GREEN

Tin Oxide and Tin

CIR EXPERT PANEL MEETING

JUNE 11-12, 2012

Cosmetic Ingredient Review
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June 11, 2012

Memorandum

To: CIR Expert Panel

From: Wilbur Johnson, Jr.
Manager/Lead Specialist

Subject: Draft Report on Tin and Tin Oxide

A Scientific Literature Review (SLR) on these ingredients was announced in February of 2012. Use concentration and safety test data received from the Council have been added for the Expert Panel's review at this meeting. Additionally, technical comments received from the Council have been addressed.

A copy of the draft report on these ingredients is included along with the CIR report history, Literature search strategy, Ingredient Data profile, 2011 FDA VCRP data, and technical comments received from the Council (pcpc1 pdf file). The unpublished data included with this report are:

1. Safety test data submitted on 1-09-2012 (data 1 pdf file);
2. Use concentration data submitted on 1-11-2012 (data 2 pdf file)

After reviewing the draft report, the Expert Panel needs to determine whether additional data are needed for completion of this safety assessment, or if the available data are sufficient for arriving at a conclusion on the safety of tin and tin oxide in cosmetic products.

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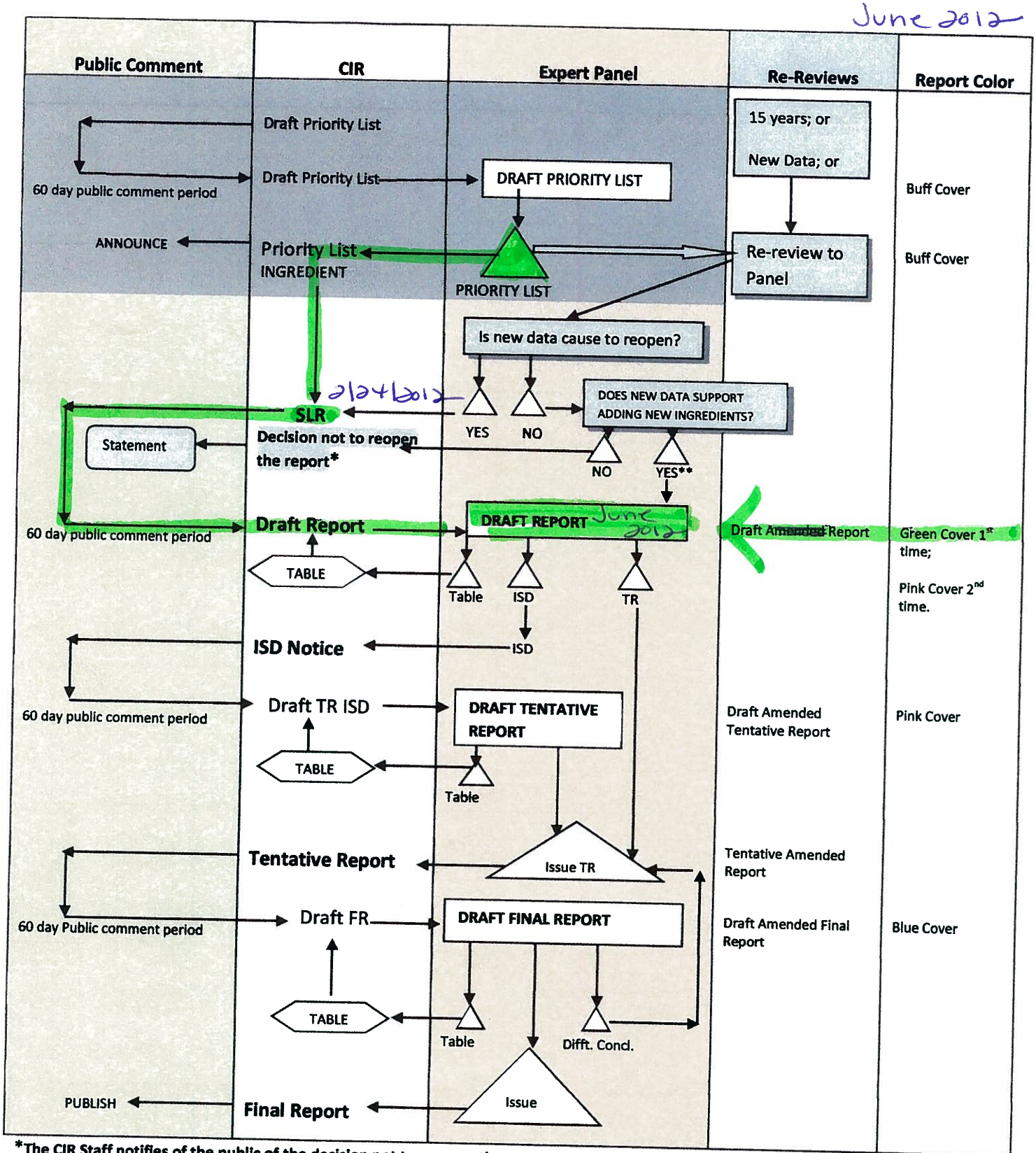
Tin & Tin Oxide

SAFETY ASSESSMENT FLOW CHART

June 2012



*The CIR Staff notifies of the public of the decision not to re-open the report and prepares a draft statement for review by the Panel. After Panel review, the statement is issued to the Public.

**If Draft Amended Report (DAR) is available, the Panel may choose to review; if not, CIR staff prepares DAR for Panel Review.

△ Expert Panel Decision

▭ Document for Panel Review

⇨ Option for Re-review

CIR History of:

Tin and Tin Oxide

A Scientific Literature Review (SLR) on these ingredients was issued in February of 2012. Use concentration and safety test data received from the Council were incorporated prior to announcement of the SLR.

1st Review, Belsito and Marks Teams/Panel: June 11-12, 2012

The following data on tin oxide (included in draft report) were received from the Council prior to announcement of the SLR: (1) RIPT on an eye shadow (0.3% tin oxide); (2) ophthalmological in-use safety evaluation of an eye shadow (0.3% tin oxide); (3) RIPT on a lipstick (0.5% tin oxide); RIPT on a lipgloss (0.35% tin oxide); and use concentration data on tin oxide.

Tin and Tin Oxide Checklist for June, 2012. Analyst – Wilbur Johnson																				
			Acute toxicity					Repeated dose toxicity				Irritation			Sensitization					
	Skin Penetration	Penetration Enhancement	ADME	Oral	Parenteral	Dermal	Inhale	Oral	Parenteral	Dermal	Inhale	Ocular Irritation	Dermal Irr. Animal	Dermal Irr Human	Sensitization Animal	Sensitization Human	Repro/Devel toxicity	Genotoxicity	Carcinogenicity	Phototoxicity
Tin			X		X			X				X		X	X	X	X		X	
Tin Oxide								X			X	X		X		X		X		

Literature Search on Tin and Tin Oxide*

Ingredients	Toxline &PubMed	ChemIDplus	Multidatabase (See legend*)	DART	SciFinder	RTECS
Tin	2920	1	3	18	127,283	
Tin Oxide	1962	1	1	6	37,151	

*Data in Table: Publications found; Multidatabase = HSDB, CCRIS, ITER, IRIS, Gene-Tox, and LacMed

Searches Performed on12/22/2011
Search Performed on 2/24/2012

Ingredients/Search Terms

Tin Oxide
Tin Dioxide
18282-10-5
1332-29-2

Tin
7440-31-5

Search Strings (NLM databases)

Tin Oxide OR Tin Dioxide OR 18282-10-5 OR 1332-29-2
Tin OR 7440-31-5

SciFinder Search Terms

18282-10-5
7440-31-5

Report

Draft Report on the Safety Assessment of

Tin and Tin Oxide as Used in Cosmetics

June 11, 2012

The 2012 Cosmetic Ingredient Review Expert Panel members are: Chair, Wilma F. Bergfeld, M.D., F.A.C.P.; Donald V. Belsito, M.D.; Curtis D. Klaassen, Ph.D.; Daniel C. Liebler, Ph.D.; Ronald A Hill, Ph.D. James G. Marks, Jr., M.D.; Ronald C. Shank, Ph.D.; Thomas J. Slaga, Ph.D.; and Paul W. Snyder, D.V.M., Ph.D. The CIR Director is F. Alan Andersen, Ph.D. This report was prepared by Wilbur Johnson, Jr., M.S., Manager/Lead Specialist.

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INTRODUCTION

The safety of tin oxide and tin as used in cosmetics is reviewed in this safety assessment. Tin oxide functions as an abrasive, bulking, and opacifying agent and tin functions as a surface modifier in cosmetic products.[1]

CHEMISTRY

Definition and Structure

Tin oxide (CAS Nos. 1332-29-2 and 18282-10-5), dioxide of tin, is an inorganic oxide that conforms to the following structure:

Other names for this chemical include: stannic oxide, white tin oxide, tin dioxide, stannic anhydride, and flowers of tin.[1,2]

Tin (CAS No. 7440-31-5) is a metallic element that conforms to the following empirical formula:

Sn

Physical and Chemical Properties

Tin is a silver-white metal that is malleable and somewhat ductile. It has a highly crystalline structure and exists in two allotropic forms at normal pressures. Gray tin exists below 13.2 °C and has a cubic structure. At 13.2 °C, gray tin is converted to white tin, which has a tetragonal structure.[3,4] The white form is known as the common, stable form at room temperature.[5] In compounds, tin can exist in the +2 or +4 oxidation state.[3,4] In compounds, tin in divalent and tetravalent oxidation states are designated as stannous and stannic, respectively. The Stock Oxidation-Number system denotes the oxidation state using Roman numerals in parentheses following the metal's name: tin(II) and tin(IV).[6] The cosmetic ingredient, tin oxide is tin(IV) oxide.

Chemical and physical properties of Tin and Tin Oxide are found in Table 1.

Method of Manufacture

The earth's crust contains approximately 2 to 3 ppm tin, comprising 0.0006% of the earth's crust.[2,7] The most important tin-containing mineral is cassiterite, SnO_2. Other tin minerals are stannite, teallite, cylindrite, and canfieldite. After tin-containing ores are mined, they undergo further separation processing, resulting in concentrates containing 70–77% tin by weight, almost pure cassiterite, and are ready for smelting.[8] Elemental tin is obtained from cassiterite by reduction with coal in a reverberatory furnace.[5] Although tin oxide occurs naturally in mineral form, this is not the source of the commercial product. It is manufactured directly from tin metal by thermal oxidation (from mined or recycled tin), either by exposing molten tin to air in a furnace at elevated temperatures, or by blowing tin powder in a stream of air through a furnace at approximately 700°C.

According to one source, the commercial production of tin oxides yielded the following grades: average particle size of 0.3 µm (bulk density = 0.72 g/cm^3), average particle size of 0.4 µm (bulk density = 1.15 g/cm^3), and average particle size of 0.5 µm (bulk density = 1.35 g/cm^3).[9] Each grade is > 99.0% pure and has a specific gravity of 6.9.

Impurities

Commercially available metallic tin is approximately 99.8% pure.[5]

USE

Cosmetic

Tin oxide functions as an abrasive, bulking, and opacifying agent and tin functions as a surface modifier in cosmetic products.[1] According to information supplied to the Food and Drug Administration (FDA) by industry as part of the Voluntary Cosmetic Registration Program (VCRP) in 2011, tin oxide was being used in cosmetic products, whereas, elemental tin was not.[10] These data are summarized in Table 2. Results from a survey of ingredient use concentrations provided by the Personal Care Products Council (also included in Table 2) in 2011 indicate that tin oxide was being used at concentrations up to 0.4% (rinse-off products) and up to 5 % (leave-on products).[11]

Cosmetic products containing tin oxide may be applied to the skin and hair, or, incidentally, may come in contact with the eyes and mucous membranes. Products containing these ingredients may be applied as frequently as several times per day and may come in contact with the skin or hair for variable periods following application. Daily or occasional use may extend over many years.

Tin oxide is used in dusting powders and cosmetic sprays, other fragrance preparations, and body and hand sprays, and could possibly be inhaled. In practice, 95% to 99% of the droplets/particles released from cosmetic sprays have aerodynamic equivalent diameters >10 μm, with propellant sprays yielding a greater fraction of droplets/particles below 10 μm when compared with pump sprays.[12,13] Therefore, most droplets/particles incidentally inhaled from cosmetic sprays would be deposited in the nasopharyngeal region and would not be respirable (i.e., they would not enter the lungs) to any appreciable amount.[14,15] However, the potential for inhalation toxicity is not limited to respirable droplets/particles deposited in the lungs. Inhaled droplets/particles deposited in the nasopharyngeal and thoracic regions of the respiratory tract may cause toxic effects, depending on their chemical and other properties.

Noncosmetic

Tin(IV) oxide is used in a variety of manufacturing applications, including polishing glass and other metals.[2] Elemental tin is present mainly in solder alloys used in the electronics industry, and is also used as a protective coating for other metals, especially those used for food containers.[16] Foods usually contain tin at levels < 4 μg/g, but higher levels may be found in processed foods because of tin-based preservatives and stabilizers and/or leaching from containers.[17] The Food and Agriculture Organization of the World Health Organization's Joint Expert Committee on Food Additives has established a provisional tolerable weekly intake of 14 mg Sn/kg body weight.[18] The European Union has established maximum levels for certain contaminants, inorganic tin included, to achieve a high level of public health protection, especially for sensitive population groups such as children or individuals with allergies.[19] Maximum levels of 200 mg/kg and 100 mg/kg were established for inorganic tin in canned foods and canned beverages, respectively.

TOXICOKINETICS

Oral Studies

Tin

After a single gavage dose of 20 mg/kg body weight of radiolabeled ^{113}Sn(II) or ^{113}Sn(IV) as the fluoride or citrate**,** the tissue distribution of tin in female Charles River (CD) or Cox Charles River rats after 48 h as a percentage of the administered tin(II) or tin(IV), respectively, was as follows: 1.0% and 0.24% (skeleton), 0.08% and 0.02% (liver), and 0.09% and 0.02% (kidneys).[20] Female rats excreted 95% of the radiolabeled tin in the feces and less than 1% in the urine. When oral tin doses of 20 mg/kg body weight were administered 6 days/week for 4 weeks, only the bone contained higher tin concentrations after day 28 when compared to tin concentrations after day 1. The half-life of tin in the femur was estimated to be 34 to 40 days. It was concluded that, of the soft tissues, only liver and kidneys were likely to accumulate significant amounts of tin as a result of the oral ingestion of tin salts. ^{113}Sn was found in the brain of rats at 48 h post-administration of ^{113}Sn(II) or ^{113}Sn(IV) (as the citrate or fluoride) as a single oral dose (4 mg), as oral doses of 20 mg/kg body weight on 6 days/week for 4 weeks, or as a single i.v. dose (0.4 mg).

