Evidence available for prioritization of *N,N* – Dimethylformamide and 2,4,6-Trinitrotoluene

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Available evidence for consideration

- Epidemiological data
  - — identified during human data screen
- Animal carcinogenicity data
- Other relevant data

N,N – Dimethylformamide: Epidemiological data – Introduction

- *N,N* – Dimethylformamide (DMF) is a solvent used in fabric and fiber production, industrial paint stripping and other solvent applications
- Available human studies include three types of occupationally exposed groups:
  - — Aircraft repairmen
  - — Leather tanners
  - — Workers in DMF production and use facilities

N,N – Dimethylformamide: Epidemiological data

DMF human studies

- Testicular cancer
  - Cluster investigation of repairmen of F4 aircraft: Ducatman *et al.* (1986)
  - Case series in leather tanners: Levin *et al.* (1987)
  - Case-control study in leather tanners: Frumin *et al.* (1989)
  - Cohort study in leather tanners: Frumin *et al.* (1989); Calvert *et al.* (1990)
- Range of cancers in workers in DMF production and use facilities
  - Case-control study: Walraith *et al.* (1989)
  - Cohort study: Chen *et al.* (1988)

N,N – Dimethylformamide
Animal carcinogenicity data

Two year inhalation bioassays

- F344/DuCrj (SPF) rats: Senoh *et al.* (2004)
- Crj:BDF1 (SPF) mice: Senoh *et al.* (2004)

Eighteen month inhalation bioassays

- Crl:CD BR rats: Malley *et al.* (1994)
- Crl:CD-1 (ICR)BR mice: Malley *et al.* (1994)

N,N – Dimethylformamide
Other relevant data

Genotoxicity

- IARC (1999) summary of effects in human and experimental systems

Reviews

- IARC (1999)

Discussion

Committee recommendations regarding next steps on *N,N* – Dimethylformamide

2,4,6-Trinitrotoluene
Epidemiological data – Introduction

- 2,4,6-Trinitrotoluene (TNT) is an explosive, used in military and industrial applications. Exposure may occur during production, in manufacture and loading of munitions, during blasting operations, and from water or soil contaminated by discarded munitions or manufacturing waste.

- Available human studies include two types of exposed groups:
  - Residential exposure to contaminated soil and water
  - Factory workers making ordnance

2,4,6-Trinitrotoluene Epidemiological data

TNT human studies

- Leukemia – residentially exposed
  - —Case-control study: Kilian *et al.* (2001)
  - —Descriptive study: Kolb *et al.* (1993)
- Hematological abnormalities – ordnance workers
  - — Case-control study: West and Stafford (1997)

2,4,6-Trinitrotoluene
Animal carcinogenicity data

Two-year bioassays of TNT in diet

- Fischer 344 rats: Army (1984a)
- B6C3F1 mice: Army (1984b)

2,4,6-Trinitrotoluene
Other relevant data - Genotoxicity

Genotoxicity evidence

- IARC (1996) summary
- Frameshift mutagen in *Salmonella* strain TA-98 & TA100: Won *et al.*, 1976; Tan *et al.*, 1992
- Mouse lymphoma gene mutation assay: Styles and Cross, 1983
- Chinese hamster ovary cell mutation assay: Kennel *et al.*, 2000
- Chromosomal aberrations in exposed workers carrying the *NAT1* rapid acetylator genotype: Sabbioni et al., 2007

2,4,6-Trinitrotoluene
Other relevant data

Hemoglobin adducts in exposed workers

- Health effects (Sabbioni *et al.*, 2005)
- Biomarkers of exposure (Liu *et al.*, 1995; Sabbioni et al., 2006)

Reviews

- Bolt *et al.* (2006)
- IARC (1996)

Discussion

Committee recommendations regarding next steps on 2,4,6-Trinitrotoluene