# Regulatory Synopsis

# for

# Titanium Dioxide 3328 USP BC

CAS Number: 13463-67-7
EINECS Number: 236-675-5
Color Index Name: Pigment White 6
Color Index Number: CI 77891

## Composition:

| | | | |
|---|---|---|---|
| Titanium Dioxide | 99.0 to 100.5% | Assay | Main constituent |
| Aluminum Oxide | <0.1% | XRF Analysis | Natural impurity |
| Amorphous Silica | <0.1% | XRF Analysis | Natural impurity |

## Inventories:

| | |
|---|---|
| **Australia (AICS)** | On the inventory |
| **Austria** | On the inventory |
| **China (IECSC)** | On the inventory |
| **European Community (EINECS)** | On the inventory |
| **Japan (MITI)** | On the inventory |
| **Canada (DSL)** | On the inventory |
| **Korea (ECL)** | In compliance* |
| **New Zealand** | On the inventory |
| **Philippines (PICCS)** | On the inventory |
| **Switzerland** | On the inventory |
| **Taiwan (ECN)** | On the inventory |
| **USA (TSCA)** | On the inventory |

**Remarks:**
"On the inventory" means the product is listed in the respective inventory.
* Korea: Certificate of Components required

**Toxicology:**

| | | |
|---|---|---|
| oral | $LD_{50}$ | > 5.000 mg/kg, |
| dermal | $LD_{50}$ | > 5.000 mg/kg, |
| inhalative | $LC_{50}$ | > 6.80 mg/l/4h, |

**Ecology:**

| | | |
|---|---|---|
| Pimephales Promelas | $LC_{50}$ | > 1.000 mg/l/96h |
| Daphia Magna (Crustacea) | $LC_{50}$ | > 100 mg/l/48h |
| Pseudokirchnerella Subcapitata | $EC_{50}$ | > 16 mg/l/72h |

Water Hazard Class (Germany) Not Hazardous for Water.

**U.S. Regulations:**

| | |
|---|---|
| 21CFR73.575 (Food) | Conforms to requirements. |
| 21CFR73.1575 (Drugs) | Conforms to requirements. |
| 21CFR73.2575 (Cosmetics) | Conforms to requirements. |
| U.S. Pharmacopeia | Conforms to requirements. |
| Food Chemicals Codex | Conforms to requirements. |
| 21CFR175.105 (Adhesives) | Conforms to requirements. |
| 21CFR175.300 (Resinous and Polymeric Coatings) | Conforms to requirements. |
| 21CFR176.170 (Paper and Paperboard Fatty Foods) | Conforms to requirements. |
| 21CFR176.180 (Paper and Paperboard Dry Foods) | Conforms to requirements. |
| 21CFR177.2600 (Rubber Articles) | Conforms to requirements. |
| 21CFR178.3297 (Colorants for Polymers) | Conforms to requirements. |
| CONEG Regulations | Conforms to requirements. |
| Conflict Minerals (Dodd-Frank Act) | Conflict minerals not incorporated in or utilized in the production of the material |
| California Proposition 65 | On September 2, 2011, the State of California listed titanium dioxide as a Carcinogen under Proposition 65 using Labor Code mechanism. The listing is a qualified listing of "Titanium dioxide (airborne, unbound particles of respirable Size)." The listing does not cover titanium dioxide when it remains bound within a product mix. |
| California Safe Cosmetics Act (SB484) | Titanium dioxide is included on the list as a carcinogen based on IARC. |

**EC Regulations:**

| | |
|---|---|
| European Pharmacopeia | Meets requirements. |
| EC Directive 231/2012 | Meets requirements. |
| EC Directive 95/45/EC (Food) | Meets E-171 Specifications (Purity criteria concerning colors for use in foodstuffs). |
| EC Directive 1223/2009 (Cosmetics) | Suitable for use in cosmetics. (Annex II, II and IV, List of Colorants allowed in cosmetic Products.) |
| EC Directive 2011/65/EU (RoHS2) | In compliance. |
| Resolution AP(89)1 | Meets the requirements for colorants in plastic materials coming into contact with food. |
| Resolution AP(2002) 1 | Meets the requirements for colorants on paper and board materials and articles intended to come into contact with food. |
| Resolution AP(2004)1 | Meets the requirements for colorants in surface coatings intended to come into contact with foodstuffs. |
| EN 71-3 Safety of Toys | Titanium dioxide is allowed to be applied. Testing of the final product is required. (Part 3: Migration of certain elements). |
| REACH | Registered. |
| Substances of Very High Concern | This product does not contain any of the 211 SVHCs on the list published on January 19, 2021 |

