

Setting the Record Straight:

Allowable Sterilization Methods for Botanical Ingredients



On June 25, 2007, the FDA published its final rule on current good manufacturing practices for dietary supplements. Since then, many companies have scrambled to understand and

meet the various requirements set forth in the rule by the appropriate deadline. However, unless you're a very careful reader of the 447 pages of GMP regulations, you might miss something at the bottom of page 34860 of the Federal Register (the official compendium that encompasses all of the rules and proposed rules of federal agencies). There, the agency makes clear that irradiation of dietary ingredients and dietary supplements as a means to reduce or eliminate microbial loads is not permitted. Combine this new information with the fact that treatment of

botanicals with the common fumigant ethylene oxide (EtO) has been prohibited for years, and you begin to grasp the enormity of the sterilization issue facing dietary supplement manufacturers.

What the Regs Say

"With respect to sterilization of dietary ingredients and supplements, there are a limited number of options," said Loren Israelsen, Director of the United Natural Products Alliance and an expert on regulations affecting dietary supplements. "Irradiation and ethylene oxide are not among them." When manufacturers hear that, the first question they ask is: "Where does it say that?"

For EtO, the answer lies in the Federal Food, Drug and Cosmetic Act (FFDCA), which defines adulterated food as any food that "bears or contains a pesticide chemical residue that is unsafe within the meaning of section 346(a)" of the FFDCA (21 U.S.C. Sec. 342). Section 346(a) sets limits on pesticide chemical residues. EtO is a pesticide. Therefore, the only way it is legal to use EtO as a sterilization method is if a tolerance for EtO residue on a particular food has been established (or if there is an exemption from the tolerance

requirement). As specified in 40 CFR 180.151, there is an EtO tolerance level set for whole and ground spices of 50 ppm. The problem is that spices are not considered the same as herbs. Since there is not an established tolerance for EtO for use on herbs, it is not an acceptable method of herbal sterilization. Bottom line: Any herb treated with EtO is automatically adulterated.

That's not the only legal issue with EtO. "As far back as 1987, EtO has been included on California's Proposition 65 list of chemicals known to cause cancer or reproductive toxicity," stated Rupa Das, Vice President



of Global Quality for raw materials supplier BI Nutraceuticals. "Therefore, any herbal product sold in California that exceeds the safe harbor level of 2 micrograms per day for EtO must be accompanied by a warning stating that the product contains a chemical known to the state of California to cause cancer, birth defects, and other reproductive harm."

Aside from the regulatory concerns surrounding EtO is its environmental impact. Because of its potentially harmful effects on humans and the environment, EtO treatment has been banned by the 27 member states of the European Union, as well as Belize, Burundi (Africa), Cambodia, and Malaysia.

The prohibition against irradiation is even more clearly stated. By law, every food that is irradiated has to be approved individually by the FDA and bear the Radura symbol. So far, the list of approved foods includes meat, poultry, wheat flour, some fresh fruits and vegetables, and spices. But once again, spices are not the same as herbs. In case there was any

confusion, FDA cleared it up once and for all in the preamble of the cGMPs. On page 34860 of the Federal Register 72 FR 34751 June 25, 2007, the agency states that it is currently reviewing a food additive petition for the use of irradiation on dietary ingredients and dietary supplements. Until the review process is completed, however, "Irradiation of dietary ingredients and dietary supplements as a means to reduce or eliminate microbial loads is not permitted." A similar mention is made on page 34897. Of note: The American Herbal Products Association has submitted a letter to the FDA requesting the agency deny the petition.

Importantly, the ban on irradiation of dietary supplements is not part of the new cGMPs, which are being phased in over a three-year period depending on company size. The new wording appears in the preamble to the cGMPs, which means that the FDA is clarifying its current position on the issue. In other words, manufacturers are disallowed from using irradiation on supplements right now — not one or two years

from now. And, like EtO, irradiation is also prohibited throughout Europe.

