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Figure 3.2.P.4.4-v0501-injectable: 1
Certificate of Analysis for Sodium Chloride



Certificate of Analysis

Sodium Chloride, Granular, U.S.P.
Multi-Compendial
Formula NaCl

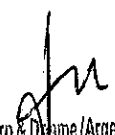
Product No. 3627

Lot No. A11338

F.W. 58.44

Release Date 03/16/2004

TEST	SPECIFICATION	RESULT
GMP Manufactured Product		
Meets U.S.P. Requirements		
Identification	Passes Test	Passes Test
Acidity or Alkalinity	Passes Test	Passes Test
Appearance of Solution	Passes Test	Passes Test
Aluminum (Al)	0.2 ppm max.	< 0.2 ppm
Arsenic (As)	1 ppm max.	< 1 ppm
Barium (Ba)	Passes Test	Passes Test
Bromides (Br)	0.010 % max.	< 0.010 %
Ferrocyanide	Passes Test	Passes Test
Heavy Metals (as Pb)	5 ppm max.	< 5 ppm
Iodides (I)	Passes Test	Passes Test
Iron (Fe)	2 ppm max.	< 2 ppm
Loss on Drying at 105°C	0.5 % max.	< 0.1 %
Magnesium and Alkaline Earth Metals	0.01 % max.	< 0.01 %
Nitrite (NO ₂)	Passes Test	Passes Test
Phosphate (PO ₄)	0.0025 % max.	< 0.0025 %
Potassium (K)	0.05 % max.	0.005 %
Sulfate (SO ₄)	0.020 % max.	< 0.020 %
Assay (NaCl) (dried basis)	99.0 – 100.5 %	99.9 %
Meets BP/Ph.Eur. Chemical Specifications		
Identification A	Passes Test	Passes Test
Identification B	Passes Test	Passes Test
Appearance of Solution	Passes Test	Passes Test
Acidity or Alkalinity	Passes Test	Passes Test
Bromide (Br)	50 ppm max.	< 50 ppm
Ferrocyanide	Passes Test	Passes Test
Iodide (I)	Passes Test	Passes Test
Nitrite (NO ₂)	Passes Test	Passes Test
Phosphate (PO ₄)	25 ppm max.	< 25 ppm
Sulfate (SO ₄)	200 ppm max.	< 200 ppm
Arsenic (As)	1 ppm max.	< 1 ppm
Barium (Ba)	Passes Test	Passes Test
Heavy Metals (as Pb)	5 ppm max.	< 5 ppm
Iron (Fe)	2 ppm max.	< 2 ppm
Magnesium and Alkaline Earth Metals	100 ppm max.	< 10 ppm
Loss on Drying at 105°C	0.5 % max.	< 0.5 %
Potassium (K)	500 ppm max.	50 ppm
Assay (NaCl) (dried basis)	99.0 – 100.5 %	99.6 %
Endotoxin Concentration, IU/g	2.5 max.	< 0.001


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Figure 3.2.P.4.4-v0501-injectable: 1 (cont.)
Certificate of Analysis for Sodium Chloride

TEST	SPECIFICATION	RESULT
Meets JP Chemical Specifications		
Assay (NaCl) (dried basis)	99.0 – 100.5 %	100.1 %
Identification	Passes Test	Passes Test
pH (1 in 10)	4.5 – 7.0	6.5
Acidity or Alkalinity	Passes Test	Passes Test
Clarity and Color of Solution	Passes Test	Passes Test
Bromide (Br)	Passes Test	Passes Test
Ferrocyanide	Passes Test	Passes Test
Iodide (I)	Passes Test	Passes Test
Iron (Fe)	Passes Test	Passes Test
Magnesium and Alkaline Earth Metals	Passes Test	Passes Test
Phosphate (PO ₄)	Passes Test	Passes Test
Sulfates (as SO ₄)	Passes Test	Passes Test
Heavy Metals (as Pb)	3 ppm max.	< 3 ppm
Barium (Ba)	Passes Test	Passes Test
Arsenic (As)	2 ppm max.	< 2 ppm
Loss on Drying	0.5 % max.	< 0.5 %

Bulk Pharmaceutical Chemical

Country of Origin: USA

Manufacturer: MORTON SALT DIVISION
MORTON INTERNATIONAL
151 SOUTH INDUSTRIAL ST.
P.O. BOX 337
RITTMAN OH 44270
(330)927-1070



