

2.1.P.4.2 Analytical Procedures

1 Opadry white, OY-L-28900 (CoA and BSE/TSE statement are attached)

1.1 Acceptance criteria

Appearance:	White powder
Identification (Ti)	Identical
Sulphated ash	34.0 –46.0 %

1.2 Test procedures

Appearance

Test:

Check by visual examination

Requirement: White powder

Identification (Ti)

Test:

Mix 0.25 g residue received in test with 2.5 g of anhydrous sodium sulphate R in a long-necked combustion flask. Add 10 ml of water and mix. Add 10 ml of sulphuric acid R and boil vigorously, with the usual precautions, after 15 min allow cooling, and filtering through an appropriate filter. To the clear solution add slowly a cooled mixture of 30 ml water and 10 ml of sulphuric acid R, cool again and dilute to 50 ml with water. (*Test Solution*)

To 5 ml of *Test Solution* add 0.1 ml of strong hydrogen peroxide solution R. An orange red colour appears.

To 5 ml of *Test Solution* add 0.5 g of zinc R in granules. After 45 min, the mixture has a violet blue colour.

Requirement: Identical

Sulphated ash

Test:

Ignite a suitable porcelain or quartz crucible for 30 minutes; allow cooling in a desiccator over silica gel and weighing. Place 1.000 g of the substance in the crucible and weigh. Moisten the substance to be examined with a small amount of sulphuric acid R (usually 1 ml) and heat gently at as low a temperature as practicable until the sample is thoroughly charred. After cooling, moisten the residue with a small amount of sulphuric acid R, heat gently until white fumes are no longer evolved and ignite until the residue is completely incinerated. Ensure that flames are not produced at any time during the procedure. Allow the crucible to cool in a desiccator over silica gel, weigh it again and calculate the mass of the residue.

If the residue so obtained exceeds the prescribed limit, continue the ignition, as previously, to constant mass.

Requirement: 34.0 – 46.0 %

Product Name: OPADRY® II COMPLETE FILM COATING SYSTEM OY-L-28900 WHITE
Product Number: OY-L-28900
Material Description: White Powder
Lot No: DT649992
Quantity Supplied: 125 KG
Ship To: Meditop Ltd. HU
Bill To: Meditop Ltd. HU
Sales Order No: CCUK1217660
Customer PO NO: 201600382
Customer Item: AL-0069-0

Compliance Statement: This Product meets all agreed upon specifications

Test	Method	Specifications		Result	Analyst
		Minimum	Maximum		
ASH, %	GLO-QC-TM-0699	21.00	31.00	25.79 %	LR
APPEARANCE	GLO-QC-TM-0733	WHITE POWDER		WHITE POWDER	LR
COLOR DIFFERENCE DE, CIE	GLO-QC-TM-0576/D3	0.0	1.0 Or Visual Match	VISUAL MATCH	LR
COLOR DIFFERENCE VISUAL	GLO-QC-TM-0576	COMPARES		COMPARES	LR
DISPERSION	GLO-QC-TM-0729	PASS		PASS	LR
IR SCAN	GLO-QC-TM-0744	COMPARES		COMPARES	LR
SPECK CHECK	GLO-QC-TM-0730	PASS		PASS	LR

Ingredients

LACTOSE MONOHYDRATE (DERIVED FROM MILK)
 HYPROMELLOSE
 TITANIUM DIOXIDE
 POLYETHYLENE GLYCOL / MACROGOL

USFDA Pigment Certification

N/A
 N/A
 N/A
 N/A

Regarding the solvents identified in the ICH Guideline on Residual Solvents Q3C and in the USP/NF General Chapter <467> Residual Solvents, only Class 2 and Class 3 solvents are likely to be present depending on the components of the specific product formulation. If present, residual Class 2 solvents are below the Option 1 limit and residual Class 3 solvents are below 0.5%. See the Colorcon Product Regulatory Datasheet for this product for detailed information on the solvents and levels that may be present in this particular product.

This Product was manufactured in a facility that is registered with the United States FDA under the provisions of the Bioterrorism Preparedness and Response Act.

The information contained in this document is proprietary to Colorcon, Inc. and may not be used or disseminated inappropriately.

Manufactured By: COLORCON
Manufacturing Site: Dartford, UK

Date Of Manufacture: 31-MAY-2016
Re-evaluation Date: 31-MAY-2018

The above analytical data has been reviewed and authenticated electronically by an authorised representative of the Quality Unit as evidence by the application of an electronic signature.

