Miller, Diane M. (CDC/NIOSH/EID)

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Sent: Tuesday, November 24, 2009 2:45 PM

To: NIOSH Docket Office (CDC)

Subject: Docket Number NIOSH-150

Attachments: Alternative Duty-HD Handlers.doc; Children's Hospital.pdf; Job Modification CA 1007.pdf; HSE Safehandling.pdf; New and Expectant Mothers HSE_1.pdf

Attached are comments and documents regarding the above-mentioned -- Request for Information on Alternative Duty: Temporary Reassignment for Health Care Workers Who Work With Hazardous Drugs.

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"Worry looks around, sorry looks back, faith looks up."

November 24, 2009

Dear Dr. Connor,

Thank you for the opportunity to provide information to NIOSH regarding the need for additional guidance in providing alternative duty to pregnant women, those actively trying to conceive and breast-feeding mothers who handle hazardous drugs. By way of this letter, we wish to encourage NIOSH to draft and provide this important information to employers and healthcare workers engaged in oncology services.

We know that this information is sorely needed as we are quite regularly approached to supply such guidance by individual healthcare workers or medical institutions. There is a patch work of policy that approaches but does not fully address this issue with some facilities providing alternative duty options and others leaving the issue unaddressed. In this climate, there is a need for clear guidance, bolstered by sound science and awareness of both employment law and privacy concerns.

Indeed, the U.S. is not alone in addressing this issue and is in fact, 'late to the table', with both Canada and the UK developing alternative duty and other protective reassignment solutions, specifically describing the handling of hazardous drugs and other pharmaceuticals as a potentially 'triggering' exposure.

Below, please find a summary of the science which we believe argues for the need for such a policy with some additional materials in the appendix. Appendicle material includes:

1) A schedule of aerosolized medication safety practices from Children's Hospital in Boston which suggests an approach to a hierarchy of exposure controls which may include alternative duty for some types of medication handling.
2) A PowerPoint presentation (The Job Modification Prescription) summarizing some of the scientific and human resource issues that impacts an alternative duty program.
3) Two documents from the UK Health and Safety Executive (HSE): the first the HSE information sheet for safe handling of cytotoxic drugs which mentions specific considerations of workers 'at particular risk' including ' new and expectant mothers'. It references an additional HSE document 'New and Expectant Mothers at Work', which suggests an outline for evaluating the occupational risk to pregnant or breast-feeding mothers. The handling of drugs is a specific example given of a potentially risky job that may suggest alternative duty.

If we can be of any further assistance, please do not hesitate to contact us.

Sincerely,

Melissa A. McDiarmid, M.D., MPH

Marian Condon, MS, RN

Introduction:

Pregnant women and mothers who are occupationally exposed to hazardous drugs (HDs), through drug preparation or administration, or through patient care activities, in turn may well expose their unborn or breast-feeding offspring as well. The transfer of medications and chemical agents either through prenatal, transplacental exposure or through contaminated breast milk is well documented. The reproductive and developmental effects in health care workers (HCWs) handling HDs are unambiguous, with data accruing now for almost 20 years. Effects observed in this population include; spontaneous abortion,[1;2-5] subfertility,[6] low birth weight[7], menstrual dysfunction[4], and birth defects[8-11]. These studies are summarized in Table 1 (Summary of Studies of Adverse Reproductive Outcomes in Workers Exposed to Antineoplastic Drugs). While positive studies might have been expected 20 years ago, prior to the use of safe handling practices, some of the most recent work reporting positive results were performed in hospitals supposedly using safe handling guidelines[11]. Little research has been conducted on the long-term developmental effects in the offspring of workers exposed to HDs. One recent study, however, found an association between occupational exposure to HDs and learning disabilities in offspring of female oncology nurses[12].

The American Society of Hospital Pharmacists (ASHP) defines HDs as drugs that possess any of these criteria:

1. Carcinogenicity
2. Teratogenicity of other developmental toxicity
3. Reproductive toxicity
4. Organ toxicity at low doses
5. Genotoxicity
6. Structure and toxicity that mimics existing hazardous drugs

Many HDs are anti-cancer agents, but not all are with some anti-viral agents also falling into the HD category.

Evidence for Developmental and Reproductive Effects: Nearly all HDs have some teratogenic and embryotoxic effects that have been well documented in experimental animal studies (see Table 2). These effects arise from the drugs' mechanisms of action, which involve either covalent binding to cellular macro-molecules or otherwise interfering with DNA or protein synthesis and normal cell division. Vainio postulates that these agents share mechanisms leading to carcinogenesis and teratogenesis, including mutation and disrupted intercellular communication[13].

Developmental Effects (Animal Studies): Male-mediated developmental effects that have been reported for HDs include: malformed and growth-retarded fetuses[14]; and behavioral deficits[15]. Female-mediated effects associated with the alkylating agent drug class include: anomalies of the toes[16;17]; eye abnormalities, and cleft palate[18]; hydronephroses and absent right kidney[19]; absence of kidney and ureter[20]; foot and toe abnormalities[21]; and malpositioned

small kidneys[22]. The antimetabolite class of drugs have been associated with further female-mediated developmental effects: cranial anomalies; cleft palate; digital abnormalities[14]; and multiple abnormalities of the hands and internal organs[23].

Reproductive Effects (Animal Studies): In this category the male -mediated effects found for HDs are pre and postimplantation loss[14]. Female-mediated effects include spontaneous abortions.[14;24].

Reproductive Health Effects (Patient-treated Case Reports): Reproductive health effects in patients treated with HDs have been noted. Males treated with the alkylating agents have demonstrated: oligospermia and azoospermia[25;26]; aspermia[27]; male sterility[28]; and testicular atrophy.[29] Females have also exhibited adverse effects from the alkylating agents, including: loss of ovarian primordial follicles; cessation of menses[30]; and amenorhhea[26;31].

Exposure to HDs Through Breast Milk: There are two primary sources of information on drugs found in human breast milk. One of these is a policy statement of The American Academy of Pediatrics (AAP) that was recently up-dated in September, 2001 entitled The Transfer of Drugs and Other Chemicals Into Human Milk[32]. This document describes drugs that a mother could take that are transferred into human milk and the possible effects of these agents on the breast-fed infant. The AAP document lists many classes of drugs that are found in breast milk and are of concern, including some anti-cancer HDs that may interfere with cellular metabolism in the nursing infant. These drugs are: cyclophosphamide, doxorubicin and methotrexate. Under the "Reasons for Concern" section, the AAP lists possible side effects to the infant from exposure to these drugs, including: possible immune suppression, unknown effect on growth or association with carcinogenesis, and neutropenia. The document is careful to state that if a drug does not appear in the table, it does not mean that it is not transferred into human milk, or does not have an effect on the infant, but that there was no information on the drug found in the literature.

Another major source of information about drugs and human breast milk is the text, Drugs In Pregnancy and Lactation, sixth edition[33]. Most of these HDs fall into risk category D, while a few are in category X (see Table 3). This source's definition for category D is: "There is positive evidence of human fetal risk, but the benefits from use in pregnant women may be acceptable despite the risk." Category X is defined in these terms: "Studies in animals or human beings have demonstrated fetal abnormalities or there is evidence of fetal risk based on human experience or both, and the risk of the use of the drug in pregnant women clearly outweighs any possible benefit" (Ref 30, page xxiv). Evidence for adverse effects seen in humans or in animal studies provides the basis for these categorizations.

Populations Affected: The magnitude of potentially affected occupational populations who come into contact with, and are exposed to HDs, is large. NIOSH estimates the number of potentially exposed workers at about 5.5 million[34]; these estimates can be derived from examining the 'life cycle' of a HD, and mapping the various stages of the cycle to workers encountering it at each stage. We make the assumption that up to one third of the 6 million workers identified in Table 4 (**Exposure Opportunities in "Life Cycle" of Hazardous Drugs**), primarily in healthcare jobs, but also a large fraction of some 600,000 in drug manufacture and transportation, may have significant opportunity to be exposed to HDs. Pharmacy and nursing

personnel who mix these drugs and administer intravenous infusions to patients are likely to experience the highest exposure intensity. However, the elimination of these drugs in the urine of a treated patient enlarges the number of direct caregivers potentially at-risk at the lesser skilled (nursing assistant) level of health care worker (HCW).

Exposure opportunities: Beginning in the mid-1970s, potential risks to HCW were postulated based on these drugs' genotoxic characterization, their toxic side effects, and "second" therapy-related malignancies observed in patients treated with these drugs[35-38]. In the last twenty years, evidence of worker exposure has accumulated. In both the pharmacy and clinical care areas there is documentation of environmental drug contamination[39-42]. Also, a recent study demonstrated dermal exposure to HDs of cleaning personnel, as well as pharmacy technicians and oncology nurses[43].

- **Exposure opportunities related to work practice:** Healthcare workers (HCW) can be exposed to these agents through a number of scenarios. The work environment is subject to contamination and HCW to potential exposure from work tasks related to drug preparation, handling and administration. Exposure can occur to workers performing these tasks in a variety of ways. Drug preparation outside of biological safety cabinets (BSC), or using the wrong type of BSC and improper use of personal protective equipment (PPE) are two ways a great deal of work area contamination occurs. Other sources of contamination include: splattering or aerosolization that can occur when drug ampules are opened; during withdrawal or transfer of drugs from vials; when trapped air is expelled from drug-filled syringes; leakages in tubing and stopcock connections; spills or accidents, and improper handling of patient body fluids or waste disposal practices. Workers unknowingly contact drug-contaminated work areas, and can spread the contamination from the pharmacy and/or clinic area to other sites and persons or parts of the patient care environment. Recognizing the potential health risks from unprotected exposure to antineoplastic drugs, the Occupational Safety & Health Administration (OSHA), in 1986, issued handling guidelines for HCW protection which were subsequently updated in 1995[44-45]. However, more recent studies suggest that HCWs may still become exposed through fairly wide-spread work area contamination. A wipe sample study of six North American cancer centers showed 75% of pharmacy and 65% of oncology clinic area wipe samples to be positive for drug contamination despite use of BSCs and safe handling practices[40]. Other studies documenting volatilization at room temperature of some commonly used antineoplastic drug solutions suggest reliance on BSCs, which filter particulate drug aerosols, may not be as protective as once thought if some of the drug exposure occurs through a vapor-inhalation route.[46]

Biomonitoring results in HCW: Biological monitoring (biomonitoring) is the measurement of a toxicant or its metabolite in a specimen (body fluid or tissue). Biomarkers can either document exposure (by looking for the toxicant or its metabolite directly-classical biomonitoring), or they can document an effect, such as a change in cellular or molecular endpoint, for example, frequency of mutations[47]. Biomonitoring methods help characterize the relationship between a toxicant exposure and a health effect. Biomonitoring of both blood and urine of HD-exposed HCWs have identified both types of biomarkers in this population.

