known, that information; and
15(3)(b)	The study must be sufficiently identified to enable consumers to access it.

Detailed comments regarding the references cited:

1. Harvard Medical School 2014, How To Boost Immune System

This reference is incomplete and incorrect. The closest match to this appears to be an article on a website which has no listed author, has no references to support the claims made, and appears to be part of a commercial partnership selling health information. Regardless, "Centrum" is not mentioned on the webpage.

<https://www.health.harvard.edu/staying-healthy/how-to-boost-your-immune-system>

2. Shaik Y, et al. J Nutr Food Sci. 2016;6(1):456-458.

An incomplete reference, the journal title is not provided. The journal may be the 'Journal of Nutrition & Food Sciences', an open access journal of dubious quality. Volume 6, Issue 1 of this journal can be found online: <https://www.longdom.org/archive/jnfs-volume-6-issue-1-year-2016.html>. However, the author does not appear in this issue. Various other searching methods where tried, all failed to find the paper. Cannot be found.

¹ <https://www.legislation.gov.au/Details/F2018L01524/Controls/>

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3. Sorice A, et al. *Mini Rev Med Chem*. 2014;14(5):444-452.

Another incomplete reference, the journal title is not provided. Probably this paper: Sorice A, Guerriero E, Capone F, Colonna G, Castello G, Costantini S. *Ascorbic Acid: Its Role in Immune System and Chronic Inflammation Diseases. Mini-Reviews in Medicinal Chemistry*. 2014;14(5):444-452. The full paper can be found here: http://www.liposhell.pl/images/pdf/6_Sorice_A_et_al_2014.pdf. It is a narrative review (not a systematic review) of vitamin C, it is not a clinical trial of Centrum. The review does not mention Centrum. The paper does not confirm the benefits supplementation and notes there are risks associated with vitamin C consumption. “Individuals who have a history of kidney stone formation and those who experience iron overload should exercise caution before using AA supplemental...”. The paper suggests it would not be appropriate to consume vitamin C supplementation without a medical assessment.

4. Puertollano MA, et al. *Curr Top Med Chem*. 2011;11(14):1752-1766.

Yet another incomplete reference, the journal title is not provided. Probably this paper: Puertollano M, Puertollano E, Alvarez de Cienfuegos G, A. de Pablo M. *Dietary Antioxidants: Immunity and Host Defense. Current Topics in Medicinal Chemistry*. 2011;11(14):1752-1766. Only an abstract could be found here: <https://pubmed.ncbi.nlm.nih.gov/21506934/>. It is a narrative review (not a systematic review) relating to antioxidants. The review does not confirm that Centrum is beneficial to human health.

5. Sasazuki S, et al. *Eur J Clin Nutr*. 2006;60(1):9-17; 5. Hemila H. *Nutrition*. 1996;12(11-12):804-809.

This appears to be two references combined, a formatting error has occurred, both references are without the titles of the papers.

5A, Sasazuki S, et al. *Eur J Clin Nutr*. 2006;60(1):9-17

Probably this paper: Sasazuki S, Sasaki S, Tsubono Y, Okubo S, Hayashi M, Tsugane S. *Effect of vitamin C on common cold: randomized controlled trial. European Journal of Clinical Nutrition*. 2005;60(1):9-17. Only the abstract could be found: <https://pubmed.ncbi.nlm.nih.gov/16118650/>. This is a clinical trial. Population: n=305, diagnosed as having atrophic gastritis, not consistent with the population targeted by the advertising of Centrum. Intervention: 500mg vitamin C (not Centrum). Control: 50mg (low dose) vitamin C. Outcome measure: Total number of colds per month. Note the primary outcome measure was stated without confidence intervals. However, a different outcome measure was stated in the results: “After adjustment for several factors, the relative risks (95% confidence interval (CI)) of suffering from a common cold three or more times during the survey period was 0.34 (0.12-0.97) for the high-dose group.” Probable P-hacking at the reporting stage. This caution is noted in the conclusion: “However, considering several limitations due to protocol amendment, the findings should be interpreted with caution.” The outcome is not consistent with other trials of vitamin C and the common cold: https://www.cochrane.org/CD000980/ARI_vitamin-c-for-preventing-and-treating-the-common-cold

5B Hemila H. *Nutrition*. 1996;12(11-12):804-809;

Probably this paper: Hemilä H. *Vitamin C supplementation and common cold symptoms: Problems with inaccurate reviews. Nutrition*. 1996;12(11-12):804-809. Only the paper abstract could be found, here: <https://pubmed.ncbi.nlm.nih.gov/8974108/>. This is a critical review. It is critical of other poorly conducted reviews which investigate vitamin C and the common cold. This review does not agree that vitamin C is efficacious for the common cold.

