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TOXICITY TESTS ON POST OFFICE CANCELLING INK 1882-17

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FOREWORD

In December, 1967, the Office of Research and Engineering, Post Office Department, requested the Public Health Service to determine whether a new cancelling ink would be safe to use. This report details the toxicity testing performed as a preliminary to the field testing.

Occupational Health Program personnel participating in the study included:

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TOXICITY TESTS ON POST OFFICE CANCELLING INK 1882-17

SUMMARY

Post Office Cancelling Ink 1882-17 was submitted to a battery of tests:

1. Rabbit eye irritation test;
2. Acute oral toxicity for rats;
3. Acute dermal toxicity for rabbits;
4. Test for primary irritation on rabbit skin;
5. Guinea pig skin sensitization test;
6. Prophetic patch tests on 324 human volunteers; and
7. Phototoxicity test on six human volunteers.

None of the tests suggested that the ink was sensitizing, toxic, or unduly irritating. No skin reactions were experienced by the two ink formulators at the Bureau of Engraving and Printing where the ink was developed. A search of the literature for toxicity of the ingredients revealed no reports of toxicity which would preclude the intended use of the ink.

In view of these findings, the investigators are of the opinion that the ink may be used as proposed by the Post Office Department, without detectable risk of adverse effect on postal employees or the using public. As a final safeguard, however, we suggest that the employees using the ink be subjected to some form of medical surveillance during the proposed trial period of use.

POST OFFICE CANCELLING INK

BACKGROUND

The purpose and method of use of the cancelling ink under investigation is as follows:

The ink will be used in ink pads and automatic cancellers for cancellation of postage stamps and for printing postmarks. Two pints of Post Office Cancelling Ink 1882-17 (P.O. Item #788) were obtained from the Bureau of Engraving and Printing for toxicity testing.

METHODS AND RESULTS

GENERAL EVIDENCE

The composition of Post Office Cancelling Ink 1882-17 was reported by the Office of Research and Development Engineering, Bureau of Engraving and Printing, Treasury Department, as follows:

Ingredient	% Weight
Varnish 120 RDE	30
Carbon Black	10
Butyl Carbitol	50
Isopropanol	10
Total	100%

The formula for Varnish 120 RDE is as follows:

Ingredient	% Weight
1120 Maleic Resin	40
#70 Phthalic Anhydride Soya Alkyd	15
Methyl Carbitol	25
Butyl Carbitol	20
Total	100%

POST OFFICE CANCELLING INK

Carbon black is a general term for several types of carbonaceous material made by the channel, furnace, and other processes. It is essentially carbon, combined with residual hydrogen from the hydrocarbon raw material. It also contains chemisorbed oxygen and less than 0.1% ash.[1] Animals exposed for prolonged periods of time by inhalation were without significant effects other than accumulation of dust in the pulmonary system.[2] Ingestion[1] and skin contact[3] studies in animals have also been negative. Surveys of industrial workers exposed to carbon black have revealed no evidence that carbon black is carcinogenic, and the morbidity and mortality experience of exposed employees is as good if not better than expected for comparable non-exposed populations.[4]

Diethylene glycol monobutyl ether (butyl Carbitol)[5] is a colorless liquid with a mild odor. In rats it is low in single-dose oral and vapor toxicity, moderately toxic in repeated-dose oral toxicity, moderately irritating and injurious to the eyes, not appreciably irritating to the skin, and not absorbed through the skin in acutely toxic amounts except at high dosage levels. Narcosis can be produced in rats by oral administration. Diethylene glycol monobutyl ether has had a long industrial experience, and no adverse human experiences have been reported. No threshold limit has been set.

Diethylene glycol monomethyl ether (methyl Carbitol)[5] is a colorless liquid with a mild odor and a bitter taste. In rats, it is low in oral toxicity and can produce narcosis by the oral route. It is slightly irritating to the eyes, but the injury is transitory. It is not irritating to the skin; and percutaneous absorption, although possible under certain conditions, is unlikely to be a problem in ordinary industrial operations. Because of its low volatility at normal room temperature and its low oral toxicity, diethylene glycol monomethyl ether presents no unusual hazards from inhalation. No adverse human experience has been reported. No threshold limit has been set.

POST OFFICE CANCELLING INK

Maleic resin and phthalic anhydride soya alkyd[5] are alkyd resinous materials of the ester type. These synthetic resins are physiologically inert. They do not cause skin irritation nor sensitization and do not show specific pulmonary reactions upon inhalation as dusts.

Isopropanol (isopropyl alcohol)[5] is not usually considered an industrial health hazard. At extremely high concentrations (not very likely in industrial operations) the inhalation of its vapors produces a narcotic effect and may be followed by rhinitis and bronchitis. It can be rather irritating to the mucous membranes. With repeated application of isopropyl alcohol on the skin of experimental animals no untoward effects were noted.

EXAMINATION OF FORMULATORS

Since persons involved in developing the ink would probably be exposed to much greater concentrations of the substances in question than the user public, the senior investigator questioned and examined the two formulators (an ink technologist and a technician) at the Bureau of Engraving and Printing, Treasury Department, Washington, D.C., where the ink was developed. There was no indication or evidence of adverse skin effects from the ink.

RABBIT EYE IRRITATION TEST

The eye irritation test was performed according to the Food and Drug Administration's regulations for the Federal Hazardous Substances Labeling Act[6], Section 191.12.