The Consequences of Violation

According to an FDA official, use of irradiation and EtO will be reviewed during GMP inspections. “When we’re at the manufacturing facility, we look at what processes they’re using,” said the official, who declined to be named. “And if the manufacturer is getting ingredients from other facilities, they need to have the appropriate specifications in place to make sure that the material they’re getting is what it purports to be, so that there is a big onus on the finished product manufacturer to make sure that what they’re using is appropriate.”

What kind of penalty could a manufacturer incur for selling products treated with ionizing radiation or EtO? “A product that would be irradiated because we don’t have a food additive petition in place would be considered to be adulterated and a product that has an illegal pesticide would also be considered to be adulterated, so

conceivably a firm could receive a warning letter if we had evidence of that, or we could seize the product, or we could enjoin the firm from doing those practices,” explained the FDA official. Repeat violators could be hit with a permanent injunction, which would essentially put them out of business.

Identifying Adulterated Herbs

When EtO is used to sterilize an herb, it leaves several residues: EtO itself, as well the byproducts ethylene chlorohydrine (ECH) and ethylene bromohydrine (EBH). All three residuals can be tested for using a gas chromatograph. It is also possible to detect whether an herb has been treated with ionizing radiation by using a screening device called photo-stimulated luminescence, which measures energy particles.

It’s impossible to tell just by looking at an herb whether it has been treated with EtO or irradiation. Therefore, unless a raw materials supplier has the appropriate analytic equipment in-house to test all of their botanicals, they may be



unwittingly selling adulterated materials.

Legal Alternatives to EtO and Irradiation.

It's generally assumed that use of EtO and irradiation as methods of sterilization has been widespread in the supplement industry. For years, there were simply no other viable ways to reduce microbial counts.

Recently, though, several alternative sterilizations techniques have been developed, including high heat, ozone, hydrogen peroxide, and steam sterilization. Unfortunately,

nearly all of them have significant drawbacks. Subjecting an herb to high heat can burn it, discolor it, or flash off the volatile oils. Ozone, a powerful oxidizing agent, can chemically alter the antioxidant profile of a plant. And hydrogen peroxide is not widely commercially available.

“There are new technologies coming on line which are very helpful, such as dry steam,” commented Israelsen. BI Nutraceuticals pioneered the use of dry steam sterilization in the United States for botanicals in 2002. The process, which



they've named Protexx HP™, involves treating herbal materials with steam at a high temperature under pressure for a specified amount of time. However, it's not a one-size-fits-all formula. The 40+ settings, which control the heat, moisture, time, and pressure parameters, can be tailored for each individual botanical, as different combinations work better for one herb than they do for another.

It took BI Nutraceuticals over three years to fine-tune their process. Now the company has over 700 herb-specific validated protocols to reduce microbial load while retaining the herbs' color, volatile oils, and marker compounds. “Dry steam sterilization has been found to be as effective as EtO and irradiation at reducing micro loads. Unlike EtO and irradiation, however, the process

does not leave any toxic residue and is completely natural and environmentally friendly. In fact, Protexx HP™ has been certified organic by Quality Assurance International,” said Das.

Whichever method suppliers choose to sterilize their botanical ingredients, one thing is clear: irradiation and EtO are not allowable. Since manufacturers are ultimately responsible for the ingredients used in their products, they will want to get assurance from their suppliers that their botanical ingredients have not been processed using either of these methods.


BI
Nutraceuticals

Identilok is a registered trademark,
and Protexx HP and UltraHD are trademarks
of BI Nutraceuticals
© 2008 BI Nutraceuticals

For more information, or to place an order call 310-669-2100

www.binutraceuticals.com

BI Nutraceuticals(West), 2550 El Presido Street, Long Beach, CA 90810-1193 • Tel (310) 669-2100 • Fax (310) 637-3644

BI Nutraceuticals(East), 120 Hoffman Lane, Islandia, NY 11749-5008 • Tel (631) 232-1105 • Fax (631) 232-0369

BI Nutraceuticals(Asia), C-2 Export Processing Zone of Suzhou, New & High-tech District (SND), Suzhou, 215151 PRC

contact@binutraceuticals.com