G12-3

Certificate of Analysis

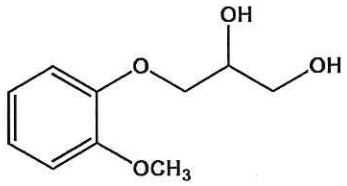
ISO GUIDE 34
ANAB Cert# AR-1470

ISO/IEC 17025
ANAB Cert# AT-1467

G12-3

GUAIFENESIN

CERTIFIED REFERENCE MATERIAL



CERTIFIED PURITY:

99.96%, U_{crm} = ±0.2% k = 2.1(Mass Balance/dried basis)

99.96%, U_{crm} = ±0.2% k = 2.1(Mass Balance/as is basis)

NOMINAL PACKAGE SIZE: 1g

CATALOG #: PHR1027 **LOT #:** LRAB3706

CERTIFICATE VERSION: LRAB3706.2 **ISSUE DATE:** 31 March 2018

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 2021 (Proper Storage and Handling Required).

RECEIPT DATE: _____

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

STORAGE: Store at Room Temperature, keep container tightly closed. Attachment of a 20 mm aluminum crimp seal recommended for unused portions.

CHEMICAL FORMULA: $C_{10}H_{14}O_4$ **MW:** 198.22

PHYSICAL DESCRIPTION: White powder in amber vial **CAS #:** 93-14-1

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.

NATIONAL QUALITY CONTROL LABORATORY
RECEIVED
03 SEP 2018
TEL: 2726963 / 3544525/30
FAX: 2710073
P. O. Box 29720 - 00625 NAIROBI

SIGMA-ALDRICH®

INSTRUCTIONS FOR USE: For USP application, dry at 60°C under vacuum not below 10mmHg to constant weight prior to use. For EP application, do not dry, use on the as is basis. Hygroscopic, keep container tightly closed. 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 (dried basis)

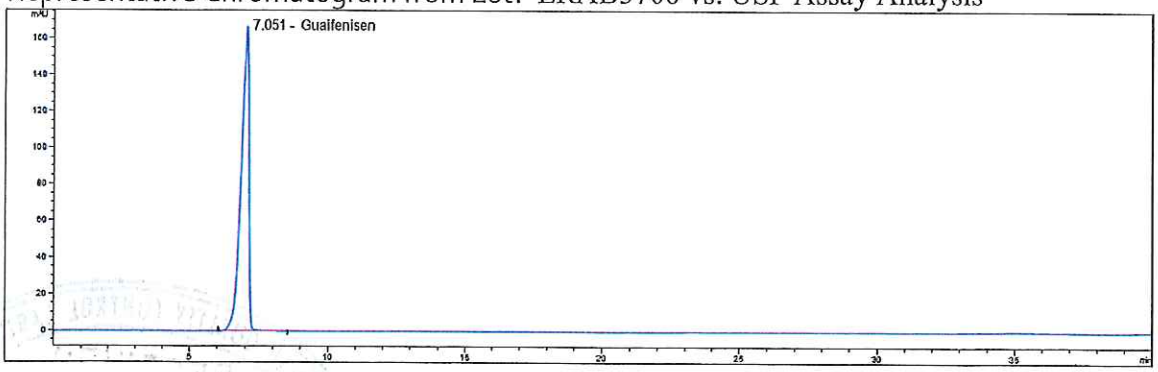
ASSAY VALUE	vs. USP LOT
99.1%	**J0G257**
	Labeled Content = 0.994 mg/mg

METHOD: HPLC (ref.: Guaifenesin, Current Compendial Monographs)
Column: Supelcosil LC-18-DB, 4.6 × 250mm, 5µm
Mobile Phase A: 1% Acetic acid in water,
Mobile Phase B: Acetonitrile
Gradient:

Time (min)	% A	% B
0-32	80→50	20→50
32-35	50→80	50→20

Flow Rate: 1.0 mL/min
Column Temperature: 30 °C
Injection: 10 µL
Detector: 276 nm

