



COLOR PIGMENTS MANUFACTURERS ASSOCIATION, INC.

May 15, 2006

NIOSH Docket Office,
Robert A. Taft Laboratories,
4676 Columbia Parkway, M/S C-34,
Cincinnati, Ohio 45226,

ATTN: Docket Number NIOSH-033, Ms. Diane Miller

Telephone 513/533-8450, fax 513/533-
8285.

**Re: Comments of the Color Pigments Manufacturers
Association, Inc. on the Draft NIOSH Current
Intelligence Bulletin, Evaluation of Health Hazard
and Recommendations for Occupational Exposure to
Titanium Dioxide**

Dear Ms. Miller:

The following comments are submitted to the National Institute of Occupational Safety and Health ("NIOSH") on the Draft Current Intelligence Bulletin, Evaluation of Health Hazard and Recommendations for Occupational Exposure to Titanium Dioxide (the "Draft Bulletin") by the Color Pigments Manufacturers Association, Inc. ("CPMA") regarding the use, safety and exposure to titanium dioxide in special effect pearlescent pigments and as an important formulation component in many other color pigments.

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CPMA strongly supports the comments submitted by the American Chemistry Council through its Titanium Dioxide Panel, including specifically that:

- 1) NIOSH has relied on outdated information to estimate the extent of titanium dioxide exposure.
- 2) NIOSH has not reasonably categorized or described the extensive epidemiological studies of workers exposed to titanium dioxide.
- 3) NIOSH has erroneously characterized and misinterpreted the available animal studies and fails completely to consider several studies of critical importance.
- 4) NIOSH relies on studies which emphasize highest dose effects and ignore evidence from studies at relevant levels of exposure.

Introduction

The Color Pigments Manufacturers Association, Inc. (CPMA), formerly DCMA -- the Dry Color Manufacturers' Association, is an industry trade association representing color pigment companies in Canada, Mexico, and the United States. CPMA represents small, medium, and large color pigments manufacturers throughout Canada, Mexico, and the United States, accounting for 95% of the production of color pigments in North America. Color Pigments are widely used in product compositions of all kinds, including paints, inks, plastics, glass, synthetic fibers, ceramics, colored cement products, textiles, cosmetics, and artists' colors. Color pigment manufacturers located in other countries with sales in Canada, Mexico, and the United States and suppliers of intermediates to the color pigments industry are also members of the Association.

Background

Pearlescent Special Effect Pigments

Pearlescent pigments are generally mixtures where color effect is achieved through the layering of mica flakes with one or more component pigments. The U.S. Food and Drug Administration recently issued a Final Rule affirming the safety

for use in food-contact applications of many of the components used in pearlescent pigments.¹

Acute Toxicity of Pearlescent Special Effect Pigments

Acute studies performed on these pigments show extremely low toxicity. Evaluation of potential impact to human health resulting from normal occupational exposure to pearlescent pigment revealed no adverse effects.² All the acute oral toxicity tests performed to date indicate LD50 values of greater than 5000 mg/kg.^{3,4}

¹ Federal Register, Volume 56, pp. 42927-42935, August 30, 1991, "Colorants for Polymers" Final Rule, Food and Drug Administration, 21 CFR 178.3297.

² Bruch, Dr. J., Expert Report on Health Hazards Caused by Pearl Lustre Pigments in Occupational Medicine and Toxicology. University Clinic Essen (Germany), Institute of Hygiene and Occupational Medicine. Provided at the request of E. Merck, Darmstadt, Germany, pp. 19-28.

³ Heusener, A. and Eberstein, M. "Report No. 4/51/88, T 13 180: Acute Toxicity Study in Rats after Oral Administration of iriodin® 502 C 63", E. Merck Institute of Toxicology, September 27, 1988.

