Safe handling of cytotoxic drugs

HSE Information Sheet MISC615

Introduction

1 This guidance aims to raise awareness among employers and employees of the hazards associated with cytotoxic drugs and the precautions to take when handling them. In particular, it focuses on the relevant regulatory framework, including risk assessment, and prevention and control of exposure. It will interest pharmacists, pharmacy technicians, medical and nursing staff, veterinary practitioners and others involved in handling these drugs and related waste. It is not specifically aimed at manufacturers of such drugs. The guidance does not provide detailed information on technical aspects of preparing and administering cytotoxic drugs or on individual drugs. Relevant material on these aspects can be found in other publications – see 'Further reading' at the end of the information sheet.

2 The information and advice in this information sheet can be used to prepare more detailed local guidance.

Uses

3 Cytotoxic drugs, sometimes known as antineoplastic, anticancer or cancer chemotherapy drugs, include a wide range of chemical compounds. Because of their ability to kill tumour cells by interfering with cell division, they are extensively used to treat cancer, and some have other medical applications. However, their actions are not specific to tumour cells and normal cells may also be damaged. As a result, they can produce significant side effects in patients or others exposed. This, together with the increasing use and complexity of chemotherapy, has raised concerns about the risks to health care workers involved in preparing and administering cytotoxic drugs and/or caring for patients undergoing treatment.

4 Administration of chemotherapy is carried out in a range of settings. They include hospitals, specialist oncology units, hospices, care homes, charitable organisations, domestic homes and veterinary clinics. An increasing number of patients are being treated in the community and at home.

Exposure

5 Cytotoxic drugs are commonly administered by injection of single doses or by continuous infusion. Some are given orally in tablet, capsule or liquid form. The potential for exposure exists during various tasks, eg drug reconstitution and mixing, connecting and disconnecting intravenous tubing, and disposing of waste equipment or patient waste.

6 The more common routes of exposure are contact with skin or mucous membranes (eg spillage/splashing), inhalation (eg overpressurising vials) and ingestion (eg through eating, drinking or smoking in contaminated areas or from poor hygiene). Less likely routes of exposure include needlestick injuries which could occur during the preparation or administration of drugs.

Health hazards

Acute health effects

7 Some cytotoxic drugs can irritate the skin, eyes and mucous membranes. Other acute effects, such as light-headedness and nausea, have been reported but in circumstances where measures to control exposure have probably been inadequate.

Chronic health effects

8 Information on the chronic health effects of cytotoxic drugs mainly comes from data in animals and from patients given therapeutic doses. It is not certain how relevant this is to workers. Any occupational exposures are likely to be at much lower levels, although there is potential for them to be repeated over a prolonged period. Little is known about the consequences of repeated exposure to small quantities of cytotoxic drugs, but some of these compounds are mutagenic and carcinogenic.

9 The International Agency for Research on Cancer (IARC) has assessed a number of cytotoxic drugs as being mutagenic and carcinogenic, based on the findings of in vitro and animal studies. It has classified some of these as *possibly* or *probably carcinogenic to humans.* Others have been classified as *carcinogenic to humans*, usually where additional studies have demonstrated the development of secondary tumours in patients undergoing chemotherapy with specified drugs.

10 IARC evaluations have also shown that a number of cytotoxic drugs are teratogenic in laboratory animals. Several studies have investigated the relationship between occupational exposure and reproductive outcomes, including miscarriage, birth defects and low birth weight. Both positive and negative findings have been reported.

Legal considerations

Employers

11 Under the Health and Safety at Work etc Act 1974 and the Management of Health and Safety at Work Regulations 1999, as an employer you have a legal duty to protect the health of your employees and anyone else, eg the public, who may be affected by your work. You must have a health and safety policy and should consult employees and safety representatives on the risks identified in the workplace and the measures needed to prevent or control these risks. You must take steps to ensure employees are familiar with the health and safety policy.

12 In general, cytotoxic drugs are hazardous substances, as defined by the Control of Substances Hazardous to Health Regulations 2002 (COSHH). Some are considered carcinogenic and are therefore subject to Appendix 1 of the COSHH Approved Code of Practice (ACOP) which provides additional guidance on the control of carcinogenic substances. Under COSHH, you have a legal duty to assess the risks from handling cytotoxic drugs for employees and anyone else affected by this type of work, and to take suitable precautions to protect their health.

