

N,N-ジメチルアセトアミドのマウスを用いた
吸入によるがん原性試験報告書

試験番号：0754

APPENDICES

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APPENDIX 1-1

IDENTITY OF *N,N*-DIMETHYLACETAMIDE
IN THE 2-YEAR INHALATION STUDY

IDENTITY OF *N,N*-DIMETHYLACETAMIDE IN THE 2-YEAR INHALATION STUDYTest Substance : *N,N*-Dimethylacetamide (Wako Pure Chemical Industries, Ltd.)

A. Lot No. : PEJ4938

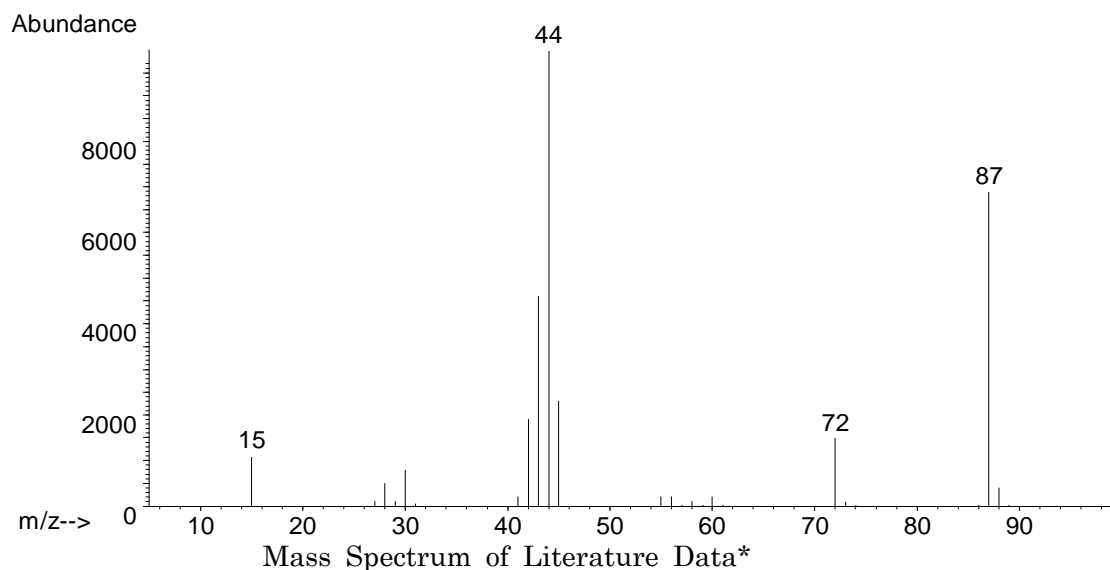
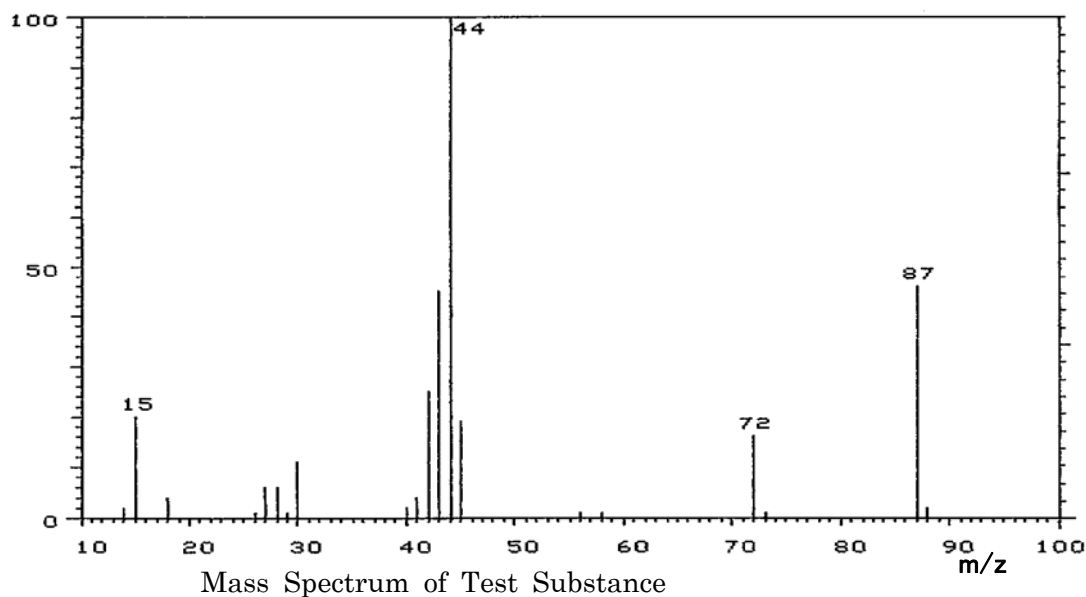
1. Spectral Data

Mass Spectrometry

Instrument : Hitachi M-80B Mass Spectrometer

Ionization : EI (Electron Ionization)

