

Law Matters, March 2011

FDA announces enforcement actions against hundreds of marketed, unapproved cough, cold and allergy drug products



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The FDA announced on March 2 that it will take enforcement action against unapproved oral cough, cold, and allergy prescription products. The products covered by the notice lack approved NDAs or ANDAs, and many, according to the agency, are inappropriately labeled for use in infants and young children. Included in the enforcement notice are three types of products: sustained- or extended-release products, which have required an NDA or ANDA since 1959; tannates, concerning which the FDA has recently denied several citizens petitions, and immediate release products. The tannates include tannate salts of brompheniramine, carbetapentane, chlorpheniramine, dexbrompheniramine, dexchlorpheniramine, dextromethorphan, diphenhydramine, ephedrine, phenylephrine, pseudoephedrine, pyrilamine, and triprolidine. The FDA noted that a few of the immediate-release products conform to the OTC monograph for cough and cold products, but are labeled as prescription only, and cannot be marketed as such without an NDA or ANDA. Some of the immediate-release products contain ingredients that are included in the OTC monograph, but have nonconforming indications or dosing regimens. The remaining immediate-release products contain ingredients that are not in the OTC final monograph, and which the FDA has investigated and concluded are not GRASE. These ingredients include atropine, carbetapentane, cyproheptadine, dyphylline, hyoscyamine, methscopolamine nitrate, phenyltoloxamine, potassium guaiacolsulfonate, promethazine, and scopolamine.

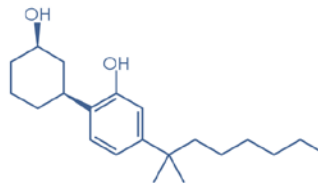
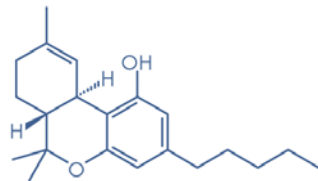
The list of drugs believed to be covered by this announcement is available on the FDA website (<http://1.usa.gov/gb9tKH>). Products that are currently listed with FDA in compliance with §510 of the FDCA, and are marketed in the US with an NDC number may not be manufactured after June 1, 2011 nor shipped after August 30, 2011. [DHHS, FDA. Drugs for Human Use; Unapproved and Misbranded oral Drugs Labeled for Prescription Use and Offered for Relief of Symptoms of Cold, Cough, or Allergy; Enforcement Dates. 76 Fed. Reg. 11794-11798, 2011 Mar 3; <http://1.usa.gov/e9VL7R>]
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DEA temporarily places “Spice” synthetic cannabinoids in Schedule I

Effective March 1, five synthetic cannabinoids, JWH-018, JWH-073, JWH-200, CP-47,497, and cannabicyclohexanol, are subject to regulatory controls and civil and criminal sanctions imposed by the CSA and DEA regulations for Schedule I controlled substances. The temporary Schedule I designation may be assigned for up to 1 year if DEA finds the action necessary to avoid an imminent public health hazard. The substances have been sold as either incense (eg, “Spice” or “K2”) or plant food (eg, “Bonsai-18”), labeled “not for human consumption.” DEA noted that 18

states, the military and other countries have banned these substances. These compounds are also Schedule I in Washington.

The synthetic cannabinoids were first developed as research tools in the early 1980s, and all have high binding affinity for cannabinoid (CB₁) receptors. For the medicinal-chemistry-inclined among us, the chemical names of the five substances are: 1-butyl-3-(1-naphthoyl)indole; 1-pentyl-3-(1-naphthoyl)indole; 1-[2-(4-morpholinyl)ethyl]-3-(1-naphthoyl)indole; 5-(1,1-dimethylheptyl)-2-[(1R,3S)-3-hydroxycyclohexyl]-phenol; and 5-(1,1-dimethyloctyl)-2-[(1R,3S)-3-hydroxycyclohexyl]-phenol. Shown below are structures for Δ^9 -THC (left) and CP-47,947 (right):



[DOJ, DEA. 21 CFR Part 1308. Schedules of Controlled Substances: Temporary Placement of Five Synthetic Cannabinoids into Schedule I, 76 Fed. Reg. 11075-11078, March 1, 2011] (Reprinted from Pharma-Law e-News, 2011 Mar; www.aspl.org)