Assessing the risk

13 The Health and Safety Executive (HSE) has produced general guidance on carrying out a risk assessment (*Five steps to risk assessment,* see 'Further reading'). More specific information can be found in the COSHH ACOP. You need to:

- identify the hazards – which cytotoxic drugs are handled and what are their potential adverse effects on health?
- decide who might be harmed and how – which employees and others might be exposed to cytotoxic drugs and how this might happen? For example through surface contamination of drug vials or leakage of drugs during preparation and administration. Pay attention to groups of workers who may be at particular risk, eg young workers, trainees and new and expectant mothers. Pregnant workers are especially relevant, as some drugs may be harmful to the unborn child. Further guidance is contained in *New and expectant mothers at work: A guide for employers* (see 'Further reading'). Consider others who could be indirectly exposed, such as cleaners, contractors and maintenance workers too;
- assess how likely it is that cytotoxic drugs could cause ill health and decide if existing precautions are adequate or whether more should be done. Exposure from all routes should be prevented or adequately controlled and you should protect the health of employees from any potential adverse effects. Factors to consider include:
  - the frequency and scale of contact with cytotoxic drugs;
  - any relevant information available from accident records;
  - the effectiveness of control measures;
- record the significant findings of the assessment and keep a written record for future reference;
- review the risk assessment if there are any significant changes and revise it if necessary. It is good practice to review the assessment from time to time anyway, to ensure that precautions are still working effectively.

Employees

14 As an employee you have a legal duty to take care of your own health and safety and that of others affected by your actions. You must make full and proper use of control measures put in place by your employer. In addition, you should cooperate with your employer, so they can comply with any legal duties placed on them.

Control of exposure

15 Measures to control exposure should be applied in the following order:

- use totally enclosed systems as the first choice for controlling exposure to carcinogens, unless this is not reasonably practicable;
- control exposure at source, including for example use of adequate ventilation systems and appropriate organisational measures;
- issue personal protective equipment where adequate control of exposure cannot be achieved by other measures alone.

16 The broad measures described above will include more specific controls, such as:

- organising work to reduce the quantities of drugs used, the number of employees potentially exposed and their duration of exposure, to the minimum;
- arranging for the safe handling, storage and transport of cytotoxic drugs and waste material containing or contaminated by them;
- using good hygiene practices and providing suitable welfare facilities, eg prohibiting eating, drinking and smoking in areas where drugs are handled and providing washing facilities;
- training all staff who may be involved in handling cytotoxic drugs or cleaning areas likely to be contaminated, in the risks and the precautions to take.

Personal protective equipment

17 Under the Personal Protective Equipment at Work Regulations 1992, personal protective equipment (PPE) should be provided and used wherever there are risks to health and safety that cannot be adequately controlled in other ways. The selection of PPE should be based on the risk assessment carried out under COSHH. It is important to ensure that PPE offers adequate protection for its intended use. PPE manufactured on or after 1 July 1995, should be 'CE'-marked to signify that it satisfies minimum legal requirements. Employers need to ensure that employees are trained in the use of PPE and that the equipment is adequately maintained and stored.

18 Effective protection will only be obtained if the PPE chosen is:

- suitable for the task;
- suited to the wearer and environment;
- compatible with other PPE in use;
- in good condition;
- worn correctly.

Gloves

19 Where contact with cytotoxic drugs is possible, and methods of control other than protective gloves are not reasonably practicable, protective gloves must be provided for employees.

20 No glove material will provide unlimited protection from cytotoxic drugs. Advice on the issues to consider when choosing suitable gloves is available from HSE (see 'Further reading'). Latex is often used in the manufacture of protective gloves. It can cause skin irritation or an allergic reaction in susceptible individuals. Under COSHH, employers must carry out a risk assessment where exposure to latex is possible.

Eye and face protection

21 Eye and face protection is relevant, particularly where cytotoxic drugs are being handled outside an enclosed system and there is a risk of splashing. A number of options are available including a face shield or visor, goggles and safety spectacles.

Respiratory protection

22 Preparation of cytotoxic drugs should be carried out in a suitable safety cabinet or pharmaceutical isolator (see paragraph 27). However, if it is not reasonably practicable to control exposure using total enclosure/local exhaust ventilation, you will need to consider respiratory protective equipment (RPE) if exposure to powders or aerosols is possible. Surgical masks will not protect against the inhalation of fine dust or aerosols.

23 HSE has produced guidance on the selection, use and maintenance of RPE (see 'Further reading').

Protective clothing

24 Protective clothing such as gowns and aprons can help prevent contamination of clothes and subsequently, the skin. The choice of material is important as their absorptive properties may vary. Standard laboratory coats are unsuitable as cytotoxic drug solutions may soak through them. Consider the comfort of staff wearing protective clothing.