- **Recovery of drugs in the urine of HCW:** Many biomonitoring studies have identified HDs in the urine of HCW. In some cases the drugs have been recovered in the urine of HCWs in proximity to, but not directly handling these agents, implying exposure through contaminated work environments[48-56] (bystander exposure). Exposure can also occur in an acute incident, as was documented in a reported case of acute symptoms deemed to have resulted from exposure of an unskilled HCW to drug contaminated patient urine[57]. Table 5 (Selected recent studies finding HDs in urine of HCW handling HDs) lists representative studies that document the presence of HDs (including the two selected for this study) in the urine of HCW handling these drugs. Most recently, in a study performed in three University hospital Cancer Centers expressing use of safe handling practices, 3 out of 63 exposed HCWs had measurable levels of HDs in their urine[58].

- **Biomonitoring for cytogenetic alterations in HCWs:** The mutagenicity and genotoxicity of the HDs drove the early concerns about HCW exposure to these drugs. Consequently there is a body of data examining biomarkers of effect in HCWs handling HDs. Studies of urine mutagenicity were performed early on[59-64], but more recently blood specimens to identify cytogenetic alterations in lymphocytes have been more common. The two primary methods used are sister chromatid exchanges (SCEs), and chromosomal aberrations. A less frequently used biomonitoring marker is the presence of micronuclei. Baker & Connor conducted a review of the cytogenetic effects of HDs[71]. Of the 46 studies they reviewed, about half were positive for the marker being examined, and four more were equivocal. Multiple studies have reported increases in genotoxicity measures in HCWs[65-71].

- Importantly, signature chromosome 5 and 7 abnormalities observed in hazardous drug – treated cancer patients who develop therapy – related leukemias, were observed in a statistical excess in exposed HCWs by McDiarmid and Collegues[58]. This demonstrates biologically important exposure to HDs is continuing to occur despite hospital endorsement of safe handling practices. This evidence suggests opportunity for exposure to pregnant and breast feeding HCWs even where safe handling programs exist. Therefore, alternative duty for these HCWs is a reasonable and necessary accommodation.

Table 1: Summary of Studies of Adverse Reproductive Outcomes in Workers Exposed to Antineoplastic Drugs

YEAR	AUTHOR	POPULATION	BIRTH DEFECT	FETAL LOSS	OTHER
1985	Hemminki	ONC Nurses	+*	-	
1985	Selevan	ONC Nurses		*	
1986	Taskinen	Pharm Mfgr		+	
1987	Rogers	ONC Nurses		+*	
1988(a)	McDonald	RN + MDs	+*		
1988(b)	McDonald	RN + MDs		-	
1990	Stucker	ONC Nurses		*	
1992	Skov	ONC Nurses	+	-	+ Ectopic preg.
1993	Stucker	ONC Nurses			+LBW, -SGA
1993	Saurel-Cubizolles	OR/ONC Nurses			* Ectopic preg.
1995	Shortridge	ONC Nurses			* Menstrual dysfunction
1997	Valanis	Pharm + RNs			* infertility (F); +(M)
1999	Valanis	RN, Pharm (M+F)		*(F); +(M)	
1999	Peelen	ONC Nurses Admin. Drug	-	-	+
		ONC Nurses Prep. Drug	+*		+*LBW

Key: (+) = effect seen, (-) = no effect seen, (*) = statistically significant effect seen (F) = female; (M) = male; (LBW) = low birth wt; (SGA) = small for gestational age.

Table 2 - Developmental Toxicity and Genotoxicity of Some Common Anticancer Agents

	Developmental Toxicity			Genotoxicity	
	Animal				
Drug Class	T	E	Human	PM	CE
Alkylating Agents					
BCNU	+	+		+	+
Busulfan	+		+	+	+
Chlorambucil	+	+	+	+	+
Cyclophosphamide	+	+	+	+	+
Ifosfamide	+	+	+	+	+
Nitrogen Mustard	+	+	+	+	+
Thiotepa	+			+	+
Cis-diaminedichloroplatinum		+		+	+
Antibiotics					
Actinomycin	+	+		+	+
Adriamycin				+	+
Bleomycin				±	+
Daunomycin			+	+	+
Antimetabolites					
Cytosine arabinoside			+		
5-Fluorouracil	+	+	+		+
6-Mercaptopurine	+	+	+	+	+
Methotrexate	+	+	+	+	+
Mitotic Function					
Vincristine	+	+	+	-	+
Vinblastine	+	+	+	-	+
Taxol	+	+	+		+
Miscellaneous					
DTIC (Dacarbazine)	+	+		+	
Procarbazine	+	+	+	±	+
Topoisomerase II Function					
Etoposide*	+	+	+	+	

(+) = effect seen; (-) = no effect seen. (T)=Teratogenic; (E)=Embryotoxic, (PM)=Point Mutation, (CE)=Chromosomal Effects

***Data summarized from Sorsa M, Hemminki K, Vainio H. Occupational exposure to anticancer drugs: potential and real hazards. Mutat Res 1985;154:135-149. Updated by McDiarmid, MA. Antineoplastics, Anesthetic Agents, Sex Steroid Hormones in Paul, M Occupational and Environmental Reproductive Hazards, 1993.**

Table 3: Pregnancy and Breast Feeding Risk of Some Common Antineoplastic Agents

Name of Drug	Pregnancy Category	*Comments on Breast-Feeding*
ALKYLATING AGENTS		
Busulfan	D	Breast –feeding is not recommended [33].
Chlorambucil	D	Breast-feeding while on this drug not recommended due to potential for severe adverse effects.
Cyclophosphamide*	D	**Excreted in human breast milk in large quantities and acute toxic effects on the breastfed infant are possible [35]. AAP considers use while breast-feeding contraindicated due to one case of neutropenia in a breast-fed infant and potential adverse effects to immune suppression, growth, and carcinogenesis.**
Ifosfamide	D	Excreted in human breast milk. Potential for serious adverse events including tumorigenicity shown in animal studies.
Thiotepa	D	Due to low molecular weight, excretion in human milk expected.
Cisplatin	D	Excreted in human breast milk in large quantities and acute toxic effects on the breastfed infant are possible [35]. Because may be in a reactive form, nursing is not recommended [33].
ANTIBIOTICS		
Dactinomycin	C or D	Breast-feeding while on this drug not recommended due to potential for severe adverse effects.
*Doxorubicin**	D	Excreted in human breast milk [36]. AAP considers use while breast-feeding contraindicated due to concerns for possible immune suppression, carcinogenesis, neutropenia, and unknown effects on growth.
Bleomycin	D	No data available.
Daunomycin	D	No data available.
Epirubicin	D	Breast-feeding while on this drug not recommended due to potential for severe adverse effects such as immune suppression, carcinogenesis, neutropenia, and unknown effects on growth.

ANTIMETABOLITES		
Ara-C	D	Breast-feeding while on this drug not recommended due to potential for severe adverse effects.
*Fluorouracil**	D (Risk Factor X according to 2 manufacturers)	Due to low molecular weight, excretion in human milk expected. Not recommended due to potential for severe adverse effects.
Methotrexate	X	Excreted in human breast milk. AAP considers use while breast-feeding contraindicated due to several potential problems, including immune suppression, neutropenia, adverse effects on growth and carcinogenesis.
Hydroxurea		Excreted in small amounts in milk, breast-feeding is not advised [33].
Gemcitabine	D	Drug, or it metabolites, cross the rat placenta and appear in rat milk after administration of compound to pregnant and lactating rats [37].
Cytarabine	D	Cytarabine liposome is not recommended in nursing women because of the potential for serious adverse effects in nursing infants [38].

Table 3 (cont.)

Name of Drug	Pregnancy Category	*Comments on Breast-Feeding*
MITOTIC FUNCTION		
Vincristine	D	Breast-feeding not recommended [33].
Paclitaxel (taxol)*	**D**	**It is not known if paclitaxel is excreted in breast milk. Due to the potential hazards of paclitaxel exposure, it is not recommended that mothers breast feed while receiving paclitaxel [38].**
Docetaxel	D	It is not known if paclitaxel is excreted in breast milk. Due to the potential hazards of paclitaxel exposure, it is not recommended that mothers breast feed while receiving paclitaxel [38].
Vinblastine	D	No data available.
TOPOISOMERASE I FUNCTION		
Irinotecan	D	Human data is unavailable; in the rat, a 65-fold higher concentration in milk versus plasma was noted at 4 hours [38].
TOPOISOMERASE II FUNCTION	D	
Etoposide	D	Excreted into human breast milk. Because of the potential for severe toxicity in a nursing infant, such as bone marrow depression, alopecia, and carcinogenicity, breast feeding should be stopped for at least 55 hrs. after the last dose of etoposide.
MISCELLANEOUS		
Dacarbazine	D	Breast-feeding while on this drug not recommended due to the potential for severe effects , such as hemopoietic depression to infant, should not be used while breast feeding.
Procarbazine	D	Breast-feeding while on this drug not recommended because of the potential for tumorigenicity, Due to low molecular weight, excretion in human milk expected.

*= drugs for which NIOSH has developed lab methods

(Unless otherwise noted, information in table from Briggs et al.2002) (Ref 30)

Table 4: Exposure Opportunities in "Life Cycle" of Hazardous Drugs

Exposure Pathway in Life of the Drug	Populations Affected	Numbers	SIC/OES
A) Drug Development/Manufacturing	Manufacturing Personnel R&D Personnel	212,000 199,500	2830 8731
B) Transport/Distribution	Transporters Drug Distributors	184,597 197,702	4210 5722
C) Healthcare Facility Pharmacy	Pharmacists Pharmacy Techs	174,540 145,430	32517 32519
D) Drug Administration	Hospital-based Registered Nurses Outpatient Clinic-based	 2,000,000 1,600,000	 32502 8011
E) Home Care	Home Care Workers/Aides	925,000	8082
F) Waste Stream Issues • Patient Waste • Chemical contaminated equipment, tubing, packaging, etc.	Hospital/clinic/home Nursing Aides/ orderlies/attendants • Spill Responders • Family	1,255,210	66008

SIC= Standard Industry Codes, from County Business Patterns 1997 OES= Occupational Employment Statistics, from 1997 National Occupational Employment and Wage Estimates, *= Numbers given are totals employed in given SIC or OES. Those potentially exposed to hazardous drugs are a subset.[49]