Approved By: Susan Hoare

Date: 03-JUN-2016

Electronic Signature ID: 1972668-1816981

intermediate

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ÉRKEZETT

Product Regulatory Datasheet

Section 1 - Product Information

Product : OPADRY[®] II Complete Film Coating System OY-L-28900 White

Scope : This datasheet pertains only to the product listed above.

Section 2 - Manufacturing, Packaging, And Release Site Information

Manufacturing Site

Included in Appendix 1 of this document is a list of Colorcon's dispersion manufacturing locations. This product type may be manufactured at any of these locations unless specified contractually or limited by regulations or customs restrictions. Consult the certificate of analysis for the manufacturing location of a specific product lot. See Section 5 for an explanation of the lot numbering system.

GMP Compliance Statement

All manufacturing and associated activities comply with appropriate excipient GMP requirements based on the IPEC-PQG *Good Manufacturing Practices Guide for Bulk Pharmaceutical Excipients* and USP General Chapter <1078>, *Good Manufacturing Practices For Bulk Pharmaceutical Excipients*. Each manufacturing site is designed to comply with appropriate additional local and regional regulatory requirements. For detailed GMP compliance information for a specific Colorcon manufacturing site, see the Site Quality Overview for that site.

Section 3 - Physical/Chemical Information

This dispersion product contains the following ingredients:

Ingredient	Source	CAS #	Country of Origin
LACTOSE MONOHYDRATE (DERIVED FROM MILK)	A (BOVINE)	64044-51-5	NETHERLANDS
HYPROMELLOSE	V (WOOD PULP)	9004-65-3	USA, KOREA, JAPAN, GERMANY
TITANIUM DIOXIDE	M	13463-67-7	CANADA
POLYETHYLENE GLYCOL / MACROGOL	S	25322-68-3	GERMANY

A = Animal; V = Vegetable; S = Synthetic; F = Product of Fermentation; M = Mineral; N = Natural; + = Fully Refined Oil

Maximum Elemental Iron Content: 0.0 %

Maximum Aluminum Content (from aluminum lakes): 0.0 %

Elemental iron and aluminum content are provided for reference only and should not be construed as a specification.

Section 4 - Regulatory Information

Compendial/Regulatory Compliance

Colorcon dispersion products are non-compendial excipient mixtures. These products are designed with ingredients that meet appropriate regulatory/compendial requirements for intended uses. The compendial compliances certified by Colorcon for each ingredient used in this Colorcon product is specified in the product specification. Detailed regulatory information for this Colorcon product related to your target market and the product specification can be requested from Colorcon's Global Regulatory Affairs group via our on-line request system <http://www.colorcon.com/regulatory-compliance/request-information> or by contacting your local Colorcon representative directly.

Drug Master Files

Colorcon's dispersion products are mixtures of commonly used compendial excipients and/or colorants. DMFs for these types of products are generally not needed for filing in the US or Canada. The key information needed for filing, including the quantitative formulation, ingredient grades and regulatory/compendial references is routinely provided by Colorcon directly to Sponsors under confidentiality agreements for inclusion in their regulatory filings. Placing this information directly in the filing can help streamline the drug review process. Colorcon does maintain DMFs for certain products however. More information about Colorcon's DMFs can be found at <http://www.colorcon.com/regulatory-compliance/request-information>.

TSE/BSE Information

Colorcon has reviewed our products with respect to the 1997 European Commission Directive for restricting the use of certain animal materials used in the manufacture of drug products and the CPMP/CVMP *Note for Guidance on Minimising the Risk of Transmitting Animal Spongiform Encephalopathy Agents via Human and Veterinary Medicinal Products* (EMA/410/01 rev 3, July 2011) and can make the following statements.

This Colorcon product does not contain and is not derived from specified risk materials as defined in the European Commission Regulation 1326/2001 dated 29 June 2001. This product does not contain and is not derived from any category A or B materials as defined in EMA/410/01-Rev 3, July 2011. This product does contain lactose monohydrate, which is classified as a category C material which indicates "no detected infectivity". The lactose used in Colorcon products has been certified by our suppliers as produced from milk obtained from healthy animals in the same condition as those used to collect milk for human consumption. The lactose used in the manufacture of this product has been prepared without the use of ruminant material, other than calf rennet, according to the description given in EMEA/CPMP/571/02, *Lactose Prepared Using Calf Rennet: Risk Assessment in Relationship to Bovine Spongiform Encephalopathies (BSE)*, which is based on EMEA/CPMP/BWP/337/02, *Risk and Regulatory Assessment of Lactose and Other Products Prepared Using Calf Rennet*, and states that the CPMP concludes that the BSE risk in pharmaceutical grade lactose is negligible. In cases where calf rennet is used in the production of the lactose, our suppliers have further certified that the rennet has been manufactured as required by EMA/410/01 Rev-3, July 2011. Copies of our suppliers' certifications can be provided upon request. This product does not come into contact with any other materials of animal origin during its manufacture, packaging or storage.