Drug preparation

25 In hospitals where preparation of cytotoxic drugs produces a significant workload, it should preferably be centralised in a pharmacy under the direction of a suitably trained and experienced pharmacist. Alternatively, if there is a major point of use such as an oncology clinic, it may be more appropriate to operate the centralised service from an outstationed pharmacy unit within the clinic. This should also be under the direction of a suitably trained and experienced pharmacist. The work area should be clearly designated for drug preparation and access restricted to authorised staff.

26 There may be rare circumstances where cytotoxic drugs have to be prepared outside a centralised area, eg where a particular drug has a very short half-life. In such cases, every effort should be made to segregate drug preparation from other ward or clinic activities. Procedures should only be undertaken by staff who are suitably trained and experienced. The same applies in hospitals where cytotoxic drugs are used infrequently and there is no centralised service. However, in this situation, consider purchasing drugs prepared by another hospital or commercially.

27 Aseptic preparation of cytotoxic drugs can be carried out using a suitable safety cabinet or a pharmaceutical isolator. There is a distinction between measures designed to protect sterility of the product and those designed to provide operator protection. HSE and the Medicines Control Agency (now known as the Medicines and Healthcare Products Regulatory Agency) have jointly produced guidance on factors to consider when selecting a negative or positive pressure isolator for aseptic reconstitution of drugs (see 'Further reading').

28 Totally enclosed systems should be used to control exposure to carcinogenic compounds. Where this cannot be achieved, engineering controls, processes or systems of work should be designed and operated to minimise the generation of, and to suppress and contain, carcinogenic compounds - eg by partial enclosure of processes and handling systems, appropriate local exhaust ventilation and general ventilation.

29 Manipulation of oral or topical medicines containing cytotoxic drugs should be avoided if possible. If unavoidable, tasks such as dividing or crushing tablets should be restricted to a controlled environment, ideally within a pharmacy department. Carrying out these procedures on wards or in clinics should be actively discouraged.

30 There should be clear procedures for dealing with any spillages and for the safe disposal of waste (see paragraphs 45-51).

31 Once prepared, a drug should be clearly labelled as cytotoxic and packaged to ensure it will not spill or leak when transported to the area where it will be administered.

Drug administration

32 Detailed advice on procedures for administering cytotoxic drugs is beyond the scope of this guidance but may be found elsewhere (see 'Further reading'). However, the following points on controlling exposure during administration are relevant:

- the drugs should be available in a form that is ready to administer without any need for additional manipulation;
- administration should be carried out in quiet, designated areas, away from passing 'traffic' and welfare areas where food and drink may be consumed;
- when handling oral preparations, direct contact with the skin should be avoided. Tablets are preferred to solutions and should be blister or foil-packed;
- procedures should be in place for dealing with any spillages that occur and for the safe disposal of waste (see paragraphs 45-51).

Monitoring exposure in the workplace

33 Monitoring exposure can include any periodic test or measurement which helps to confirm the ongoing effectiveness of controls. Under COSHH, monitoring is necessary when any of the following circumstances apply:

- when failure or deterioration of control measures could result in a serious health effect;
- when measurement is required to ensure an occupational exposure limit or in-house working standard is not exceeded;
- as an additional check on the effectiveness of control measures;
- when any change occurs in the conditions affecting employees' exposure which could mean that adequate control of exposure is no longer being maintained.

34 In accordance with the COSHH ACOP (Appendix 1 provides additional guidance on the control of carcinogenic substances), monitoring is normally necessary where there is potential for exposure to carcinogenic compounds.

35 Monitoring is not appropriate if suitable procedures do not exist or cannot be devised. Similarly, monitoring is not necessary where another method of evaluation is used that demonstrates the control measures in place are adequately controlling exposure.

36 Where a risk assessment indicates that monitoring exposure to cytotoxic drugs is necessary, for certain drugs it is possible to measure their concentration on surfaces, in the air or in body fluids. There is no recognised standard against which test data can be compared for any of these methods. However, performing serial measurements and observing trends in the data can be useful to help demonstrate that control measures are still adequate or the need to review them. These monitoring techniques can also help confirm restoration of adequate control if there is a failure of the measures put in place.

37 Dermal exposure is dependent on working practices and the frequency and adequacy of decontamination procedures. Surface wipe tests will provide some information on levels of work surface contamination and standards of cleanliness. They can help provide reassurance after decontamination of significant spillages. Airborne measurements may be warranted if there is concern about inhalation of drugs.

