TECHNICAL INFORMATION PAPER

APHC U.S. ARMY PUBLIC HEALTH CENTER

ADMINISTRATIVE CONTROLS FOR MANAGING HAZARDOUS DRUGS

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PURPOSE

This paper describes several administrative controls for the safe handling of hazardous drugs (HDs): HD identification, HD risk assessments, HD Officer (HDO), HD safety and health plan (HDSHP), worker education and training, warning signs, and medical surveillance. These practices educate healthcare workers (HCWs) on the risks associated with working with HDs, and they reduce occupational exposure when they are used together with engineering controls and personal protective equipment (PPE). An additional administrative control, environmental wipe sampling, will be addressed in greater detail in a separate HD technical information paper.

POINTS OF MAJOR INTEREST AND FACTS

Background

The U.S. Army Medical Command published Technical Bulletin-Medical (TB MED) 515, Occupational Health and Industrial Hygiene Guidance for the Management, Use and Disposal of Hazardous Drugs on 22 April 2014. The TB MED 515 consolidated the safety practices for handling HDs that were recommended in numerous federal and national consensus standards. Two key takeaways from the TB MED 515 are (1) there is no acceptable level of occupational exposure to HDs and (2) all potential occupational exposures must be kept to the lowest possible level through the use of engineering and administrative controls, safe work practices, and PPE.

The U.S. Pharmacopeial Convention (USP) published General Chapter <800> Hazardous Drugs – Handling in Healthcare Settings on 1 February 2016. The USP also published an erratum to Chapter <800> that revised the exhaust ventilation requirements for the containment secondary engineering controls (C-SEC) on 26 May 2016. The Chapter <800> focuses on protecting HCW from occupational exposure to HDs in healthcare settings. This paper integrates the latest health and safety information published in Chapter <800> with the TB MED 515 guidance.

It is important to note that the Chapter <800> adds to, but does not replace, the USP General Chapters <795> Pharmaceutical Compounding – Nonsterile Preparations and <797> Pharmaceutical Compounding – Sterile Preparations. The Chapter <800> will become federally enforceable on 1 July 2018.

Hazardous Drug Identification

The first step in protecting HCWs from occupational exposure to HD is to develop a comprehensive list of all of the HDs handled in the facility.

The Food and Drug Administration (FDA) defines a drug as—

- A substance recognized by an official pharmacopoeia or formulary.
- A substance intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease.
- A substance (other than food) intended to affect the structure or any function of the body.
- A substance intended for use as a component of a medicine but not a device or a component, part, or accessory of a device.
- Biological products are included in the FDA's definition of a drug and are generally covered by the same laws and regulations, but differences exist regarding their manufacturing processes (chemical process versus biological process).

A drug's effect on the body can be positive, negative, intentional, or a side-effect (a harmful, unwanted effect that occurs along with the desired effect). Drugs are deemed hazardous when they pose a health risk to the HCW who handle, prepare, or administer them. Examples of adverse health effects resulting from occupational exposure to HDs include, but are not limited to, skin rashes, infertility, miscarriages, birth defects, leukemia, and other cancers.

The National Institute for Occupational Safety and Health (NIOSH) maintains a list of HDs that healthcare facilities must use as a starting point when developing their respective HD lists. The most recent version of the NIOSH list is available online at NIOSH List of Antineoplastic and Other Hazardous Drugs in Healthcare Settings, 2016. The NIOSH considers a drug hazardous and includes the drug on its list when it exhibits one or more of the following six criteria—

- Carcinogenicity
- Teratogenicity or developmental toxicity
- Reproductive toxicity in humans
- Organ toxicity at low doses in humans or animals
- Genotoxicity
- New drugs that mimic existing HD in structure or toxicity

- The NIOSH groups its list of HDs into three categories—

    - Group 1: Antineoplastic drugs (American Hospital Formulary Service (AHFS) Classification 10:00)
    - Group 2: Non-antineoplastic drugs that meet one or more of the NIOSH criteria for a HD
    - Group 3: Drugs that primarily have adverse reproductive effects

- The NIOSH updates its HD list every 2 to 3 years, adding newly identified HDs and removing HDs when they no longer meet the HD criteria.