Allergen Information

The materials listed in the table below are included based on the current allergen legislation in the U.S., EU and Japan and other materials of interest.

This product contains ingredients derived from and/or may come in to contact with this material during manufacturing, packaging or storage.		
	Yes	No
Cereals containing gliadin gluten (wheat, rye, barley, oats, spelt and kamut)		X
Milk (lactose)/dairy products	X	
Eggs		X
Fish/crustacean/molluscs/shellfish including abalone and squid		X
Peanuts		X
Tree nuts		X
Soybeans		X
Celery		X
Mustard		X
Sesame seeds		X
Lupin		X
Buckwheat, oranges, kiwifruit, peaches, apples, yams or mushrooms		X
Gelatin		X
Azo dyes		X
Sulphur dioxide/sulphites at concentrations greater than 10 mg/kg as SO ₂		X
BHT (E321)/BHA (E320)		X
Benzoates (E210-E213)		X
p-hydroxybenzoates (parabens) (E214-E219)		X

Latex Information

Latex is not used in the manufacture of any Colorcon products and, to the best of our knowledge, none of the ingredients used in the manufacture of our products contain latex. Colorcon products do not come into contact with latex during manufacture or packaging.

GMO Information

To the best of our knowledge, this product does not contain any materials derived from genetic modification (GM). Additionally, this product has not come into contact with GM materials during its manufacture, packaging or storage.

According to the following regulations, use of this product would not generate labeling requirements for consumer products with regard to genetic modification.

- EC Regulation 1829/2003 on genetically modified feed
- EC Regulation 1830/2003 Amending EU Directive 2001/18/EC concerning the traceability and labeling of genetically modified organisms and the traceability of food and feed produced from genetically modified organisms

Aflatoxin Information

Ingredients used in Colorcon products that have the potential for aflatoxin contamination are routinely monitored by the suppliers of these ingredients for such contamination and, to the best of our knowledge, are in compliance with the requirements related to aflatoxin contamination of Commission Regulation (EC) 1881/2006 of 19 December 2006 setting maximum levels for certain contaminants in foodstuffs as well as the U.S. FDA's action levels for aflatoxins present in human food.

Dioxin Information

To the best of our knowledge, the ingredients used in the manufacture of Colorcon products meet the requirements related to dioxin contamination of Commission Regulation (EC) 1881/2006 of 19 December 2006 setting maximum levels for certain contaminants in foodstuffs.

Residual Solvent Information

Regarding the solvents identified in the ICH Guideline on Residual Solvents Q3C and in the USP/NF General Chapter <467> Residual Solvents, none of the solvents are used in or generated during the manufacture of this Colorcon product. Additionally, based on information received during the evaluation of our suppliers of the ingredients used to manufacture this product, the following Class 2 or Class 3 solvents (see table below) are likely to be present in the ingredients. Additional details of Colorcon's Supplier and Raw Material Qualification can be provided upon request.

Other than the solvents indicated here, no other solvents are used in the manufacture of this product nor are we aware of the use of any other solvents in the manufacture of the ingredients.

Ingredient Potentially Containing Solvent	Solvent	Class	Option 1 Limit	Maximum Expected Amount in Finished Colorcon Product
HYPROMELLOSE	METHANOL	2	3000 ppm	84 ppm
POLYETHYLENE GLYCOL / MACROGOL	ETHYLENE GLYCOL	2	620 ppm	50 ppm
	1,4-DIOXANE	2	380 ppm	1 ppm

Metal Catalyst Information

With regard to the EMEA CHMP Guideline on the Specification Limits for Residues of Metal Catalysts or Metal Reagents (EMEA/CHMP/SWP/4446/2000), we can confirm that no metal catalysts or metal reagents are used in the manufacture of this Colorcon product.

Additionally, according to information received during the evaluation of our suppliers, no metal catalysts or metal reagents specified in this Guideline are used in the manufacture of the ingredients used in this product.