38 Exposure can also be assessed by biological monitoring – measuring concentrations of cytotoxic drugs or their metabolites in body fluids, usually urine (see 'Further reading' for detailed guidance on biological monitoring programmes). A number of compounds can be evaluated in this way. The advantage of biological monitoring is being able to measure total uptake by all routes of exposure. If you are setting up a biological monitoring programme, obtain advice from appropriate occupational health professionals.

39 The adequacy of control measures can be demonstrated, in part, through good supervision and monitoring of the efficiency of equipment. The latter includes examination and testing of equipment and keeping suitable records. If appropriate, this might be supplemented by surface wipe tests at suitable intervals and following decontamination of any significant spillages. Biological monitoring may be useful in particular circumstances (eg following failure of control measures) but is not recommended for routine use.

Health surveillance

40 Detailed guidance on health surveillance is available (see 'Further reading').

41 Health surveillance is appropriate where:

- exposure to a hazardous substance is such that an identifiable disease or adverse health effect may be related to exposure;
- there is a reasonable likelihood that the disease or effect may occur under the particular conditions of the work undertaken;
- there are valid techniques for detecting indications of the disease or effect; and
- the technique of investigation is of low risk to the employee.

42 The results of the risk assessment for staff potentially exposed to cytotoxic drugs should be used to determine whether health surveillance is necessary. Where this has shown that exposure is most unlikely to result in any disease or adverse health effect, health surveillance is not required.

43 In practice, the criteria for health surveillance in paragraph 41 are unlikely to be met for employees handling cytotoxic drugs. However, it is recommended that employers keep a health record on all staff potentially exposed to these compounds. The health record should contain at least the following: surname, forenames, gender, date of birth, permanent address and postcode, National Insurance Number, date when present employment started and a historical record of jobs in this employment involving exposure to cytotoxic drugs.

44 A number of published studies have used biological monitoring (see paragraph 38) and biological effect monitoring (measurement and assessment of early biological effects caused by absorption of chemicals) to try and draw inferences about the health of workers exposed to cytotoxic drugs. However, data produced from using these techniques are difficult to interpret in the context of the health of an individual employee and are therefore not recommended for routine use in health surveillance.

Dealing with spillages and contamination

45 Put clear procedures, based on a risk assessment, in place for dealing with spillages or contamination of people or work surfaces. All staff involved in handling cytotoxic drugs should be familiar with these procedures. Measures to prevent or contain spillages should be used at all times. Any spillages that do occur should be dealt with promptly.

46 Staff should wear suitable PPE and be given spillage kits where appropriate. Contaminated materials should be clearly labelled and appropriately packaged for disposal.

47 Any drugs that come into direct contact with the skin should be washed off with soap and water and medical advice obtained.

48 If drugs come into direct contact with the eye, they should be washed out with water or an eye wash bottle containing water or normal saline. Medical advice should be obtained.

Waste disposal

49 After completing a suitable risk assessment, put procedures in place for the safe disposal of waste. All relevant staff should be familiar with these procedures. Excreta from treated patients may contain unchanged cytotoxic drugs or active metabolites. When handling waste, including waste from treated patients, staff should wear suitable PPE.

50 Suitable containers, clearly labelled and reserved solely for the use of cytotoxic drug waste, should be available. Sharps containers should be used for the safe disposal of needles etc. Waste should not be allowed to accumulate.

51 The Health Services Advisory Committee has produced guidance on the safe disposal of clinical waste (see 'Further reading'). Drugs or other pharmaceutical products are considered to be clinical waste. In addition, waste containing or consisting of prescription-only medicines is classified as *special waste* and subject to controls under the Special Waste Regulations 1996.

Information, instruction and training

52 Employers need to ensure that employees handling cytotoxic drugs are given suitable and sufficient information, instruction and training that is relevant to their work. This should be enough to make employees aware of the risks of working with cytotoxic drugs and the precautions they should take when handling them.

Reporting accidents

53 Under the requirements of the Reporting of Injuries, Diseases and Dangerous Occurrences Regulations 1995 (RIDDOR), employers have a legal duty to report certain incidents and dangerous occurrences to the relevant enforcing authority. The accidental release of any substance which could damage health is classed as a dangerous occurrence. A small spillage of a cytotoxic drug which is well contained and easily dealt with, is not reportable. Spillage of a large amount, to which people could have been exposed, is reportable.

