NIOSH

Current Intelligence Bulletin 44

July 5, 1985

Dinitrotoluenes (DNT)

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
Centers for Disease Control
National Institute for Occupational Safety and Health

DISCLAIMER

Mention of the name of any company or product does not constitute endorsement by the National Institute for Occupational Safety and Health.

DHHS (NIOSH) Publication No. 85-109

FOREWORD

Current Intelligence Bulletins (CIB's) are reports issued by the National Institute for Occupational Safety and Health (NIOSH), Centers for Disease Control, Atlanta, Georgia, for the purpose of disseminating new scientific information about occupational hazards. A CIB may draw attention to a hazard previously unrecognized or may report new data suggesting that a known hazard is either more or less dangerous than was previously thought.

CIB's are prepared by the staff of the Division of Standards Development and Technology Transfer, NIOSH (Robert A. Taft Laboratories, 4676 Columbia Parkway, Cincinnati, Ohio 45226) and are distributed to representatives of organized labor, industry, public health agencies, academia, and public interest groups as well as to those federal agencies, such as the Department of Labor, which have responsibilities for protecting the health of workers. It is our intention that anyone with the need to know should have ready access to the information contained in these documents; we welcome suggestions concerning their content, style, and distribution.

This CIB describes the results of research indicating the potential for various technical grade mixtures of dinitrotoluene isomers (TDNT) and the 2,6- isomer of dinitrotoluene (2,6-DNT) to induce cancer and adverse reproductive effects in animals exposed to these substances. Although there is limited evidence indicating that 2,4-dinitrotoluene (2,4-DNT) poses a risk to human health, the existing animal and *in vitro* data are suggestive of such a potential. NIOSH estimates that 1,300 workers are potentially exposed to the isomers of dinitrotoluene (DNT) during the manufacture of TDNT; in the production of munitions; and in the synthesis of toluenediamine (TDA), an intermediate in the production of polyurethane.

NIOSH recommends that TDNT and the 2,6- isomer of DNT be regarded as potential human carcinogens in the workplace and possible inducers of adverse reproductive effects. The excess risk of cancer and of adverse reproductive effects in workers exposed to specific concentrations of TDNT or 2,6-DNT and the potential of the other DNT isomers to induce these adverse health effects have not yet been precisely determined, but the probability of developing such effects would be decreased by reducing exposure.

It is also recommended that producers and users of TDNT or the isomers of DNT disseminate this information to their workers and customers, that professional and trade associations and unions inform their members of the potential hazards of working with DNT, and that appropriate engineering controls and work practices be used to reduce worker exposure to the fullest feasible extent.

J. Donald Millar, M.D., D.T.P.H. (Lond.)
Assistant Surgeon General
Director, National Institute for
Occupational Safety and Health
Centers for Disease Control

CURRENT INTELLIGENCE BULLETIN #44

DINITROTOLUENE

JULY 1985

ABSTRACT

Rats which over a 1-year period ingested diets containing a technical grade mixture of dinitrotoluenes (TDNT), primarily composed of the 2,4- and the 2,6- isomers, or which were fed only 2,6-dinitrotoluene (2,6-DNT) developed cancers of the liver. The liver cancers consisted of hepatocellular carcinomas and in some cases cholangiocarcinomas. Two-year TDNT ingestion studies in rats produced subcutaneous fibromas and fibrosarcomas, mammary fibroadenomas, and the liver cancers. Male mice fed TDNT for 2 years developed papillary and cortical carcinomas of the kidney and nonmalignant kidney tumors diagnosed as papillary and cortical adenomas. Rats fed 2,4-dinitrotoluene (2,4-DNT) throughout a 2-year carcinogenicity study developed statistically significant incidences of subcutaneous fibromas and mammary fibroadenomas and low incidences of hepatocellular carcinomas and subcutaneous fibrosarcomas which were not statistically significant. Feeding or oral administration of TDNT or 2,6-DNT for up to 2 years induced decreased spermatogenesis, aspermatogenesis, or testicular atrophy in dogs, rats, or mice. Nonfunctioning ovaries were found in mice fed TDNT for 2 years.

Based on these data, the National Institute for Occupational Safety and Health (NIOSH) recommends that TDNT and 2,6-DNT be regarded as potential human carcinogens in the workplace and possible inducers of adverse reproductive effects. Although there is limited evidence indicating that 2,4-DNT poses a risk to human health, the existing animal and *in vitro* data are suggestive of such a potential. The potential of the other DNT isomers to induce adverse health effects has not been determined, but the probability of developing such effects would be decreased by reducing exposure. Therefore, NIOSH recommends that occupational exposures to TDNT and the isomers of DNT be controlled to the fullest feasible extent.

BACKGROUND

Physical and Chemical Properties

The six isomers of dinitrotoluene (DNT)*, 2,3-; 2,4-; 2,5-; 2,6-; 3,4-; and 3,5-DNT, are stable, yellow, crystalline solids at room temperature [1]. When heated, technical grade dinitrotoluene (TDNT)* forms a combustible, oily liquid [2]. The TDNT used in the synthetic organic chemicals industry is composed of approximately 76% 2,4-dinitrotoluene (2,4-DNT)*, 19% 2,6-dinitrotoluene (2,6-DNT)*, and 5% of the other four isomers. Chemical and physical properties of 2,4- and 2,6-DNT are listed in Table 1.

Production, Use, and Potential for Occupational Exposure

DNT is produced by a two-step nitration of toluene in a closed system process [3]. DNT is used in the manufacture of dyes, munitions, and explosives, but its major use today (99%) is in the synthesis of toluenediamine (TDA)*, an organic intermediate in the production of polyurethane [4,5]. In 1982, approximately 720 million pounds of DNT were produced in the United States [6].

It is estimated that up to 1,300 workers are exposed to various forms of DNT, of which an estimated 750-800 workers are potentially exposed to TDNT in its manufacture and use in the production of TDA [3,5] and an additional 500 workers are potentially exposed to 2,4-DNT in the production of munitions and explosives [7]. Based on a projected increase in demand for TDA, annual TDNT production through 1989 is expected to increase approximately 1-4% [5] with a potential increase in the number of workers exposed to TDNT. Anticipated increases in the production of munitions and explosives may contribute to an increase in employment and a potential for an increase in occupational exposure to 2,4-DNT.

