

FDA Notification to Industry
**Products using oils, glycerin, or protein that were
derived from the *Jatropha* plant may have toxic effects**

The U.S. Food and Drug Administration (FDA) is notifying the regulated community that oils, glycerin, and proteins commonly used in the production of human and animal food, medical products, cosmetics, and other FDA-regulated products may contain toxins if they are derived from the *Jatropha* plant.

When vegetable oils and animal fats are used in biodiesel fuel production, the co-products include oils, glycerin and protein. Recently, the *Jatropha* plant¹ has become an attractive source material for biodiesel fuel because of the high oil content of its seed, availability of the plant in certain parts of the world, and relatively low cost. *Jatropha* is a drought-resistant shrub that grows well in tropical and semi-tropic climates throughout the world. However, unlike other benign materials used to produce biodiesel fuel, *Jatropha* plants may contain toxic compounds, including phorbol esters.^{2,3} These compounds exhibit potential toxicity, both acute and chronic, to exposed humans and animals.

As part of the biodiesel fuel production process, oil is extracted from the *Jatropha* plant. This oil contains a portion of the toxic compounds; however, toxic compounds are retained in the glycerin and protein co-products. Consequently, the oils, glycerin, and protein derived from *Jatropha* seeds may contain toxic compounds.^{4,5,6} Even though crude *Jatropha* extracts have protein levels comparable to soybeans and, therefore, could be an attractive protein source for human and animals, *Jatropha*-derived protein may contain these toxic ingredients.^{7,8} Conventional impurity test methods may not detect the presence of these toxins.

At this time, the FDA is unaware of any intentional substitution or contamination in FDA-regulated finished products or components derived from the *Jatropha* plant. However, given the significant overlap among the supply chains of FDA-regulated products, the FDA is advising industry to be aware of the potential for substitution or use of oils, glycerin, and proteins derived from the *Jatropha* plant. This increased attention to supply chains is important for ingredient suppliers and manufacturers of FDA-regulated products, both in the U.S. and abroad. Suppliers and manufacturers should take steps to prevent the use of ingredients that might be intentionally, or otherwise, adulterated with *Jatropha*. The following practices may help suppliers and manufacturers identify the presence of *Jatropha*-derived ingredients:

- Know, monitor, and audit supply chains of naturally-derived ingredients⁹.
- Unless the composition of ingredients has been verified and does not pose a risk, conduct comprehensive risk assessments for naturally-derived ingredients.¹⁰
- Confirm the composition of naturally-derived ingredients and conduct appropriate testing of these ingredients.¹¹

The FDA is monitoring this situation to assess impacts on FDA-regulated products and is working to develop test methods for *Jatropha*-based ingredients. As additional information becomes available, the FDA intends to provide updates. FDA welcomes relevant information from suppliers and manufacturers of FDA-regulated products. In particular, please share findings with FDA if validated testing methodologies are developed, for the detection of *Jatropha*-based toxins, or if *Jatropha*-based toxins are suspected, by sending an email to: IntentionalAdulteration@fda.hhs.gov.

¹ For the purpose of this notification, the term *Jatropha* refers to ingredients or materials that are derived from the plant *Jatropha* of the Euphorbiaceae family.

² A New Tumor Promoter from the Seed Oil of *Jatropha curcas* L., an Intramolecular Diester of 12-Deoxy-16-hydroxyphorbol (1988) *Cancer Res.* 48: 5800-5804.

³ Toxicity Studies of Detoxified *Jatropha* Meal (*Jatropha curcas*) in Rats (2008) *Food and Chem. Toxicol.* 46: 3621-3625.

⁴ Dynamic Analysis of Phorbol Esters in the Manufacturing Process of Fatty Acid Methyl Esters from *Jatropha curcas* Seed Oil (2011) *J. Am. Oil Chem. Soc.* 88: 851-861.

⁵ *Jatropha* Toxicity – A Review (2010) *J. Toxicology and Environmental Health, Part B*, 13: 476-507.

⁶ Comparative Evaluation of Non-toxic and Toxic Varieties of *Jatropha curcas* for Chemical Composition, Digestibility, Protein Degradability and Toxic Factors (1998) *Food Chemistry* 62: 207-215.

⁷ Nutritional, Biochemical, and Pharmaceutical Potential of Proteins and Peptides from *Jatropha*: Review (2010) *J. Agric. Food Chem.* 58: 6543-6555.

⁸ Ozone for Phorbol Esters Removal from Egyptian *Jatropha* Oil Seed Cake (2011) *Adv. Appl. Sci. Research* 2: 221-232.

⁹ See, e.g. 21 CFR Part 110; 21 CFR Part 211; 21 CFR Part 820

¹⁰ This is a general industry recommendation whenever a manufacturer of medical products uses any mixture containing undeclared or undisclosed components. See, e.g., ICH Q9 and/or ISO14971 for guidance on risk management.

¹¹ See, e.g., Isolation, Stability and Bioactivity of *Jatropha curcas* Phorbol Esters (2012) *Fitoterapia* 83: 586-592.