

# Carcinogens in the workroom air in the rubber industry

by Bertold Spiegelhalder, PhD<sup>1</sup>

SPIEGELHALDER B. Carcinogens in the workroom air in the rubber industry. *Scand j work environ health* 9 (1983): suppl 2, 15-25. Only a few data are available on the occurrence of carcinogenic compounds in the air at workplaces in the rubber industry, with the exception of data on total particulates and solvents. The available information allows the indication of some specific workplaces with elevated exposure levels. Recent investigations of nitrosamines in the rubber industry indicate the widespread occurrence of considerable levels of nitrosodimethylamine and nitrosomorpholine. In an effort to elucidate the origin and formation of nitrosamines in this industry, chemicals as well as the air in various areas were analyzed. All chemicals used for rubber compounding contain nitrosamines if they are derivatives of secondary amines, eg, tetramethylthiuram, zinc diethyldithiocarbamate or N-oxydiethylene benzothiazolylsulfenamide. Accordingly, variable concentrations of airborne nitrosamines could be detected at places where rubber products are manufactured or stored. The nitrosamines found correspond to the compounded chemicals. The original nitrosamine level in rubber chemicals is not high enough to explain the amounts found in rubber products and in air. Therefore additional nitrosation had to be considered. The responsible nitrosating agents are described. Preliminary results show that, in most cases, either by elimination of the nitrosating agent or by the exchange of rubber chemicals nitrosamine levels in the work area can be drastically reduced.

**Key terms:** air monitoring, by-products, carcinogenicity, nitrosamines, rubber chemicals, toxicology, workplace exposure, workplace monitoring.

A great number of epidemiologic studies deal with the excess cancer risk of workers in the rubber industry. In a monograph (10), published recently by the International Agency for Research on Cancer (IARC), on the evaluation of the carcinogenic risk in the rubber industry about 33 epidemiologic studies, including case reports and cohort and case-referent studies, were considered. Most of them were based on data from the United States and Great Britain, but also Swiss and Finnish data were used. Although it is accepted that increased cancer rates are evident for rubber workers, little progress could be made to establish with reason-

able certainty a direct causal link between usage of (or exposure to) certain chemicals and the excess of distinct cancer types.

Only for 2-naphthylamine and solvents (benzene) has an association been found between exposure to these chemicals and an increased risk of bladder cancer and lymphatic leukemia, respectively. Other increased cancer rates (stomach and lung cancer) could only be related to specific job descriptions rather than to specific chemicals. Other types of cancer could not be associated to either specific jobs or chemicals. The reason for this lack is the fact that most epidemiologic studies have not been exposure-specific (historical industrial hygiene data are not available) or have used job descriptions as a substitute for exposure categories. The difficulty is to estimate individual exposure that occurred several decades ago in relation to currently occurring cancer. A further difficulty is the enormous number of dif-

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**Table 1.** Occurrence of carcinogenic compounds in the rubber industry (summary of individual publications not mentioned in the text).

| Material                                          | Year      | Reference                                                              |
|---------------------------------------------------|-----------|------------------------------------------------------------------------|
| Carbon black                                      | 1972–1977 | Occupational Safety and Health Administration (18)                     |
| Carbon black                                      | 1961      | National Institute for Occupational Safety and Health (13, 14, 15, 16) |
| Ethylene thiourea                                 | 1977–1980 | National Institute for Occupational Safety and Health (13, 15, 16)     |
| Ethylene thiourea                                 | 1982      | Enwald (3)                                                             |
| Benzo(a)pyrene (polycyclic aromatic hydrocarbons) | 1978      | Otto & Schmidt (19)                                                    |
| Benzo(a)pyrene                                    | 1976      | Nutt (17)                                                              |
| Benzo(a)pyrene (oil mist)                         | 1982      | Enwald (3)                                                             |
| Styrene                                           | 1976      | Fraser & Rappaport (6)                                                 |

ferent chemicals used in the rubber industry. Only for a small number of chemicals are some exposure data available. The need for systematic monitoring of the industrial environment has been recognized only in recent years. The limited number of surveys available until now should therefore be considered only as a starting signal rather than as a valuable data base for evaluations.

### Carcinogens found in the workroom air

As was previously mentioned, the currently available data on the exposure levels of carcinogens in the rubber industry are limited to a small number of compounds (table 1). Primarily these are benzene, styrene, ethylenethiourea, benzo(a)pyrene, 4,4'-methylene bis (2-chloroaniline), and N-nitrosamines. Available data on total particulate are also of interest due to its possible content of benzo(a)pyrene.

Valuable reviews on the levels of exposure to particulates and solvents in the rubber industry of the United States were published by William et al (26) and Van Ert et al (25). Results of sampling studies in 14 tire and tube manufacturing plants were reported by plant and by occupational title groups within plants, and about 1,000 determinations of various solvent vapor components in air samples were made in 10 tire manufacturing plants. In a further study in 10 tire factories in the United Kingdom (21) samples were taken

in which total particulates, cyclohexane-soluble particulates, and benzo(a)pyrene concentrations were estimated at various sites. In a follow-up study on benzene exposure (20) in the rubber-coating industry air analysis data were compared with the biological monitoring and health status of 38 workers exposed for 1 to 24 years to benzene. In a number of smaller surveys the occurrence of other compounds was investigated.

The occurrence of airborne nitrosamines in the rubber and tire industry was recently discovered by Fajen et al (4) in the United States. They reported the occurrence of nitrosodimethylamine and nitrosomorpholine in three out of four surveyed factories. Another American study (11) reported the results of four separate surveys of a single tire plant. Analyses for nitrosodiphenylamine and for volatile nitrosamines were carried out. No nitrosodiphenylamine could be detected, but nitrosodimethylamine, nitrosopyrrolidine, and nitrosomorpholine were found. In our own studies (24) from 1979 to 1982 a total of 24 separate surveys was carried out in 17 factories of 14 different companies in the Federal Republic of Germany.

