

Target Ingredient Announcement
AAFCO Recommended Enforcement Event
Enforcement Strategy for Marketed Ingredients (ESMI) Working Group

During the AAFCO Annual Meeting in August 2002, the Enforcement Strategy for Marketed Ingredients (ESMI) Working Group announced the target ingredient recommended for a future regulatory enforcement event. The target ingredient, comfrey, has been shown to be a health and safety concern for animals and humans, prompting regulatory action by the United States, Canada and Germany. Comfrey does not meet any of the recognized criteria for use as an animal feed ingredient or animal feed.

Comfrey was identified by the ESMI Working Group based on the following published scientific information provided by the United States Food and Drug Administration (FDA), Center for Veterinary Medicine with references provided at the end of this document:

The leaf and root of the comfrey (*Symphytum officinale*) plant have been used in supplements. Supplement use has been orally for ulcers, diarrhea, cough, bronchitis, and rheumatism or topically for the treatment of inflammation, arthritis, wounds, and bruises. This supplement has been banned in Germany and Canada due to safety concerns.

Comfrey has shown to be hepatotoxic in both humans and rats. The toxic compounds found are pyrrolizidine alkaloids (8 have been identified), which include lasiocarpine and symphitine. The highest content of these substances were found in products containing bulk comfrey root or leaf.

Pyrrolizidine alkaloids have also been associated with lung and liver cancer. The primary liver ailment associated with comfrey consumption is veno-occlusive disease (a form of Budd-Chiari syndrome), a non-thrombotic destruction of small hepatic veins leading to cirrhosis and eventual liver failure. Consumption of 85 mg pyrrolizidine alkaloids (15mg/kg BW/d) for 6 months resulted in venoocclusive disease in a 49-year old woman. Signs of liver toxicity have been seen in rats consuming low doses of comfrey (50mg/kg BW three times a week for three weeks) which included loss of sinusoidal lining cells, sinusoids filled with cellular debris (hepatocyte organelles and red blood cells), and narrowing of terminal hepatic venules.

Pyrrolizidine alkaloids extracted from comfrey were shown to damage chromosomes when administered to human lymphocytes at concentrations of 140 mg/mL and 1400 mg/mL. At these concentrations, sister-chromatid exchange and chromosome aberrations were observed. On July 6, 2001, the FDA advised dietary supplement manufacturers that comfrey should not be used in dietary supplements due to safety concerns.

AAFCO recommended to feed control officials that an enforcement event occur to clarify the regulatory status of ingredients sold for consumption by animals as animal feed, including livestock feed and pet food. All feed ingredients must be shown to be safe and efficacious for their intended use prior to distribution. Feed manufacturers have several methods for meeting this requirement that are summarized in an ingredient fact sheet entitled, "Options Available for Acceptance of a Proposed Feed Ingredient", available on the AAFCO Website. Feed ingredients not recognized or acceptable for their intended purpose may be subject to regulatory action by the feed control official and the FDA.

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