Temperature:

	Time (min)	Temperature (°C)
Column	0 - 39	60 - 290
	39 - 50	290
Injection port		275
Detector		300

Detection: flame ionisation.

Injection: 1 µl.

Relative retentions with reference to squalane (retention time = about 41 min): internal standard = about 0.2; methyl erucate = about 0.9; cyclosqualane = 1.05.

System suitability: reference solution (b):

– *resolution*: minimum 5 between the peaks due to methyl erucate and squalane.

Calculate the percentage content of squalane from the areas of the peaks and the declared content of *squalane CRS*.

LABELLING

The label states the origin of squalane (vegetable or animal).

01/2005:1438

St. JOHN'S WORT

Hyperici herba

DEFINITION

St. John's wort consists of the whole or cut, dried flowering tops of *Hypericum perforatum* L., harvested during flowering time. It contains not less than 0.08 per cent of total hypericins expressed as hypericin ($C_{30}H_{16}O_8$; M_r 504.4), calculated with reference to the dried drug.

CHARACTERS

It has the macroscopic and microscopic characters described under identification tests A and B.

IDENTIFICATION

A. The branched and bare stem shows 2 more-or-less prominent longitudinal ridges. The leaves are opposite, sessile, exstipulate, oblong-oval and 15 mm to 30 mm long; present on the leaf margins are glands which appear as black dots and over all the surface of the leaves many small, strongly translucent excretory glands which are visible in transmitted light. The flowers are regular and form corymbose clusters at the apex of the stem. They have 5 green, acute sepals, with black secretory glands on the margins; 5 orange-yellow petals, also with black secretory glands on the margins; 3 staminal blades, each divided into many orange-yellow stamens and 3 carpels surmounted by red styles.

B. Reduce to a powder (355). The powder is greenish-yellow. Examine under a microscope using *chloral hydrate solution R*. The powder shows the following diagnostic characters: fragments of polygonal cells of the epidermis with thickened and beaded walls and paracytic or anomocytic stomata (*2.8.3*); fragments of the leaf and sepal with large oil glands and red pigment cells; thin-walled, elongated cells of the petal epidermis with straight or wavy anticlinal walls; tracheids and tracheidal vessels with pitted walls and groups of thick-walled fibres; fragments of rectangular, lignified and pitted parenchyma; fibrous layer of the anther and elongated, thin-walled cells of the filament with a striated cuticle; numerous pollen grains with 3 pores and a smooth exine, occur singly or in dense groups, and calcium oxalate cluster crystals.

C. Examine by thin-layer chromatography (*2.2.27*), using a *TLC silica gel plate R*.

Test solution. Stir 0.5 g of the powdered drug (500) in 10 ml of *methanol R* in a water-bath at 60 °C for 10 min and filter.

Reference solution. Dissolve 5 mg of *rutin R* and 5 mg of *hyperoside R* in *methanol R* and dilute to 5 ml with the same solvent.

Apply to the plate as 10 mm bands 10 µl of the test solution and 5 µl of the reference solution. Develop over a path of 10 cm using a mixture of 6 volumes of *anhydrous formic acid R*, 9 volumes of *water R* and 90 volumes of *ethyl acetate R*. Allow the plate to dry at 100-105 °C for 10 min. Spray the plate with a 10 g/l solution of *diphenylboric acid aminoethyl ester R* in *methanol R* and then with a 50 g/l solution of *macrogol 400 R* in *methanol R*. Examine the plate after about 30 min in ultraviolet light at 365 nm. The chromatogram obtained with the reference solution shows in the lower third the zone due to rutin and above it the zone due to hyperoside, both with yellow-orange fluorescence. The chromatogram obtained with the test solution shows in the lower third the reddish-orange fluorescent zones of rutin and hyperoside and in the lower part of the upper third the zone of pseudohypericin and above it the zone of hypericin, both with red fluorescence. Other yellow or blue fluorescent zones are visible.

TESTS

Foreign matter (*2.8.2*). Not more than 3 per cent of stems with a diameter greater than 5 mm, and not more than 2 per cent of other foreign matter.