Phillipsburg, NJ 9001
Paris, KY 9002
Mexico City, Mexico 9003
Dover, Holland 9004
Kuala Lumpur, Malaysia 9005

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Figure 3.2.P.4.4-v0501-injectable: 2
Certificate of Analysis for Polysorbate 80

Croda Analysis Report

Manufacture Date 02/28/03
Test Date 02/28/03

Product Name CRILLET 4 HP (POLYSORBATE 80 NF / EP / JP)
Lot Number T4H-1032
Part Number CRLLT4HP
CAS Number(s) 8005-85-4
Reference OCP-315

Product Note: THIS PRODUCT UTILIZES INGREDIENTS OF NON-ANIMAL AND NON-PEANUT ORIGIN. THIS PRODUCT IS PACKED UNDER NITROGEN TO INCREASE SHELF-LIFE. MAINTENANCE OF THE NITROGEN BLANKET AFTER CONTAINER HAS BEEN OPENED IS RECOMMENDED. THIS PRODUCT IS MANUFACTURED IN MILL HALL, PA, USA

Test	Specification	Result
NF REQUIREMENTS		
IDENTIFICATION A	Must Pass	PASSES
IDENTIFICATION B	Must Pass	PASSES
IDENTIFICATION C	Must Pass	PASSES
SPECIFIC GRAVITY (25°C)	1.06 - 1.08	1.07
VISCOSITY (25°C)	300 - 500cp	385.5 m
ACID VALUE	2.2 Max	0.7
HYDROXYL VALUE	65.0 - 80.0	74.2
SAPONIFICATION VALUE	45.0 - 65.0	48.3
WATER CONTENT	3.0% Max	0.1 %
RESIDUE ON IGNITION	0.25% Max	0.07 %
HEAVY METALS	0.001% Max	<0.001 %
ORGANIC VOLATILE IMPURITIES	Meets Requirements	PASSES
EP REQUIREMENTS		
ASSAY (Fatty Acid Fraction % Oleic Acid)	50% Min	78.4 %
2-CHLOROETHANOL	10ppm Max	NOT PRESENT ppm
ETHYLENE + DIETHYLENE GLYCOL	0.25% Max	<0.01 %


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Figure 3.2.P.4.4-v0501-injectable: 2 (cont.)
 Certificate of Analysis for Polysorbate 80

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Test	Specification	Result
EP REQUIREMENTS - continued		
IDENTIFICATION A	Must Pass	PASSES
IDENTIFICATION B	Must Pass	PASSES
IDENTIFICATION C	Must Pass	PASSES
IDENTIFICATION D	Must Pass	PASSES
IDENTIFICATION E	Must Pass	PASSES
ACID VALUE	2.0 Max	0.8
HYDROXYL VALUE	85.0 - 80.0	71.8
PEROXIDE VALUE	10.0 Max	0.7
SAPONIFICATION VALUE	45.0 - 55.0	48.8
RESIDUAL ETHYLENE OXIDE	1ppm Max	0.0 ppm
RESIDUAL 1,4-DIOXANE	10ppm Max	0.0 ppm
HEAVY METALS	10ppm Max	<10 ppm
WATER CONTENT	3.0% Max	0.1 %
SULFATED ASH	0.25% Max	0.07 %
PYROGENS	Complies	PASSES

Test	Specification	Result
JP REQUIREMENTS		
pH (5% Aqueous)	5.5 - 7.5	6.0
IDENTIFICATION (1)	Must Pass	PASSES
IDENTIFICATION (2)	Must Pass	PASSES
IDENTIFICATION (3)	Must Pass	PASSES
IDENTIFICATION (4)	Must Pass	PASSES
VISCOSITY (25°C)	345 - 445 mm ² /s	365.5 mm ² /s
SPECIFIC GRAVITY (20°C)	1.085 - 1.095	1.077
ACID VALUE	2.0 Max	0.7
SAPONIFICATION VALUE	45.0 - 55.0	48.8
IODINE VALUE	19.0 - 24.0	22.0
PURITY (1) HEAVY METALS	20ppm Max	<10 ppm
PURITY (2) ARSENIC	2ppm Max	<0.01 ppm
WATER CONTENT	3.0% Max	0.1 %
RESIDUE ON IGNITION	0.15% Max	0.07 %


