



April 16, 2018

Barbara MacKenzie National Institute for Occupational Safety and Health 1090 Tusculum Ave, MS-C26 Cincinnati, OH 45226

Re: NIOSH List of Antineoplastic and Other Hazardous Drugs in Healthcare Settings: Proposed Additions to the NIOSH Hazardous Drug List 2018 (Dockets CDC-2018-0004 and NIOSH-233-B)

Dear Barbara MacKenzie,

The National Community Pharmacists Association ("NCPA") appreciates the opportunity to provide comments on the National Institute for Occupational Safety and Health's ("NIOSH") proposed additions to the *NIOSH List of Antineoplastic and Other Hazardous Drugs in Healthcare Settings, 2018* ("NIOSH List"). In 83 Fed. Reg. 6563 (Feb. 14, 2018), NIOSH invited comments on "any topic related to the drugs identified" in the *Federal Register* notice (Feb. 14, 2018).

NCPA represents the interests of America's community pharmacists, including the owners of more than 22,000 independent community pharmacies. Together, they represent an \$80 billion health care marketplace and employ more than 250,000 individuals on a full or part-time basis. By volume, 52 percent of the total prescriptions our members fill is covered by Medicaid or Medicare Part D.

Our comments will primarily focus on the impact of hazardous drug exposure beyond hospitals; for example, the impact on community pharmacies. NCPA suggests that NIOSH revise its guidance to include that the packaging of a hazardous drug product is relevant to the product's risk assessment, especially in a community pharmacy setting. In addition, NCPA recommends that the NIOSH List include a table that outlines which hazardous drugs pose the highest risk to healthcare workers.

NIOSH identifies hazardous drugs as drugs that exhibit carcinogenicity, teratogenicity, reproductive toxicity, organ toxicity at low doses, genotoxicity, or structural/toxicity profiles of new drugs that mimic existing drugs in humans or animals. In a retail or community pharmacy, instead of liquid form, hazardous drug products are usually in solid dosage form, such as a tablet, capsule or suppository. The pharmacies receive these solid form products in secure packaging, which are manufacturer-sealed. When assessing the risk of a product, it is reasonable to conclude that leaks are not likely to occur in unpacking and storing these drug products.

Retail pharmacies also receive hazardous drug products in ready-to-dispense form, which are securely packaged with many layers of packaging. These drug products are dispensed directly to the patient for the first time and are not handled by the community pharmacist. These packages are not manipulated by the pharmacist. Examples of these drug products include, blister packs of oral contraceptives;



testosterone gels and films; estradiol films, creams and emulsions; dinoprostone suppositories; cyclosporine ophthalmic emulsions; and progesterone gels and inserts. Therefore, NCPA proposes that NIOSH add text to the second full paragraph on page 2 of the 2016 document stating that drug products contained in ready-to-dispense form, such as blister packs, pose a lower risk of exposure as long as they stay intact through the receipt, storage, and dispensing of the drug.

Further, an essential purpose of the list of hazardous drugs is to assist health care facilities, such as retail pharmacies, in creating their own risk management procedures for any drugs and formulations that are used in their facilities, which may be hazardous.¹ Studies cited by OSHA consistently show that the most significant risk to workers in healthcare settings stems from volatile cytotoxic & cytostatic drugs.² Because certain drugs pose higher risks to healthcare workers than others, it is vital that the NIOSH List include a table that highlights the substances that pose the highest risk to healthcare workers, based on their volatility and dose-related toxic potential. This new table would prioritize risk and thus allow healthcare facilities to appropriately implement precautions to be taken in handling and storing these drugs. Regarding the placement of drugs in specific tables, drugs listed on the 2016 NIOSH HD list are classified into three categories.

- Category 1: Includes antineoplastic drugs.
- Category 2: Non-antineoplastic drugs that meet one or more of the NIOSH criteria for hazardous drugs.
- Category 3: Includes drugs that primarily pose a reproductive risk to men and woman who are actively trying to conceive and women who are pregnant or breast-feeding.