Tin(II) chloride was injected orally (intagastric [i.g.], using stomach tube) into mice, Sprague-Dawley rats, African white-tailed rats, monkeys, and dogs.[21] Less than 5% was absorbed from the gut, and bone was the chief site of tin deposition.

The absorption of tin from the gastrointestinal tract and its distribution in the tissues was studied using groups of male Wistar rats dosed orally(gastric intubation) with ^{113}Sn(II) chloride together with the following other food components: sucrose, ascorbic acid, and potassium nitrate (given with the tin salt either separately or together), ethanol (given as 20% solution), a solution of albumin, and an emulsion of sunflower oil and 1% Tween 20.[22] In all groups, 90% to 99% of the administered radioactivity was excreted in the feces within 48 h, at which time fecal excretion and retention in the alimentary tract accounted for 98.7% to 99.9% of the dose. Only traces of ^{113}Sn were detected in organs and tissues examined, irrespective of the other components administered with the tin salt.

In another study, rats reportedly absorbed 7.65% of a single oral dose of tin(IV) chloride.[23] The recovery of 99% of administered tin in the feces and the lack of detectable urinary tin in the 24 h following ingestion of tin (7 to 20 mg/kg body weight) in orange juice by rats and cats indicated very low gastrointestinal absorption of tin.[24]

The concentrations of tin in the tibias (µg/g) of rats fed diets supplemented with tin(II) chloride (100 to 2,000 mg of tin per kg of diet) were more than 5 times greater than the tin concentrations in the kidneys and nearly 20 times greater than the concentrations in the liver.[25] No other organs were analyzed. Tin accumulated in the tibia and kidneys in a dose-dependent manner.

Male Wistar rats were given either 100 mg $SnCl_2$ per liter (0.44 mM), 250 mg/l (1.11 mM) or 500 mg/l (2.22 mM) in drinking water for 18 weeks.[26] Control rats received tap water. The tin content of the right cerebral hemispheres ranged from 5 to 10 pmol/g wet weight in control rats, and the following ranges were reported for the remaining groups: 7 to 19 pmol/g wet weight (0.44 mM in drinking water), 5 to 22 pmol/g (1.11 mM in drinking water), and 16 to 60 pmol/g (2.22 mM in drinking water). At the highest dose (2.22 mM), tin accumulated in the cerebrum throughout the experiment. In the right cerebral hemispheres, tin concentrations greater than the 1.11mM dose were only found after 15 and 18 weeks. Tin did not increase in the right cerebral hemispheres after dosing with 0.44 mM. After one week at the highest dose (2.22 mM), blood tin increased promptly, and there was no evidence of further accumulation. Blood tin at the 0.44 mM dose level did not differ from controls. Effects on cerebral and muscle acetylcholinesterase activity reported in this study are included in the Toxicology section later in the report text. Data from other animal studies suggest that inorganic tin does not readily cross the blood-brain barrier.[21,27,26]

A study using the radioactive tin isotope ^{113}Sn was performed using rats (Wistar AF/Han and Sprague-Dawley strains) and rabbits (strain not stated) to determine the kinetics of tin and of its absorption and excretion following oral administration.[28,29] Study details presented are from a translation of this German publication. ^{113}Sn was acquired as $SnCl_2$ dissolved in hydrochloric acid, and the specific activity amounted to 5-10 mCi/mg of Sn. Fourteen rats were killed within a time period between 1 and 21 days post-administration. The anuses of 6 rats were sutured (to ensure that urine was not contaminated with feces) after dosing and these animals were examined on days 2 and 5 post-administration. The anuses of 2 of the 5 rabbits used in the study were also sutured after dosing. ^{113}Sn content in the feces and urine and in the following organs was determined: liver, spleen, muscles, lungs, intestine, femur, testicles, heart, kidneys, and blood. Results for the group of 14 rats (1 died due to ileus) indicated that, primarily, the absorption of ^{113}Sn from the gastrointestinal tract was very minor, i.e., < 2%. Following oral administration, ^{113}Sn was excreted predominantly via the urine. In the other group of 6 rats (anuses sutured), ^{113}Sn absorption was < 1% and urinary excretion was somewhat higher. Both rabbits (anus sutured) died due to ileus; however, in 1 rabbit, ~ 5% of the administered radioactivity was excreted via the urine. In the remaining 3 rabbits, urinary excretion of administered radioactivity amounted to < 2%. An increased uptake of ^{113}Sn was not found in any organ (rats or rabbits).

The absorption of tin in the gastrointestinal tract was small and was dependent upon the amount administered. An increased uptake of tin was not found in any organ; absorbed tin was excreted via the kidneys. This information is from an English summary of a German publication. Additional details will be included after this publication has been translated.

The average daily tin intake of an adult in the United States was estimated at 4.003 mg (4 mg from food and 0.003 mg from air), and with undetectable levels contributed by drinking water. The most important source for exposure to tin is from food, especially canned food products. Tin-lined cans used to package food are the most important contributor to dietary tin intake.[30]

Eight healthy volunteers were fed mixed diets containing 0.11 mg tin (control diet) and 49.67 mg tin (test diet) daily for 20days. [31] The tin content of the control diet was typical of that found in diets that contained fresh and frozen foods. The

tin content of the test diet was typical of the amount found in diets that containing several servings of certain canned foods. When fed the test and control diets, 3% and 50% of their dietary tin intake, respectively, was absorbed .

When 9 healthy volunteers were given diets consisting of fresh foods (10 mg tin per day), or cold-stored canned foods (26 mg of tin per day), or warm-stored canned foods (163 mg of tin per day) for 24 days, fecal excretion accounted for the whole dose, and none was detected in the urine.[32]

Four human volunteers (2 males, 2 females) with tin blood levels of < 2 ng/ml (< 17 nmol/liter) each consumed 60 mg of tin in fruit juice from an unlacquered can, and blood samples were taken after 2 h, 5 h, and 24 h.[33] The 2 females had detectable tin blood levels (3 ng/ml) only in the 5-h blood samples. However, the 2 males had peak blood tin concentrations of 4.7 ng/ml after 2 h and 3.9 ng/ml after 24 h.

Intravenous/Intraperitoneal Study

Intravenous (i.v.) dosing of ^{113}Sn(II) or ^{113}Sn(IV) (each as the citrate) in rats resulted in the excretion of significant fractions of administered tin in the urine. [20] The presence of tin in the feces after i.v. dosing indicated that the biliary system can contribute significantly to tin clearance.

Tin(II) chloride was injected by intraperitoneal (i.p.), and intravenous (i.v.) routes into mice, Sprague-Dawley rats, and African white-tailed rats and i.v. into monkeys and dogs.[21] Less than 5% was absorbed, and bone was the chief site of tin deposition.

Subcutaneous Study

Ten female Wistar rats received repeated subcutaneous (s.c.) doses (2 mg Sn/kg) of tin(II) chloride every other day (7 doses total).[34] A second group of animals was exposed (same method) to tin(II) chloride labeled with ^{113}Sn. The control group consisted of 6 rats. The animals were killed 24 h after the last dose. Approximately 60% of the metal was retained in the body. Of this amount, approximately 95% accumulated in the skin and hair. The total dose of tin administered in the study was approximately 3,400 µg/animal, of which an average of 2,035 µg was retained. In the remaining organs and tissues, tin concentrations (expressed as µg Sn/g tissue) were lower by 1 to 2 orders of magnitude, which corresponded to 2.57 to 0.0001% of the retained dose. Most of the ^{113}Sn was retained in the kidneys (0.20 ± 0.35 µg Sn/kg) and muscles + bones (0.59 ± 0.18 µg Sn/kg).

Environmental Study

The levels of trace elements in maternal blood, umbilical cord blood, and the placenta were studied using 198 female subjects (16 to 39 years old) who, collectively, were from areas of the United States identified as the Southeast (Charlotte and Birmingham), NewYork-New Jersey (Riverhead and Elizabeth), Utah (Ogden and Salt Lake City), and California (East and West Los Angeles).[35] All participants lived in their respective areas for at least the entire duration of pregnancy. Blood/tissue specimens were obtained from obstetrics departments in local hospitals, and 25 maternal-fetal sets were collected from each of the 8 areas. Venous blood specimens were collected from the mother after delivery. Umbilical cord blood specimens were drawn after the cord was cut, but before delivery of the placenta. Samples of the placenta (free of gross pathology) consisted of 3 peripheral wedges cut in full thickness after placental delivery. Sample sizes ranged from 177 to 187 for cord and maternal blood and 160 to 169 for the placenta. Mean blood levels of tin were 4.6 µg/100 ml blood (maternal blood) and 5.6 µg/100 ml blood (cord blood). The mean level of tin in the placenta was 5.0 µg/100 g.

PBPK Model

According to The International Commission on Radiological Protection (ICRP) model,[36] the fraction of ingested tin that is absorbed from the gastrointestinal tract (uptake to blood) is assumed to be 0.02. Absorbed tin is assumed to enter the blood, from where 50% is immediately transferred to excreta (specific routes not specified in the model), 35% is transferred to bone mineral, and 15% is uniformly distributed to all other tissues. Tin in any tissue or organ is retained with elimination half-times of 4 (20% of tissue burden), 25 (20%), and 400 (60%) days.

The ICRP also provides classifications for clearance of inhaled tin compounds in the respiratory tract, for use in an inhalation model.[30,36] Sulfides, oxides, hydroxides, halides, and nitrates of tin, and stannic phosphate are assigned Type M,

and all other tin compounds are assigned to Type F. With Type F compounds, rapid absorption (100%) is assumed to occur within 10 minutes of material deposition in the bronchi (BB), bronchiole (bb), and alveolar interstitial (AI) regions. Fifty percent of Type F compounds deposited in the extrathoracic region transfer to the gastrointestinal tract (ET_2). During breathing through the nose, approximately 25% of the tin deposited in the extrathoracic region is absorbed rapidly, and breathing through the mouth yields 50% absorption. With Type M compounds, approximately 70% of the tin deposited in AI regions is eventually transferred to the blood, approximately 10% of the tin deposited in BB and bb is absorbed rapidly, and 5% of the tin is deposited in ET_2. During breathing through the nose, approximately 2.5% of the tin deposit in the extrathoracic region is absorbed rapidly and 5% is absorbed rapidly during breathing through the mouth.

TOXICOLOGY

Acute Toxicity

Parenteral Studies

Tin

Reportedly, the results of studies in which animals (species not stated) were injected intravenously (i.v.) with tin indicated a lethal dose of 100 mg/kg body weight.[37]

Using a laryngeal tube, tin dust (50 mg, in saline) was injected into the trachea of rats (number and strain not stated) and then blown into the lungs.[38] At 3 months post-injection, microscopic examination revealed many areas with dust cells lining the alveoli. Tin particles were observed in phagocytes, in the pleural lymphatics, and in the mediastinal lymph glands. In another experiment, tin dust was injected i.v. into the tail vein of mice (number and strain not stated). Particles of tin dust were found in the lungs, spleen, and, particularly, in the liver. No cellular reactions were observed and all mice were very healthy. In both mice and rats, no fibrous response in the lungs was observed up to a year post-evaluation.

Repeated Dose Toxicity

Oral Studies

Tin Compounds

Various tin compounds were fed to weanling Wistar rats for either 4 or 13 weeks. Groups of 10 males and 10 females were fed diets containing 0, 0.03, 0.10, 0.30, or 1.0% of the following: tin(IV) oxide, tin(II) chloride, tin(II) orthophosphate, tin(II) sulfate, tin(II) sulfide, tin(II) oleate, tin(II) oxalate or tin(II) tartrate for 28 days.[39] Additional groups of 10 males and 10 females were fed either tin(II) chloride or tin(II) oxide in the diet at the levels previously mentioned for 90 days. Endpoints monitored included: mortality, growth, food consumption and utilization, hematology, urinalysis, serum biochemistries, and gross and microscopic pathology. No compound-related adverse effects were observed among rats fed tin(IV) oxide, tin(II) sulfide, or tin(II) oleate for 4 weeks. Anemia and reductions in growth, food consumption and food use efficiency were observed, however, among rats fed either 0.3 or 1% of tin(II) chloride, tin(II) orthophosphate, tin(II) sulfate, tin(II) oxalate, or tin(II) tartrate. Microscopic evidence of liver damage (homogeneous liver cell cytoplasm; slight but definite oval cell type hyperplasia of bile ducts) was also observed in male and females fed 1.0% of the same compounds. Similar hepatic changes, though of lesser intensity and frequency, were observed among rats fed 0.3% tin(II) chloride, tin(II) oxalate or tin(II) orthophosphate. Females given tin(II) orthophosphate had a dose-related increase in relative liver weight at $\geq 0.1\%$.

No compound-related adverse effects were observed among rats fed tin(II) oxide for 13 weeks. In the 13-week study with tin(II) chloride, rats fed 1.0% were killed after 8 weeks on test because of high mortality. Necropsy of these rats revealed anemia, distinct liver changes (described above), severe pancreatic atrophy, enteritis, moderate testicular degeneration, " a spongy state of the white matter of the brain", and acute broncho-pneumonia. It was speculated that some of these changes were due to starvation. Poor appetite and reduced growth were also observed among rats fed 0.3% stannous chloride, but these changes were observed only for the first 2 weeks. Thereafter, growth and food consumption among rats fed 0.3% were similar to controls. Slight anemia (males only) and other changes (described above) were also observed among rats fed 0.3%. No compound-related adverse effects were observed among rats fed 0.03 or 0.1% tin(II) chloride for

13 weeks. The authors concluded that 0.1% of tin compounds in the diet (22 to 33 mg of tin/kg/day; estimated by investigators) was a "no-effect-level." [39]

Tin

The tolerability of tin migrated from canned food (tomato soup) packaging at concentrations < 0.5 mg/kg (tomato soup without tin) and 201 mg Sn/kg and 267 mg Sn/kg in 250 ml tomato soup was evaluated using 24 normal volunteers.[40] The main focus of this study was to determine the dose-response of tin acute gastrointestinal effects in man. Tomato soup samples (250 ml) were heated to the temperature range of 65ºC to 70ºC and consumed within 15 minutes after nominal dosing time (8:00 a.m.) in a 3-way crossover design with wash out periods of at least 48 h between the different dose levels. There were 3 treatment periods, and the subjects were evaluated for adverse effects at 4 h post-dosing. No clinically significant adverse effects were reported. Similarly, no toxic effects were observed when 9 volunteers were given canned food with tin concentrations of 13, 33, and 204 mg/kg for three 24-day periods, respectively.[32]

At the 64th Joint FAO/WHO Expert Committee on Food Additives (JECFA) meeting in 2005, the Committee reiterated its opinion, expressed at the 33rd and 55th Committee meetings, that the available data for humans indicated that inorganic tin at concentrations > 150 mg/kg in canned beverages or > 250 mg/kg in canned foods may produce acute gastric irritation in certain individuals.[16] Therefore, ingestion of inorganic tin at concentrations equal to the proposed standard for canned beverages (200 mg/kg) may lead to adverse reactions.