Representative Chromatogram from Lot: LRAB3706 vs. USP Assay Analysis



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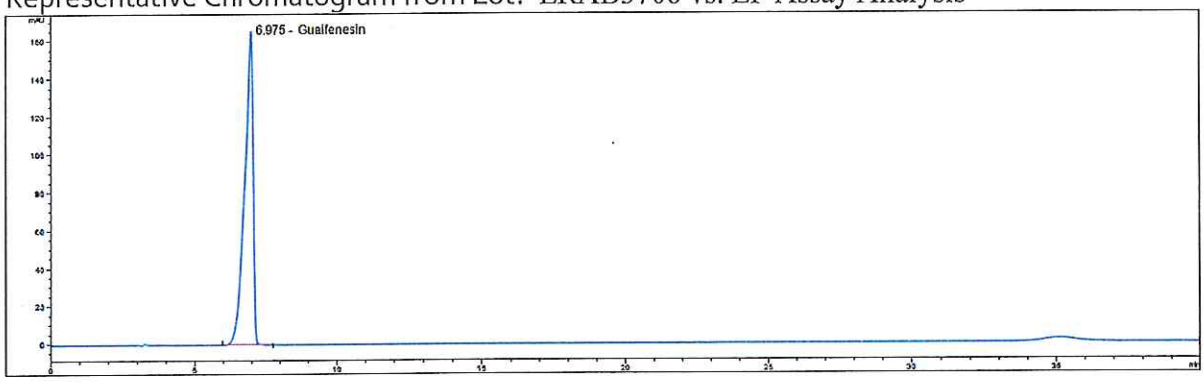
ASSAY vs. EP CRS (as is basis)

ASSAY VALUE	vs. EP BATCH
99.99%	**3.0**
	Labeled Content = 100.0 %

METHOD: HPLC (ref.: Guaifenesin, Current Compendial Monographs)

See USP Assay

Representative Chromatogram from Lot: LRAB3706 vs. EP Assay Analysis



PURITY DETERMINATION BY MASS BALANCE

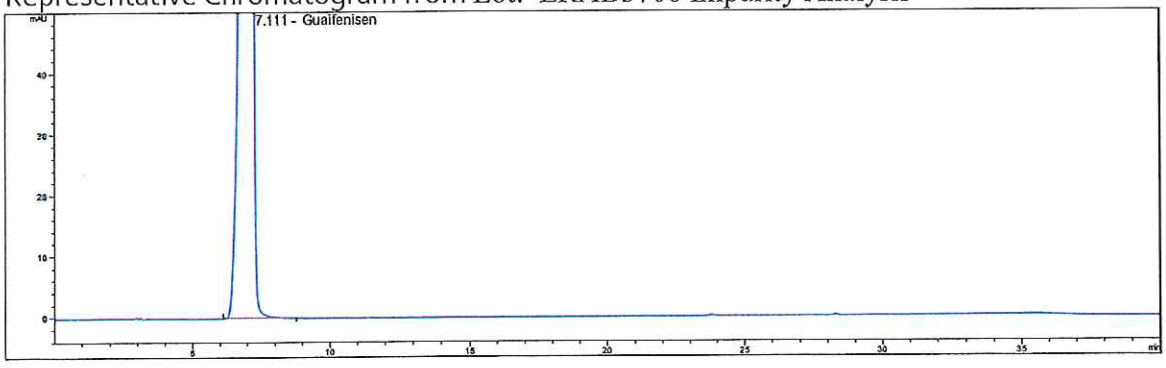
CHROMATOGRAPHIC IMPURITY ANALYSIS
METHOD: HPLC (ref.: Guaifenesin, Current Compendial Monographs)

See Assay

Impurities Detected:

None Detected

Representative Chromatogram from Lot: LRAB3706 Impurity Analysis



RESIDUAL SOLVENTS

Method: GC-MS Headspace (ref.: Adapted from Residual Solvents USP <467>)
Column: SPB-624
Carrier gas: He
Flow: 1.2 mL/min
Split Ratio: 1:5
Injection/Temperature: 1 mL/250 °C
Temperature Program: 40 °C for 8 min, 8 °C/min to 200 °C, hold 8 min

Solvents Detected: None

LOSS ON DRYING/VOLATILES

Method: Dry at 65°C to constant weight under vacuum of 10 mm (Hg) (ref.: Current Compendial Monographs)
Mean of three measurements, Loss = **0.0%**

RESIDUE ANALYSIS

Method: Sulfated Ash) (ref.: Current Compendial Monographs)
Sample Size: ~100 mg
Mean of three measurements, Residue = **0.037%**