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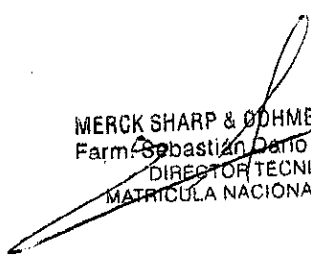

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Figure 3.2.P.4.4-v0501-injectable: 2 (cont.)
 Certificate of Analysis for Polysorbate 80

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Test	Specification	Result	
ITEMS BELOW ARE ADDITIONAL CRODA SPECIFICATIONS PLEASE NOTE THAT THESE SPECIFICATIONS WILL EXCEED COMPENDIAL SPECIFICATIONS WHERE APPLICABLE			
APPEARANCE	Yellow Liquid	PASSES	
COLOR (Gardner, 1933)	7 Max	5+	
ODOR	Slight	PASSES	
WATER CONTENT	0.2% Max	0.1	%
PEROXIDE VALUE	2.0 Max	0.4	
ORGANIC VOLATILE IMPURITIES			
Free Ethylene Oxide	1ppm Max	0.0	ppm
1,4-Dioxane	5ppm Max	0.0	ppm
Chloroform, Methylene Chloride, Trichloroethylene: Not present in manufacture			
MICROBIOLOGICAL			
Total Plate Count (opc)	100 Max	<10	
Escherichia coli	Absent	PASSES	
Pseudomonas aeruginosa	Absent	PASSES	
Salmonella	Absent	PASSES	
Staphylococcus aureus	Absent	PASSES	
Yeast & Mold (opc)	50 Max	<10	

Remarks

CRODA

Witnessed: *David Masoch* Recorded by: *[Signature]*

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Figure 3.2.P.4.4-v0501-injectable: 3
 Certificate of Analysis for L-Histidine HCL Monohydrate

KYOWA HAKKO KOGYO CO., LTD.
 1-6-1 Okinashi, Chiyoda-ku, Tokyo, JAPAN
 TEL: 3-2327-0279



CERTIFICATE OF ANALYSIS

Commodity : L-HISTIDINE HCL MONOHYDRATE
 Lot No. : 0220202
 Quantity : 100 KG
 Manufacturing date : MAR 28, 2008
 Analyzing date : MAY 24, 2008
 Release date : MAR 28, 2008

HYCLONE
 PO# 030-15734

Part# SV10026
 Qty: 1.00 kg

SPECIFICATION	ACCEPTANCE CRITERIA	RESULT
APPEARANCE	WHITE CRYSTALLINE POWDER	WHITE CRYSTALLINE POWDER
IDENTIFICATION	PASS TEST	PASS TEST
STATE OF SOLUTION (2%)	NOT LESS THAN 99.9 %	NOT LESS THAN 99.9 %
pH	4.5 to 4.8	4.8
SPECIFIC ROTATION (20°C)	18.5 to 19.5	18.7
AMMONIUM CHLORIDE	NOT MORE THAN 0.050 %	NOT MORE THAN 0.050 %
CALCIUM CHLORIDE	11.0 to 17.0 %	11.7 %
SULFATE (SO4)	NOT MORE THAN 0.050 %	NOT MORE THAN 0.050 %
IRON (Fe)	NOT MORE THAN 10 ppm	NOT MORE THAN 10 ppm
HEAVY METALS (Pb)	NOT MORE THAN 10 ppm	NOT MORE THAN 10 ppm
ARSENIC (As)	NOT MORE THAN 1 ppm	NOT MORE THAN 1 ppm
PERMANGANATE ACIDS	NOT MORE THAN 0.2% (COC. 100%)	NOT MORE THAN 0.2% (COC. 100%)
LOSS ON DRYING	NOT MORE THAN 0.20 %	0.07 %
RESIDUE ON FILTRATION	NOT MORE THAN 0.10 %	0.01 %
ENDOTOXIN	NOT MORE THAN 40 EU/10g	NOT MORE THAN 40 EU/10g
ASSAY (DRY BASIS)	99.0 to 101.0 %	99.7 %

WE HEREBY CERTIFY THAT THE COMMODITY DESCRIBED ABOVE MEETS THE REQUIREMENTS OF THE CURRENT EP AND FCC.

