

**VI. Results of Testing**

Chemical Name	CAS No.	Study Code/Type	Protocol/Guidline	Species	Exposure	Dose/Concentration	No. per Group	Results	Reference
<i>N</i> -Methylpyrrolidone	872-50-4	HEADME Pharmacokinetics	40 CFR 795.232 (modified)	rat	inhalation	10 and 100 ppm	4/sex	No NMP was detected in plasma after exposure to 10 ppm. The half-life of NMP could not be determined. Approximately 7% of 10 ppm [ <sup>2-14</sup> C] NMP vapor was absorbed and 9% of 100 ppm [ <sup>2-14</sup> C] NMP was absorbed. Once absorbed NMP was distributed, metabolized, and eliminated in the urine with negligible tissue residues remaining after 4-5 days post dose.	61 FR 3403; 1/31/96, Docket OPPTS-44620
<i>N</i> -Methylpyrrolidone	872-50-4	HEADME Pharmacokinetics	40 CFR 795.232 (modified)	rat	dermal	10 mg/kg	5/sex	No NMP was detected in plasma after exposure to 10 mg/kg. The half-life of NMP could not be determined after dermal exposure. Approximately 44% and 43% of the topically applied dose was absorbed by male and female rats, respectively. NMP was readily absorbed after dermal exposure. Once absorbed NMP was distributed, metabolized, and eliminated in the urine with negligible tissue residues remaining after 4-5 days post dose.	61 FR 3403; 1/31/96, Docket OPPTS-44620
<i>N</i> -Methylpyrrolidone	872-50-4	HEADME Pharmacokinetics	40 CFR 795.232 (modified)	rat	oral, 7 days	5, 50 mg/kg	10/sex (5 mg/kg), 4/sex (50 mg/kg)	No NMP was detected in plasma after exposure to 5 mg/kg. The time to reach C <sub>max</sub> (T <sub>max</sub> ) was 2 hours after the multiple oral high dose. The half-life of NMP could not be determined after low oral exposure. The oral bioavailability of NMP was 48% for male rats and 101% for female rats. NMP was readily absorbed after inhalation exposure. Once absorbed NMP was distributed, metabolized, and eliminated in the urine with negligible tissue residues remaining after 4-5 days post dose.	61 FR 3403; 1/31/96, Docket OPPTS-44620
<i>N</i> -Methylpyrrolidone	872-50-4	HEADME Pharmacokinetics	40 CFR 795.232 (modified)	rat	intravenous	50 mg/kg	9	The concentration of NMP in plasma (C <sub>max</sub> ) was highest after intravenous administration as compared with oral, dermal, or inhalation routes of exposure. The bioavailability of NMP in female rats was probably lower than 101%. The volume of distribution was 0.7 L/kg for male rats and 1.8 L/kg for female rats. Once absorbed NMP was distributed, metabolized, and eliminated in the urine with negligible tissue residues remaining after 4-5 days post dose.	61 FR 3403; 1/31/96, Docket OPPTS-44620

**G067**  
**N-Methylpyrrolidone [872-50-4]**

Chemical Name	CAS No.	Study Code/Type	Protocol/Guideline	Species	Exposure	Dose/Concentration	No. per Group	Results	Reference
N-Methylpyrrolidone	872-50-4	HECTOXCARC Oncogenicity	40 CFR 798.3300 (modified)	B6C3F1 mice	oral (gavage)	0, 600, 1200 or 7200 ppm	50 male; 50 female	Under the conditions of this study, NMP was carcinogenic in male or female mice, inducing hepatocellular adenomas and carcinomas in the top dose (7,200 ppm) groups. The incidences of liver foci (preneoplastic lesions) were also significantly increased in the high dose male and female mice. Should the mid-dose level was higher, a dose-response relationship of these neoplastic and preneoplastic lesions might be observed.	65 FR 4606, 1/31/00
N-Methylpyrrolidone	872-50-4	HECTOXCARC Oncogenicity	40 CFR 798.3300 (modified)	rat	oral (diet)	0, 1600, 5000 or 15000 ppm	62 male; 62 female	Based on the observed decrements in body weight and body weight gain in the high-dose males and females, and the increase in the incidence of nephropathy in the high-dose males, a MTD (maximum tolerated dose) appeared to have been achieved. Under the conditions of this study, NMP was not carcinogenic in male and female rats at dietary concentrations up to 15000 ppm.	63 FR 35587; 6/30/98, Docket OPPTS-44649
N-Methylpyrrolidone	872-50-4	HENEUR Functional Observational Battery: Subchronic	40 CFR 798.6050 (modified)	rat	oral (diet), 90 days	3000, 7500, 18,000 ppm	20/sex (3000 and 7500 ppm), 26/sex (18000 ppm)	A statistically increase in foot splay was observed in high- and mid-dose males, no such change occurred in females. A statistically significant increase in the incidence of "low" arousal was observed in low-dose males at week 4, but not after that. Similarly, a statistically significant increase in slight palpebral closure was observed in low- and high-dose animals, but only on weeks 4 and 13. It was concluded that the test substance was not neurotoxic.	61 FR 3403; 1/31/96 OTS0513411-7, Docket OPPTS- 44620
N-Methylpyrrolidone	872-50-4	HENEUR Motor Activity: Subchronic	40 CFR 798.6200 (modified)	rat	oral (diet), 90 days	3000, 7500, 18,000 ppm	20/sex (3000 and 7500 ppm), 26/sex (18000 ppm)	A statistically increase in foot splay was observed in high- and mid-dose males, no such change occurred in females. A statistically significant increase in the incidence of "low" arousal was observed in low-dose males at week 4, but not after that. Similarly, a statistically significant increase in slight palpebral closure was observed in low- and high-dose animals, but only on weeks 4 and 13. There were no statistically significant effects on motor activity in any dose group of either sex. It was concluded that the test substance was not neurotoxic.	61 FR 3403; 1/31/96 OTS0513411-7, Docket 44620