Ionization Voltage : 70eV



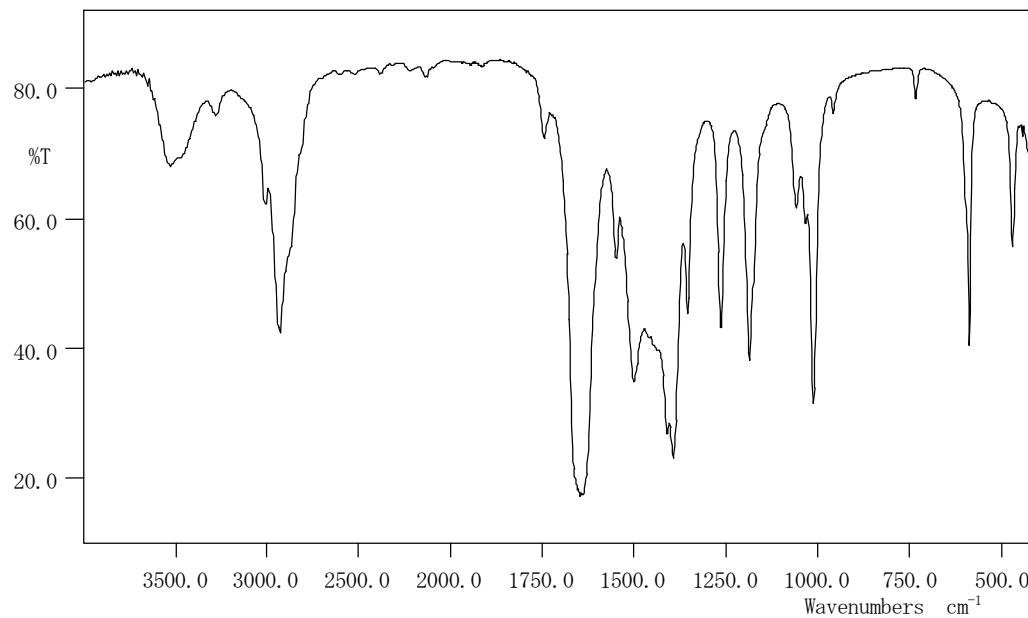
Result: The mass spectrum was consistent with literature spectrum.

(*McLafferty FW, ed. 1994. Wiley Registry of Mass Spectral Data. 6th ed. New York, NY:John Wiley and Sons.)

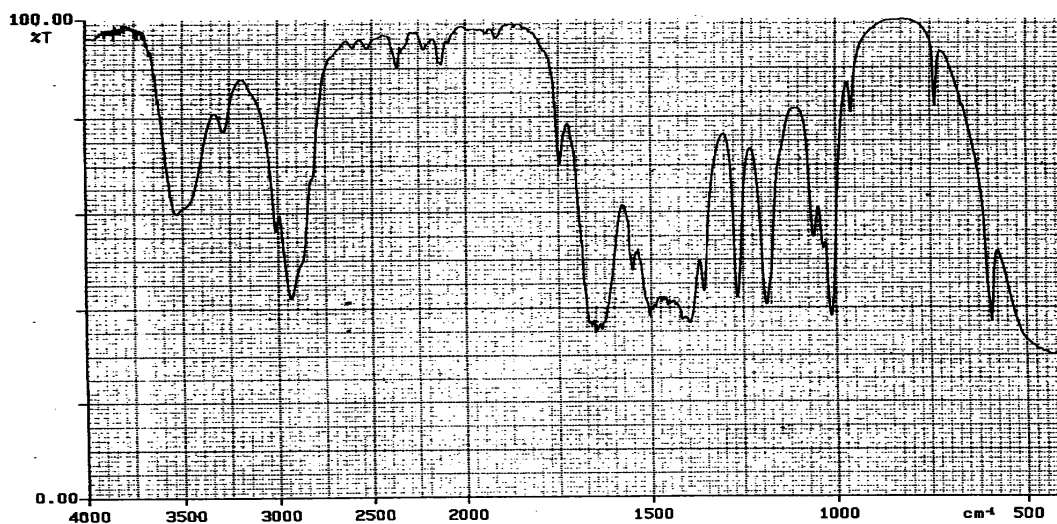
Infrared Spectrometry

Instrument : Shimadzu FTIR-8200PC Infrared Spectrometer

Cell : KBr Liquid Cell

Resolution : 4 cm^{-1} 

Infrared Spectrum of Test Substance



Infrared Spectrum of Literature Data*

Result: The infrared spectrum was consistent with literature spectrum.
(*Performed by Wako Pure Chemical Industries, Ltd.)