NO ORGANIC VOLATILE IMPURITIES AS IDENTIFIED IN THE CURRENT USP ARE INTRODUCED IN THE MANUFACTURING PROCESS OF THE ABOVE DESCRIBED COMMODITY.

The undersigned affirms that contents mentioned above are truly reported in accordance with the analysis by Quality Control Center.

M. Hayashi

Bio-Chemicals Company



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 Jose Verone
 Apod...

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Figure 3.2.P.4.4-v0501-injectable: 4
 Certificate of Analysis for Sodium Borate

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Certificate of Analysis

Sodium Borate, 10-Hydrate, N.F. (Borax)
 Multi-Compendial
 Formula $\text{Na}_2\text{B}_4\text{O}_7 \cdot 10\text{H}_2\text{O}$ F.W. 381.37

Product No. 3575

Lot No. A11479

Release Date 03/24/2004

TEST	SPECIFICATION	RESULT
GMP Manufactured Product		
Meets N.F. Requirements		
Assay	99.0 – 105.0 %	100.7 %
Identification	Passes Test	Passes Test
Carbonate and Bicarbonate	Passes Test	Passes Test
Heavy Metals (as Pb)	0.002 % max.	< 0.002 %
Endotoxin Concentration (EU/g)	2.5 max.	1.3
Organic Volatile Impurities (1)	Conforms to USP/NF	Conforms to USP/NF
(1) The manufacturer has assurance, based on knowledge of the manufacturing process and controlled handling, shipping, and storage of the material, that there is no potential for organic volatile impurities to be present as described in the current U.S.P. In this case "unnecessary testing may be avoided".		
Meets BP/Ph.Eur. Chemical Specifications		
Assay ($\text{Na}_2\text{B}_4\text{O}_7 \cdot 10\text{H}_2\text{O}$)	99.0 – 103.0 %	100.0 %
Identification A	Passes Test	Passes Test
Identification B	Passes Test	Passes Test
Identification C	Passes Test	Passes Test
Appearance of Solution	Passes Test	Passes Test
pH of 4% Solution at 25°C	9.0 – 9.6	9.2
Sulfate (SO_4)	50 ppm max.	< 50 ppm
Ammonium (NH_4)	10 ppm max.	< 10 ppm
Arsenic (As)	5 ppm max.	< 5 ppm
Calcium (Ca)	100 ppm max.	< 100 ppm
Heavy Metals (as Pb)	25 ppm max.	< 25 ppm
Meets JP Chemical Specifications		
Assay ($\text{Na}_2\text{B}_4\text{O}_7 \cdot 10\text{H}_2\text{O}$)	99.0 – 103.0 %	100.7 %
Identification	Passes Test	Passes Test
pH (1 in 20)	9.1 – 9.6	9.2
Clarity and Color of Solution	Passes Test	Passes Test
Carbonate and Bicarbonate	Passes Test	Passes Test
Heavy Metals (as Pb)	20 ppm max.	< 20 ppm
Arsenic (As)	5 ppm max.	< 5 ppm

Bulk Pharmaceutical Chemical
 COUNTRY OF ORIGIN: USA
 Manufacturer: US BORAX 300 FALCON STREET
 WILMINGTON CA 90744 310-522-5323

ISO 9000
 Phillipsburg, NJ 9001
 Paris, KY 9002
 Mexico City, Mexico 9002
 Deventer, Holland 9001
 Kuala Lumpur, Malaysia 9002

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Figure 3.2.P.4.4-v0501-injectable: 5
Certificate of Analysis for Aluminum Potassium Sulfate



Certificate of Analysis

Aluminum Potassium Sulfate, 12-Hydrate, Crystal
"BAKER ANALYZED"® A.C.S. Reagent

Formula $AlK(SO_4)_2 \cdot 12H_2O$ F.W. 474.39

Product No. 0546

Lot No. A36594

Release Date
09/09/2004

TEST	SPECIFICATION	RESULT
Exceeds A.C.S. Specifications		
Meets Reagent Specifications for testing USP/NF monographs		
Assay ($AlK(SO_4)_2 \cdot 12H_2O$) (by EDTA titrn)	98.0 – 102.0 %	100.1 %
Insoluble Matter	0.005 % max.	< 0.005 %
pH of 5% Solution at 25°C	2.0 – 4.0	3.3
Ammonium (NH_4)	0.005 % max.	< 0.005 %
Iron (Fe)	0.001 % max.	< 0.001 %
Sodium (Na)	0.02 % max.	< 0.02 %
Trace Impurities (in ppm):		
Chloride (Cl)	5 max.	< 5
Heavy Metals (as Pb)	5 max.	< 5