⁴ Heusener, A. and Jacobs, M. "Report No. 40/59/89, T 13279: Acute Toxicity Study in Rats after

Chronic Toxicity of Pearlescent Special Effect Pigments

In the case of uncoated mica, any potential chronic effects would be no different than exposure to mica particulates with the notable exception that mica pigments would be completely free of impurities. Chronic health effects have not been identified as a result of exposure to pearlescent pigments containing titanium dioxide, this is despite many years of industry use. Any exposure to titanium dioxide in manufacturing processes which use pearlescent pigments would be controlled by existing regulations. Pearlescent special effect pigments used in consumer products are encapsulated in the inks, paints and resins which make up these products, as a result, there should not be any exposure to titanium dioxide from these products in consumer use.

Titanium Dioxide in Color Pigment Formulations

Titanium dioxide is indispensable as an agent in many formulations of color pigments used in the printing ink, coatings and plastics industries. Titanium dioxide is used to tint color pigments, to standardize color pigments for specific

Oral Administration of EM 140537", E. Merck
Institute of Toxicology, July 5, 1989.

color shades and as an important opacifying agent. There is little if any exposure to titanium dioxide in these applications, since the pigment formulation is non-soluble and non-bioavailable and the formulation, including the titanium dioxide is encapsulated in the final resin which makes up the ink, coating or plastic.

It is our understanding that, after two years as a "high carcinogenicity concern" substance, titanium dioxide remains assigned to a priority candidate list. From this candidate list, NIOSH may determine to prepare a hazard identification document after which titanium dioxide may be assessed by the California Carcinogen Identification Committee. As discussed below, we believe that the NIOSH findings contradict the conclusions reached by the American Conference of Governmental Industrial Hygienists ("ACGIH"). After review of the cited studies and related information, we continue to believe that their is not data sufficient to warrant further assessment of titanium dioxide.

**NIOSH Evaluation of Carcinogenicity
And Exposure Data, Titanium Dioxide**

The following discussion will review the NIOSH Draft Bulletin for carcinogenicity studies (dated November, 2005) involving titanium dioxide and its relevance to pearlescent

pigments and formulation of color pigments used in various applications. We note that NIOSH describes but does not sufficiently consider the available information from human epidemiological studies. These studies include Chen and Fayerweather (1989), Siemiatycki et al. (1994), Boffetta et al. (2001), and an update of Siemiatycki et al. (1994) found no significant increase in lung cancer among workers occupationally exposed to titanium dioxide. If no significant connection between higher concentration workplace exposures and lung cancer can be determined from four studies, there would appear to be little evidence to support the NIOSH assessment that titanium dioxide exposures pose a high concern warranting review and possible listing in the California Proposition 65 list of carcinogens. Particularly if we consider that ordinary exposures to consumers would be no more than a fraction of that experienced by workers in an epidemiological study.

NIOSH has based its concern with respect to titanium dioxide on a number of studies which were done in the mid to late 1980s involving extremely high doses of titanium dioxide administered to the breathing zone of laboratory animals. These experiments, Lee et al. (1985),⁵ Dungworth et al. (1994), Thyssen

⁵ See also, Lee et al. "Pulmonary Response to Impaired Lung Clearance in Rats Following Excessive TiO₂ Dust Deposition. Environ. Res. 41:144-167 (1986)

et al. (1978) and Mohr et al. (1984), all involved doses of titanium dioxide which were many times the allowable limit for nuisance dust exposures in the workplace. Such doses of any dust material are known to overwhelm the clearance mechanisms which the animals use to clear particles from the lungs.

The additional studies reviewed in the Draft Bulletin indicate that, for both intraperitoneal injection experiments and high dose feeding studies there was no evidence of carcinogenic activity associated with titanium dioxide. Nor do the available studies for mutagenicity indicate that titanium dioxide poses any concern despite numerous studies.

Therefore, the Draft Bulletin fails to justify the NIOSH high level of concern for exposure to titanium dioxide. It is true that titanium dioxide is widely used in thousands of formulations and products. Since titanium dioxide has been used for over fifty years in so many applications without significant concern, and despite a number of workplace studies, there is little evidence which in any way questions the safety of this extremely important compound.

Additionally, as noted in the Draft Bulletin, titanium dioxide is an established food colorant. Titanium dioxide has been proven safe in use as a food colorant for decades. We are not aware of any reports of health related concerns associated

with the use of titanium dioxide in food and pharmaceutical preparations.