EXPOSURE LIMITS

The Occupational Safety and Health Administration (OSHA) promulgated its permissible exposure limit (PEL) of 1.5 milligrams of DNT per cubic meter of air (mg/m^3) for occupational exposure to DNT determined as an 8-hour time-weighted average (TWA) concentration [8] based on the 1968 Threshold Limit Value (TLV®) of the American Conference of Governmental Industrial Hygienists (ACGIH) [9]. The TLV, which has remained unchanged at 1.5 mg/m^3 through 1984 [10], was based on the prevention of hematologic effects in exposed humans and by analogy with the TLV's adopted

*Abbreviations:
DNT -- dinitrotoluene
TDNT -- technical grade dinitrotoluene
2,4-DNT -- 2,4-dinitrotoluene
2,6-DNT -- 2,6-dinitrotoluene
TDA -- toluenediamine

TABLE 1. CHEMICAL AND PHYSICAL PROPERTIES OF 2,4- and 2,6-DINITROTOLUENE ISOMERS [1,11]

Chemical Identity:	2,4-Dinitrotoluene	2,6-Dinitrotoluene
CAS[a] Registry No.	121-14-2	606-20-2
RTECS[b] Accession No.	XT1575000	XT1925000
Synonyms	2,4-Dinitrotoluol 1-Methyl-2,4-dinitrobenzene	2,6-Dinitrotoluol 1-Methyl-2,6-dinitrobenzene
Molecular Weight	182.14	182.14
Empirical Formula	$C_7H_6N_2O_4$	$C_7H_6N_2O_4$
Boiling Point (at 760 mmHg)	Decomposes at 300°C (572°F)	Decomposes at 260°C (500°F)
Melting Point	71°C (160°F)	66°C (151°F)
Specific Gravity	1.321 (71°C, 160°F)	1.283 (111°C, 232°F)
Solubility		
water	Insoluble	Not available
alcohol	Soluble	Soluble
ether	Soluble	Not available
acetone	Very soluble	Not available
benzene	Soluble	Not available

[a]Chemical Abstract Service
[b]Registry of Toxic Effects of Chemical Substances

for nitro- and dinitro-benzenes [12], rather than on the prevention of cancer. Both the OSHA PEL and the ACGIH TLV include a "Skin" notation which refers to the potential contribution to the overall exposure by the cutaneous route by either airborne or direct contact with DNT. At the present time, the National Institute for Occupational Safety and Health (NIOSH) has no recommended exposure limit (REL) for DNT.

TOXICITY

Results of Animal Studies

Acute Effects

Oral administration of 2,4-DNT (98% purity) or 2,6-DNT (purity >99%) has shown the lethal dose in milligrams per kilogram of body weight (mg/kg) for 50 percent (LD_{50}) of the rats and mice tested to be as follows:

ORAL LD50 VALUES (mg/kg body weight)

	RAT		MOUSE	
	Male	Female	Male	Female
2,4-DNT	568	650	1954	1340
2,6-DNT	535	795	621	807

Signs of DNT toxicity included muscular incoordination, cyanosis, central nervous system depression, and respiratory depression followed by death. Both 2,4- and 2,6-DNT were found to be nonirritating to the eyes and mildly irritating to the skin of rabbits [13].

Metabolism

TDNT, 2,4-, and 2,6-DNT are believed to be metabolized by a three stage process. Following absorption from the site of administration, TDNT, 2,4-, or 2,6-DNT undergoes initial metabolism in the rat liver to dinitrobenzyl alcohol glucuronide (DNBAG) [14,15], which is excreted in the bile and subsequently transferred to the intestine where it is further metabolically altered by intestinal bacteria to aminonitrobenzyl alcohol [16,17]. These bacteria are present in the gastrointestinal flora of rodents and humans [18]. Aminonitrobenzyl alcohol is thought to be reabsorbed and returned to the liver where it is further metabolized to an unidentified but mutagenically active metabolite(s) or its precursor(s) which is capable of covalent binding and genotoxicity [17]. The binding of the genotoxic metabolite(s) to liver DNA, RNA, and protein has been shown to be two to five times greater following administration of 2,6-DNT than with 2,4-DNT. This greater binding capacity indicates a greater genotoxic potential for the 2,6- isomer when compared to the 2,4- isomer [19].

Mutagenic Effects

The six isomers of DNT have been shown to be weakly mutagenic in bacterial assays using several strains of Salmonella typhimurium including TA98 and TA100, nitro-reductase active bacteria [20,21,22]. The DNT isomers, when tested in strain TA100NR3 which lacked nitro-reductase activity, demonstrated no mutagenic response [21].

In vitro assays were performed to test the ability of isolated mammalian cells in culture to produce a mutagenic metabolite of DNT. In Chinese hamster ovary cell assays, TDNT and the six individual DNT isomers showed no mutagenic activity either with or without metabolic activation [16,23,24]. In an assay using metabolically competent rat liver cells, there was no observed increase in DNA repair of liver cell damage when TDNT or the six individual DNT isomers were used [25]. This indicates that the unidentified toxic DNT metabolite(s) or precursor(s) is probably not produced in the liver alone and that subsequent metabolism in the gastrointestinal tract and then the liver appears necessary for the production of the ultimate active mutagenic agent(s) [16,17].

A liver cell DNA repair assay which measures genotoxicity expressed as DNA repair was conducted to establish the role of nitro-reductase active gastrointestinal bacteria in DNT-induced genotoxicity. Rats with normal gastrointestinal bacteria and germfree rats which lacked such bacteria were administered a single 100 mg/kg dose of TDNT by gavage. The rats with normal gastrointestinal bacteria showed an increase in DNA repair of genotoxic liver cell damage, while germfree rats showed no increase [26].

These mutagenicity test results indicate that the mutagenic potential of TDNT and the DNT isomers depends on metabolism in the intestinal tract presumably by nitro-reductase active bacteria and subsequent metabolism in the liver for the formation of the active mutagenic metabolite(s) or its precursor(s).

In another study, TDNT, 2,4-DNT, or 2,6-DNT was administered by gavage to rats in a liver cell DNA repair assay to measure genotoxicity expressed as DNA repair [27]. Results of this study indicated that TDNT and 2,6-DNT were potent inducers of DNA repair; whereas 2,4-DNT produced only a weak response. This research indicates that most of the genotoxic activity of TDNT is probably attributable to 2,6-DNT.

Carcinogenic Effects

Studies of the cancer initiation or promotion potential of DNT, expressed as increased numbers of liver cell alterations, have been reported. These alterations may be precursors of hepatocellular neoplastic nodules [28]. TDNT and the 2,6-DNT isomer demonstrated a cancer initiating activity in rats; whereas the other five DNT isomers had no detectable initiating activity [29]. In a cancer promotion study using TDNT, 2,4-DNT, or 2,6-DNT, all three compounds demonstrated a cancer promoting activity by inducing liver cell alterations [28]. No promotion studies have been reported for the other DNT isomers.

