Defining a Hazardous Agent

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Objectives

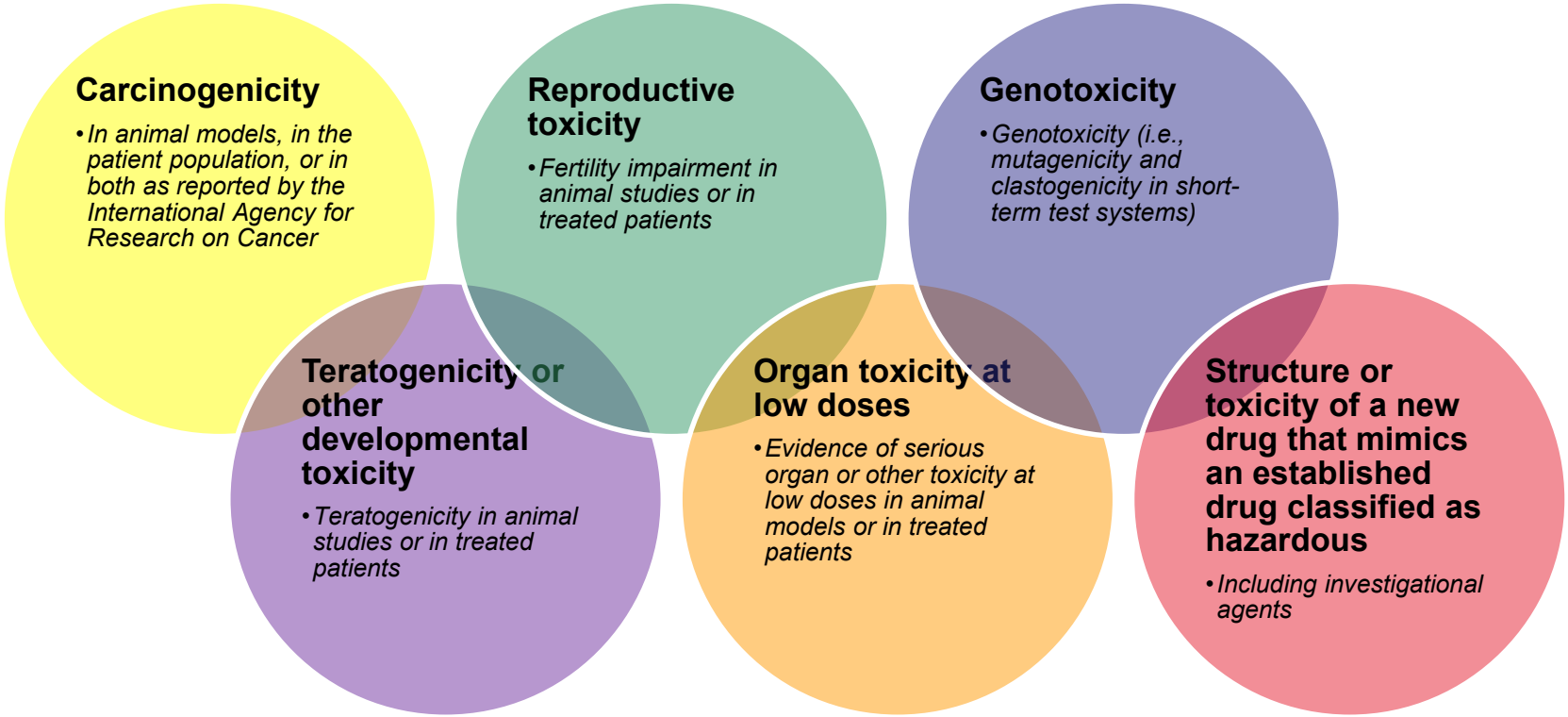
By the end of this presentation, the participant should be able to:

- Identify guidelines which define hazardous agents/drugs
- Describe the characteristics which classify an agent/drug as hazardous
- Design a list of agents/drugs which are considered hazardous

Relevant International Guidelines

Guideline/Recommendation	Group; Year Updated
United States Pharmacopoeia (USP) Chapter <800>	United States Pharmacopoeia; 2019
ASHP Guidelines on Handling Hazardous Drugs	American Society of Health System Pharmacists (ASHP); 2018
OSHA technical Manual: Controlling Occupational Exposure to Hazardous Drugs	Occupational Safety & Health Administration (OSHA); 2014
Safe Handling of Hazardous Chemotherapy Drugs in Limited-Resource Settings	Pan American Health Organization of the WHO; 2013
Chemotherapy Administration Safety Standards	American Society of Clinical Oncology & Oncology Nursing Society; 2013
ISMP International Medication Safety Self assessment for Oncology	Institute for Safe Medication Practices (ISMP); 2012
QuapoS 4: Quality Standard for the Oncology Pharmacy Service with Commentary, DGOP e.V	German Society of Oncology Pharmacy
ISOPP Standards of practice	International Society of Oncology Pharmacy Practitioners (ISOPP); 2007
Bonnes Pratiques de préparation (BPP)	Agence française de sécurité sanitaire de produits de santé (Afssaps); 2007
Suvapro: sécurité dans l'emploi des cytostatiques	Swiss Accident Insurance Fund; 2004

