

SAFETY INSTRUCTIONS FOR WORK WITH CYTOTOXIC/ CHEMOTHERAPIC MATERIALS

GENERAL:

DO NOT USE THE MATERIALS BEFORE RECEIVING TRAINING FROM A QUALIFIED PERSON AND BEFORE UNDERSTANDING THE MATERIAL SDS AND ALL ITS RISKS.

1. Cytotoxic materials are materials known or suspected as carcinogenic, teratogenic (harmful for the fetus) or mutagenic used for the treatment of humans or animals.
2. All purchase or storage of cytotoxic material is accompanied by the material SDS to be reviewed.
3. Store cytotoxic materials in a secured, locked cabinet, with access reserved to authorized persons only.
4. Affix a label indicating that those are dangerous cytotoxic materials.
5. Work should be performed only after receiving training from a person familiar with the risks of the materials including training on issues such as personal protective equipment, work processes, knowing the risks, enforcing cleanliness and order, disposal of cytotoxic waste and actions/ response to spill and exposure incidents.
6. Women's work with cytotoxic materials shall be according to Women's Work Regulations (prohibited works, limited works, dangerous works) 2001, updated, including regulations 4, 5, 6, 7, 8, 9
7. According to the regulations, it is permitted to work with diluted material ready for injection.
8. It is recommended that pregnant or breast feeding women do not perform procedures involving cytotoxic materials – assess each material according to its SDS and act accordingly.
9. All works shall be performed in the biological or chemical hood, over absorbent pads.
10. Following is the personal protective equipment to be mandatorily used with cytotoxic materials:
 - 10.1. Long sleeved coat
 - 10.2. Goggles
 - 10.3. Nitrile gloves (without talc) – it is recommended to use two pairs of protective gloves.
 - 10.4. Safety boots
11. Solution preparation from powder: it is recommended to order materials in known weight ampoules to avoid the need for weighting in the lab. If needed, transfer of material for weighing

shall be done in a chemical or biological hood into a closed volumetric flask in which the solution shall be prepared on the analytical weights.

12. Nobody shall be found in the vicinity when working with cytotoxic powders, weighing or adding liquids.
13. Clean the hood and the work surfaces on completion of work.
 - 13.1. The most efficient material for cleaning and inactivating cytotoxic substances is sodium hypochlorite 0.5% (dilute fresh solution once a week). Surfaces sensitive to this material (such as stainless steel must then be rinsed with sterile water and alcohol to remove remnants that can cause corrosion. Alternatively, it is possible to use recommended commercial materials)
 - 13.2. Fluorouracil and Oxaliplatin can be harmful to the fetus, therefore it is recommended to handle them with utmost care, especially pregnant and breast feeding women. The first material is included in the third addendum to the **Women's Work Regulations (prohibited works, limited works, dangerous works) 2001**. According to the regulation, it is permitted to work with a diluted substance, ready for injection.
 - 13.3. When using chemotherapy substances included in the list of cytotoxic materials registered in Israel (Gemcitabine, Paclitaxel, Oxaliplatin, Fluorouracil, for example) handle them according to the Medical Directorate circulars no. 06/2004 and 28/2010 – "Handling cytotoxic drugs – guidelines" and "Guidelines for the prevention of workers exposure to cytotoxic remnants" respectively (see list in Annex 2).
14. Storage of cytotoxic materials requires labeling the container with: material name, quantity, concentration, preparation date and cytotoxic warning sign (In a closed cabinet, refrigerator or freezer with access to authorized workers only).
15. Material leftovers shall be discarded as hazardous chemical waste marked cytotoxic in a closed container labeled with material details, date and lab manager name.
16. On work completion, remove the gloves and wash hands thoroughly with water and soap.
17. Activities to be performed during an accident are detailed in Annex 1.
18. Material which was diluted in the lab and must subsequently be transferred to the animals' facility shall be placed in a secondary, non leak, closed and non breakable package.
19. When injecting to animal, it is mandatory to use suitable personal protective equipment including double gloves, coat, protective glasses, respiratory mask and shoe covers.
20. Instructions for injecting to animals – receive permission from Preclinical Research Authority prior to working with animals.
21. It is recommended to give the injection to anesthetized animals.

22. It is recommended to give the injections in the biological hood
23. Mark cages accordingly.
24. Animal bedding during the first three days after the injection of some cytotoxic materials might be infected, therefore collect and send for burning – like the animals
25. Opening of the cages up to 3 days after injection and changing of the first bedding must be done in the biological hood.
26. On work completion, remove gloves (discard to cytotoxic wwaste) and wash hands thoroughly with water and soap.

Annex 1

Instructions for activities to be performed during a spill incident or accident with cytotoxic materials:

A. Instructions concerning behavior during cytotoxic materials spill:

- Liquid spill:** absorb with absorbent paper/ pad and discard as cytotoxic waste. Wipe the area again with 0.5% sodium hypochlorite then with water
- Powder spill:** cover carefully with an absorbent pad to prevent powder spread. Pour a little water on the pad and collect to cytotoxic waste. Wipe the area again with 0.5% sodium hypochlorite then with water.

Discard all that was mentioned above and mark as cytotoxic waste

B. Instructions concerning behavior during accidents with cytotoxic materials:

- Splash into eyes** – use eye washer to rinse for at least 15 minutes, keep eyes open while rinsing and seek medical attention (immediate and/ or preventive).
- Splash into nose, mouth, on body or hands** - wash thoroughly with water and soap for several minutes, encourage wounds to bleed
- Reporting/ notification** – immediate notification of lab manager, Head of Administration and Safety Unit (2146/7)

Annex 2

LIST OF CYTOTOXICS SUBSTANCES:

Altretamine, Aminoglutethimide, Azathioprine, L-Asperaginase,
Bleomycin, Bromodeoxyuridine (BrDU), Busulfan,
Carboplatin, Carmustine, Chlorambuscil, Chloramphenicol, Chlorotianisene,
Chlorozotocin, Cyclosporin, Cisplatin, Cyclophosphamide, Cytarrabine,
Dacarbazine, Dactinomycin, Daunorubincin, Diethylstilbestrol, Doxorubincin,
Estradiol, Estramustine, Ethinyl Estradiol, Etoposide,
Floxuridine, Fluorouracil, Flutamide,
Ganciclovir,
Hydroxyurea,
Idarubicin, Ifosfamide, Interferon-A, Isotretinoin,
Leuprolide, Levamisole, Lomustine,
Mechlorethamine, Medroxygrogesterone, Megestrol, Melphalan,
Mercaptopurine, Methotrexate, Mitomycin, Mitotane, Mitoxantrone, Nafarelin,
Pipobroman, Plicamycin, Procarbazine,
Ribavirin,
Streptozocin,
Tamoxifen, Testolactone, Thioguanine, Thiotepa,
Uracil Mustard,
Vidarabine, Vinblastine, Vincristine,
Zidovudine