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Chemical Name	CAS No.	Study Code/Type	Protocol/Guideline	Species	Exposure	Dose/Concentration	No. per Group	Results	Reference
N-Methylpyrrolidone	872-50-4	HENEUR Neuropathology: Subchronic	40 CFR 798.6400 (modified)	rat	oral (diet), 90 days	3000, 7500, 18,000 ppm	20/sex (3000 and 7500 ppm), 26/sex (18000 ppm)	Administration of 7500 and 18000 ppm caused decrements in body weight and body weight gain which were correlated with lower food consumption and food efficiency. There were no compound-related adverse effects on survival, clinical signs of toxicity, ophthalmoscopically visible structures of the eyes, or clinical pathology parameters. No compound-related changes were detected in nervous system tissue or muscle tissue in any treated animal. There were no compound-related adverse effects on organ weight parameters or tissue morphology in any treated animals. The NOEL was 3000 ppm for this study.	61 FR 3403; 1/31/96 OTS0513411-7, Docket 44620
N-Methylpyrrolidone	872-50-4	STOX Repeated dose toxicity study	OECD (Organization of European Commu- nity Development) 407	B6C3F <sub>1</sub> mice	oral (diet), 4 wk	0, 500, 2500, 7500, 10,000 ppm (nominal)	5/sex/group	At 10,000 ppm, one male died during the study, and cloudy swelling of the epithelia of the distal parts of the renal tubules was observed in 4 males and 3 females. At 7500 ppm, no animals died. Cloudy swelling of the epithelia of the distal parts of the renal tubules occurred in 2 males at 7500 ppm. The No Observed Adverse Effect Level (NOAEL) was 2500 ppm.	59 FR33291; 6/28/94 OTS0513411-7, Docket OPPTS- 44610
N-Methylpyrrolidone	872-50-4	STOX Subchronic oral toxicity	40 CFR 798.2650 (modified)	rat	oral (diet), 28 days	0, 2000, 6000, 18,000, 30,000 ppm (nominal)	5/sex/group	Decreased food consumption and efficiency resulted in significant body weight decrements in males and females at the 30,000 ppm level, and in male rats at 18,000 ppm. Alterations in clinical chemical parameters indicate possible compound related changes in lipid, protein, and carbohydrate metabolism at 30,000 ppm. The hematologic and organ weight changes observed were due to reduced body weight, except for centrilobular hepatocellular hypertrophy found at 30,000 and 18,000 ppm levels. The No Observed Adverse Effect Level (NOAEL) was 6000 ppm.	59 FR33291; 6/28/94 OTS0513411-7, Docket OPPTS- 44610

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Chemical Name	CAS No.	Study Code/Type	Protocol/Guideline	Species	Exposure	Dose/Concentration	No. per Group	Results	Reference
N-Methylpyrrolidone	872-50-4	STOX Subchronic oral toxicity	40 CFR 798.2650 (modified)	B6C3F <sub>1</sub> mice	diet, 3 months (main group), 4 wks (satellite)	1000, 2500, 7500 ppm	10/sex	Substance-related findings in the 2500 and 7500 ppm groups treated for 4 week included dark yellow staining of urine, increase in cholesterol in the females, decrease in triglycerides in the males; a decrease in alkaline phosphatase and calcium was seen in the males in the 7500 ppm group. No substance-related effects were noted in the 1000 ppm satellite dose groups. Substance-related findings in the main group included dark yellow staining of urine, significantly increased mean absolute and relative liver weights in male mice at 2500 and 7500 ppm. Centrolobular hypertrophy of the liver cells occurred in the 7500 ppm dose group. No substance-related effects were found in the main group at 1000 ppm. The NOEL was 1000 ppm for this study.	61 FR 3403; 1/31/96, Docket OPPTS-44620
N-Methylpyrrolidone	872-50-4	STOX Subchronic oral toxicity	40 CFR 798.2650 (modified)	rat	oral (diet), 90 days	3000, 7500, 18,000 ppm	20/sex (3000 and 7500 ppm), 26/sex (18,000 ppm)	There were no compound-related effects on organ weight parameters or tissue morphology in males or females at any dietary concentration. No compound-related changes were detected in the nervous system tissue or muscle tissue at any concentration in either males or females. The NOEL was considered to be 3000 ppm for both sexes based on compound-related adverse effects on body weight, body weight gain, food consumption, food efficiency, and changes in 3 neurobehavioral parameters (male rats only) at 7500 and 18000 ppm.	61 FR 3403; 1/31/96, Docket OPPTS-44610