Hazardous Drug Criteria/Characteristics



All characteristics must be considered.
A drug does *not* need to meet all criteria to be considered "hazardous" - it may be hazardous by only meeting 1 of the criteria above.
The handling approach may vary based on the risk criteria.

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USP <800> Implementation Details

- **A single designated person must oversee hazardous drug handling in the institution**
  - Must have proper knowledge, training, and qualifications

- **A health system must establish a hazardous drugs list**
  - Must be based on the model list by NIOSH
    - NIOSH classifies agents into one of 3 categories based on personnel risk
  - Must be updated annually

- **When implementing safe handling guidelines, the institution must also annually evaluate the following**
  - NIOSH classification of each agent
  - Dosage forms used
  - Need for manipulation based on presentation/patient population
  - Manufacturer's packaging
  - The overall risk of exposure

NIOSH Hazardous Drugs List (2016)

Group 1
- Antineoplastic drugs
- Identified by American Hospital Formulary Service (AHFS) Classification 10:00

Group 2
- Non-antineoplastic drugs that meet one or more of the 6 NIOSH criteria

Group 3
- Drugs that pose a reproductive risk for men and women who are actively trying to conceive and women who are pregnant or breast-feeding (as some agents may be present in breast milk)

The NIOSH list has been updated about every 2 years since first published in 2004. The next update is pending for 2019.

Group 1: Antineoplastic Drugs

Select agents based on Pediatric Hematology/Oncology use; not a comprehensive list

Agent	Additional Details
Arsenic trioxide	IARC Group 1 carcinogen; NTP*; FDA Pregnancy Cat D
Bleomycin	IARC Group 2B carcinogen; FDA Pregnancy Category D
Carboplatin	FDA Pregnancy Category D
Cisplatin	IARC Group 2A carcinogen; NTP**; FDA Pregnancy D
Cyclophosphamide	IARC Group 1 carcinogen*; NTP; FDA Pregnancy Cat D
Cytarabine	FDA Pregnancy Category D
Dacarbazine	NTP**; FDA Pregnancy Category C
Dactinomycin	FDA Pregnancy Category D
Daunorubicin	IARC Group 2B carcinogen; FDA Pregnancy Category D
Doxorubicin	IARC Group 2A carcinogen; NTP**; FDA Pregnancy Category D
Etoposide	IARC Group 1 carcinogen; FDA Pregnancy Category D

Agent	Additional Details
Fluorouracil	FDA Pregnancy Category D
Hydroxyurea	FDA Pregnancy Category D
Ifosfamide	FDA Pregnancy Category D
Imatinib	FDA Pregnancy Category D
Mercaptopurine	FDA Pregnancy Category D
Methotrexate	FDA Pregnancy Category X
Paclitaxel	FDA Pregnancy Category D
Procarbazine	IARC Group 2A carcinogen; NTP**; FDA Pregnancy Category D
Temozolomide	FDA Pregnancy Category D
Vinblastine	FDA Pregnancy Category D
Vincristine	FDA Pregnancy Category D

*FDA: U.S. Food & Drug Administration; IARC: International Agency for Research on Cancer; Group 1 = Carcinogenic, Group 2A = Probably Carcinogenic, Group 2B = Possibly Carcinogenic; NTP = National Toxicology Program *Known or **Reasonably Accepted as Human Carcinogens; MHRD = maximum recommended human dose*

Group 2: Other Drugs Meeting NIOSH Criteria

Select agents based on Pediatric Hematology/Oncology use; not a comprehensive list
Agents meeting ≥1 NIOSH criteria & agents with manufacturer's safe-handling guidance

Agent	Additional Details
Carbamazepine	Boxed warning for aplastic anemia; congenital malformations in offspring; rapid transplacental passage; FDA Pregnancy Category D
Chloramphenicol	IARC Group 2A carcinogen; NTP**; FDA Pregnancy C
Cidofovir	FDA Pregnancy Category C
Cyclosporine	IARC Group 1 carcinogen; NTP*; FDA Pregnancy Category C
Dexrazoxane	FDA Pregnancy Category C; secondary malignancies; genotoxic in vitro and in vivo; testicular atrophy at or below human dose (in lab studies)
Estrogens	IARC Group 1 carcinogen; NTP*; Pregnancy Category X; (see specific agent for more details)
Fosphenytoin & phenytoin	IARC Group 2B; NTP**; FDA Pregnancy Category D
Ganciclovir & valganciclovir	FDA Pregnancy Category C