Chronic 2-year carcinogenicity feeding studies with TDNT induced liver (hepatocellular) carcinomas, bile duct (cholangio-) carcinomas, or subcutaneous fibrosarcomas in rats and renal carcinomas in mice [30,31]. Rats fed 2,6-DNT (99.9% purity) for 1 year developed hepatocellular carcinomas [32]. Feeding 2,4-DNT (approximate purity 99% [33]) to rats for 2 years induced statistically significant incidences of subcutaneous fibromas and mammary fibroadenomas and low incidences of hepatocellular carcinomas and subcutaneous fibrosarcomas which were not statistically significant [34].

In a 2-year study [30] with male and female rats, three diets containing TDNT composed of 76% 2,4-DNT and 19% 2,6-DNT were ingested at daily dosages of approximately 35, 14, or 3.5 milligrams per kilogram of body weight per day (mg/kg/day). Hepatocellular carcinomas were found in 10 of 10 male and 4 of 10 female animals in the 35 mg/kg/day dosage group that were killed at week 52 of the study. No hepatocellular carcinomas were observed in control animals. Because of the high incidence of hepatocellular carcinomas, the remaining rats in the 35 mg/kg/day group were killed at week 55. Of the 40 rats examined at this time, 20 of 20 males and 11 of 20 females had hepatocellular carcinomas. Cholangiocarcinomas also were found in 5 of these high dose male rats killed at weeks 52 and 55 but not in the females. At the end of the 2-year study, autopsied male and female rats fed 14 mg/kg/day of TDNT had an increased incidence over controls of hepatocellular carcinomas, cholangiocarcinomas, mammary fibroadenomas, and subcutaneous fibromas and fibrosarcomas. Rats fed 3.5 mg/kg/day of TDNT had an increased incidence of hepatocellular carcinomas and subcutaneous fibromas in males when compared to controls.

In subsequent 1-year ingestion studies [32] intended to confirm the results of the 55 week study cited above [30], groups of male rats were fed TDNT composed of 76% 2,4-DNT and 19% 2,6-DNT at a dosage of 35 mg/kg/day or only the 2,6-DNT (99.9% purity) isomer at dosages of 14 or 7 mg/kg/day. Regardless of dosage, all groups of animals fed TDNT or 2,6-DNT developed hepatocellular carcinomas. Rats fed a diet containing only the 2,4-DNT (99.9% purity) for 1 year at a dosage of 35 mg/kg/day did not develop hepatocellular carcinomas [32].

In another 2-year rat feeding study [31], TDNT containing 98% 2,4-DNT and 1.7% 2,6-DNT induced increases over controls in the incidence of hepatocellular carcinomas in male rats fed 34.5 mg/kg/day and female rats fed 45.3 mg/kg/day of the TDNT. At the same dosages, treatment-related increases in the incidence of subcutaneous fibromas in the male rats and mammary fibroadenomas in the females, as compared with controls, also occurred. In addition, an increased incidence of subcutaneous fibrosarcomas was found in the male rats when compared to controls, but the importance of this response was not discussed. The authors concluded that the tumors noted in their study were induced by 2,4-DNT; however, the possible role played by the 2,6- isomer that was present in the TDNT in producing these tumors was not addressed.

In another study, male mice fed TDNT of the same composition (98% 2,4-DNT, 1.7% 2,6-DNT) at dosages of 96.9 or 13.3 mg/kg/day for 24 months developed papillary and cortical carcinomas of the kidney and nonmalignant kidney tumors diagnosed as papillary and cortical adenomas [31]. The possible role of the 2,6- isomer in the observed tumorigenicity was not discussed.

A 2-year carcinogenicity study with rats that ingested a diet containing 2,4-DNT (approximate purity 99%) for 18 months followed by a 6-month observation period on untreated diet has been reported [34]. Dietary intake of approximately 14 mg/kg/day of the 2,4-DNT induced a statistically significant incidence of subcutaneous fibromas ($p=0.003$) in males and mammary fibroadenomas ($p=0.016$) in the females, when compared to controls. Ingestion of approximately 5.7 mg/kg/day of the 2,4-DNT induced a statistically significant incidence of only subcutaneous fibromas ($p=0.008$) in male rats. A low incidence of hepatocellular carcinomas and subcutaneous fibrosarcomas, although not statistically significant, was also observed at both dosages, but only in the male rats. The importance of these reported cancers was not discussed in the report; however, these tumor incidences exceeded not only those in the study control group but also those of the National Toxicology Program's historical control data for such tumors identified in 13 other studies initiated in the same reporting laboratory from 1977 through 1979 [35]. In addition, the tumor types present and the target tissues affected in this study [34] were the same as those reported for TDNT [30,31] and the 2,6-DNT isomer [32]. These data indicate that 2,4-DNT may also have the capacity for inducing a tumorigenic response. However, the possible presence of other DNT isomers, particularly the 2,6-isomer, in the compound administered in this study and their potential for playing a role in the observed tumorigenicity was not discussed and cannot be discounted.

Unlike rats which did show the tumorigenic response, mice fed 2,4-DNT (approximate purity 99%) at dosages of approximately 14 or 5.7 mg/kg/day for 18 months followed by a 3-month observation period on untreated diet showed no treatment-related increases in tumors [34].

All of the cited animal carcinogenicity studies have used the oral route of administration for TDNT, 2,4-DNT, or 2,6-DNT. Although the primary routes of worker exposure are through inhalation or dermal contact, studies using oral administration are relevant since DNT absorbed from any site of administration is ultimately transferred to the liver for the initial stage of metabolism. In addition, TDNT and 2,6-DNT have induced malignant tumors of the liver, bile duct, kidneys, or subcutaneous tissue, all of which were distant from the site of administration. No carcinogenicity studies have been reported for the 2,3-; 2,5-; 3,4-; or 3,5-DNT isomers.

Reproductive Effects

In short-term or chronic studies, feeding or oral administration of TDNT or 2,6-DNT induced testicular atrophy, decreased spermatogenesis, or aspermatogenesis in treated rats, mice, and dogs when compared to their respective controls [16,23,31]. Nonfunctioning ovaries were found in mice chronically fed TDNT [31].

In studies with 2,6-DNT (purity >99%), ingestion of 144.7 mg/kg/day by groups of rats for 4 or 13 weeks resulted in decreased spermatogenesis or aspermatogenesis and testicular atrophy in all treated animals. Mice fed 2,6-DNT at 288.8 mg/kg/day for 4 weeks showed aspermatogenesis and testicular atrophy. Oral administration of 2,6-DNT to dogs for 8 weeks at 100 mg/kg/day resulted in decreased spermatogenesis and testicular atrophy [23].