Table 5: Selected recent studies finding HDs in urine of HCW handling HDs

Author/ Year	Population (HD handlers)	Drug measured	Method used	*Detection limit*	Range of concentrations of drug in urine	No. of workers	% of specimens testing positive
Evelo et al., 1986	HCWs (not described)	CP	NR	0.5µg/24h	0.7-2.5µg/24h	20	25%
Sessink et al., 1992	RNs & pharmacy personnel	CP & IF	GC- MS	<0.1µg/L	0.1µg-0.5µg	18	43%
Ensslin et al, 1993	RNs & pharmacy personnel	PL	GC-ED	4ng/L	4.1ng/L-34.4ng/L	21	26%
Sessink, et al, 1994	Pharmacy technicians	CP	GC-MS	0.2ng/ml	0.2-19.4Mµg/24h	9	66%
Ensslin et al., 1997	Pharmacy personnel	CP	GC-ED	2.5µg/L	5-9µg/L	13	15%
		PL	NR	NR	22.3 ng/g (one specimen +)	13	7%
Petran et al., 2003	RNs & pharmacy personnel	CP	GC-MS	0.04µg/L	0.05-0.76µg/L	100	40%, 23.4%, 7.3%*
		IF		0.05µg/L	0.08-1.90µg/L		14%, 7.4%, 2.4%
		DX	HPLC	NR	5-127 ng/L		5.5%
		EP		NR	10-182 ng/L		
Wick et al., 2003	RNs & pharmacy personnel	CP	HPLC-ESI-MS-MS	0.1ng/ml	0.1->100ng	7	37%
		IF					20%

NR= Not reported, CP= Cyclophosphamide, IF=Ifosfamide, PL=Platinum (Carboplatin & Cisplatin), DX= Doxorubicin, EP = Epirubicin

*Measurements taken at three different times with the same population over a period of three years (decrease in amount from first sampling to the last presumes 'learning effect' of safety precautions during study)

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Children's Hospital

Aerosolized Medication Administration Guidelines

PHARMACY					SAFETY				
Medication Administration					Staff/Environmental Precautions				
Drug	Use	Dose (Aerosolized)	Administration	Equipment Category	Employee Safety Category	Room Type▼ NSP or PR	HEPA Filter▪	Respiratory Protection▲	PPE ◆
Acetylcysteine (Mucomyst®) 20% Solution	Mucolytic	Infants: 1 - 2 mL TID - QID Children: 3 - 5 mL TID - QID	Dilute with 1 - 2 mL NS	V	1	NSP	NO	NONE	NO
●Albuterol (Proventil®) 0.5% Solution	Bronchodilator	Intermittent: 0.01 - 0.05 mL/kg/dose Q15min-Q6h ± PRN Max = 1 mL	Dilute with 1 - 2 mL NS.	V	1	NSP	NO	NONE	NO
Amphotericin (Fungizone®) 5 mg/mL	Anti-Fungal	15 mg QD - BID	Requires no further dilution	B	2	PR	YES	PAPR/ N-95	YES
Aztreonam (Azactam®) 200 mg/mL	Anti-Bacterial	Cystic Fibrosis: 500 - 1000 mg Q12h	Requires no further dilution	B	2	PR	YES	PAPR/ N-95	YES
Budesonide (Pulmicort®) 0.25 mg/mL	Anti-Inflammatory	0.25 - 0.5 mg BID *OR* 0.5 - 1 mg QD	Requires no further dilution	B	2	PR	YES	PAPR/ N-95	YES
Ceftazidime (Fortaz®) 200 mg/mL	Anti-Bacterial	Cystic Fibrosis: 500 - 1000 mg Q12h	Requires no further dilution	B	2	PR	YES	PAPR/ N-95	YES
Colistin Sulfate (Coly-Mycin®) 75 mg/mL	Anti-Bacterial	37.5 - 150 mg Q8 - 12h	Requires no further dilution	P	2	PR	YES	PAPR/ N-95	YES
●Cromolyn (Intal®) 10 mg/mL	Antihistamine	>2 yo: 20 mg QID	Requires no further dilution.	V	1	NSP	NO	NONE	NO
Dornase alfa (Pulmozyme®) 1 mg/mL	Mucolytic	2.5 mg QD - BID	Do NOT dilute or mix with other meds.	V	1	NSP	NO	NO	NO
Furosemide (Lasix®) 20 mg/mL	Broncho-pulmonary dysplasia	1 mg/kg/dose	Dilute to 2 mL with NS	V	1	NSP	NO	NONE	NO
●Ipratropium (Atrovent®) 0.02% (500 mcg/2.5 mL)	Bronchodilator/ Anticholinergic	Neonatal: 25 mcg/kg/dose TID Infants/Children: 125 - 250 mcg TID >14 yo: 500 mcg TID - QID	Requires no further dilution.	V	1	NSP	NO	NONE	NO
Levalbuterol (Xopenex®) 0.63 mg/3 mL	Bronchodilator	0.63 - 1.25 mg Q6 - 8h ± PRN	Requires no further dilution	V	1	NSP	NO	NONE	NO
Pentamidine (Pentam®) 50 mg/mL	Anti-Protozoal	<5 yo: 8 mg/kg/month (max 300 mg/dose) ≥5 yo: 300 mg/month	Dilute 300 mg vial with 6 mL NS. Do not mix with other meds.	B	2	PR	YES	PAPR/ N-95	YES
Racemic Epinephrine (Racemic Epi®) 2.25% Solution	Bronchodilator	0.25 - 0.5 mL Q1 - 4h PRN	Dilute with 3 mL NS	V	1	NSP	NO	NONE	NO
Ribavirin (Virazole®) 20 mg/mL	Anti-Viral	Intermittent: 2 g over 2 hrs TID Continuous: 6 g over 12 - 18 hrs/day Treatment Course is 3 - 7 days.	Prepared by pharmacy. Do not mix with other meds.	SPAG-2 & Tent (Page Resp. Care #1869)	3	PR Restricted To PS, PS, ISW	YES	PAPR/ N-95	YES
Tobramycin (TOBI®) 300 mg/5 mL	Anti-Bacterial	300 mg BID	Do not dilute or mix with other meds	P	2	PR	YES	PAPR/ N-95	YES

●Albuterol, Cromolyn, and/or Ipratropium may be mixed together for administration.

▼Room Type: NSP = No Special Precautions. PR = Precaution Room (Negative Pressure, Private and/or Treatment Room).

▪HEPA Filter = High Efficiency Particulate Air Filter. Two filters are available on each nursing unit.

▲To use an N-95 respirator, staff must be cleared by Occupational Health Services and fit tested by Safety and Environmental Health. Otherwise use a PAPR (Powered Air Purifying Respirator).
PAPRs are available from Materials Management x8336.

◆PPE = Personal Protective Equipment (Gown, Gloves, Goggles)

04/25/03

Aerosolized Medication Safety Category

For questions regarding precautions, please contact Safety & Environmental Health by paging "SAFE" (#7233).

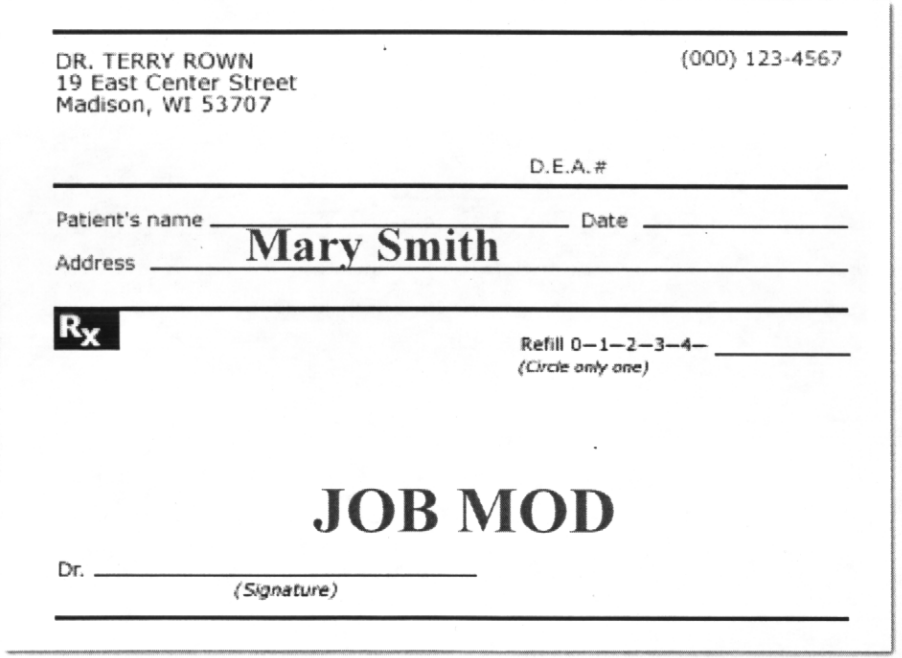
1	2	3
No Specific Precautions Required	**Moderate Level of Precaution**	**High Level of Precaution**
✓ Medications not classified as teratogens and not known to impair fertility ✓ Medications have not been shown to cause significant or persistant adverse health effects with secondary exposure ✓ Systemic absorption of medication is considered minimal ✓ Physical state of medication is not an aerosol particle. It will not settle out of the air onto surfaces or be transported outside of the treatment area to cause secondary exposures	✓ Medications not classified as teratogens and not known to impair fertility ✓ Medications in which no studies have been conducted on potential health effects related to healthcare worker exposure ✓ Patients who directly receive these aerosolized medications may exhibit 1 or more serious adverse health effects indicating a potential for secondary exposure effects with repeated exposure scenarios ✓ Physical state of medication is not an aerosol particle. It will not settle out of the air onto surfaces or be transported outside of the treatment area to cause secondary exposures	✓ Medications are considered to be potential teratogens (capable of causing fetal defects) ✓ Medications that exclude childbearing or lactating females from administering the medication ✓ Physical state of medication is an aerosol particle that is capable of settling out of the air onto surfaces and being transported outside of the treatment area causing secondary exposures.

