

Response from the National Institute for Occupational Safety and Health (NIOSH) on the Inclusion of Tamiflu as a Hazardous Drug

NIOSH has not reviewed Tamiflu for inclusion in its hazardous drug list. The approach that NIOSH has taken in classifying drugs as hazardous is based on the six criteria in the NIOSH definition of a hazardous drug. (NIOSH 2004)

1. Carcinogenicity
2. Teratogenicity or other developmental toxicity ^{††}
3. Reproductive toxicity ^{††}
4. Organ toxicity at low doses ^{††}
5. Genotoxicity ^{‡‡}
6. Structure and toxicity profiles of new drugs that mimic existing drugs determined hazardous by the above criteria.

^{††} All drugs have toxic side effects, but some exhibit toxicity at low doses. The level of toxicity reflects a continuum from relatively nontoxic to production of toxic effects in patients at low doses (for example, a few milligrams or less). For example, a daily therapeutic dose of 10 mg/day or a dose of 1 mg/kg per day in laboratory animals that produces serious organ toxicity, developmental toxicity, or reproductive toxicity has been used by the pharmaceutical industry to develop occupational exposure limits (OELs) of less than 10 µg/m³ after applying appropriate uncertainty factors [Sargent and Kirk 1988; Naumann and Sargent 1997; Sargent et al. 2002]. OELs in this range are typically established for potent or toxic drugs in the pharmaceutical industry. Under all circumstances, an evaluation of all available data should be conducted to protect health care workers.

NIOSH evaluates each drug on an individual basis, not by drug class or category. The majority of the drugs listed by NIOSH as hazardous are classified as antineoplastic (AHFS, 2009). However, not all drugs classified as antineoplastic are listed as hazardous. Similarly, not all monoclonal antibodies, immunosuppressant drugs or antiviral drugs are listed as hazardous.

The statement in the introduction to the Alert may be the source of these concerns.

“Health care workers who work with or near hazardous drugs may be exposed to these agents in the air or on work surfaces, clothing, medical equipment, or patient urine or feces. Hazardous drugs include those used for cancer chemotherapy, antiviral drugs, hormones, some bioengineered drugs, and other miscellaneous drugs (see [Appendix A](#) of *NIOSH Alert: Occupational Exposures to Antineoplastic and Other Hazardous Drugs in Health Care Settings for a List of Hazardous Drugs*). The health risk depends on how much exposure a worker has to these drugs and how toxic they are.” (NIOSH 2004)

The key part of this statement is “...and how toxic they are.” Tamiflu has never been formally evaluated by NIOSH as to its potential to be a hazardous drug. However, there is no indication in the drug package insert that would indicate that it would be listed if it were to undergo a full expert review. It is Pregnancy Category C, which is pretty much a default for any drug that is not a category D or X. There is no reported carcinogenicity in laboratory animals or humans. There is one positive test for genotoxicity, but this alone

would not warrant it being listed as hazardous. There are no teratogenic effects listed and it does not produce organ toxicity at low doses.

NIOSH is aware that some powders and capsules and/or tablets are manipulated for compounding or to facilitate their administration to pediatric and/or geriatric patients or patients who are not able to swallow intact capsules or tables. The NIOSH Alert addresses this issue.

“Some drugs defined as hazardous may not pose a significant risk of direct occupational exposure because of their dosage formulation (for example, coated tablets or capsules—solid, intact medications that are administered to patients without modifying the formulation). However, they may pose a risk if solid drug formulations are altered, such as by crushing tablets or making solutions from them outside a ventilated cabinet.”

This statement is based on the drug in question having intrinsic toxic properties regardless of the formulation. As one of the authors of the NIOSH Alert and the manager of the NIOSH Hazardous Drug List, in my opinion, Tamiflu does not possess any characteristics that would categorize it as hazardous.