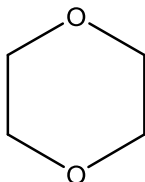


Certificate of Analysis

ISO GUIDE 34
ACCLASS Cert# AR-1470

ISO/IEC 17025
ACCLASS Cert# AT-1467

1,4-DIOXANE CERTIFIED REFERENCE MATERIAL



CERTIFIED PURITY: 99.9%, $U_{\text{crm}} = \pm 0.4\%$ $k = 2$
(Mass Balance/as is basis)

NOMINAL PACKAGE SIZE: 3X1.2mL

CATALOG #: PHR1549

LOT #: LRAA4465

CERTIFICATE VERSION: LRAA4465.1

ISSUE DATE: 13 June 2014

*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 2018 (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. Dispose of unused portions after opening.

CHEMICAL FORMULA: C₄H₈O₂

MW: 88.1

PHYSICAL DESCRIPTION: Clear liquid in amber ampule

CAS #: 123-91-1

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.

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 R&D use only. Not for drug, household or other uses.

TRACEABILITY ASSAY

Comparative assay demonstrates direct traceability to Pharmacopeial Standards

METHOD: GC

Column: SPB-624, 30m x 0.53mm x 3.0 μ m

Carrier gas: H₂

Flow: 2.5mL/min

Split Ratio: 5:1

Injection/Temperature: 1 μ L/250 $^{\circ}$ C

Temperature Program: 40 $^{\circ}$ C for 20min, 10 $^{\circ}$ C/min to 200 $^{\circ}$ C

Detector/Temperature: FID/230 $^{\circ}$ C

Internal Standard: Tetrahydrofuran

ASSAY vs. USP REFERENCE STANDARD (as is basis)

