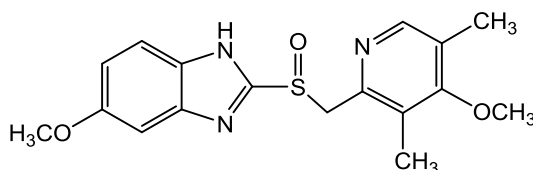


Certificate of Analysis

ISO 17034
ANAB Cert# AR-1470

ISO/IEC 17025
ANAB Cert# AT-1467

OMEPRAZOLE CERTIFIED REFERENCE MATERIAL



CERTIFIED PURITY: 99.6 %, $U_{\text{crm}} = \pm 0.2 \%$ $k = 2.1$
(Mass Balance/as is basis)

NOMINAL PACKAGE SIZE: 1g

CATALOG #: PHR1059

LOT #: LRAC0716

CERTIFICATE VERSION: LRAC0716.1

ISSUE DATE: 15 January 2019

*Note: Certificates may be updated due to Pharmacopeial Lot changes or the availability of new data.
Check our website at: www.sigma-aldrich.com for the most current version.*

CRM EXPIRATION: 31 December 2023 (Proper Storage and Handling Required).

RECEIPT DATE: _____

Note: this space is provided for convenience only and its use is not required.

STORAGE: Store in a Refrigerator, keep container tightly closed. Protect from moisture, Keep in a wash thoroughly after handling. Avoid breathing dust. Attachment of a 20 mm aluminum crimp seal recommended for unused portions.

CHEMICAL FORMULA: C₁₇H₁₉N₃O₃S

MW: 345.4

PHYSICAL DESCRIPTION: White powder in amber vial

CAS #: 73590-58-6

HAZARDS: Read Safety Data Sheet before using. All chemical reference materials should be considered potentially hazardous and should be used only by qualified laboratory personnel.

INSTRUCTIONS FOR USE: Do not dry, use on the as is basis. The internal pressure of the container may be slightly different from the atmospheric pressure at the user's location. Open slowly and carefully to avoid dispersion of the material. This material is intended for Laboratory Use only. Not for drug, household or other uses.

TRACEABILITY ASSAY

Comparative assay demonstrates direct traceability to Pharmacopeial Standards

ASSAY vs. USP REFERENCE STANDARD (as is basis)

ASSAY VALUE

100.3 %

vs. USP LOT

R065N0

Labeled Content = 0.999 mg/mg

ASSAY vs. EP CRS (as is basis)

ASSAY VALUE

100.9 %

vs. EP BATCH

5.0

Labeled Content = 99.9 %

ASSAY vs. BP CRS (as is basis)

ASSAY VALUE

100.0 %

vs. BP BATCH

3840

Labeled Content = 99.6 %

METHOD: HPLC (ref: Omeprazole, Current Compendial Monographs)

Column: Ascentis Express C8, 4.6 x 100 mm, 2.7µm

Mobile Phase A: 0.18g/L NaH₂PO₄ + 1.118 g/L Na₂HPO₄ in Water (pH: 7.5)

