

アクリル酸メチルのラットを用いた吸入によるがん原性試験報告書

試験番号：0831

APPENDICES

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APPENDIX 1-1

IDENTITY OF METHYL ACRYLATE IN THE 2-YEAR
INHALATION STUDY

IDENTITY OF METHYL ACRYLATE IN THE 2-YEAR INHALATION STUDY

Test Substance : Methyl acrylate (Wako Pure Chemical Industries, Ltd.)

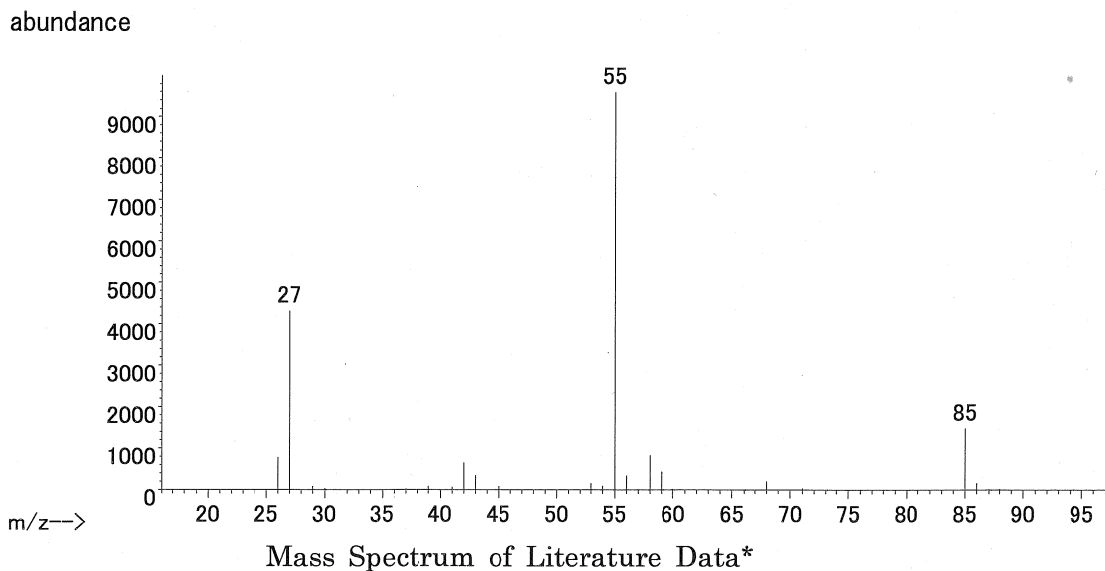
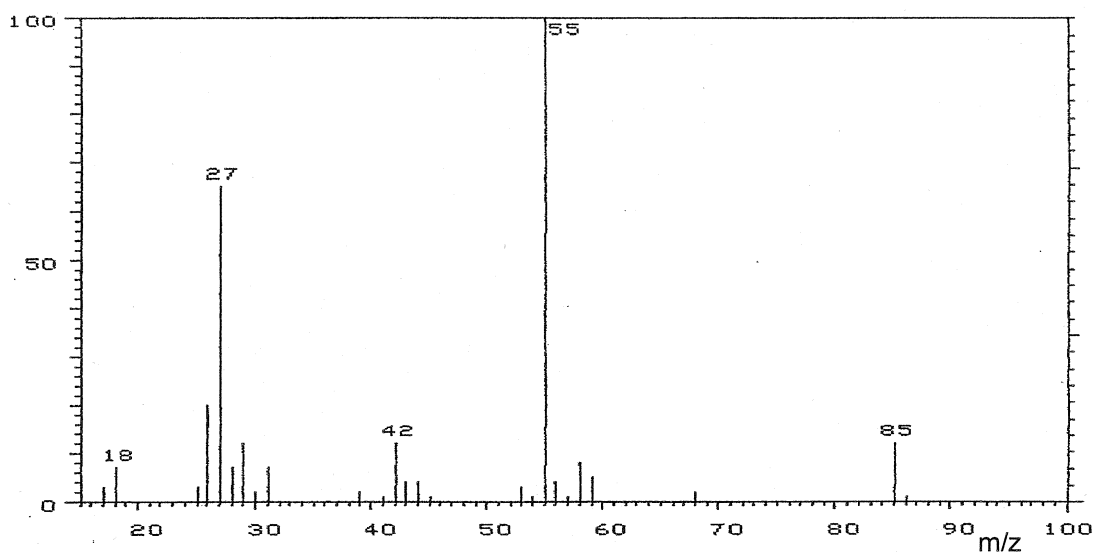
A. Lot No. : AWF1535

1. 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.)

