APPENDIX A

DRUGS CONSIDERED HAZARDOUS

General Approach to Handling Hazardous Drugs

In this Alert, NIOSH presents a *standard precautions* or *universal precautions* approach to handling hazardous drugs safely: that is, NIOSH recommends that all hazardous drugs be handled as outlined in this Alert. Therefore, no attempt has been made to perform drug risk assessments or propose exposure limits. The area of new drug development is rapidly evolving as unique approaches are being taken to treat cancer and other serious diseases.

Defining Hazardous Drugs

Hazardous drugs include those used for cancer chemotherapy, antiviral drugs, hormones, some bioengineered drugs, and other miscellaneous drugs. This definition of hazardous drugs is used in this Alert and is based on an ASHP definition that was originally developed in 1990 [AHSP 1990]. Thus the definition may not accurately reflect the toxicity criteria associated with the newer generation of pharmaceuticals entering the health care setting. For example, bioengineered drugs target specific sites in the body; and although they may be toxic to the patient, some may not pose a risk to health care workers.

NIOSH and other organizations are still gathering data on the potential toxicity and health effects related to highly potent drugs and bioengineered drugs. Therefore, when working with any hazardous drug, health care workers should follow a standard precautions approach along with any recommendations included in the manufacturer's MSDSs.

ASHP Definition of Hazardous Drugs

The ASHP defines hazardous drugs in their 1990 revision of *Technical Assistance Bulletin on Handling Hazardous Drugs* [ASHP 1990]. The bulletin gives criteria for identifying potentially hazardous drugs that should be handled in accordance with an established safety program [McDiarmid et al. 1991; Arrington and McDiarmid 1993]. The criteria are prioritized to reflect the hierarchy of potential toxicity described below. Since the hazardous drugs covered by this Alert were designed as therapeutic agents for humans, human toxicity profiles should be considered superior to any data from animal models or in vitro systems. Additional guidance for defining hazardous drugs is available in the following citations: carcinogenicity [61 Fed. Reg. 17960–18011 (1996b); IARC 2004], teratogenicity [56 Fed. Reg. 63798–63826 (1991)], developmental toxicity [56 Fed. Reg. 63798–63826 (1991)], and reproductive toxicity [61 Fed. Reg. 56274–56322

(1996a)]. Physical characteristics of the agents (such as liquid versus solid, or water versus lipid solubility) also need to be considered in determining the potential for occupational exposure.

NIOSH Revision of ASHP Definition

The 1990 ASHP definition of hazardous drugs** was revised by the NIOSH Working Group on Hazardous Drugs for this Alert. Drugs considered hazardous include those that exhibit one or more of the following six characteristics in humans or animals:

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.

Determining Whether a Drug is Hazardous

Many hazardous drugs used to treat cancer bind to or damage DNA (for example, alkylating agents). Other antineoplastic drugs, some antivirals, antibiotics, and bioengineered drugs interfere with cell growth or proliferation, or with DNA synthesis. In some cases, the nonselective actions of these drugs disrupt the growth and function of both healthy and diseased cells, resulting in toxic side effects for treated patients. These nonselective actions can also cause adverse effects in health care workers who are inadvertently exposed to hazardous drugs.

Early concerns about occupational exposure to antineoplastic drugs first appeared in the 1970s. Although the antineoplastic drugs remain the principal focus of this Alert, other drugs may also be considered hazardous because they are potent (small quantities produce a physiological effect) or cause irreversible effects. As the use and number of these potent drugs increase, so do opportunities for hazardous exposures among health care workers. For example, antineoplastic drugs such as cyclophosphamide have immunosuppressant effects proved beneficial for treating nonmalignant

**ASHP [1990] definition of hazardous drugs:
1. Genotoxicity (i.e., mutagenicity and clastogenicity in short-term test systems)
2. Carcinogenicity in animal models, in the patient population, or both, as reported by the International Agency for Research on Cancer (IARC)
3. Teratogenicity or fertility impairment in animal studies or in treated patients
4. Evidence of serious organ or other toxicity at low doses in animal models or treated patients.

††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 $\mu g/m^3$ 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 effects.

‡‡In evaluating mutagenicity for potentially hazardous drugs, responses from multiple test systems are needed before precautions can be required for handling such agents. The EPA evaluations include the type of cells affected and in vitro versus in vivo testing [51 Fed. Reg. 34006–34012 (1986)].

diseases such as rheumatoid arthritis and multiple sclerosis [Baker et al. 1987; Moody et al. 1987; Chabner et al. 1996; Abel 2000].

This appendix presents useful criteria and sources for determining whether a drug is hazardous. When a drug has been judged to be hazardous, the various precautions outlined in this Alert should be applied as appropriate when handling that drug. Also included is a list of drugs that should be handled as hazardous. This list is based on a compilation of lists from four health care facilities and one drug manufacturers' organization.