**United Nations:**

| | |
|---|---|
| Specifications for Identity and Purity of Food Colors | Conforms to specifications. |

**Other Jurisdictions:**

| | |
|---|---|
| Japanese Pharmacopeia | Complies with specifications for Titanium Dioxide |
| British Pharmacopeia | Complies with specifications for Titanium Dioxide |

Dust Explosion Hazard: This material is an inert inorganic chemical substance. It is neither flammable nor explosive and cannot be assigned to any dust explosion class as defined under national and international standards on dust explosions.

Nitrosamines: A risk assessment including testing for the presence of nitrosamines by an independent, accredited analytical laboratory using appropriately validated and sensitive methods (CAM-0658501-18D), has been performed for Titanium Dioxide 3328 USP BC. It was determined that there are no nitrosamine impurities present in this material at concentrations above corresponding detection limits.

Residual Solvents: This material does not contain nor is processed with any organic solvents identified in USP <467> or any of the Class 1, 2, 3 or other solvents listed in the ICH Residual Solvent Guidelines Q3C (R6) (including 2-methyltetrahydrofuran, cyclopentylmethylether and tert-butanol in R8) and the United States Pharmacopeia. Organic solvents are not used in or around the production, processing, handling, or shipping of this product. There are no solvents used or generated in the manufacturing process for this material. Thus, if tested, this material will comply with ICH Q3C and USP<467> requirements.

BSE/TSE Statement: This product does not contain any material of animal origin and is, therefore, not of concern in regard to BSE/TSE transmission.

Animal Testing Statement: This product has not been tested on animals since July 1976. It is currently the policy of Brenntag Specialties, LLC to not subject our materials to any testing that requires the use of animals as test subjects.

Vegan/Vegetarian Statement: Titanium dioxide is a naturally occurring oxide of titanium. No animal or animal bi-products are used in the creation of this product. Therefore, this product can be considered safe for vegans and vegetarians.

Nano-Particles: European Regulation EC 1223/2009 – defines nanomaterials as insoluble or biopersistant and intentionally manufactured materials with one or more external dimensions, or an internal structure, on the scale from 1 to 100 nm. This definition does not apply to this product.

This material is milled to achieve a consistent particle size range, but is not intentionally manufactured using nanotechnology, or to have nanomaterial properties or particle size, nor does it meet accepted definitions of a nanomaterial. Particle size greater than 100 nanometers is needed in the pigment products to achieve desired properties, including opacity. The milling process results in a primary particle size range following a normal or Gaussian distribution curve, where it can be assumed that a small percentage of primary particles are <100 nm (i.e. nanoparticles in terms of ISO/TS 80004).

This pigmentary grade contains less than 50% of particles in the number size distribution, where one or more external dimensions is between 1 nm and 100 nm. Consequently, this product is not nanomaterial according to the definition given in European Commission Recommendation 2011/696/EU dated 10-18-2011. Furthermore, this product does not fall within the scope of the French Decree No. 2012-232 of February 17, 2012, the Belgian Royal Decree C-2014/24329 of May 27, 2014, or the Canadian Section 71 Notice of July 25, 2015 requiring the declaration of nanomaterials.

Other Chemicals: Based on an extensive knowledge of the product and the manufacturing process, though not actually tested, we do not have any reason to believe that this material contains the following chemicals.

