1 Introduction

Obviously, when working with chemicals you will always take care to neither risk your own safety and health, nor those of others. This applies especially to working with substances that are carcinogenic, mutagenic, or reprotoxic. We call these substances CMR substances. In case of mutagenic or reprotoxic substances or agents, the effects may stretch to the health of future offspring and/or fertility. Please see Chapter 4 for a clarification of these concepts.

The information herein applies to all employees. To some vulnerable groups of employees additional rules apply in working with these substances. For example, pregnant women are not allowed to work with genotoxic (mutagenic and reprotoxic) substances, and with carcinogenic (non-genotoxic) substances only if there is a known safe exposure limit, which is patently not crossed. During breastfeeding the risk arises that exposed mothers (unwittingly) pass on hazardous substances to the child through the mother’s milk. Please note: mutagenic and reprotoxic effects may also occur in male reproductive cells! Please read the information on the intention to have children and pregnancy (in Dutch) on the website for specific guidelines and regulations.

2 Inventory of carcinogenic, mutagenic, or reprotoxic substances

2.1 General information regarding the inventory

The Dutch Ministry of Social Affairs and Employment publishes a list with the currently registered carcinogenic and mutagenic substances and processes, and those that are toxic to the reproduction, as well as those that are suspected to be (in Dutch, but with CAS numbers). These lists are regularly updated and announced in the Dutch Government newspaper “Staatscourant”. However, these do not contain all substances with risks; they are not limiting. That is why it is important to check the properties of the substances one works with using the labels and MSDSs, and, if possible, make an assessment of the risk-inducing properties of one’s own preparations.

Do you need more information? Please contact the AMD: amd@science.leidenuniv.nl
Please pay attention to the following R sentences (on old labels) or H sentences (Health), and symbols on labels or MSDSs, or to the hazards information in Chemicals registration (Gros):

<table>
<thead>
<tr>
<th>Code</th>
<th>Risk</th>
<th>Effect</th>
<th>Symbol</th>
</tr>
</thead>
<tbody>
<tr>
<td>R40 or R68</td>
<td>Irreversible effects cannot be ruled out</td>
<td>Mutagenic/carcinogenic</td>
<td>Not recognizable by a separate symbol in the old system!</td>
</tr>
<tr>
<td>R45</td>
<td>May cause cancer</td>
<td>Carcinogenic</td>
<td></td>
</tr>
<tr>
<td>R46</td>
<td>May cause hereditary genetic damage</td>
<td>Mutagenic</td>
<td></td>
</tr>
<tr>
<td>R49</td>
<td>May cause cancer by inhalation</td>
<td>Carcinogenic</td>
<td></td>
</tr>
<tr>
<td>R60</td>
<td>May harm the fertility</td>
<td>Reprotoxic</td>
<td></td>
</tr>
<tr>
<td>R61</td>
<td>May harm the unborn child</td>
<td>Reprotoxic</td>
<td></td>
</tr>
<tr>
<td>R62</td>
<td>Possible hazard of reduced fertility</td>
<td>Reprotoxic</td>
<td></td>
</tr>
<tr>
<td>R63</td>
<td>Possible hazard of harm to the unborn child</td>
<td>Reprotoxic</td>
<td></td>
</tr>
<tr>
<td>R64</td>
<td>May be harmful through breast feeding</td>
<td></td>
<td></td>
</tr>
<tr>
<td>H340</td>
<td>May cause genetic damage &lt;possibly with exposure route&gt;</td>
<td>Mutagenicity in reproductive cells</td>
<td></td>
</tr>
<tr>
<td>H341</td>
<td>Suspected of causing genetic damage &lt;possibly with exposure route&gt;</td>
<td>Mutagenicity in reproductive cells</td>
<td></td>
</tr>
<tr>
<td>H350</td>
<td>May cause cancer &lt;possibly with exposure route&gt;</td>
<td>Carcinogenic</td>
<td></td>
</tr>
<tr>
<td>H351</td>
<td>Suspected of causing cancer &lt;possibly with exposure route&gt;</td>
<td>Carcinogenic</td>
<td></td>
</tr>
<tr>
<td>H360</td>
<td>May harm the fertility or the unborn child &lt;mention specific effect if known &gt; &lt;possibly with exposure route&gt;</td>
<td>Reprotoxic</td>
<td></td>
</tr>
<tr>
<td>H361</td>
<td>May possibly harm the fertility or the unborn child &lt;mention specific effect if known &gt; &lt;possibly with exposure route&gt;</td>
<td>Reprotoxic</td>
<td></td>
</tr>
<tr>
<td>H362</td>
<td>May be harmful through breast feeding</td>
<td>Toxic to reproduction, supplementary category, effects on and through lactation</td>
<td>No symbol</td>
</tr>
</tbody>
</table>

*Sentences in italics: substance is suspected of having said effect (insufficient evidence in man and animal, but strong indications of).*

The CMR substances used should be known per department by keeping a list of these substances. This is often a challenge in a research environment in which everyone orders his/her own chemicals. We, therefore, ask everyone who works with chemicals, to please check if he or she works with CMR substances. If such is the case, then please inform your superior and colleagues.
2.2 Specific CMR sources to check for

2.2.1 Laboratory chemicals and dyes
The CMR lists do not only contain exotic chemicals, but also a number of standard organic solvents and certain reagents, such as acrylamide, acetonitrile, ethanol, methanol, phenolphthalein, formaldehyde, and propylene oxide.