Because the NIOSH list can become outdated quickly due to new drugs being continually introduced into the marketplace, the availability of new information, and the lag time between the NIOSH updates, facilities should also reference the following resources when developing and updating their HD lists—

- AHFS Pharmacologic-Therapeutic Classification System (Therapeutic Category 10:00, Antineoplastic Agent)
- International Agency for Research on Cancer Monographs on the Evaluation of Carcinogenic Risks to Humans (Group 1, Carcinogenic to humans; Group 2A, probably carcinogenic to humans; and Group 2B, possibly carcinogenic to humans)
- Manufacturers' safety data sheets (SDS) and labels where the use of special isolation or other techniques in a drug's handling, administration, or disposal are recommended
- National Toxicology Program's Report on Carcinogens (known human carcinogens or reasonably anticipated to be human carcinogens)
- Manufacturers' package inserts for specific pharmaceutical agents (e.g., drug classification, pregnancy category and reproductive toxicity, organ toxicities, secondary cancers that may develop with exposure, and drug warnings)
- FDA Approved Drug Products available on line at http://www.accessdata.fda.gov/scripts/cder/daf/index.cfm
- All investigational drugs should be handled as HD where there is insufficient information available to make a determination

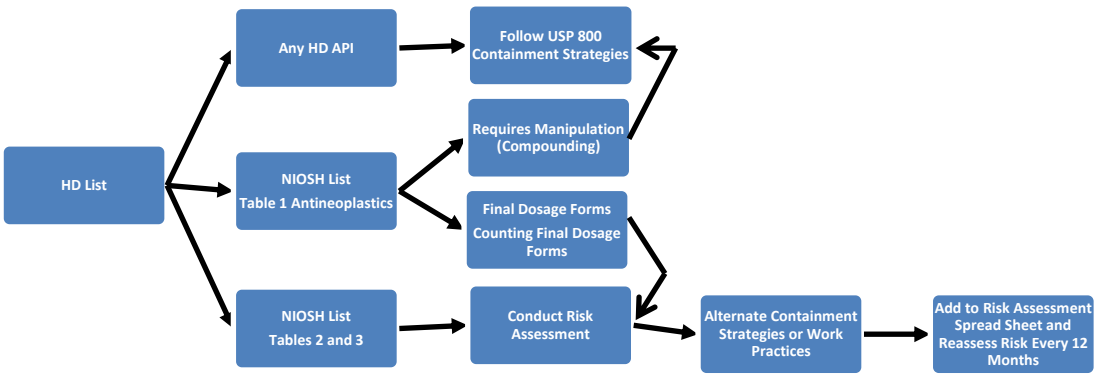
Chapter <800> requires facilities to review their HD lists every 12 months and update them whenever new drugs or dosage forms are introduced in the workplace.

Risk Assessments

Facilities must use all containment strategies described in Chapter <800> for activities having a higher exposure risk, such as manipulating antineoplastic drugs (NIOSH List

Table 1) and compounding with any HD active pharmaceutical ingredient (API). However, some activities pose a lesser exposure risk due to the HD type and its dosage form. Examples of lower exposure risk activities include counting antineoplastics (NIOSH List Table 1) that are in final dosage form (e.g., coated, solid, intact tablets or capsules) and manipulating non-antineoplastics (NIOSH list Table 2) and reproductive hazards (NIOSH List Table 3). For these lesser risk activities, facilities must decide to follow all of the Chapter <800> containment strategies or to conduct a risk assessment and choose the alternate containment strategies or work practices to minimize occupational exposure. The flow chart below shows a simple process for conducting a risk assessment.

HD Risk Assessment



The risk assessment must take the following information under consideration—

- The HD type (e.g., antineoplastic, non-antineoplastic, reproductive risk)
- The HD's dosage form—

  - Solid orals that must be counted or packaged or in the unit-of-use or unit-dose
  - Liquid orals that must be measured or in unit-of-dose
  - Topical in unit-of-use or unit-dose or that must be manipulated or repackaged
  - Injections to be dispensed/distributed without manipulation or that require manipulation under Chapter <800> compliant conditions
  - The HD that are manipulated outside Chapter <800> compliant conditions (e.g., Bacillus Calmette-Guerin (BCG) or ophthalmic mitomycin)
  - The monoclonal antibodies listed on NIOSH List Table 1 that are conjugated to another hazardous substance (e.g., cytotoxic or radiopharmaceutical agents)

  - Infusions that are dispensed/distributed without manipulation or from a compounding pharmacy or outsourcer that is dispensed/distributed without manipulation
  - Ophthalmics, irrigations, inhalants, etc.