Aerosolized Medication-Equipment Guide

Equipment Category	V	B	P
Nebulizer Type	Vicrone® Small Volume Medication Nebulizer	Baxter® Airlife Misty-Neb Medication System with Filter	Pari® LC Plus Nebulizer and Pari Filter/Valve Set
Description	Multi-purpose medication jet nebulizer	Medication jet nebulizer with expiratory filter. Intended to reduce care-giver exposure.	Medication jet nebulizer for administration of TOBI® and Colistin.
Flow Rate	8-10 L/min	6-8 L/min	4-6 L/min
General Stores #	9427	9035	Stat Room Item #9504 & #9505
Goals of Treatment	Optimize drug particle delivery to the lungs.	Optimize drug particle delivery while minimizing caregivers' exposure to particles.	Effective delivery of TOBI® and Colistin while minimizing caregivers' exposure to particles
Optimizing Treatment	Provide a reservoir of aerosolized particles for the patient to breathe from. "Blow-by" treatments provide the least particle delivery.	A closed conduit between the apparatus and the patient ensures that the majority of aerosolized particles pass through the filter.	Pari® LC Plus is the only nebulizer recommended for the effective delivery of TOBI®
Patient Use	Infants: Attach infant-sized aerosol mask or resuscitation mask to nebulizer. Hold mask as close to infant's face as possible. Children <6 yo: Attach pediatric aerosol mask to nebulizer. Strap nebulizer to child's head. Instruct child to take deep breaths. Children ≥6 yo & adults: Connect mouth-piece to one end of a T-piece and a corrugated reservoir to the opposite end. Instruct patient to take slow deep breaths with a brief inspiratory pause.	Infants & Children <6 yo: Attach appropriate size resuscitation mask to apparatus. Hold mask tightly over patient's nose and mouth. Children ≥6 yo & adults: Attach mouth-piece to apparatus. Instruct patient to maintain a tight seal around mouth-piece, and inhale and exhale through mouth-piece. Patients should be instructed to take deep breaths with a brief inspiratoy pause.	Remove mouthpiece with blue flap valve. Connect filter set and mouthpiece. Instruct patient to maintain a tight seal around mouth-piece, and inhale and exhale through mouth-piece. Patients should be instructed to take deep breaths with a brief inspiratory pause.
Via Trach	Attach nebulizer to trach collar.	Cannot be connected to a trach tube. Page Resp. Care for an adapter (#1089).	Cannot be used with a trach collar. Page Resp Care for adapter (#1089). The Baxter® Airlife filtered nebulizer may be used as a substitute, however, drug effectiveness has not been confirmed with this apparatus.
Infection Control	Between treatments on the same patient, rinse with sterile water and air dry. Replace every 7 days. Change between patients.	Between treatments on the same patient, rinse nebulizer with sterile water and air dry. Replace medication nebulizer with Vicrone® every 24 hours. Replace entire unit every 7 days. Change between patients.	Between treatments on the same patient, rise nebulizer with sterile water and air dry. Replace entire unit every 7 days. Change between patients.

04/25/03

THE JOB MODIFICATION PRESCRIPTION


DR. TERRY ROWN
19 East Center Street
Madison, WI 53707

(000) 123-4567

D.E.A.#

Patient's name _____ Date _____

Address Mary Smith

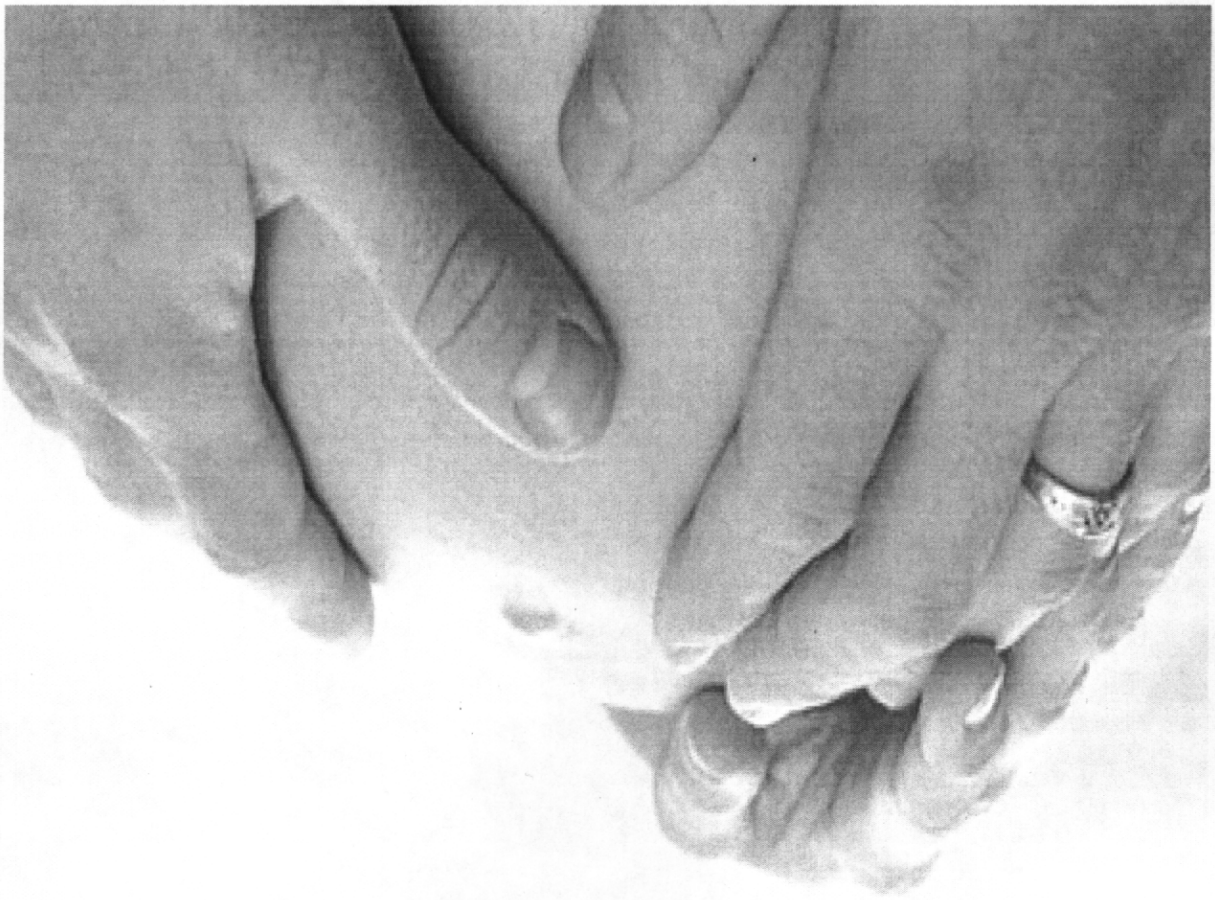
Rx

Refill 0–1–2–3–4– _____
(Circle only one)

JOB MOD

Dr. _____
(Signature)

Melissa McDiarmid, M.D., M.P.H.



Why Job Modification Prescriptions are needed?

1) Risk to reproductive/developmental health from occupational exposures are not well characterized.

2) Most occupational exposure limits are set without considering reproductive/developmental health effects.

Report

Preconception Brief: Occupational/Environmental Exposures

Melissa A. McDiarmid[1] – and Kim Gehle[1], 2006

"…many toxicants with unambiguous reproductive and developmental effects are still in regular commercial or therapeutic use and thus present exposure potential to workers."

Historically…Job Modification has referred primarily to physical stresses as standing and lifting - i.e. AMA Guidelines, 1984.

Recommendations Regarding Exposure During Pregnancy

Exposure	Recommendation
Anesthetic gases on a daily basis if no scavenging system is in place	Mandatory transfer
Lead, if blood-lead level has been greater than 30	Mandatory transfer
Direct application and use of organic mercurial compounds	Mandatory transfer
Radiation exposure potentially greater than 0.5 Rems for the duration of the pregnancy	Mandatory transfer
Direct mixing of cytotoxic drugs without protective clothing and a hood	Mandatory transfer
Use of hexachlorophene for hand washing	Substitute material
A job that entails more than 3 hours of standing, lifting more than 15 pounds on a regular basis, or significant exposure to vibration or extremes of temperature	Transfer or job modification in the third trimester: modification consists of flexible work schedule to avoid fatigue and allow frequent breaks
Carbon monoxide if carboxyhemoglobin level is greater than 5	Transfer or job modification (smoking cessation if patient smokes)
Glycol ethers	Job transfer or rigorous exposure controls (note: exposure control may be impossible in trade uses such as painting)
Other organic solvents	Job transfer or modification to minimize exposure
PCBs, PBBs, organochlorine pesticides , and defoliants	Job transfer or rigorous exposure controls

From Welch, LS, 1986

Protective Reassignment

- Retrait Preventive, Quebec - 1981
- EU Countries – 1990s
- Variable corporate programs
- ACOEM – 1994*
- U.S. Navy – 2001*

*includes risk to working men also

Workplace Reproductive Hazards Management

- Plan/Policy in place
  - Hazard Identification
  - Assessment of Risk
- Hazard Communication (Right to Know)
- Notification or Pregnancy
  - Validation with caregiver note
- Workplace Response to Notification
  - Job hazard evaluation
  - Risk Reduction
  - Job Modification – with benefit protection
    - Communication of Job Modification to Worker & Supervisor

Job Modification Considerations for Clinicians

- ***Hazard Recognition***/Assessment of Risk
  - Literature
  - MSDS
  - Specialty Consultants
- Patient Participation
- Social Context (lost wages, benefits)
- Determination of Job Modification need
  - Consultation with patient's employee health unit
- Description of Modification Duties
- Duration of Modified Duties
  - Address Breast Feeding

Employment sectors and associated reproductive/developmental toxicants

Sector	Toxicant	Examples
Agriculture	Pesticides/Herbicides	Metam Sodium Methyl Bromide Ethylene Dibromide
Manufacturing	Organic Solvents Heavy Metals	Glycol ethers, lead, Cadmium
Dry Cleaning	Solvents	Perchloroethylene
Printing	Solvents/inks	
Pharmaceutical Compounding/Manufacture	Hazardous Drugs	Antineoplastics, hormones, immunologic modifiers
Nail Salons	Organic Solvents/Chemicals	Toluene Dibutyl Phthalate
Health Care	Biologics	Rubella, CMV, Hepatitis virus
	Physical Agents	Ionizing Radiation/Heat
	Chemicals	Antineoplastics/ Hazardous Drugs Anesthetic Gases Sterilants
	Physical Exertion	Lifting/Prolonged Standing Shift Work

From McDiarmid & Gehle, 2006

Pregnancy Outcome Following Gestational Exposure to Organic Solvents

A Prospective Controlled Study

Sohail Khattak, MD, FRCPC

GuitiK-Moghtader, BSc

Kristen McMartin, MSc

Maru Barrera, PhD

Debbie Kennedy, MD

Gideon Koren, MD, FRPC

Significantly more major malformations occurred among fetuses of women exposed to organic solvents than controls (RR= 13.0; 95% CI= 1.8 - 99.5)

JAMA 1999 Vol 281, No.12 pp. 1106-1109

Job Modification Considerations for Clinicians

- Hazard Recognition/Assessment of Risk
  - Literature
  - MSDS
  - Specialty Consultants
- **Patient Participation**
- **Social Context (lost wages, benefits)**
- **Determination of Job Modification need**
  - **Consultation with patient's employee health unit**
- **Description of Modification Duties**
- Duration of Modified Duties
  - Address Breast Feeding

