## INTERNATIONAL NUTRITION, INC.

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## Dear Customer,

We have made formula revisions to our Nutrivene-D Daily Supplements that you will see instituted over the next few months beginning with the Daily Supplement Powder, Daily Supplement Microencapsulated Powder and lastly, the Daily Supplement Capsules. The formula changes we have made are outlined below.

Rutin, a bioflavonoid, has been added to the product. Research suggests that "rutin may be a promising neuroprotective compound for the treatment of neurodegenerative diseases." Abnormal tau is a characteristic of Alzheimer's disease which is more common in Down syndrome.

In the mouse model of tauopathy, "rutin reduced pathological tau levels, suppressed gliosis and neuroinflammation by downregulating NF-kB pathway, and rescued synapse loss in mouse brains, resulting in a significant improvement of cognition."<sup>2</sup>

Luteolin, another natural bioflavonoid, has also been added. Research on luteolin suggests that it "protects against behavioral deficits and enhances hippocampal learning" in mouse models of Down syndrome.<sup>3</sup> Further studies indicate that flavonoids like luteolin may have some benefit in potentially targeting the ageing process<sup>4</sup> and neurodegenerative diseases.<sup>5,6</sup>

We have reduced vitamin B12 levels slightly as we have observed a pattern of elevated B12 levels in blood tests. Should additional amounts be recommended by your healthcare practitioner, this ingredient can be provided as a separate product in liquid or sublingual lozenges.

The carotenoid lycopene has been eliminated from the formula as there have been concerns with skin conditions in some children. Further, the increasing costs of this ingredient warranted its elimination or the product would have substantially increased in price. If you wish to continue using lycopene, it is readily available in softgel form.

Please note the reduced dosages for the Daily Supplement products that correspond to these formula revisions. Should you have any questions or concerns, don't hesitate to contact us at 1-800-899-3413 or email us at ask@nutrivene.com.

Sincerely,

Robert M. Pugaczewski

President

Rober M. Puzayush

<sup>&</sup>lt;sup>1</sup> Oxid Med Cell Longev 2018 June 27;2018:6241017

<sup>&</sup>lt;sup>2</sup> Neuroinflammation 2021 Jun 11; 18(1):131

<sup>&</sup>lt;sup>3</sup> Neural Regen Res 2019 Apr; 14 (4):613-620

<sup>&</sup>lt;sup>4</sup> Pharmaceut Med 2022 Sept 13;1-22

<sup>&</sup>lt;sup>5</sup> Chemosphere 2022 Nov;307

<sup>&</sup>lt;sup>6</sup> Int J Mol Sci 2022 Sep; 23 (17):10020