- Areas where handled (e.g., Pharmacy, Oncology Units, Medical/Surgical Units, Urology Clinic, Emergency Department, Obstetrics, Surgical Services, etc.)
- Possible route(s) of exposure (e.g., dermal, mucosal absorption, inhalation, injection, ingestion)
- Packaging (e.g., dispensed directly to the patient in the manufacturer's original packaging)
- Manipulation (e.g., repackaging, crushing/opening the dosage form, compounding)
- Volume/Frequency (e.g., typical amount of the HD handled daily, monthly, quarterly, or annually)
- Information from the Manufacturer's package inserts
- Risk assessment (high risk, low risk, or no risk activities)
- Alternate engineering controls and work practices for purchasing; receipt; transport; storage; sterile and non-sterile compounding areas; deactivating, decontaminating, and cleaning procedures; administration; disposal; handling spills; etc.

Risk assessments must be recorded (see sample spreadsheet below) and reviewed every 12 months.

Sample Risk Assessment Spreadsheet

Drug Name	Drug Type	Dosage Form	Areas Where the Drug is Handled	Route(s) of Exposure	Packaging	Manipulation	Volume and Frequency	Manufacturer's Package Insert	Risk Assessment	Follow USP Chapter <800>	Follow Alternate Engineering Controls and Work Practices

Hazardous Drug Safety and Health Officer (HDO)

Each facility that handles HDs must designate a HDO to oversee the development and implementation of HD safety and health policies and procedures.

Leaders should designate a knowledgeable individual responsible for—

- Recognizing the occupational safety and health risks associated with handling HDs.
- Informing leadership on compliance with Chapter <800>, TB MED 515, and other applicable laws, regulations, guidelines, and standards, such as the Joint Commission's (TJC) standards for managing HDs and HD waste.
- Verifying that the HDSHP is implemented and effective.
- Collecting data related to worker safety and health, deficiencies (including HD spills and worker exposures), and opportunities for improving the HDSHP.
- Submitting data collection reports to the facility's HD Committee and/or the Safety/Environment of Care Committee routinely and evaluating the HDSHP and related standing operating procedures (SOP) for effectiveness annually.
- Assisting work-area supervisors in conducting and documenting risk assessments.
- Making sure all required documentation is maintained and readily available to inspectors/surveyors.
- Coordinating periodic environmental wipe sampling to determine the need for engineering controls, the effectiveness of the cleaning and decontamination processes used, and the types of PPE required.

Written HDSHP

To keep occupational exposures to the lowest possible level, facilities should develop and implement a comprehensive HDSHP that addresses the following practices for the safe handling of HD—

- Identifying all HD handled in the facility and maintaining a comprehensive HD list
- Conducting HD risk assessments and deciding the appropriate containment strategies for the HDs handled in the facility
- Complying with the facility's Hazard Communication Program, including procedures for maintaining a written HD inventory, hazard warning labels, and SDS
- Monitoring worker health through the facility's Medical Surveillance Program
- Designating HD areas (e.g., storage, non-sterile and sterile compounding, administration, etc.)
- Developing a work area specific SOP for—

    - Receiving HDs
    - Storing HDs
    - Compounding sterile and non-sterile HDs

- Using and maintaining engineering controls (e.g., containment primary engineering controls (C-PEC), C-SEC, and closed-system drug transfer devices (CSTD))
- Practicing hand hygiene
- Using PPE based on the job duties performed
- Deactivating, decontaminating, cleaning, and disinfecting work areas and equipment
- Dispensing HDs
- Transporting HDs
- Administering HDs
- Monitoring for contamination in work areas where HDs are handled (e.g., environmental wipe sampling)
- Disposing of HD waste
- Preventing and responding to spills

The HDO must review and assess the HDSHP for effectiveness every 12 months and update the plan as needed.

The HDO should make sure that comprehensive records related to the HDSHP are maintained. At a minimum, associated records should include—

- Results of the annual HDSHP evaluation. Records should be maintained 3 years from the date of the facility's last full TJC survey and no more than 6 years after the date the evaluation was completed.
- Certification, maintenance, and testing records for engineering controls (e.g., compounding aseptic containment isolators (CACI) and biological safety cabinets (BSC), and clean room ventilation systems.) Records should be maintained for life of the equipment or system.
- The Industrial Hygiene survey and workplace monitoring results. Results must be recorded in Defense Occupational and Environmental Health Readiness System-Industrial Hygiene (DOEHRS-IH) and kept as stated in Department of Army Pamphlet (DA PAM) 40-503, the Army Industrial Hygiene Program.
- The HCWs' medical records. Occupational medical surveillance examinations for Service members and civilian personnel must be recorded and maintained as stated in Army Regulation (AR) 40-66, Medical Record Administration and Health Care Documentation. Records must be maintained for at least the duration of employment plus 30 years.
- The HCWs' education and training records. Records should be maintained 3 years from the date of the facility's last full TJC accreditation survey.
- Investigational HD approvals and reports if applicable. Records must be kept as stated in AR 40-7, Use of U.S. Food and Drug Administration-Regulated Investigational Products in Humans Including Schedule I Controlled Substances.