Abietic Acid
Aflatoxins
Alcohol
Aldehyde
Allergenic Raw Materials
Animal Derived Substances
Aromatic Amines
Asbestos
Azo Dyes
Biocides
Bioengineered Food/Ingredients as defined in 7 CFR 66
Bisphenol A
Chloroacetamide
Chloromethylisothiazolinone/ Methylisothiazolinone (CMIT/MIT)
CMR Substances
Colophony
DEA (diethanolamine)
Dimethyl Fumerate
DIPA (diisopropanolamine)
Dioxins/Furans
Epoxy Derivatives
Ethylene Oxide (ETO)
Flame Retardants (PBB, PBDE)
Formaldehyde
Fragrance
Genetically Modified Organisms (GMO)
Gluten
Glycol
Halogenated Organic Substances
Iodine
Lactose
Melamine
Mycotoxins
Nonylphenol
Ozone Depleting Substances
Polycyclic Aromatic Hydrocarbons (PAH)
Palm Oil
Parabens
Polychlorinated Biphenyls (PCB)
Perfluorinated Tensides (PFOA, PFOS)
Pesticides
Petrolatum
Phenols
Phthalates
Plasticizers
Preservatives
PVC
Rubber Latex
Salicylates
Sewer Sludge
Sodium Lauryl Sulfate (SLS)
Solvents
Synthetic scrubbing beads
Tourmaline
Tributyl Tin
Triclosan
Trisnonylphosphite

**Allergen Statement:**

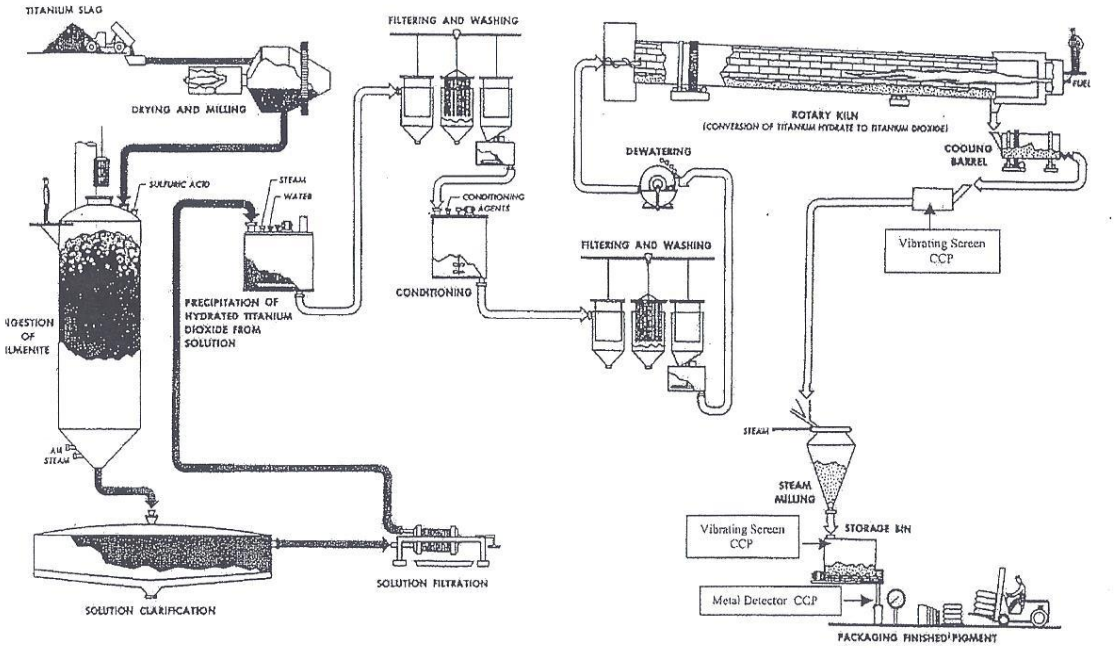
| Potential Allergens | Present in Material | Potential Risk for Cross Contamination |
|---|---|---|
| Aspartame | No | No |
| Cereals Containing Gluten (wheat, rye, barley, oats, spelt, kamut, and products thereof.) | No | No |
| Corn / Corn Derivatives | No | No |
| Crustaceans | No | No |
| Egg/ Egg Derivatives | No | No |
| Fish | No | No |
| Shellfish | No | No |
| Peanuts/ Peanut Derivatives | No | No |
| Soy/ Soy Derivatives | No | No |
| Milk/ Milk Derivatives | No | No |
| Tree Nuts | No | No |
| Legumes | No | No |
| Mollusks and products thereof | No | No |
| Celery | No | No |
| Mustard | No | No |
| Sesame Seeds | No | No |
| Sulfur Dioxide/ Sulfites (>10ppm) | No | No |
| Poppy Seeds | No | No |
| Sunflower Seeds | No | No |
| Yeast/ Extracts of Yeast | No | No |
| Lupin and products thereof | No | No |
| Molds | No | No |
| Latex | No | No |
| Antioxidants | No | No |
| Preservatives | No | No |
| Glutamates | No | No |
| Phenylalanine | No | No |
| Organic Colorants | No | No |

