

**G104**  
**Dibasic Esters**

**Results of Testing**

| Chemical Name    | CAS No.       | Study Code/Type                  | Protocol/Guideline                | Species                           | Exposure                             | Dose/Concentration          | No. per Group        | Results  | Reference  |
|------------------|---------------|----------------------------------|-----------------------------------|-----------------------------------|--------------------------------------|-----------------------------|----------------------|--|--|
| DBE Mixture      | Not available | In vitro dermal penetration rate | 64 FR 42692                       | Sprague-Dawley rat and human skin | Ex vivo<br>1, 2, 3, 4, 5 and 6 hours |                             | 6                    | All three of the dibasic esters used in this study penetrated rat skin from 32 to 44 times faster than they penetrated human skin when applied as single compounds. When the three dibasic esters were applied as mixture they still penetrated rat-skin quicker than human skin but the difference was less (14-31 times). The permeability coefficients (Kp), whether the DBE homologue was applied alone or as part of the 1:3:1 (DMS:DMG:DMA) % blend, were comparable for each homologue within a species and higher for rat skin compared to human skin. The Kp values for rat and human skin ranged from $2.12 \times 10^{-3}$ to $4.18 \times 10^{-3}$ cm/hr and from $6.81 \times 10^{-5}$ to $1.69 \times 10^{-4}$ cm/hr, respectively.  | 68 FR 44949<br>7/31/03<br>OPPT-42190<br>OPPT-2002-0009 |
| DBE Mixture      | Not available | HE Dermal (14-day) Toxicity      | 64 FR 42692                       | <i>rats</i>                       | Dermal,<br>6 hours/day<br>2 weeks    | 100, 300 and 1000 mg/kg/day | 10 female<br>10 male | Low incidences (typically one to five animals) of test article-related erythema and/or edema, generally graded as very slight, were observed for DMA, DMS, DMG and DBE. For males and females combined, minimal to mild erythema was observed in all three DMA, DMG and DBE groups. Various findings (generally minimal to mild) consistent with dermal irritation were observed for animals treated with all four test materials, most prominently eschar (focal) and erythema. Considering the results of 14 daily exposures, none of the chemicals would be considered very irritating. Within that context, DMG and the DBE mixture would be considered more irritating than DMA and DMS. DMS would be considered the least irritating of the chemicals tested. Any dermal findings observed were completely reversible. Based on the results of this study, the no-observed-effect level (NOEL) for systemic toxicity of DMA, DMS, DMG and DBE when administered dermally to male and female rats for 14 consecutive days was 1000 mg/kg/day. | 8/02<br>OPPT-42190<br>OPPT-2002-0009                   |
| Dimethyl adipate | 627-93-0      | HEGTOXCHRM Micronucleus test     | National Toxicology Program (NTP) | <i>Not specified</i>              | Not specified                        | Not specified               | Not specified        | Equivocal  | NTP Results Report<br>8/8/96                           |
| Dimethyl adipate | 627-93-0      | HEGTOXMUTA Ames test             | National Toxicology Program (NTP) | <i>Salmonella typhimurium</i>     | <i>in vitro</i>                      | Not specified               | Not specified        | Negative response  | NTP Results Report<br>8/8/96                           |