2. Conclusion: The test substance was identified as methyl acrylate by mass spectrum.

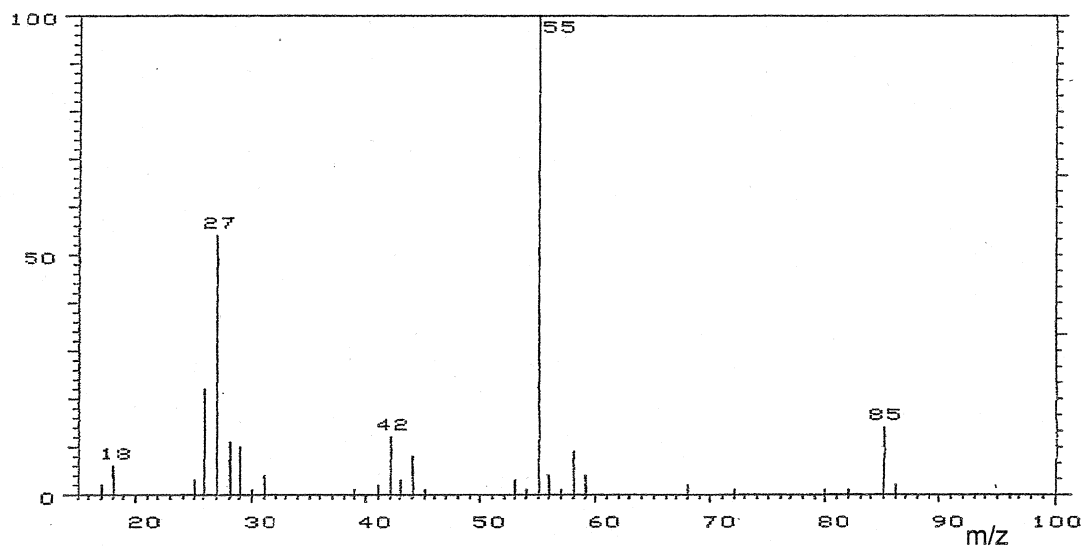
B. Lot No. : KPJ3619

1. Mass Spectrometry

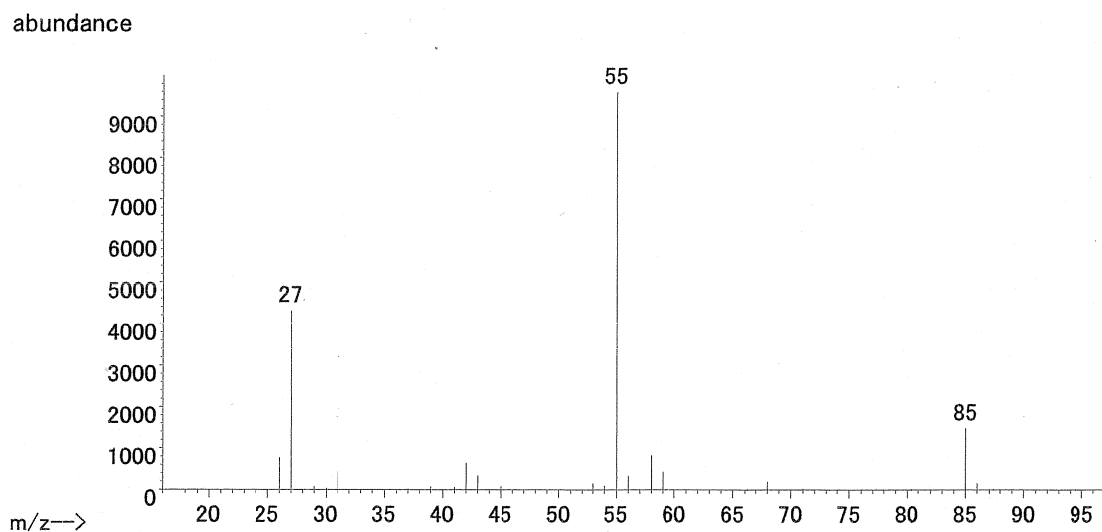
Instrument : Hitachi M-80B Mass Spectrometer

Ionization : EI (Electron Ionization)

Ionization Voltage : 70eV



Mass Spectrum of Test Substance



Mass Spectrum of Literature Data*

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.)

