SUMMARY STATEMENT

EXPERT GUIDANCE ON THE ROLE OF MICRONUTRIENTS IN SUPPORT OF THE IMMUNE RESPONSE AGAINST VIRUS INFECTIONS

An Expert Panel ("the Panel") was invited by Prof. Manfred Eggersdorfer and DSM Nutritional Products to independently review the global scientific evidence regarding the roles micronutrients play in support of the immune response, including against viral infections. Viral infections can be of particular concern, as highlighted by both seasonal influenza, and the recent outbreak of 2019 Novel Coronavirus (2019-nCoV). Indeed, viral infections are a leading cause of morbidity and mortality worldwide. For example, the WHO estimates seasonal influenza results in 3-5 million cases annually, while 2019-nCoV is spreading rapidly within China and beyond.

A number of standard public health practices, including hand washing and covering of coughs, are well-accepted to help reduce the spread of respiratory tract infections. A well-functioning immune system is also important to help reduce the risk of infections. For some viruses, such as influenza, effective vaccination programs have been developed to help prime the immune system in case of exposure.

Proper nutrition can also help support optimal immune function. The purpose of this document is to provide expert guidance regarding the safety and efficacy of micronutrients and omega-3 fatty acids in supporting immunity, particularly with respect to respiratory virus infections. The experience of the members of the Panel in the field of micronutrients, including the roles they play in immunity, was a key criterion in their selection to participate.

To assist in the Panel's review, the Panel members received a background document regarding the specific topic as well as a series of questions to be addressed by the experts. The Panel was encouraged to conduct its own literature survey.

Following the review of the above and other information considered relevant by the individual members, the Panel convened for a webinar on 6 February 2020, with Professor Calder providing input independently.

The panel considers that proper nutrition, including ensuring adequate micronutrient status, is one way to support effective immune function. Several vitamins, including vitamins A, B_6, B_{12}, C, D, E, and folate; and trace elements, including zinc, iron, selenium, magnesium, and copper, play important roles in supporting the cells and tissues of the immune system. Deficiencies or low status in micronutrients have the potential to negatively affect immune function and may therefore decrease resistance to infections. Other nutrients such as omega-3 fatty acids also support an effective immune system. In spite of the inconclusive clinical evidence, supplementation with micronutrients and omega-3 fatty acids appears to be a safe and low-cost way to support optimal function of the immune system, with the potential to reduce the risk and consequences of infection, including viral respiratory infections. It is important to stress that supplementation should be in addition to a healthy diet and fall within recommended upper safety limits set by scientific expert bodies, such as EFSA or the US Institute of Medicine.

CONCLUSIONS

In the opinion of the Panel, the following conclusions regarding the utility of micronutrients to support the immune response against viral infections can be made:

1. A well-functioning immune system is important to reduce the risk of viral infections, including respiratory tract infections. **Several micronutrients are understood to work together to support an effective immune system,** based on a variety of mechanistic and clinical data. These include vitamins - e.g. vitamins A, B_6, B_{12}, C, D, E, and folate - and minerals - e.g. zinc, iron, selenium, magnesium, and copper. As such, it is desirable to ensure optimal intake of all of these micronutrients to help support optimal functioning of the immune system.

2. **For some micronutrients, intakes above the nutrient requirements (e.g. recommended daily allowance [RDA]) may better support optimal immune function.** In addition, the requirements for certain micronutrients appear to increase during illness. As an example, vitamin C stores in the body decrease during times of infection.

3. **Optimal intakes of these micronutrients would ideally be achieved through a well-balanced diet, but this can sometimes be difficult to accomplish.** Indeed, gaps in micronutrient intakes relative to the RDA are common in both

developing and developed countries. For example, dietary sources of vitamin D are limited and synthesis in the skin is affected by season, climate, skin color, avoidance of sun exposure either actively or due to lifestyle.

4. **Micronutrient supplements offer a safe option to complement the diet to eliminate these gaps and help support the immune system.** Micronutrient intake should follow recommended upper safety limits set by expert authorities, such as EFSA and IOM.

5. **Omega-3 fatty acids support the immune system.** The omega-3 fatty acids EPA and DHA are key components for the immune response. An adequate intake may support resolution of inflammation which may be protective against symptoms of infection.

6. **The goal of micronutrient and omega-3 fatty acid supplementation is to help sustain optimal function of the immune system.** Indeed, the clinical data, while admittedly inconsistent, appears to support a potential for micronutrient supplementation to reduce the risk and/or severity of infections. Nevertheless, it is important to recognize that nutritional supplementation will not necessarily prevent infections, or cure the disease, but may help decrease symptoms and facilitate recovery.

RECOMMENDATIONS

In the opinion of the Panel, the following recommended intakes of selected nutrients may support a healthy immune system:

1. **Multivitamin and trace element supplementation**: A multivitamin and mineral supplement that supplies the nutrient requirements (e.g. RDA) for vitamins and minerals is recommended.

2. **Vitamin C supplementation:** Additional supplementation to a total intake of 200-500 mg/day for healthy individuals is supported. Vitamin C requirements depend on health status, and 1 – 2 g/day may be necessary to restore normal blood levels in individuals who are sick.

3. **Vitamin D supplementation:** Daily supplementation of vitamin D has been reported to be effective in reducing the risk of acute respiratory tract infections. Supplementation to 2,000 IU (50 μg) per day is recommended.

4. **Zinc supplementation:** Low status of zinc can impact the immune system. Therefore, a daily intake in the range of 8 – 11 mg is recommended.

5. **Omega-3 fatty acid supplementation:** Omega-3 fatty acid intake of 250 mg EPA + DHA per day is recommended.

In the opinion of the Panel, this guidance takes into consideration the latest scientific evidence and it is of the Panel's opinion that other experts qualified by their experience, would reach the similar conclusion on the basis of the totality of available scientific information.

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