ASSAY VALUE

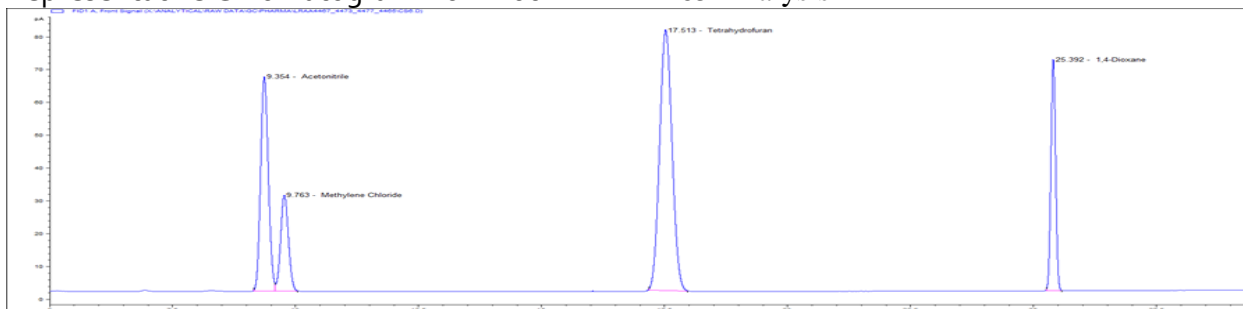
99.6%

vs. USP LOT

G0I251

Labeled Content = 1.88mg/mL

Representative Chromatogram from Lot: LRAA4465 Analysis



PURITY DETERMINATION BY MASS BALANCE

CHROMATOGRAPHIC IMPURITY ANALYSIS

METHOD: GC Headspace

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

Carrier gas: He

Flow: 1.2mL/min

Split Ratio: 20:1

Injection/Temperature: 1mL/220 $^{\circ}$ C

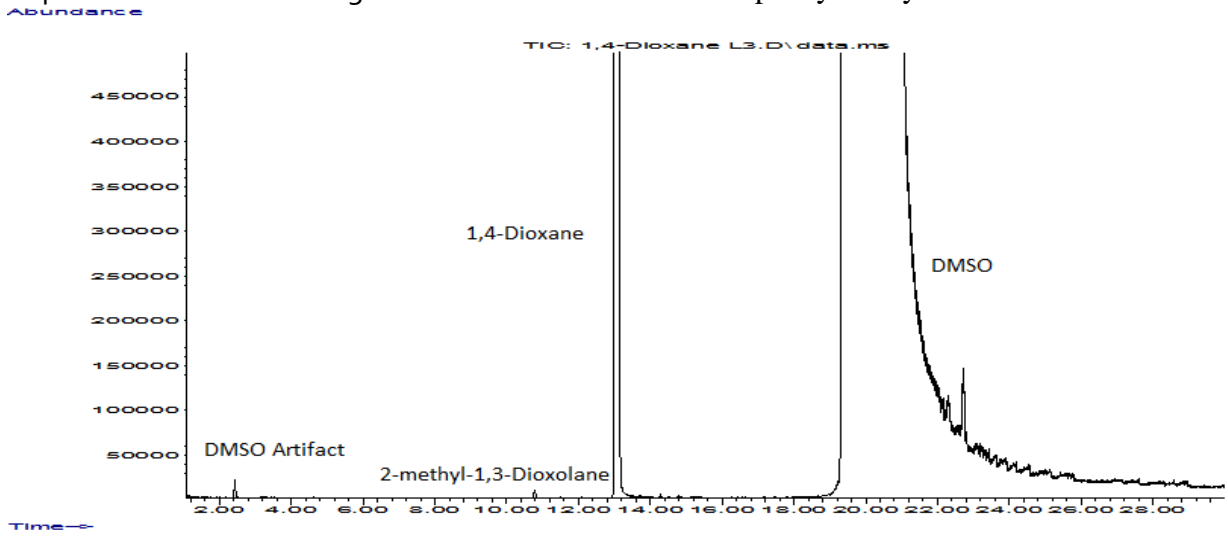
Temperature Program: 40 $^{\circ}$ C for 2min, 8 $^{\circ}$ C/min to 200 $^{\circ}$ C, hold 5min

Detector/Temperature: MS/230 $^{\circ}$ C

Impurities Detected:

2-Methyl-1,3-Dioxolane: **0.1%**

Representative Chromatogram from Lot: LRAA4465 Impurity Analysis



WATER DETERMINATION

Method: Karl Fisher titration

Mean of three measurements, Water Content = **0.02%**

RESIDUE ANALYSIS

Method: Evaporation

Sample Size: ~1g

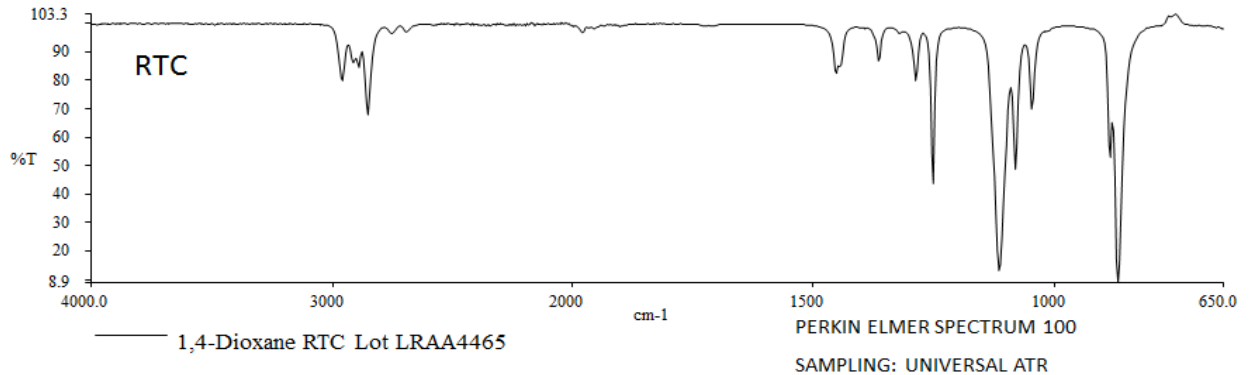
Mean of three measurements, Residue = **0.01%**