Cytotoxicity

Metallic tin (powdered form; particle size = < 125 μm) was not cytotoxic in an *in vitro* cell culture test involving human fibroblasts incubated for 24 h.[41]

Effect on Acetylcholinesterase

Male Wistar rats were given either 100 mg $SnCl_2$ per liter (0.44 mM), 250 mg/l (1.11 mM) or 500 mg/l (2.22 mM) in drinking water for 18 weeks.[26] At the 2 higher doses, tin exposure caused a dose-dependent increase in cerebral (left cerebral hemispheres) and muscle acetylcholinesterase activity.

Respiratory Irritation

Reportedly, tin powder is moderately irritating to the airways.[37]

Ocular Irritation

Tin Oxide

The ocular irritation potential of an eyeshadow containing 0.3% tin oxide was evaluated using 34 female subjects (18 to 65 years old), 3 of whom withdrew for reasons unrelated to conduct of the study.[42] The participants were instructed to use the test material at least once daily for 4 weeks. A comprehensive ocular examination was performed at the end of the 4-week period. There were no adverse events, and all ophthalmologic examinations remained within normal limits. Study results did not indicate a potential for ocular irritation or hypersensitivity.

Tin

Reportedly, tin powder is moderately irritating to the eyes.[37]

Skin Irritation and Sensitization

Tin Oxide

The skin irritation and sensitization potential of a powder eye shadow containing 0.3% tin oxide was evaluated in a repeated insult patch test (RIPT) using 111 male and female subjects (18 to 75 years old), 98 of whom completed the study.[43] Withdrawal from the study was not related to application of the test material. A 1" x 1" semi-occlusive patch containing 0.2 g of the test material was applied to the upper back (between the scapulae) of each subject 3 times per week for a total of 9, 24 h induction applications. After a 2-week non-treatment period, challenge patches were applied for 24 h to a new test site. Reactions were scored at 24 h and 72 h post-application. No reactions were observed, and it was concluded that the test material did not have skin irritation or allergic contact sensitization potential.

The skin irritation and sensitization potential of a lipstick containing 0.5% tin oxide was also evaluated in an RIPT (same procedure) using 112 male and female subjects (16 to 79 years old), 103 of whom completed the study. Withdrawal from the study was not related to application of the test material. No reactions were observed, and it was concluded that the test material did not have the potential for causing dermal irritation or allergic contact sensitization.[44] In another study, the skin irritation and sensitization potential of a lipgloss product containing 0.35% tin oxide was evaluated in an RIPT (amount per patch not stated) using 112 male and female subjects (18 to 70 years old), 108 of whom completed the study.[45] The test protocol was identical to that used in the preceding test, with the exception that challenge sites were evaluated at 24 h, 48 h, and 72 h post-application. No reactions were observed, and it was concluded that the test material did not demonstrate a clinically significant potential for eliciting dermal irritation or sensitization.

Tin

Seventy-three nickel-sensitive patients (age range not stated) were patch-tested with copper discs (12 mm diameter) plated with a tin coating.[46] The discs were applied directly to skin of the upper back and secured with Scanpor® tape for 48 h. Reactions were scored at 48 h and 72 h post-application. Positive reactions were observed in 6 subjects (age range: 7 to 74 years). Five subjects had a ++ allergic reaction and 1 subject had a +++ allergic reaction to the tin discs. An additional 4 subjects were classified as having doubtful reactions. Patch test results also indicated that it is unlikely that metallic tin is a skin irritant. It was noted that if pure metallic tin were an irritant, one would have expected a higher number of doubtful reactions.

Fifty workers in the ceramics industry (12 males, 38 females) were patch tested with 2.5% metallic tin. A positive reaction was observed in only one subject. [47]

Allergenicity

Intraperitoneal (i.p.) or intravenous (i.v.) injections of metallic tin powder (200 mg in saline) produced a striking plasmacellular hyperplasia in the draining lymph nodes and spleen of Lewis rats.[48,49] The lymph node response to metallic tin varied from a very mild response to insoluble foreign particles to a marked granulomatous hyperplasia (August rats) and intense plasmacellular hyperplasia (Lewis rats and F_1 hybrids of Lewis rats).[50]

Occupational Studies/Case Reports

Tin Oxide

Two-hundred fifteen workers (ages not stated) were exposed to tin oxide fumes at a plant, 95% of whom had at least 3 years of service.[51] Of the 215 workers that received chest X-rays, 121 had changes identified as pneumoconiosis. None of the X-ray films were suggestive of massive fibrosis or significant emphysema, and there was no evidence of massive fibrosis or nodulation. There were no differences in the following between the 121 pneumoconiotic workers and 94 non-pneumoconiotic workers: respiratory symptoms, vital capacity, chest expansion, loss time due to chest illness, and incidence of tuberculosis.

A clinical study of 19 male employees (most < 30 years old) exposed to tin oxide dust and fumes at a plant was performed.[52] Impairment of pulmonary function was not observed in any of the subjects, and there were no reports of work disability from any clinical cause. Physical examinations did not reveal any abnormal lung findings or significant findings in general. All of the values for vital capacity, maximal breathing capacity, resting minute volume, and respiratory reserve were within normal limits. The absence of alteration in these ventilatory tests indicae that there was no significant degree of obstructive emphysema or of diffuse pulmonary fibrosis. Based on the methods used, it was noted that the only type of pulmonary function alteration that could have escaped detection would have been impaired diffusion of the alveolo-capillary block type, which is found in cases of asbestosis and berylliosis.

Based on chest roentgenograms, one subject was classified as completely normal, 8 were classified as stannosis suspects, and 10 were classified as having tin oxide pneumoconiosis. It was noted that subjects with less than 3 years of exposure may be classified as either normal or suspects, but do not present with pulmonary nodulation. After 3 years of exposure to tin oxide, nodular stenosis was found in all cases, and advanced stages occurred with increasing frequency as the years of exposure increased. Of the 10 employees with roentgenographic changes classified as stannosis, 6 had been exposed to tin oxide fume. The most advanced changes were observed in 4 of these 6 employees. One of the 4 subjects probably had been exposed exclusively to tin oxide dust and had first stage stannosis, and the remaining 3 subjects (exposure to dust and fumes) had varying degrees of change. Six of the 10 employees with lung changes were asymptomatic and the following signs were reported for the remaining 4: moderate anorexia (2 subjects), cough with serious expectoration (1 subject), and scapular pain (1 subject). For the 10 cases of stannosis, the hemograms and sedimentation rates were within normal limits. Traces of albumin in the urine were reported for 3 of the cases, and the blood Kahn reaction was normal in all cases. The authors noted that the results of this study corroborate the conclusion that tin oxide fume, and not tin oxide dust, is more likely to be the cause of stannosis.[52]

Stannosis is the form of pneumoconiosis (non-fibrotic form) that results from the inhalation of tin in the form of tin oxide fumes or dust. Tin oxide accumulates in the pulmonary parenchyma. Lung radiography results for a man (age not stated) who had worked in the smelter of a tin mine for 26 years revealed moderately profuse small nodules, some of which were metallic in density.[53] The patient was asymptomatic and clinically normal. Lung function tests were not performed. Results 8 years later revealed an increase in the profusion of small opacities, particularly in the left mid-zone of the lung. The patient remained asymptomatic. Another case report involved a 55-year-old male employee of a detinning plant for 15 years. He was exposed to tin fumes as well as clouds of coal dust on the job, and lung function test results yielded a forced vital capacity of 90% and a forced expiratory volume that was 96% of predicted values. Lung radiography results revealed very profuse bilateral nodules (~ 3 mm in diameter). At lung biopsy, focal aggregations of macrophages containing dust particles (black particles) were observed in some of the air spaces and in the perivascular and peribronchiolar connective tissue. Electron probe analysis results indicated that tin was present in the dust.[53]

A 50-year-old female (non-smoker) with stannosis was exposed to tin fume for 33 years. There were also exposures to biomass fuels and asbestos. A chest X-ray revealed common nolular lesions and thorax high resolution computed tomography revealed widespread interlobular thickening and peribronchial thickening. Subpleural nodules with metallic density were observed in the upper and middle lobe of the right lung. Bronchial lavage cytology was defined as class II, and histiocytic cells and focal fibrosis were detected on transbronchial lung biopsy. The patient died 6 months later due to respiratory failure.

Tin

Toxicity (e.g., nausea, vomiting, and diarrhea) in humans due to the consumption of food highly contaminated with tin has been reported.[5,54,24,55,56,57]

In a Belgian case-control study (n = 272 men and women), a significantly increased risk (odds ratio 3.72, 95% confidence interval 1.22 to 11.3) of chronic renal failure was found for occupational exposure to tin (Nuyts et al. 1995). [58] Exposures were reconstructed from self-reported occupational histories by 3 industrial hygienists independently.

REPRODUCTIVE AND DEVELOPMENTAL TOXICITY

Tin

The placental transfer of tin was studied using groups of 12 pregnant Sprague-Dawley rats fed tin salts in the diet from day 0 to day 20 of gestation. Fetal tin values were slightly elevated (0.8 to 1.3 mg/kg body weight) in Sprague-Dawley rats on day 20 of gestation when the maternal diets contained tin salts (tin(II) fluoride, sodium pentachlorostannite, or sodium pentafluorostannite) at 125 to 625 mg/kg in the feed (approximately 10 to 50 mg of tin per kg body weight per day).[59] The increases were generally dose-related. Untreated rats had fetuses containing 0.64 mg of tin per kg body weight. Reproductive performance was normal in all dietary groups, and the number of viable fetuses per litter ranged from 9 to 14. Only one nonviable (unresorbed) fetus was observed in the 154 females that delivered viable fetuses.

GENOTOXICITY

Tin Oxide and Tin Ore Powder

Tin(IV) oxide and 5 kinds of Yunnan tin ore powder were administered to rats through the trachea, and cytological preparations were made at various intervals in order to determine effects on micronucleus frequency and karyorrhexis of rat bone marrow cells and lung macrophages.[60] Results indicated that tin(IV) oxide and each of the 5 kinds of Yunnan tin ore powder can induce micronuclei and karyorrhexis in bone marrow cells. On the first and tenth day, the frequency of karyorrhexis was higher than that of micronuclei, and differed significantly from that of the control, and vice versa, on the 20th and 30th days. Tin(IV) oxide and each of the 5 kinds of Yunnan tin ore powder also can induce micronuclei and karyorrhexis in lung macrophages. On the 10th and 20th days, the frequency of karyorrhexis was the same as that in bone marrow cells.

CARCINOGENICITY

Tin

The tumorigenicity of tin foil was evaluated using 25 male Wistar rats.[61] Circles or squares of tin foil (~ 1.5 cm wide) were sterilized in Zephiran and washed in sterile saline. The pieces of metal (2 per animal) were then imbedded s.c. in the abdominal wall, just ventral to the fascia. The animals were then evaluated for tumor formation at weekly intervals. The percentage production of tumors was calculated on the basis of the number of animals that survived beyond the minimum latent period (300 days) necessary for tumor production. The tin foil did not induce tumor formation in any of the animals.

Sterilized 4 mm cylinders of pure tin foil (0.0015" thick) were inserted anteriorally, parallel with the surface of the cranial arc, into 39 male Marsh mice.[62] The skin was then sutured. Implantation was followed by a 19-month observation period. Thirty-eight mice subjected to the same surgical procedure served as controls. Of the 33 mice that survived the implantation procedure, 16 died before the 7th month, 7 died between the 7th and 9th month, and 10 died between the 10th and 19th month. Thirty-two of the 39 surgical controls survived 13 to 19 months. Compared to surgical controls, the lower survival rate for test animals was due to genital urinary disorders that resulted from fighting. Local neoplasms did not develop in any of the mice. Various degrees of gliosis were observed histologically after 3, 4, 5, 6, 11, 14, and 19 months.

In another study, an intrathoracic injection (0.2 ml per mouse) of a 20 mg/ml tin needles suspension in isotonic saline was made into each of 43 male Marsh mice.[63] The needles were 1μ in diameter and needle lengths were defined as follows: $\leq$ 3.3 μ (46% of the needles), 3.3 to 6.6 μ (12%), 6.6 to 9.9 μ (8%), and > 9.9 μ (34%). Control mice (44) were given the same volume of isotonic saline. The study was terminated 19 months later. Three female mice were injected i.p. with 0.5 ml of a 10 mg suspension of tin needles in isontonic saline and killed 40 days later. At 24 h post-injection (intrathoracic), water and food intake were reduced markedly in mice. Of the 41 mice that survived 10 to 19 months after intrathoracic injection, 16 had tin particles within the thorax, 9 had tin particles within the peritoneum, and 1 had tin particles within the thorax and peritoneum. Adhesions to the following tissues were observed: lung (6 adhesions), pericardium (7), diaphragm (2), thoracic wall (5), and intrathoracic site (6 diffuse adhesions). At the i.p. site, there were 6 adhesions to the liver, 3 to the diaphragm, and 3 diffuse adhesions. At 40 days post-i.p. injection of tin needles, the foreign body reaction was primarily lymphohistiocytic. Tin needles were found on the gut, mesentery, and liver. Histologic examination (14 mice) of the local reaction to tin was performed at 13.5 to 19 months after after intrathoracic injection. At 11 intrathoracic injection sites, most of the tin needles were engulfed by giant cells and rested in the cytoplasm. Additionally, adjacent nodular fibroplasia was observed and a network of capillaries had developed.

Gross examination of the bladder, liver, and kidney in mice (intrathoracic injection) did not reveal any statistically significant differences in organ damage between test and control animals. Observations for the development of neoplasms intrathoracically revealed l lung papillary adenoma, 2 reticulum cell sarcomas, and 1 lymphosarcoma. Four reticulum cell sarcomas and 2 malignant lymphomas at multiple sites (mesenteric, thymic, parotid, and leukemic) also developed. These tumors were also observed in control mice and were not considered treatment-related. The tin needles did not induce local or general neoplasm development.[63]

HEALTH EFFECTS ASSESSMENT

According to a health effects assessment on tin and tin compounds by the U. S. Environmental Protection Agency, an oral reference dose (RfD) of 0.62 mg Sn/kg/day or (43.4 mg Sn/day) was recommended.[64] The RfD is defined as an estimate of an exposure level that would not be expected to cause adverse effects when exposure occurs for a significant portion of the lifespan.