European Fragrance Allergens: This product does not contain any of the 26 fragrance allergens listed in EC Directive 2003/15/EC.

- Kosher Certified
- Halal Certified
- No Nutritional Value

**Manufacturing Process:**

This titanium dioxide pigment has an anatase crystal structure and is produced by the sulfate process. This process utilizes ilmenite ore slag. The ilmenite slag is digested with concentrated sulfuric acid. This reaction coverts the iron oxide in the slag to the by-product Iron (II) Sulfate which is crystallized and filtered-off to yield only the titanium salt in the digestion solution. This is further processed by hydrolysis, washing and calcination to yield the titanium dioxide pigment. The processing results in a purified grade of finished pigment, which is tested and certified to meet compendial standards. This material is considered to be a synthetic inorganic colorant. The process flow diagram for the anatase pigment produced by the Sulfate Process is illustrated below.




Good Manufacturing Practices: The product is manufactured, packaged, labeled, tested, stored and shipped in accordance with the current Good Manufacturing Practices as stated in 21CFR Parts 210 and 211 for bulk inactive ingredients.

Manufacturing Site: KRONOS Canada, Inc.
3390 Boul. Marie-Victorin
Varennes, Quebec

The manufacturing site has been assessed and registered under ISO 9001:2015 and FSSC 22000 v4.1 standards.

Bacteria Control: This pigment is not gamma-irradiated or gassed. The material is calcined at approximately 1,000 $^{o}$C and enters a closed system after calcination to the packaging station.

Foreign Object Controls: The pigment is sieved prior to packaging and passes through a state of the art metal detection system. The packaging system is fully automated and the final package is sealed.

Storage: The product should be stored in a clean, dry area at ambient temperature.

Shelf Life: A retest date of 5 years from the date of manufacture has been established and shelf life may be extended by rechecking the moisture and microbial content to verify the integrity of the material.

Lot Number Explanation: The lot sequence is seven-digit number, generated by a "batch generator" and then, entered into SAP HANA (Kronos' internal computer system) to link the lot number to the appropriate production batch. The lot number is a sequential number worldwide.

Elemental Impurities:

| Elemental Impurity | | Class | Likely to be Present | | | If Known, Please Identify the Expected Concentration /Units (or Range) | Analytical Method Used (and Limit of Detection if Available) | Comments regarding source of information (i.e.; frequency of testing, process understanding, etc.) |
|---|---|---|---|---|---|---|---|---|
| Arsenic (inorganic) | As | 1 | Yes ☐ | No ☒ | Unknown ☐ | < 0.1 ppm | ICP-MS / EN ISO 17294-2 | Tested every lot |
| Cadmium | Cd | 1 | Yes ☐ | No ☒ | Unknown ☐ | < 0.2 ppm | ICP-MS / EN ISO 17294-2 | Tested every lot |
| Mercury (inorganic) | Hg | 1 | Yes ☐ | No ☒ | Unknown ☐ | < 0.1 ppm | ICP-MS / EN ISO 17294-2 | Tested every lot |
| Lead | Pb | 1 | Yes ☒ | No ☐ | Unknown ☐ | 2.0 ppm | ICP-MS / EN ISO 17294-2 | Tested every lot |
| Cobalt | Co | 2A | Yes ☐ | No ☒ | Unknown ☐ | < 0.1 ppm | ICP-MS / EN ISO 17294-2 | Tested once per year |
| Nickel | Ni | 2A | Yes ☒ | No ☐ | Unknown ☐ | < 1 ppm | ICP-MS / EN ISO 17294-2 | Tested once per year |
| Vanadium | V | 2A | Yes ☒ | No ☐ | Unknown ☐ | < 7 ppm | ICP-MS / EN ISO 17294-2 | Tested once per year |
| Silver | Ag | 2B | Yes ☐ | No ☒ | Unknown ☐ | < 0.2 ppm | ICP-MS / EN ISO 17294-2 | Tested once per year |
| Gold | Au | 2B | Yes ☐ | No ☒ | Unknown ☐ | < 0.1 ppm | ICP-MS / EN ISO 17294-2 | Tested once per year |

