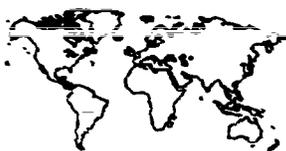


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Chemical Category		POLYMERIC DIPHENYLMETHANE DIISOCYANATE			

A 03



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INTERNATIONAL ISOCYANATE INSTITUTE, INC.

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April 26, 2000

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Attn: 8(e) Coordinator

RE: Polymeric diphenylmethane diisocyanate
9016-87-9

Dear Sir/Madam:

The following information is being submitted by the International Isocyanate Institute (III) on behalf of its members¹ pursuant to current guidance issued by EPA indicating EPA's interpretation of Section 8 (e) of the Toxic Substance Control Act. Neither III nor any member of III has made a determination as to whether a significant risk of injury to health or the environment is actually presented by the findings.

The report enclosed, III Ref 11377, Polymeric MDI: Feasibility generation study, by J. D. Kilgour was recently issued by the III Scientific Office. The study was conducted to determine whether a respirable atmosphere of MDI at concentrations greater than 2 mg/liter could be generated under laboratory conditions. The study indicated that it was feasible, and the one rat that was exposed to 2.48 mg/liter for one hour was killed humanely on the day after exposure to prevent suffering. Generating this atmosphere required sophisticated laboratory equipment, and therefore, the study may be of limited relevance to any non-laboratory exposure scenario.

Sincerely,

M.J. Blankenship
Managing Director



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- cc: J. Chapman
- D. Gilbert
- J. Jadlocki
- J. Lyon
- T. Landry
- R. Robert
- M. Spence

Contain NO CBI

¹ BASF Corporation, Bayer Corporation, Dow Chemical Company, Huntsman, and Lyondell Chemical

A 04

III Project 173

iii ref. 11577

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Polymeric MDI: Feasibility generation study

**Author
J D Kilgour**

**Central Toxicology Laboratory
Macclesfield
Cheshire
UK**

April 2000

Number of pages: 6

III Report

International Isocyanate Institute Inc.

The Scientific Office, Bridgewater House, Whitworth Street, Manchester M1 6LI.



The Scientific Office of the International Isocyanate Institute Inc.,
Bridgewater House, Whitworth Street, Manchester M1 6LI.

**CENTRAL TOXICOLOGY LABORATORY
ALDERLEY PARK MACCLESFIELD
CHESHIRE UK**

CTL/HR2365/SUMMARY REPORT
**POLYMERIC MDI: FEASIBILITY GENERATION
STUDY**

STUDY DETAILS

Sponsor:	International Isocyanate Institute Inc. Scientific Office, Floor 9, Bridgewater House, Whitworth Street, Manchester M1 6LT
Sponsor Reference:	CO9183
CTL Test Substance Reference Number:	Y00122/021
CTL Study Number:	HR2365
Document Number:	CTL/HR2365/SUM/REPT

AUTHOR

Dr J D Kilgour

DATE OF ISSUE

11-Apr-2000

1. INTRODUCTION

The purpose of this study was to determine the feasibility of generating an aerosol of polymeric MDI at a target concentration of $\geq 2\text{mg/l}$ and to measure the gravimetric concentration and particle size distribution of the trial atmosphere. If a suitable atmosphere was generated, a 1 hour trial exposure of one animal would be conducted. This study was conducted for purposes of classification issues raised by the Fire Marshalls of the United States.

2. TEST SUBSTANCE

Name	Polymeric MDI
Source	Huntsman ICI Polyurethanes (UK) Limited
Colour	Dark brown
Physical state	Liquid
Batch number	6032
Viscosity (mPa s)	220 approx (at 25°C)
CTL test substance reference number	Y00122/025
Purity (%w/w)	Not specified
Storage conditions	Ambient temperature in the dark. Once opened, containers should be overlaid with an inert gas to prevent exposure to air/moisture.
Stability	Not specified

3. EXPERIMENTAL PROCEDURES

3.1 Atmosphere generation

3.1.1 Trial generation

Two trial generations were conducted; the first to determine the appropriate generation systems and conditions, to confirm whether the target concentration could be achieved, and to provide information on particle size distribution of the aerosol; the second to assess reproducibility, and since the target concentration was achieved, to allow exposure of one animal for a period of one hour.

3.1.2 Generation conditions

The test atmosphere was generated using a glass concentric - jet atomiser. The test substance was pumped to the atomiser using a peristaltic pump supplied by Watson Marlow. Clean, dry air (dried and filtered using equipment supplied by Atlas-Copco, Sweden) was passed through the atomiser at a nominal flow rate of 8 l/minute (at 20 PSI) and carried the atmosphere to the exposure chamber, having an internal volume of 27.6 litres, in order to achieve a minimum of 12 air changes per hour. Since diluting air was not employed, the flow rate through the exposure chamber was the same as that employed in the generation of the test atmosphere. Air flows were monitored continuously and recorded at least 3 times using variable area flowmeters (KDG Flowmeters, Burgess Hill, Sussex, UK) and were altered as necessary to maintain the target concentration.