In a series of studies [16,31], rats, mice, and dogs were fed or orally administered TDNT (98% 2,4-DNT, 1.7% 2,6-DNT) for periods as long as 2 years. Groups of rats fed TDNT at 265.6 or 92.8 mg/kg/day for 13 weeks developed decreased spermatogenesis or aspermatogenesis and testicular atrophy in all treated animals [16]. Ingestion of TDNT by rats for 2 years at a dosage of 34.5 mg/kg/day caused decreased spermatogenesis and testicular atrophy in treated animals. Mice fed TDNT for 2 years at dosages of 885 mg/kg/day or 96.9 mg/kg/day developed decreased spermatogenesis and testicular atrophy. Nonfunctioning ovaries were found in mice fed TDNT at 911 mg/kg/day for 2 years [31]. Oral administration of TDNT at 25 mg/kg/day to dogs for 4 or 13 weeks caused decreased spermatogenesis [16].

A three-generation reproductive study in rats fed TDNT (98% 2,4-DNT, 1.7% 2,6-DNT) in the diet at dosages as high as 45 mg/kg/day produced no treatment-related effects in any of the offspring [31]. No embryotoxic or teratogenic effects were observed in offspring of pregnant rats dosed by gavage with up to 100 mg/kg/day of TDNT (76% 2,4-DNT, 19% 2,6-DNT) on days 7 through 20 of gestation [36].

Human Health Effects

In humans, the acute toxic effects of exposure to DNT are caused by the chemical's ability to produce methemoglobin, which decreases the oxygen carrying capacity of the blood [37]. The clinical manifestation of methemoglobinemia is cyanosis, which may be accompanied by headache, irritability, dizziness, weakness, nausea, vomiting, dyspnea, drowsiness, unconsciousness, and possibly death. Repeated or prolonged exposure may cause anemia [38].

Studies of reproductive effects resulting from human exposure to TDNT are equivocal. A NIOSH Health Hazard Evaluation (HHE) [39] conducted in a chemical plant which used TDNT in the production of TDA included the determination of workers' exposure to TDNT from analysis of 7 personal and 3 area samples. Concentrations of TDNT ranged from not detected to 0.42 mg/m^3 (one area sample). Concentrations of TDA determined from 14 samples ranged from not detected to 0.39 mg/m^3. Medical evaluation of nine workers potentially exposed to TDNT and TDA in this plant found decreased sperm counts and a reduction in the number of large morphologic sperm forms. An excess of spontaneous abortions, although not statistically significant, was also reported for the wives of the exposed workers. Another HHE of 20 male TDNT-exposed workers [40] indicated no statistically significant differences in the rates of fertility or spontaneous abortions between the wives of exposed and unexposed workers. A subsequent HHE [41]

of male TDNT-exposed workers found no statistically significant differences between exposed and unexposed workers in sperm counts, sperm morphology, fertility, and the rates of spontaneous abortions in their wives. However, the evaluation of male TDA-exposed workers in the same plant showed a statistically significant ($p<0.05$) increase in the number of spontaneous abortions in their wives. Seven area samples analyzed for DNT indicated concentrations in the work areas that ranged from 0.026 to 0.89 mg/m^3. TDA concentrations in area samples from this plant ranged from not detected to 0.687 mg/m^3.

An epidemiologic study to assess reproductive effects in 84 male workers exposed to TDNT and TDA indicated no significant differences between the exposed and 119 unexposed workers in any of the reproductive parameters examined. This assessment included fertility, sperm counts, and sperm morphology for the workers and spontaneous abortions in their wives [42]. In another study to evaluate the fertility of 579 workers employed at three chemical plants producing TDNT and TDA, no statistically significant differences between exposed and unexposed workers were noted [43].

Epidemiologic studies for carcinogenicity in DNT-exposed workers have not been reported.

CONCLUSIONS

The research data presented in this bulletin have focused on the mutagenic, carcinogenic, and adverse reproductive effects produced in animals exposed to TDNT or the DNT isomers.

TDNT and the six isomers of DNT have been shown to be mutagens using *in vitro* assay methods. When these compounds were tested as tumor initiators, only TDNT and 2,6-DNT were active. However, in tumor promotion studies using TDNT, 2,6-DNT, or 2,4-DNT, all three compounds were promotors. These data indicate that 2,4-DNT acts as a promotor only, while TDNT and 2,6-DNT can act as both initiators and promotors.

Animal studies indicate a potential for carcinogenicity from exposure to TDNT or 2,6-DNT. The liver, bile duct, mammary glands, kidneys, and subcutaneous tissue are the primary sites identified with carcinogenic or tumorigenic responses. Studies on the metabolism of DNT indicate that the carcinogenic potential appears to be dependent upon a three-stage metabolic activation of the compound. Although the primary routes of worker exposure are through inhalation and dermal contact rather than the oral route used in animal studies, DNT absorbed from any site of administration is transferred to the liver for the initial stage of metabolism. The DNT metabolite produced in this initial stage of metabolism is thought to undergo gastrointestinal bacterial nitro-reduction with subsequent further activation in the liver to a genotoxic metabolite(s).

A 2,4-DNT carcinogenicity experiment has demonstrated that this isomer may have a tumorigenic capacity in animals. In addition, the types of tumors produced and the target tissues affected in this experiment are the same as those identified in the TDNT or 2,6-DNT studies. Data adequate to permit evaluation of the carcinogenic potential from exposure to the 2,3-; 2,5-; 3,4-; and 3,5-DNT isomers are not available.

Epidemiologic studies of carcinogenicity in humans exposed to TDNT or the DNT isomers have not been reported.

Data from animal studies using TDNT or 2,6-DNT which show reduced spermatogenesis, aspermatogenesis, or testicular atrophy in exposed dogs, rats, and mice and nonfunctioning ovaries in TDNT-exposed mice indicate a potential for adverse reproductive effects from exposure to these compounds. No animal reproductive data have been published for the other DNT isomers. Results from studies of reproductive effects from human exposure to TDNT are equivocal.

The studies which indicate the potential for these compounds to induce cancer and adverse reproductive effects in experimental animals are not without their shortcomings. The strains of animals used, the route and doses selected for administration of the test compounds, and the short duration of several studies impose limitations on the interpretation of the results. However, NIOSH believes that the collective toxicologic data on metabolism, mutagenicity, carcinogenicity, and reproductive effects provide sufficient evidence to warrant concern for adverse health effects from occupational exposure to TDNT or 2,6-DNT. Although there is limited evidence indicating that 2,4-DNT poses a risk to human health, the existing animal and in vitro data are suggestive of such a potential.