Mobile Phase B: Acetonitrile

Mobile Phase Ratio: 75:25

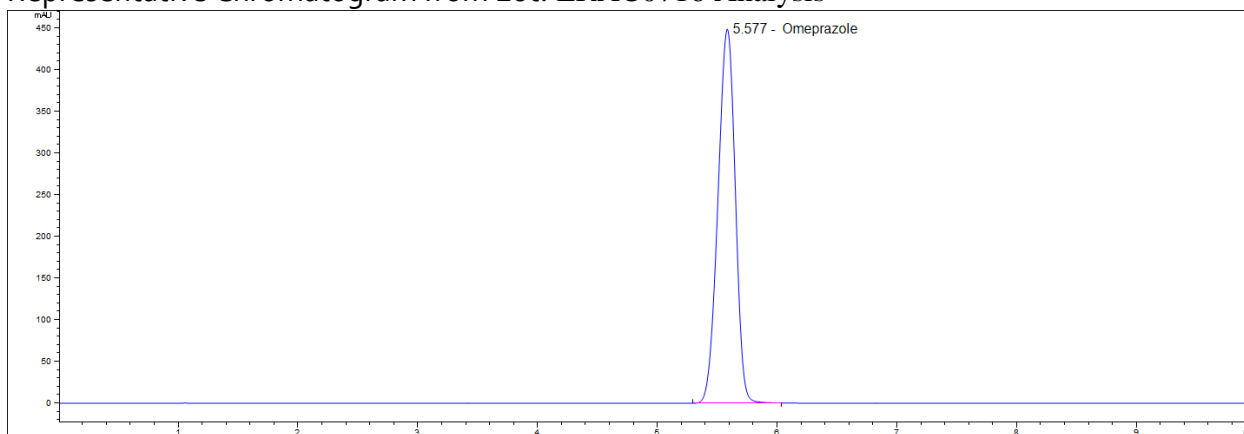
Flow: 1.0 mL/min

Column Temperature: 30 °C

Injection: 20 µL

Detector: 280 nm

Representative Chromatogram from Lot: LRAC0716 Analysis



PURITY DETERMINATION BY MASS BALANCE

CHROMATOGRAPHIC IMPURITY ANALYSIS

METHOD: HPLC (ref: Omeprazole, Current Compendial Monographs)

Column: Ascentis Express C8, 4.6 x 100 mm, 2.7 μ m

Mobile Phase A: 0.18g/L NaH_2PO_4 + 1.118 g/L Na_2HPO_4 in Water (pH: 7.0)

Mobile Phase B: Acetonitrile

Gradient:

Time (min)	% A	% B
0-2.6	75	25
2.6-5	75-50	25-50
5-9.7	50	50
9.7-9.8	50-75	50-25
9.8-16	75	25

Flow Rate: 1.0 mL/min

Column Temperature: 35 $^{\circ}\text{C}$

Injection: 40 μL

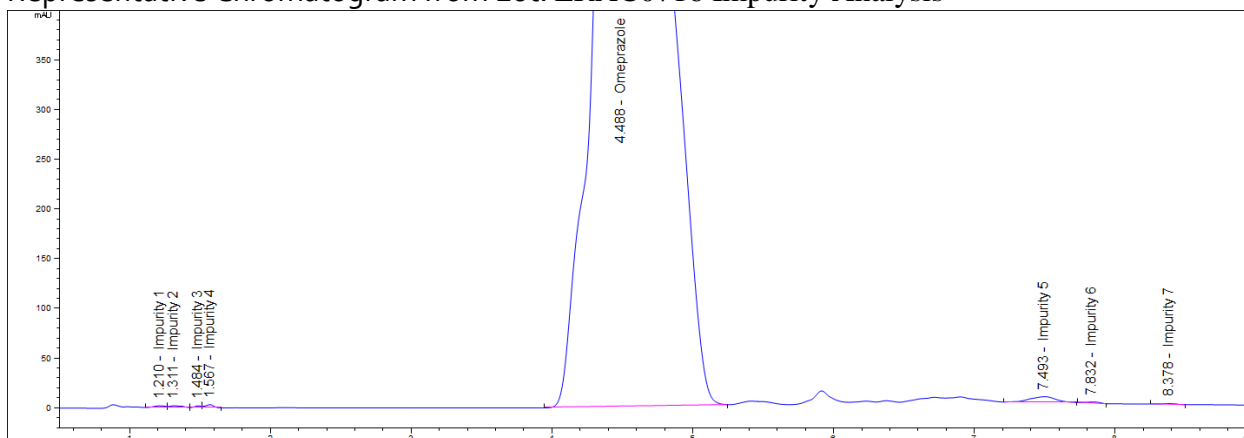
Detector: 264 nm

Impurities Detected:

Impurity 1:	0.030%	Impurity 2:	0.031%
Impurity 3:	0.017%	Impurity 4:	0.043%
Impurity 5:	0.205%	Impurity 6:	0.039%
Impurity 7:	0.047%		