2. Conclusion: The test substance was identified as *N,N*-dimethylacetamide by mass spectrum and infrared spectrum.

B. Lot No. : CDE2493

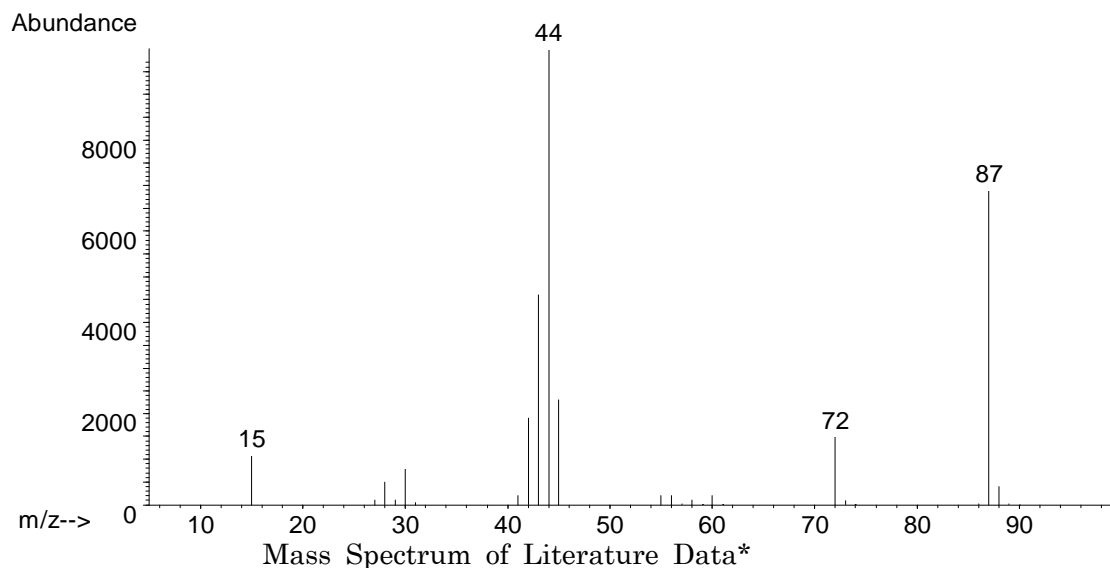
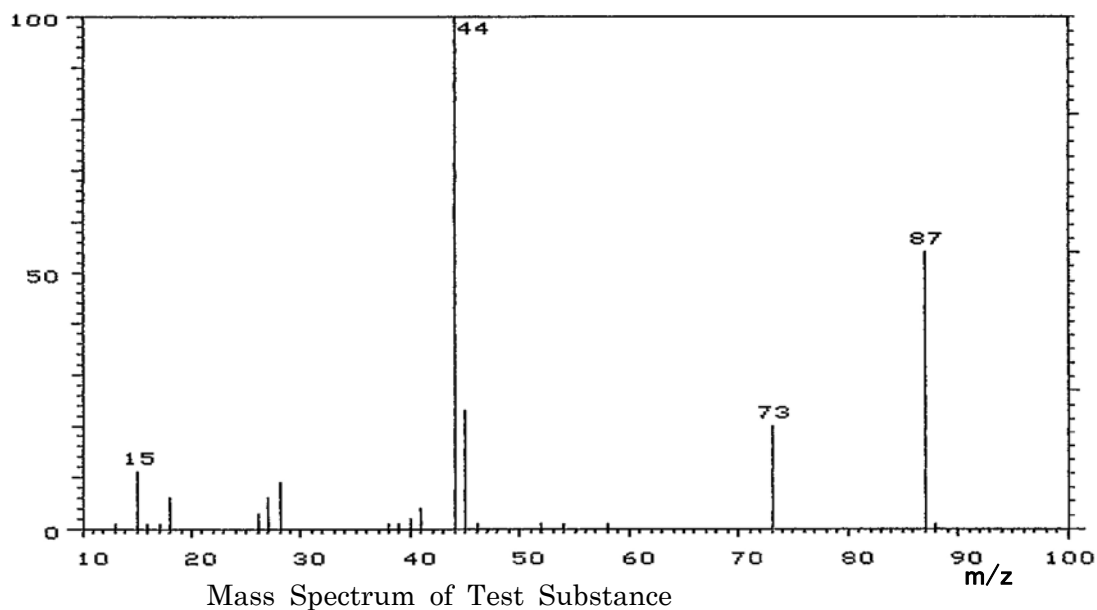
1. Spectral Data

Mass Spectrometry

Instrument : Hitachi M-80B Mass Spectrometer

Ionization : EI (Electron Ionization)

Ionization Voltage : 70eV



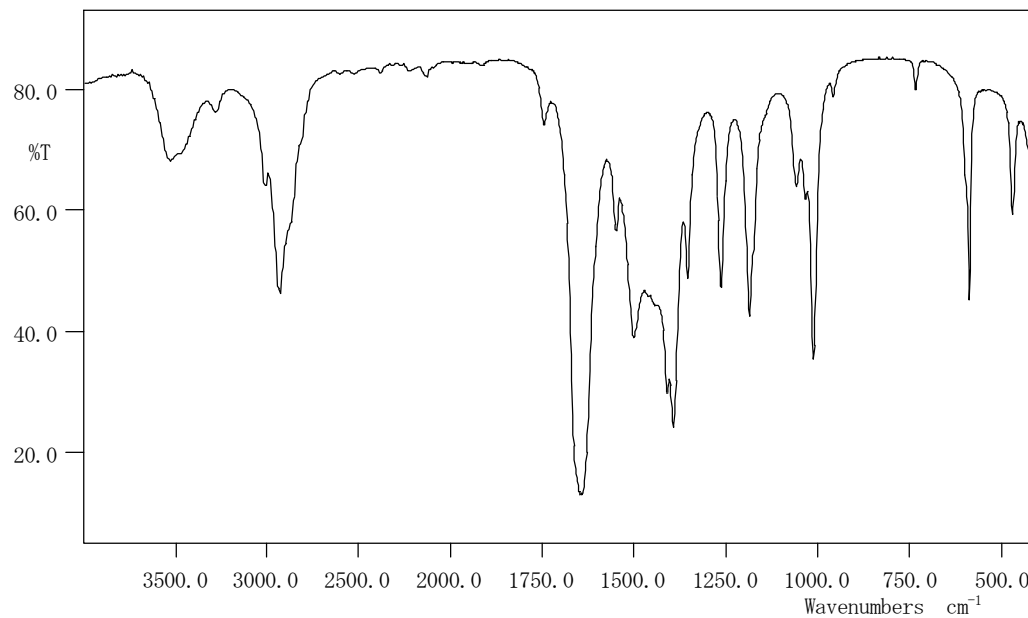
Result: The mass spectrum was consistent with literature spectrum.

(*McLafferty FW, ed. 1994. Wiley Registry of Mass Spectral Data. 6th ed. New York, NY:John Wiley and Sons.)