Country of Origin: JAPAN



Phillipsburg, NJ 9001
Paris, KY 9002
Mexico City, Mexico 9002
Deventer, Holland 9001
Kuala Lumpur, Malaysia 9002

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Figure 3.2.P.4.4-v0501-injectable: 6
 Certificate of Analysis for Sodium Hydroxide 50% (w/w) Solution



Certificate of Analysis

Sodium Hydroxide, 50%(w/w) Solution
 "BAKER ANALYZED"® Reagent
 Formula NaOH F.W. 40.00

Product No. 3727

Lot No. A12A00

Release Date 03/24/2004

TEST	SPECIFICATION	RESULT
Assay (NaOH) (by acidimetry)	50 - 52 %	50.8 %
Sodium Carbonate (Na ₂ CO ₃)	0.1 % max.	< 0.1 %
Chloride (Cl)	0.002 % max.	< 0.002 %
Sulfate (SO ₄)	0.001 % max.	< 0.001 %
Ammonium Hydroxide Precipitate	0.01 % max.	< 0.01 %
Silica (SiO ₂)	Information Only %	< 0.001 %
Heavy Metals (as Ag)	0.001 % max.	< 0.001 %
Potassium (K)	0.01 % max.	0.0007 %

Trace Impurities (in ppm):

Nitrogen Compounds (as N)	5 max.	< 5
Phosphate (PO ₄)	5 max.	< 5
Iron (Fe)	5 max.	< 5
Mercury (Hg)	Information Only	< 0.01
Nickel (Ni)	5 max.	< 0.01

IMPORTANT: Material will freeze if stored below 60°F (16°C).
 For Laboratory, Research or Manufacturing Use
 Protect from air to avoid absorption of carbon dioxide.

COUNTRY OF ORIGIN: USA



Phillipsburg, NJ 9001
 Paris, KY 9002
 Mexico City, Mexico 9002
 Dordrecht, Holland 9001
 Kuala Lumpur, Malaysia 9002

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Figure 3.2.P.4.4-v0501-injectable: 7
 Certificate of Analysis for Sodium Phosphate Dibasic

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Certificate of Analysis

Sodium Phosphate, Dibasic, Anhydrous, U.S.P.
 Multi-Compendial
 Formula Na₂HPO₄

Product No. 3804

Lot No. A11H24

F.W. 141.96

Release Date 03/22/2004

TEST	SPECIFICATION	RESULT
GMP Manufactured Product		
Meets U.S.P. Requirements		
Assay (Na ₂ HPO ₄) (dried basis)	98.0 – 100.5 %	100.4 %
Identification	Passes Test	Passes Test
Loss on Drying at 130°C	5.0 % max.	< 0.1 %
Insoluble Substances	0.4 % max.	< 0.004 %
Chloride (Cl)	0.06 % max.	< 0.06 %
Sulfate (SO ₄)	0.2 % max.	< 0.2 %
Arsenic (As)	16 ppm max.	< 3 ppm
Heavy Metals (as Pb)	0.002 % max.	< 0.001 %
Endotoxin Concentration (2.5 EU/g max.)	Passes Test	Passes Test

The following test results are derived from testing Sodium Phosphate, Dibasic, Anhydrous, U.S.P. to the JP Chemical specifications for Dibasic Sodium Phosphate, Dodecahydrate.

Identification	Passes Test	Passes Test
Assay (Na ₂ HPO ₄) (dried basis)	98.0 – 101.0 %	100.4 %
pH	9.0 – 9.4	9.1
Clarity and Color of Solution	Passes Test	Passes Test
Chloride (Cl)	0.014 % max.	< 0.014 %
Sulfate (SO ₄)	0.038 % max.	< 0.038 %
Carbonate (CO ₃)	Passes Test	Passes Test
Heavy Metals	10 ppm max.	< 10 ppm
Arsenic (As)	2 ppm max.	< 2 ppm