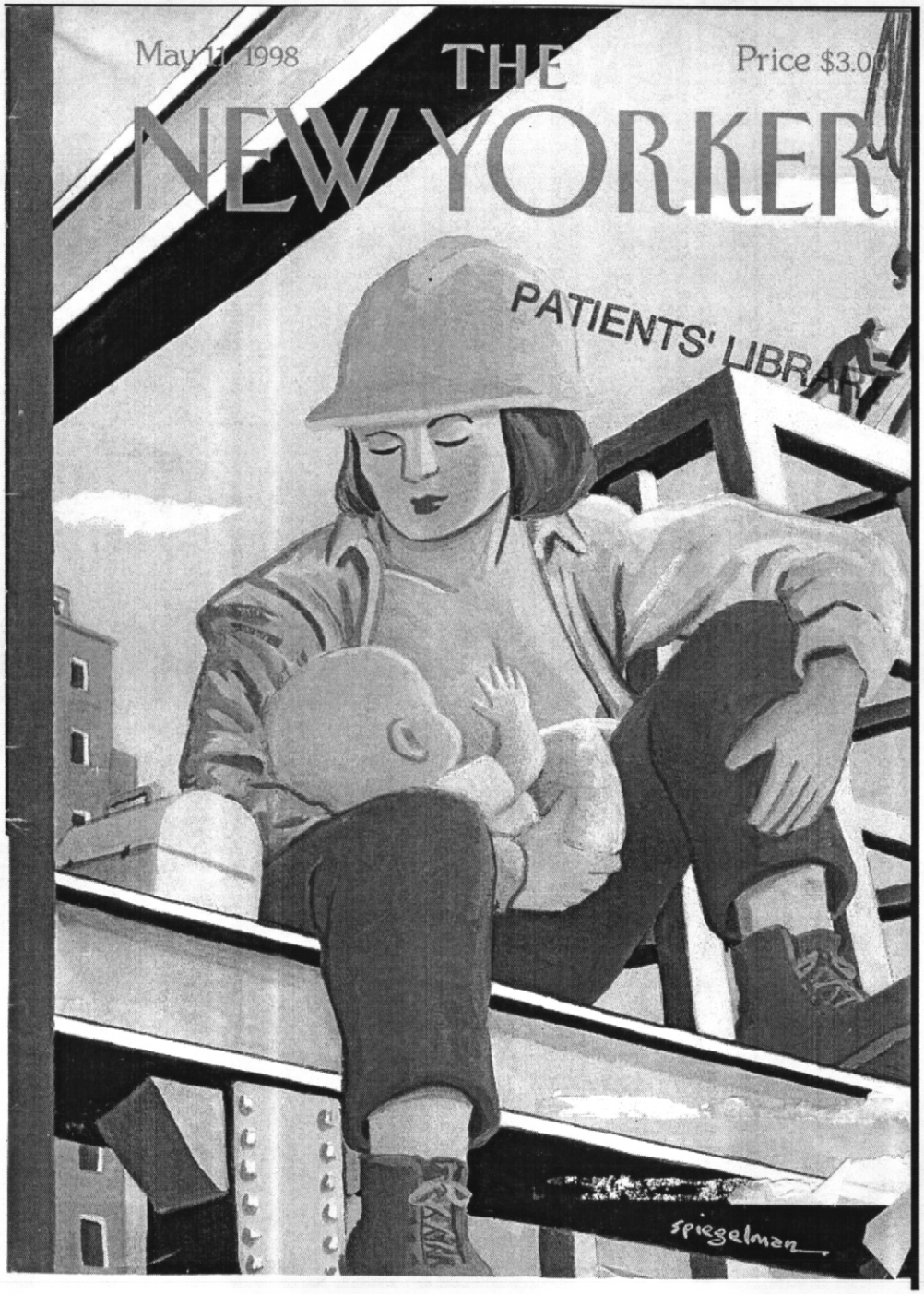
Job Modification

- **Consider Temporary Reassignment**
  - when potential for exposure cannot be adequately controlled through engineering or work-practices
  - Medical history or risk factors suggest need

- **Temporary Protective Reassignment**
  - Reassignment of Duties Within Same Job OR True Position Reassignment Needed
  - Identify specific Duties within a Job as Hazardous
  - Explore Scenarios of Temporary Duty Transfer rather than position re-assignment
  - Discussions with affected Parties and Supervisors

Job Modification Considerations for Clinicians

- Hazard Recognition/Assessment of Risk
  - Literature
  - MSDS
  - Specialty Consultants
- Patient Participation
- Social Context (lost wages, benefits)
- Determination of Job Modification need
  - Consultation with patient's employee health unit
- Description of Modification Duties
- **Duration of Modified Duties**
  - Address Breast Feeding


May 11, 1998
THE NEW YORKER
Price $3.00
PATIENTS' LIBRARY
Spiegelman

Chemical Found in Breast Milk	Occupation at Risk of Exposure
Mercury	Medical/dental staff
Cadmium	Battery manufacturing, metal soldering or welding
Drugs/Medications	Medical/dental staff
Tetrachloroethylene	Dry cleaners
Polycyclic Aromatic Hydrocarbons (PAHs)	Coke, coal-tar, and asphalt production plants, smokehouses, and municipal trash incineration facilities
Lead	Artists, work in construction, smelters, radiator repair shops, and firing ranges
Dioxin	Pesticides production, work at paper and pulp mills, or operating incinerators
Pesticides	Farming, nursery workers, pesticide manufacturing
Nitrosamines	Work in tanneries, pesticide manufacturing plants, and rubber and tire plants

Sonawane, BR (1995) Chemical Contaminants in Human Milk: An Overview, Environmental Health Perspectives, 103:6 pages 197-205., Committee on Drugs (1983) The Transfer of Drugs and Other Chemicals into Human Breast Milk, Pediatrics 72:3, pages 375-383., Wolff, MS (1983) Occupationally Derived Chemicals in Breast Milk, American Journal of Industrial Medicine, 4, pages 259-281.

DR. TERRY ROWN
19 East Center Street
Madison, WI 53707

(000) 123-4567

D.E.A. #

Patient's name Mary Smith Date

Address

Rx

Refill 0—1—2—3—4— _____
(Circle only one)

JOB MOD

Dr. _____
(Signature)

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

The Stationery Office (formerly HMSO) publications are available from The Publications Centre, PO Box 276, London SW8 5DT Tel: 0870 600 5522 Fax: 0870 600 5533 Website: www.tso.co.uk (They are also available from bookshops).

HSE priced and free publications are available by mail order from HSE Books, PO Box 1999, Sudbury, Suffolk CO10 2WA Tel: 01787 881165 Fax: 01787 313995 Website: www.hsebooks.co.uk (HSE priced publications are also available from bookshops and free leaflets can be downloaded from HSE's website: www.hse.gov.uk).

Further printed copies of this information sheet are not available. You can print further copies from the HSE website.

For information about health and safety ring HSE's Infoline Tel: 08701 545500 Fax: 02920 859260 e-mail: hseinformationservices@natbrit.com or write to HSE Information Services, Caerphilly Business Park, Caerphilly CF83 3GG.

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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New and expectant mothers at work

A guide for health professionals

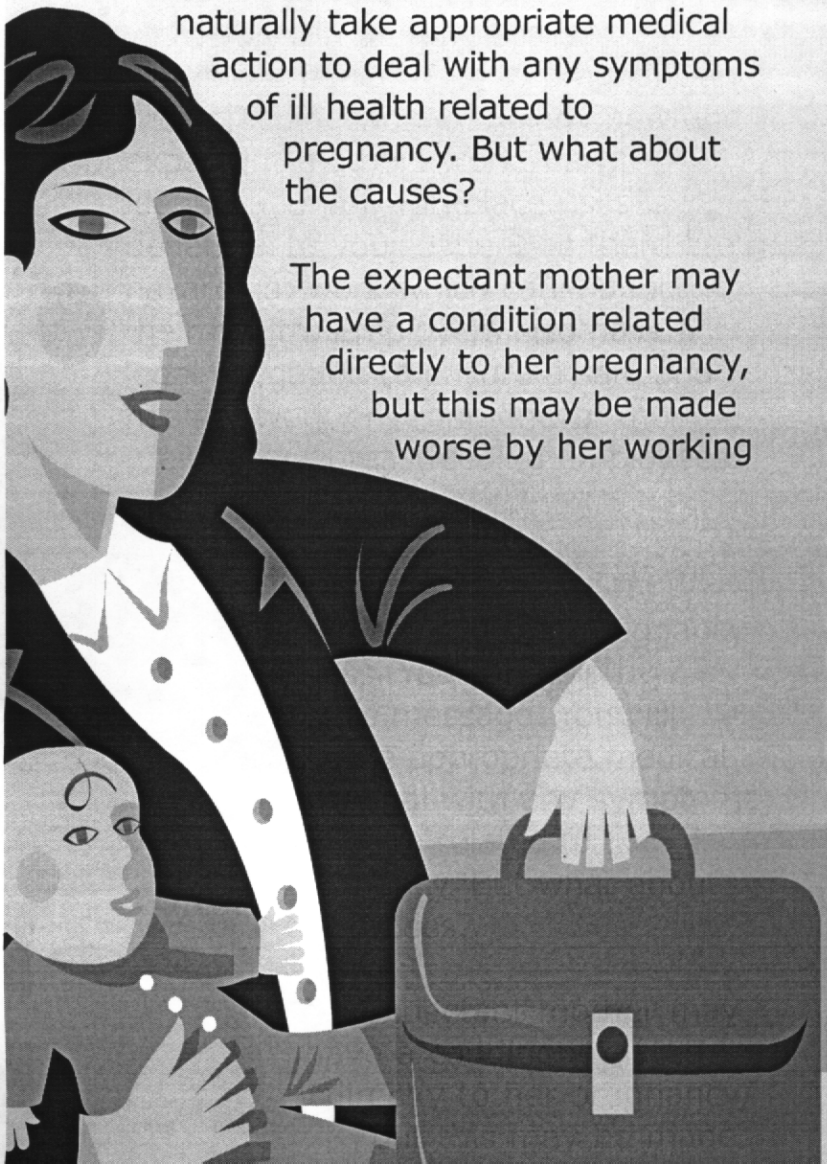
HSE

This leaflet tells you, as a professional providing advice to new and expectant mothers, about the health and safety responsibilities of employers. It advises what you can do to minimise workplace health risks to pregnant and breastfeeding workers. Many new and expectant mothers work. Early identification of workplace risks is beneficial to your patient as there are hazards at work which could affect their health. Employers also have a legal obligation to ensure a safe and healthy work environment for their pregnant or breastfeeding employees.

How you can help

Employers are advised that pregnancy is not an illness. You can help by reinforcing this message. You will naturally take appropriate medical action to deal with any symptoms of ill health related to pregnancy. But what about the causes?