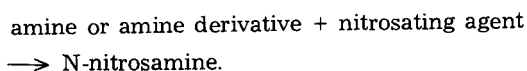
With a few exceptions none of these studies on airborne exposures to carcinogenic material include follow-up measurements. From these data therefore only limited information can be obtained on the exposure of individual workers with respect to certain chemicals. This

situation explains why it was not possible until now to show the contribution that any one of the many chemicals used in the rubber industry may make to the cancer experience of workers in specific job categories, with the exceptions already discussed. Some of the reasons for this difficulty to assess individual risks by exposure measurements are: (i) there is a multiplicity of exposures arising from the variety of chemicals used at given workplaces and cross contamination between jobs, (ii) there is movement between jobs exhibiting different exposure situations, (iii) currently observed cancer excesses almost certainly result from exposures that occurred many years ago, a period for which no exposure data are available, and (iv) not only rubber chemicals have to be considered but also by-products produced during the manufacturing process, as for example N-nitrosamines.

For future evaluations I think that it is necessary to establish representative data bases on individual exposure levels in combination with prospective epidemiologic studies. Under these conditions it might be possible to identify carcinogenic agents that could account for the observed excess cancer rates in the rubber industry. For the support of retrospective studies, an understanding of all factors which contribute to and influence the occurrence of chemicals in the workroom air is necessary. As an example of both the investigation of conditions which lead to the formation of chemicals at the workplace and the establishing of data bases on the occurrence of these compounds in the workroom air, including follow-up, I would like to present the results of our own studies, which I have already mentioned.

### Chemistry of nitrosamine formation in the rubber industry

The formation of N-nitrosamines from precursors (eg, 9) can be described as the following reaction:



In addition to the familiar nitrosation of secondary amines, reactions involving

tertiary amines or amine derivatives such as dialkyl dithiocarbamates, dialkyl thiuram sulfides and sulfenamides are possible in the rubber industry, where these types of chemicals are used as vulcanization accelerators and stabilizers (fig 1).

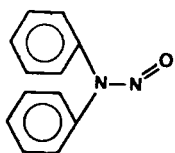
Nitrosation can occur in aqueous and in solid systems, as well as in the gas phase. Nitrosatable compounds dissolved or dispersed in a latex solution may be nitrosated during the production of latex articles. Nitrogen oxides from the air probably act as nitrosating agents.

Chemicals that contain nitro or nitroso groups are potential nitrosating agents. As some of these chemicals may decompose thermally during processing to form nitrogen oxides, direct nitrosation of nitrosatable compounds contained in solid rubber is possible. Fig 2 shows potential nitrogen oxide-releasing chemicals used in the rubber industry. From these compounds N-nitrosodiphenylamine is of major interest since it is (or was) used in many tire factories. Laboratory tests (23), and also measurements in industry (11), clearly show that this chemical is a primary source of nitrosating activities. Replacement of N-nitrosodiphenylamine by other retarders results in a decreased level of detectable nitrosamines in rubber factories (5, 11, 24).

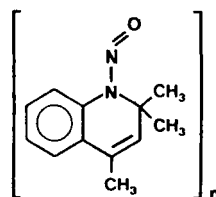
In Western Europe, and to a less extent in the United States, some rubber products are cured in a bath consisting of a mixture of molten nitrate and nitrite salts (salt-bath curing). In continuous vulcanization the extruded rubber material is transferred continuously through the molten heat-transfer salt. Nitrosatable chemicals present at the surface of solid rubber can react directly with nitrite or nitrogen oxides to form nitrosamines.

Ubiquitously occurring nitrosating agents are nitrogen oxides in the air. Their natural level is about 30–70 ppb, caused by oxidation of nitrogen under sunlight or other ultraviolet sources. Combustion processes, such as open flames, industrial pollution, and exhausts from gas and diesel-powered forklift trucks and other transport vehicles, increase the nitrogen oxide levels. Especially propane-powered trucks and cars, which emit low levels of carbon monoxide, for indoor use contri-

## RETARDERS

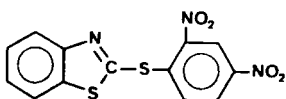


*N*-nitrosodiphenylamine

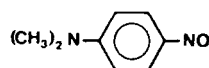


poly-*N*-nitroso-2,2,4-trimethyl-1,2-dihydroquinoline

## ACCELERATORS

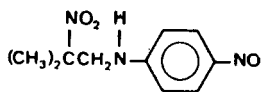


2-(2,4-dinitrophenylthio)-benzothiazole



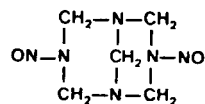
*N,N*-dimethyl-*para*-nitrosoaniline

## PROMOTOR



*N*-(2-methyl-2-nitropropyl)-4-nitrosoaniline

## BLOWING AGENT

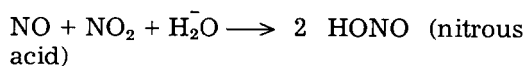


dinitrosopenta-methylenetetramine

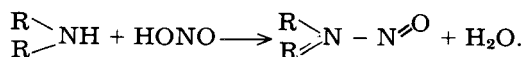
Fig 1. Groups of chemicals convertible to *N*-nitrosamines.

bute to nitrogen oxides in air by their high nitrogen oxide emissions. An increase of up to 5,000 ppb can be observed near gas-powered forklift trucks.

The atmospheric chemistry of nitrosamines has been studied in model experiments only by Hanst et al (8), Gehler & Rolle (7), Pitts et al (22), and Crosby et al (2). The formation of nitrosamines in the gas phase can be explained by a reaction of nitrogen oxides with amines in the presence of water according to the following reactions:



and



These reactions can occur at the surface of particulates. Secondary amines react rapidly in the dark, whereas tertiary amines react also in sunlight to form nitrosamines. The limiting factor of nitrosamine formation under real conditions seems to be the amount of nitrous acid in the air. In dry air nitric oxide and nitrogen dioxide do not react with amines at a rate that could be appreciable in the atmosphere.