Agent	Additional Details
Lenalidomide	Analog of thalidomide; Black Box warning/animal data for limb abnormalities; FDA Pregnancy Category X
Medroxyprogesterone acetate	IARC Group 2B; FDA Pregnancy Category X
Mycophenolate mofetil	Black Box warning for embryo fetal toxicity, malignancies, serious infections; increased risk of first trimester loss and congenital malformations; FDA Pregnancy Category D
Nevirapine	FDA Pregnancy Category B; hepatocellular adenomas and carcinomas at doses lower than human dose
Oxcarbazepine	Tumors in lab studies at 1/10 the MHRD; FDA Pregnancy Category C
Sirolimus	Increased risk of lymphomas and other malignancies; embryotoxic and fetotoxic at 0.2 human dose; FDA Pregnancy Category C
Tacrolimus	Increased risk of lymphomas and other malignancies; reproductive effects in lab studies below MRHD; excreted in breast milk; FDA Pregnancy Category C
Zidovudine	IARC Group 2B; FDA Pregnancy Category C

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Group 3: Agents with Adverse Reproductive Effects

Select agents based on Pediatric Hematology/Oncology use; not a comprehensive list

Agent	Additional Details
Fluconazole	FDA Pregnancy Category C; case reports of congenital anomalies in infants exposed in utero to maternal fluconazole during the first trimester
Ribavirin	Teratogenic and embryotoxic effects in lab studies; contraindicated in women who are pregnant and male partners of women who are pregnant; FDA Pregnancy Category X
Tretinoin	Black Box warning for severe birth defects; FDA Pregnancy Category X
Valproate/valproic acid	Black Box warning for teratogenicity; congenital malformations, including neural tube defects; FDA Pregnancy Category D
Voriconazole	FDA Pregnancy Category D
Warfarin	FDA Pregnancy Category D
Zoledronic acid	Increased number of still births and decreased neonatal survival in lab studies at low doses; FDA Pregnancy Category D

Hazardous Agents: Next Steps

- An institutional approach to classifying and handling hazardous agents must be established
  - *The NIOSH model list must be used as a starting point*
- The approach to safe handling will vary based on the drug dosage form, preparation approach, toxicity characteristics, and more
- Additional details on safe handling of hazardous agents are discussed in other modules

What's Next?

- Complete practice questions
- Review answer file

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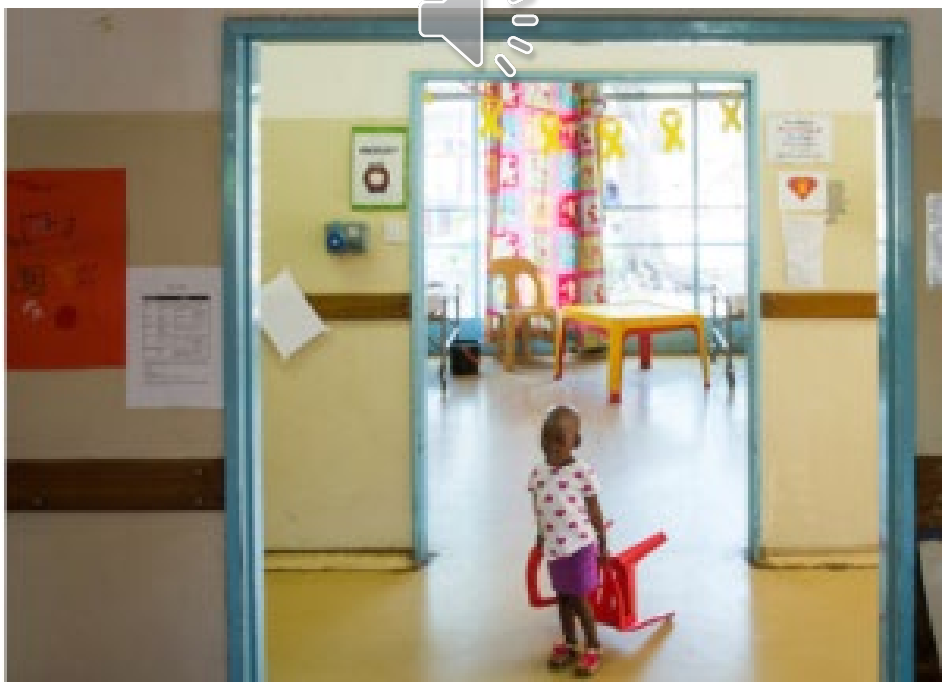

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