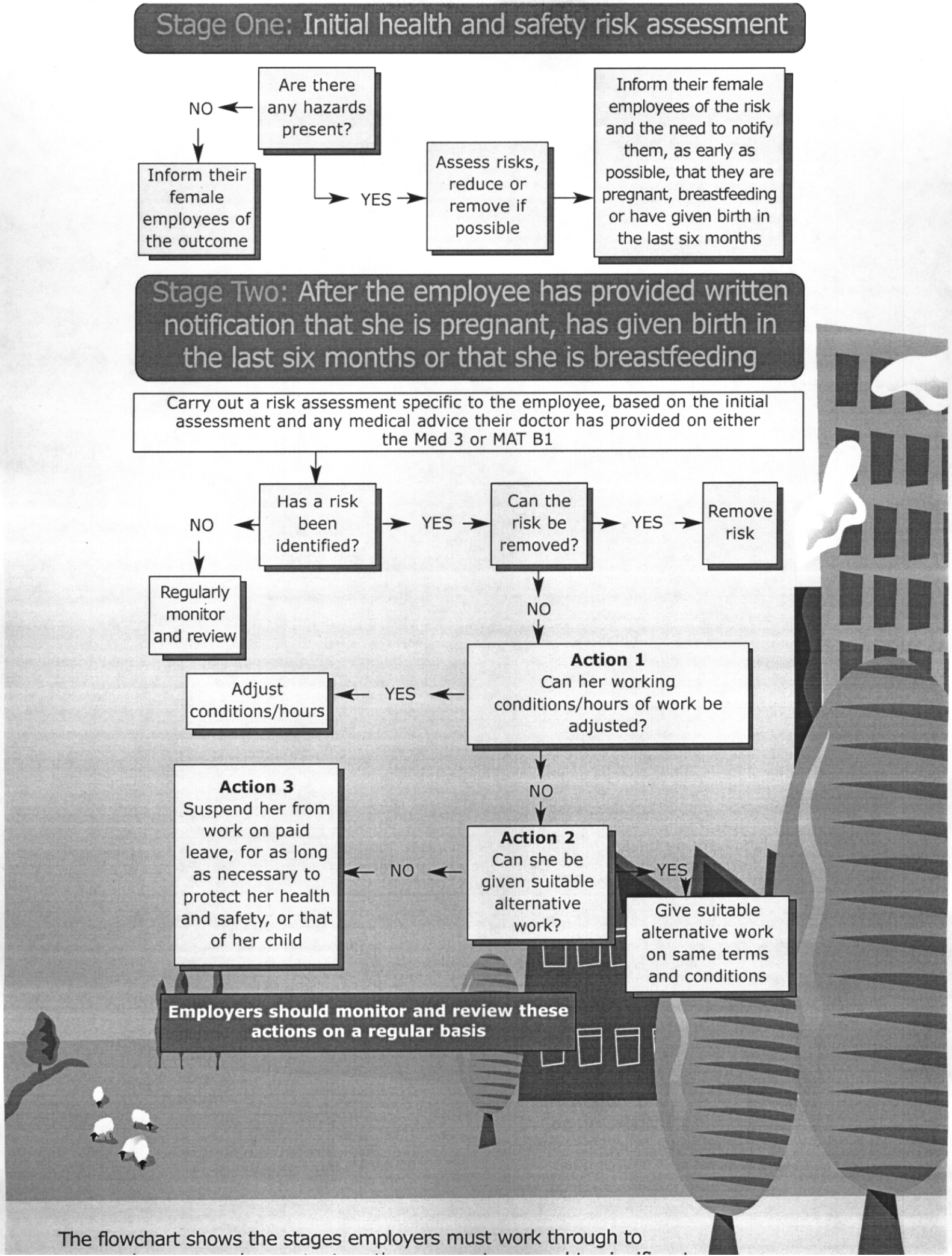
The expectant mother may have a condition related directly to her pregnancy, but this may be made worse by her working conditions or hazards at work. If this is the case then employers need to do something about it. Issuing a medical certificate (Med 3) may not resolve the problem and the woman might still have to consult you more frequently than would normally be expected. It is also possible that by being off work sick the woman could suffer financial loss during her pregnancy and maternity leave.



Duties on employers under the Management of Health and Safety at Work Regulations 1999

The law requires every employer to assess workplace risks for all their employees, and take practical action to control those risks. In addition, employers must take particular account of risks to new and expectant mothers. The definition of a new or expectant mother is someone who is pregnant, has given birth within the previous six months, or is breastfeeding.

Employers must identify hazards in their workplace that could pose a health or safety risk to new and expectant mothers and take appropriate action to remove or reduce the risk. They must also make this information known to all their female employees of childbearing age, not just those who have informed them they are pregnant. This is particularly important for expectant mothers, as it is possible for the first 4-6 weeks of pregnancy to go undetected.



The flowchart shows the stages employers must work through to

Protecting the woman's health and safety at her workplace

The expectant mother must inform her employer in writing that she is pregnant. Her employer can ask for written medical evidence to confirm this and the employee has to provide it. The reason for this is so that employers can carry out a specific risk assessment for the woman concerned (Stage Two of the flowchart). The following certificates can be used to convey any advice.

Medical Statement (Med 3)

Doctors are required to record advice given to patients about their ability to perform their own or usual type of occupation on medical statements. Where the doctor considers work adjustments are required during pregnancy and breastfeeding, the doctor should:

- record this advice to the employee (and employer) in the 'remarks' section on the Med 3; and
- select section (a) 'You need not refrain from work'.

Maternity Certificate (MAT B1)

When the pregnant woman wishes to claim Statutory Maternity Pay (SMP) or Maternity Allowance (MA) she should provide her employer with certificate MAT B1, which is issued around the twentieth week of pregnancy. A doctor or a registered midwife can complete the MAT B1.

Employers must ask the woman to help with the risk assessment. This is particularly to take account of any medical advice she has received. In providing this advice it may be helpful to consider the following points.

Pregnancy-related medical conditions (eg high blood pressure)

Employers must conduct a specific risk assessment after receiving the Med 3 and should take into account any medical advice you have given. If risks are identified, which go beyond the level of risk found outside the

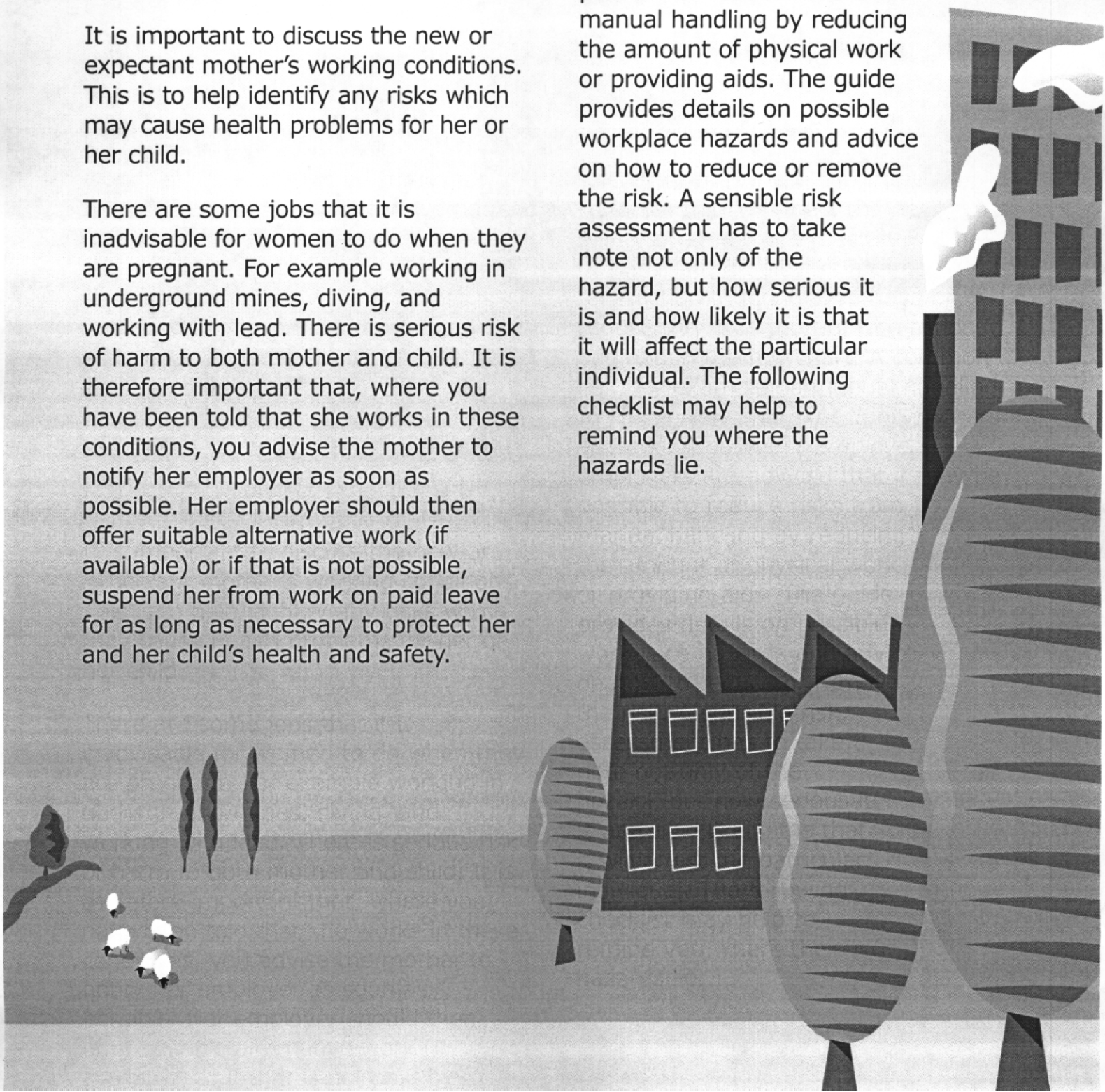
workplace, but cannot be removed, employers should adjust the woman's working conditions or hours. If there is still a risk, she must be offered suitable alternative work or if that is not possible, suspended on full pay for as long as is necessary to protect her and her child's health.

Health problems caused by the woman's work

It is important to discuss the new or expectant mother's working conditions. This is to help identify any risks which may cause health problems for her or her child.

There are some jobs that it is inadvisable for women to do when they are pregnant. For example working in underground mines, diving, and working with lead. There is serious risk of harm to both mother and child. It is therefore important that, where you have been told that she works in these conditions, you advise the mother to notify her employer as soon as possible. Her employer should then offer suitable alternative work (if available) or if that is not possible, suspend her from work on paid leave for as long as necessary to protect her and her child's health and safety.

There are many other workplace hazards that can affect the health and safety of a new or expectant mother or her child. Employers are required to take action to identify, remove or reduce the risks through the actions outlined in the flowchart. A common risk, for example, is manual handling. In HSE's *New and expectant mothers at work: A guide for employers*, employers are advised that it may be possible to reduce risks from manual handling by reducing the amount of physical work or providing aids. The guide provides details on possible workplace hazards and advice on how to reduce or remove the risk. A sensible risk assessment has to take note not only of the hazard, but how serious it is and how likely it is that it will affect the particular individual. The following checklist may help to remind you where the hazards lie.