2. Conclusion: The test substance was identified as methyl acrylate by mass spectrum.

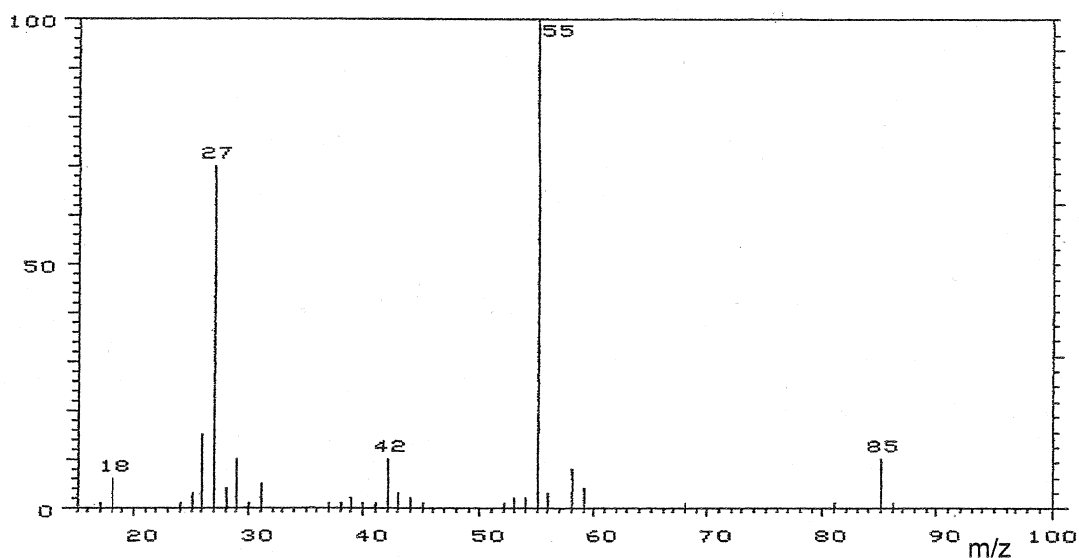
C. Lot No. : ECL0060

1. Mass Spectrometry

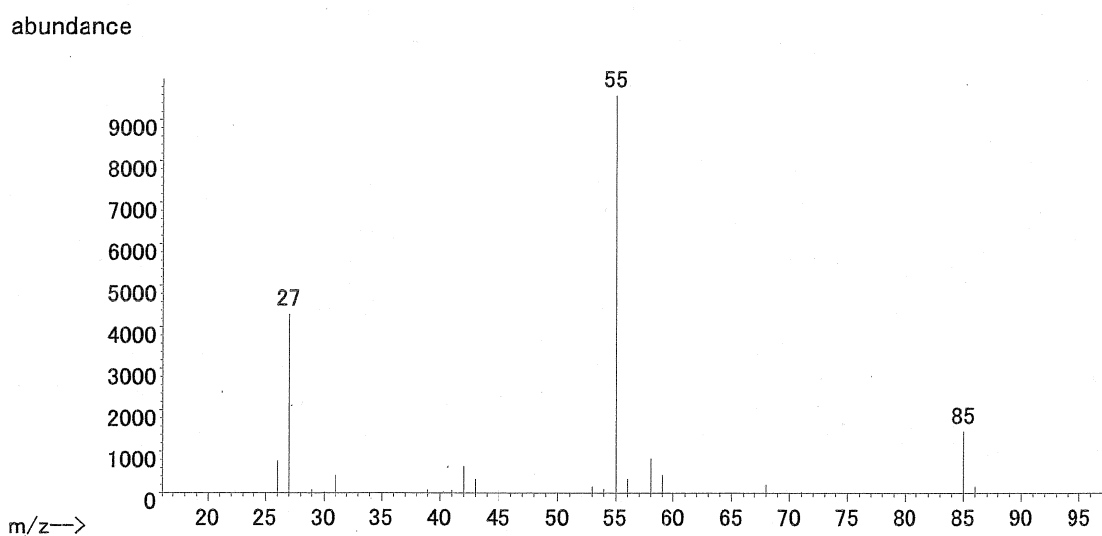
Instrument : Hitachi M-80B Mass Spectrometer

Ionization : EI (Electron Ionization)

Ionization Voltage : 70eV



Mass Spectrum of Test Substance



Mass Spectrum of Literature Data*

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.)