In addition to using the list of hazardous drugs presented here, each organization should create its own list of drugs considered to be hazardous. This appendix presents guidance for making such a facility-specific list (see section entitled *How to Generate your own List of Hazardous Drug*s). Once this list is made, newly purchased drugs should be evaluated against the organization's hazardous drug criteria and added to the list if they are deemed hazardous.

Some organizations may have inadequate resources for determining their own list of hazardous drugs. If so, the sample list of hazardous drugs in this appendix (current only to the printing date of this document) will help employers and workers to determine when precautions are needed. However, reliance on such a published list is a concern because it quickly becomes outdated as new drugs continually enter the market and listed drugs are removed when additional information becomes available. To fill this knowledge gap, NIOSH will update an internet list at regular intervals, adding new drugs considered to be hazardous and removing those that require reclassification. This hazardous drug list will be posted on the NIOSH Web site at www.cdc.gov/niosh, under the topic page *Hazardous Drug Exposures in Health Care*.

How to Generate Your Own List of Hazardous Drugs

The OSHA hazard communication standard [29 CFR 1910.1200] requires employers to develop a hazard communication program appropriate for their unique workplace. An essential part of the program is the identification of all hazardous drugs a worker may encounter in the facility. Compliance with the OSHA hazard communication standard entails (1) evaluating whether these drugs meet one or more of the criteria for defining hazardous drugs and (2) posting a list of the hazardous drugs to ensure worker safety. Institutions may wish to compare their lists to the sample listing in this document or on the NIOSH Web site.

It is not probable that every health care provider or facility will use all drugs that have received U.S. Food and Drug Administration (FDA) approval, and the OSHA hazard communication standard does not mandate evaluation of every marketed drug. Instead, compliance requires practice-specific assessments for drugs used at any one time by a facility. However, hazardous drug evaluation is a continual process. Local hazard communication programs should provide for assessment of new drugs as they enter the marketplace, and when appropriate, reassessment of their presence on hazardous drug lists as toxicological data become available to support recategorization. Toxicological data are often incomplete or unavailable for investigational drugs. However, if the mechanism of action suggests

that there may be a concern, it is prudent to handle them as hazardous drugs until adequate information becomes available to exclude them.

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.

Where to Find Information Related to Drug Toxicity

Practice-specific lists of hazardous drugs (usually developed by pharmacy or nursing departments) should be comprehensive, including all hazardous medications routinely used or very likely to be used by a local practice. Some of the resources that employers can use to evaluate the hazard potential of a drug include, but are not limited to, the following:

- MSDSs
- Product labeling approved by the U.S. FDA (package inserts)
- Special health warnings from drug manufacturers, FDA, and other professional groups and organizations
- Reports and case studies published in medical and other health care profession journals
- Evidence-based recommendations from other facilities that meet the criteria defining hazardous drugs

Examples of Hazardous Drugs

The following list contains a sampling of major hazardous drugs. The list was compiled from information provided by (1) four institutions that have generated lists of hazardous drugs for their respective facilities, (2) the American Hospital Formulary Service Drug Information (AHFS DI) monographs [ASHP/AHFS DI 2003], and (3) several other sources. The OSHA hazard communication standard requires hazardous drugs to be handled using special precautions. The mandate applies not only to health care professionals who provide direct patient care but also to others who support patient care by participating in product acquisition, storage, transportation, housekeeping, and waste disposal. Institutions may want to adopt this list or compare theirs with the list on the NIOSH Web site.

Caution: Drugs purchased and used by a facility may have entered the marketplace after the list below was assembled. Therefore, this list may not be all-inclusive.

If you use a drug that is not included in the list of examples, check the available literature to see whether the unlisted drug should be treated as hazardous. Check the MSDS or the proper handling section of the package insert; or check with other institutions that might be using the same drug. If any of the documents mention carcinogenicity, genotoxicity, teratogenicity, or reproductive or developmental toxicity, use the precautions stipulated in this Alert. If a drug meets one or more of the criteria for hazardous drugs listed in this Alert, handle it as hazardous.

The listing below is a sample of what will be available on the NIOSH Web site [www.cdc.gov/niosh], and this list will be updated annually.