In a toxicological profile for tin and tin compounds, prepared by the Agency for Toxic Substances and Disease Registry of the U.S. Department of Health and Human Services, a minimal risk level (MRL) of 0.3 mg/kg/day was derived for intermediate-duration oral exposure (15 to 364 days) to inorganic tin.[30] An MRL is defined as an estimate of daily human exposure to a substance that is likely to be without an appreciable risk of adverse effects (noncarcinogenic) over a specified duration of exposure.

The National Institute for Occupational Safety and Health (NIOSH) has established a recommended exposure limit for tin and tin (IV) oxide of 2 mg/m^3 of air as a time-weighted average for up to a 10-h workday during a 40-h work week.[65]

SUMMARY

The safety of tin oxide (dioxide of tin) and elemental tin in cosmetics is reviewed in this report. Elemental tin is obtained from cassiterite by reduction with coal in a reverberatory furnace. Tin oxide is manufactured directly from tin metal by thermal oxidation. According to information supplied to the Food and Drug Administration (FDA) by industry as part of the Voluntary Cosmetic Registration Program (VCRP) in 2011, tin oxide, but not elemental tin, was being used in cosmetics. Furthermore, results from a survey of ingredient use concentrations provided by the Personal Care Products Council in 2011 indicate that tin oxide was being used at concentrations up to 0.4% in rinse-off products and up to 5% in leave-on products.

The results of toxicokinetic studies involving rats, cats, monkeys, and dogs indicated that more than 90% of orally or parenterally (i.v. and i.p.) administered tin (as tin salts) was excreted. The skeleton was the main site of deposition, but tin was also deposited in the liver and kidneys. There was also very little absorption of tin from the GI tract of man. Following s.c. dosing in rats, approximately 60% of the metal was retained in the body. Of this amount, approximately 95% accumulated in the skin and hair. PBPK modeling (ingestion) indicated that tin in any tissue or organ is retained with elimination half-times of 4 (20% of tissue burden), 25 (20% of tissue burden), and 400 (60% of tissue burden) days. An inhalation model for tin compounds (oxides included) indicated that 70% of the tin was deposited in alveolar interstitial regions and eventually transferred to the blood. Approximately 10% of the tin deposited in the bronchi and bronchioles was absorbed rapidly. Tin in maternal blood, umbilical cord blood, and the placenta was detected in a study involving 198 female subjects from various areas of the United States.

Reportedly, i.v. dosing of animals yielded a lethal dose of 100 mg/kg body weight. No test substance-related adverse effects were observed in rats fed tin(IV) oxide at dietary concentrations up to 1.0% for 4 or 13 weeks. Toxic effects were not observed when 9 volunteers were given canned food with tin concentrations of 13, 33, and 204 mg/kg for three 24-day periods, respectively. Elemental tin was not cytotoxic to human fibroblasts *in vitro*.

Reportedly, tin powder is moderately irritating to the airways. An eyeshadow containing 0.3% tin oxide did not cause ocular irritation in 31 subjects who participated in a 4-week product use study (daily applications). In repeated insult patch tests, neither a lipstick (0.5% tin oxide, 103 subjects), lipgloss product (0.35% tin oxide, 108 subjects), nor a powder eye shadow (0.3% tin oxide, 98 subjects) induced skin irritation or allergic contact sensitization. A positive reaction was observed in 1 of 50 workers in the ceramics industry patch-tested with 2.5% metallic tin. Of 73 nickel-sensitive patients patch-tested with copper disks plated with a pure tin coating, 6 had allergic reactions and 4 had doubtful reactions. Tin was not classified as a skin irritant. Intraperitoneal or i.v. injections of metallic tin powder (200 mg in saline) induced plasmacellular hyperplasia in the spleen and draining lymph nodes.

In occupational settings, stannosis has been observed in workers exposed to tin oxide fumes. In a case-control study (272 men and women), a significantly increased risk (odds ratio = 3.72) of chronic renal failure was found for occupational exposure to tin.

In pregnant rats, dietary exposure to tin salts resulted in a dose-related elevation (0.8 to 1.3 mg/kg body weight) of tin values in fetuses. Reproductive performance was normal in all dietary groups.

Tin(IV) oxide administered intratracheally induced micronuclei and karyorrhexis in rat bone marrow cells *in vivo*. The s.c. implantation of tin foil into the abdominal wall of 25 rats did not induce malignant tumor formation during the 300-day latent period necessary for tumor formation. Local neoplasms also did not develop during a 19-month observation period after 39 mice were surgically implanted with pure tin foil. Similarly, over the same observation period, neither local nor general neoplasm development was noted in any of 43 mice injected intrathoracically with a tin needle saline suspension.

Table 1. Properties of Tin Oxide and Tin[66]

Chemical	Form	Molecular Weight	logP	Density	Water Solubility	Boiling Point	Melting Point
Tin Oxide	Gray tetragonal crystals	150.71	NA*	6.85 g/cm^3	Insoluble	NA	1630°C
Tin	Cubic crystals (gray tin); silvery tetragonal crystals (white tin)	118.71	NA	7.287 g/cm^3 (white tin); 5.769 g/cm^3 (gray tin)	Insoluble	2602°C (gray and white tin)	231.93°C (white tin); gray tin transition to white tin at 13.2°C

*NA = Not Available

Table 2. Frequency and Concentration of Use According to Duration and Type of Exposure Provided in 2011[10,11]

	Tin Oxide		
	# of Uses	Conc. (%)	
Exposure Type			
Eye Area	223	0.003 to 5	
Incidental Ingestion	342	0.008 to 1	
Incidental Inhalation-sprays	15	0.0005 to 0.08	
Incidental Inhalation-powders	42	0.0005 to 1	
Dermal Contact	472	0.000003 to 5	
Deodorant (underarm)	NR	NR	
Hair - Non-Coloring	9	0.0008 to 0.4	
Hair-Coloring	NR	0.04	
Nail	45	0.002 to 1	
Mucous Membrane	376	0.0005 to 1	
Baby Products	NR	NR	
Duration of Use			
Leave-On	833	0.000003 to 5	
Rinse off	38	0.0003 to 0.4	
Diluted for (bath) use	1	NR	
Totals*/Conc. Range**	872	0.000003 to 5	

NR = Not Reported; Totals = Rinse-off + Leave-on Product Uses

NOTE: Because each ingredient may be used in cosmetics with multiple exposure types, the sum of all exposure type uses may not be equal to sum total uses.

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Data

Personal Care Products Council
Committed to Safety, Quality & Innovation

Memorandum

TO: F. Alan Andersen, Ph.D.
Director - COSMETIC INGREDIENT REVIEW (CIR)

FROM: Halyna Breslawec, Ph.D.
Industry Liaison to the CIR Expert Panel

DATE: January 9, 2012

SUBJECT: Studies of Products Containing Tin Oxide

Consumer Product Testing Co. 2011. Repeated insult patch test of an eye shadow containing 0.3% Tin Oxide. Experiment Reference Number: C11-1390.03.

Consumer Product Testing Co. 2011. Ophthalmological in-use safety evaluation of an eye shadow containing 0.3% Tin Oxide. Experiment Reference Number: C11-2693.01.

Consumer Product Testing Co. 2011. Repeated insult patch test of a lipstick containing 0.5% Tin Oxide. Experiment Reference Number: C11-0704.03.

Clinical Research Laboratories, Inc. 2008. Repeated insult patch test of a lipgloss containing 0.35% Tin Oxide. CRL Study Number: CRL34408-4.

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Consumer Product Testing Co.

FINAL REPORT

CLIENT:

ATTENTION:

TEST: Repeated Insult Patch Test
Protocol No.: 1.01L

TEST MATERIAL: POWDER EYE SHADOW -
contains 0.3% Tin oxide

EXPERIMENT REFERENCE NUMBER: C11-1390.03

Reviewed by: Richard R. Eisenberg, M.D.
Medical Director
Board Certified Dermatologist

Approved by: Michael Caswell, Ph.D., CCRC, CCRA
Director, Clinical Evaluations

Approved by: Joy Frank, R.N.
Executive Vice President, Clinical Evaluations

70 New Dutch Lane • Fairfield, New Jersey 07004-2514 • (973) 808-7111 • Fax (973) 808-7234

Consumer Product Testing Co

QUALITY ASSURANCE UNIT STATEMENT

Study Number: C11-1390.03

The Consumer Product Testing Company, Incorporated (CPTC) Quality Assurance Unit (QAU) is responsible for monitoring the conduct, content and reporting of all clinical laboratory studies that are conducted at CPTC.

This study has been conducted in accordance with ICH Guideline E6 for *Good Clinical Practice*, the requirements of 21 CFR Parts 50 and 56, other applicable regulations, CPTC Standard Operating Procedures, and the approved Study Protocol.

The CPTC QAU has reviewed all data, records, and documents relating to this study and also this Final Report. The following QAU representative signature certifies that all data, records, and documents relating to this study and also this Final Report have been reviewed and are deemed to be acceptable, and the study conforms to all of the requirements as indicated above.

All records and documents pertaining to the conduct of this study shall be retained in the CPTC archives for a minimum of ten (10) years. At any time prior to the completion of the tenth archival year, a Sponsor may submit a written request to the CPTC QA Department to obtain custody of study records once the CPTC archive period has been completed. This transfer shall be performed at the Sponsor's expense. In the absence of a written request, study-related records shall be destroyed at the end of the CPTC archive period in a manner that renders them useless.

Quality Assurance Representative

6/10/11
Date

70 New Dutch Lane • Fairfield, New Jersey 07004-2514 • (973) 808-7111 • Fax (973) 808-7234
Clinical • Toxicology • Analytical Chemistry • Microbiology

Objective: To determine by repetitive epidermal contact the potential of a test material to induce primary or cumulative irritation and/or allergic contact sensitization.

Participants: One hundred eleven (111) qualified subjects, male and female, ranging in age from 18 to 75 years, were selected for this evaluation. Ninety-eight (98) subjects completed this study. The remaining subjects discontinued their participation for various reasons, none of which were related to the application of the test material.

Inclusion Criteria:

a. Male and female subjects, age 16[a] and over.
b. Absence of any visible skin disease which might be confused with a skin reaction from the test material.
c. Prohibition of use of topical or systemic steroids and/or antihistamines for at least seven days prior to study initiation.
d. Completion of a Medical History form and the understanding and signing of an Informed Consent form.
e. Considered reliable and capable of following directions.

Exclusion Criteria:

a. Ill health.
b. Under a doctor's care or taking medication(s) which could influence the outcome of the study.
c. Females who are pregnant or nursing.
d. A history of adverse reactions to cosmetics or other personal care products.

Test Material: POWDER EYE SHADOW -

Study Schedule:

Panel #	Initiation Date	Completion Date
20110100	March 30, 2011	May 12, 2011
20110110	April 6, 2011	May 12, 2011

[a]With parental or guardian consent

Methodology:

The upper back between the scapulae served as the treatment area. Approximately 0.2 g of the test material, or an amount sufficient to cover the contact surface, was applied to the 1" x 1" absorbent pad portion of a clear adhesive dressing. This was then applied to the appropriate treatment site to form a semi-occlusive patch.

This pad was moistened with several drops of water to ensure adherence of the test material.

Induction Phase:

Patches were applied three (3) times per week (e.g., Monday, Wednesday, and Friday) for a total of nine (9) applications. The site was marked to ensure the continuity of patch application. Following supervised removal and scoring of the first Induction patch, participants were instructed to remove all subsequent Induction patches at home, twenty-four hours after application. The evaluation of this site was made again just prior to re-application. If a participant was unable to report for an assigned test day, one (1) makeup day was permitted. This day was added to the Induction period.

With the exception of the first supervised Induction Patch reading, if any test site exhibited a moderate (2-level) reaction during the Induction Phase, application was moved to an adjacent area. Applications were discontinued for the remainder of this test phase, if a moderate (2-level) reaction was observed on this new test site. Applications would also be discontinued if marked (3-level) or severe (4-level) reactivity was noted.

Rest periods consisted of twenty-four hours following each Tuesday and Thursday removal, and forty-eight hours following each Saturday removal.

Challenge Phase:

Approximately two (2) weeks after the final Induction patch application, a Challenge patch was applied to a virgin test site adjacent to the original Induction patch site, following the same procedure described for Induction. The patch was removed and the site scored at the clinic twenty-four and seventy two hours post-application.

Methodology (continued):

Evaluation Criteria (Erythema and additional Dermal Sequelae):

0	=	**No visible skin reaction**	**E**	=	**Edema**
0.5	=	**Barely perceptible**	**D**	=	**Dryness**
1	=	**Mild**	**S**	=	**Staining**
2	=	**Moderate**	**P**	=	**Papules**
3	=	**Marked**	**V**	=	**Vesicles**
4	=	**Severe**	**B**	=	**Bullae**
			U	=	**Ulceration**
			Sp	=	**Spreading**

Erythema was scored numerically according to this key. If present, additional Dermal Sequelae were indicated by the appropriate letter code and a numerical value for severity.

Results:

The results of each participant are appended (Table 1).

Observations remained negative throughout the test interval.

Subject demographics are presented in Table 2.

Summary:

Under the conditions of this study, test material, POWDER EYE SHADOW - .id not indicate a potential for dermal irritation or allergic contact sensitization.

Table 1
Panel #20110100

Individual Results

POWDER EYE SHADOW -

Subject Number	24*hr	Induction Phase 1	2	3	4	5	6	7	8	9	Virgin Challenge Site 24*hr	72 hr
1	0	0	0	0	0	0	0	----DID NOT COMPLETE STUDY----				
2	0	0	0	0	0	0	0	0	0	0	0	0
3	0	0	0	0	0	0	0	0	0	0	0	0
4	0	0	0	0	0	0	0	0	0	0	0	0
5	0	0	0	0	0	0	0	0	0	0	0	0
6	0	0	0	0	0	0	0	0	0	0	0	0
7	0	0	0	0	0	0	0	0	0	0	0	0
8	0	0	0	----------DID NOT COMPLETE STUDY----------								
9	0	0	0	0	0	0	0	0	0	0	0	0*
10	0	0	0	0	0	0	0	0	0	0	0	0
11	0	0	0	0	0	0	0	0	0	0	0	0
12	----------DID NOT COMPLETE STUDY----------											
13	0	0	0	0	0	0	0	0	0	0	0	0
14	0	0	0	0	0	0	0	0	0	0	0	0
15	0	0	0	0	0	0	0	0	0	0	0	0
16	0	0	0	0	0	0	0	0	0	0	0	0
17	0	0	0	0	0	0	0	0	0	0	0	0
18	0	0	0	0	0	0	0	0	0	0	0	0
19	0	0	0	0	0	0	0	0	0	0	0	0
20	0	0	0	0	0	0	0	0	0	0	0	0
21	0	0	0	0	0	0	0	0	0	0	0	0
22	0	0	0	0	0	0	0	0	0	0	0	0
23	0	0	0	0	0	0	0	0	0	0	0	0
24	0	0	0	0	0	0	0	0	0	0	0	0
25	0	0	0	0	0	0	0	0	0	0	0	0
26	0	0	0	0	0	0	0	0	0	0	0	0
27	0	0	0	0	0	0	0	0	0	0	0	0
28	0	0	0	0	0	0	0	0	0	0	0	0
29	0	0	0	0	0	0	0	0	0	0	0	0

24* = Supervised removal of 1st Induction and Challenge Patch
* = Observation recorded 96 hours post challenge application. Subject unable to report, as scheduled.