RECOMMENDATIONS

There are several classifications for identifying a substance as a carcinogen. Such classifications have been developed by the National Toxicology Program (NTP) [44], the International Agency for Research on Cancer (IARC) [45], and OSHA in its "Identification, Classification, and Regulation of Potential Occupational Carcinogens" 29 CFR 1990 [46], also known as "The OSHA Cancer Policy" [47]. NIOSH considers the OSHA classification the most appropriate for use in identifying potential occupational carcinogens* [48]. Since exposure to TDNT or 2,6-DNT has been

*"'Potential occupational carcinogen' means any substance, or combination or mixture of substances, which causes an increased incidence of benign and/or malignant neoplasms, or a substantial decrease in the latency period between exposure and onset of neoplasms in humans or in one or more experimental mammalian species as the result of any oral, respiratory or dermal exposure, or any other exposure which results in the induction of tumors at a site other than the site of administration. This definition also includes any substance which is metabolized into one or more potential occupational carcinogens by mammals" (29 CFR 1990.103).

shown to produce malignant tumors in rats and mice, they meet the OSHA criteria. Therefore, NIOSH recommends that the technical grade mixtures of DNT (TDNT) and the 2,6- isomer of DNT be considered potential human carcinogens in the workplace. In addition, a reproductive hazard may exist for workers exposed to TDNT or 2,6-DNT. Testicular atrophy, decreased spermatogenesis, or aspermatogenesis seen in three species of experimental animals exposed to TDNT or 2,6-DNT and nonfunctioning ovaries in mice exposed to TDNT form the basis for this concern.

The excess risk of cancer and of adverse reproductive effects in workers exposed to specific airborne concentrations of TDNT or 2,6-DNT and the potential of the other DNT isomers to induce these adverse health effects have not yet been precisely determined. However, the probability of developing such effects would be decreased by reducing exposure. As prudent public health policy, employers should voluntarily assess the conditions under which workers may be exposed to TDNT or the isomers of DNT and take all reasonable precautions to reduce exposure to the fullest feasible extent.

Research is needed to definitively clarify the sequence of events and the role of gastrointestinal bacteria in the reported metabolic pathway for DNT and the associated mutagenic and carcinogenic effects. In addition, animal and epidemiologic research is necessary to further assess the carcinogenic, mutagenic, and adverse reproductive effects observed in animals exposed to TDNT or a specific DNT isomer and the potential for similar effects in workers exposed to TDNT or a DNT isomer. Such studies should use pure isomers of DNT as well as a technical grade mixture.

Guidelines recommended in the Appendix for minimizing worker exposure to DNT are general in nature and should be adapted to specific work situations as required.

REFERENCES

1. Weast RC (ed): CRC Handbook of Chemistry and Physics - A Ready Reference Book of Chemical and Physical Data. Sixty-Fourth Edition. The Chemical Rubber Company, Boca Raton, Florida, pp. C-542 - C-543 (1983-1984).

2. Hawley GG (ed): The Condensed Chemical Dictionary. Tenth Edition. Van Nostrand Reinhold Company, New York, p. 375 (1981).

3. Chemical Manufacturers Association: Comments of the CMA toluenediamines panel on EPA's ANPR for phenylenediamines under section 4 of TSCA. Washington, DC, Docket No. OPTS-42008, pp. 49 (1982).

4. Chemical Economics Handbook: Toluene. SRI International, Menlo Park, California, p. 300.7202 I (1979).

5. Smith, HJ: Written communication to NIOSH on the NIOSH Special Hazard Review of Dinitrotoluenes. Air Products and Chemicals, Inc., Allentown, Pennsylvania (July 1, 1982).

6. Synthetic Organic Chemicals: United States Production and Sales, 1982 (Investigation No. 332-135) USITC Publication 1422, p. 27, U.S. Government Printing Office, Washington, DC (1983).

7. Coleman LC: Written communication to NIOSH submitted to Department of the Army by Gardner CC of Hercules Incorporated, Radford Army Ammunition Plant, Radford, Virginia (June 28, 1984).

8. Code of Federal Regulations, U.S. Department of Labor, Occupational Safety and Health Administration, 29 CFR 1910.1000, Table Z-1, pp. 660-664 (1983).

9. American Conference of Governmental Industrial Hygienists: Threshold Limit Values of Air-borne Contaminants for 1968, Recommended and Intended Changes. ACGIH, Cincinnati, Ohio (1968).

10. American Conference of Governmental Industrial Hygienists: TLVs® Threshold Limit Values for Chemical Substances and Physical Agents in the Work Environment and Biological Exposure Indices with Intended Changes for 1984-85. ACGIH, Cincinnati, Ohio (1984).

11. Dean JA (ed): Lange's Handbook of Chemistry. Twelfth Edition. McGraw Hill, New York, pp. 7-198 to 7-199 (1979).

12. American Conference of Governmental Industrial Hygienists, Inc.: Documentation of the Threshold Limit Values. Fourth Edition. Cincinnati, Ohio, pp. 153-154 (1980).

13. Lee CC, Dilley JV, Hodgson JR, et al.: Mammalian toxicity of munition compounds: Phase I. Acute oral toxicity, primary skin and eye irritation, dermal sensitization, and disposition and metabolism. Report No. 1. Midwest Research Institute Project No. 3900-B (1975).

14. Long RM, Rickert DE: Metabolism and excretion of 2,6-dinitro [^{14}C] toluene *in vivo* and in isolated perfused rat livers. Drug Metab Dispos 10(5):455-458 (1982).

15. Rickert DE, Long RM: Metabolism and excretion of 2,4-dinitrotoluene in male and female Fischer 344 rats after different doses. Drug Metab Dispos 9(3):226-232 (1981).

16. Lee CC, Ellis HV III, Kowalski JJ, et al.: Mammalian toxicity of munitions compounds: Phase II. Effects of multiple doses. Part II: 2,4-Dinitrotoluene. Report No. 3. Midwest Research Institute Project No. 3900-B (1976).

17. Rickert DE, Butterworth BE, Popp JA: Dinitrotoluene: Acute toxicity, oncogenicity, genotoxicity, and metabolism. CRC Crit Rev Toxicol 13:(3) 217-234 (1984).