Meets BP/Ph. Eur. chemical specifications as Disodium Phosphate, Anhydrous

Assay (Na ₂ HPO ₄) (dried basis)	98.0 – 101.0 %	100.4 %
Appearance of Solution	Passes Test	Passes Test
Identification A	Passes Test	Passes Test
Identification B	Passes Test	Passes Test
Identification C	Passes Test	Passes Test
Identification D	Passes Test	Passes Test
Reducing Substances	Passes Test	Passes Test
Arsenic (As)	2 ppm max.	< 2 ppm
Chloride (Cl)	200 ppm max.	< 200 ppm
Heavy Metals (as Pb)	10 ppm max.	< 10 ppm
Iron (Fe)	20 ppm max.	< 20 ppm
Loss on Drying	1.0 % max.	< 0.1 %
Monosodium Phosphate	0.025 max.	< 0.025
Sulfate (SO ₄)	500 ppm max.	< 500 ppm

Bulk Pharmaceutical Chemical COUNTRY OF ORIGIN: USA
 Manufacturer: MALLINCKRODT BAKER, INC. 600 NORTH BROAD ST
 PHILLIPSBURG NJ 08865 908-859-2151



Phillipsburg, NJ 9001
 Paris, KY 9002
 Mexico City, Mexico 9002
 Dusseldorf, Holland 9001
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Figure 3.2.P.4.4-v0501-injectable: 8
 Certificate of Analysis for Sodium Phosphate Monobasic Monohydrate



Certificate of Analysis

Sodium Phosphate, Monobasic, Monohydrate, U.S.P.
 Multi-Compendial
 Formula $\text{NaH}_2\text{PO}_4 \cdot \text{H}_2\text{O}$

Product No. 3802

Lot No. A12H07

F.W. 137.99


Release Date 03/25/2004

TEST	SPECIFICATION	RESULT
GMP Manufactured Product		
Meets U.S.P. Requirements		
Appearance (White crystals or granules)	Passes Test	Passes Test
Assay (anhydrous basis)	98.0 – 103.0 %	98.1 %
Aluminum, Calcium, and Related Elements	Passes Test	Passes Test
Arsenic (As)	8 ppm max.	< 3 ppm
Chloride (Cl)	0.014 % max.	< 0.014 %
Heavy Metals (as Pb)	0.002 % max.	< 0.002 %
Identification	Passes Test	Passes Test
Insoluble Substances	0.2 % max.	< 0.01 %
Organic Volatile Impurities (1)	Conforms to USP/NF	Conforms to USP/NF
pH (1 in 20)	4.1 – 4.5	4.2
Sulfate (SO_4)	0.15 % max.	< 0.15 %
Water (H_2O)	10.0 – 15.0 %	14.2 %

(1) The manufacturer has assurance, based on knowledge of the manufacturing process and controlled handling, shipping, and storage of the material, that there is no potential for organic volatile impurities to be present as described in the current U.S.P. in this case "unnecessary testing may be avoided".

The following test results are derived from testing Sodium Phosphate, Monobasic, Monohydrate, U.S.P. to the EP Chemical specifications for Sodium Dihydrogen Phosphate Dihydrate.

Identification A	Passes Test	Passes Test
Identification B	Passes Test	Passes Test
Identification C	Passes Test	Passes Test
Assay (anhydrous basis)	98.0 – 100.5 %	99.7 %
Chloride (Cl)	200 ppm max.	< 200 ppm
Sulfate (SO_4)	300 ppm max.	< 300 ppm
Arsenic (As)	2 ppm max.	< 2 ppm
Reducing Substances	Passes Test	Passes Test
Heavy Metals (as Pb)	10 ppm max.	< 10 ppm
Endotoxin Concentration (EU/g)	5 max.	1
Iron (Fe)	10 ppm max.	< 10 ppm
Appearance of Solution	Passes Test	Passes Test
pH	4.2 – 4.5	4.2


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Figure 3.2.P.4.4-v0501-injectable: 8 (cont.)
Certificate of Analysis for Sodium Phosphate Monobasic Monohydrate