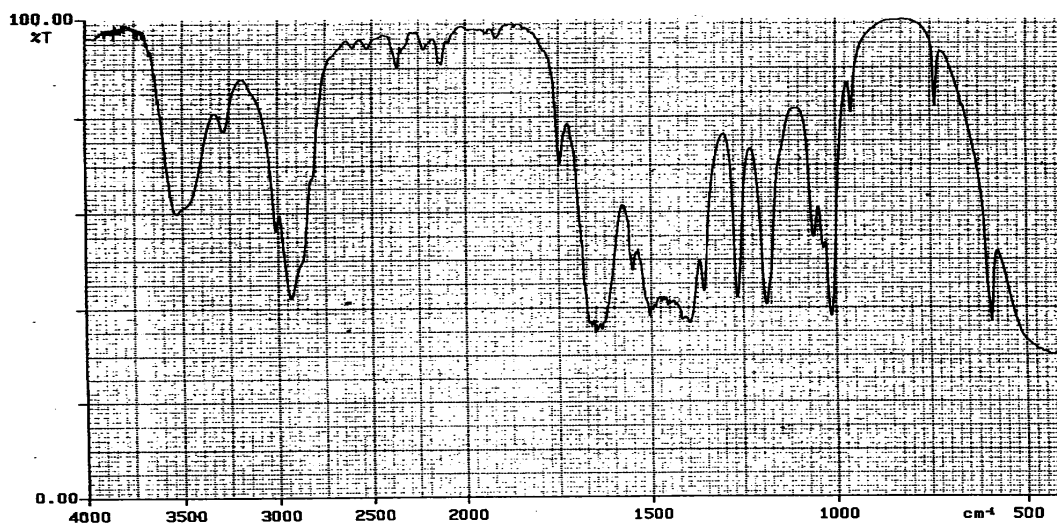
Infrared Spectrometry

Instrument : Shimadzu FTIR-8200PC Infrared Spectrometer

Cell : KBr Liquid Cell

Resolution : 4 cm^{-1} 

Infrared Spectrum of Test Substance



Infrared Spectrum of Literature Data*

Result: The infrared spectrum was consistent with literature spectrum.
(*Performed by Wako Pure Chemical Industries, Ltd.)

2. Conclusion: The test substance was identified as *N,N*-dimethylacetamide by mass spectrum and infrared spectrum.

C. Lot No. : STF2171

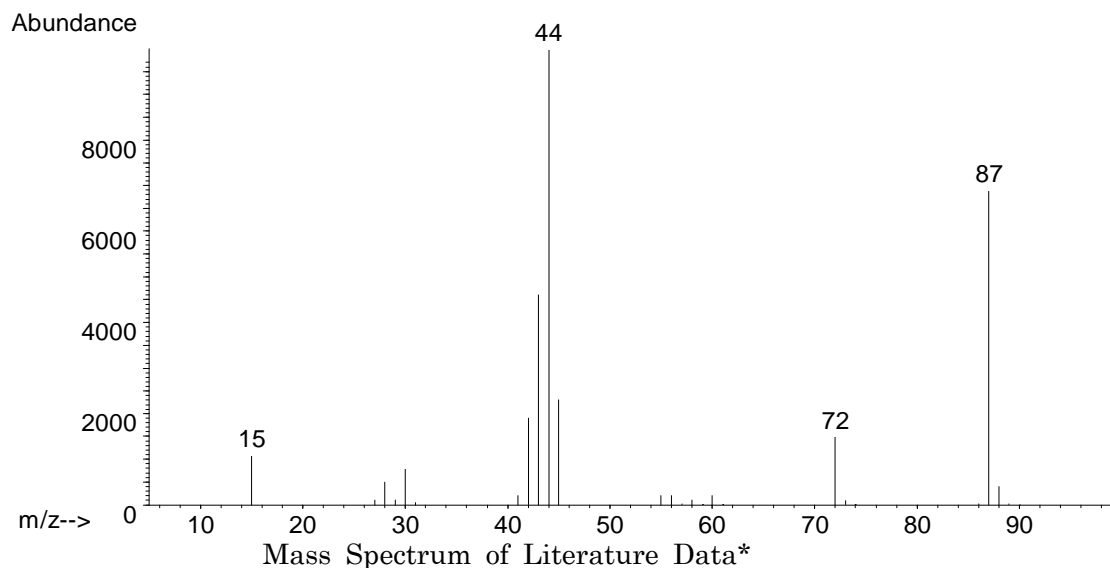
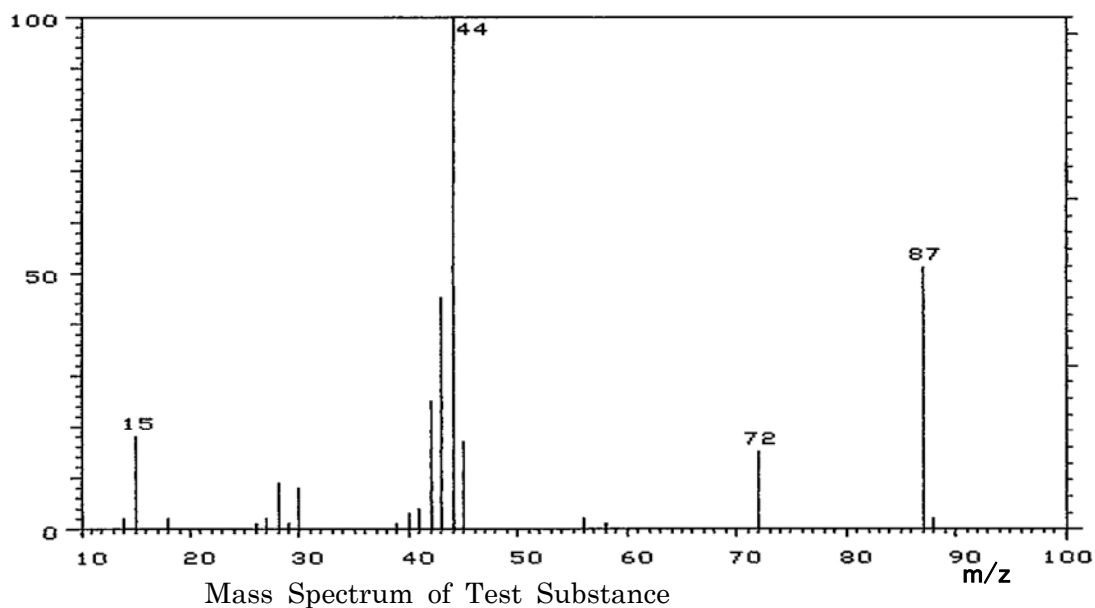
1. Spectral Data

Mass Spectrometry

Instrument : Hitachi M-80B Mass Spectrometer

Ionization : EI (Electron Ionization)