Total Impurities: **0.413%**

Representative Chromatogram from Lot: LRAC0716 Impurity Analysis



RESIDUAL SOLVENTS

Method: GC-MS Headspace (ref.: Adapted from Residual Solvents USP <467>)

Column: SPB-624, 30 m x 0.25 mm, 1.4 mm

Carrier gas: He

Flow: 1.2 mL/min

Split Ratio: 1:5

Injection/Temperature: 1 mL/220 °C

Temperature Program: 40 °C for 5 min, 8 °C/min to 200 °C, hold 5 min

Solvents Detected: **None**

LOSS ON DRYING/VOLATILES

Method: 60 °C under vacuum for 4 hours (ref.: Current Compendial Monographs)

Mean of three samples, Loss = **0.027 %**

RESIDUE ANALYSIS

Method: Sulfated Ash (ref.: Current Compendial Monographs)

Sample Size: ~ 90 mg

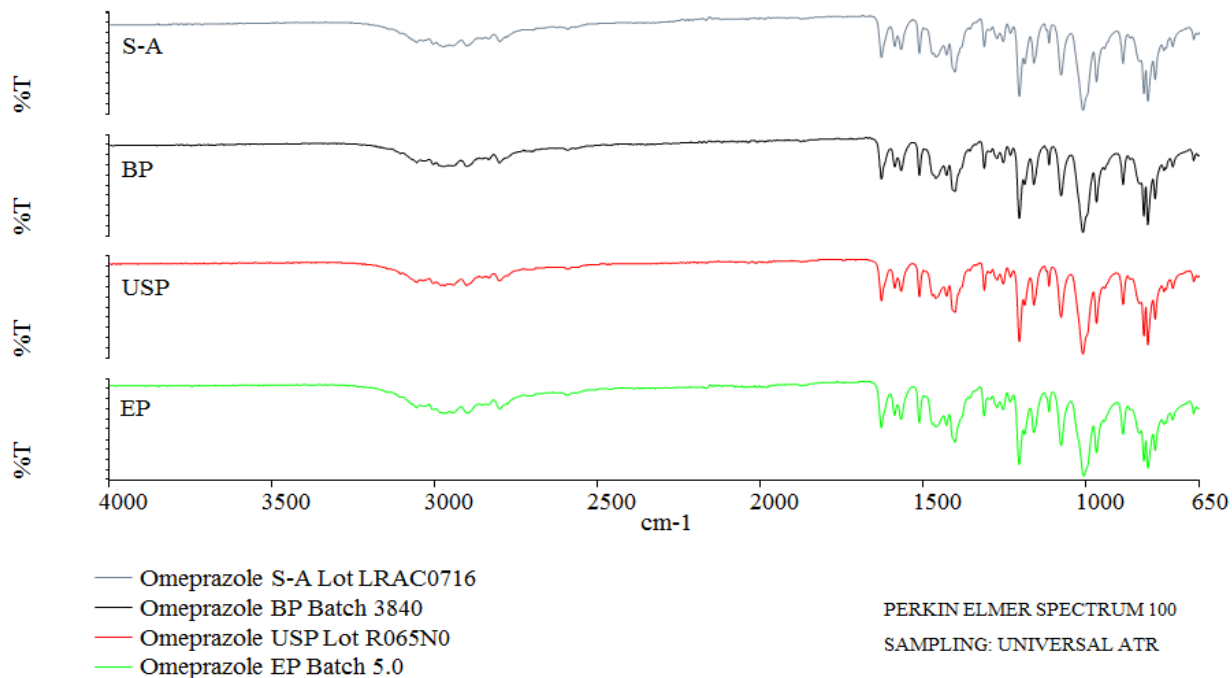
Mean of three determinations, Residue = **0.0085 %**

CERTIFIED PURITY BY MASS BALANCE [100% - Impurities (normalized)]

99.6 % $U_{\text{crm}} = \pm 0.2 \%$, $k = 2.1$
(as is basis)