Nitrosamines are not only formed during the manufacture of rubber but may also be present in rubber chemicals as contaminants (table 2). The origin of these nitrosamines is probably nitrosation by ambient nitrogen oxides during production or storage. Knowing the chemical composition of a rubber formulation, one can predict the nature of the nitrosamines which might be formed. It should also be

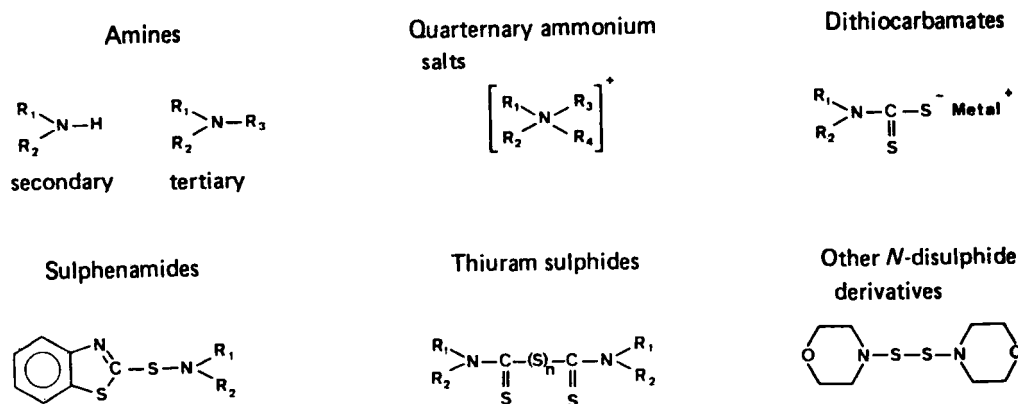


Fig. 2. Nitro and nitroso compounds that can act as precursors of nitrogen oxides in the rubber industry.

Table 2. Examples of nitrosamine contamination in commercial samples of rubber chemicals.

| Accelerator                                       | Nitrosamine present    | Concentration (µg/kg) |
|---------------------------------------------------|------------------------|-----------------------|
| N-pentamethylene dithiocarbamate, piperidine salt | N-nitrosopiperidine    | 200                   |
| Tetramethylthiuram disulfide                      | N-nitrosodimethylamine | 4-800                 |
| Tetraethylthiuram disulfide                       | N-nitrosodiethylamine  | 25-80                 |
| Zinc pentamethylene dithiocarbamate               | N-nitrosopiperidine    | 60-450                |
| Zinc dibutyldithiocarbamate                       | N-nitrosodibutylamine  | 65-2,500              |
| Zinc diethyldithiocarbamate                       | N-nitrosodiethylamine  | 10-100                |
| Morpholine derivatives                            | N-nitrosomorpholine    | 60-3,500              |

possible to use nitrosamine measurements for the identification of rubber compositions and for the clarification of the nature of accelerators.

### Nitrosamine exposure in the workplace

From 1979 to 1982 a total of 24 separate surveys was carried out in 17 factories of 14 different companies in the Federal Republic of Germany. In all factories volatile N-nitrosamines could be detected. In the tire industry nitrosodimethylamine and nitrosomorpholine could be found in all cases. In technical rubber product factories nitrosodimethylamine, nitrosodiethylamine, nitrosodibutylamine, nitrosopiperidine, and nitrosomorpholine could be found. All the results were from work area samples or from personal monitoring (breathing zone samples). An

overview of all the results is given in table 3.

### Tire industry

In contrast to the results from Fajen et al (4) and McGlothlin et al (11), in our investigation, the levels of nitrosodimethylamine and nitrosomorpholine in the hot processes of the tire industry were not unusually high. The nitrosodimethylamine concentration was between nondetectable ( $< 0.01 \mu\text{g}/\text{m}^3$ ) and  $2 \mu\text{g}/\text{m}^3$ . Nitrosomorpholine was found in concentrations from 0.1 to  $17 \mu\text{g}/\text{m}^3$ . Only in one factory were consistently low results found for both nitrosodimethylamine and nitrosomorpholine (no value  $> 0.7 \mu\text{g}/\text{m}^3$ ). In contrast to the other factories neither nitrosodiphenylamine nor nitrogen oxide emitting transportation systems had been

**Table 3.** Overview of the exposure situation for N-nitrosamines in the rubber industry.

| Job description                         | Concentration in the air<br>( $\mu\text{g}/\text{m}^3$ ) |       | Remarks on sampling, industry or process                                                                                        |
|-----------------------------------------|----------------------------------------------------------|-------|---------------------------------------------------------------------------------------------------------------------------------|
| Raw material handling, weighing, mixing |                                                          |       |                                                                                                                                 |
| Nitrosodimethylamine                    | 0.2–                                                     | 0.9   | Tire                                                                                                                            |
| Nitrosomorpholine                       | 0.1–                                                     | 2     | Tire                                                                                                                            |
| Milling, extruding, calendaring         |                                                          |       |                                                                                                                                 |
| Nitrosodimethylamine                    | 0.1–                                                     | 2     | Tire and industry products                                                                                                      |
| Nitrosomorpholine                       | 0.1–                                                     | 9     | Tire and industry products                                                                                                      |
| Assembly and building                   |                                                          |       |                                                                                                                                 |
| Nitrosodimethylamine                    | 0.1–                                                     | 1     | Tire and industry (personal sampling)                                                                                           |
| Nitrosomorpholine                       | 0.5–                                                     | 3     | Tire and industry (personal sampling)                                                                                           |
| Curing or vulcanizing                   |                                                          |       |                                                                                                                                 |
| Nitrosodimethylamine                    | 0.1–                                                     | 2     | Tire (personal sampling)                                                                                                        |
| Nitrosodimethylamine                    | 15–                                                      | 130   | Tube (nitrosodiphenylamine used)                                                                                                |
| Nitrosodimethylamine                    | 1–                                                       | 4.5   | Tube (nitrosodiphenylamine not used, personal sampling)                                                                         |
| Nitrosomorpholine                       | 0.1–                                                     | 17    | Tire (personal sampling)                                                                                                        |
| Nitrosodimethylamine                    | 1–                                                       | 40    | Salt-bath curing (personal sampling)                                                                                            |
| Nitrosodiethylamine                     | 0.1–                                                     | 5     | Salt-bath curing (personal sampling)                                                                                            |
| Nitrosomorpholine                       | 0.1–                                                     | 3     | Salt-bath curing (personal sampling)                                                                                            |
| Nitrosodimethylamine                    | 40–                                                      | 90    | Injection molding, tetramethylthiuram disulfide, dithiomorpholine together with nitrosodiphenylamine in use (personal sampling) |
| Nitrosomorpholine                       | 120–                                                     | 380   | Injection molding, tetramethylthiuram disulfide, dithiomorpholine together with nitrosodiphenylamine in use (personal sampling) |
| Nitrosodimethylamine                    | 500–                                                     | 1,060 | Injection molding (stationary sampling <sup>a</sup> )                                                                           |
| Nitrosomorpholine                       | 200–                                                     | 4,700 |                                                                                                                                 |
| Nitrosodimethylamine                    | 1                                                        |       | Water hose production                                                                                                           |
| Nitrosodiethylamine                     | 5                                                        |       | Water hose production                                                                                                           |
| Nitrosopiperidine                       | 0.3                                                      |       | Water hose production                                                                                                           |
| Nitrosomorpholine                       | 0.1                                                      |       | Water hose production                                                                                                           |
| Nitrosodimethylamine                    | 1–                                                       | 3.5   | Window seals                                                                                                                    |
| Nitrosomorpholine                       | 3–                                                       | 9     | Window seals                                                                                                                    |
| Nitrosodimethylamine                    | 0.2–                                                     | 3.5   | Injection molding, sole production                                                                                              |
| Nitrosodimethylamine                    | 1                                                        |       | Latex goods production                                                                                                          |
| Nitrosodiethylamine                     | 3                                                        |       | Latex goods production                                                                                                          |
| Inspection and finishing                |                                                          |       |                                                                                                                                 |
| Nitrosodimethylamine                    | 0.1–                                                     | 1.5   | Tire (personal sampling)                                                                                                        |
| Nitrosomorpholine                       | 0.1–                                                     | 20    | Tire (personal sampling)                                                                                                        |
| Nitrosodimethylamine                    | 1–10                                                     |       | Tube (personal sampling)                                                                                                        |
| Storage and dispatch                    |                                                          |       |                                                                                                                                 |
| Nitrosodimethylamine                    | 0.2–                                                     | 10    | Tire (personal sampling)                                                                                                        |
| Nitrosodimethylamine                    | 1–                                                       | 19    | Tube (personal sampling)                                                                                                        |
| Nitrosomorpholine                       | 0.3–                                                     | 17    | Tire (personal sampling)                                                                                                        |
| Nitrosodimethylamine                    | 0.2–                                                     | 1     | Industrial rubber                                                                                                               |