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

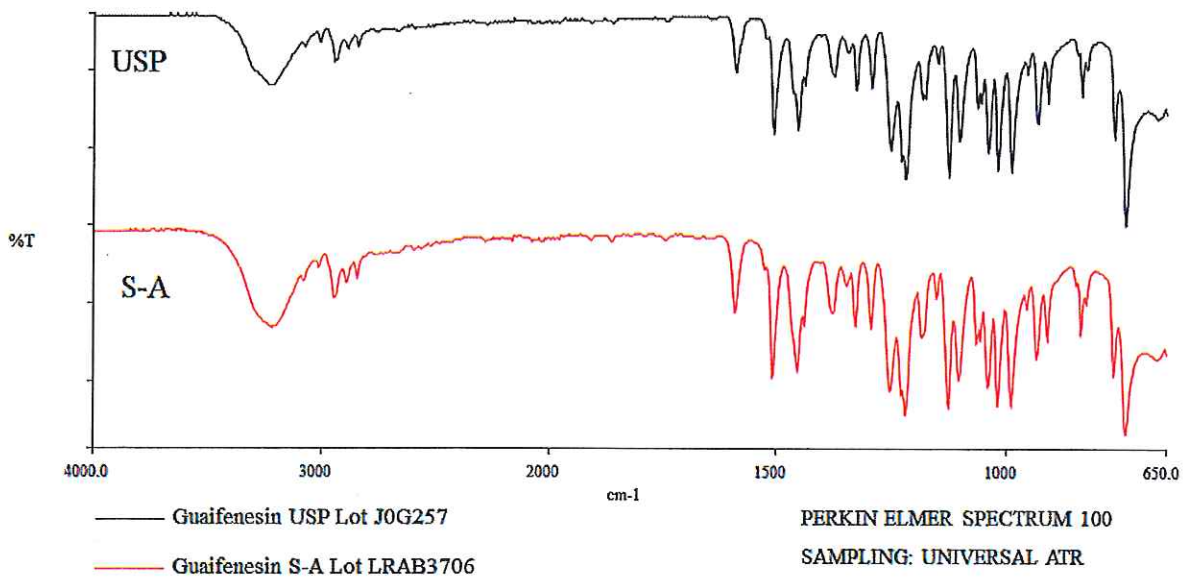
99.96% U_{crm} = ±0.2%, k = 2.1 (dried basis)
99.96% U_{crm} = ±0.2%, k = 2.1 (as is basis)

