The causes of adverse effects on the human reproductive process are very varied and, on the whole, poorly understood. Hereditary factors are usually accepted as being responsible for a large proportion of reproductive malfunction. Environmental and lifestyle factors, including exposure to natural and synthetic chemicals, drugs, ionising radiation and alcohol consumption are also contributors but the magnitude of each contribution is unknown. Other factors also need to be considered, such as changes in reproductive behaviour. Some of the possible reproductive effects seen can at least in part be associated with having children later in life (both mothers and fathers being older than in the relatively recent past) and also having fewer children.

Reproduction is a complex, multi-stage process covering pertinent events between the development of germ cells in both male and female, starting early in life right through to the status of the offspring as a healthy sexually mature adult. Interference at any of these stages may cause adverse effects, collectively described as "reproductive impairment". It is difficult to estimate the overall rate of reproductive impairment in the "normal" human population. This is because figures quoted for specific types of impairment are often incomplete and, in particular, because most spontaneous abortions occur very early and may be perceived as late menstruation. 36 80.

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Cocaine use during pregnancy has been associated with abruptio placentae, prematurity, foetal loss, decreased birth weight, microcephaly, limb defects, urinary tract malformations, and poorer neurodevelopmental performance.

Hydantoins (phenytoin and trimethadione) have been associated with a recognisable pattern of malformation termed the foetal hydantoin syndrome. The clinical features include craniofacial dysmorphology.

Lithium treatment for bi-polar disorder may rarely produce heart defects in the foetus during the first trimester. However the risks are generally considered lower than with other drugs for this condition.

Sodium valproate in the first trimester is associated with, , neural tube defects.

Other compounds which may be teratogens include D-penicillamine, methimazole and diazepam.

Development of the nervous, immune, endocrine, reproductive and metabolising systems continues after birth. Some chemicals absorbed by the mother are excreted in breast milk, unchanged or as metabolites. Hence the opportunity for toxic insult to the newborn baby by those chemicals is significant following sufficient exposure. Heavy metals, PCBs and PBBs have all been associated with this route of exposure.

The identification of the reproductive effects of chemicals and their dose-effect relationships is in many respects a rapidly developing science. However it has many features in common with other forms of chemical toxicity. Detailed assessment of risk requires reliable, high-quality data covering exposure and outcome. Except in a very few cases such data are not available.

Reproductive effects are only one of the potential risks to health that have to be controlled in the workplace. In general it is desirable that legislation to control the use of chemicals at work should so far as is practicable protect against adverse reproductive effects by controlling and minimising exposure, and hence risk.

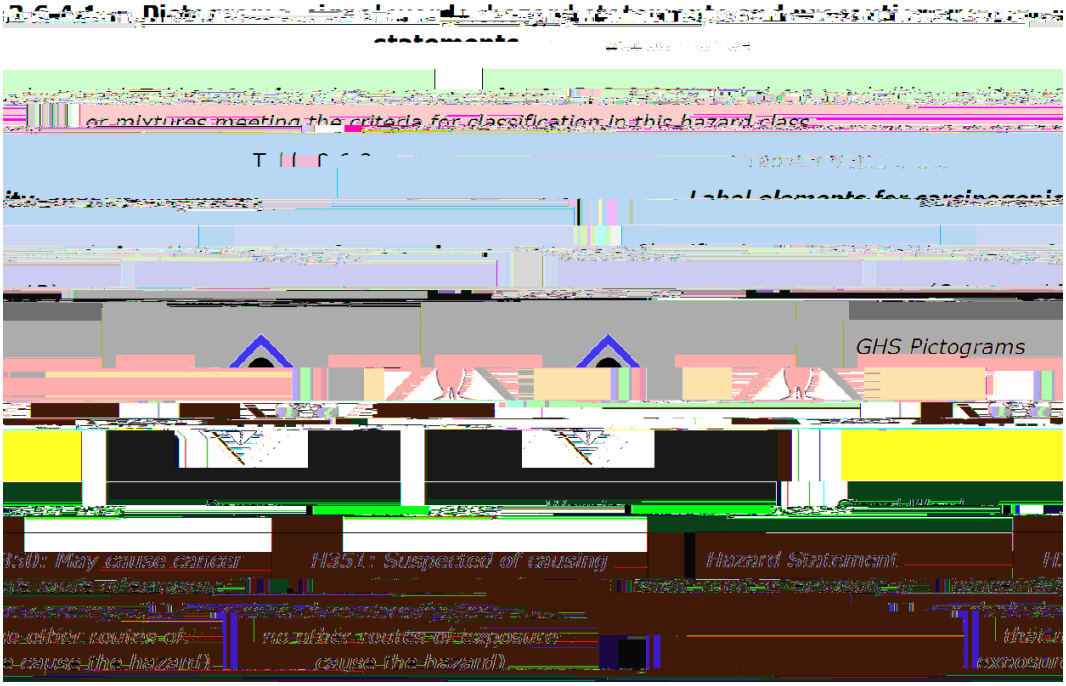
Women of child-bearing age are often considered a group of particular concern in relation to chemical reproductive hazards requiring special provisions. However it is clear from the information above that the possibility of adverse pre-conception effects exists at any time in either sex, and not just during pregnancy. More importantly there may be adverse effects before pregnancy is recognised, or during breast feeding after the pregnancy. Of particular relevance here is that a woman is born with all the eggs needed for her child-bearing lifetime. Moreover, fertility treatment has extended the age range of women potentially at risk and introduced possible donors who may have been previously exposed to chemicals. It is thus important that, as far as practicable, adequate protection be afforded to all persons at risk at work. This must be a standard feature of all COSHH hazard assessments, as set out in the HSE publication “COSHH Assessments; a step0.353 RG[a)4(s fa)-2(r a)6

either a weight of evidence approach using existing information, or the conduct of experimental studies (reproductive toxicity screen, and developmental/reproductive toxicity at higher tonnages). It is to be hoped that advances in knowledge will lead to a better understanding of which chemicals may affect reproduction, and of the relevant dose-response relationships, and hence to a consequent improvement in risk assessment and control.

The main way that chemicals can be identified as being a possible risk to reproduction in the workplace is via their classification and labelling. This is based on the GHS system which is implement in the UK and EU as the CLP Regulations, currently based on the EU Guidance. The three main classifications which indicate a need to manage the risk from possible exposure, are those for Germ cell mutagens, Carcinogens and specifically for Toxicity to reproduction.

Casarett and Doull's Essentials of Toxicology 2010 2nd ed. Klaassen C D, Watkins J. McGraw-Hill Publishing Co.

Carcinogens are another class of substances which may possibly pose a risk to reproduction, in particular those which are considered to be genotoxic carcinogens. These have the potential in addition to causing cancer in the parent to also adversely affect a foetus.



The category of substances which are of specific concern for their risk to reproduction are those specifically classified as Toxic to Reproduction, this includes both adverse effects on fertility in either males or females but also adverse effect on the foetus during pregnancy or during lactation.