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6. Wu D, et al. J Leukoc Biol. 2008;84(4):900-914;

An incomplete reference, the journal title is not provided. Probably this paper: *Wu D, Meydani S. Age-associated changes in immune and inflammatory responses: impact of vitamin E intervention. Journal of Leukocyte Biology. 2008;84(4):900-914.* Via Monash Uni library, it can be found here: <https://jlb-onlinelibrary-wiley-com.ezproxy.lib.monash.edu.au/doi/full/10.1189/jlb.0108023>. This is a narrative review (not a systematic review) relating to T cells, the immune response, aging and vitamin E. The review makes positive comments about vitamin E supplementation which are not well supported with evidence. Centrum is not mentioned.

7. 1. Puertollano MA, et al. Curr Top Med Chem. 2011;11(14):1752-1766

(repetition of reference 4)

8. Takeda S, et al. Biosci Biotechnol Biochem. 2008;72(6):1595-1600

Another incomplete reference, the journal title is not provided. Could not be found.

9. Huang Z, et al. Antioxid Redox Signal. 2012;16(7):705-743;

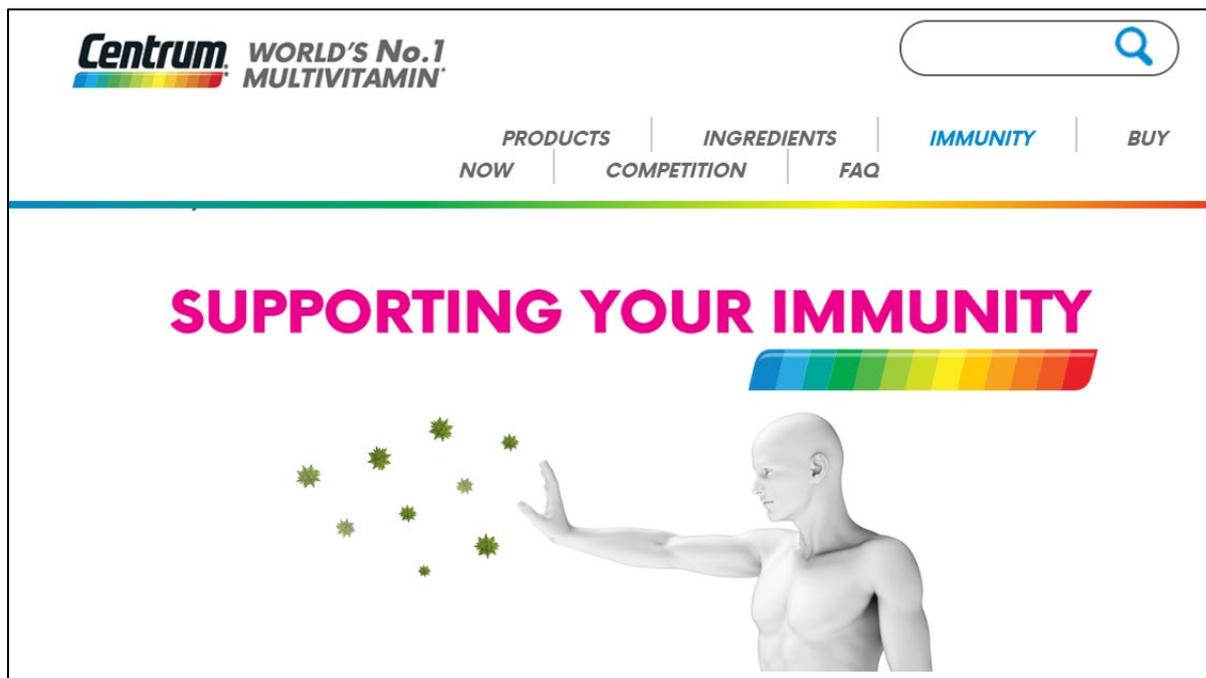
Another incomplete reference, the journal title is not provided. Probably this paper: *Huang Z, Rose A, Hoffmann P. The Role of Selenium in Inflammation and Immunity: From Molecular Mechanisms to Therapeutic Opportunities. Antioxidants & Redox Signaling. 2012;16(7):705-743.* The full text can be found here: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3277928/>. A narrative review of the evidence in relation to selenium and the immune system (not Centrum). The author expresses concern at the lack of available evidence: *“Once mechanistic studies have provided insights regarding the effects of Se supplementation on immune cells and networks, this information should be used to choose appropriate uses of this nutritional supplement for treating particular disorders or diseases.”* This paper does not recommend selenium supplementation.

10. AARP 2020, Boost Your Immune System

Probably from this Journal of Nutrition & Food Sciences <https://www.aarp.org/health/healthy-living/info-2020/boosting-immune-response.html> –commercial rubbish!

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Screen shots



Vitamins and minerals that support immune system function

There are a number of vitamins and minerals that help build immunity.

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⁸Takeda S, et al. Biosci Biotechnol Biochem. 2008;72(6):1595-1600

⁹Huang Z, et al. Antioxid Redox Signal. 2012;16(7):705-743;

¹⁰AARP 2020, Boost Your Immune System

where dietary intake is inadequate

<https://www.centrum.net.au/immunity>