Physical hazards

- Awkward spaces and workstations.
- Vibration.
- Noise.
- Radiation (covered by specific legislation).

Biological agents

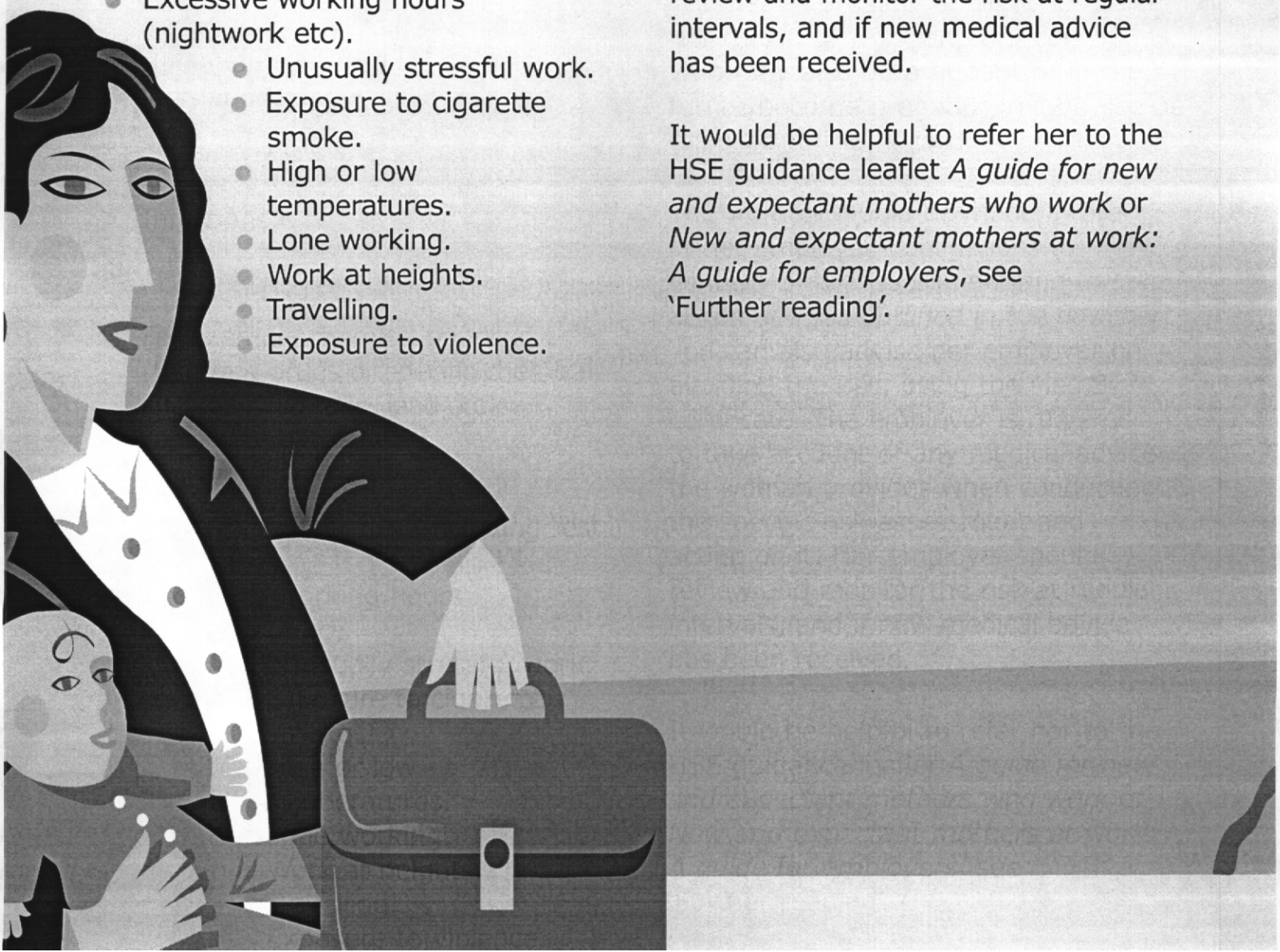
- Infections.

Chemical hazards

- For example chemical handling (handling drugs or specific chemicals such as pesticides, lead etc).

Working conditions

- Inadequate facilities (including rest rooms).
- Excessive working hours (nightwork etc).
- Unusually stressful work.
- Exposure to cigarette smoke.
- High or low temperatures.
- Lone working.
- Work at heights.
- Travelling.
- Exposure to violence.



Signing the pregnant woman off sick from work, by issuing a Med 3, may not address the cause of her ill health. The health problem could reoccur on her return to work and her colleagues, who may also be pregnant or in the future become pregnant, might also be exposed to the hazard.

The woman should be made aware of her employer's obligations to conduct a risk assessment *and to take action on it as outlined in the flowchart*. You can also advise her employer on avoiding the risk, using the Med 3 certificate. The employer is required to take account of any medical advice the woman provides when conducting the specific risk assessment and acting on it. Her employer should review and monitor the risk at regular intervals, and if new medical advice has been received.

It would be helpful to refer her to the HSE guidance leaflet *A guide for new and expectant mothers who work* or *New and expectant mothers at work: A guide for employers*, see 'Further reading'.

Rest facilities for pregnant and breastfeeding women

Many pregnant women feel tired and need to rest. Breastfeeding mothers need a clean, private place to express and store their milk. Employers are legally required to provide suitable rest facilities for workers who are pregnant or breastfeeding. Also, although not a legal requirement, employers are encouraged to provide a healthy and safe environment for nursing mothers to express and store milk. This could be provided in the suitable rest facilities. However, it is not suitable for toilets to be used for this purpose.

Night work

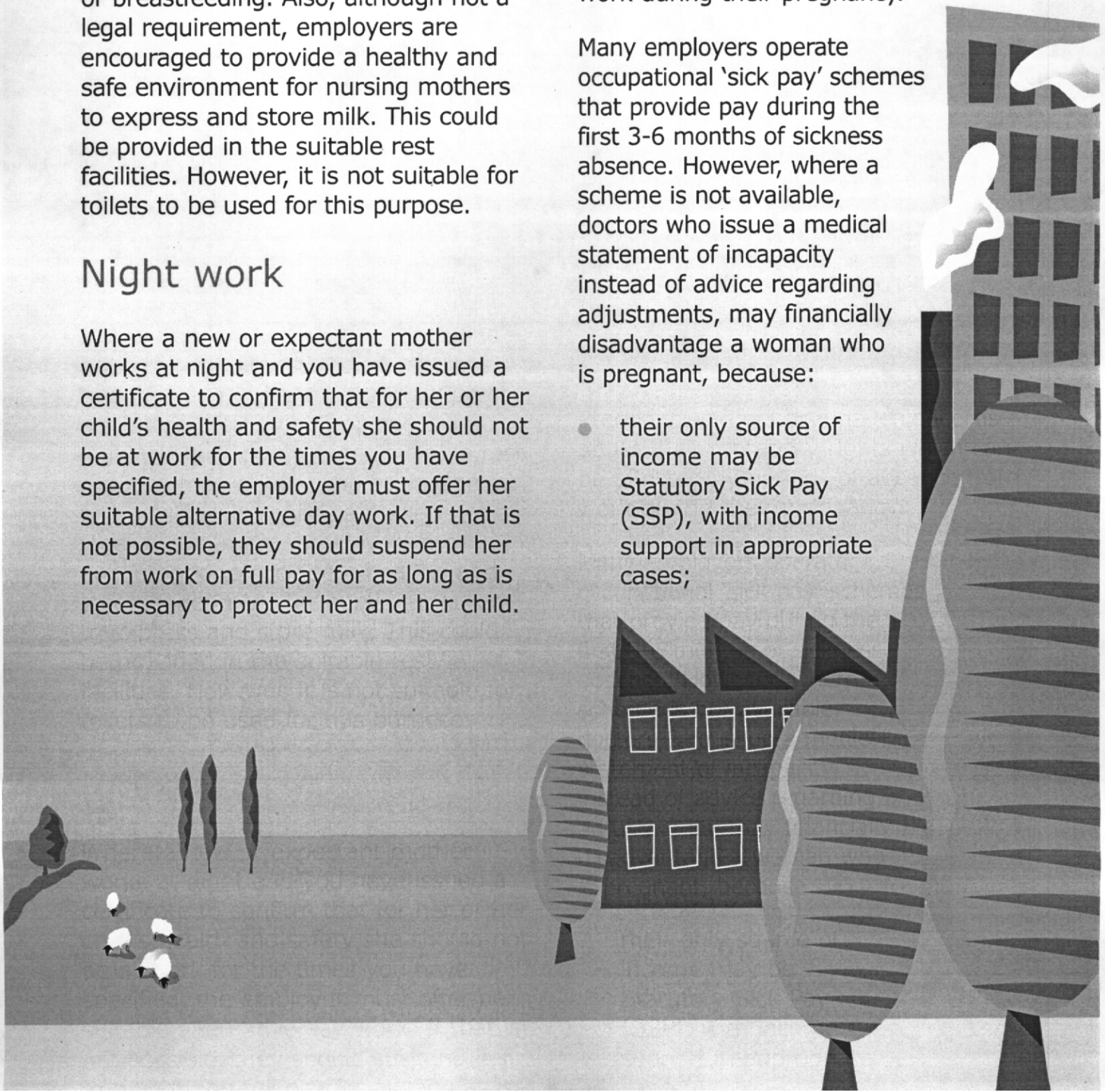
Where a new or expectant mother works at night and you have issued a certificate to confirm that for her or her child's health and safety she should not be at work for the times you have specified, the employer must offer her suitable alternative day work. If that is not possible, they should suspend her from work on full pay for as long as is necessary to protect her and her child.

Impact on maternity rights, including maternity pay, of issuing a Medical Statement, eg Med 3

Pregnant workers also have concerns about their maternity rights which can be affected by periods of absence from work during their pregnancy.

Many employers operate occupational 'sick pay' schemes that provide pay during the first 3-6 months of sickness absence. However, where a scheme is not available, doctors who issue a medical statement of incapacity instead of advice regarding adjustments, may financially disadvantage a woman who is pregnant, because:

- their only source of income may be Statutory Sick Pay (SSP), with income support in appropriate cases;



- women getting only SSP in the period used for calculating their earnings towards Statutory Maternity Pay (SMP) may not qualify, although they may be able to claim Maternity Allowance; and
- if a woman is signed off sick for a pregnancy-related reason at any time after the beginning of the sixth week before her expected week of childbirth (this will be reduced to the fourth week for women with an expected week of childbirth on or after 6 April 2003), her maternity leave will automatically be triggered, irrespective of when she intended to start it.