Certain drugs in Category 1 of the 2016 NIOSH HD list are approved for antineoplastic indications yet the drugs themselves are not antineoplastic agents since they do not have any effects on disrupting cellular

¹ See Connor TH, Mackenzie BA, DeBord DG. Clarification about hazardous drugs. Am J Health-Syst Pharm. 2012; 69(22):1949-1950.

² See American Society of Health-System Pharmacists. ASHP guidelines on handling hazardous drugs. Am J Health-Syst Pharm. 2006; 63:1172-1193;

see also Sessink PJ, Boer KA, Scheefhals AP et al. Occupational exposure to antineoplastic agents at several departments in a hospital: environmental contamination and excretion of cyclophosphamide and ifosfamide in urine of exposed workers. Int Arch Occup Environ Health. 1992; 64:105–12;

see also Kiffmeyer TK, Ing KG, Schoppe G. External contamination of cytotoxic drug packing: safe handling and cleaning procedures. J Oncol Pharm Pract. 2000; 6:13;

see also Connor TH, Sessink PJ, Harrison BR et al. Surface contamination of chemotherapy drug vials and evaluation of new vial-cleaning techniques: results of three studies. Am J Health-Syst Pharm. 2005; 62:475–84; see also Kiffmeyer TK, Kube C, Opiolka S, Schmidt KG, Schöppe G, Sessink PJM [2002]. Vapor pressures, evaporation behaviour and airborne concentrations of hazardous drugs: implications for occupational safety. Pharmeaceut J 268:331–337;

see also International Society of Oncology Pharmacy Practitioners Standards Committee. ISOPP standards of practice. Safe handling of cytotoxics. J Oncol Pharm Pract. 2007; 13 Suppl:1–81.



activity. These agents should be reclassified into Category 2 based on their mechanism. NCPA strongly recommends the following drugs be moved from Category 1 to Category 2.

Drug	Mechanism	Information
Anastrozole	Selective nonsteroidal aromatase inhibitor- lowers serum estradiol concentrations and has no detectable effect on formation of adrenal corticosteroids or aldosterone.	https://www.accessdata.fda. gov/drugsatfda_docs/label/2 011/020541s026lbl.pdf
Leuprolide	Synthetic analog of a gonadotropin hormone (GnRH)- results in suppression of ovarian and testicular steroidogenesis due to decreased levels of LH and FSH with subsequent decrease in testosterone (male) and estrogen (female) levels.	https://www.accessdata.fda. gov/drugsatfda_docs/label/2 010/019010s033,019732s031 s035s036,020517s024s028s0 29lbl.pdf
Megestrol	Synthetic oral progestin	https://www.accessdata.fda. gov/drugsatfda_docs/label/2 007/021778s002s003lbl.pdf
Tamoxifen	Selective Estrogen Modulator- competes with estrogen for binding sites in target tissues such as breast and uterus.	https://www.accessdata.fda. gov/drugsatfda_docs/label/2 005/17970s053lbl.pdf
Letrozole	Aromatase inhibitor inhibits the aromatase enzyme by competitively binding to the heme of the cytochrome P450 subunit of the enzyme, resulting in a reduction of estrogen biosynthesis in all tissues.	https://www.accessdata.fda. gov/drugsatfda_docs/label/2 014/020726s027lbl.pdf
Degorelix	GnRH antagonist- It binds reversibly to the pituitary GnRH receptors, thereby reducing the release of gonadotropins and consequently testosterone.	https://www.accessdata.fda. gov/drugsatfda_docs/label/2 008/022201lbl.pdf

Conclusion

NCPA greatly appreciates the opportunity to share with you our comments and suggestions on NIOSH's proposed guidance and additions to the NIOSH List.



Sincerely,

Ronna Hauser, PharmD

Vice President, Pharmacy Affairs National Community Pharmacists Association