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Comparative study on toxicological profile and no observed adverse effect level of 2,4-dinitrophenol in newborn and young rats

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The starting ages of experimental animals in 28 days repeated dose toxicity study are 5 to 6 weeks old according to Japanese Official Test Guideline. There are no informations on chemical safety for newborn to infant. To elucidate the chemical safety for very young children, 2,4-dinitrophenol was given by gavage to newborn SD rats from 4 days after birth to 21 days and the result was compared to that of the 28 days repeated dose toxicity study using 5 weeks old SD rats. In newborn study, a part of animals was kept up to 12 weeks old. In 28 days study, abnormal behavior such as decreased locomotor activity, abdominal position, shallow respiration, etc. was observed and no observed adverse effect level (NOAEL) was considered to be 10 mg/kg/day. In newborn study, low body weight gain, decrease of absolute/relative thymus weight, increased relative organ weight of kidney and heart were observed and NOAEL was the same as that of 28 days study. These changes got back to normal by the withdrawal. It is presumed that the reason for the same toxicity level is partially due to the immediate toxicity action and quick metabolism rate of 2,4-dinitrophenol.

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Comparative study on toxicological profile and no observed adverse effect level of 4-nitrophenol in newborn and young rats

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INTRODUCTION: Generally, 28 days repeated dose toxicity study on chemical safety assessment in Chemical Control Act was conducted using 5 to 6 weeks old rats. However a neonate age, the fastest growth period, is not included in this repeated dose toxicity study. If neonates received adverse effects of chemicals, there is a significant possibility that those changes might have continued during their whole lives. As a lot of 28 days toxicity data using young rats are already obtained to date, those could be much more valuable if neonate toxicity information were given. In this experiment, to elucidate the chemical safety for very young children, 4-nitrophenol sodium salt chosen as the first sample chemical was repeatedly given to newborn rats and the result was compared to that of the 28 days repeated dose toxicity study using 6 weeks old rats.

MATERIALS and METHODS: 4-Nitrophenol sodium salt (CAS No. 824-78-2) was suspended in 0.5 % carboxymethyl cellulose. 28 days repeated dose study was conducted in SPF male and female Crj:CD(SD) IGS rats in doses of 80, 160, 400 and 1000 mg/kg/day. In newborn study, 4-nitrophenol sodium was given by gavage to SPF male and female Crj:CD(SD) IGS rats from 4 days after birth to 21 days in doses of 80, 110 and 160 mg/kg/day. All of these studies were conducted under GLP in Chemical Control Act.

RESULTS and DISCUSSION: In 28 days study, almost all males and females died from intoxication at 1000 mg/kg and appearance of eosinophilic body in kidneys was noted in males at 400 mg/kg. No observed adverse effect level (NOAEL) was estimated to be 160 mg/kg/day for males and 400 mg/kg/day for females. In newborn study, a temporal retardation of body weight gain was observed in males at 160 mg/kg but there were no toxicological changes in females in any treated groups. Then, NOAEL was estimated to be 110 mg/kg/day for males and higher than 160 mg/kg/day females. As the results, there is no great difference between NOAEL of 4-nitrophenol sodium salt in newborn rats and that in young rats.