Further reading

Legal/guidance

Biological monitoring in the workplace: A guide to its practical application to chemical exposure HSG167 HSE Books 1997 ISBN 0 7176 1279 1

Consulting employees on health and safety: A guide to the law Leaflet INDG232 HSE Books 1996 (single copy free or priced packs of 15 ISBN 0 7176 1615 0)

Control of substances hazardous to health. The Control of Substances Hazardous to Health Regulations 2002. Approved Code of Practice and guidance L5 (Fourth edition) HSE Books 2002 ISBN 0 7176 2534 6

Five steps to risk assessment Leaflet INDG163(rev1) HSE Books 1998 (single copy free or priced packs of 10 ISBN 0 7176 1565 0)

Handling cytotoxic drugs in isolators in NHS Pharmacies HSE/Medicines Control Agency 2003. Available from the HSE website: www.hse.gov.uk

Health and Safety at Work etc Act 1974 Ch37 The Stationery Office 1974 ISBN 0 10 543774 3

Health surveillance at work HSG61 (Second edition) HSE Books 1999 ISBN 0 7176 1705 X

Latex and you Leaflet INDG320 HSE Books 2000 (single copy free or priced packs of 10 ISBN 0 7176 1777 7)

Management of health and safety at work. Management of Health and Safety at Work Regulations 1999. Approved Code of Practice and guidance L21 (Second edition) HSE Books 2000 ISBN 0 7176 2488 9

New and expectant mothers at work: A guide for employers HSG122 (Second edition) HSE Books 2002 ISBN 0 7176 2583 4

Personal protective equipment at work. Personal Protective Equipment at Work Regulations 1992. Guidance on Regulations L25 HSE Books 1992 ISBN 0 7176 0415 2

Safe disposal of clinical waste (Second edition) Guidance HSE Books 1999 ISBN 0 7176 2492 7

Selecting protective gloves for work with chemicals: Guidance for employers and health and safety specialists Leaflet INDG330 HSE Books 2000 (single copy free or priced packs of 15 ISBN 0 7176 1827 7)

Special Waste Regulations 1996 SI 1996/972 The Stationery Office 1996 ISBN 0 11 054565 6 as amended by *Special Waste (Amendment) Regulations 1996* SI 1996/2019 ISBN 0 11 062894 2

The Control of Substances Hazardous to Health Regulations 2002 SI 2002/2677 The Stationery Office 2002 ISBN 0 11 042919 2 as amended by *The Control of Substances Hazardous to Health (Amendment) Regulations 2003* SI 2003/978 ISBN 0 11 045572 X

The selection, use and maintenance of respiratory protective equipment: A practical guide HSG53 (Second edition) HSE Books 1998 ISBN 0 7176 1537 5

Technical

Allwood M, Stanley A and Wright P (editors) *The Cytotoxics Handbook* Ratcliffe Medical Press 2002 ISBN 1 85775 504 9

International Agency for Research on Cancer *Some antineoplastic and immunosuppressive agents: IARC monographs on the evaluation of the carcinogenic risk of chemicals to humans Volume 26* IARC 1981 ISBN 92 832 1226 6

International Agency for Research on Cancer *Overall evaluation of carcinogenicity an updating of IARC monographs Volumes 1-42: IARC monographs on the evaluation of carcinogenic risks to humans Supplement 7* IARC 1988 ISBN 92 832 1411 0

International Agency for Research on Cancer *Pharmaceutical drugs: IARC monographs on the evaluation of carcinogenic risks to humans Volume 50* IARC 1991 ISBN 92 832 1250 9

International Agency for Research on Cancer *Some antiviral and antineoplastic drugs and other pharmaceutical agents: IARC monographs on the evaluation of carcinogenic risks to humans Volume 76* IARC 2000 ISBN 92 832 1276 2

MARC (Management and Awareness of the Risks of Cytotoxics). Guidelines available on the website: www.marcguidelines.com

Parsons M *Guidelines for the safe use of cytotoxic chemotherapy in the clinical environment* Scottish Executive Health Department 2001 ISBN 1 84268 987 8

Goodman I (editor) *Clinical practical guidelines: The administration of cytotxic chemotherapy: Recommendations* RCN 1998 ISBN 1 873853 81 5

Goodman I (editor) *Clinical practical guidelines: The administration of cytotoxic chemotherapy: Technical Report* RCN 1998 ISBN 1 873853 80 7

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This information sheet contains notes on good practice which are not compulsory but which you may find helpful in considering what you need to do.

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