Loss on drying (*2.2.32*). Not more than 10.0 per cent, determined on 1.000 g of the powdered drug (500) by drying in an oven at 100-105 °C for 2 h.

Total ash (*2.4.16*). Not more than 7.0 per cent.

ASSAY

Test solution. In a 100 ml round-bottomed flask, introduce 0.800 g of the powdered drug (500), 60 ml of a mixture of 20 volumes of *water R* and 80 volumes of *tetrahydrofuran R* and a magnetic stirrer. Boil the mixture in a water-bath at 70 °C under a reflux condenser for 30 min. Centrifuge (2 min at 700 *g*) and decant the supernatant into a 250 ml flask. Take up the residue with 60 ml of a mixture of 20 volumes of *water R* and 80 volumes of *tetrahydrofuran R*. Heat again under a reflux condenser for 30 min. Centrifuge (2 min at 700 *g*) and decant the supernatant. Combine the extracts and evaporate to dryness. Take up the residue with 15 ml of *methanol R* with the help of ultrasound and transfer to a 25 ml measuring flask. Rinse the 250 ml flask with *methanol R* and dilute to 25.0 ml with the same solvent. Centrifuge again, filter 10 ml through a syringe filter (0.2 µm). Discard the first 2 millilitres of the filtrate. Introduce 5.0 ml of the filtrate into a measuring flask and dilute to 25.0 ml with *methanol R*.

Compensation liquid. Methanol R.

Measure the absorbance (*2.2.25*) of the test solution at 590 nm by comparison with the compensation liquid.

Calculate the percentage content of total hypericins, expressed as hypericin, from the expression:

$$\frac{A \times 125}{m \times 870}$$

i.e. taking the specific absorbance of hypericin to be 870.

A = absorbance at 590 nm,

m = mass of the drug to be examined, in grams.

STORAGE

Protected from light.

01/2005:1266

STANNOUS CHLORIDE DIHYDRATE

Stannosi chloridum dihydricum

$SnCl_2,2H_2O$ M_r 225.6

DEFINITION

Stannous chloride dihydrate contains not less than 98.0 per cent and not more than the equivalent of 101.0 per cent of $SnCl_2,2H_2O$.

CHARACTERS

A white, crystalline powder or colourless crystals, efflorescent in air, freely soluble in water (the solution becomes cloudy after standing or on dilution), freely soluble in alcohol. It dissolves in dilute hydrochloric acid.

IDENTIFICATION

A. To 1 ml of solution S1 (see Tests) add a mixture of 5 ml of *water R* and 0.05 ml of *mercuric chloride solution R*. A blackish-grey precipitate forms.

B. Dissolve 1.0 g in 3.0 ml of *water R*. Add 0.5 ml of *dilute sodium hydroxide solution R* to the cloudy solution; a yellowish flocculent precipitate is formed. Add 6.5 ml of *water R*. To 1.0 ml of the previously shaken suspension add 1.0 ml of *strong sodium hydroxide solution R*; the precipitate dissolves and the resulting solution is clear and colourless.

C. Dissolve 10 mg in 2 ml of *dilute nitric acid R*. The solution gives reaction (a) of chlorides (*2.3.1*).

TESTS

Solution S1. To 0.40 g add 1 ml of *dilute hydrochloric acid R* and dilute to 20 ml with *distilled water R*.

Solution S2. Dissolve 1.0 g in *dilute hydrochloric acid R* and dilute to 30 ml with the same acid. Heat to boiling. Add 30 ml of *thioacetamide solution R* and boil for 15 min (solution A). Use 5 ml, filter and heat the filtrate to boiling. Add 5 ml of *thioacetamide solution R* and boil for 15 min. If a precipitate is formed, add the remainder of solution A (solution A′) to the mixture. Add 10 ml of *thioacetamide solution R* and boil. Repeat the series of operations from "Use 5 ml,..." until a precipitate is no longer formed on addition of *thioacetamide solution R* to the filtrate obtained from the 5 ml of solution A (solution A′, solution A″,..., respectively). If no precipitate is formed or if no more precipitate is formed combine the solution obtained with the remainder of solution A (solution A′, solution A″,..., respectively), filter and wash the precipitate with 10 ml of *water R*. Heat the filtrate until the resulting vapour no longer turns a moistened piece of *lead acetate paper R* blackish-grey. Allow to cool and dilute to 50 ml with *water R*.

