## VII. RESEARCH NEEDS

Research focused on the prevention of adverse health effects in workers who manufacture, handle, or use NG or EGDN is needed in several areas. For workers who handle NG or EGDN directly, skin absorption appears to be the major route of exposure. Thus, investigators should develop processes that will minimize or prevent skin contact with these compounds.

NG and EGDN penetrate gloves made of neoprene, rubber, leather, or cotton that are currently worn by exposed workers. Research should be conducted to identify a material suitable for use in work clothing and gloves through which these nitroesters will not penetrate. As an interim measure, a safe compound that changes color when it comes in contact with NG or EGDN should be identified. If used on gloves and clothing, workers would be warned by the change in color that their clothing had become contaminated with nitroesters.

Compounds should be identified that will remove NG and EGDN from the skin and from surfaces in work areas more effectively than do soap and water.

Further research is needed to identify a "no effect" level for exposure to NG or EGDN in the workplace, and appropriate indices of both exposure and effect should be developed that can be used to determine whether workers are overexposed to these substances. Exposure by inhalation can be estimated from concentrations of these airborne compounds, but no method is currently available to assess the extent of exposure through the skin. Such estimates might be based on measurements of concentrations of NG or EGDN removed from the skin on swabs or in cotton

gloves, glove liners, or socks. An index of exposure by both inhalation and skin absorption could be obtained by measuring concentrations of NG and EGDN in the blood or possibly the urine of exposed workers. An index of effect might be constructed of information on symptoms, blood pressure estimations, and such measurements as fingertip volume by plethysmography. New techniques, such as echocardiography, may provide information on the effects of NG or EGDN on cardiac function.

Angina pectoris, caused by an insufficient supply of oxygen to the heart, is usually associated with sclerosis of the coronary arteries. However, it does not appear that atherosclerosis is more extensive in workers exposed to NG or EGDN than in the general population. It has been suggested that spasms of the coronary arteries may lead to angina or sudden death in exposed workers, particularly during brief periods of withdrawal from exposure, such as on weekends. The mechanism of causation of these spasms and the possibility that other factors may be associated with angina and sudden death in exposed workers, should be explored. Detailed epidemiologic studies are needed to determine the extent of the risk of developing heart disease in former workers who are no longer exposed to NG or EGDN and to identify factors, such as duration of exposure, that may be associated with this increased risk.

Reports, primarily from the turn of the century, suggest that exposure to NG alone or, especially, with alcohol can cause psychologic effects. More recent reports suggest that workers who absorb NG or EGDN through the skin can develop numbness in their fingers. Further studies are needed to determine whether these nitroesters act directly on the central or peripheral nervous systems or whether the reported effects are

secondary to the effects of these compounds on the cardiovascular system.

With the exception of one report from the late 1800's, the effects of NG or EGDN on the male and female reproductive systems or on the developing fetus have not been evaluated. The possibility that workplace exposure to these compounds may affect reproduction merits further attention. Well-designed tests are needed to determine whether NG, EGDN, or their metabolites are potentially mutagenic or carcinogenic by inhalation, ingestion, or absorption through the skin.

The US Army Medical Research and Development Command is sponsoring studies of the toxicity of NG. Dilley [161] is studying the effects of exposure to NG by inhalation and through the skin on coronary blood flow in dogs. Lee et al [162,163] are studying the effects of short-term and long-term exposures to NG in rats, mice, and dogs. The potential carcinogenicity of NG administered orally to rats and mice is also being studied by Lee et al. Since these studies [161-163] are still in progress (1978), final results from them are not yet available.

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