| Elemental Impurity | | Class | Likely to be Present | | | If Known, Please Identify the Expected Concentration /Units (or Range) | Analytical Method Used (and Limit of Detection if Available) | Comments regarding source of information (i.e.; frequency of testing, process understanding, etc.) |
|---|---|---|---|---|---|---|---|---|
| Iridium | Ir | 2B | Yes ☐ | No ☒ | Unknown ☐ | < 0.1 ppm | ICP-MS / EN ISO 17294-2 | Tested once per year |
| Osmium | Os | 2B | Yes ☐ | No ☒ | Unknown ☐ | < 0.1 ppm | ICP-MS | Tested once per year |
| Palladium | Pd | 2B | Yes ☐ | No ☒ | Unknown ☐ | < 0.1 ppm | ICP-MS / EN ISO 17294-2 | Tested once per year |
| Platinum | Pt | 2B | Yes ☐ | No ☒ | Unknown ☐ | < 0.1 ppm | ICP-MS / EN ISO 17294-2 | Tested once per year |
| Rhodium | Rh | 2B | Yes ☐ | No ☒ | Unknown ☐ | < 0.1 ppm | ICP-MS / EN ISO 17294-2 | Tested once per year |
| Ruthenium | Ru | 2B | Yes ☐ | No ☒ | Unknown ☐ | < 0.1 ppm | ICP-MS / EN ISO 17294-2 | Tested once per year |
| Selenium | Se | 2B | Yes ☐ | No ☒ | Unknown ☐ | < 0.5 ppm | ICP-MS / EN ISO 17294-2 | Tested once per year |
| Thallium | Tl | 2B | Yes ☐ | No ☒ | Unknown ☐ | < 0.1 ppm | ICP-MS / EN ISO 17294-2 | Tested once per year |
| Barium | Ba | 3 | Yes ☒ | No ☐ | Unknown ☐ | < 8 ppm | ICP-MS / EN ISO 17294-2 | Tested every lot |
| Chromium | Cr | 3 | Yes ☒ | No ☐ | Unknown ☐ | < 5 ppm | ICP-MS / EN ISO 17294-2 | Tested every lot |
| Copper | Cu | 3 | Yes ☐ | No ☒ | Unknown ☐ | < 2.0 ppm | ICP-MS / EN ISO 17294-2 | Tested every lot |

| Elemental Impurity | | Class | Likely to be Present | | | If Known, Please Identify the Expected Concentration /Units (or Range) | Analytical Method Used (and Limit of Detection if Available) | Comments regarding source of information (i.e.; frequency of testing, process understanding, etc.) |
|---|---|---|---|---|---|---|---|---|
| Lithium | Li | 3 | Yes ☐ | No ☒ | Unknown ☐ | < 1 ppm | ICP-MS / EN ISO 17294-2 | Tested once per year |
| Molybdenum | Mo | 3 | Yes ☐ | No ☒ | Unknown ☐ | < 1 ppm | ICP-MS / EN ISO 17294-2 | Tested once per year |
| Antimony | Sb | 3 | Yes ☐ | No ☒ | Unknown ☐ | < 0.1 ppm | ICP-MS / EN ISO 17294-2 | Tested every lot |
| Tin | Sn | 3 | Yes ☒ | No ☐ | Unknown ☐ | < 0.5 ppm | ICP-MS / EN ISO 17294-2 | Tested once per year |

Date: February 1, 2021