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|--------------------|-----------|---|--------------------------------------|---|---|----------------------------------|----------------------|--|--------------------------------------|
| Dimethyl adipate   | 627-93-0  | HESTOX<br>90-day Inhalation<br>Toxicity | 64 FR 42692                          | rats                                    | inhalation,<br>6 hours/day<br>5 days/week | 400 mg/m <sup>3</sup>            | 30 female<br>30 male | The LOAEL for DMA for repeated exposure was 400 mg/m <sup>3</sup> , the only concentration tested, based on increases in epididymal sperm counts, increases in relative epididymal weight and decreases in serum estradiol concentrations. The NOAEL for DMA could not be established because effects were observed at the only exposure concentration tested.   | 8/02<br>OPPT-42190<br>OPPT-2002-0009 |
| Dimethyl adipate   | 627-93-0  | HE<br>Dermal (14-day)<br>Toxicity       | 64 FR 42692                          | rats                                    | dermal,<br>6 hours/day<br>2 weeks         | 100, 300 and 1000<br>mg/kg/day   | 10 female<br>10 male | Low incidences (typically one to five animals) of test article-related erythema and/or edema, generally graded as very slight, were observed for DMA, DMS, DMG and DBE. For males and females combined, minimal to mild erythema was observed in all three DMA, DMG and DBE groups. Various findings (generally minimal to mild) consistent with dermal irritation were observed for animals treated with all four test materials, most prominently eschar (focal) and erythema. Considering the results of 14 daily exposures, none of the chemicals would be considered very irritating. Within that context, DMG and the DBE mixture would be considered more irritating than DMA and DMS. DMS would be considered the least irritating of the chemicals tested. Any dermal findings observed were completely reversible. Based on the results of this study, the no-observed-effect level (NOEL) for systemic toxicity of DMA, DMS, DMG and DBE when administered dermally to male and female rats for 14 consecutive days was 1000 mg/kg/day. | 8/02<br>OPPT-42190<br>OPPT-2002-0009 |
| Dimethyl adipate   | 627-93-0  | HEGTOXCHRM<br>Micronucleus test         | 64 FR 42692                          | mice                                    | inhalation,<br>6 hours/days               | 0.5, 1.0 and 2.0 mg/l            | 5 female<br>5 male   | Micronucleus data on the dibasic ester DMA indicated that it is not a chromosome mutagen in rats when exposed in vivo by inhalation.   | 8/01<br>OPPT-42190<br>OPPT-2002-0009 |
| Dimethyl glutarate | 1119-40-0 | HEGTOXCHRM<br>Micronucleus test         | National Toxicology<br>Program (NTP) | Not specified                           | Not specified                             | Not specified                    | Not specified        | Equivocal  | NTP Results Report<br>8/8/96         |
| Dimethyl glutarate | 1119-40-0 | HEGTOXMUTA<br>Ames test                 | National Toxicology<br>Program (NTP) | <i>Salmonella</i><br><i>typhimurium</i> | <i>in vitro</i>                           | Not specified                    | Not specified        | Negative response  | NTP Results Report<br>8/8/96         |
| Dimethyl glutarate | 1119-40-0 | HESTOX<br>90-day Inhalation<br>Toxicity | 64 FR 42692                          | rats                                    | inhalation,<br>6 hours/day<br>5 days/week | 10, 50 and 400 mg/m <sup>3</sup> | 30 female<br>30 male | The NOAEL for repeated exposures to DMG was 10 mg/m <sup>3</sup> based on decreases in serum testosterone and serum LH concentrations and increases in epididymal sperm counts at 50 mg/m <sup>3</sup> . The LOAEL for repeated exposures to DMG was 50 mg/m <sup>3</sup> , based on decreases in serum testosterone and serum LH concentrations and increases in epididymal sperm counts.   | 8/02<br>OPPT-42190<br>OPPT-2002-0009 |