Sample list of drugs that should be handled as hazardous*

Drug	Source	AHFS Pharmacologic-Therapeutic Classification
Aldesleukin	4,5	10:00 Antineoplastic agents
Alemtuzumab	1,3,4,5	10:00 Antineoplastic agents
Alitretinoin	3,4,5	84:36 Miscellaneous skin and mucous membrane agents (Retinoid)
Altretamine	1,2,3,4,5	Not in AHFS (Antineoplastic agent)
Amsacrine	3,5	Not in AHFS (Antineoplastic agent)
Anastrozole	1,5	10:00 Antineoplastic agents
Arsenic trioxide	1,2,3,4,5	10:00 Antineoplastic agents
Asparaginase	1,2,3,4,5	10:00 Antineoplastic agents
Azacitidine	3,5	Not in AHFS (antineoplastic agent)
Azathioprine	2,3,5	92:00 Unclassified therapeutic agents (immunosuppressant)
Bacillus Calmette-Guerin	1,2,4	80:12 Vaccines
Bexarotene	2,3,4,5	10:00 Antineoplastic agents
Bicalutamide	1,5	10:00 Antineoplastic agents
Bleomycin	1,2,3,4,5	10:00 Antineoplastic agents
Busulfan	1,2,3,4,5	10:00 Antineoplastic agents
Capecitabine	1,2,3,4,5	10:00 Antineoplastic agents
Carboplatin	1,2,3,4,5	10:00 Antineoplastic agents
Carmustine	1,2,3,4,5	10:00 Antineoplastic agents
Cetrorelix acetate	5	92:00 Unclassified therapeutic agents (GnRH antagonist)
Chlorambucil	1,2,3,4,5	10:00 Antineoplastic agents
Chloramphenicol	1,5	8:12 Antibiotics
Choriogonadotropin alfa	5	68:18 Gonadotropins
Cidofovir	3,5	8:18 Antivirals
Cisplatin	1,2,3,4,5	10:00 Antineoplastic agents
Cladribine	1,2,3,4,5	10:00 Antineoplastic agents
Colchicine	5	92:00 Unclassified therapeutic agents (mitotic inhibitor)

(See footnotes at end of table)

Sample list of drugs that should be handled as hazardous* (Continued)

Drug	Source	AHFS Pharmacologic-Therapeutic Classification
Cyclophosphamide	1,2,3,4,5	10:00 Antineoplastic agents
Cytarabine	1,2,3,4,5	10:00 Antineoplastic agents
Cyclosporin	1	92:00 Immunosuppressive agents
Dacarbazine	1,2,3,4,5	10:00 Antineoplastic agents
Dactinomycin	1,2,3,4,5	10:00 Antineoplastic agents
Daunorubicin HCl	1,2,3,4,5	10:00 Antineoplastic agents
Denileukin	3,4,5	10:00 Antineoplastic agents
Dienestrol	5	68:16.04 Estrogens
Diethylstilbestrol	5	Not in AHFS (nonsteroidal synthetic estrogen)
Dinoprostone	5	76:00 Oxytocics
Docetaxel	1,2,3,4,5	10:00 Antineoplastic agents
Doxorubicin	1,2,3,4,5	10:00 Antineoplastic agents
Dutasteride	5	92:00 Unclassified therapeutic agents (5-alpha reductase inhibitor)
Epirubicin	1,2,3,4,5	10:00 Antineoplastic agents
Ergonovine/methylergonovine	5	76:00 Oxytocics
Estradiol	1,5	68:16.04 Estrogens
Estramustine phosphate sodium	1,2,3,4,5	10:00 Antineoplastic agents
Estrogen-progestin combinations	5	68:12 Contraceptives
Estrogens, conjugated	5	68:16.04 Estrogens
Estrogens, esterified	5	68:16.04 Estrogens
Estrone	5	68:16.04 Estrogens
Estropipate	5	68:16.04 Estrogens
Etoposide	1,2,3,4,5	10:00 Antineoplastic agents
Exemestane	1,5	10:00 Antineoplastic agents
Finasteride	1,3,5	92:00 Unclassified therapeutic Agents (5-alpha reductase inhibitor)
Floxuridine	1,2,3,4,5	10:00 Antineoplastic agents

(See footnotes at end of table)

Sample list of drugs that should be handled as hazardous* (Continued)