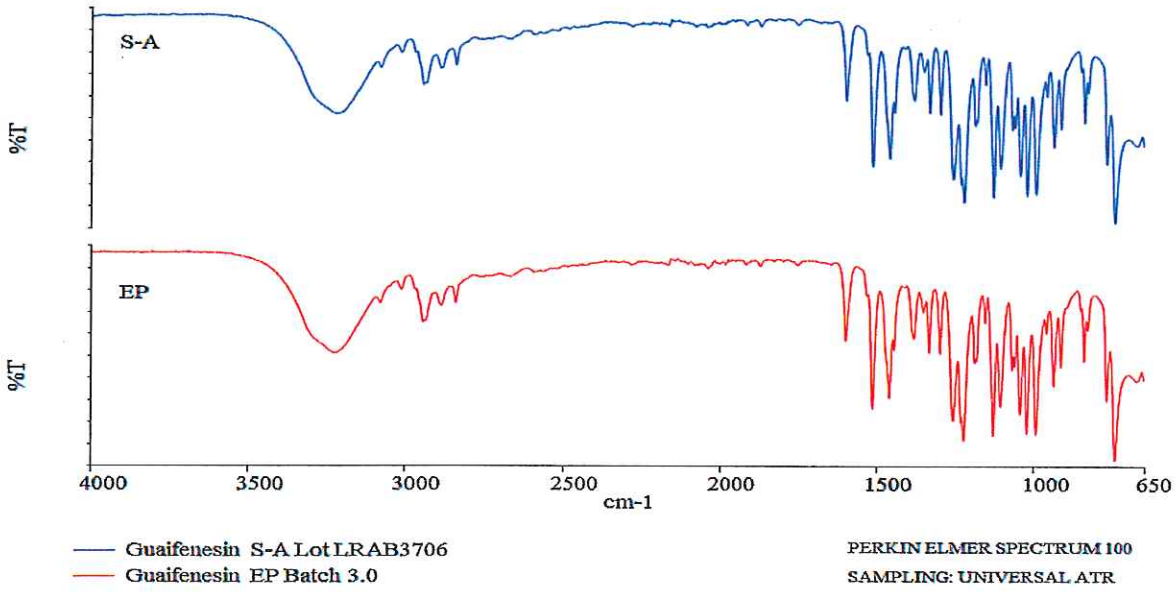
IDENTIFICATION TESTS

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

K12-3

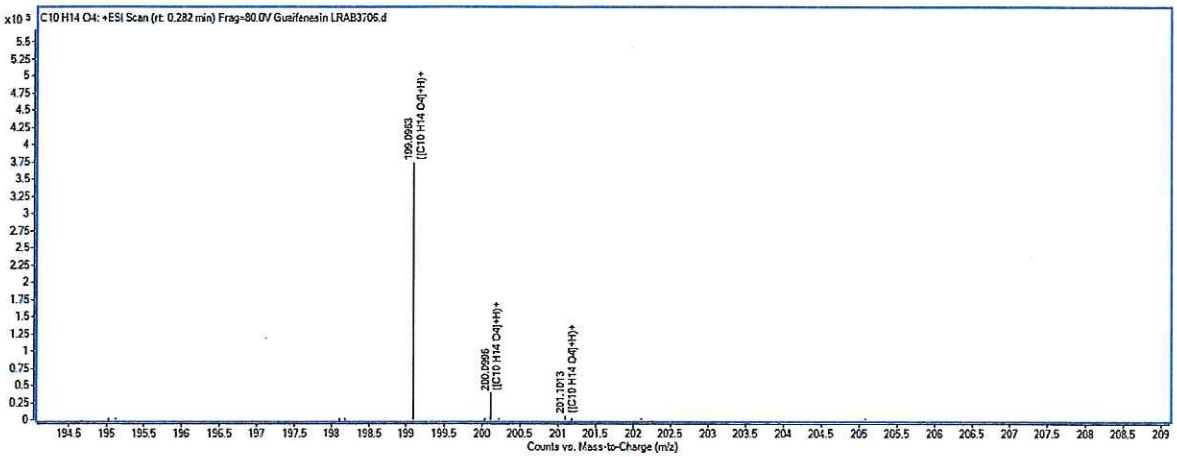
Ga 2-3





MASS SPECTRUM

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

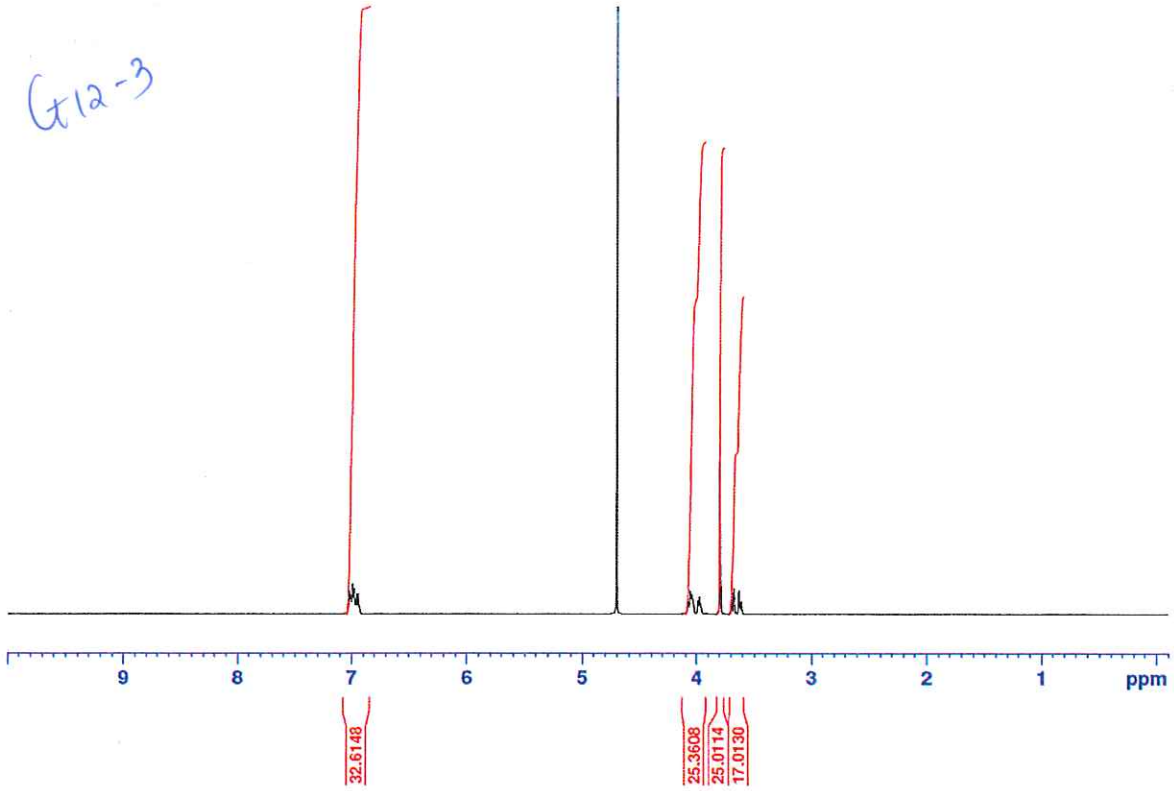


Theoretical value: 199.0970 m/z

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

^{1}H NMR (Data provided by an external laboratory; not in scope of accreditation)

LRAB3706
Guaifenesin in D2O



Consistent with structure

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MELTING RANGE

Specification: 79-83°C (EP)
Mettler Toledo FP900 Thermosystem with FP81 Measuring Cell
Mean of three measurements = **80.0–82.4°C**

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: ~25 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

QA Supervisor

APPENDIX

Original Release Date: 31 May 2017
Requalification Test Date: 31 March 2018

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Manufactured and certified by Sigma-Aldrich RTC, Inc.
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(Phone): 1-307-742-5452 (Fax): 1-855-831-9212
email: RTCTechGroup@sial.com

ANAB ACCREDITED ISO/IEC 17025 TESTING LABORATORY

ANAB ACCREDITED ISO GUIDE 34 REFERENCE MATERIAL PRODUCER