Ionization Voltage : 70eV



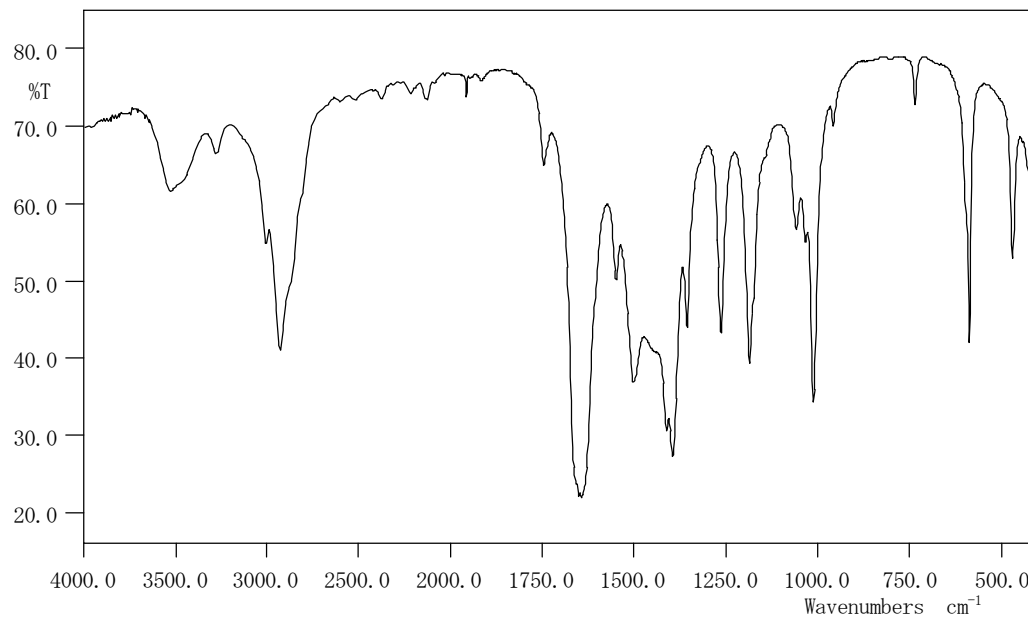
Result: The mass spectrum was consistent with literature spectrum.

(*McLafferty FW, ed. 1994. Wiley Registry of Mass Spectral Data. 6th ed. New York, NY:John Wiley and Sons.)

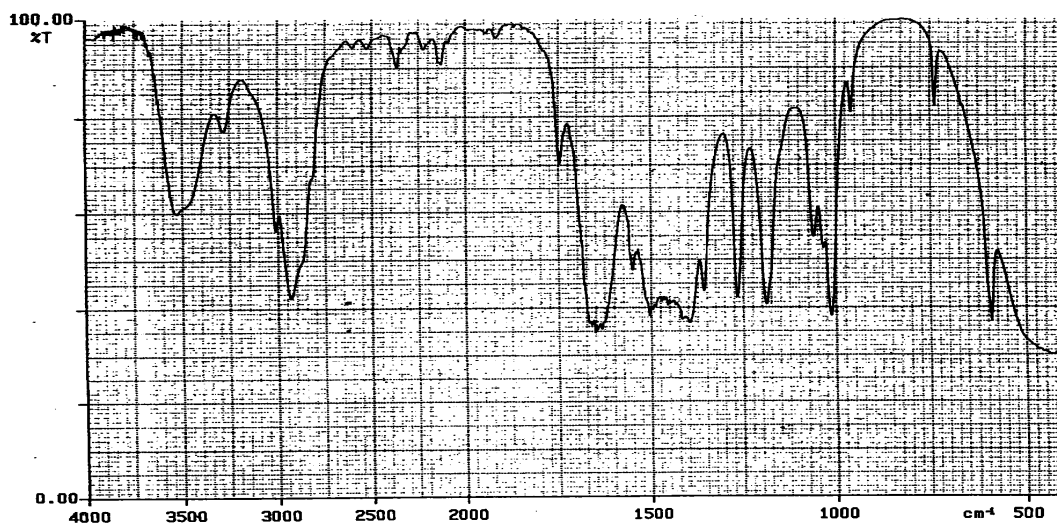
Infrared Spectrometry

Instrument : Shimadzu FTIR-8200PC Infrared Spectrometer

Cell : KBr Liquid Cell

Resolution : 4 cm^{-1} 

Infrared Spectrum of Test Substance



Infrared Spectrum of Literature Data*

Result: The infrared spectrum was consistent with literature spectrum.
(*Performed by Wako Pure Chemical Industries, Ltd.)