TEST	SPECIFICATION	RESULT
Meets BP Chemical Specifications		
Identification A	Passes Test	Passes Test
Identification B	Passes Test	Passes Test
Identification C	Passes Test	Passes Test
Identification D	Passes Test	Passes Test
Acidity	4.2 – 4.5	4.2
Clarity and Color of Solution	Passes Test	Passes Test
Arsenic (As)	2 ppm max.	< 2 ppm
Heavy Metals (as Pb)	10 ppm max.	< 10 ppm
Iron (Fe)	10 ppm max.	< 10 ppm
Chloride (Cl)	200 ppm max.	< 200 ppm
Sulfate (SO ₄)	300 ppm max.	< 300 ppm
Reducing Substances	Passes Test	Passes Test
Loss on Drying at 130°C	11.5 – 14.5 %	13.6 %
Assay (anhydrous basis)	98.0 – 100.5 %	99.7 %
Bulk Pharmaceutical Chemical		

COUNTRY OF ORIGIN: USA

Manufacturer: MALLINCKRODT BAKER, INC.
600 NORTH BROAD ST.
PHILLIPSBURG NJ 08866
908-859-2151



Phillipsburg, NJ 9001
 Paris, KY 9002
 Mexico City, Mexico 9002
 Deventer, Holland 9001
 Kuala Lumpur, Malaysia 9002

Marcy M. Matlosz
 Marcy M. Matlosz
 Director of QA & Regulatory Affairs

J.T. Baker – A Division of Mallinckrodt Baker, Inc. – 222 Red School Lane – Phillipsburg, NJ 08865
 Phone: 908-859-2151 – Fax: 908-859-6905

JN
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3) CONTROL DE CALIDAD-METODOS CONTROL PRINCIPIO ACTIVO

3.1 Especificaciones

Los ensayos analíticos que se presentan en la Tabla 13 se realizan para confirmar la calidad de la suspensión celular como producto intermedio del proceso, y del granel de producto monovalente adsorbido (PMAG), del principio activo. Tres de los ensayos para liberación del granel de producto monovalente adsorbido (PMAG) se hacen en muestras del producto acuoso final (PAF): la concentración total de proteínas, el porcentaje de pureza y el porcentaje de monómero intacto.

Tabla 13:
 Ensayos de liberación y criterios de aceptación para la sustancia farmacéutica contra el VPH

Ensayo	Muestra estudiada	Criterios de aceptación	Procedimiento
Liberación de la suspensión celular			
Pureza de los cultivos	Cultivo celular final	Sin crecimiento aparte de <i>Saccharomyces cerevisiae</i>	PC 9110.775
Identidad de el inóculo huésped		Debe identificarse como <i>S. cerevisiae</i> CANADE 3C-5	PC 9110.770
Liberación del granel de producto monovalente adsorbido			
Concentración de proteínas	PAF ^a	≥640 µg/ml, para todos los tipos	PC 9110.768
Porcentaje de pureza	PAF	≥95% para los tipos 6, 11 y 16 ≥90% para el tipo 18	PC 9110.767
Porcentaje de monómero intacto	PAF	≥80% para los tipos 6, 11 y 16 ≥75% para el tipo 18	PC 9110.767
Potencia relativa <i>in vitro</i>	PMAG ^b	≥232 unidades/ml para los tipos 6, 11 y 16 ≥189 unidades/ml para el tipo 18	PC 9110.769
Identidad	PMAG	Cumple	PC 9110.769
Esterilidad ^c	PMAG	Sin crecimiento, para todos los tipos	PC 9110.001
Endotoxina ^d	PMAG	≤10 UE/ml, para todos los tipos	PC 9110.678
Aluminio	PMAG	0.35-0.62 mg/ml, para todos los tipos	PC 9110.699
pH	PMAG	5.7-6.7, para todos los tipos	PEO 224-388

PC: procedimiento de control; PEO: procedimiento estándar de operación.

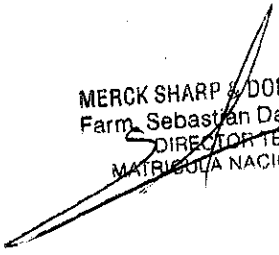
^a PAF: producto acuoso final

^b PMAG: granel de producto monovalente adsorbido

^c Esta ensayo cumple con la Farmacopea de Estados Unidos (USP), Sección <71>, la Farmacopea Europea (Ph. Eur.), Sección 2.6.1, y las normas del Código de Regulaciones Federales de Estados Unidos (21 CFR 610.12).

^d Esta ensayo cumple con la USP, Sección <85>, y la Ph. Eur., Sección 2.6.14.


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