Drug	Source	AHFS Pharmacologic-Therapeutic Classification
Fludarabine	1,2,3,4,5	10:00 Antineoplastic agents
Fluorouracil	1,2,3,4,5	10:00 Antineoplastic agents
Fluoxymesterone	5	68:08 Androgens
Flutamide	1,2,5	10:00 Antineoplastic agents
Fulvestrant	5	10:00 Antineoplastic agents
Ganciclovir	1,2,3,4,5	8:18 Antiviral
Ganirelix acetate	5	92:00 Unclassified therapeutic agents (GnRH antagonist)
Gemcitabine	1,2,3,4,5	10:00 Antineoplastic agents
Gemtuzumab ozogamicin	1,3,4,5	10:00 Antineoplastic agents
Gonadotropin, chorionic	5	68:18 Gonadotropins
Goserelin	1,2,5	10:00 Antineoplastic agents
Hydroxyurea	1,2,3,4,5	10:00 Antineoplastic agents
Ibritumomab tiuxetan	3	10:00 Antineoplastic agents
Idarubicin	1,2,3,4,5	Not in AHFS (antineoplastic agent)
Ifosfamide	1,2,3,4,5	10:00 Antineoplastic agents
Imatinib mesylate	1,3,4,5	10:00 Antineoplastic agents
Interferon alfa-2a	1,2,4,5	10:00 Antineoplastic agents
Interferon alfa-2b	1,2,4,5	10:00 Antineoplastic agents
Interferon alfa-n1	1,5	10:00 Antineoplastic agents
Interferon alfa-n3	1,5	10:00 Antineoplastic agents
Irinotecan HCl	1,2,3,4,5	10:00 Antineoplastic agents
Leflunomide	3,5	92:00 Unclassified therapeutic agents (antineoplastic agent)
Letrozole	1,5	10:00 Antineoplastic agents
Leuprolide acetate	1,2,5	10:00 Antineoplastic agents
Lomustine	1,2,3,4,5	10:00 Antineoplastic agents
Mechlorethamine	1,2,3,4,5	10:00 Antineoplastic agents
Megestrol	1,5	10:00 Antineoplastic agents
Melphalan	1,2,3,4,5	10:00 Antineoplastic agents

(See footnotes at end of table)

Sample list of drugs that should be handled as hazardous* (Continued)

Drug	Source	AHFS Pharmacologic-Therapeutic Classification
Menotropins	5	68:18 Gonadotropins
Mercaptopurine	1,2,3,4,5	10:00 Antineoplastic agents
Methotrexate	1,2,3,4,5	10:00 Antineoplastic agents
Methyltestosterone	5	68:08 Androgens
Mifepristone	5	76:00 Oxytocics
Mitomycin	1,2,3,4,5	10:00 Antineoplastic agents
Mitotane	1,4,5	10:00 Antineoplastic agents
Mitoxantrone HCl	1,2,3,4,5	10:00 Antineoplastic agents
Mycophenolate mofetil	1,3,5	92:00 Immunosuppressive agents
Nafarelin	5	68:18 Gonadotropins
Nilutamide	1,5	10:00 Antineoplastic agents
Oxaliplatin	1,3,4,5	10:00 Antineoplastic agents
Oxytocin	5	76:00 Oxytocics
Paclitaxel	1,2,3,4,5	10:00 Antineoplastic agents
Pegaspargase	1,2,3,4,5	10:00 Antineoplastic agents
Pentamidine isethionate	1,2,3,5	8:40 Miscellaneous anti-infectives
Pentostatin	1,2,3,4,5	10:00 Antineoplastic agents
Perphosphamide	3,5	Not in AHFS (antineoplastic agent)
Pipobroman	3,5	Not in AHFS (antineoplastic agent)
Piritrexim isethionate	3,5	Not in AHFS (antineoplastic agent)
Plicamycin	1,2,3,5	Not in AHFS (antineoplastic agent)
Podoflilox	5	84:36 Miscellaneous skin and mucous membrane agents (mitotic inhibitor)
Podophyllum resin	5	84:36 Miscellaneous skin and mucous membrane agents (mitotic inhibitor)
Prednimustine	3,5	Not in AHFS (antineoplastic agent)
Procarbazine	1,2,3,4,5	10:00 Antineoplastic agents
Progesterone	5	68:32 Progestins
Progestins	5	68:12 Contraceptives

(See footnotes at end of table)

Sample list of drugs that should be handled as hazardous* (Continued)

Drug	Source	AHFS Pharmacologic-Therapeutic Classification
Raloxifene	5	68:16.12 Estrogen agonists-antagonists
Raltitrexed	5	Not in AHFS (antineoplastic agent)
Ribavirin	1,2,5	8:18 Antiviral
Streptozocin	1,2,3,4,5	10:00 Antineoplastic agents
Tacrolimus	1,5	92:00 Unclassified therapeutic agents (immunosuppressant)
Tamoxifen	1,2,5	10:00 Antineoplastic agents
Temozolomide	3,4,5	10:00 Antineoplastic agents
Teniposide	1,2,3,4,5	10:00 Antineoplastic agents
Testolactone	5	10:00 Antineoplastic agents
Testosterone	5	68:08 Androgens
Thalidomide	1,3,5	92:00 Unclassified therapeutic agents (immunomodulator)
Thioguanine	1,2,3,4,5	10:00 Antineoplastic agents
Thiotepa	1,2,3,4,5	10:00 Antineoplastic agents
Topotecan	1,2,3,4,5	10:00 Antineoplastic agents
Toremifene citrate	1,5	10:00 Antineoplastic agents
Tositumomab	3,5	Not in AHFS (antineoplastic agent)
Tretinoin	1,2,3,5	84:16 Cell stimulants and proliferants (retinoid)
Trifluridine	1,2,5	52:04.06 antivirals
Trimetrexate glucuronate	5	8:40 Miscellaneous anti-infectives (folate antagonist)
Triptorelin	5	10:00 Antineoplastic agents
Uracil mustard	3,5	Not in AHFS (antineoplastic agent)
Valganciclovir	1,3,5	8:18 Antiviral
Valrubicin	1,2,3,5	10:00 Antineoplastic agents
Vidarabine	1,2,5	52:04.06 Antivirals
Vinblastine sulfate	1,2,3,4,5	10:00 Antineoplastic agents