2. Conclusion: The test substance was identified as methyl acrylate by mass spectrum.

APPENDIX 1-2

STABILITY OF METHYL ACRYLATE IN THE 2-YEAR
INHALATION STUDY

STABILITY OF METHYL ACRYLATE IN THE 2-YEAR INHALATION STUDY

Test Substance : Methyl acrylate (Wako Pure Chemical Industries, Ltd.)

A. Lot No. : AWF1535

1. Gas Chromatography

Instrument : Agilent Technologies 5890A Gas Chromatograph

Column : INNOWAX (0.53 mm ϕ \times 60 m)

Column Temperature : 78 $^{\circ}$ C

Flow Rate : 5 mL/min

Detector : FID (Flame Ionization Detector)

Injection Volume : 1 μ L

| Date Analyzed | Peak No. | Retention Time (min) | Area (%) |
|---------------|----------|----------------------|----------|
| 2014.01.17 | 1 | 4.732 | 100 |
| 2014.11.06 | 1 | 4.759 | 100 |

Result: Gas chromatography indicated one major peak (peak No.1) analyzed on 2014.1.17 and one major peak (peak No.1) analyzed on 2014.11.6. No new trace impurity peak in the test substance analyzed on 2014.11.6 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. : KPJ3619

1. Gas Chromatography

Instrument : Agilent Technologies 5890A Gas Chromatograph

Column : INNOWAX (0.53 mm ϕ \times 60 m)

Column Temperature : 78 $^{\circ}$ C

Flow Rate : 5 mL/min

Detector : FID (Flame Ionization Detector)

Injection Volume : 1 μ L

| Date Analyzed | Peak No. | Retention Time (min) | Area (%) |
|---------------|----------|----------------------|----------|
| 2014.10.31 | 1 | 4.763 | 100 |
| 2015.08.20 | 1 | 4.720 | 100 |

Result: Gas chromatography indicated one major peak (peak No.1) analyzed on 2014.10.31 and one major peak (peak No.1) analyzed on 2015.8.20. No new trace impurity peak in the test substance analyzed on 2015.8.20 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. : ECL0060

1. Gas Chromatography

Instrument : Agilent Technologies 5890A Gas Chromatograph

Column : INNOWAX (0.53 mm ϕ \times 60 m)

Column Temperature : 78 $^{\circ}$ C

Flow Rate : 5 mL/min

Detector : FID (Flame Ionization Detector)

Injection Volume : 1 μ L

| Date Analyzed | Peak No. | Retention Time (min) | Area (%) |
|---------------|----------|----------------------|----------|
| 2015.08.18 | 1 | 4.716 | 100 |
| 2016.02.05 | 1 | 4.722 | 100 |

Result: Gas chromatography indicated one major peak (peak No.1) analyzed on 2015.8.18 and one major peak (peak No.1) analyzed on 2016.2.5. No new trace impurity peak in the test substance analyzed on 2016.2.5 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 METHYL ACRYLATE

ENVIRONMENTAL CONDITIONS OF INHALATION CHAMBER
IN THE 2-YEAR INHALATION STUDY OF METHYL ACRYLATE

| Group Name | Temperature (°C) | Humidity (%) | Ventilation Rate (L/min) | Air Change (time/h) |
|------------|---------------------|-----------------|-----------------------------|------------------------|
| | Mean ± S.D. | Mean ± S.D. | Mean ± S.D. | Mean |
| Control | 23.0 ± 0.1 | 53.4 ± 1.0 | 1697.3 ± 8.7 | 12.0 |
| 10 ppm | 23.0 ± 0.0 | 53.9 ± 1.0 | 1693.6 ± 8.9 | 12.0 |
| 40 ppm | 23.0 ± 0.0 | 53.8 ± 1.1 | 1700.1 ± 9.3 | 12.0 |
| 160 ppm | 23.0 ± 0.0 | 54.0 ± 1.1 | 1698.6 ± 9.1 | 12.0 |

APPENDIX 3

METHODS, UNITS AND DECIMAL PLACE FOR
HEMATOLOGY AND BIOCHEMISTRY IN THE 2-YEAR
INHALATION STUDY OF METHYL ACRYLATE

METHODS, UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY
IN THE 2-YEAR INHALATION STUDY OF METHYL ACRYLATE

| 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 | BOD 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 | 1 |
| Creatine kinase (CK) | JSCC method ²⁾ | U/L | 0 |
| Urea nitrogen | Urease·GLDH method ²⁾ | mg/dL | 1 |
| Creatinine | Creatinase·SOD·POD method ²⁾ | mg/dL | 2 |
| 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.)