<sup>a</sup> No estimation of workers' exposure is possible from these values.

used in this factory during the last 10 years. Higher levels can be explained either by the use of nitrosodiphenylamine with nitrosodimethylamine levels of up to  $2 \mu\text{g}/\text{m}^3$  and nitrosomorpholine levels of up to  $17 \mu\text{g}/\text{m}^3$  or by high nitrogen oxide levels (up to 5,000 ppb could be measured) in the air from gas or diesel-powered forklift trucks.

A comparison of airborne nitrosamine levels in 10 different tire manufacturing plants is given in table 4. Plant 1 was investigated in four different visits over a period of two years.

### Tube production

Measurements in tire factories in which also tubes are produced showed some extraordinarily high results (table 5). The highest value in a tube curing room (nitrosodimethylamine,  $130 \mu\text{g}/\text{m}^3$ ) was caused by the simultaneous use of nitrosodiphenylamine and tetramethylthiuram disulfide. But reformulation of the chemicals used for compounding showed a significant decrease in the nitrosodimethylamine levels to  $1\text{--}5 \mu\text{g}/\text{m}^3$ . The

**Table 4.** Nitrosodimethylamine and nitrosomorpholine concentrations ( $\mu\text{g}/\text{m}^3$ ) in the air during tire and tube production. Parameters given under personal monitoring describe the investigator's exposure during visit. (· = measurements were not carried out or impossible, trace =  $\sim 0.05 \mu\text{g}/\text{m}^3$ )

|                             | Mixer room | Extruding & calendaring | Tire building | Tire curing | Final inspection | Tire storage | Tube curing & inspection | Tube storage | Personal monitoring during visit (average of 6 h) |
|-----------------------------|------------|-------------------------|---------------|-------------|------------------|--------------|--------------------------|--------------|---------------------------------------------------|
| <i>Nitrosodimethylamine</i> |            |                         |               |             |                  |              |                          |              |                                                   |
| Plant 1                     | —          | 2                       | ·             | 0.5–2       | ·                | 3.5–7        | ·                        | ·            | 0.1                                               |
| 1st visita                  | ·          | ·                       | ·             | 0.3–1       | 0.1–1            | 0.4–4        | 50–130                   | 6–19         | 3.5                                               |
| 2nd visita                  | ·          | ·                       | ·             | 0.1–1       | 0.5              | 0.2–1        | 1                        | 1–2.5        | 0.5                                               |
| 3rd visitb                  | 0.3–0.9    | ·                       | ·             | 0.6         | ·                | 1            | 1–2                      | 3            | 1.5                                               |
| 4th visitb                  | ·          | ·                       | ·             | 0.5         | 0.6–1            | 0.5          | ·                        | ·            | 0.4                                               |
| Branch of plant 1b          | 0.3        | 0.4                     | 0.2           | 0.3         | 0.2              | 0.2–0.5      | ·                        | ·            | 0.5                                               |
| Plant 2b, c                 | 0.2        | 0.1–0.9                 | 0.3           | 0.1–0.4     | 0.2              | 0.2          | ·                        | ·            | 0.3                                               |
| Plant 3d                    | 0.7        | 0.1–0.7                 | ·             | 0.1–1.5     | 0.3–1.5          | 1.5          | 15–40e                   | 3            | 1.6                                               |
| Plant 4a                    | 0.2        | 0.1–0.4                 | ·             | 0.1–0.3     | 0.1–0.8          | 5–10         | 1–4.5                    | 17           | 2                                                 |
| Plant 5d                    | 0.1–0.7    | ·                       | ·             | 1–2         | 1                | 0.5          | 2–18f                    | 4            | 0.6                                               |
| Plant 6d                    | 0.5        | ·                       | 0.4–1         | 0.2         | 0.2              | 0.5          | 0.1                      | ·            | < 0.1                                             |
| Plant 7d                    | 0.4        | 0.5                     | 0.2           | 0.2–0.4     | Trace            | 0.1–1.1      | ·                        | ·            | 0.1                                               |
| Plant 8d, g                 | 0.3        | 1                       | 0.2           | 0.3         | 0.1–0.3          | Trace        | ·                        | ·            | 0.1                                               |
| Plant 9d, g                 | ·          | ·                       | 1.6           | ·           | ·                | ·            | ·                        | ·            | ·                                                 |
| <i>Nitrosomorpholine</i>    |            |                         |               |             |                  |              |                          |              |                                                   |
| Plant 1                     | ·          | 0.7                     | 0.5           | 0.3–2       | ·                | 5–9          | ·                        | ·            | 0.5                                               |
| 1st visita                  | 0.1        | ·                       | ·             | 0.1–3       | 0.7–1            | 4–14         | 0.5                      | 4–10         | 1.2                                               |
| 2nd visita                  | ·          | ·                       | ·             | ≤ 1         | ·                | 0.2–3        | ·                        | 2–4.5        | 0.2                                               |
| 3rd visitb                  | ·          | ·                       | ·             | 0.8         | ·                | 2.5          | ·                        | 4            | 1                                                 |
| 4th visitb                  | ·          | ·                       | ·             | ·           | ·                | ·            | ·                        | ·            | ·                                                 |
| Branch of plant 1b, c       | 0.4–1      | 2–2.5                   | 0.5–2         | 0.3–2       | 16–21            | 10–17        | ·                        | ·            | 2.5                                               |
| Plant 2b, c                 | 0.7–2      | 2–9                     | 3             | 4–5         | 4                | 0.7–6        | ·                        | ·            | 2.5                                               |
| Plant 3d                    | ·          | ·                       | ·             | < 0.1       | ≤ 0.1            | ·            | ·                        | ·            | 0.1                                               |
| Plant 4a                    | 0.2        | 0.7–5                   | ·             | 1–17        | 1–7              | 7–11         | ·                        | 2.5          | 2                                                 |
| Plant 5d                    | < 0.1      | ·                       | ·             | < 0.1       | < 0.1            | 1            | < 0.1                    | ·            | < 0.1                                             |
| Plant 6d                    | 0.1        | ·                       | 1             | 1–2         | 2                | 0.6–1        | 3                        | ·            | 0.5                                               |
| Plant 7d                    | 0.6        | 0.8                     | 2.5           | 1.5         | 1.5–4            | 3            | ·                        | ·            | 0.6                                               |
| Plant 8d, g                 | 0.2        | Trace                   | Trace         | 0.1–0.5     | Trace            | Trace        | ·                        | ·            | Trace                                             |
| Plant 9d, g                 | ·          | Trace                   | 1.9           | 0.2         | 0.3              | 0.2          | ·                        | ·            | Trace                                             |