(See footnotes at end of table)

Sample list of drugs that should be handled as hazardous* (Continued)

Drug	Source	AHFS Pharmacologic-Therapeutic Classification
Vincristine sulfate	1,2,3,4,5	10:00 Antineoplastic agents
Vindesine	1,5	Not in AHFS (antineoplastic agent)
Vinorelbine tartrate	1,2,3,4,5	10:00 Antineoplastic agents
Zidovudine	1,2,5	8:18:08 Antiretroviral agents

*These lists of hazardous drugs were used with the permission of the institutions that provided them and were adapted for use by NIOSH. The sample lists are intended to guide health care providers in diverse practice settings and should not be construed as complete representations of all of the hazardous drugs used at the referenced institutions. Some drugs defined as hazardous may not pose a significant risk of direct occupational exposure because of their dosage formulation (for example, intact medications such as coated tablets or capsules that are administered to patients without modifying the formulation). However, they may pose a risk if solid drug formulations are altered outside a ventilated cabinet (for example, intact medications such as coated tablets or capsules that are administered to patients without modifying the formulation). However, they may pose a risk if solid drug formulations are altered outside a ventilated cabinet (for example, if tablets are crushed or dissolved, or if capsules are pierced or opened).

[1]The NIH Clinical Center, Bethesda, MD (Revised 8/2002).
The NIH Health Clinical Center Hazardous Drug (HD) List is part of the NIH Clinical Center's hazard communication program. It was developed in compliance with the OSHA hazard communication standard [29 CFR 1910.1200] as it applies to hazardous drugs used in the workplace. The list is continually revised and represents the diversity of medical practice at the NIH Clinical Center; however, its content does not reflect an exhaustive review of all FDA-approved medications that may be considered hazardous, and it is not intended for use outside the NIH.

[2]The Johns Hopkins Hospital, Baltimore, MD (Revised 9/2002).

[3]The Northside Hospital, Atlanta, GA (Revised 8/2002).

[4]The University of Michigan Hospitals and Health Centers, Ann Arbor, MI (Revised 2/2003).

[5]This sample listing of hazardous drugs was compiled by the Pharmaceutical Research and Manufacturers of America (PhRMA) using information from the AHFS DI monographs published by ASHP in selected AHFS Pharmacologic-Therapeutic Classification categories [ASHP/AHFS DI 2003] and applying the definition for hazardous drugs. The list also includes drugs from other sources that satisfy the definition for hazardous drugs [PDR 2004; Sweetman 2002; Shepard 2001; Schardein 2000; REPROTOX 2003]. Newly approved drugs that have structures or toxicological profiles that mimic the drugs on this list should also be included. This list was revised in June 2004.

APPENDIX B

ABBREVIATIONS AND GLOSSARY

Abbreviations

ACGIH	American Conference of Governmental Industrial Hygienists
ACOEM	American College of Occupational and Environmental Medicine
AHFS	American Hospital Formulary Service
AHFS DI	American Hospital Formulary Service Drug Information
AGS	American Glovebox Society
ANSI	American National Standards Institute
ASHP	American Society of Health-System Pharmacists (before 1995, American Society of Hospital Pharmacists)
BSC	Biological safety cabinet
CDC	Centers for Disease Control and Prevention
FDA	U.S. Food and Drug Administration
ft	foot (feet)
HEPA	high-efficiency particulate air
HIV	human immunodeficiency virus
HVAC	heating, ventilating, and air conditioning
IARC	International Agency for Research on Cancer
IV	intravenous
kg	kilogram(s)
LPN	licensed practical nurse
m^3	cubic meter(s)
mg	milligram(s)
min	minute (s)
MSDS	material safety data sheet
NIH	National Institutes of Health

NIOSH	National Institute for Occupational Safety and Health
NSF	National Sanitation Foundation
OEL(s)	occupational exposure limit(s)
ONS	Oncology Nursing Society
OSHA	Occupational Safety and Health Administration
PDA	PDA (formerly, the Parenteral Drug Association)
PEL(s)	permissible exposure limit(s)
PPE	personal protective equipment
RCRA	Resource Conservation and Recovery Act
REL(s)	recommended exposure limit(s)
RN	registered nurse
SCE(s)	sister chromatid exchange(s)
TLVs®	threshold limit values of the ACGIH
μg	microgram
WEEL	workplace environmental exposure limit

Glossary

Antineoplastic drug: A chemotherapeutic agent that controls or kills cancer cells. Drugs used in the treatment of cancer are cytotoxic but are generally more damaging to dividing cells than to resting cells.

