Comparison of Vitamin B12 Forms
By Michael Mooney and Research Associates

I have been asked if cyanocobalamin as a usable and nontoxic form of Vitamin B-12. I am also asked if methylcobalamin is more easily absorbed than cyanocobalamin. This document addresses these questions.

Biochemically, even in an imaginary scenario, cyanocobalamin toxicity is unlikely although still remotely possible...but it doesn't ever occur.

It's important to note that questions I get have not addressed the relative risk of toxicity of consumption of cyanocobalamin in the body. The relative risk of toxicity is actually "zero" with cyanocobalamin or with hydroxycobalamin or methylcobalamin or any of the forms of Vitamin B12 contained in the dietary supplements found in health food stores.

In fact, the body handles cyanocobalamin safely and adequately. Where is the proof? Well, the proof is given by conservative scientific research organizations.

Simply, over several dozens of years with millions of consumers there are no registered reports of Vitamin B-12 toxicity from cyanocobalamin or hydroxycobalamin or methylcobalamin, ever. Thus, there is in fact, zero risk with any of them.

In fact, although some of the questions I’ve gotten have stated that cyanocobalamin is a toxic form of Vitamin B-12 because of the “cyano” part of the molecule, I have to take strong exception. There is no indication that cyanocobalamin is toxic in supplements anywhere in the scientific literature, medical journal studies or safety reports.

Furthermore, the mechanisms by which the body metabolizes and uses cyanocobalamin are well documented and show that the "cyano" part of B-12 is easily and normally metabolized by the body.

Vitamin B-12, whatever form, is among the safest of all the vitamins, which of themselves are among the safest things we put in our mouths, including food and drink.

WHERE IS THE PROOF?
We’ll refer to three conservative agencies of the U.S. government and a state university.
1. The U. S. National Library of Medicine houses all the health and medical journal studies reported in accredited journals from around the world. (More than 15 million scientific articles)

As of September 13, 2007 there were 19,813 scientific studies that investigated Vitamin B-12 that were accessible there. Of these only 665 investigated hydroxycobalamin. This is about 3 percent. 490 investigated methylcobalamin. This is a little over 2 percent. 16,251 investigated cyanocobalamin. This is about 82 percent. There are no reports of toxicity from cyanocobalamin, hydroxycobalamin or methylcobalamin in the 19,813 studies that investigated Vitamin B-12. Cyanocobalamin is, by a great margin – over 82 percent, the most studied form of Vitamin B12.
2. There are no reports of cyanocobalamin toxicity registered with the U.S. Centers for Disease Control and Prevention.

3. In the Vitamin Toxicity Chart, developed by Dr. John Hathcock, PhD., of the Department of Food and Nutrition, Iowa State University (he is now the senior scientist for the Council For Responsible Nutrition), and published in Pharmacy Times, May 1985:104-113, there was shown to be no known toxicity for Vitamin B-12.

4. The U.S. National Academy of Sciences, Institute of Medicine's Food and Nutrition Board sets upper limit for various nutrients to be sure there is virtually no possibility of any toxicity in the nutrients that up to 300 million Americans take daily. In their publication, Dietary Reference Intakes, they report no upper limit for Vitamin B-12 because of a lack of reports of adverse effects, even at higher doses.

So, (1) the National Library of Medicine (which houses all the scientific studies published in accredited scientific journals), finds no toxicity from any of these three forms of Vitamin B-12; (2) The U.S. Center for Disease Control and Prevention has no reports of Vitamin B-12 toxicity; (3) The Food and Nutrition Department of the State University of Iowa reported they could find no adverse effects for any of these forms of Vitamin B-12; and finally, (4) the scientists in the Institute of Medicine report that there are no defined upper limits for these forms of Vitamin B-12 because of a lack of reports of any adverse effects ever.

If three U.S. Government agencies and a major university study can find no evidence of toxicity from these forms of Vitamin B-12 in 19,813 studies conducted over dozens of years, and over 150 million Americans have taken cyanocobalamin daily for dozens of years with no reports of toxicity, it’s clear that there is zero risk of toxicity.

Additionally, cyanocobalamin is used by more Americans every day than any other form of Vitamin B12 without any reports of toxicity. There is absolutely no effective difference in the safety of these three forms.