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

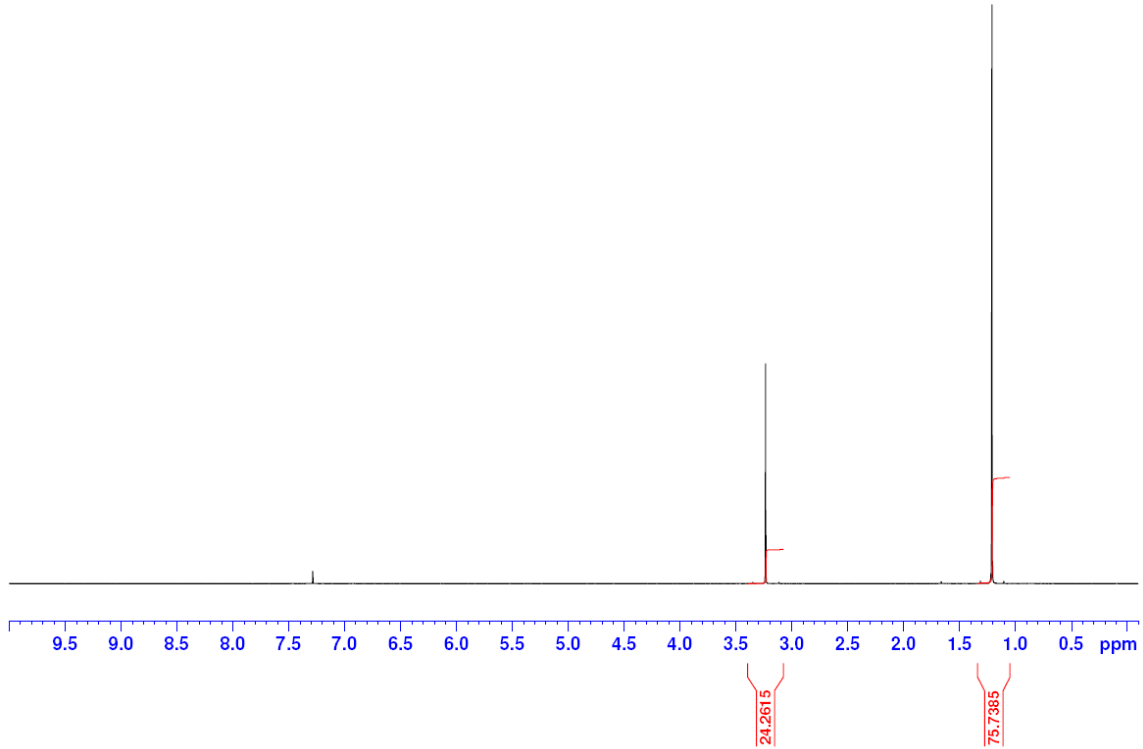
99.9% $U_{\text{crm}} = \pm 0.4\%$, $k = 2$
(as is basis)

IDENTIFICATION TESTS

INFRARED SPECTROPHOTOMETRY (For Information Purposes)



¹H NMR (Data provided by an external laboratory; not in scope of accreditation)
RTC LRAA4476 Tert-Butylmethylether



Consistent with structure

ELEMENTAL ANALYSIS (Data provided by an external laboratory; not in scope of accreditation)

Exeter Analytical 440 Elemental Analyzer

Combustion method

%	Theoretical	Result 1	Result 2	Mean
C	54.53	54.67	54.65	54.66
H	9.15	9.44	9.25	9.35

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: GC

Sample size: ~100mg

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.



Operations Manager



QA Supervisor

APPENDIX

Original Release Date: 13 June 2014