Aseptic: Free of living pathogenic organisms or infected materials.

Barrier system: An open system that can exchange unfiltered air and contaminants with the surrounding environment.

Barrier isolator: This term has various interpretations, especially as they pertain to hazard containment and aseptic processing. For this reason, it has been omitted from this Alert.

Biohazard: An infectious agent or hazardous biological material that presents a risk to the health of humans or the environment. Biohazards include tissue, blood or body fluids, and materials such as needles or other equipment contaminated with these infectious agents or hazardous biological materials.

Biomarker: A biological, biochemical or structural change that serves as an indicator of potential damage to cellular components, whole cells, tissues, or organs.

BSC (biological safety cabinet): A BSC may be one of several types, as described here [CDC/NIH 1999; NSF/ANSI 2002]:

> ***Class I BSC:*** A BSC that protects personnel and the work environment but does not protect the product. It is a

negative-pressure, ventilated cabinet usually operated with an open front and a minimum face velocity at the work opening of at least 75 ft/min. A Class I BSC is similar in design to chemical fume hood except all of the air from the cabinet is exhausted through a HEPA filter (either into the laboratory or to the outside).

Class II BSC: A ventilated BSC that protects personnel, product, and the work environment. A Class II BSC has an open front with inward airflow for personnel protection, downward HEPA-filtered laminar airflow for product protection, and HEPA-filtered exhausted air for environmental protection.

Type A1 (formerly, Type A): These Class II BSCs maintain a minimum inflow velocity of 75 ft/min, have HEPA-filtered downflow air that is a portion of the mixed downflow and inflow air from a common plenum, may exhaust HEPA-filtered air back into the laboratory or to the environment through an exhaust canopy, and may have positive-pressure contaminated ducts and plenums that are not surrounded by negative-pressure plenums. They are not suitable for use with volatile toxic chemicals and volatile radionucleotides.

Type A2 (formerly, Type B3): These Class II BSCs maintain a minimum inflow velocity of 100 ft/min, have HEPA-filtered downflow air that is a portion of the mixed downflow and inflow air from a common exhaust plenum, may exhaust HEPA-filtered air back into the laboratory or to the environment through an exhaust canopy, and have all contaminated ducts and plenums under negative-pressure or surrounded by negative-pressure ducts and plenums. If these cabinets are used for minute quantities of volatile toxic chemicals and trace amounts of radionucleotides, they must be exhausted through properly functioning exhaust canopies.

Type B1: These Class II BSCs maintain a minimum inflow velocity of 100 ft/min, have HEPA-filtered downflow air composed largely of uncontaminated, recirculated inflow air, exhaust most of the contaminated downflow air through a dedicated duct exhausted to the atmosphere after passing it through a HEPA filter, and have all contaminated ducts and plenums under negative pressure or surrounded by negative-pressure ducts and plenums. If these cabinets are used for work involving minute quantities of volatile toxic chemicals and trace amounts of radionucleotides, the work must be done in the directly exhausted portion of the cabinet.

Type B2 (total exhaust): These Class II BSCs maintain a minimum inflow velocity of 100 ft/min, have HEPA-filtered downflow air drawn from the laboratory or the outside, exhaust all inflow and downflow air to the atmosphere after filtration through a HEPA filter without recirculation inside the cabinet or return to the laboratory, and have all contaminated ducts and plenums under negative pressure or surrounded by directly exhausted negative-pressure ducts and plenums. These cabinets may be used with volatile toxic chemicals and radionucleotides.

Class III BSC: A BSC with a totally enclosed, ventilated cabinet of gas-tight construction in which operations are conducted through attached rubber gloves and observed through a nonopening view window. This BSC is maintained under negative pressure of at least 0.50 inch of water gauge, and air is drawn into the cabinet through HEPA filters. The exhaust air is treated by double HEPA filtration or single HEPA filtration/incineration. Passage of materials in and out of the cabinet is generally performed through a dunk tank (accessible through the cabinet floor) or a double-door pass-through box (such as an autoclave) that can be decontaminated between uses. For a more detailed description, refer to CDC/NIH [2000], *Primary Containment for Biohazards: Selection, Installation and Use of Biological Safety Cabinets*, 2nd edition. [www.cdc.gov/od/ohs/biosfty/bsc/bsc.htm].

Chemotherapy drug: A chemical agent used to treat diseases. The term usually refers to a drug used to treat cancer.

Chemotherapy glove: A medical glove that has been approved by the FDA for use when handling antineoplastic drugs.