18. Guest D, Schnell SR, Rickert DE, Dent JG: Metabolism of 2,4-dinitrotoluene by intestinal microorganisms from rat, mouse, and man. Toxicol Appl Pharm 64:160-168 (1982).

19. Rickert DE, Schnell SR, Long RM: Hepatic macromolecular covalent binding and intestinal disposition of [^{14}C] dinitrotoluenes. Toxicol Environ Health 11:555-567 (1983).

20. Couch DB, Allen PF, Abernethy DJ: The mutagenicity of dinitrotoluenes in Salmonella typhimurium. Mutat Res 90:373-383 (1981).

21. Spanggord RJ, Mortelmans KE, Griffin AF, Simmon VF: Mutagenicity in Salmonella typhimurium and structure-activity relationships of wastewater components emanating from the manufacture of trinitrotoluene. Environ Mutagen 4:163-179 (1982).

22. Tokiwa H, Nakagawa R, Ohnishi Y: Mutagenic assay of aromatic nitro compounds with Salmonella typhimurium. Mutat Res 91:321-325 (1981).

23. Lee CC, Ellis HV III, Kowalski JJ, et al.: Mammalian toxicity of munitions compounds: Phase II. Effects of multiple doses. Part III: 2,6-Dinitrotoluene. Report No. 4. Midwest Research Institute Project No. 3900-B (1976).

24. Abernethy DJ, Couch DB: Cytotoxicity and mutagenicity of dinitrotoluenes in Chinese hamster ovary cells. Mutat Res 103:53-59 (1982).

25. Bermudez E, Tillery D, Butterworth BE: The effect of 2,4-diaminotoluene and isomers of dinitrotoluene on unscheduled DNA synthesis in primary rat hepatocytes. Environ Mutagen 1:391-398 (1979).

26. Mirsalis JC, Hamm TE Jr, Sherrill JM, Butterworth BE: Role of gut flora in the genotoxicity of dinitrotoluene. Nature 295:322-323 (1982).

27. Mirsalis JC, Butterworth BE: Induction of unscheduled DNA synthesis in rat hepatocytes following in vivo treatment with dinitrotoluene. Carcinogenesis 3:241-245 (1982).

28. Popp JA, Leonard TB: The use of in vivo hepatic initiation-promotion systems in understanding the hepatocarcinogenesis of technical grade dinitrotoluene. Toxicol Pathol 10(2):190-196 (1982).

29. Leonard TB, Lyght O, Popp JA: Dinitrotoluene structure dependent initiation of hepatocytes in vivo. Carcinogenesis 4(8):1059-1061 (1983).

30. Chemical Industry Institute of Toxicology: 104-Week Chronic Toxicity Study in Rats - Dinitrotoluene. Final Report, Volume I of II. CIIT Docket No. 12362. Research Triangle Institute, Research Triangle Park, North Carolina (1982).

31. Ellis HV III, Hagensen JH, Hodgson JR, et al.: Mammalian toxicity of munitions compounds: Phase III. Effects of life-time exposure. Part I: 2,4- dinitrotoluene. Final report No. 7. Midwest Research Institute Project No. 3900-B (1979).

32. Popp JA, Leonard TB: Hepatocarcinogenicity of 2,6-dinitrotoluene (DNT). Proc Am Assoc Cancer Res 24:361 (1983).

33. Jameson, CW: Written communication to NIOSH on the chemical analysis of 2,4-dinitrotoluene. National Institute of Environmental Health Sciences (October 22, 1984).

34. National Cancer Institute: Bioassay of 2,4-dinitrotoluene for possible carcinogenicity. DHEW (NIH) Publication No. 78-1360. U.S. Department of Health, Education, and Welfare, Public Health Service, National Institutes of Health, National Cancer Institute Carcinogenesis Technical Report Series No. 54 (1978).

35. Haseman JK: Written communication to NIOSH on control tumor incidences in F-344 rats. National Institute of Environmental Health Sciences (March 12, 1985).

36. Jones-Price C, Marks TA, Ledoux TA, Reel JR, Langhoff-Paschke L, Wolkowski-Tyl R,: Teratological and postnatal evaluation of dinitrotoluene in Fischer 344 rats. CIIT Docket No. 10992. Research Triangle Institute, Research Triangle Park, North Carolina (1982).

37. Proctor NH, Hughes JP: Chemical Hazards of the Workplace. J B Lippincott Company, Philadelphia, pp 233-235 (1978).

38. Key M, et al. (ed): Occupational Diseases, A Guide to Their Recognition. DHEW (NIOSH) Publication No. 77-181. Revised Edition. U.S. Department of Health, Education, and Welfare, Public Health Service, Center for Disease Control, National Institute for Occupational Safety and Health, pp. 278-279 (1977).

39. Ahrenholz SA, Meyer CR: Health Hazard Evaluation Determination Report No. 79-113-728, Olin Chemical Company, Brandenburg, Kentucky. U.S. Department of Health and Human Services, Public Health Service, Center for Disease Control, National Institute for Occupational Safety and Health, Cincinnati, Ohio (1980).

40. Ahrenholz SA, Meyer CR: Health Hazard Evaluation Determination Interim Report No. 1, 81-118, Mobay Chemical Corporation, New Martinsville, West Virginia. U.S. Department of Health, Education, and Welfare, Public Health Service, Centers for Disease Control, National Institute for Occupational Safety and Health, Cincinnati, Ohio (1980).

41. Ahrenholz SA, Meyer CR: Health Hazard Evaluation Determination Report No. 81-295-1155, Olin Chemical Company, Moundsville, West Virginia. U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control, National Institute for Occupational Safety and Health, Cincinnati, Ohio (1982).

42. Hamill PVV, Steinberger E, Levine RJ, et al: The epidemiologic assessment of male reproductive hazard from occupational exposure to TDA and DNT. J Occup Med 24(12):985-993 (1982).

43. Levine RJ, Dal Corso RD, Blunden PB: Fertility of workers exposed to dinitrotoluene and toluene diamine at three chemical plants. In: Rickert DE (ed): Toxicity of Nitroaromatic Compounds. Hemisphere Publishing Corp., New York, pp. 243-254 (1985).

44. National Toxicology Program: Technical Report on the Toxicology and Carcinogenesis Studies of 1,3-Butadiene (CAS No. 106-99-0) in B6C3F$_1$, Mice (Inhalation Studies). U.S. Department of Health and Human Services, Public Health Service, National Institutes of Health Publication No. 84-2544 (August 1984).

45. World Health Organization: IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. IARC Monographs, Volumes 1-20, Supplement 1 (1979).

46. Code of Federal Regulations, U.S. Department of Labor, Occupational Safety and Health Administration, 29 CFR 1990 (July 1, 1984).