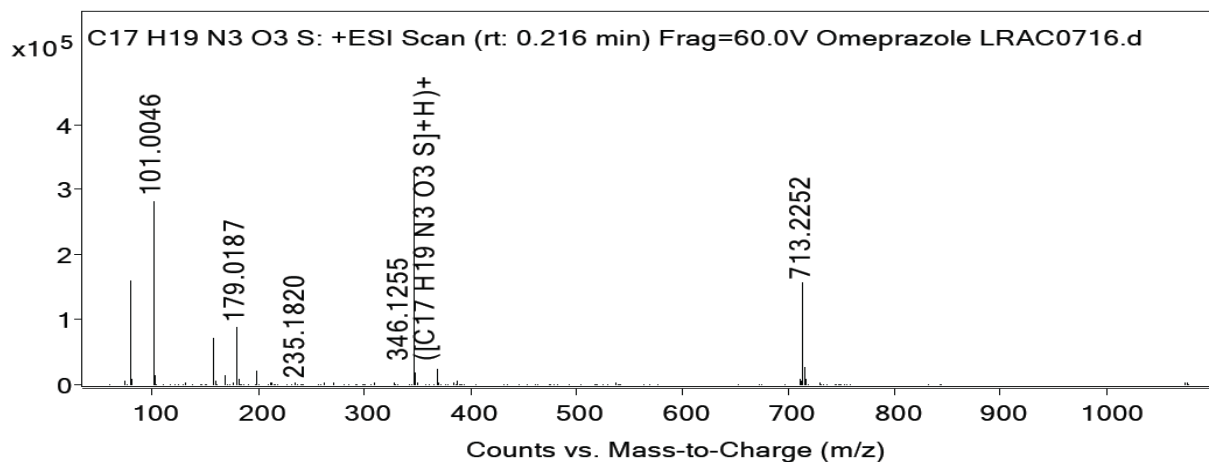
IDENTIFICATION TESTS

INFRARED SPECTROPHOTOMETRY (Comparative identification analysis demonstrates direct traceability to Pharmacopeial standards)



MASS SPECTRUM

Method: HR-QTOF; 4.0 kV ESI+; temperature: 325 °C



Theoretical value: 346.1225 m/z

The signal of the MS spectrum is consistent with the theoretical value and its interpretation is consistent with the structural formula.

HOMOGENEITY ASSESSMENT

Homogeneity was assessed in accordance with ISO Guide 35. Completed units were sampled using a random stratified sampling protocol. The results of chemical analysis were then compared by Single Factor Analysis of Variance (ANOVA). The uncertainty due to homogeneity was derived from the ANOVA. Heterogeneity was not detected under the conditions of the ANOVA.

Analytical Method: HPLC

Sample size: ~ 20 mg

UNCERTAINTY STATEMENT

Uncertainty values in this document are expressed as Expanded Uncertainty (U_{crm}) corresponding to the 95% confidence interval. U_{crm} is derived from the combined standard uncertainty multiplied by the coverage factor k , which is obtained from a t -distribution and degrees of freedom. The components of combined standard uncertainty include the uncertainties due to characterization, homogeneity, long term stability, and short term stability (transport). The components due to stability are generally considered to be negligible unless otherwise indicated by stability studies.

STABILITY ASSESSMENT

Significance of the stability assessment will be demonstrated if the analytical result of the study and the range of values represented by the Expanded Uncertainty do not overlap the result of the original assay and the range of its values represented by the Expanded Uncertainty. The method employed will usually be the same method used to characterize the assay value in the initial evaluation.

Long Term Stability Evaluation - An assessment, or re-test, versus a Compendial Reference Standard may be scheduled, within the 3 year anniversary date of a release of a Secondary Standard. The re-test interval will be determined on a case-by-case basis.

Short Term Stability Study - It is useful to assess stability under reasonably anticipated, short term transport conditions by simulating exposure of the product to humidity and temperature stress. This type of study is conducted under controlled conditions of elevated temperature and humidity.



QC Manager



Head Quality Assurance

APPENDIX

Original Release Date: 15 January 2019