Chemotherapy waste: Discarded items such as gowns, gloves, masks, IV tubing, empty bags, empty drug vials, needles and syringes, and other items generated while preparing and administering antineoplastic agents.

Closed system: A device that does not exchange unfiltered air or contaminants with the adjacent environment.

Closed system drug-transfer device: A drug transfer device that mechanically prohibits the transfer of environmental contaminants into the system and the escape of hazardous drug or vapor concentrations outside the system.

Cytotoxic: A pharmacologic compound that is detrimental or destructive to cells within the body.

Deactivation: Treating a chemical agent (such as a hazardous drug) with another chemical, heat, ultraviolet light, or other agent to create a less hazardous agent.

Decontamination: Inactivation, neutralization, or removal of toxic agents, usually by chemical means.

Engineering controls: Devices designed to eliminate or reduce worker exposures to chemical, biological, radiological, ergonomic, or physical hazards. Examples include laboratory fume hoods, glove bags, retracting syringe needles, sound-dampening materials to reduce noise levels, safety interlocks, and radiation shielding.

Genotoxic: Capable of damaging the DNA and leading to mutations.

Glove box: A controlled environment work enclosure providing a primary barrier from the work area. Operations are performed through sealed gloved openings to protect the worker, the ambient environment, and/or the product.

Glove bag: A glove box made from a flexible plastic film. Operations are performed through sealed gloved openings to protect the worker, the work environment, and/or the product.

Hazardous drug: Any drug identified by at least one of the following six criteria: carcinogenicity, teratogenicity or developmental

toxicity, reproductive toxicity in humans, organ toxicity at low doses in humans or animals, genotoxicity, or new drugs that mimic existing hazardous drugs in structure or toxicity.

Hazardous waste: Any waste that is a RCRA-listed hazardous waste [40 CFR 261.30–33] or that meets a RCRA characteristic of ignitability, corrosivity, reactivity, or toxicity as defined in 40 CFR 261.21–24.

Health care settings: All hospitals, medical clinics, outpatient facilities, physicians' offices, retail pharmacies, and similar facilities dedicated to the care of patients.

Health care worker: All workers who are involved in the care of patients. These include pharmacists, pharmacy technicians, nurses (registered nurses [RNs], licensed practical nurses [LPNs], nurses aids, etc.), physicians, home health care workers and environmental services workers (housekeeping, laundry, and waste disposal).

HEPA filter: High-efficiency particulate air filter rated 99.97% efficient in capturing 0.3-micron-diameter particles.

Horizontal laminar flow hood (horizontal laminar flow clean bench): A device that protects the work product and the work area by supplying HEPA-filtered air to the rear of the cabinet and producing a horizontal flow across the work area and out toward the worker.

Isolator: A device that is sealed or is supplied with air through a microbially retentive filtration system (HEPA minimum) and may be reproducibly decontaminated. When closed, an isolator uses only decontaminated interfaces (when necessary) or rapid transfer ports (RTPs) for materials transfer. When open, it allows for the ingress and/or egress of materials through defined openings that have been designed and validated to preclude the transfer of contaminants or unfiltered air to adjacent environments. An isolator can be used for aseptic processing, for containment of potent compounds, or for simultaneous asepsis and containment. Some isolator designs allow operations within the isolator to be conducted through attached rubber gloves without compromising asepsis and/or containment.

> ***Aseptic isolator:*** A ventilated isolator designed to exclude external contamination from entering the critical zone inside the isolator.
>
> ***Aseptic containment isolator:*** A ventilated isolator designed to meet the requirements of both an aseptic isolator and a containment isolator.
>
> ***Containment isolator:*** A ventilated isolator designed to prevent the toxic materials processed inside it from escaping to the surrounding environment.

Lab coat: A disposable or reusable open-front coat, usually made of cloth or other permeable material.

MSDS: Material safety data sheet. These sheets contain summaries provided by the manufacturer to describe the chemical properties and hazards of specific chemicals and ways in which workers can protect themselves from exposure to these chemicals.

Mutagenic: Capable of increasing the spontaneous mutation rate by causing changes in the DNA.

OEL: Occupational exposure limit. An industry or other nongovernment exposure limit usually based on scientific calculations of airborne concentrations of a substance that are considered to be acceptable for healthy workers.

PDA: An international trade association serving pharmaceutical science and technology. Formerly known as the Parenteral Drug Association.

PEL: OSHA permissible exposure limit: The time-weighted average concentration of a substance to which nearly all workers may be exposed for up to 8 hours per day, 40 hours per week for 30 years without adverse effects. A PEL may also include a skin designation.

PPE: Personal protective equipment. Items such as gloves, gowns, respirators, goggles, face shields, and others that protect individual workers from hazardous physical or chemical exposures.

REL: NIOSH recommended exposure limit: An occupational exposure limit recommended by NIOSH as being protective of worker health and safety over a working lifetime. The REL is frequently expressed as a time-weighted average exposure to a substance for up to a 10-hour workday during a 40-hour work week.