47. Code of Federal Regulations, U.S. Department of Labor, Occupational Safety and Health Administration, 29 CFR 1990.101 (July 1, 1984).

48. Code of Federal Regulations, U.S. Department of Labor, Occupational Safety and Health Administration, 29 CFR 1990.103 (July 1, 1984).

49. Leidel NA, Busch KA, Lynch JR: Occupational Exposure Sampling Strategy Manual. DHEW (NIOSH) Publication No. 77-173. U.S. Department of Health, Education, and Welfare, Public Health Service, Center for Disease Control, National Institute for Occupational Safety and Health, Cincinnati, Ohio (1977).

50. NIOSH Manual of Analytical Methods. Second Edition. DHEW (NIOSH) Publication No. 78-175 Volume 4, pp. S215-1 to S215-7. U.S. Department of Health, Education, and Welfare, Public Health Service, Center for Disease Control, National Institute for Occupational Safety and Health, Cincinnati, Ohio (1978).

51. Hagopian JH, Bastress EK: Recommended Industrial Ventilation Guidelines. DHEW (NIOSH) Publication No. 76-162. U.S. Department of Health, Education, and Welfare, Public Health Service, Center for Disease Control, National Institute for Occupational Safety and Health, Cincinnati, Ohio (1976).

52. Industrial Ventilation--A Manual of Recommended Practice. Eighteenth Edition. American Conference of Governmental Industrial Hygienists, Cincinnati, Ohio, pp. 2-1 to 14-1 (1984).

53. American National Standard: Fundamentals Governing the Design and Operation of Local Exhaust Systems, ANSI Z9.2-1979. American National Standards Institute, Inc., New York (1979).

54. Summary Plant Observation Report and Evaluation. (submitted to NIOSH under Contract No. 210-78-0017) JRB Associates, Inc., McLean, Virginia (1979).

55. Steere NV (ed): Handbook of Laboratory Safety. Second Edition. The Chemical Rubber Company, Cleveland, Ohio, pp. 128-129, 133-136 (1971).

56. Code of Federal Regulations, U.S. Department of Labor, Occupational Safety and Health Administration, 29 CFR 1910.134 (1983).

APPENDIX

GUIDELINES FOR MINIMIZING WORKER EXPOSURE TO DINITROTOLUENE

It is recommended that the technical grade mixtures of dinitrotoluene (TDNT) and the 2,6- isomer of dinitrotoluene (2,6-DNT) be regarded as potential human carcinogens in the workplace and possible inducers of adverse reproductive effects. These recommendations are based on animal studies which demonstrated carcinogenicity and adverse reproductive effects. Although there is limited evidence indicating that the 2,4- isomer of dinitrotoluene (2,4-DNT) poses a risk to human health, the existing animal and in vitro data are suggestive of such a potential. Consequently, appropriate engineering and work-practice controls should be used to reduce worker exposure to TDNT and all the isomers of dinitrotoluene (DNT) to the fullest feasible extent. The area in which TDNT or the isomers of DNT are used should be restricted to only those workers essential to the process or operation. The guidelines below are general in nature and should be adapted to specific work situations as required.

EXPOSURE MONITORING

Initial and periodic worker exposure surveys should be made by qualified industrial hygiene personnel. These surveys are necessary to determine the extent of worker exposure and to ensure that controls already in place are operational and effective. The NIOSH Occupational Exposure Sampling Strategy Manual may be helpful in developing efficient programs to monitor worker exposure to DNT [49]. The manual discusses how to determine the need for exposure measurements and how to select sampling times.

Worker exposures should be estimated by 8-hour or other full shift TWA and short-term (15-minute) exposures calculated from personal or breathing zone samples. Short-term samples should be taken during periods of maximum expected exposure by using all available knowledge of the work areas, procedures, and processes. Area and personal measurements may be useful in identifying sources of exposure at processes and operations.

A detailed analytical method for DNT is in the NIOSH Manual of Analytical Methods, Second Edition [50].

CONTROLLING WORKER EXPOSURE

Proper maintenance procedures and worker education are all vital aspects of a good control program. Workers should be informed of the materials to which they are exposed, the nature of their hazard, the methods for their control, and appropriate personal hygiene procedures. There are three basic methods of limiting worker exposure to DNT. Careful planning and thought should precede implementation.

Contaminant Controls

Engineering controls should be used to eliminate the potential for DNT exposure in the workplace and to prevent fires and explosions. Achieving and maintaining reduced concentrations of airborne DNT in the workplace depend upon the implementation of engineering control measures, such as properly constructed and maintained closed system operations and ventilation, with appropriate safety designs.

Closed system operations provide the most effective means for minimizing worker exposures to DNT. Closed system equipment should be used for manufacturing, storing, and processing DNT. Where closed systems cannot be employed or do not effectively control DNT emissions, local exhaust ventilation should be provided to direct dust, vapors, and gases away from workers and to prevent the recirculation of contaminated exhaust air. Exhaust ventilation systems for quality control laboratories or laboratories where samples are prepared for analyses should be designed to adequately capture and contain DNT dust, vapors, or gases. Special consideration should be given to the releasing of these compounds from pressurized sampling containers. Guidance for designing local exhaust ventilation systems can be found in Recommended Industrial Ventilation Guidelines [51], Industrial Ventilation--A Manual of Recommended Practice [52], and Fundamentals Governing the Design and Operation of Local Exhaust Systems, ANSI Z9.2-1979 [53].

Ventilation equipment should be checked at least every 3 months to ensure adequate performance. System effectiveness should also be checked when there are any changes in production, process, or control that might result in significant increases in airborne exposure to DNT.

Worker Isolation

If feasible, workers may be isolated from direct contact with the work environment by the use of automated equipment operated from a closed control booth or room. The control room should be maintained at a greater air pressure than that surrounding the process equipment so that air flows out of, rather than into, the room. This type of control will not protect workers who must perform process checks, adjustments, maintenance, and related operations. Therefore, special precautions are often necessary to prevent or limit worker exposure in these situations and frequently involve the use of personal protective equipment.

Personal Protective Equipment

Workers should prevent direct skin contact with DNT by wearing fully encapsulating protective clothing made of butyl rubber, which has proven to be an effective barrier against DNT [54,55]. Any clothing that becomes contaminated with DNT should be removed and discarded or cleaned before

re-use. Areas of the body which come in contact with DNT should be thoroughly washed with soap and water. As a general hygienic measure, facilities (e.g., change rooms, showers, etc.) for personal cleanliness should be provided.