**ABSORPTION**

The other question I get is whether cyanocobalamin absorbs as well as methylcobalamin. Methylcobalamin is a form of Vitamin B12 that cyanocobalamin converts to in the body, so there is a hypothesis that methylcobalamin will be absorbed better than cyanocobalamin.

I found a study of humans that used precisely controlled radioisotope measurements that compared absorption of several forms of Vitamin B12, including cyanocobalamin, methylcobalamin, hydroxycobalamin, and the co-enzymated form of Vitamin B12 called dibencozide. Dibencozide is the main naturally occurring form of B12 found in human tissues. These three other supplemental forms of Vitamin B12 are converted into dibencozide in the body. The study looked at people with a variety of diseases who may have worse absorption than healthy people.

The study was conducted to investigate whether supplemental forms of B12 absorb as well as dibencozide, with the common notion being that dibencozide, which is the main naturally occurring form of B12 found in human tissues, should absorb best.
RESULTS
What the study found was:
At a 1 mcg dose:
Hydroxocobalamin absorbed 55.7 percent;
Cyanocobalamin absorbed 49.2 percent;
Methylcobalamin absorbed 44.4 percent;
Dibencozide absorbed 33.7 percent.

At a 5 mcg dose:
Cyanocobalamin absorbed 20.4 percent;
Methycobalamin absorbed 18.8 percent;
Hydroxycoobalamin absorbed 16.3 percent;
Dibencozide absorbed 12.9 percent.

At a 25 mcg dose:
Dibencozide absorbed 7.9 percent;
Hydroxycoobalamin absorbed 7.4 percent;
Methycobalamin absorbed 6.1 percent;
Cyanocobalamin absorbed 5.6 percent.

Contrary to common notions, cyanocobalamin performed well. The study discussed why cyanocobalamin absorbed as well as it does, and hypothesized in complex biochemical terms that its “mass and molecular structure” were responsible for its efficient absorption.

CYANOCOBALAMIN COMPARED TO FOOD SOURCE B12
FOOD PROTEINS CAN INHIBIT ABSORPTION
The study also looked at Vitamin B12 in Vitamin B12-rich foods noting that several studies have shown that in spite of common notions to the contrary, there is similar absorption between cyanocobalamin and food-source (liver) Vitamin B12. However, for some individuals who have problems digesting proteins, especially people over 50 years of age, food-source Vitamin B12 may not absorb as well as isolated supplemental Vitamin B12 forms, like cyanocobalamin. This is because food-source B12 is bound to proteins in the food. If protein digestion is poor,
B12 might not be easily liberated from its protein bindings, so it will not be well absorbed. (See the study abstract below.) This is why the National Academy of Sciences’ Institute of Medicine recommends that these people consume a majority of their Vitamin B12 in its isolated supplemental form rather than depending on food sources.

Cyanocobalamin is the most widely used form of B12, being included in over 80 percent of dietary supplements. Since methylcobalamin costs over two times more than cyanocobalamin, cyanocobalamin is the more logical choice for use in dietary supplements for consumers when cost versus benefit is considered.

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References

The following abstract recommends that people with protein-digestion problems (this study focused on people over 50 years of age) take supplemental Vitamin B12 rather than depending on Vitamin B12 found in food.


Abstract
In response to research findings that 10% to 30% of people aged 51 years and older may have protein-bound vitamin B-12 malabsorption, the National Academy of Sciences’ Institute of Medicine recommends that these people consume a majority of the new Recommended Dietary Allowance (RDA) of 2.4μg/day in its synthetic form rather than in its food form. Protein-bound vitamin B-12 malabsorption in older adults has been attributed to reduced pepsin activity and gastric acid secretion, which interfere with cleavage of vitamin B-12 from dietary protein before absorption. Unlike patients with pernicious anemia, most people with protein-bound vitamin B-
12 malabsorption produce intrinsic factor and have the ability to absorb synthetic vitamin B-12 normally. Early diagnosis is necessary to prevent the untoward effects of vitamin B-12 deficiency. A thorough assessment of vitamin B-12 status entails measurement of multiple biochemical assessment indexes, including serum vitamin B-12, methylmalonic acid, and homocysteine concentrations. Dietitians and other health care professionals should be aware of the prevalence of vitamin B-12 deficiency in older adults and be familiar with sources of synthetic vitamin B-12 to facilitate implementation of the new RDA.