Table 1
(continued)
Panel #20110100

Individual Results

POWDER EYE SHADOW -

Subject Number	24*hr	Induction Phase 1	2	3	4	5	6	7	8	9	Virgin Challenge Site 24*hr	72 hr
30	0	0	0	0	0	0	0	0	0	0	0	0
31	0	0	0	0	0	0	0	0	0	0	0	0
32	----------DID NOT COMPLETE STUDY----------											
33	0	0	0	0	0	0	0	0	0	0	0	0
34	0	0	0	0	0	0	0	0	0	0	0	DNC
35	0	0	0	0	0	0	0	0	0	0	0	0
36	0	0	0	0	0	0	0	0	0	0	0	0
37	0	0	0	0	0	0	0	0	0	0	0	0
38	0	0	0	0	0	0	0	0	0	0	0	0
39	0	0	0	0	0	0	0	0	0	0	0	0
40	0	0	0	0	0	0	0	0	0	0	0	0
41	0	0	0	0	0	0	0	0	0	0	0	0
42	0	0	0	0	0	0	0	0	0	0	0	0
43	0	0	0	0	0	0	0	0	0	0	0	0
44	0	0	0	0	0	0	0	0	0	0	0	0
45	0	0	0	0	0	0	0	0	0	0	0	0
46	0	0	0	0	0	0	0	0	0	0	0	0
47	0	0	0	0	0	0	0	0	0	0	0	0
48	0	0	0	0	0	0	0	0	0	0	0	0
49	0	0	0	0	0	0	0	0	0	0	0	0
50	0	0	0	0	0	0	0	0	0	0	0	0
51	0	0	0	0	0	0	0	0	0	0	0	0
52	0	0	0	0	0	0	0	0	0	0	0	0
53	0	0	0	0	0	0	0	0	0	0	0	0
54	0	0	0	0	0	0	0	0	0	0	0	0
55	0	0	0	0	0	0	0	0	0	0	0	0
56	0	0	0	0	0	0	0	0	0	0	0	0

24* = Supervised removal of 1st Induction and Challenge Patch
DNC = Did not complete study

Table 1
(continued)
Panel #20110110

Individual Results

POWDER EYE SHADOW -

Subject Number	24*hr	Induction Phase 1	2	3	4	5	6	7	8	9	Virgin Challenge Site 24*hr	72 hr
1	0	0	0	0	0	0	0	0	0	0	0	0
2	0	0	0	0	0	0	0	0	0	0	0	0
3	0	0	0	0	0	0	0	0	0	0	0	0
4	0	0	0	0	0	0	0	0	0	0	0	0
5	0	0	0	0	0	0	0	0	0	0	0	0
6	0	DID NOT COMPLETE STUDY										
7	DID NOT COMPLETE STUDY											
8	0	0	0	0	0	0	0	0	0	0	0	0
9	0	0	0	0	0	0	0	0	0	0	0	0
10	0	0	0	0	0	0	0	0	0	0	0	0
11	0	0	DID NOT COMPLETE STUDY									
12	0	0	DID NOT COMPLETE STUDY									
13	0	0	0	0	0	0	0	0	0	0	0	0
14	0	0	0	0	0	0	0	0	0	0	0	0
15	0	0	0	0	0	0	0	0	0	0	0	0
16	0	0	0	0	0	0	0	0	0	0	0	0
17	0	0	0	DID NOT COMPLETE STUDY								
18	0	0	0	0	0	0	0	0	0	0	0	0
19	0	0	DID NOT COMPLETE STUDY									
20	0	0	0	0	0	0	0	0	0	0	0	0
21	0	0	0	0	0	0	0	0	0	0	0	0
22	0	0	0	0	0	0	0	0	0	0	0	0
23	0	0	0	0	0	0	0	0	0	0	0	0
24	0	0	0	0	0	0	0	0	0	0	0	0
25	0	0	0	0	0	0	0	0	0	0	0	0
26	0	0	0	0	0	0	0	0	0	0	0	0
27	0	0	0	0	0	0	0	0	0	0	0	0
28	0	0	0	0	0	0	0	0	0	0	0	0
29	0	0	0	0	0	0	0	0	0	0	0	0

24* = Supervised removal of 1st Induction and Challenge Patch

Table 1
(continued)
Panel #20110110

Individual Results

POWDER EYE SHADOW -

Subject Number	24*hr	Induction Phase 1	2	3	4	5	6	7	8	9	Virgin Challenge Site 24*hr	72 hr
30	0	0	0	0	0	0	0	0	0	0	0	0
31	0	0	DID NOT COMPLETE STUDY									
32	0	0	0	0	0	0	0	0	0	0	0	0
33	0	0	0	0	0	0	0	0	0	0	0	0
34	0	0	0	0	0	0	0	0	0	0	0	0
35	DID NOT COMPLETE STUDY											
36	0	0	0	0	0	0	0	0	0	0	0	0
37	0	0	0	0	0	0	0	0	0	0	0	0
38	0	0	0	0	0	0	0	0	0	0	0	0
39	0	0	0	0	0	0	0	0	0	0	0	0
40	0	0	0	0	0	0	0	0	0	0	0	0
41	0	0	0	0	0	0	0	0	0	0	0	0
42	0	0	0	0	0	0	0	0	0	0	0	0
43	0	0	0	0	0	0	0	0	0	0	0	0
44	0	0	0	0	0	0	0	0	0	0	0	0
45	0	0	0	0	0	0	0	0	0	0	0	0
46	0	0	0	0	0	0	0	0	0	0	0	0
47	0	0	0	0	0	0	0	0	0	0	0	0
48	0	0	0	0	0	0	0	0	0	0	0	0
49	0	0	0	0	0	0	0	0	0	0	0	0
50	0	0	0	0	0	0	0	0	0	0	0	0
51	0	0	0	0	0	0	0	0	0	0	0	0
52	0	0	0	0	0	0	0	0	0	0	0	0
53	0	0	0	0	0	0	0	0	0	0	0	0
54	0	0	0	0	0	0	0	0	0	0	0	0
55	0	0	0	0	0	0	0	0	0	0	0	0

24* = Supervised removal of 1st Induction and Challenge Patch

Table 2
Panel #20110100

Subject Demographics

Subject Number	Initials	Age	Sex
1	JA	29	F
2	MJB	38	M
3	AB	68	M
4	MRP	71	F
5	EB	44	F
6	NHB	43	F
7	REM	44	M
8	JC	21	F
9	JJP	21	F
10	JCJ	34	F
11	JB	61	F
12	RJP	32	M
13	JC	45	F
14	JEP	75	F
15	KAN	56	F
16	JM	59	M
17	CYK	58	F
18	LMC	48	F
19	PYM	48	F
20	AWO	51	F
21	LCO	20	M
22	DMD	56	F
23	CMB	44	F
24	RAS	71	F
25	HJM	58	F
26	RAO	33	F
27	KWL	62	M
28	MP	40	F
29	PR	48	M

Table 2
(continued)
Panel #20110100

Subject Demographics

Subject Number	Initials	Age	Sex
30	LKS	64	F
31	JR	71	M
32	LT	52	F
33	JEF	73	F
34	JBO	21	M
35	MMK	66	F
36	VF	46	M
37	LMF	68	F
38	NAG	49	F
39	MP	45	F
40	RDR	37	F
41	RMD	51	M
42	JB	47	F
43	GAA	40	M
44	MSM	71	F
45	QCM	33	F
46	SMS	27	F
47	DA	34	F
48	JB	44	F
49	FT	51	M
50	TLG	62	M
51	PMG	63	F
52	SAB	45	F
53	MVC	46	F
54	JH	62	M
55	CFD	68	M
56	BTD	31	F

Table 2
(continued)
Panel #20110110

Subject Demographics

Subject Number	Initials	Age	Sex
1	JPP	64	M
2	AJM	42	F
3	JOT	26	M
4	KVR	39	F
5	REV	45	M
6	YD	50	F
7	RIV	39	F
8	DGD	75	F
9	MKS	35	M
10	RBP	56	F
11	TSS	31	F
12	CTH	30	M
13	JI	75	F
14	EPC	48	F
15	DLB	27	F
16	AA	52	M
17	MAT	40	F
18	LST	38	F
19	EJN	22	M
20	AD	26	F
21	AR	47	F
22	NLR	46	F
23	LKR	53	M
24	ZC	41	F
25	HVS	20	F
26	DEC	18	F
27	GTC	20	M
28	FMS	20	F
29	VLA	46	F

Table 2
(continued)
Panel #20110110

Subject Demographics

Subject Number	Initials	Age	Sex
30	WLK	56	M
31	TNT	23	F
32	CR	53	F
33	AMR	54	F
34	KAM	57	F
35	TMM	56	F
36	CMR	41	F
37	NJC	62	F
38	TKW	39	F
39	DRC	50	F
40	BRS	50	F
41	REP	46	F
42	LAP	22	F
43	TV	49	F
44	WM	61	F
45	SDW	29	F
46	WMA	60	F
47	LAF	24	M
48	MTD	58	F
49	JJO	45	M
50	CMM	22	F
51	SDD	57	M
52	KM	57	F
53	TMM	70	M
54	SMP	45	F
55	BFP	70	F

Consumer Product Testing

FINAL REPORT

CLIENT:

ATTENTION:

TEST: Ophthalmological In-Use Safety Evaluation
Protocol No.: BNIW02-206

TEST MATERIAL: EYESHADOW -
Contains 0.3% Tin Oxide

EXPERIMENT REFERENCE NUMBER: C11-2693.01

Reviewed by: Charles J. Kronengold, M.D.
Board Certified Ophthalmologist

Approved by: Michael Caswell, Ph.D., C.C.R.C., C.C.R.A.
Director, Clinical Evaluations

Approved by: Joy Frank, R.N.
Executive Vice President, Clinical Evaluations

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QUALITY ASSURANCE UNIT STATEMENT

Study Number: C11-2693.01

The Consumer Product Testing Company, Incorporated (CPTC) Quality Assurance Unit (QAU) is responsible for auditing the conduct, content and reporting of all clinical trials that are conducted at CPTC.

This trial has been conducted in accordance with the Declaration of Helsinki, the ICH Guideline E6 for *Good Clinical Practice*, the requirements of 21 CFR Parts 50 and 56, other applicable laws and regulations, CPTC Standard Operating Procedures, and the approved protocol.

The CPTC QAU has reviewed all data, records, and documents relating to this trial and also this Final Report. The following QAU representative signature certifies that all data, records, and documents relating to this trial and also this Final Report have been reviewed and are deemed to be acceptable, and that the trial conforms to all of the requirements as indicated above.

All records and documents pertaining to the conduct of this trial shall be retained in the CPTC archives for a minimum of ten (10) years. At any time prior to the completion of the tenth archival year, a Sponsor may submit a written request to the CPTC QAU to obtain custody of trial records once the CPTC archive period has been completed. This transfer shall be performed at the Sponsor's expense. In the absence of a written request, trial-related records shall be destroyed at the end of the CPTC archive period in a manner that renders them useless.

Quality Assurance Representative

8/22/11
Date

70 New Dutch Lane • Fairfield, New Jersey 07004-2514 • (973) 808-7111 • Fax (973) 808-7234
Clinical • Toxicology • Analytical Chemistry • Microbiology

Objective: To evaluate the safety and ocular irritation potential of an eye shadow following repetitive, daily use conditions.

Participants: Thirty-four female subjects, ages 19 to 64 years, were recruited for this trial. Thirty-one subjects completed the trial. Subject #17 was disqualified at the baseline visit due to pregnancy. Subject #'s 7 and 8 discontinued their participation due to reasons unrelated to test material use.

Inclusion Criteria:

a. Approximately 30 healthy female subjects, ages 18 to 65 years, inclusive.
b. Must have agreed to discontinue use of their current product with similar function and use only the test material.
c. Must have agreed to arrive at the Testing Facility without makeup.
d. Absence of any visible skin or eye disease that might have been confused with a reaction to the test material.
e. Approximately 50% of subjects must have been soft contact lens wearers and approximately 50% had self-perceived sensitive eyes.
f. Must have been a regular user of a product with similar function.
g. Must have agreed not to introduce the use of any new cosmetic, toiletry or personal care products during the course of the trial.
h. Must have had an acceptable ophthalmic examination to ensure eye health and, if appropriate, the correct fit and condition of their contact lenses.
i. Completion of a Medical History Form and understood and signed an Informed Consent Form that included a HIPAA statement.
j. Considered dependable and capable of following directions as outlined in the protocol.

Exclusion Criteria:

a. Ill health or taking medication, other than birth control, which could have influenced the purpose, integrity or outcome of the trial.
b. Subjects using any systemic or topical corticosteroid, anti-inflammatory, antihistamine therapy or any other medication that, in the opinion of the Investigator, could have influenced the outcome of the trial.
c. Females who were pregnant, nursing or planning on becoming pregnant during the course of this trial.
d. A history of adverse reactions to similar products being tested.

Test Material: EYESHADOW

Trial Schedule:

Initiation Date	Completion Date
July 1, 2011	July 29, 2011

Methodology: Prior to acceptance, each subject received a qualifying ophthalmic examination by a Board Certified Ophthalmologist to ensure eye health and if appropriate, the correct fit of their contact lenses.

The Ophthalmologist evaluated by gross and/or slit lamp examination the subjects' eyelids, corneas, conjunctivae, anterior chambers and pupillary reactions, in addition to measuring visual acuity.

Findings were noted on subjects' Ocular Examination Record Forms.

After completion of the ophthalmic examination, qualified subjects received the test material and were instructed to use the test material at least once daily for 4 weeks, according to the following directions:

Instructions:

Discontinue the use of your current eyeshadow and use only the test material provided for the duration of this trial.