All HCWs that handle HDs must have free access to the HDSHP and work area SOP.

Education and Training

Hazard Communication.

- All HCWs who handle HDs must attend hazard communication training and be informed of—

  - Any operation or procedure in their work area where HDs are present.
  - The location and availability of the facility's written Hazard Communication Program.
  - The location and availability of the list(s) identifying the HD present in the work area.
  - The location and availability of the SDS for all HDs in the work area.
  - The hazards associated with the HD present in their work area.
  - The control measures that will prevent occupational exposure.

- Hazard communication training must occur—

  - Before a HCW handles HDs (e.g., at the time of their initial assignment to a work area where a HD is present and before carrying out tasks involving the HD).
  - When a new HD is introduced into the work place.
  - When new equipment used to handle a HD is introduced into the work place.
  - When there is a significant change in procedures or work practices.

The HDO should attend education and training to develop the knowledge and skills necessary to effectively carryout their assigned responsibilities. Education and training topics should include—

- An overview of the facility's list of HD and their risks.
- A review of the facility's HDSHP and work area SOP.
- Selection and proper use of PPE.
- Proper use of equipment and devices, including an overview of safe aseptic manipulation practices; negative pressure techniques when using a BSC or a CACI; and the correct use of CSTD.
- Decontamination/deactivation, cleaning, and disinfection procedures.
- Environmental wipe sampling procedures for HD residue.
- An overview of compounding and dispensing procedures together with the HD labeling and packaging requirements and the precautions for transporting HD within the facility.

- Medical surveillance procedures, including procedures for responding to a known or suspected HD exposure and treatment of a HCW following a contact or inhalation exposure.
- Containment, clean-up, and disposal procedures for spills and breakages.
- Proper HD disposal procedures.

Supervisors of an affected HCW must know the facility-wide and work area-specific SOP for handling HDs. They should receive additional training as needed to enable them to effectively—

- Evaluate their respective work area and work practices to detect and eliminate HD hazards and reduce HCW's risk of occupational exposure.
- Verify control measures (e.g., engineering and administrative controls, safe-work practices and PPE) are available, functional, effective, and properly used.
- Reinforce worker knowledge and assess worker competency in safe handling procedures.

All HCWs who handle HDs must receive initial and on-going (e.g., annual) education and training based on their assigned roles and the tasks they perform (e.g., receiving, storing, compounding, repackaging, dispensing, administering, and disposing of HD). They must be familiar with the HD list, risk of exposure, and facility-wide and work area-specific SOPs for handling HDs. Also, workers must be able to demonstrate that they can perform the following safe handling procedures—

- Properly use safety equipment and devices.
- Use PPE correctly, including respiratory protection where it is required to be worn.
- Respond to a known or suspected HD exposure.
- Follow HD spill prevention, clean-up, and reporting procedures.
- Dispose of HDs and trace-contaminated materials properly.

Compounding personnel must receive additional training on the following safe handling procedures—

- Proper use of equipment and devices, including an overview of safe aseptic manipulation practices; negative pressure techniques when using a BSC or a CACI; and the correct use of CSTD.
- Decontamination/deactivation, cleaning, and disinfection procedures.

Supervisors must assess each HCW's competency in safe handling practices after the initial training session, and then reassess their competency at least every 12 months thereafter. Competency assessments may involve written or oral exams and direct

observation of their HD handling skills (e.g., safe aseptic manipulation practices, proper use of safety equipment, proper techniques for donning and doffing PPE, hand hygiene, spill response procedures, etc.)