a Nitrosodiphenylamine in use.

b Nitrosodiphenylamine no longer used.

c Nitrogen oxide emissions from gas-powered forklift trucks.

d Nitrogen oxide emissions from diesel- and gas-powered forklift trucks.

e Nitrosodiphenylamine together with tetramethylthiuram disulfide in same rubber stock.

f Salt-bath curing of tubes.

g Remold and retreat shops.

**Table 5.** Change in airborne nitrosamine levels ( $\mu\text{g}/\text{m}^3$ ) after introduction of a new retarder in one factory at three different times.

| Area             | First introduction<br>(Nitrosodiphenylamine in use) | Second introduction<br>(Cyclohexylthio-<br>phthalimide in use) | Third introduction |
|------------------|-----------------------------------------------------|----------------------------------------------------------------|--------------------|
| Tube curing area | 50–130 <sup>a</sup>                                 | 1 <sup>a</sup>                                                 | 1–2 <sup>a</sup>   |
| Tube warehouse   | 6–20 <sup>a</sup>                                   | 1–2.5 <sup>a</sup>                                             | 3 <sup>a</sup>     |
| Tire warehouse   | 4–10 <sup>b</sup>                                   | 2–4.5 <sup>b</sup>                                             | 4 <sup>b</sup>     |

a Nitrosodimethylamine.

b Nitrosomorpholine.

**Table 6.** Nitrosamines ( $\mu\text{g}/\text{m}^3$ ) in the air of the salt-bath curing areas.

| Type of process                                                | Nitrosodimethylamine | Nitrosoethylamine | Nitrosomorpholine |
|----------------------------------------------------------------|----------------------|-------------------|-------------------|
| Curing of profiles                                             | 1–10                 | Trace             | Trace             |
| Curing of tubes 1981                                           | 9–18                 | 3–5               | 3                 |
| Curing of tubes 1982                                           | 7–24                 | 0.5–2             | —                 |
| Curing of hoses and foam rubber                                |                      |                   |                   |
| 1981                                                           | 10–40                | Trace             | 1                 |
| 1982                                                           | 12–41                | Trace             | 0.5               |
| Curing of profiles (compounded with peroxides as accelerators) | 0.1                  | —                 | —                 |

**Table 7.** Carcinogenicity of chemicals used in the rubber industry and of chemicals found as by-products. (IARC = International Agency for Research on Cancer)