2. Conclusion: The test substance was identified as *N,N*-dimethylacetamide by mass spectrum and infrared spectrum.

D. Lot No. : STF3169

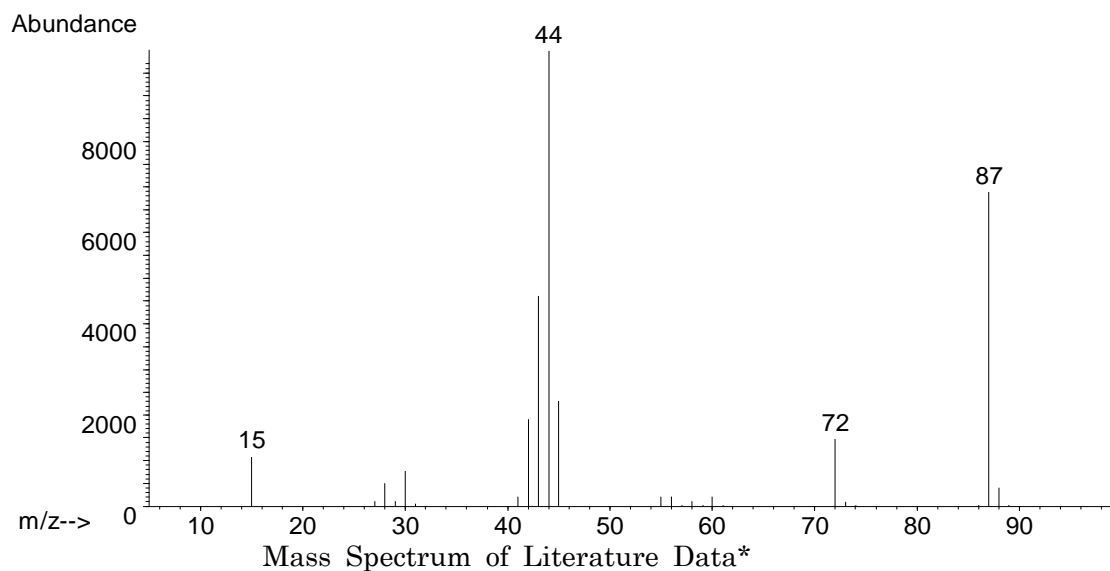
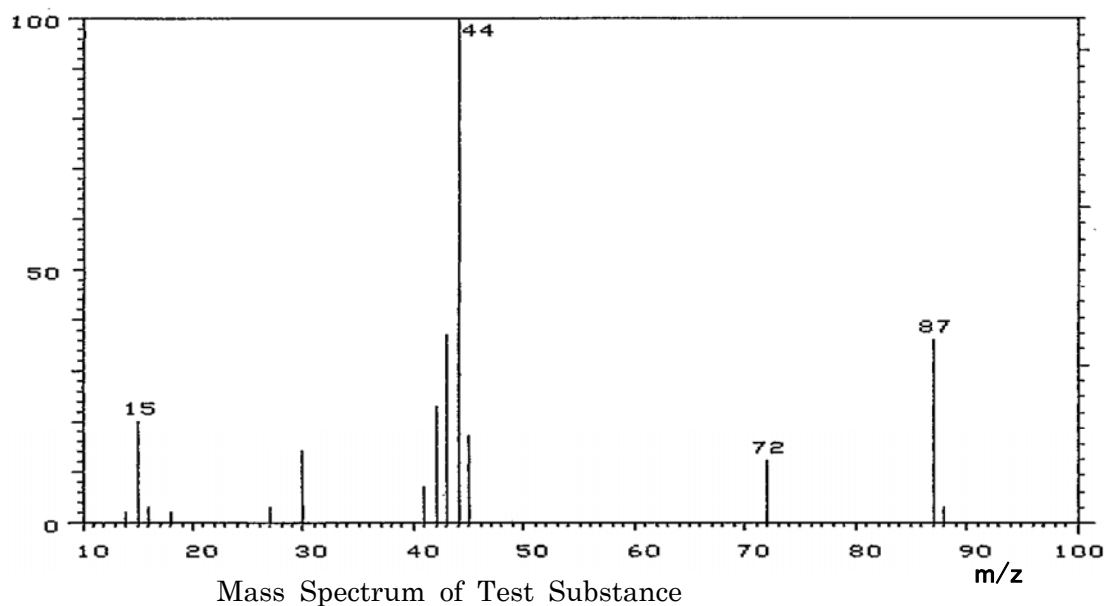
1. Spectral Data

Mass Spectrometry

Instrument : Hitachi M-80B Mass Spectrometer

Ionization : EI (Electron Ionization)

Ionization Voltage : 70eV



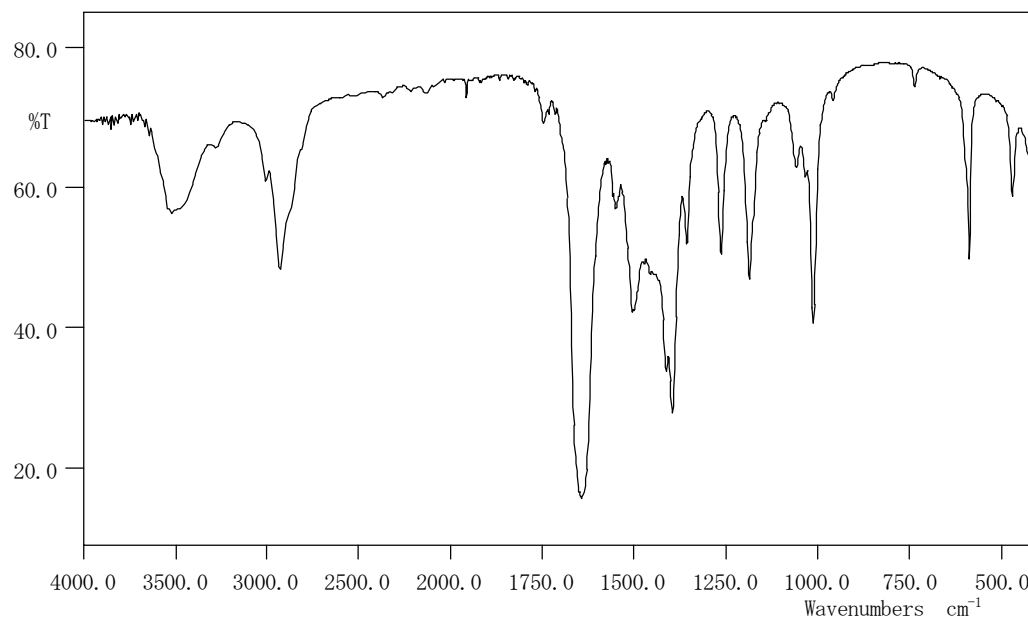
Result: The mass spectrum was consistent with literature spectrum.

(*McLafferty FW, ed. 1994. Wiley Registry of Mass Spectral Data. 6th ed. New York, NY:John Wiley and Sons.)