The undiluted ink (0.1 ml) was instilled into the lower lid of the right eye of each of six albino rabbits. The upper and lower lids were gently held together for one second before releasing to prevent loss of material, and the eyes were not washed following instillation. Readings were made at 24, 48, and 72 hours after instillation. In no case was a positive reaction observed. The untreated eyes served as controls.

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ACUTE ORAL TOXICITY FOR RATS

Thirty male rats weighing between 225-250 gm. each, were divided into five groups of six animals each. Six animals in each of four groups were given the ink intragastrically (1 gram, undiluted) immediately following a 24-hour period of fasting. One group of six rats was used for control purposes and received an equivalent volume of saline intragastrically. Within five minutes after administration of the ink, narcosis was observed in the rats for periods lasting up to about 20 minutes. The first group was sacrificed at the end of six hours, the second at 24 hours, the third at 7 days, and the fourth at 14 days post exposure. One control rat was sacrificed at each of the early sacrifice times, and three at 14 days post exposure.

No differences were observed in body weight gains between the exposed and control rats. The lungs, heart, liver, spleen, kidneys, stomach, esophagus, small intestine and large intestine were examined grossly and microscopically in the 24 exposed and six control rats following the scheduled sacrifices. No consistent pathological changes that could be attributed to the ink were seen in the tissues.

An equivalent amount of one of the solvents, butyl Carbitol, was subsequently administered to three additional control rats, with the production of a narcotic effect similar, but of shorter duration, to that produced by the ink.

ACUTE DERMAL TOXICITY FOR RABBITS

This test was performed in accordance with Sections 191.10 of the Food and Drug Administration's Regulations of the Federal Hazardous Substances Labelling Act[6] as modified by Kettering Laboratory (use of three animals instead of six, for test materials which are relatively non-toxic). Three male albino rabbits weighing between 2 to 3 kg. were used. The animals were prepared by clipping the skin of the trunk free of hair. Abrasions were made on the skin of two rabbits only. A plastic sleeve (2-quart size plastic bag) was fitted around the shaved area so that the central portion formed a "balloon". The ink (36 ml per kg.) was introduced under

the sleeve which was then wrapped with a cloth towel. Each rabbit was placed in a stock for 24 hours. At the end of this time they were released and the ink removed from the skin. After two weeks of observation, during which the rabbits appeared normal, they were sacrificed along with one control rabbit.

The skin, lungs, kidneys, spleen, heart, pancreas, adrenals, thyroid, thymus, testes, esophagus, bladder, and small and large intestines were examined grossly and microscopically. No consistent pathologic changes that could be attributed to the ink were seen in the tissues.

TEST FOR PRIMARY IRRITATION ON RABBIT SKIN

The undiluted ink, in 0.1 ml amounts, was applied in open and closed patch tests to shaved areas on the backs of rabbits. Six male albino rabbits were used. Readings at 24 and 48 hours were negative.

GUINEA PIG SKIN SENSITIZATION TEST

A modification[7] of the Landsteiner and Jacobs' test[8] for detecting strong cutaneous sensitizers was used.

Ten male albino guinea pigs weighing approximately 350 grams each were used as test animals. After the animals were clipped and shaved, an area of skin on the back was scarified (four $\frac{1}{2}$-inch-long crosshatch scratches), and a drop of undiluted ink was rubbed into the freshly scarified area with a glass rod. This procedure was performed nine times in a $2\frac{1}{2}$-week period. After a rest period of two weeks, the animals were challenged by applying the ink to scarified skin and were observed daily for three days. Except for minimal erythema from the scarifications, no reaction was observed in any of the animals.

POST OFFICE CANCELLING INK

PROPHETIC PATCH TESTS ON 324 HUMAN VOLUNTEERS

A modified Schwartz prophetic patch test technique[9] was used on 324 volunteers with the following three patch test materials:

1. Wet cancelling ink (full strength) on 3/4" flannel square;
2. Dry cancelling ink on white paper; and
3. Unprinted white paper (control).

Standard closed patch tests were applied to the lateral aspect of the left arm for 48 hours. The patch test sites were read 15 minutes after removal of patches to detect any immediate irritation or pre-existing sensitivity. After a rest period of two weeks, the patch tests were re-applied in the same location for 24 hours. The patch test sites were read on removal and 24, 48 and 72 hours after removal to ascertain if allergic eczematous reactions had developed. All patch tests of the second series were negative, except for 8 subjects who had transient erythema under the patches, interpreted as physical or fatiguing reactions. These eight subjects were subsequently patch tested with 10% ink in olive oil, and all were negative during the 72 hour observation period, indicating no sensitization.

The patch test population ranged in age from 16 to 64, and consisted of 127 males and 197 females. Eighty-seven percent were Caucasians; the remainder were Negroes and Orientals.

According to the statistical analysis of Henderson and Riley[10] on the basis of these results, no positive reactions in a sample of 324, it can be predicted with 95% statistical certainty that the maximum possible sensitization from the ink will not exceed 0.9% in the exposed population at large.

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PHOTOTOXICITY TEST ON SIX HUMAN VOLUNTEERS

Undiluted ink was applied to two adjacent areas on the inner surface of the forearms of six adult volunteers (four males and two females). At the end of 24 hours, the patches were removed, the ink cleaned off with acetone, and one test site exposed to noon-day sunlight for 30 minutes. The other test site was shielded from sunlight exposure. Both irradiated and non-irradiated test sites were observed at 24, 48, and 72 hours. All were negative. Previous studies have showed that the action spectra for phototoxic reactions are greater than 3200A, and that an exposure of 30 minutes to April sunlight at the test latitude would be sufficient to produce a reaction to a phototoxic material.