| Compound                                                                                                                                                    | Class of compound <sup>a</sup>         | Evaluation in IARC monograph 28 (10) |                                |                   | Evaluation in another IARC monograph (volume/page) |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------|--------------------------------------|--------------------------------|-------------------|----------------------------------------------------|
|                                                                                                                                                             |                                        | Data on occurrence <sup>b</sup>      | Data on standards <sup>b</sup> | Page of reference |                                                    |
| <i>Known carcinogens to humans</i>                                                                                                                          |                                        |                                      |                                |                   |                                                    |
| Benzene + by-product                                                                                                                                        | Solvent<br>(> 100,000,000 t)           | +                                    | (+)                            | 332               | 11/295                                             |
| Vinyl chloride                                                                                                                                              | Contaminant                            | (+)                                  | (+)                            | . <sup>c</sup>    | 19/377                                             |
| 4-Aminobiphenyl + by-product                                                                                                                                | —                                      | —                                    | — <sup>d</sup>                 | 265               | 10/343                                             |
| Benzidine + by-product                                                                                                                                      | —                                      | —                                    | — <sup>d</sup>                 | 266               | 1/ 80                                              |
| 2-Naphthylamine + by-product                                                                                                                                | Contaminant                            | —                                    | — <sup>d</sup>                 | .                 | 4/ 97                                              |
| Asbestos                                                                                                                                                    | Filler                                 | —                                    | —                              | .                 | 14/123                                             |
| Mineral oils                                                                                                                                                | Solvent                                | —                                    | —                              | .                 | 3/ 30                                              |
| Soots and tars                                                                                                                                              | Filler                                 | —                                    | —                              | .                 | 9/ 22                                              |
| <i>Suspected carcinogens to humans</i>                                                                                                                      |                                        |                                      |                                |                   |                                                    |
| Styrene                                                                                                                                                     | By-product                             | +                                    | +                              | 356               | 19/231                                             |
| Naphthylamine-acetaldehyde-condensate (mixed $\alpha$ + $\beta$ ) (NONOX S) + by-product (Talc) via asbestos                                                | —                                      | —                                    | — <sup>d</sup>                 | 258               | —                                                  |
|                                                                                                                                                             | Filler<br>( $\leq$ 100,000,000 t)      | —                                    | +                              | 349               | 17/351                                             |
| Acrylonitrile                                                                                                                                               | By-product                             | (+)                                  | (+)                            | . <sup>c</sup>    | 19/ 73                                             |
| Carbontetrachloride                                                                                                                                         | Solvent<br>(> 100,000,000 t)           | —                                    | +                              | 328               | 20/371                                             |
| Cadmium compounds                                                                                                                                           | —                                      | —                                    | —                              | .                 | —                                                  |
| <i>Carcinogens in animal experiments</i>                                                                                                                    |                                        |                                      |                                |                   |                                                    |
| Ethylene thiourea                                                                                                                                           | Accelerator<br>( $\leq$ 100,000 t)     | —                                    | —                              | 297               | 7/ 45                                              |
| Dioxane                                                                                                                                                     | Solvent<br>(500—10,000 t)              | —                                    | +                              | 322               | 11/247                                             |
| Ethylenedichloride                                                                                                                                          | Solvent<br>(> 100,000,000 t)           | +                                    | +                              | 329               | 20/429                                             |
| Acrylonitrile                                                                                                                                               | —                                      | (+)                                  | (+)                            | .                 | 19/ 73                                             |
| Vinyl chloride                                                                                                                                              | —                                      | (+)                                  | (+)                            | .                 | 19/377                                             |
| Epichlorhydrin                                                                                                                                              | —                                      | (-)                                  | (+)                            | .                 | 11/131                                             |
| Carbon black                                                                                                                                                | Filler<br>(> 100,000,000 t)            | —                                    | +                              | 344               | —                                                  |
| Benzo(a)pyrene (total particulate)                                                                                                                          | —                                      | +                                    | +                              | 352               | 3/ 91                                              |
| Tris(2,3-dibromopropyl)phosphate                                                                                                                            | Flame retardant<br>(500—10,000 t)      | —                                    | —                              | 327               | 20/575                                             |
| 2,4-Diaminotoluene                                                                                                                                          | Antioxidant<br>( $\leq$ 100,000,000 t) | —                                    | +                              | 253               | 16/ 83                                             |
| 4,4'-Methylene bis(2-chloro-aniline) + by-product                                                                                                           | Antioxidant<br>( $\leq$ 1,000,000 t)   | —                                    | +                              | 256               | 4/ 65                                              |
| Di(2-ethylhexyl)phthalate                                                                                                                                   | Plasticizer<br>(> 100,000,000 t)       | —                                    | —                              | 314               | 29/269                                             |
| Nitrosamines (nitrosodimethylamine, nitrosodiethylamine, nitrosodipropylamine nitrosobutylamine, nitrosopiperidine, nitrosopyrrolidine, nitroso-morpholine) | By-products                            | +                                    | —                              | 355               | 17/-                                               |
| p-Nitroso-N,N-dimethylaniline                                                                                                                               | Accelerator<br>( $\leq$ 100,000 t)     | —                                    | —                              | 267               | —                                                  |
| Carbontetrachloride                                                                                                                                         | Solvent<br>(> 100,000,000 t)           | —                                    | +                              | 328               | 20/371                                             |
| Cadmium compounds                                                                                                                                           | —                                      | —                                    | —                              | .                 | 11/39—74                                           |
| Chloroform                                                                                                                                                  | Solvent                                | —                                    | —                              | .                 | 20/401                                             |
| Formaldehyde gas                                                                                                                                            | Contaminant                            | —                                    | —                              | .                 | —                                                  |
| Hydrazine                                                                                                                                                   | —                                      | —                                    | —                              | .                 | —                                                  |
| <i>Insufficient data or limited evidence relative</i>                                                                                                       |                                        |                                      |                                |                   |                                                    |
| Tetramethylthiuram disulfide                                                                                                                                | Accelerator<br>(500—10,000 t)          | —                                    | +                              | 291               | 12/225                                             |
| Tetramethylthiuram monosulfide                                                                                                                              | Accelerator<br>(500—10,000 t)          | —                                    | +                              | 291               | —                                                  |
| Tetraethylthiuram disulfide                                                                                                                                 | Accelerator<br>(500—10,000 t)          | —                                    | —                              | 290               | 12/ 85                                             |

(continued)

**Table 7.** (Continued)

| Compound                                    | Class of compound                | Evaluation in IARC monograph 28 (10) |                                |                   | Evaluation in another IARC monograph (volume/page) |
|---------------------------------------------|----------------------------------|--------------------------------------|--------------------------------|-------------------|----------------------------------------------------|
|                                             |                                  | Data on occurrence <sup>b</sup>      | Data on standards <sup>b</sup> | Page of reference |                                                    |
| Trichloroethylene                           | Solvent<br>(> 100,000,000 t)     | —                                    | +                              | 331               | 11/263                                             |
| 1,1,1-Trichloroethane                       | Solvent<br>(> 100,000,000 t)     | +                                    | +                              | 331               | 20/515                                             |
| Perchloroethylene                           | —                                | —                                    | —                              | .                 | 20/491                                             |
| Styrene                                     | By-product                       | +                                    | +                              | 356               | 19/231                                             |
| Benzene + by-product                        | Solvent<br>(> 100,000,000 t)     | +                                    | +                              | 332               | 11/295                                             |
| 1-Naphthylamine                             | —                                | —                                    | —                              | .                 | 4/ 87                                              |
| 2,5-Diaminotoluene                          | Antioxidant<br>(> 100,000,000 t) | —                                    | +                              | 253               | 16/ 97                                             |
| Meta-phenylenediamine                       | —                                | —                                    | — <sup>d</sup>                 | .                 | 16/111                                             |
| N-phenyl-2-naphthylamine                    | Antioxidant<br>(≤ 1,000,000 t)   | —                                    | —                              | 269               | 16/325                                             |
| N-methyl-N,4-dinitroso-aniline + by-product | Accelerator<br>(< 1,000,000 t)   | —                                    | — <sup>d</sup>                 | 268               | 1/141                                              |
| Nitrosodiphenylamine                        | Retarder<br>(≤ 1,000,000 t)      | —                                    | —                              | 255               | 27/213                                             |
| Mercaptobenzthiazole                        | Accelerator<br>(≤ 100,000 t)     | —                                    | —                              | 285               | —                                                  |
| Di(2-ethylhexyl)-adipate                    | Plasticizer<br>(< 100,000,000 t) | —                                    | —                              | 314               | 29/257                                             |

<sup>a</sup> Amount of production in the United States per year in parentheses.