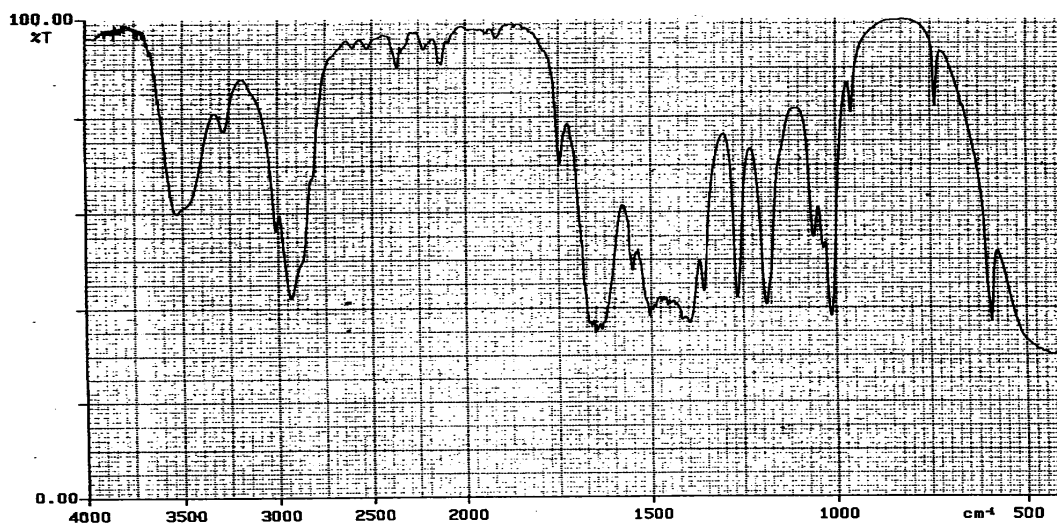
Infrared Spectrometry

Instrument : Shimadzu FTIR-8200PC Infrared Spectrometer

Cell : KBr Liquid Cell

Resolution : 4 cm^{-1} 

Infrared Spectrum of Test Substance



Infrared Spectrum of Literature Data*

Result: The infrared spectrum was consistent with literature spectrum.
(*Performed by Wako Pure Chemical Industries, Ltd.)

2. Conclusion: The test substance was identified as *N,N*-dimethylacetamide by mass spectrum and infrared spectrum.

APPENDIX 1-2

STABILITY OF *N,N*-DIMETHYLACETAMIDE
IN THE 2-YEAR INHALATION STUDY

STABILITY OF *N,N*-DIMETHYLACETAMIDE IN THE 2-YEAR INHALATION STUDY

Test Substance : *N,N*-Dimethylacetamide (Wako Pure Chemical Industries, Ltd.)

A. Lot No. : PEJ4938

1. Gas Chromatography

Instrument : Agilent Technologies 5890A Gas Chromatograph

Column : Methyl Silicone (0.53 mm ϕ \times 60 m)

Column Temperature: 160° C

Flow Rate : 10 mL/min

Detector : FID (Flame Ionization Detector)

Injection Volume : 1 μ L

| Date (date analyzed) | Peak No. | Retention Time (min) | Area (%) |
|-------------------------|----------|-------------------------|-------------|
| 2010.01.27 | 1 | 3.766 | 100 |
| 2010.06.10 | 1 | 3.767 | 100 |

Result: Gas chromatography indicated one major peak (peak No.1) analyzed on 2010.1.27 and one major peak (peak No.1) analyzed on 2010.6.10.
No new trace impurity peak in the test substance analyzed on 2010.6.10 was detected.

2. Conclusion: The test substance was stable for the period that the test substance had been used for the study.

B. Lot No. : CDE2493

1. Gas Chromatography

Instrument : Agilent Technologies 5890A Gas Chromatograph

Column : Methyl Silicone (0.53 mm ϕ \times 60 m)

Column Temperature: 160° C

Flow Rate : 10 mL/min

Detector : FID (Flame Ionization Detector)

Injection Volume : 1 μ L

| Date (date analyzed) | Peak No. | Retention Time (min) | Area (%) |
|-------------------------|----------|-------------------------|-------------|
| 2010.06.04 | 1 | 3.765 | 100 |
| 2011.03.30 | 1 | 3.776 | 100 |

Result: Gas chromatography indicated one major peak (peak No.1) analyzed on 2010.6.4 and one major peak (peak No.1) analyzed on 2011.3.30. No new trace impurity peak in the test substance analyzed on 2011.3.30 was detected.

2. Conclusion: The test substance was stable for the period that the test substance had been used for the study.

C. Lot No. : STF2171

1. Gas Chromatography

Instrument : Agilent Technologies 5890A Gas Chromatograph

Column : Methyl Silicone (0.53 mm ϕ \times 60 m)

Column Temperature: 160° C

Flow Rate : 10 mL/min

Detector : FID (Flame Ionization Detector)

Injection Volume : 1 μ L

| Date (date analyzed) | Peak No. | Retention Time (min) | Area (%) |
|-------------------------|----------|-------------------------|-------------|
| 2011.03.25 | 1 | 3.776 | 100 |
| 2011.12.28 | 1 | 3.774 | 100 |

Result: Gas chromatography indicated one major peak (peak No.1) analyzed on 2011.3.25 and one major peak (peak No.1) analyzed on 2011.12.28. No new trace impurity peak in the test substance analyzed on 2011.12.28 was detected.

2. Conclusion: The test substance was stable for the period that the test substance had been used for the study.

D. Lot No. : STF3169

1. Gas Chromatography

Instrument : Agilent Technologies 5890A Gas Chromatograph

Column : Methyl Silicone (0.53 mm ϕ \times 60 m)

Column Temperature: 160° C

Flow Rate : 10 mL/min

Detector : FID (Flame Ionization Detector)

Injection Volume : 1 μ L

| Date (date analyzed) | Peak No. | Retention Time (min) | Area (%) |
|-------------------------|----------|-------------------------|-------------|
| 2011.12.26 | 1 | 3.776 | 100 |
| 2012.02.27 | 1 | 3.776 | 100 |

Result: Gas chromatography indicated one major peak (peak No.1) analyzed on 2011.12.26 and one major peak (peak No.1) analyzed on 2012.2.27.
No new trace impurity peak in the test substance analyzed on 2012.2.27 was detected.