The (azo) dyes that are used in biological research (e.g. histology), for example, colouring coupes, and dyes for dye lasers are almost all (suspected) CMR substances. Their use in combination with solvents makes penetration through the skin even easier. Therefore, please check for the proper kind of gloves (see “Chemiekaart” or MSDS) and always work in a fumehood when handling (weighing, dissolving, etc.) dyes.

When working with silica you should always be aware of the presence or formation of quartz. Please weigh silica in the fumehood, use a P2 respirator, and immediately remove dusted silica with a wet absorbent.

2.2.2 Asbestos in buildings and equipment
Buildings dating from before 1980 are very likely to contain asbestos in their construction, especially in the technical rooms, shafts, etc., as insulation and fire protection material. As long as asbestos materials remain intact, there is no health hazard. Only in cases of (re)processing or damage inhalable fibres may be released. Please note, asbestos belongs to the category of non-genotoxic carcinogens, for which a safe exposure limit exists.

Because asbestos may be present, certain technical actions, such as work above the modular ceilings, may not be performed at will. Air samples are taken on a regular basis in the Faculty of Science’s (W&N’s) buildings to check for the presence of asbestos fibres. In cases of alterations and renovations the presence of asbestos will be checked for. If asbestos is found, a prior sanitation will take place by a specialized firm. This firm will build a “tent” around the object to be sanitized, so no asbestos fibres will be released into the environment.

In some old laboratory equipment, such as old drying stoves and ovens, asbestos may be present as insulation or sealant. These equipment are, if all is well, provided with the warning sticker shown to the right: “voorzichtig bevat asbest” (“careful, contains asbestos”). If the sticker is missing, and you suspect the presence of asbestos, or if there are deficiencies in this type of equipment, please always warn the AMD (as well). A special protocol has to be followed in the dismantling or disposal of asbestos containing equipment.

Do you need more information? Please contact the AMD: amd@science.leidenuniv.nl
2.2.3 Ionizing radiation
The effects due to ionizing radiation are specific. In cases of uncontrolled exposure carcinogenic, mutagenic, and/or reprotoxic effects may occur. That is why employees who are about to start working with (equipment involving) ionizing radiation (x-rays and radioactivity), have to follow a special, external training. After successfully completing the accompanying exam, they are able to assess the risks and are authorized to work safely with ionizing radiation. More information may be found on the AMD website under the heading: "Working safely with ionizing radiation".

3 Dealing with CMR substances in the workplace

The following applies in general:
- Make sure you know what you are working with or may be released: are there safe exposure limits, what are the preventive measures and what (not!) to do when in the unforeseen event something goes wrong? Are your colleagues aware of the hazards of the substances you work with or your activities?

In het laboratory:
- In working with CMR substances there is a legal obligation to first look for an alternative method or substance. Working with CMR substances should be avoided as much as possible.
- When the application of alternatives for the research is demonstrably impossible, all actions (weighing, pouring, reactions, refining/reprocessing, etc.) with these substances take place in a properly functioning fumehood using the correct gloves (see product MSDS), lab coat, and safety spectacles, and all colleagues are informed about the hazards of these operations.
- The operations are performed in a closed system as much as possible. This also means that the packages are opened for as short a time period as possible.
- Work with CMR substances should always take place in a fumehood. Please check for proper functioning beforehand. See AMD information sheet RhL023 The fumehood.
- Preferably a fumehood in a small laboratory, for example, a night laboratory, is used to limit the number of people exposed in case of calamities as much as possible.

Other (technical) operations:
- Please check if carcinogenic/mutagenic/reprotoxic substances may be present or be released in the course of the operations (for example, demolishing or drilling in technical rooms, processing hardwood or metal compositions).
Prior to processing materials with the above properties (check the SZW list), in which dusting or atomization, and such occurs, or may occur, a risk assessment should be performed. See AMD Information sheet RhL010 Research risk assessment. After the assessment it will be determined if the operations can be performed in a safe manner, and, if so, under what conditions.

The removal of asbestos must be performed by specialized firms.

4. Explanation of the terms used

Substances or physical phenomena are considered to be carcinogenic agents when these (may) cause cancer. These may have a genotoxic or mutagenic, or a non-genotoxic effect mechanism.

Mutagenic or genotoxic agents may (slowly) alter (or mutate) the DNA in the cell nucleus in such a manner that they cause cancer or a defect in the reproductive cells (resulting in miscarriage or defects in the unborn child). Exposure to small amounts of such substances may, in principle, already cause mutations. Therefore, there are no safe lower exposure limits for these substances.

Non-genotoxic carcinogens may, by exposure above a certain lower limit, cause cancer by way of a cell damaging effect. Examples of such substances are asbestos, quartz, and cadmium, but also the dust that is released in the processing of several types of hardwood.

Reprotoxic substances are substances that may present hazards to the reproduction. These may have detrimental effects on the fertility of men as well as women, and on the reproduction.
The effects may be divided in:
- effects on the hormone balance (and, thus, the reproductive organs)
- diminished fertility (effects on sperm and/or female ova cells, and/or the conception);
- developmental defects in the unborn child in the womb (teratogenic substances);
- effects on the child by way of mother’s milk ingestion.
An example of a standard reprotoxic substance is alcohol (ethanol).

Teratogenic agents are substances and biological agents that have the property of causing congenital defects when the woman is exposed to them during pregnancy. A well-known pathogenic organism with this property is the rubella virus. Another example is thalidomide (trademark: Softenon), a sleep-inducing drug from the fifties that, when used during pregnancy, resulted in babies with underdeveloped or even missing limbs.