CENTER FOR
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Dr. Lori White (whiteld@niehs.nih.gov)
Designated Federal Officer for the Board of Scientific Counselors
Office of Liaison, Policy and Review
Division of National Toxicology Program
National Institute of Environmental Health Sciences
PO Box 12233, K2-03
Research Triangle Park, NC 27709

Dear Dr. White:

These comments pertain to the meeting of the NTP Board of Scientific Counselors scheduled for December 9-10, 2014, specifically the agenda item on *Ginkgo biloba*.

The Center for Science in the Public Interest is a non-profit consumer advocacy organization which conducts research and advocacy programs in health and nutrition, and provides consumers with current, useful information about their health and well-being.

The American Botanical Council, which receives support from companies[1] that make and sell ginkgo extracts, has argued that the NTP used an extract of *Ginkgo biloba* that is not representative of Ginkgo supplements sold in the United States. But as the National Toxicology Program report notes, the composition of the extract it tested falls within the range of what is available in the marketplace[2] and is from a company known to supply U.S. companies[3]. Obviously, it is not possible to test all of the compositions that are on the market, and it appears that the NTP researchers obtained the most representative extract possible, given that the standardized extract EGb 761® was not available.[4]

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[1] For example, Enzymatic Therapy, GNC, Inc., Hain Celestial Group Inc., Hongjiu Ginseng Co. Ltd, Irwin Naturals, Korea Ginseng Corp., Natural Factors Nutritional Products Inc., Nature's Plus, Nature's Way Products, Inc., NOW Foods and Vitamins, Prince of Peace, and Swanson Health Products. Source: http://abc.herbalgram.org/site/PageServer?pagename=Sponsors

[2] The report states "the *Ginkgo biloba* products available in the marketplace have a wide range of concentrations, and the test article's composition fell within the range of what is on the market."

[3] The report states "The *Ginkgo biloba* extract used in the current studies was procured from a supplier known to provide material to United States companies."

[4] The report states, "The test article was selected based on a wide distribution in commerce and that the ratio of active ingredients was similar to marketed leaf extract EGb 761® (which was not available)," and "The original intent was to use standardized extract EGb 761®, manufactured by Wilhelm Schwabe, due to its use in many human studies. However, this material was not available

The Council has also claimed that the concentrations of three important constituents (flavonol glycosides, terpene lactones, and ginkgolic acids) of Ginkgo were significantly different in the NTP product from what is generally available in the marketplace. However, the differences between different Ginkgo extracts are modest, and would not be expected to lead to significant differences in study outcomes. While it is not known which component or components of *G. biloba* are responsible for the NTP carcinogenicity findings, it is reasonable to think that quercetin, a known mutagen, might be at least partially responsible. Quercetin is a flavone glycoside. EGb 761® contains 24% flavone glycosides. The extract used by NTP contains 31.2% flavone glycosides. There is no reason to think that testing an extract with 24% flavone glycosides would produce results that differed in any significant way from an extract containing 31.2% flavone glycosides.

The Council has also argued that the dosage levels administered to the test animals were 5-108 times higher than the levels of ginkgo extract that are normally ingested by consumers. However, it is well known that using lower dosages would lower the sensitivity of the bioassay; the range of doses used is unremarkable and perfectly acceptable in the context of rodent bioassays. Rodent cancer bioassays, of course, have a long history of identifying chemicals that are carcinogenic. They are currently the best approach and indeed the only practical, reasonably reliable way available for predicting carcinogenic risk to humans from chemicals in the food supply and many other chemicals that might cause cancer.

Sincerely,

[Redacted]

Michael F. Jacobson, PhD
Executive Director

Lisa Y. Lefferts, MSPH
Senior Scientist

David Schardt, MS
Senior Nutritionist

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to the NTP because unformulated EGb 761® was exclusively sold to pharmaceutical companies at the time of procurement for the NTP studies. Through industry contacts, the NTP learned that Shanghai Xing Ling Science and Technology Pharmaceutical Company, Ltd (Shanghai, China), produced an extract comparable to the Schwabe extract that was widely distributed in commerce (personal communication to Dr. P.C. Chan, NIEHS)."