Do not introduce any new cleansing products, moisturizers or other cosmetics during the trial interval.

Please wear your contacts on examination days.

Usage Directions:
Apply as you normally would any eyeshadow at least once a day. Use all colors during the trial. Use both wet and dry.

Keep out of reach of children. Do not let anyone else use the test material.

Methodology (continued):

Record the times of use on the daily diary.

Report any adverse reactions or problems immediately to the Testing Facility staff.

To document compliance, subjects were required to maintain a daily diary to record each use.

A comprehensive ocular examination, as previously described, was conducted for each subject after 4 weeks of test material usage.

All unused test material and daily diaries were returned to the Testing Facility at the final visit.

Daily diaries were reviewed for completeness, prior to dismissal of the subjects.

Deviations: There were no deviations.

Adverse Events: There were no adverse events.

Results: All ophthalmologic examinations remained within normal limits throughout the test interval.

Questionnaire responses to Question #1 are presented in Table 1.

Questionnaire response tallies are presented in Tables 2 and 3.

Subject demographics are listed in Table 4.

The panel was comprised of the following:
21 out of 34 subjects (62%) had self-perceived sensitive eyes
13 out of 34 subjects (38%) had non-sensitive eyes
17 out of 34 subjects (50%) wore soft contact lenses
17 out of 34 subjects (50%) were non-contact lens wearers

All ophthalmological examination records, questionnaires and daily diaries are provided under separate cover.

Summary: Under the conditions of this trial, test material, EYESHADOW - [illegible] not indicate a potential for ophthalmologic irritation or hypersensitivity. This test material can be considered safe for use by both contact lens and non-contact lens wearers, as well as for individuals with normal and self-perceived sensitive eyes.

Consumer Product Testing

FINAL REPORT

CLIENT:

ATTENTION:

TEST: Repeated Insult Patch Test
Protocol No.: 1.01L

TEST MATERIAL: LIPSTICK ENG050657-0.1.1.0. LNYC3-71.1
Contains 0.5% Tin Oxide

EXPERIMENT REFERENCE NUMBER: C11-0704.03

Reviewed by: Richard R. Eisenberg, M.D.
Medical Director
Board Certified Dermatologist

Approved by: Michael Caswell, Ph.D., C.C.R.C., C.C.R.A.
Director, Clinical Evaluations

Approved by: Joy Frank, R.N.
Executive Vice President, Clinical Evaluations

70 New Dutch Lane • Fairfield, New Jersey 07004-2514 • (973) 808-7111 • Fax (973) 808-7234

QUALITY ASSURANCE UNIT STATEMENT

Study Number: C11-0704.03

The Consumer Product Testing Company, Incorporated (CPTC) Quality Assurance Unit (QAU) is responsible for monitoring the conduct, content and reporting of all clinical laboratory studies that are conducted at CPTC.

This study has been conducted in accordance with ICH Guideline E6 for *Good Clinical Practice*, the requirements of 21 CFR Parts 50 and 56, other applicable regulations, CPTC Standard Operating Procedures, and the approved Study Protocol.

The CPTC QAU has reviewed all data, records, and documents relating to this study and also this Final Report. The following QAU representative signature certifies that all data, records, and documents relating to this study and also this Final Report have been reviewed and are deemed to be acceptable, and the study conforms to all of the requirements as indicated above.

All records and documents pertaining to the conduct of this study shall be retained in the CPTC archives for a minimum of ten (10) years. At any time prior to the completion of the tenth archival year, a Sponsor may submit a written request to the CPTC QA Department to obtain custody of study records once the CPTC archive period has been completed. This transfer shall be performed at the Sponsor's expense. In the absence of a written request, study-related records shall be destroyed at the end of the CPTC archive period in a manner that renders them useless.

Quality Assurance Representative

4/1/11
Date

70 New Dutch Lane • Fairfield, New Jersey 07004-2514 • (973) 808-7111 • Fax (973) 808-7234
Clinical • Toxicology • Analytical Chemistry • Microbiology

Objective: To determine by repetitive epidermal contact the potential of a test material to induce primary or cumulative irritation and/or allergic contact sensitization.

Participants: One hundred twelve (112) qualified subjects, male and female, ranging in age from 16 to 79 years, were selected for this evaluation. One hundred three (103) subjects completed this study. The remaining subjects discontinued their participation for various reasons, none of which were related to the application of the test material.

Inclusion Criteria:

a. Male and female subjects, age 16[a] and over.
b. Absence of any visible skin disease which might be confused with a skin reaction from the test material.
c. Prohibition of use of topical or systemic steroids and/or antihistamines for at least seven days prior to study initiation.
d. Completion of a Medical History form and the understanding and signing of an Informed Consent form.
e. Considered reliable and capable of following directions.

Exclusion Criteria:

a. Ill health.
b. Under a doctor's care or taking medication(s) which could influence the outcome of the study.
c. Females who are pregnant or nursing.
d. A history of adverse reactions to cosmetics or other personal care products.

Test Material: LIPSTICK ENG050657-0.1.1.0. LNYC3-71.1

Study Schedule:

Panel #	Initiation Date	Completion Date
20110039	February 14, 2011	March 24, 2011
20110046	February 14, 2011	March 25, 2011

[a]With parental or guardian consent

Methodology:

The upper back between the scapulae served as the treatment area. Approximately 0.2 g of the test material, or an amount sufficient to cover the contact surface, was applied to the 1" x 1" absorbent pad portion of a clear adhesive dressing. This was then applied to the appropriate treatment site to form a semi-occlusive patch.

Induction Phase:

Patches were applied three (3) times per week (e.g., Monday, Wednesday, and Friday) for a total of nine (9) applications. The site was marked to ensure the continuity of patch application. Following supervised removal and scoring of the first Induction patch, participants were instructed to remove all subsequent Induction patches at home, twenty-four hours after application. The evaluation of this site was made again just prior to re-application. If a participant was unable to report for an assigned test day, one (1) makeup day was permitted. This day was added to the Induction period. Due to a holiday weekend, subjects who needed a makeup day may have experienced a delay in patch application.

With the exception of the first supervised Induction Patch reading, if any test site exhibited a moderate (2-level) reaction during the Induction Phase, application was moved to an adjacent area. Applications were discontinued for the remainder of this test phase, if a moderate (2-level) reaction was observed on this new test site. Applications would also be discontinued if marked (3-level) or severe (4-level) reactivity was noted.

Rest periods consisted of twenty-four hours following each Tuesday and Thursday removal, and forty-eight hours following each Saturday removal.

Challenge Phase:

Approximately two (2) weeks after the final Induction patch application, a Challenge patch was applied to a virgin test site adjacent to the original Induction patch site, following the same procedure described for Induction. The patch was removed and the site scored at the clinic twenty-four and seventy two hours post-application.

Methodology (continued):

Evaluation Criteria (Erythema and additional Dermal Sequelae):

0	=	No visible skin reaction	E	=	Edema
0.5	=	Barely perceptible	D	=	Dryness
1	=	Mild	S	=	Staining
2	=	Moderate	P	=	Papules
3	=	Marked	V	=	Vesicles
4	=	Severe	B	=	Bullae
			U	=	Ulceration
			Sp	=	Spreading

Erythema was scored numerically according to this key. If present, additional Dermal Sequelae were indicated by the appropriate letter code and a numerical value for severity.

Results:

The results of each participant are appended (Table 1).

Observations remained negative throughout the test interval.

Subject demographics are presented in Table 2.

Summary:

Under the conditions of this study, test material, LIPSTICK ENG050657-0.1.1.0. LNYC3-71.1, did not indicate a potential for dermal irritation or allergic contact sensitization.

Table 1
Panel #20110039

Individual Results

LIPSTICK ENG050657-0.1.1.0. LNYC3-71.1

Subject Number	24*hr	Induction Phase 1	2	3	4	5	6	7	8	9	Virgin Challenge Site 24*hr	72 hr
1	0	0	0	0	0	0	0	0	0	0	0	0
2	0	0	0	0	0	0	0	0	0	0	0	0
3	0	0	0	0	0	0	0	0	0	0	0	0
4	0	0	0	0	0	0	0	------DID NOT COMPLETE STUDY-------				
5	0	0	0	0	0	0	0	0	0	0	0	0
6	0	0	0	0	0	0	0	0	0	0	0	0
7	0	0	----------DID NOT COMPLETE STUDY----------									
8	0	0	0	0	0	0	0	0	0	0	0	0
9	0	0	0	0	0	0	0	0	0	0	0	0
10	0	0	0	0	0	0	0	0	0	0	0	0
11	0	0	0	0	0	0	0	0	0	0	0	0
12	0	0	0	0	0	0	0	0	0	0	0	0
13	0	0	0	0	0	0	0	0	0	0	0	0
14	0	0	0	0	0	0	0	0	0	0	0	0
15	0	0	0	0	0	0	0	0	0	0	0	0
16	0	0	0	0	0	0	0	0	0	0	0	0
17	0	0	0	0	0	0	0	0	0	0	0	0
18	0	0	0	0	0	0	0	0	0	0	0	0
19	0	0	0	0	0	0	0	0	0	0	0	0
20	0	0	0	0	0	0	0	0	0	0	0	0
21	0	0	0	0	0	0	0	0	0	0	0	0
22	0	0	0	0	0	0	0	0	0	0	0	0
23	0	0	0	0	0	0	0	0	0	0	0	0
24	0	0	0	0	0	0	0	0	0	0	0	0
25	0	0	0	0	0	0	0	0	0	0	0	0
26	0	0	0	0	0	0	0	0	0	0	0	0
27	0	0	0	0	0	0	0	0	0	0	0	0
28	0	0	0	0	0	0	0	0	0	0	0	0
29	0	0	0	0	0	0	0	0	0	0	0	0

24* = Supervised removal of 1st Induction and Challenge Patch

Table 1
(continued)
Panel #20110039

Individual Results

LIPSTICK ENG050657-0.1.1.0. LNYC3-71.1

Subject Number	24*hr	Induction Phase 1	2	3	4	5	6	7	8	9	Virgin Challenge Site 24*hr	72 hr
30	0	0	0	0	0	0	0	0	0	0	0	0
31	0	0	0	0	DID NOT COMPLETE STUDY							
32	0	0	0	0	0	0	0	0	0	0	0	0
33	0	0	0	0	0	0	0	0	0	0	0	0
34	0	0	0	0	0	0	0	0	0	0	0	0
35	0	0	0	0	0	0	0	0	0	0	0	0
36	0	0	0	0	0	0	0	0	0	0	0	0
37	0	0	0	0	0	0	0	0	0	0	0	0
38	0	0	0	0	0	0	0	0	0	0	0	0
39	0	0	0	0	0	0	0	0	0	0	0	0
40	0	0	0	0	0	0	0	0	0	0	0	0
41	0	0	0	0	0	0	0	0	0	0	0	0
42	0	0	0	0	0	0	0	0	0	0	0	0
43	0	0	0	0	0	0	0	0	0	0	0	0
44	0	0	0	0	0	0	0	0	0	0	0	0
45	0	0	0	0	0	0	0	0	0	0	0	0
46	0	0	0	0	0	0	0	0	0	0	0	0
47	-	0	0	0	0	0	0	0	0	0	0	0
48	0	0	0	0	0	0	0	0	0	0	0	0
49	0	0	0	0	0	0	0	0	0	0	0	0
50	0	0	0	0	0	0	0	0	0	0	0	0
51	0	0	0	0	0	0	0	0	0	0	0	0
52	0	0	0	0	0	0	0	0	0	0	0	0
53	0	0	0	0	0	0	0	0	0	0	0	0
54	0	0	0	0	0	0	0	0	0	0	0	0
55	0	0	0	0	0	0	0	0	0	0	0	0
56	0	0	0	0	0	0	0	0	0	0	0	0

24* = Supervised removal of 1st Induction and Challenge Patch
- = Subject not present for supervised removal

Table 1
(continued)
Panel #20110046

Individual Results

LIPSTICK ENG050657-0.1.1.0. LNYC3-71.1

Subject Number	24*hr	Induction Phase 1	2	3	4	5	6	7	8	9	Virgin Challenge Site 24*hr	72 hr
1	0	0	0	0	0	0	0	0	0	0	0	0
2	0	0	0	0	0	0	0	0	0	0	0	0
3	0	0	0	0	0	0	0	0	0	0	0	0
4	0	0	0	0	0	0	0	0	0	0	0	0
5	0	0	0	0	0	0	0	0	0	0	0	0
6	0	0	0	0	0	0	0	0	0	0	0	0
7	0	0	0	0	0	0	0	0	0	0	0	0
8	0	0	0	0	0	0	0	0	0	0	0	0
9	0	0	0	0	0	0	0	0	0	0	0	0
10	0	0	0	0	0	0	0	0	0	0	0	0
11	0	0	0	0	0	0	0	0	0	0	0	0
12	0	0	0	0	0	0	0	0	0	0	0	0
13	0	0	0	0	0	0	0	0	0	0	0	0
14	0	0	0	0	0	0	0	0[m]	0	0	0	0
15	0	0	0	0	0	0	0	0	0	0	0	0
16	0	0	0	0	0	0	0	0	0	0	0	0
17	0	0	0	0	0	0	0	0	0	0	0	0
18	0	0	0	0	0	0	0	0	0	0	0	0
19	0	0	0	0	0	0	0	0	0	0	0	0
20	0	0	0	0	0	0	0	0	0	0	0	0
21	0	0	0	0	0	0	----------DID NOT COMPLETE STUDY----------					
22	0	0	0	0	0	0	0	0	0	0	0	0
23	0	0	0	0	0	0	0	0	0	0	0	0
24	0	0	0	0	0	0	0	0	0	0	0	0
25	0	0	0	0	0	0	0	0	0	0	0	0
26	0	0	0	0	0	0	0	0	0	0	0	0
27	----------DID NOT COMPLETE STUDY----------											
28	0	0	0	0	0	0	0	0	0	0	0	0
29	0	0	0	0	0	0	0	0	0	0	0	0

24* = Supervised removal of 1st Induction and Challenge Patch
m = Additional makeup day granted at the discretion of the clinic supervisor