Respirator: A type of PPE that prevents harmful materials from entering the respiratory system, usually by filtering hazardous agents from workplace air. A surgical mask does not offer respiratory protection.

Risk assessment: Characterization of potentially adverse health effects from human exposure to environmental or occupational hazards. Risk assessment can be divided into five major steps: hazard identification, dose-response assessment, exposure assessment, risk characterization, and risk communication.

Sister chromatid exchange: The exchange of segments of DNA between sister chromatids.

Standard precautions (formerly universal precautions): The practice in health care of treating all patients as if they were infected with HIV or other similar diseases by using barriers to avoid known means of transmitting infectious agents [CDC 1987, 1988]. These barriers can include nonporous gloves, goggles, and face shields. Careful handling and disposal of sharps or the use of needleless systems are also important.

TLVs®: Threshold limit values. These values are exposure limits established by the ACGIH. They refer to airborne concentrations of chemical substances and represent conditions under which it is believed that nearly all workers may be repeatedly exposed, day after day, over a working lifetime, without adverse health effects.

Ventilated cabinet: A type of engineering control designed for purposes of worker protection (as used in this document). These devices are designed to minimize worker exposures by controlling emissions of airborne contaminants through the following:

- The full or partial enclosure of a potential contaminant source
- The use of airflow capture velocities to capture and remove airborne contaminants near their point of generation
- The use of air pressure relationships that define the direction of airflow in or out of the cabinet

Examples of ventilated cabinets include BSCs, containment isolators, and laboratory fume hoods.

WEEL (workplace environmental exposure level): Occupational exposure limits developed by the American Industrial Hygiene Association as a chemical concentration to which nearly all workers may be repeatedly exposed for a working lifetime without adverse health effects.

APPENDIX C

NIOSH HAZARDOUS DRUG SAFETY WORKING GROUP

The following members of the NIOSH Hazardous Drug Safety Working Group provided leadership, information, and recommendations for this document:

Tito Aldape, Microflex Corporation

Roger W. Anderson, Dr.P.H., University of Texas M.D. Anderson Cancer Center

Britton Berek, Joint Commission on Accreditation of Healthcare Organizations

Stephen Brightwell, NIOSH

G. Edward Burroughs, Ph.D., C.I.H., NIOSH

Thomas H. Connor, Ph.D., NIOSH

Barbara D. Coyle, B.S.N., R.N. C.O.H.N.-S., State of Wisconsin

Gayle DeBord, Ph.D., NIOSH

Robert DeChristoforo, M.S., National Institutes of Health

Phillup C. Dugger, U.S. Oncology, Inc.

Barbara A. Grajewski, Ph.D., NIOSH

Dori Greene, U.S. Oncology, Inc.

Duane R. Hammond, B.S.M.E., NIOSH

Bruce R. Harrison, M.S., R.Ph., B.C.O.P., Department of Veterans Affairs

Hye-Joo Kim, U.S. Food and Drug Administration

L.D. King, International Academy of Compounding Pharmacists

Nancy Kramer, R.N., B.S.N., Coram Healthcare

R. David Lauper, Pharm.D., SuperGen, Inc.

Melissa M. Leone, R.N., B.S.N., Apria Healthcare

Chiu S. Lin, Ph.D., U.S. Food and Drug Administration

Barbara A. MacKenzie, NIOSH

Charlene Maloney, NIOSH

Melissa A. McDiarmid, M.D., M.P.H., University of Maryland

Kenneth M. Mead, M.S., P.E., NIOSH

Martha T. O'Lone, U.S. Food and Drug Administration

Jerry Phillips, U.S. Food and Drug Administration

Marty Polovich, M.N., R.N., A.O.C.N., Oncology Nursing Society

Luci Power, M.S., R.Ph., University of California

Angela C. Presson, M.D., M.P.H.,OSHA

Hank Rahe, Containment Technologies Group, Inc

Laurence D. Reed, M.S., NIOSH

Anita L. Schill, Ph.D., M.P.H., NIOSH

Teresa Schnorr, Ph.D., NIOSH

Douglas Sharpnack, D.V.M., NIOSH

Charlotte A. Smith, M.S., R.Ph., PharmEcology Associates, LLC

Sandi Yurichuk, American Federation of State, County and Municipal Employees

American Nurses Association

American Society of Health-System Pharmacists

Oncology Nursing Society

Pharmaceutical Research and Manufacturers of America

Service Employees International Union

U.S. Environmental Protection Agency

Baxa Corporation

Nuaire, Inc

The Baker Company, Inc.

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Centers for Disease Control and Prevention
National Institute for Occupational Safety and Health
4676 Columbia Parkway
Cincinnati, Ohio 45226–1998

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