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Chemical Category	POLYMERIC DIPHENYLMETHANE DIISOCYANATE		

A 03



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**INTERNATIONAL ISOCYANATE INSTITUTE, INC.**

201 Main Street, Suite 403 • La Crosse, WI 54601 • 608/796-0880 • FAX 608/796-0882

July 10, 2000

TSCA Document Processing Center (TS-790)  
Office of Toxic Substances  
U.S. Environmental Protection Agency  
401 M Street, SW  
Washington, DC 20460

Attn: 8(e) Coordinator

RE: Polymeric diphenylmethane diisocyanate  
9016-87-9

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Dear Sir/Madam:

Enclosed is a revision to report III Ref 11377, *Polymeric MDI Feasibility generation study*, by J. D. Kilgour. The International Isocyanate Institute on behalf of its members<sup>1</sup> submitted the original report. The acknowledgement 8EHG Number is 8EHQ-00-14714.

The conclusion in the report has been revised as indicated in the letter attached from the study director.

Sincerely,

M.J. Blankenship  
Managing Director

Contain NO CB!

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

MR 37559



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<sup>1</sup> BASF Corporation, Bayer Corporation, Dow Chemical Company, Huntsman, and Lyondell Chemical

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CTL 2000 JUL 14 AM 11:24

Central Toxicology Laboratory  
Alderley Park  
Near Macclesfield  
Cheshire SK10 4TJ  
England  
Tel: +44 (0)1625 582711  
Fax: +44 (0)1625 517314

Dr M Collins  
Gilbert International Limited  
Bridgewater House  
Whitworth Street  
Manchester  
M1 6LT  
UK

Our Ref                      Direct Line                      Direct Fax                      Date 27/06/2000

Dear Dr Collins

**RE: CTL CONTRACT REFERENCE NUMBER CO9183**

**Reason for revision of report CTL/HR2365/SUMMARY REPORT**

The original report contained a comment on potential human health effects of exposure to respirable MDI aerosols. The study design and data generated were inadequate to make such comment for the following reason:

The study was a feasibility study to assess whether respirable polymeric MDI aerosols could be generated under experimental laboratory conditions at concentrations exceeding 2 mg/l. In this context it must be remembered that MDI has a very low vapour pressure (< 0.005 Pa at 20°C). This means that at ambient temperatures MDI vapour concentrations cannot exceed approximately 50 ppb (0.5 mg/m<sup>3</sup>) and the high viscosity of MDI precludes aerosol formation under normal handling or accidental spillage. Inhalation exposure would normally be to the vapour. In order to generate high concentrations of aerosols of MDI requires extremely high energy input into the generation system which can only be done achieved under experimental laboratory conditions and on a small scale. The resultant aerosols are completely artificial and not comparable to potential human exposure under normal use patterns of polymeric MDI. Therefore, a scientific evaluation of this study and the effect of exposure of one rat to such artificial experimental aerosols is judged inadequate to make any conclusion regarding potential effects in man.

Therefore, the report will be re-issued as a revision to the original report, with the comment on the potential human health effects of exposure removed. A reason for the revision will be given in the report, as required by GLP.

I hope these actions can help resolve this matter to your satisfaction, and I apologise for the difficulties encountered so far.

Regards

*Continued...*

Dr J D Kilgour (Study Director)

Dr P M Hext (Senior Toxicologist)

27/6/00  
Date

28 Jun 2000  
Date

**A 05**

**III Project 173**

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**III ref: 11377**

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# **Polymeric MDI: Feasibility generation study**

**Author  
J D Kilgour**

**Central Toxicology Laboratory  
Macclesfield  
Cheshire  
UK**

**June 2000**

**Number of pages: 6**

**A 06**

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

**CTL/HR2365/SUMMARY REPORT/REVISION - 001**

**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:	Y00122/025
CTL Study Number:	HR2365
Document Number:	CTL/HR2365/SUM/RE - 001

**AUTHOR**

Dr J D Kilgour

**DATE OF ISSUE**

26 June 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 Mariow. Clean, dry air (dried and filtered using equipment supplied by Atlas-Copco, Sweden) was passed through the atomiser at a nominal flow rate of 18//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 1<sup>st</sup> trial generation, and 4 times during exposure on the 2<sup>nd</sup> 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 1<sup>st</sup> trial, and once during the exposure period of the 2<sup>nd</sup> 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<sub>2</sub>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

##### 1<sup>st</sup> trial: Conducted on 6 January 2000

The achieved test atmosphere had the following characteristics:

Target Concentration mg/l	Aerosol Concentration mg/l	MMAD* $\mu\text{m}$	GSD*
$\geq 2$	$2.38 \pm 0.10$	2.63, 2.34	1.70, 1.72

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

\* Mass Median Aerodynamic Diameter ( $\mu\text{m}$ )

\* Geometric Standard Deviation

##### 2<sup>nd</sup> 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* $\mu\text{m}$	GSD*
$\geq 2$	$2.48 \pm 0.06$	2.86	1.72

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

\* Mass Median Aerodynamic Diameter ( $\mu\text{m}$ )

\* 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  $\geq 2\text{mg/l}$ .

## 6. DATA STORAGE

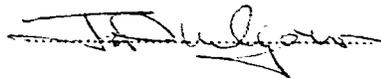
An original report, the study protocol, all raw data, samples and specimens, pertaining to this study are retained in the Archives, Central Toxicology Laboratory (CTL), Alderley Park, Macclesfield, Cheshire, UK.

## 7. REASON FOR REVISION

The conclusion of this report has been revised, following re-assessment of the limitations of the study, to state whether the aim of the study (to generate a stable aerosol of concentration  $\geq 2\text{mg/l}$ ) was achieved.

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



26 June 2000  
Date