Table 1
(continued)
Panel #20110046

Individual Results

LIPSTICK ENG050657-0.1.1.0. LNYC3-71.1

Subject Number	Induction Phase									Virgin Challenge Site	
	24*hr	1	2	3	4	5	6	7	8	9	24*hr	72 hr
30	0	0	0	0	0	0	0	0	0	0	0	0
31	0	0	0	0	0	0	0	0	0	0	0	0
32	0	0	0	0	0	0	0	0	0	0	0	0
33	0	0	0	0	0	0	0	0	0	0	0	0
34	0	0	0	0	0	0	0	0	0	0	0	0
35	0	0	0	0	0	0	0	0	0	0	0	0
36	----------DID NOT COMPLETE STUDY----------											
37	----------DID NOT COMPLETE STUDY----------											
38	0	0	0	0	0	0	0	0	0	0	0	0
39	0	0	0	0	0	0	0	0	0	0	0	0
40	0	0	0	0	0	0	0	0	0	0	0	0
41	0	0	0	0	0	0	0	0	0	0	0	0
42	0	0	0	0	0	0	0	0	0	0	0	0
43	0	0	0	0	0	0	0	0	0	0	0	0
44	0	0	----------DID NOT COMPLETE STUDY----------									
45	0	0	----------DID NOT COMPLETE STUDY----------									
46	0	0	0	0	0	0	0	0	0	0	0	0
47	0	0	0	0	0	0	0	0	0	0	0	0
48	0	0	0	0	0	0	0	0	0	0	0	0
49	0	0	0	0	0	0	0	0	0	0	0	0
50	0	0	0	0	0	0	0	0	0	0	0	0
51	0	0	0	0	0	0	0	0	0	0	0	0
52	0	0	0	0	0	0	0	0	0	0	0	0
53	0	0	0	0	0	0	0	0	0	0	0	0
54	0	0	0	0	0	0	0	0	0	0	0	0
55	0	0	0	0	0	0	0	0	0	0	0	0
56	0	0	0	0	0	0	0	0	0	0	0	0

24* = Supervised removal of 1st Induction and Challenge Patch

Table 2
Panel #20110039

Subject Demographics

Subject Number	Initials	Age	Sex
1	VEW	58	M
2	JEK	56	M
3	WCN	41	M
4	MWM	53	M
5	HC	33	M
6	MAN	32	M
7	PCK	51	M
8	BYG	38	F
9	WPC	51	M
10	YC	49	F
11	BAW	53	F
12	CJD	71	F
13	JAD	19	M
14	DAD	52	F
15	BES	44	M
16	EJE	67	F
17	CEF	40	M
18	JWC	38	M
19	IMZ	60	F
20	JPQ	58	F
21	DLT	48	F
22	SB	48	F
23	CEG	45	F
24	MK	46	M
25	TL	71	M
26	GER	63	F
27	MAW	78	F
28	DMW	18	M
29	JVH	46	M

Table 2
(continued)
Panel #20110039

Subject Demographics

Subject Number	Initials	Age	Sex
30	EEO	40	F
31	AC	53	F
32	BAR	52	F
33	BMB	71	F
34	LMR	25	F
35	LCL	49	F
36	NK	30	F
37	SC	50	F
38	SK	62	M
39	LT	57	F
40	DNB	19	M
41	MB	42	F
42	ADM	23	F
43	RF	47	F
44	KFC	62	F
45	GF	20	M
46	GF	18	M
47	LRI	53	M
48	JJV	42	M
49	MER	30	F
50	PFO	65	F
51	PAW	66	F
52	JMM	79	F
53	JSM	44	M
54	MSC	27	F
55	FAC	52	M
56	JGW	76	F

Table 2
(continued)
Panel #20110046

Subject Demographics

Subject Number	Initials	Age	Sex
1	SSC	17	F
2	TF	28	F
3	VF	28	F
4	JLP	62	F
5	TAR	33	F
6	GNG	64	F
7	TAU	63	F
8	CM	51	F
9	AMS	69	F
10	LAC	29	F
11	MLP	34	F
12	SPM	42	F
13	ACP	41	M
14	DAW	53	F
15	GV	37	F
16	DAG	50	F
17	DMC	52	F
18	NLJ	55	F
19	MJP	72	F
20	VKK	70	M
21	FHH	20	F
22	LDP	63	F
23	VAM	41	M
24	DMC	44	F
25	HSC	49	M
26	DEG	53	M
27	EBP	39	F
28	LFG	56	M
29	MDG	51	F

Table 2
(continued)
Panel #20110046

Subject Demographics

Subject Number	Initials	Age	Sex
30	MS	30	F
31	NS	36	F
32	OAS	16	M
33	BED	44	F
34	CAL	70	F
35	DJO	48	M
36	RDH	23	M
37	CGG	34	F
38	JMG	36	F
39	NS	33	F
40	MV	56	F
41	DDC	30	F
42	KLC	46	F
43	VR	66	M
44	DMC	49	F
45	PRC	26	F
46	MP	58	M
47	REO	40	M
48	QJM	18	M
49	JMS	19	M
50	ER	69	F
51	MMC	60	F
52	PLB	65	F
53	MM	53	F
54	BLP	37	F
55	BNP	58	F
56	LZD	32	F

Clinical
Research
Laboratories, Inc.

Final Report

Repeated Insult Patch Test

CLIENT:

ATTENTION:

TEST MATERIAL: Lipgloss
LSP5-30-1, ENG027914-1.1.0
containing 0.35% Tin oxide

CRL STUDY NUMBER: CRL34408-4

AUTHORIZED SIGNATURES:

Bruce E. Kanengiser, M.D.
President/Medical Director

Michael J. Muscatiello, Ph.D.
Executive Vice President/COO

George J. Neumaier, M.D.
Diplomate American Board
of Dermatology

REPORT DATE: May 30, 2008

371 Hoes Lane • Piscataway, NJ 08854 • (732) 981-1616 • FAX (732) 981-0520

Clinical
Research
Laboratories, Inc.

Good Clinical Practice
Quality Assurance Audit Statement

Clinical Study Number: CRL34408-4

Start Date: March 31, 2008

Completion Date: May 9, 2008

The clinical study listed above was conducted in accordance with Clinical Research Laboratories, Inc. Standard Operating Procedures, which incorporate the principles of Good Clinical Practice defined by applicable guidelines and regulations established by U.S. Regulatory Agencies. The conduct of the study was monitored for compliance, and the associated records, including source documents or raw data, were reviewed for documentation practices and accuracy by a Project Manager/Study Director and/or a Quality Assurance Representative. Standard Quality Assurance audit procedures for this final report and study related documents were conducted, as indicated below.

Signature of QA Auditor

5/30/08
Date

FINAL REPORT

REPEATED INSULT PATCH TEST

PURPOSE

The purpose of this study was to determine the dermal irritation and sensitization potential of a test material.

INVESTIGATIVE SITE

Clinical Research Laboratories, Inc.
371 Hoes Lane
Piscataway, New Jersey 08854
732-981-1616

TEST MATERIAL

The following test material was provided by and was received by Clinical Research Laboratories, Inc. on March 14, 2008:

Test Material	Test Condition	Patch Type
Lipgloss (ile) LSP5-30-1, ENG027914-1.1.0	Test as received	Semi-occlusive*

The test material was coded with the following CRL identification number:

CRL34408-4

STUDY DATES

This study was initiated on March 31, 2008 and was completed on May 9, 2008.

* Semi-occlusive Strip (TruMed Technologies Inc., Burnsville, Minnesota)

PANEL SELECTION

Each subject was assigned a permanent CRL identification number. All subjects signed an Informed Consent Form in compliance with 21 CFR Part 50: "Protection of Human Subjects" and a HIPAA Authorization Form in compliance with 45 CFR Parts 160 and 164. All subjects completed a Subject Profile/Medical History Form provided by Clinical Research Laboratories, Inc. prior to the study (Subject Demographics - Appendix I). Subjects who met the following criteria were impaneled:

- Male and female panelists between the ages of 18 and 70;
- Subjects who have completed a Panelist Profile/Medical History;
- Subjects who are in general good health as determined by a Panelist Profile/Medical History;
- Subjects who do not exhibit any skin diseases that might be confused with a skin reaction from the test material;
- Subjects willing to sign an Informed Consent Form in conformance with 21 CFR Part 50: "Protection of Human Subjects";
- Subjects who have completed a HIPAA Authorization Form in conformance with 45 CFR Parts 160 and 164;
- Females who are not pregnant or lactating;
- Subjects who demonstrate dependability and intelligence in following directions;
- Subjects who are not currently using any systemic or topical corticosteroids, anti-inflammatory drugs or antihistamines.

TEST METHOD

Prior to the application of the patch, the test area was wiped with 70% isopropyl alcohol and allowed to dry. The test material, which was prepared as described in the Test Material section of the report, was applied to the upper back (between the scapulae) and was allowed to remain in direct skin contact for a period of 24 hours.

TEST METHOD (Continued)

Patches were applied to the same site on Monday, Wednesday, and Friday for a total of 9 applications during the Induction Period. This schedule may have been modified to allow for missed visits or holidays. If a subject was unable to report on an assigned test date, the test material was applied on 2 consecutive days during the Induction Phase and/or a makeup day was added at the end of the Induction Phase.

The sites were graded by a CRL technician for dermal irritation 24 hours after removal of the patches by the subjects on Tuesday and Thursday and 48 hours after removal of the patches on Saturday, unless the patching schedule was altered as described above.

The sites were graded according to the following scoring system:

Dermal Scoring Scale

0 No visible skin reaction
± Barely perceptible erythema
1+ Mild erythema
2+ Well defined erythema
3+ Erythema and edema
4+ Erythema and edema with vesiculation

If a "2+" reaction or greater occurred, the test material was applied to an adjacent virgin site. If a "2+" reaction or greater occurred on the new site, the subject was not patched again during the Induction Phase but was challenged on the appropriate day of the study. At the discretion of the Study Director, patch sites with scores less than a "2+" may have been changed.

Following approximately a 2-week rest period, the challenge patches were applied to previously untreated test sites on the back. After 24 hours, the patches were removed by a CRL technician and the test sites were evaluated for dermal reactions. The test sites were re-evaluated at 48 and 72 hours. Subjects exhibiting reactions during the Challenge Phase of the study may have been asked to return for a 96-hour reading.

RESULTS

This study was initiated with 112 subjects. Four subjects discontinued study participation for reasons unrelated to the test material. A total of 108 subjects completed the study.

Individual dermal scores recorded during the Induction and Challenge Phases appear in Table I.

CONCLUSION

Based on the test population of 108 subjects and under the conditions of this study, the test material identified as Lipgloss (LSP5-30-1, ENG027914-1.1.0 did not demonstrate a clinically significant potential for eliciting dermal irritation or sensitization.

RETENTION

Test materials and all original forms of this study will be retained by Clinical Research Laboratories, Inc. as specified in CRL Standard Operating Procedures 30.6 and 30.6C, unless designated otherwise by the Sponsor.

TABLE I

Summary of Dermal Scores

Test Material:	Lipgloss .SP5-30-1, ENG027914-1.1.0

Subject Number	Induction Scores									Challenge Scores		
	1	2	3	4	5	6	7	8	9	24 Hour	48 Hour	72 Hour
1	0	0	0	0	0	0	0	0	0	0	0	0
2	0	0	0	0	0	0	0	0	0	0	0	0
3	Discontinued											
4	0	0	0	0	0	0	0	0	0	0	0	0
5	0	0	0	0	0	0	0	0	0	0	0	0
6	0	0	0	0	0	0	0	0	0	0	0	0
7	0	0	0	0	0	0	0	0	0	0	0	0
8	0	0	0	0	0	0	0	0	0	0	0	0
9	0	0	0	0	0	0	0	0	0	0	0	0
10	0	0	0	0	0	0	0	0	0	0	0	0
11	0	0	0	0	0	0	0	0	0	0	0	0
12	0	0	0	0	0	0	0	0	0	0	0	0
13	0	0	0	0	0	0	0	0	0	0	0	0
14	0	0	0	0	0	0	0	0	0	0	0	0
15	0	0	0	0	0	0	0	0	0	0	0	0
16	0	0	0	0	0	0	0	0	0	0	0	0
17	0	0	0	0	0	0	0	0	0	0	0	0
18	0	0	0	0	0	0	0	0	0	0	0	0
19	0	0	0	0	0	0	0	0	0	0	0	0
20	0	0	0	0	0	0	0	0	0	0	0	0
21	0	0	0	0	0	0	0	0	0	0	0	0
22	0	0	0	0	0	0	0	0	0	0	0	0
23	0	0	0	0	0	0	0	0	0	0	0	0
24	0	0	0	0	0	0	0	0	0	0	0	0
25	0	0	0	0	0	0	0	0	0	0	0	0

TABLE I
(Continued)

Summary of Dermal Scores

Test Material:	Lipgloss le) LSP5-30-1, ENG027914-1.1.0

Subject Number	**Induction Scores**									**Challenge Scores**		
	1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**24 Hour**	**48 Hour**	**72 Hour**
26	0	0	0	±	0	0	0	0	0	0	0	0
27	0	0	0	0	0	0	0	0	0	0	0	0
28	0	0	0	0	0	0	0	0	0	0	0	0
29	0	0	0	0	0	0	0	0	0	0	0	0
30	0	0	0	0	0	0	0	0	0	0	0	0
31	0	0	0	0	0	0	±	0	0	0	0	0
32	0	0	0	0	0	0	0	0	0	0	0	0
33	0	0	0	0	0	0	0	0	0	0	0	0
34	0	0	0	0	0	0	0	0	0	0	0	0
35	0	0	0	0	0	0	0	0	0	0	0	0
36	0	0	0	0	0	0	0	0	0	0	0	0
37	0	0	0	0	0	0	0	0	0	0	0	0
38	0	0	0	0	0	0	0	0	0	0	0	0
39	0	0	0	0	0	0	0	0	0	0	0	0
40	0	0	0	0	0	0	0	0	0	0	0	0
41	0	0	0	0	0	0	0	0	0	0	0	0
42	0	0	0	0	0	0	0	0	0	0	0	0
43	0	0	0	0	0	0	0	0	0	0	0	0
44	0	0	0	±	0	0	0	0	0	0	0	0
45	0	0	0	0	0	0	0	0	0	0	0	0
46	0	0	0	0	0	0	0	0	0	0	0	0
47	0	0	0	0	0	0	0	0	0	0	0	0
48	0	0	0	0	0	0	0	0	0	0	0	0
49	0	0	0	0	0	0	0	0	0	0	0	0
50	0	0	0	0	0	0	0	0	0	0	0	0

TABLE I
(Continued)