<sup>b</sup> + = data available, — = data not available, (+) or (—) = data from other industries available.

<sup>c</sup> Occurs in the rubber industry although not listed in IARC monograph 28.

<sup>d</sup> Withdrawn from industry or market.

retarder nitrosodiphenylamine was substituted by cyclohexylthiophthalimide, which releases no nitrogen oxides.

#### *Industrial rubber product factories*

Due to a wide variety of different formulations of rubber for technical and industrial purposes, the results are more difficult to summarize for rubber product factories. In this industry also other nitrosamines, like nitrosodiethylamine, nitrosodibutylamine and nitrosopiperidine, could be detected. The occurrence of these nitrosamines can be explained by rubber chemicals used in these areas.

Interesting results have been obtained at different salt-bath curing rooms. Normally tetramethylthiuram disulfide is used as an accelerator in products which are vulcanized by this method. Therefore, it is not surprising that nitrosodimethylamine can be found in high concentrations (up to 40 µg/m<sup>3</sup>) (table 6). In one factory, however, a peroxide accelerator was used, and a low nitrosodimethylamine level of about 0.1 µg/m<sup>3</sup> was detected. The highest

nitrosamine concentrations ever detected occurred in measurements during the injection molding and curing of conveyor belts [1,060 µg/m<sup>3</sup> (nitrosodimethylamine) and 4,700 µg/m<sup>3</sup> (nitrosomorpholine) for process samples and from personal monitoring up to 90 µg/m<sup>3</sup> (nitrosodimethylamine) and 380 µg/m<sup>3</sup> (nitrosomorpholine)].

#### *Other locations*

The continuous release of nitrosamines from rubber articles causes the occurrence of these compounds also at places where such exposure is not expected. Measurements in sales rooms, mounting halls, and storage rooms of tire and tube dealers have shown nitrosamine levels of up to 1.5 µg/m<sup>3</sup>.

### **Preventive measures**

#### *Elimination of nitrosating agents*

Available results indicate that nitrosodiphenylamine as a retarder should not be

used in the presence of nitrosatable compounds. Alternative retarders are cyclohexylthiophthalimide, phthalic anhydride or benzoic acid. In addition, it seems to be necessary to control nitrogen oxides in those areas where nitrosatable compounds are handled or stored. Indoor transportation systems should not emit nitrogen oxides. All other combustion processes should be separated from the production areas. A good example for the successful elimination of nitrosating agents is given in table 5. The replacement of nitrosodiphenylamine by cyclohexylthiophthalimide drastically reduces the levels of nitrosodimethylamine.

#### *Reformulation of rubber compositions*

Changes in rubber compositions seem to be another, even more effective way to prevent nitrosamine formation. A wide variety of different accelerators which are not nitrosatable are available and can substitute the traditional accelerators. For example:

##### *Peroxides*

2,4-Dichlorobenzoylperoxide  
Dicumylperoxide  
2,5-Dimethyl-2,5-di(tert-butylperoxy)hexane  
2,5-Dimethyl-2,5-di(tert-butylperoxy)hexene-3  
Para-chlorobenzoylperoxide  
Di-tert-butylperoxide  
Benzoylperoxide

##### *Dithiophosphoric acid derivatives*

Bis(diethylthiophosphoryl)trisulfide  
Bis(di-isopropylthiophosphoryl)disulfide  
S,S'-carbonyl-bis(di-*n*-butyl)dithiophosphate  
Zinc-di-*n*-butyl dithiophosphate  
Dicyclohexylamine salt of di-*n*-butyldithiophosphoric acid<sup>2</sup>

##### *Xanthates*

Sodium isopropylxanthate  
Zinc isopropylxanthate  
Dibutylxanthogen disulfide  
Zinc dibutylxanthate

##### *Mercaptobenzothiazoles*

Mercaptobenzothiazole  
Dibenzothiazyl disulfide  
Mercaptobenzothiazole-zinc salt  
N-cyclohexyl-2-benzothiazylsulfenamide  
N,N-dicyclohexyl-2-benzothiazylsulfenamide<sup>2</sup>  
N-tert-butyl-2-benzothiazylsulfenamide

##### *Other accelerators*

Glycoldimercaptoacetate  
Zinc laurate  
2,2'-Methylenebis(4-methyl-6-*tert*-butylphenol)  
Urea  
Tetrachloro-*para*-benzoquinone  
Zinc dibenzylthiocarbamate<sup>2</sup>

Three of the chemicals given in the preceding list might form nitrosamines which are, however, not carcinogenic in animal experiments (9). As an example for the prevention of nitrosamine formation by the reformulation of rubber composition, data are given in table 5.

The exchange of nitrosatable accelerators against peroxide accelerators allows vulcanization by salt-bath curing without the formation of considerable amounts of nitrosamines.

#### **Carcinogenicity of nitrosamines in animals**

From animal experiments it is known that the nitrosamines found in the rubber industry might represent a carcinogenic risk for workers in the rubber industry. Especially the more relevant inhalation studies with low concentrations of nitrosodimethylamine show that even amounts of 70 µg/m<sup>3</sup> induce tumors in rats. The observed tumors were located in kidney, lung, and liver (1, 12). It should be pointed out that in some cases the observed nitrosamine levels in the workers' environment were in the same range as the effective levels in animal inhalation experiments.