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|--------------------|-----------|---------------------------------------|--------------------------------------|--------------------------------------|--|---|----------------------|--|--|
| Dimethyl glutarate | 1119-40-0 | HE<br>Dermal (14-day)<br>Toxicity     | 64 FR 42692                          | rats                                 | dermal,<br>6 hours/day                     | 100, 300 and 1000<br>mg/kg/day                | 10 female<br>10 male | Low incidences (typically one to five animals) of test article-related erythema and/or edema, generally graded as very slight, were observed for DMA, DMS, DMG and DBE. For males and females combined, minimal to mild erythema was observed in all three DMA, DMG and DBE groups. Various findings (generally minimal to mild) consistent with dermal irritation were observed for animals treated with all four test materials, most prominently eschar (focal) and erythema. Considering the results of 14 daily exposures, none of the chemicals would be considered very irritating than DMA and DMS. DMS would be considered the least irritating of the chemicals tested. Any dermal findings observed were completely reversible. Based on the results of this study, the no-observed-effect level (NOEL) for systemic toxicity of DMA, DMS, DMG and DBE when administered dermally to male and female rats for 14 consecutive days was 1000 mg/kg/day. | 8/02<br>OPPT-42190<br>OPPT-2002-0009             |
| Dimethyl glutarate | 1119-40-0 | HEGTOXCHRM<br>Micronucleus test       | 64 FR 42692                          | Fischer 344<br>rats                  | inhalation,<br>6 hours/day for two<br>days | 0.5, 1.0 and 2.0 mg/l                         | 5 female<br>5 male   | Micronucleus data on the dibasic ester DMG indicated that it is not a chromosome mutagen in rats when exposed in vivo by inhalation.   | 8/01<br>OPPT-42190<br>OPPT-2002-0009             |
| Dimethyl glutarate | 1119-40-0 | HEGTOXMUTA<br>Gene Mutation test      | 64 FR 42692                          | <i>Sprague-<br/>Dawley rat</i>       | <i>in vitro</i>                            |   | Not applicable       | The dibasic ester dimethyl gluturate (DMG) is not a gene mutagen in CHO cells in vitro.  | 8/02<br>67 FR 17430<br>4/10/02<br>OPPT-2002-0009 |
| Dimethyl glutarate | 1119-40-0 | Prenatal<br>developmental<br>toxicity | 64 FR 42692                          | <i>New Zealand<br/>White Rabbits</i> | inhalation,<br>6 hours/day                 | 0, 30, 100, 300 and<br>1000 mg/m <sup>3</sup> | 22 female<br>22 male | Under the conditions of the study, the LOAEL for maternal toxicity was 300 mg/m <sup>3</sup> , based on the significant reductions in body weight and treatment-related signs of clinical toxicity. The NOAEL for maternal toxicity was considered to be 100 mg/m <sup>3</sup> . The LOAEL for developmental toxicity was the highest concentration tested, 1000 mg/m <sup>3</sup> , based on statistically significant increases in delayed ossification. The NOAEL for developmental toxicity was 300 mg/m <sup>3</sup> .  | 68 FR 44949<br>7/31/03<br>OPPT-2002-0009         |
| Dimethyl succinate | 106-65-0  | HEGTOXMUTA<br>Ames test               | National Toxicology<br>Program (NTP) | <i>Salmonella<br/>typhimurium</i>    | <i>in vitro</i>                            | Not specified                                 | Not specified        | Negative response  | NTP Results Report<br>8/8/96                     |

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|--------------------|----------|---|--------------------|---------|---|--------------------------------|----------------------|--|--------------------------------------|
| Dimethyl succinate | 106-65-0 | HESTOX<br>90-day Inhalation<br>Toxicity | 64 FR 42692        | rats    | inhalation,<br>6 hours/day<br>5 days/week | 400 mg/m <sup>3</sup>          | 30 female<br>30 male | The LOAEL for DMS for repeated exposure was 400 mg/m <sup>3</sup> , the only concentration tested, based on increases in epididymal sperm counts, increases in relative epididymal weight and decreases in serum estradiol concentrations. The NOAEL for DMS could not be established because effects were observed at the only exposure concentration tested.   | 8/02<br>OPPT-42190<br>OPPT-2002-0009 |
| Dimethyl succinate | 106-65-0 | HE<br>Dermal (14-day)<br>Toxicity       | 64 FR 42692        | rats    | dermal,<br>6 hours/day<br>2 weeks         | 100, 300 and 1000<br>mg/kg/day | 10 female<br>10 male | Low incidences (typically one to five animals) of test article-related erythema and/or edema, generally graded as very slight, were observed for DMA, DMS, DMG and DBE. For males and females combined, minimal to mild erythema was observed in all three DMA, DMG and DBE groups. Various findings (generally minimal to mild) consistent with dermal irritation were observed for animals treated with all four test materials, most prominently eschar (focal) and erythema. Considering the results of 14 daily exposures, none of the chemicals would be considered very irritating. Within that context, DMG and the DBE mixture would be considered more irritating than DMA and DMS. DMS would be considered the least irritating of the chemicals tested. Any dermal findings observed were completely reversible. Based on the results of this study, the no-observed-effect level (NOEL) for systemic toxicity of DMA, DMS, DMG and DBE when administered dermally to male and female rats for 14 consecutive days was 1000 mg/kg/day. | 8/02<br>OPPT-42190<br>OPPT-2002-0009 |