2. Conclusion: The test substance was stable for the period that the test substance had been used for the study.

APPENDIX 2

ENVIRONMENTAL CONDITIONS OF INHALATION CHAMBER IN THE 2-YEAR INHALATION STUDY OF *N,N*-DIMETHYLACETAMIDE

ENVIRONMENTAL CONDITIONS OF INHALATION CHAMBER IN THE 2-YEAR
INHALATION STUDY OF *N,N*-DIMETHYLACETAMIDE

| Group Name | Temperature (°C) | Humidity (%) | Ventilation Rate (L/min) | | Air Change (time/h) | |
|------------|---------------------|-----------------|-----------------------------|---------------------------|------------------------|--------------------|
| | Mean ± S.D. | Mean ± S.D. | Mean ± S.D. ^{*1} | Mean ± S.D. ^{*2} | Mean ^{*1} | Mean ^{*2} |
| Control | 22.5 ± 0.1 | 55.1 ± 0.8 | 371.2 ± 3.1 | 739.7 ± 4.4 | 6.0 | 12.0 |
| 12 ppm | 22.5 ± 0.1 | 51.1 ± 1.7 | 371.0 ± 2.8 | 739.7 ± 4.1 | 6.0 | 12.0 |
| 60 ppm | 22.6 ± 0.1 | 50.5 ± 2.2 | 371.7 ± 3.2 | 740.0 ± 4.3 | 6.0 | 12.0 |
| 300 ppm | 22.6 ± 0.2 | 47.4 ± 3.8 | 372.3 ± 3.4 | 740.0 ± 4.1 | 6.0 | 12.0 |

*1: Exposure period

*2: After exposure period

APPENDIX 3

METHODS, UNITS AND DECIMAL PLACE FOR
HEMATOLOGY AND BIOCHEMISTRY IN THE 2-YEAR
INHALATION STUDY OF *N,N*-DIMETHYLACETAMIDE

METHODS, UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY
IN THE 2-YEAR INHALATION STUDY OF *N,N*-DIMETHYLACETAMIDE

| Item | Method | Unit | Decimal place |
|--|---|---------------------------|---------------|
| Hematology | | | |
| Red blood cell (RBC) | Light scattering method ¹⁾ | $\times 10^6/\mu\text{L}$ | 2 |
| Hemoglobin(Hgb) | Cyanmethemoglobin method ¹⁾ | g/dL | 1 |
| Hematocrit(Hct) | Calculated as $\text{RBC} \times \text{MCV}/10$ ¹⁾ | % | 1 |
| Mean corpuscular volume(MCV) | Light scattering method ¹⁾ | fL | 1 |
| Mean corpuscular hemoglobin(MCH) | Calculated as $\text{Hgb}/\text{RBC} \times 10$ ¹⁾ | pg | 1 |
| Mean corpuscular hemoglobin concentration (MCHC) | Calculated as $\text{Hgb}/\text{Hct} \times 100$ ¹⁾ | g/dL | 1 |
| Platelet | Light scattering method ¹⁾ | $\times 10^3/\mu\text{L}$ | 0 |
| Reticulocyte | Light scattering method ¹⁾ | % | 1 |
| White blood cell(WBC) | Light scattering method ¹⁾ | $\times 10^3/\mu\text{L}$ | 2 |
| Differential WBC | Light scattering method ¹⁾ | % | 0 |
| Biochemistry | | | |
| Total protein(TP) | Biuret method ²⁾ | g/dL | 1 |
| Albumin (Alb) | BCG method ²⁾ | g/dL | 1 |
| A/G ratio | Calculated as $\text{Alb}/(\text{TP} - \text{Alb})$ ²⁾ | — | 1 |
| T-bilirubin | Azobilirubin method ²⁾ | mg/dL | 2 |
| Glucose | GlcK·G-6-PDH method ²⁾ | mg/dL | 0 |
| T-cholesterol | CE·COD·POD method ²⁾ | mg/dL | 0 |
| Triglyceride | MGLP·GK·GPO·POD method ²⁾ | mg/dL | 0 |
| Phospholipid | PLD·ChOD·POD method ²⁾ | mg/dL | 0 |
| Aspartate aminotransferase (AST) | JSCC method ²⁾ | U/L | 0 |
| Alanine aminotransferase (ALT) | JSCC method ²⁾ | U/L | 0 |
| Lactate dehydrogenase (LDH) | JSCC method ²⁾ | U/L | 0 |
| Alkaline phosphatase (ALP) | JSCC method ²⁾ | U/L | 0 |
| γ -Glutamyl transpeptidase (γ -GTP) | JSCC method ²⁾ | U/L | 0 |
| Creatine kinase (CK) | JSCC method ²⁾ | U/L | 0 |
| Urea nitrogen | Urease·GLDH method ²⁾ | mg/dL | 1 |
| Sodium | Ion selective electrode method ²⁾ | mEq/L | 0 |
| Potassium | Ion selective electrode method ²⁾ | mEq/L | 1 |
| Chloride | Ion selective electrode method ²⁾ | mEq/L | 0 |
| Calcium | OCPC method ²⁾ | mg/dL | 1 |
| Inorganic phosphorus | PNP·XOD·POD method ²⁾ | mg/dL | 1 |

1) Automatic blood cell analyzer (ADVIA120 : Siemens Healthcare Diagnostics Inc.)

2) Automatic analyzer (Hitachi 7080 : Hitachi,Ltd.)