3.1.3 Particulate concentration

The particulate concentration of the test atmosphere, close to the animals' breathing zone, was measured gravimetrically 8 times during the 1st trial generation, and 4 times during exposure on the 2nd trial. This was done by drawing the test atmosphere, at a known flow rate, for a known time, through a 25mm diameter, polyvinyl chloride (PVC) GLA 5000 filter housed in a Delrin open-faced filter holder (both filters and holders supplied by Gelman Sciences Limited, Northampton, UK). The filter was weighed before and after the sample was taken. The concentration was calculated as follows:

$$\text{Concentration (mg/l)} = \frac{\text{post wt(mg)} - \text{pre wt (mg)}}{\text{time (minutes)} \times \text{airflow (l/minute)}}$$

pre wt = weight of filter prior to sampling

post wt = weight of filter after sampling

3.1.4 Aerodynamic particle size distribution

The aerodynamic particle size distribution was measured twice during the 1st trial, and once during the exposure period of the 2nd trial. Particle size distribution was measured using a Marple Cascade Impactor (supplied by Schaeffer Instruments, Wantage, Oxon., UK) which aerodynamically separated airborne particles into pre-determined size ranges. The amount of aerosol, by weight, in each size range, was then used to calculate the aerodynamic particle size distribution of the aerosol. Using a microcomputer, the data were transformed using a log/probit transform and a linear regression derived from the cumulative data.

Using this regression line, the mass median aerodynamic diameter (MMAD) and geometric standard deviation (GSD) were calculated.

3.1.5 Trial exposure

A single male Alpk:AP_{SD}, (Wistar-derived) rat, obtained from the Rodent Breeding Unit, Alderley Park, Macclesfield, Cheshire, UK, was exposed, nose only, to the test atmosphere. (The rat was 10-11 weeks old, weighed 425g and had been acclimatised to the environment at CTL for 4 weeks at the time of exposure). Clinical observations were recorded during and immediately after exposure. Bodyweight was recorded on day -1 and the day of termination.

4. RESULTS

1st trial: Conducted on 6 January 2000

The achieved test atmosphere had the following characteristics:

Target Concentration mg/l	Aerosol Concentration mg/l	MMAD* μm	GSD*
≥ 2	2.38 ± 0.10	2.63, 2.34	1.70, 1.72

Concentration given as mean \pm SD, (n=8)

* Mass Median Aerodynamic Diameter (μm)
Geometric Standard Deviation

2nd trial conducted (to assess reproducibility) on 7 January 2000

The achieved test atmosphere had the following characteristics:

Target Concentration mg/l	Aerosol Concentration mg/l	MMAD* μm	GSD*
≥ 2	2.48 ± 0.06	2.86	1.72

Concentration given as mean \pm SD, (n=4)

* Mass Median Aerodynamic Diameter (μm)
Geometric Standard Deviation

In both trials, the atmospheres were acceptably stable and the total mass concentrations obtained by cascade impactors were consistent with atmosphere concentrations determined gravimetrically by filter samples.

During the second trial, a single male rat was exposed for 1 hour in order to assess the potential hazard of exposure to such concentrations of MDI aerosol. The ranges for temperature and relative humidity in the chamber during this time were 19.0-19.8°C and 20-25% respectively. The rat survived the 1 hour exposure period, and showed reduced breathing rate after 52 minutes exposure. Immediately after exposure, clinical signs indicative of respiratory tract irritation were seen (abnormal respiratory noise, breathing rate

reduced and depth increased). Over the following 24 hours, the condition of the animal deteriorated, to the extent that in order to prevent undue suffering, it was killed humanely.

5. CONCLUSION

This study demonstrated that it was feasible to generate a stable aerosol of polymeric MDI of concentration $\geq 2\text{mg/l}$.

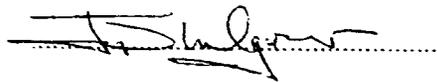
The result of this trial indicates that human exposure to respirable aerosols of MDI at concentrations similar to those tested could result in fatalities.

6. DATA STORAGE

An original report, the study protocol, all raw data, samples and specimens, pertaining to this study are retained in the Archives, Central Toxicology Laboratory (CTL), Alderley Park, Macclesfield, Cheshire, UK.

This study was not commissioned for regulatory submission. It was conducted according to the current version of the UK Principles of GLP (The United Kingdom GLP Regulations) and the OECD Principles of Good Laboratory Practice 1997 (ENV/MC/CHEM(98) 17) except that the study protocol, experimental phases and report were not subject to Quality Assurance audit although the work was conducted using the same facilities and study procedures which are subject to routine inspection under the QA Programme.

Dr J D Kilgour
Study Director



11-Apr-2000
Date