All training and competency assessments must be recorded. The HD training records should include the—

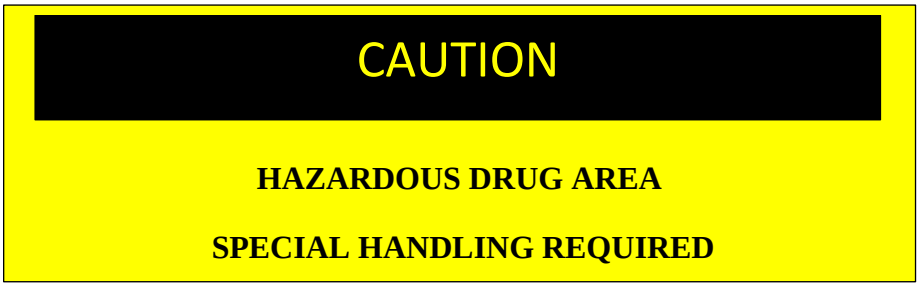
- Dates of the training sessions
- Contents or a summary of the training sessions
- Names and qualifications of the persons conducting the training
- Names and job titles of all persons attending the training sessions

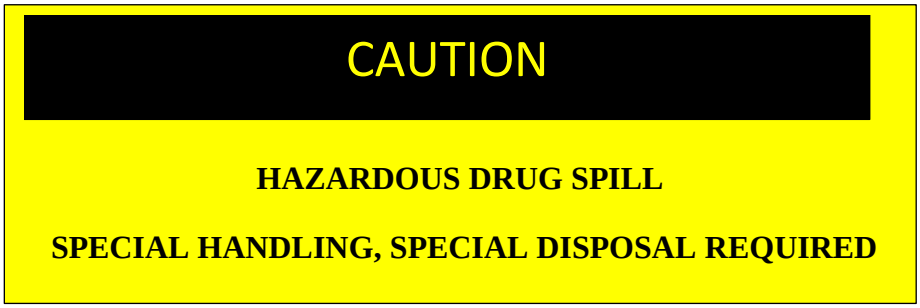
Signage

Signage stating "CAUTION: HAZARDOUS DRUG AREA; SPECIAL HANDLING REQUIRED" should be posted at entrances to work areas where HDs are stored and handled (e.g., received, compounded, and administered).

Signage stating "CAUTION: HAZARDOUS DRUG SPILL; SPECIAL HANDLING, SPECIAL DISPOSAL REQUIRED" should be posted to mark HD spills before and during clean up.

Signage should have a yellow background with black text.





Additional signage may be posted in the work areas to provide supplementary safety instructions.

Medical Surveillance

All HCWs that handle a HD as a regular part of their job duties should be included in the facility's Medical Surveillance Program. The purpose of medical surveillance is to monitor workers for adverse health effects and to determine the effectiveness of engineering and administrative controls, safe work practices, and PPE used to prevent occupational exposure.

Medical surveillance should be performed at specific intervals—

- Pre-placement examinations. Occupational medicine providers should collect medical and occupational histories and tailor the medical examinations and laboratory studies to the HCW's potential for exposure and specific toxic profiles of the HD handled (e.g., hematological studies for antineoplastic agents). Pre-placement medical histories should be very detailed and address the following—

    - Medical history should focus on the known target organ systems of the HDs handled (e.g., hematopoietic, hepatic, reproductive, skin, and urologic); symptoms thought to be caused by exposure to HDs (e.g., significant, unintentional weight loss; fever; malaise; unexplained fatigue; headache; hair loss; lightheadedness; dizziness); and information from previous medical examinations. Special consideration should be given to the HCW's reproductive history (general questions regarding problems conceiving, spontaneous abortions, fetal malformations, etc.) Female HCWs should be asked to provide a complete reproductive history of each pregnancy (dates, outcome, and work history during pregnancy) and menstrual irregularities. Male HCWs should provide information about the inability to conceive and the reproductive histories of their partners.

    - Work history should include a description of the HCW's job duties related to exposure to HDs such as the names of the HD handled, the quantities handled, hours spent handling a HD per week, and number of preparations or administrations per week. Work history should also include a description of the engineering and administrative controls, work practices, and PPE worn when handling HDs.

    - Physical examinations should be complete with emphasis on the skin, mucous membranes, cardiopulmonary and lymphatic systems, and liver. Providers must tailor the elements of the physical exam toward the target organs of the

HDs to which the worker is exposed. Additional testing may be ordered at the discretion of the provider.

- Suggested laboratory tests include a complete blood count with differential, reticulocyte count, liver transaminase concentrations (aspartate aminotransferase and alanine aminotransferase), and urine microscopy or dipstick for blood. Providers must tailor the elements of their laboratory testing toward the target organs of the HD to which the worker is exposed.