#### **Carcinogenic effect of chemicals used and found in the rubber industry**

The currently available knowledge on the carcinogenicity of chemicals used or found in the rubber industry is summarized in table 7. These chemicals or products are listed according to evaluation by IARC monographs, with a few exceptions, where other data were used for classification. Cross-reference is made to IARC monograph volume 28 (chemical and industrial hygiene data) (10), as well

<sup>2</sup> The possible nitrosation product is non-carcinogenic.

as reference to IARC monographs with respect to the evaluation of the carcinogenic risk. For each material information is also given about the way in which the chemical is used for rubber compounding. The addition of United States production data should give some idea of the importance of these products. Together with the indication of the availability of data on occurrence at the workplace and exposure limits (recommended guidelines or governmental regulations) this table could present a useful tool for industrial toxicologists and epidemiologists.

It must be kept in mind that exposure usually is not caused by one compound only. Therefore also combined effects have to be taken into account. Still unknown is to what extent smoking may play a role as a synergistically acting agent.

## References

1. Benemanskij VV, Brusakov VM, Leshenko ME. Blastogenic effect of treatment with low concentrations of nitrosodimethylamine and nitrogen oxide [in Russian]. *Vopr onkol* 27 (1981): 10, 56-62.
2. Crosby DG, Humphrey JR, Moilanen KW. The photodecomposition of dipropylnitrosamine vapor. *Chemosphere* 9 (1980) 51-54.
3. Enwald E. How safe is it to work with rubber? In: Scandinavian Rubber Society. Proceedings of the Scandinavian rubber conference, Helsinki, May. Trelleborg (in press).
4. Fajen JM, Carson GA, Rounbehler DP, Fan TY, Vita R, Goff UE, Wolf MH, Edwards GS, Fine DH, Reinhold V, Biemann K. N-nitrosamines in the rubber and tire industry. *Science* 205 (1979) 1262-1264.
5. Fine DH, Rounbehler DP. Occurrence of N-nitrosamines in the workplace: Some recent developments. In: Scanlan RA, Tannenbaum SR, ed. N-nitroso compounds. American Chemical Society, Washington, DC 1981, pp 207-216. (ASC symposium series no 174).
6. Fraser DA, Rappaport S. Health aspects of the curing of synthetic rubbers. *Environ health perspect* 17 (1976) 45-53.
7. Gehler P, Rolle W. Formation of diethylnitrosamine by reaction of diethylamine with nitrogen oxide in the gas phase. *Z Chem* 14 (1974) 579-581.
8. Hanst PL, Spence JW, Miller M. Atmospheric chemistry of N-nitrosodimethylamine. *Environ sci technol* 11 (1977) 403-405.
9. International Agency for Research on Cancer. Some N-nitroso compounds. Lyon 1978, pp 35-47. (IARC monographs on the evaluation of the carcinogenic risk of chemicals to humans, volume 17).
10. International Agency for Research on Cancer. The rubber industry. Lyon 1982. (IARC monographs on the evaluation of the carcinogenic risk of chemicals to humans, volume 28).
11. McGlothlin JD, Wilcox TC, Fajen JM, Edwards GS. A health hazard evaluation of nitrosamines in a tire manufacturing plant. In: Choudhary G, ed. Chemical hazards in the workplace, measurement and control. American Chemical Society, Washington DC 1981, pp 283-299.
12. Moiseev GE, Benmanskij VV. On the carcinogenic activity of low concentrations of nitrosodimethylamine in inhalation [in Russian]. *Vopr onkol* 21 (1975): 6, 107-109.
13. National Institute for Occupational Safety and Health. Health hazard evaluation determination. Cincinnati, OH 1977. (Report no 77-67-499, St Clair Rubber Company, Marysville, Michigan).
14. National Institute for Occupational Safety and Health. Survey report of Cincinnati rubber manufacturing company, Norwood, Ohio (PB-278 792). National Technical Information Service, Washington, DC 1977. (Chemical abstract 89 220163h).
15. National Institute for Occupational Safety and Health. Interim report no 1: Health hazard evaluation project no HHE-79-75, St Clair Rubber Company, Marysville, Michigan. Cincinnati, OH 1979.
16. National Institute for Occupational Safety and Health. Interim report no 1: Health hazards evaluation project no HHE-79-126, St Clair Rubber Company, Marysville, Michigan. Cincinnati, OH 1980.
17. Nutt A. Measurement of some potentially hazardous materials in the atmosphere of rubber factories. *Environ health perspect* 17 (1976) 117-123.
18. Occupational Safety and Health Administration. Test for hazardous substance - 527 (carbon black) (29CFR 1910.1000). US Department of Labor, Washington, DC 1977.
19. Otto J, Schmidt E. Workplace concentrations of polycyclic aromatic hydrocarbons [in German]. *Zentralbl Ges Hyg Ihre Grenzgeb* 24 (1978) 896-898.
20. Pagnatto LD, Elkins HB, Brugsch HG. Benzene exposure in the rubber coating industry - A follow-up. *Am ind hyg assoc j* 40 (1979) 137-146.
21. Parkes HG, Whittaker B, Willoighby BG. The monitoring of the atmospheric environment in UK tyre manufacturing work areas, British Rubber Manufacturers' Association, Ltd, Birmingham 1975.
22. Pitts JN, Grosjean D, Cauwenbergh KV, Schmid JP, Fitz DR. Photooxidation of aliphatic amines under simulated atmospheric conditions: Formation of nitrosamines, nitramines, amides and photochemical oxidants. *Environ sci technol* 12 (1978): 8, 946-953.
23. Rappe C, Rydström T. Occupational exposure to N-nitroso compounds. In: Walker EA, Gričič L, Castegnaro M,

- Börzsonyi M, ed. N-nitroso compounds: Analysis, formation and occurrence. International Agency for Research on Cancer, Lyon 1980, pp 565-574. (IARC scientific publication no 31).
24. Spiegelhalder B, Preussmann R. Nitrosamides and rubber. In: Bartsch H, O'Neill IK, Castegnaro M, Okada M, ed. N-nitroso compounds: Occurrence and biological effects. International Agency for Research on Cancer, Lyon 1982, pp 231-244. (IARC scientific publication no 41).
25. Van Ert MD, Arp EW, Harris RL, Symons MJ, Williams TM. Worker exposures to chemical agents in the manufacture of rubber tires: Solvent vapor studies. *Am ind hyg assoc j* 41 (1980) 212-219.
26. Williams TM, Harris RL, Arp EW, Symons MJ, Van Ert MD. Worker exposure to chemical agents in the manufacture of rubber tires and tubes: Particulates. *Am ind hyg assoc j* 41 (1980) 204-211.