The use of respiratory protection requires that a respiratory protection program be instituted which at a minimum meets the requirements of 29 CFR 1910.134 [56]. In addition to selection of respirators approved by the Mine Safety and Health Administration (MSHA) and by NIOSH, a complete respiratory protection program should include at least regular training of personnel, fit testing, periodic environmental monitoring, and maintenance, inspection, and cleaning of equipment. The program should be evaluated regularly.

It must be stressed that the use of respiratory protection is the least preferred method of controlling worker exposures and should not be used as the only means of preventing or minimizing exposures during routine operations. However, NIOSH recognizes that respirators may be required to provide protection under certain situations such as implementation of engineering controls, certain short-duration maintenance procedures, and emergencies. NIOSH maintains that only the most protective respirators should be used to protect workers from exposure to workplace carcinogens. Therefore, the following respirators are recommended for these situations:

- A self-contained breathing apparatus with a full facepiece operated in pressure-demand or other positive pressure mode or

- A combination respirator that includes a supplied-air respirator with a full facepiece operated in pressure-demand or other positive pressure mode and an auxiliary self-contained breathing apparatus operated in pressure-demand or other positive pressure mode.

MEDICAL SURVEILLANCE

A medical surveillance program should be made available that can evaluate both the acute and chronic effects of DNT exposure. The physician responsible should be provided with information concerning the adverse effects from exposure to DNT and an estimate of the worker's potential exposure to DNT, including any available workplace sampling results and a description of any protective devices or equipment the worker may be required to use. A medical and work history should be taken initially and updated periodically. As part of this medical surveillance program, workers who are or may be exposed to DNT should have preplacement and periodic evaluations focusing on the history of previous exposure to DNT and other toxic agents. The examining physician should direct particular attention to the urinary, respiratory, and nervous systems; blood; liver; and skin as these are the most likely targets of exposure to DNT.

CUMULATIVE LIST OF NIOSH CURRENT INTELLIGENCE BULLETINS

1.	Chloroprene	- January 20, 1975
2.	Trichloroethylene (TCE)	- June 6, 1975
3.	Ethylene Dibromide (EDB)	- July 7, 1975
4.	Chrome Pigment	- June 24, 1975
		- October 7, 1975
		- October 8, 1976
5.	Asbestos - Asbestos Exposure during Servicing of Motor Vehicle Brake and Clutch Assemblies	- August 8, 1975
6.	Hexamethylphosphoric Triamide (HMPA)	- October 24, 1975
7.	Polychlorinated Biphenyls (PCB's)	- November 3, 1975
		- August 20, 1976
8.	4,4'-Diaminodiphenylmethane (DDM)	- January 30, 1976
9.	Chloroform	- March 15, 1976
10.	Radon Daughters	- May 11, 1976
11.	Dimethylcarbamoyl Chloride (DMCC) Revised	- July 7, 1976
12.	Diethylcarbamoyl Chloride (DECC)	- July 7, 1976
13.	Explosive Azide Hazard	- August 16, 1976
14.	Inorganic Arsenic - Respiratory Protection	- September 27, 1976
15.	Nitrosamines in Cutting Fluids	- October 6, 1976
16.	Metabolic Precursors of a Known Human Carcinogen, Beta-Naphthylamine	- December 17, 1976
17.	2-Nitropropane	- April 25, 1977
18.	Acrylonitrile	- July 1, 1977
19.	2,4-Diaminoanisole in Hair and Fur Dyes	- January 13, 1978
20.	Tetrachloroethylene (Perchloroethylene)	- January 20, 1978
21.	Trimellitic Anhydride (TMA)	- February 3, 1978
22.	Ethylene Thiourea (ETU)	- April 11, 1978
23.	Ethylene Dibromide and Disulfiram Toxic Interaction	- April 11, 1978
24.	Direct Black 38, Direct Blue 6, and Direct Brown 95 Benzidine Derived Dyes	- April 17, 1978
25.	Ethylene Dichloride (1,2-Dichloroethane)	- April 19, 1978
26.	NIAX Catalyst ESN	- May 22, 1978
27.	Chloroethanes - Review of Toxicity	- August 21, 1978
28.	Vinyl Halides - Carcinogenicity	- September 21, 1978
29.	Glycidyl Ethers	- October 12, 1978
30.	Epichlorohydrin	- October 12, 1978
31.	Adverse Health Effects of Smoking and the Occupational Environment	- February 5, 1979
32.	Arsine (Arsenic Hydride) Poisoning in the Workplace	- August 3, 1979

CUMULATIVE LIST OF NIOSH CURRENT INTELLIGENCE BULLETINS (CONTINUED)

33.	Radiofrequency (RF) Sealers and Heaters: Potential Health Hazards and Their Prevention	- December 4, 1979
34.	Formaldehyde: Evidence of Carcinogenicity	- April 15, 1981
35.	Ethylene Oxide (EtO): Evidence of Carcinogenicity	- May 22, 1981
36.	Silica Flour: Silicosis	- June 30, 1981
37.	Ethylene Dibromide (EDB) Revised	- October 26, 1981
38.	Vibration Syndrome	- March 29, 1983
39.	The Glycol Ethers, with Particular Reference to 2-Methoxyethanol and 2-Ethoxyethanol: Evidence of Adverse Reproductive Effects	- May 2, 1983
40.	2,3,7,8-Tetrachlorodibenzo-p-dioxin (TCDD, "Dioxin")	- January 23, 1984
41.	1,3-Butadiene	- February 9, 1984
42.	Cadmium	- September 27, 1984
43.	Monohalomethanes: Methyl Chloride Methyl Bromide Methyl Iodide	- September 27, 1984
44.	Dinitrotoluenes (DNT)	- July 5, 1985

NOTE: For the convenience of those who desire a complete series of Current Intelligence Bulletins, #1 through #18 and #19 through #30 have been reprinted as NIOSH publications #78-127 and #79-146, respectively. These publications and single copies of Bulletins #31 and higher are available from Publications Dissemination, DSDTT; National Institute for Occupational Safety and Health; 4676 Columbia Parkway; Cincinnati, Ohio 45226; (513) 841-4287.

☆ U.S. GOVERNMENT PRINTING OFFICE:1985--559-112/10955

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
CENTERS FOR DISEASE CONTROL
NATIONAL INSTITUTE FOR OCCUPATIONAL SAFETY AND HEALTH
ROBERT A. TAFT LABORATORIES
4676 COLUMBIA PARKWAY, CINCINNATI, OHIO 45226

Third Class Mail

DHHS (NIOSH) Publication No. 85-109