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Mera Pharmaceuticals
Bringing the Ocean to Life

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To whom it may concern:

I have been asked if the phytochemical profile of *Haematococcus pluvialis*, when produced commercially using very similar production methods, can be expected to be substantially equivalent, even if different strains of the algae were used as the basis of the production. In my opinion, the answer to that question is yes.

The chemical structure of astaxanthin consists of a long chain of carbon atoms held together by conjugated double bonds with two carbon rings at both ends. For that reason, astaxanthin can exist as a number of geometrical isomers (*cis* or *trans*). The all-*trans* carotenoid isomers are usually the more stable ones, and thus the most abundant in nature and in *H. pluvialis*. The presence of chiral centers at the 3 and 3' carbon atoms on the rings allow for the presence of three different stereoisomers: 3S,3'S; 3S,3'R; and 3R,3'R. The 3S,3'S is the most common form found in nature, including in *H. pluvialis* and wild Pacific and Atlantic salmon species [1,2].

We have recently reviewed the methods used to produce astaxanthin commercially from *H. pluvialis*[3]. Most commercial producers induce astaxanthin accumulation in *H. pluvialis* by modifying the cultivation conditions from growth-promoting to stress-promoting (*e.g.*, lower nutrient concentrations, increased irradiance and temperature). Under such stress conditions, the *H. pluvialis* cells respond by slowing the synthesis of nitrogen-rich compounds (such as proteins) and instead accumulate carbon-based compounds, such as lipids. Astaxanthin is a carbon-rich compound (a carotenoid) that appears to help stabilize the lipids accumulated by *H. pluvialis*. Indeed, lipid accumulation accompanies, and may be required for, astaxanthin accumulation in *H. pluvialis* [4,5]. Thus, astaxanthin accumulates in oil droplets in the cells' cytoplasm [6]. For the most part, astaxanthin accumulates in the form of esters [7,8,9].

From our experience in cultivating *H. pluvialis* to produce astaxanthin. and in our review of the literature on the topic of astaxanthin production from that organism, it appears that *H. pluvialis* responds consistently to the environmental stresses used to induce astaxanthin accumulation. Stated directly, it is my opinion that the phytochemical profile of commercially produced *H. pluvialis* would not vary meaningfully as a result of the strain used in the production process. From that, I conclude that the astaxanthin derived from H. pluvialis would be substantially equivalent, regardless of the strain used to produce it, provided the production methods used were similar in most regards.

Sincerely,

Miguel Olaizola, Ph.D.
Enclosure (1)

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