Further information

For health and safety issues:
Contact HSE's Infoline: 08701 545500 or see the HSE website: www.hse.gov.uk.

For the following maternity rights issues:

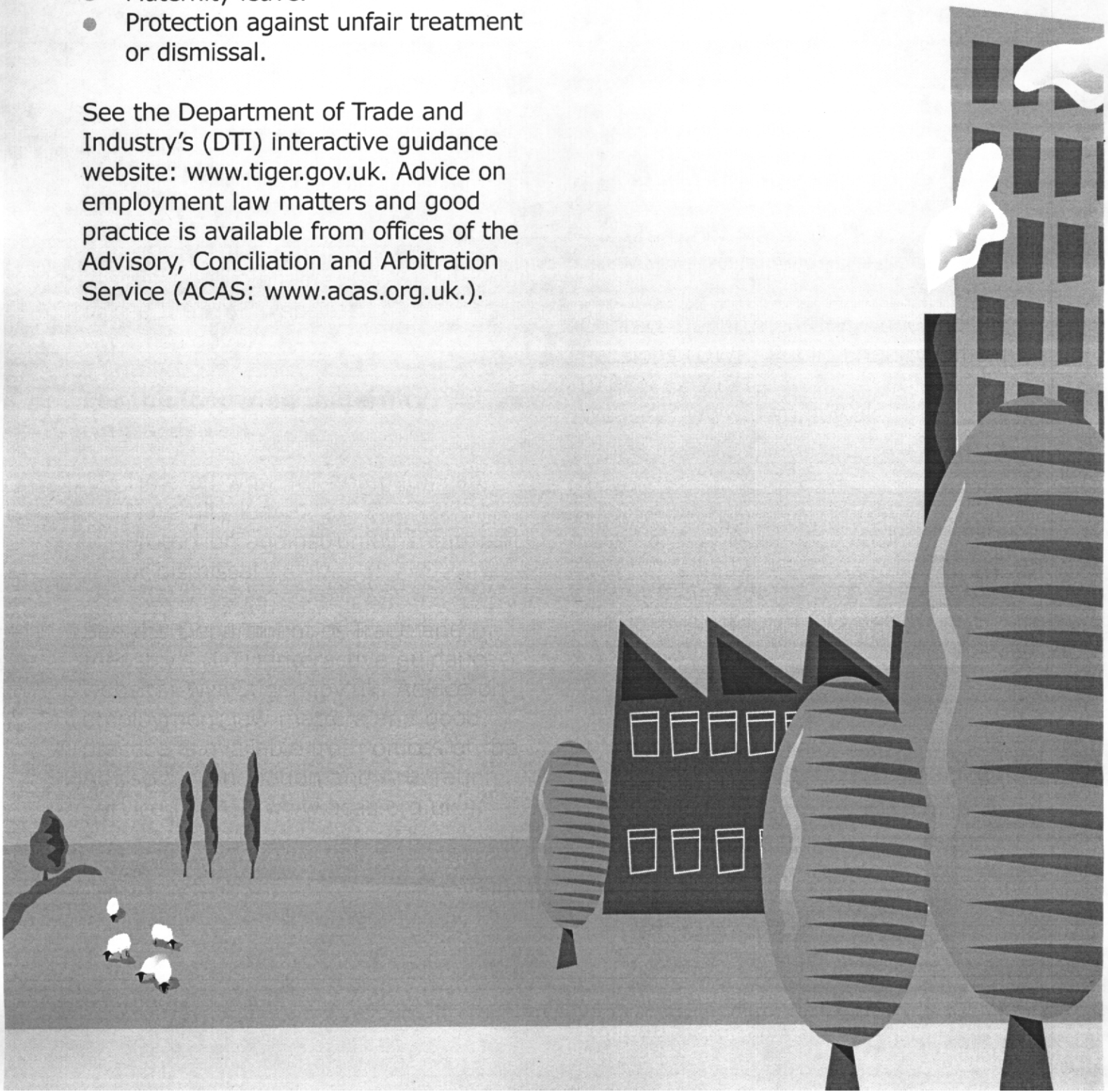
- Time off work for antenatal care.
- Maternity leave.
- Protection against unfair treatment or dismissal.

See the Department of Trade and Industry's (DTI) interactive guidance website: www.tiger.gov.uk. Advice on employment law matters and good practice is available from offices of the Advisory, Conciliation and Arbitration Service (ACAS: www.acas.org.uk.).

For maternity benefits issues:

- Statutory Maternity Pay.
- Maternity Allowance.

Contact Department for Work and Pensions (DWP) Public Enquiry Office: 0207 712 2171,
Website: www.dwp.gov.uk.



Further reading

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

Workplace health, safety and welfare. Workplace (Health, Safety and Welfare) Regulations 1992. Approved Code of Practice L24 HSE Books 1992 ISBN 0 7176 0413 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)

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

A guide for new and expectant mothers who work INDG373 HSE Books 2003 (single copy free or priced packs of 10 ISBN 0 7176 2614 8)

Maternity rights: A guide for employers and employees 02/904 available at www.dti.gov.uk/er/individual/maternity.pdf and from DTI Publications Orderline: 0870 1502 500

Working safely with ionising radiation: Guidance for expectant or breastfeeding mothers Leaflet INDG334 HSE Books 2001 (single copy free)

Infection risks to new and expectant mothers in the workplace: A guide for employers Guidance booklet HSE Books 1997 ISBN 0 7176 1360 7

Sex Discrimination Act 1975 The Stationery Office ISBN 0105465755

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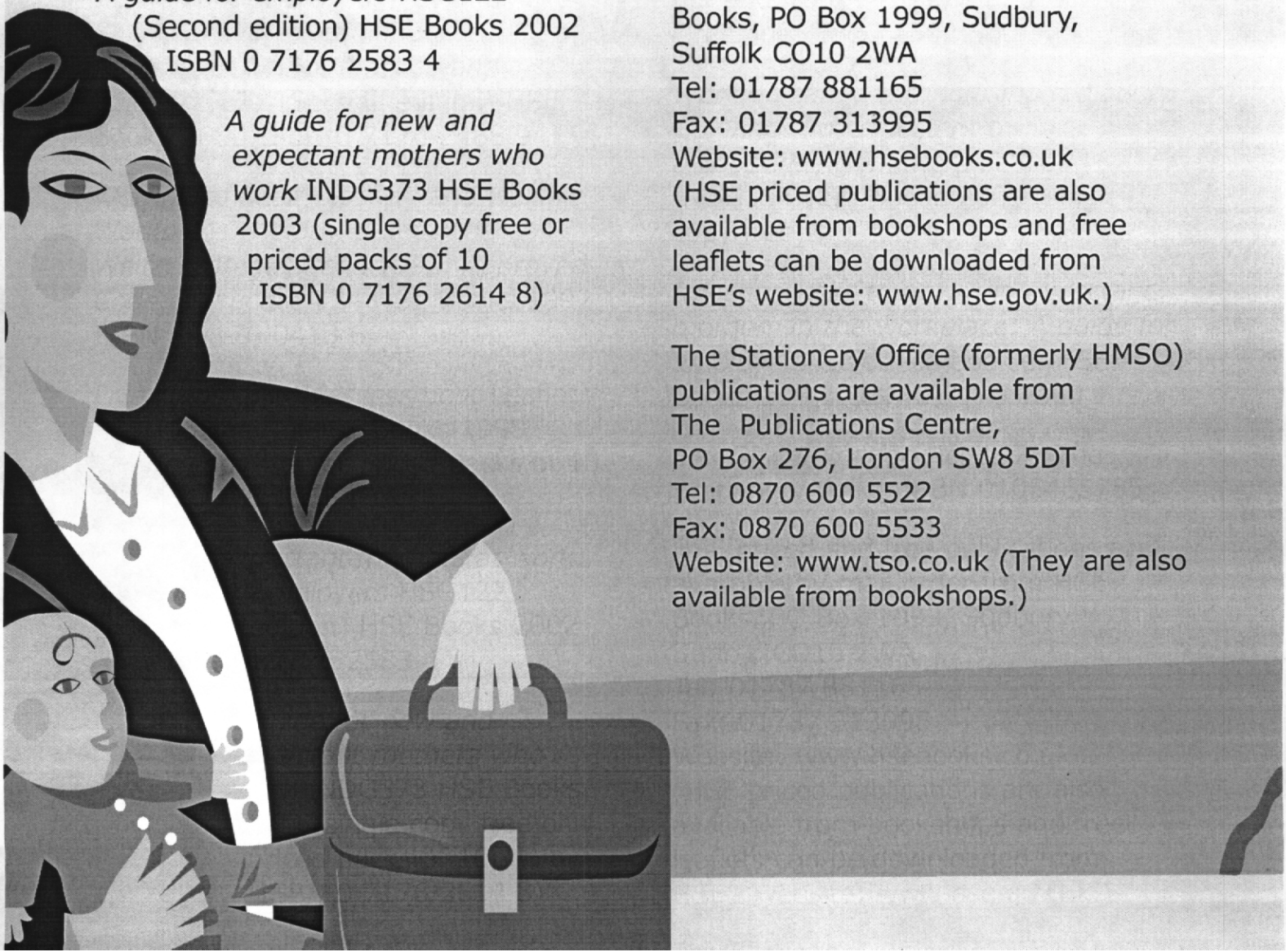

Sources of help

HSE Information Services
Caerphilly Business Park
Caerphilly
CF83 3GG
Infoline: 08701 545500
Fax: 02920 859260
email:
hseinformationservices@natbrit.com
Website: www.hse.gov.uk

Department for Work and Pensions
Public Enquiry Office
The Adelphi
1-11 John Adam Street
London
WC2N 6HT
Tel: 020 7712 2171
Fax: 020 7712 2386
Website: www.dwp.gov.uk

Department for Trade and Industry
General Enquiry Unit
1 Victoria Street
London
SW1H 0ET
Tel: 020 7215 5000
email: enquiries@dti.gsi.gov.uk
Website: www.dti.gov.uk

Equal Opportunities Commission
Arndale House, Arndale Centre
Manchester
M4 3EQ
Tel: 0845 601 5901
Fax: 0161 838 8312
email: info@eoc.org.uk
Website: www.eoc.org.uk

The Maternity Alliance
Information and Publications
3rd Floor West
2-6 Northburgh Street
London
EC1V 0AY
Information Line: 020 7490 7639
Fax: 020 7014 1350
email:
info@maternityalliance.org.uk

Tommy's the Baby Charity
1 Kennington Road
London
SE1 7RR
Tel: 0870 777 3060
Fax: 020 7928 6628
Website: www.tommys.org

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

03/03 C40

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