APPENDIX D—COMBINED EXPOSURE TO NOISE AND OTOTOXIC SUBSTANCES

Ototoxic substances came gradually to the attention of occupational health and safety professionals in the 1970s, when the ototoxicity of several industrial chemicals, including solvents, was recognized. The possibility of noise/solvent interaction was raised more recently, when Bergström and Nyström (1986) published the results of a 20-year epidemiological follow-up study in Sweden, started in 1958 and involving regular hearing tests in workers. Interestingly, a large proportion of workers employed in the chemicals divisions of companies suffered from hearing impairment, although noise levels were significantly lower than those in sawmills and paper pulp production. The authors suspected that industrial solvents were an additional causative factor in hearing loss.

Workers are commonly exposed to multiple agents. Physiological interactions with some mixed exposures can lead to an increase in the severity of harmful effects. This applies not only to the combination of interfering chemical substances, but also in certain cases to the co-action of chemical and physical factors. In this case, effects of ototoxic substances on ear function can be aggravated by noise, which remains a well-established cause of hearing impairment.

According to the European Agency for Safety and Health at Work (2009), experiments with rats have shown that combined exposure to noise and solvents induced synergistic adverse effects on hearing. “Good evidence” has been accumulated on the adverse effects on hearing of the following solvents:

Toluene, ethylbenzene, n-propylbenzene
Styrene and methylstyrenes
Trichloroethylene
p-Xylene
n-Hexane
Carbon disulfide

The rat cochlea is sensitive to aromatic solvents, unlike that of the guinea pig or chinchilla (Campo et al., 1993; Cappaert et al., 2003; Davis et al., 2002; Fechter, 1993). These findings have been attributed to metabolic and other toxicokinetic differences (Campo and Maguin, 2006; Davis et al., 2002; Gagnaire et al., 2007). Because of their metabolism, rats are considered comparatively good animal models for the investigation of the ototoxic properties of aromatic solvents in humans (Campo and Maguin, 2006; Kishi et al., 1988).

Examples of relevant literature on interactions between noise and specific substances include:

Toluene (Brandt-Lassen et al., 2000; Johnson et al., 1988; Lataye and Campo, 1997; Lund and Kristiansen, 2008)
Styrene (Lataye et al., 2000; Lataye et al., 2005; Mäkitie et al., 2003)
Ethylbenzene (Cappaert et al., 2001)
Trichloroethylene (Muijser et al., 2000)
Carbon monoxide (Lacerda et al., 2005)
Lead (CDC-HHE, 2011)
Lataye et al. (2005) found interactive effects of noise at 85 dB with a styrene exposure concentration of 400 parts per million (ppm). In general, though, high levels of noise and high concentrations of solvents were used in most of these investigations. Because of these special conditions, extrapolation to occupational exposure conditions can be challenging (Cary et al., 1997).

Investigators suggest that exposure to these solvents can provoke irreversible hearing impairment, with the cochlear hair cells (organ of Corti) being considered a target tissue for these solvents (Figure 5; Campo et al., 2007).

Scanning electron micrograph of a rat organ of Corti prior to (left panel) and after (right panel) toluene exposure (from European Agency for Safety and Health, 2009, as published in Lataye et al., in 1999).

Although the cochlea suffers damage, particularly during co-exposure, recent studies have reported that solvents reduce the protective role played by the middle-ear acoustic reflex, an involuntary muscle contraction that normally occurs in response to high-intensity sound stimuli. A disturbance of this reflex would allow more acoustic energy into the inner ear (Campo et al., 2007; Lataye et al., 2007; Maguin et al., 2009).

A number of epidemiological studies have investigated the relationship between hearing impairments and co-exposure to both noise and industrial solvents (Chang et al., 2003; De Barba et al., 2005; Johnson et al., 2006; Kim et al., 2005; Morata, 1989; Morata et al., 1993, 2002; Morioka et al., 2000; Prasher et al., 2005; Sliwinska-Kowalska et al., 2003, 2005). Due to confounding factors, straightforward conclusions could not easily be drawn from these studies. However, the evidence of additive or synergistic ototoxic effects due to combined exposure to noise and solvents is very strong (Lawton et al., 2006; Hoet and Lison, 2008).

A recent longitudinal study (Schäper et al., 2003; Schäper et al., 2008) on the relationship between hearing impairment measured by pure tone audiometry and occupational exposure to toluene and noise has not found ototoxic effects in workers exposed to a concentration of toluene lower than 50 ppm. The observed hearing loss was associated only with noise intensity. However, the use of hearing protection was not taken into account in the conclusions relative to the potential interaction between noise and toluene on hearing.

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4 To put this exposure level in perspective, 29 CFR 1910.1000, Table Z-2, lists OSHA's 8-hour time-weighted average permissible exposure limit for styrene as 100 ppm, with a 200 ppm peak, and up to 600 ppm permitted for no more than 5 minutes in a 3-hour period.
A clear relationship between solvent and hearing impairment is difficult to assess through the available epidemiological studies. The workplace environments where noise and solvents can be simultaneously present are typically complex (for example, see critical review of Lawton et al., 2006; Hoet and Lison, 2008). Quite often, the workers were exposed to multiple substances. Furthermore, most of these studies had a cross-sectional design that featured a number of weaknesses in the interpretation of the findings. For instance, chronic effects were related to currently measured exposures. In some cases, the exposure concentrations measured at the time of the study were markedly lower than those ascertained in past years (Morata et al., 1993).

All in all, there are limited data on dose-response relationships or clear effects on auditory thresholds in humans (for reviews, see Lawton et al., 2006; Hoet and Lison, 2008). However, animal data clearly show an effect. Further human studies are needed for clarification of these issues. However, in the interim, one cannot rule out a likely relationship between solvent exposure and hearing impairments.

Overall, in combined exposure to noise and organic solvents, interactive effects may be observed depending on the parameters of noise (intensity, impulsiveness) and the solvent exposure concentrations. In cases of concomitant exposures, animal studies suggest that solvents might exacerbate noise-induced impairments even though the noise intensity is below the permissible limit value.
References Cited in This Appendix