- Pregnancy. Workers, both male and female, starting any job that requires routine handling of a HD should be fully informed of the potential reproductive and other health hazards. These HCWs must confirm in writing that they understand the safety and health risks of handling a HD.

- Additionally, HCWs who are pregnant, breast-feeding, or are trying to conceive a child should be given the option of being transferred to other comparable duties that do not involve handling HDs.

- Periodic examinations during employment. Periodic examinations may be less detailed than pre-placement examinations by focusing on the signs and symptoms related to exposure to HD and changes in the worker's health status. All HCW working with HD should receive a medical examination annually or more often at the discretion of the occupational medicine provider (based on the worker's potential for exposure, duration of exposure, history, and age) as well as an incidental examination as required (such as, after an acute exposure). Periodic examinations may detect changes in—

  - The HCW's general health as might be affected by subsequent exposure to HD.
  - Specific diagnoses secondary to exposure to HD.

- Post-exposure examinations.

  - Post-exposure examinations should focus on the exposed area of the body and other organ systems commonly affected. The treating medical practioner must document the acute exposure evaluation in the HCW's medical record.

  - Acute exposures include, but are not limited to—

    - A needle-stick from a needle attached to a syringe or intravenous (IV) catheter containing an HD.
    - A spill or splash on exposed skin or in the eye(s).

  - Ingestion resulting from inadvertent hand contact with HDs when handling food, drink, cosmetics, and smoking materials.
  - Inhalation of aerosols or droplets.

- First-aid for an acute exposure requires immediate action to include decontamination and medical care or evaluation. Treat overt contamination of gloves or gown and direct skin or eye contact as follows—

  - Immediately remove contaminated PPE and any underlying clothing that is contaminated due to soak through. Discard disposable items in an appropriate waste container.
  - Wash contaminated skin with soap and water. For splashes to the eye(s), rinse the affected eye(s) with tepid water for at least 15 minutes or until the pH of the conjunctival surface is neutral; then refer the worker to an eye-care provider.
  - Refer to the manufacturer's SDS for additional emergency and first-aid procedures.
  - Follow-up with medical attention, especially for inhalation of HDs in powder form.

- The HCW's immediate supervisor should investigate the accident as stated by the facility's accident reporting procedures and send a copy of the accident report to the HDO and safety manager. The investigation should include—

  - A comparison between the current administrative, engineering controls, and the relevant regulations, guidelines, and standards.
  - Verification that engineering controls were operational.
  - Verification that the HCW complied with practices described in the HDSHP and work area SOP.
  - Verification that the appropriate PPE was available and used.
  - A review of any environmental wipe sampling results conducted in the work area.
  - An action plan to prevent additional exposure to workers.
  - A follow-up survey to verify the actions plan was implemented and effective.
  - Ongoing communication between the Occupational Health Department and the exposed worker regarding any adverse health effects, and potential alternative duty or temporary assignment.

- Medical surveillance serves as an additional tool to evaluate the effectiveness of engineering and administrative controls, safe work practices, and PPE. Therefore, any occurrence of HD exposure-related disease or adverse health effects should initiate an immediate investigation into the effectiveness of the

HD handling practices currently in use. Investigations should be conducted in the same manner as an investigation following an acute exposure.

- Termination examinations. Termination examinations are provided on termination of assignment or termination of employment for all workers who have been included in a periodic job-related medical surveillance program, unless an examination has been conducted within the past 90 days. The examination and laboratory evaluation should be guided by the worker's exposure history and follow procedures for conducting a periodic evaluation.

CONCLUSION

The administrative controls discussed in this paper describe a number of ways to reduce occupational exposure to HDs. The first step for reducing occupational exposure is to identify the HDs handled in the facility, the specific locations where HDs are present, and the workers at risk for occupational exposure. The second step is to develop a written HDSHP that establishes the framework for carrying out other important processes such as assessing risk, designating knowledgeable individuals to oversee the program, establishing SOPs, educating and training workers, and monitoring workers' health through medical surveillance. Administrative controls should always be used to prevent occupational exposure to HDs; however, they are prone to human error and failure from time to time. Therefore, administrative controls must always be used together with engineering controls and PPE to protect workers from occupational exposure to HDs.

POINT OF CONTACT FOR FURTHER INFORMATION

For more information, contact the U.S. Army Public Health Center, Industrial Hygiene Program Management at commercial 410-436-2439 or DSN 584-2439.

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Dated: 5 April 2017

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