The NIOSH Data Draft Bulletin is contradicted by the ACGIH Assessment for titanium dioxide. The ACGIH monograph for titanium dioxide, dated 2001, reviewed the same body of evidence that the NIOSH has described in its Draft Bulletin. ACGIH specifically reviewed the high dose rat inhalation studies that appear to be a concern to NIOSH. ACGIH concluded that the Lee et al. study, which produced tumors a 250 milligrams titanium dioxide per cubic meter over two years was:

"of questionable relevance for extrapolation of results to humans. Given the amount of dust in the lungs, the carcinomas were postulated to be the result of saturation of normal pulmonary clearance mechanisms. At 50 milligrams per cubic meter, massive accumulations of dust laden macrophages, foamy dust cells, and free particles were considered indicative of such an overload." ACGIH Titanium Dioxide Monograph p.2.

The ACGIH concluded that, "[t]here is a lack of conclusive evidence to support a relationship between occupational exposure to titanium dioxide and pulmonary fibrosis, cancer, or other adverse health effects." ACGIH Titanium Dioxide Monograph p.2. ACGIH set its recommended Threshold Limit Value at 10 milligrams per cubic meter air. This recommended limit is 25 times less than the level found to pose a concern in chronic animal experiments.

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It should be noted that ACGIH recommends a limit of 5 milligrams per cubic meter of air for all respirable dusts. Federal Occupational Safety and Health Administration mandates a limit to respirable nuisance dusts at no more than 5 milligrams per cubic meter air. As a result it is extremely unlikely that any person in California would encounter an exposure to titanium dioxide above the ACGIH limit.

**Exposure to Titanium Dioxide from
Products Represented by CPMA**

Titanium dioxide is coated on platelets of mica or various compositions to produce special effect pigments. The relatively small amounts of titanium dioxide used in the formulations cannot be separated from the pigment formulation. These pigments are further encapsulated in the resin which makes up the final ink, paint or plastic of the final products made from these pigments. As a result, no exposure in use has any potential to approach nuisance dust levels. Labeling or warning language involving extremely high levels of dust which are not possible in use would lead to unwarranted confusion. Similarly, there is no relevant exposure to titanium dioxide which could result from the use of titanium dioxide in formulations of color pigments as an opacifier, or color standardization additive. The amounts of titanium dioxide are too low and the exposures,

if any, far to short to create any possible concern with nuisance type, extreme, dust exposures.

Additionally, it must be kept in mind that titanium dioxide is a valuable industrial commodity. For practical financial reasons there is a strong incentive to avoid waste or lost product. High concentration dust exposures imply extensive losses of titanium dioxide as fugitive dust, such a waste of valuable products in business would be rare in today's competitive economy.

Furthermore, regulation of chemicals which have been proven safe and nontoxic over a period of more than fifty years, such as titanium dioxide, can create an unwarranted incentive to replace the proven product with products which may be far more hazardous in the application, simply because the substitute does not have such a labeling requirement.

Conclusion

The NIOSH policy identifying potential carcinogens based on only one exposure without regard to dose or controls and without consideration of other existing studies is not scientifically sound. As long as NIOSH works from this definition as a policy, then all of the technical or scientific discussion about the human studies becomes irrelevant to the decision about

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identification of carcinogens. For example, if there were a perfect epidemiological study with no observed increase in cancer, it would not change the NIOSH position regarding identification of carcinogens because of this policy and a single animal study at extremely high irrelevant doses.

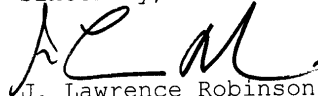
NIOSH's approach to titanium dioxide as a carcinogenicity concern is not warranted from the data cited in the Draft Bulletin. ACGIH, reviewing much of the same data, could not conclude that exposure to titanium dioxide posed a significant risk. Special effect and color pigment formulations could not produce an exposure relevant to the exposures identified in animal experiments and should be specifically excluded from any further consideration.

Titanium dioxide should not be considered as a potential carcinogen and does not warrant further consideration as such.

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Please call if there are any further questions or if we can
assist in your inquiry.

Sincerely,



J. Lawrence Robinson
President

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