Summary of Dermal Scores

Test Material:	Lipgloss , LSP5-30-1, ENG027914-1.1.0											
Subject Number	**Induction Scores**									**Challenge Scores**		
	1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**24 Hour**	**48 Hour**	**72 Hour**
51	0	0	0	0	0	0	0	0	0	0	0	0
52	0	0	0	0	0	0	0	0	0	0	0	0
53	0	0	0	0	0	0	0	0	0	0	0	0
54	0	0	0	0	0	0	0	0	0	0	0	0
55	0	0	0	0	0	0	0	0	0	0	0	0
56	0	0	0	0	0	0	0	0	0	0	0	0
57	0	0	0	0	0	0	0	0	0	0	0	0
58	0	0	0	0	0	0	0	0	0	0	0	0
59	0	0	0	0	0	±	0	0	0	0	0	0
60	0	0	0	0	0	0	0	0	0	0	0	0
61	0	0	0	0	0	0	0	0	0	0	0	0
62	0	0	0	0	0	0	0	0	0	0	0	0
63	0	0	0	0	0	0	0	0	0	0	0	0
64	0	0	0	0	0	0	0	0	0	0	0	0
65	0	0	0	0	0	0	0	0	0	0	0	0
66	0	0	0	0	0	0	0	0	0	0	0	0
67	0	0	0	0	0	0	0	0	0	0	0	0
68	0	0	0	0	0	0	0	0	0	0	0	0
69	0	0	0	0	0	0	0	0	0	0	0	0
70	0	0	0	0	0	0	0	0	0	0	0	0
71	0	0	0	0	0	0	0	0	0	0	0	0
72	0	0	0	0	0	0	0	0	0	0	0	0
73	0	0	0	0	0	0	0	0	0	0	0	0
74	0	Discontinued										
75	0	0	±	0	0	0	0	0	0	0	0	0

TABLE I
(Continued)

Summary of Dermal Scores

Test Material:	Lipglos e) LSP5-30-1, ENG027914-1.1.0

Subject Number	Induction Scores									Challenge Scores		
	1	2	3	4	5	6	7	8	9	24 Hour	48 Hour	72 Hour
76	0	0	0	0	0	0	0	0	0	0	0	0
77	0	0	0	0	0	0	0	0	0	0	0	0
78	0	0	0	0	0	0	0	0	0	0	0	0
79	0	0	0	0	0	0	0	0	0	0	0	0
80	0	0	0	0	0	0	0	0	0	0	0	0
81	0	0	0	0	0	0	0	0	0	0	0	0
82	0	0	0	0	0	0	0	0	0	0	0	0
83	0	0	0	0	0	0	0	0	0	0	0	0
84	0	0	0	0	0	0	0	0	0	0	0	0
85	0	0	0	0	0	0	0	0	0	0	0	0
86	0	0	0	0	0	0	0	0	0	0	0	0
87	0	0	0	0	0	0	0	0	0	0	0	0
88	0	0	0	0	0	0	0	0	0	0	0	0
89	0	0	0	0	0	0	0	0	0	0	0	0
90	Discontinued											
91	0	0	0	0	0	0	0	0	0	0	0	0
92	0	0	0	0	0	0	0	0	0	0	0	0
93	0	0	0	0	0	0	0	0	0	0	0	0
94	0	0	0	0	0	0	0	0	0	0	0	0
95	0	0	0	0	0	0	0	0	0	0	0	0
96	0	0	0	0	0	0	0	0	0	0	0	0
97	0	0	0	0	0	0	0	0	0	0	0	0
98	0	0	0	0	0	0	0	0	0	0	0	0
99	0	0	0	0	0	0	0	0	0	0	0	0
100	0	0	0	0	0	0	0	0	0	0	0	0

TABLE I
(Continued)

Summary of Dermal Scores

Test Material:	Lipgloss					LSP5-30-1, ENG027914-1.1.0						
Subject Number	Induction Scores									Challenge Scores		
	1	2	3	4	5	6	7	8	9	24 Hour	48 Hour	72 Hour
101	Discontinued											
102	0	0	0	0	0	±	0	0	0	0	0	0
103	0	0	0	0	0	0	0	0	0	0	0	0
104	0	0	0	0	0	0	0	0	0	0	0	0
105	0	0	0	0	0	0	0	0	0	0	0	0
106	0	0	0	0	0	0	0	0	0	0	0	0
107	0	0	0	0	0	0	0	0	0	0	0	0
108	0	0	0	0	0	0	0	0	0	0	0	0
109	0	0	0	0	0	0	0	0	0	0	0	0
110	0	0	0	0	0	0	0	0	0	0	0	0
111	0	0	0	0	0	0	0	0	0	0	0	0
112	0	0	0	0	0	0	0	0	0	0	0	0

Appendix I

Subject Demographics

Subject Number	Subject Initials	CRL ID #	Age	Sex
1	MB	18220	57	F
2	BF	00054	51	F
3	DC	12376	48	F
4	AS	01584	46	F
5	PG	13984	43	F
6	RP	16060	21	F
7	JT	09713	53	F
8	CL	14668	60	F
9	CK	09605	63	F
10	PK	18678	54	M
11	SB	13858	64	F
12	JM	07179	44	F
13	LA	16749	46	F
14	AM	18842	24	M
15	MP	16022	66	F
16	PA	02727	65	F
17	SM	12510	24	F
18	NS	16253	69	F
19	KH	15618	55	F
20	JR	08854	43	F
21	CM	03444	67	F
22	KC	13388	60	F
23	NF	14449	47	F
24	KM	14519	37	F
25	HS	07067	49	F
26	AC	14858	39	F
27	PM	18953	54	F
28	MM	15443	43	F

Subject Number	Subject Initials	CRL ID #	Age	Sex
29	MP	03505	46	F
30	NK	17220	40	F
31	MB	03650	60	F
32	AS	16567	32	F
33	AA	18956	23	F
34	PN	03277	47	F
35	AR	18777	65	M
36	KM	08600	46	F
37	ED	17217	65	F
38	MH	01132	66	F
39	IA	10338	62	F
40	JP	15332	30	F
41	DW	10884	43	F
42	BL	18894	26	M
43	WW	16548	35	F
44	RH	18256	69	M
45	JC	06977	47	F
46	LL	10701	57	F
47	SH	18975	50	F
48	PM	09260	49	F
49	DM	18979	40	F
50	JV	18978	39	F
51	AC	05637	57	F
52	LA	15065	63	F
53	HP	17132	58	F
54	SC	18974	21	F
55	JB	12170	60	F
56	VJ	04247	62	F

Appendix I
(Continued)

Subject Demographics

Subject Number	Subject Initials	CRL ID #	Age	Sex
57	TP	07612	40	F
58	JW	08904	45	F
59	ET	09473	65	F
60	DP	08438	48	F
61	CS	14389	66	F
62	KT	06277	49	F
63	PM	03457	67	F
64	SA	18981	38	F
65	EW	18412	43	F
66	KW	14133	34	F
67	LF	15023	68	F
68	LL	07031	48	F
69	CS	18814	18	F
70	JK	14141	64	F
71	RK	14142	66	M
72	FA	18719	50	F
73	SS	18791	26	M
74	MC	13494	55	F
75	RB	08241	26	F
76	MV	02437	58	F
77	JL	13249	25	F
78	MP	18840	22	M
79	DS	15209	45	M
80	KC	12260	32	F
81	TR	13698	38	F
82	SI	18989	40	F
83	NP	17123	40	F
84	JG	18387	21	F

Subject Number	Subject Initials	CRL ID #	Age	Sex
85	HJ	18846	38	F
86	NO	01162	57	F
87	TM	13580	26	F
88	MZ	00237	52	F
89	MH	11093	46	F
90	CN	18252	51	F
91	BG	14700	20	F
92	TR	18931	34	F
93	AG	17450	28	F
94	CW	18095	43	F
95	SF	07438	29	F
96	AB	18851	20	F
97	BC	10128	54	F
98	LT	04909	55	F
99	BC	10444	57	F
100	CP	09254	38	F
101	LT	06804	35	F
102	RB	05376	56	M
103	MG	14013	35	F
104	SJ	13519	54	F
105	JB	14759	53	F
106	LF	18999	26	F
107	RS	09790	54	F
108	CN	19001	18	F
109	IV	10514	53	F
110	CT	19004	24	F
111	SN	16751	41	M
112	DH	19006	36	F

Personal Care Products Council
Committed to Safety, Quality & Innovation

Memorandum

TO: F. Alan Andersen, Ph.D.
Director - COSMETIC INGREDIENT REVIEW (CIR)

FROM: Halyna Breslawec, Ph.D.
Industry Liaison to the CIR Expert Panel

DATE: January 11, 2012

SUBJECT: Concentration of Use by FDA Product Category: Tin Oxide

1101 17th Street, N.W., Suite 300 | Washington, D.C. 20036-4702 | 202.331.1770 | 202.331.1969 (fax) | www.personalcarecouncil.org

Concentration of Use by FDA Product Category
Tin Oxide

Product Category	Maximum Concentration of Use
Eyebrow pencil	0.01-0.03%
Eye liner	0.06-2%
Eye shadow	0.07-5%
Eye lotion	0.004-0.09%
Eye makeup remover	0.3%
Mascara	0.003-0.08%
Other eye makeup preparations	0.01%
Colognes and toilet waters	0.0005%
Powders (dusting and talcum)	0.0005-0.03%
Other fragrance preparations	0.04-0.08%
Hair conditioners	0.001-0.003%
Shampoos (noncoloring)	0.0008-0.4%
Tonics, dressings and other hair grooming aids	0.001-0.002%
Hair dyes and colors (all types requiring caution statement and patch testing)	0.04%
Blushers (all types)	0.02-0.3%
Face powders	0.03-1%
Foundations	0.01-0.1%
Leg and body paints	0.09%
Lipstick	0.008-1%
Makeup bases	0.03%
Rouges	0.005-0.3%
Other makeup preparations	0.000003-0.02%
Basecoats and undercoats (manicuring preparations)	1%

Nail polish and enamel	0.002-1%
Bath soaps and detergents	0.0005-0.2%
Other personal cleanliness products	0.0005%
Skin cleansing (cold creams, cleansing lotions, liquids and pads)	0.0003-0.006%
Depilatories	0.002%
Face and neck creams, lotions and powders	0.02-0.05%
Body and hand creams, lotions and powders spray	0.0009-0.05% 0.002-0.06%
Moisturizing creams, lotions and powders	0.00005-0.01%
Other skin care preparations	0.002-0.3%
Suntan gels, creams and liquids	0.02% (not sprays)

Information collected in 2011
Table prepared January 10, 2012

Personal Care Products Council
Committed to Safety, Quality & Innovation

Memorandum

TO: F. Alan Andersen, Ph.D.
Director - COSMETIC INGREDIENT REVIEW (CIR)

FROM: Halyna Breslawec, Ph.D.
Industry Liaison to the CIR Expert Panel

DATE: March 9, 2012

SUBJECT: Comments on the Scientific Literature Review on Tin and Tin Oxide as Used in Cosmetics

Key Issue

p.2, 9, 11, Table 2 - Where did the concentration of use of 1% in rinse-off products come from (stated in the Cosmetic Use section, the Summary and Table 2)? The results of the Council concentration of use survey indicated 1% concentrations for face powders, lipsticks, basecoats and undercoats, and nail polish and enamel. None of these product categories are considered rinse-off products.

Additional Comments

p.2 - In the Cosmetic Use section, please provide the specific FDA product categories associated with the stated use concentrations.

p.2 - As the Cosmetic Use section should focus on exposure, please delete the following sentences. "However, the potential for inhalation toxicity is not limited to respirable droplets/particles deposited in the lungs. Inhaled droplets/particles deposited in the nasopharyngeal and thoracic regions of the respiratory tract may cause toxic effects, depending on their chemical and other properties."

p.2 - The following sentence should note the material (food?) to which the European Union limits apply. "The European Union has established maximum levels for certain contaminants, inorganic tin included, to achieve a high level of health protection, especially for sensitive population groups such as children or individuals with allergies."

p.5 - Since studies of many tin compounds are presented under the Tin Oxide subheading, perhaps this subheading is not necessary.

p.5 - Please indicate what endpoints were evaluated in humans fed tomato soup containing tin.

p.5 - The reports of adverse effects in humans eating food highly contaminated with tin appear to be case reports and should be presented in the case report section.

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p.8 - Although it is a study of workers, the study of the ceramics workers should be presented in the Skin Irritation and Sensitization section.
p.8 - In the description of the rat study in the Reproductive and Developmental Toxicity section, please include the days of gestation the dams were treated and the levels of tin found in offspring of treated dams.
p.8 - The study that examines tin levels in human maternal blood, umbilical cord blood and placenta should be presented in the Toxicokinetics section.
p.8 - Please include the doses used in the genotoxicity study.
p.8 - If available, please provide some measure of dose for the Tin implanted in the carcinogenicity studies (reference 66, 67?, 68 [reference 67 does not seem to be correct as it is the Belgian case-control study]).
p.9 - The Belgian case-control study (reference 67) should be moved to the section on Occupational Studies and Case Reports.
p.9 - On p.5 it states that the exposures of the 9 volunteers was "for three 24-day periods" on p.9 it says "over a 24-h period". Which exposure protocol is correct?
p.9 - The study in ceramics workers should be presented in the Summary with the other dermal irritation and sensitization studies.
p.10 - All the information in the first paragraph on p.10 concerns toxicokinetics. Therefore, this information should be presented with the other toxicokinetic information.
p.11, Table 1 - Please present use information by FDA product category when use information for only one ingredient is presented in a report.

2011 FDA VCRP Data
Tin Oxide

02D - Other Bath Preparations	1
03A - Eyebrow Pencil	1
03B - Eyeliner	34
03C - Eye Shadow	172
03D - Eye Lotion	1
03F - Mascara	4
03G - Other Eye Makeup Preparations	11
04A - Cologne and Toilet waters	4
04B - Perfumes	2
04C - Powders (dusting and talcum, excluding aftershave talc)	11
04E - Other Fragrance Preparation	9
05A - Hair Conditioner	1
05F - Shampoos (non-coloring)	2
05G - Tonics, Dressings, and Other Hair Grooming Aids	4
05I - Other Hair Preparations	2
07A - Blushers (all types)	22
07B - Face Powders	31
07C - Foundations	20
07D - Leg and Body Paints	1
07E - Lipstick	342
07F - Makeup Bases	5
07G - Rouges	4
07H - Makeup Fixatives	1
07I - Other Makeup Preparations	31
08D - Nail Extenders	1
08E - Nail Polish and Enamel	44
10A - Bath Soaps and Detergents	13
10E - Other Personal Cleanliness Products	20
12A - Cleansing	1
12C - Face and Neck (exc shave)	7
12D - Body and Hand (exc shave)	9
12F - Moisturizing	55
12G - Night	1
12H - Paste Masks (mud packs)	1
12J - Other Skin Care Preps	4
13B - Indoor Tanning Preparations	6
Total	**878**