Kosher/Halal Information

Some Colorcon dispersion products may be Kosher certified when produced at Colorcon sites evaluated by a Rabbinical service. A Kosher certificate for a specific Colorcon product produced at a specific Colorcon site can be requested via our online request system: <http://www.colorcon.com/services/reg/RequestInformation> or by contacting your local Customer Care representative.

Certain Colorcon products produced at specific Colorcon sites are Halal certified. A Halal certificate for a specific Colorcon product produced at a specific Colorcon site can be requested via our online request system <http://www.colorcon.com/services/reg/RequestInformation>.

California Proposition 65 Information

Information regarding California Proposition 65 can be found on the US Safety Data Sheet. Because Proposition 65 also concerns the content of heavy metals, we can confirm that typical heavy metal values for this product are below 10 ppm.

Irradiation/Ethylene Oxide Information

No Colorcon products themselves are subject to irradiation or treatment with ethylene oxide and, to the best of our knowledge, none of the raw materials used in the manufacture of this product have been subjected to irradiation or post-manufacture treatment with ethylene oxide.

Organic Certification

This Colorcon product is not certified organic under the United States Department of Agriculture (USDA) National Organic Program (NOP).

Other Regulatory Information

Requests for additional regulatory information about this product can be made via our on-line request system: <http://www.colorcon.com/services/reg/RequestInformation> or by contacting your local Colorcon representative directly.

Section 5 - Miscellaneous Product Information

Lot/Batch Numbering System

Colorcon's products are identified with both a product number and a lot/batch number. An auto-lot numbering system is used that is preceded by a two letter code which identifies the manufacturing location. Listed below are the lot/batch number prefixes and their corresponding manufacturing location.

Prefix	Manufacturing Location
WP	West Point, Pennsylvania, USA
PR	Humacao, Puerto Rico
DT	Dartford, Kent, England
JP	Fujinomiya-shi, Shiizuoka, Japan
GA	Goa, India
SH	Shanghai, People's Republic of China

Batch Definition

Dispersion products are produced in various batch sizes depending on the amount ordered and equipment limitations. Each batch is homogeneously blended and packaged.

Re-evaluation Period

Information regarding the re-evaluation period for this product can be found on the product specification. A product specification can be requested via our online request system: <http://www.colorcon.com/services/reg/RequestInformation> or by contacting your local Customer Care representative.

Nutritional Information

A nutritional disclosure is available for all Colorcon products. A nutritional disclosure for a specific Colorcon product can be requested via our online request system: <http://www.colorcon.com/services/reg/RequestInformation> or by contacting your local Customer Care representative.

Section 6 - Revision History

Effective Date: 10-MAR-17

Changes Since Last Revision:

This document is prepared electronically and is valid without a signature.

Section 7 - Contact Information

Questions or requests for additional information regarding the information provided in this document can be made via our online request system <http://www.colorcon.com/services/reg/RequestInformation> or by contacting your local Colorcon representative directly.

APPENDIX 1

COLORCON DISPERSION MANUFACTURING LOCATIONS

Site Prefix	Location	Telephone	Fax #
WP	Colorcon, Inc. 415 Moyer Blvd West Point PA 19486-0021, United States	215-699-7733	215-661-2605
PR	Colorcon P.R., Inc. 160 Calle Cacique Jumacao Humacao PR 00791-5606, United States	787-852-3815	787-852-0030
JP	Colorcon Japan LLC 2441-5 Nishiyama, Fujinomiya-shi, Shizuoka 419-0313, Japan	81-544-65-2711	81-544-65-2730
SH	Shanghai Colorcon Coating Technology Limited No 588 Chundong Road, Shanghai Xinzhuang Industry Zone Minhang Shanghai 201108, People's Republic of China	86-21-6198-2300	86-21-5442-2229
GA	Colorcon Asia Pvt. Limited Plot Nos. M-14 to M-18 Verna Industrial Estate, Verna - Goa 403722, India	91-832-6727373	91-832-6625870
DT	Colorcon Limited Flagship House Victory Way Crossways Dartford Kent DA2 6QD, United Kingdom	44-1322-293000	44-1322-627200

The information contained herein, to the best of our knowledge is true and accurate. Any recommendations or suggestions are made without warranty or guarantee, since the conditions of use are beyond our control. Any information contained herein is intended as a recommendation for use of our products so as not to infringe on any patent.

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