Appearance of solution. Dissolve 10.0 g in *dilute hydrochloric acid R* and dilute to 20 ml with the same acid. The solution is clear (*2.2.1*) and colourless (*2.2.2, Method II*).

Substances not precipitated by thioacetamide. Evaporate 25 ml of solution S2 to dryness and ignite at 600 °C. The residue weighs not more than 1 mg (0.2 per cent).

Sulphates (*2.4.13*). 15 ml of solution S1 complies with the limit test for sulphates (500 ppm).

Iron(*2.4.9*). Dilute 5 ml of solution S2 to 10 ml with *water R*. The solution complies with the limit test for iron (100 ppm).

Heavy metals. Dissolve 1.0 g in 2 ml of a mixture of 1 volume of *nitric acid R* and 3 volumes of *hydrochloric acid R*. Heat the solution on a water-bath until nitrous vapour is no longer evolved. Dissolve the residue in *water R* and dilute to 25 ml with the same solvent. To 5 ml of the solution add 3 ml of *strong sodium hydroxide solution R* and 2 ml of *water R*. Heat until a clear solution is obtained, then cool and add 0.5 ml of *thioacetamide reagent R*. After 2 min, any colour in the solution is not more intense than that of a mixture of 1.0 ml of *lead standard solution (10 ppm Pb) R*, 6 ml of *water R*, 3 ml of *strong sodium hydroxide solution R* and 0.5 ml of *thioacetamide reagent R* (50 ppm).

ASSAY

Dissolve 0.100 g in 1.5 ml of *hydrochloric acid R1* and dilute to 50 ml with *water R*. Add 5 g of *sodium potassium tartrate R*, 10 g of *sodium hydrogen carbonate R* and 1 ml of *starch solution R*. Titrate immediately with *0.05 M iodine*. Carry out a blank titration.

1 ml of *0.05 M iodine* is equivalent to 11.28 mg of $SnCl_2,2H_2O$.

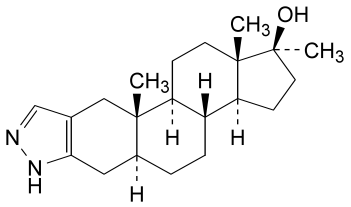
STORAGE

Store in an airtight container.

01/2005:1568

STANOZOLOL

Stanozololum



$C_{21}H_{32}N_2O$ M_r 328.5

DEFINITION

Stanozolol contains not less than 98.5 per cent and not more than the equivalent of 101.0 per cent of 17-methyl-2′*H*-5α-androst-2-eno[3,2-*c*]pyrazol-17β-ol, calculated with reference to the dried substance.

CHARACTERS

A white or almost white crystalline powder, hygroscopic, practically insoluble in water, soluble in dimethylformamide, slightly soluble in alcohol, very slightly soluble in methylene chloride.

It shows polymorphism.

IDENTIFICATION

A. Examine by infrared spectrophotometry (*2.2.24*), comparing with the spectrum obtained with *stanozolol CRS*. If the spectra obtained in the solid

01/2005:1477

TANNIC ACID

Tanninum

DEFINITION

Tannic acid is a mixture of esters of glucose with gallic acid and 3-galloylgallic acid.

CHARACTERS

A yellowish-white or slightly brown amorphous light powder or shiny plates, very soluble in water, freely soluble in acetone, in alcohol and in glycerol (85 per cent), practically insoluble in methylene chloride.

IDENTIFICATION

A. Dilute 0.1 ml of solution S (see Tests) to 5 ml with *water R*. Add 0.1 ml of *ferric chloride solution R1*. A blackish-blue colour is produced which becomes green on the addition of 1 ml of *dilute sulphuric acid R*.

B. To 1 ml of solution S, add 3 ml of a 1 g/l solution of *gelatin R*. The mixture becomes turbid and a flocculent precipitate is formed.

C. Dilute 0.1 ml of solution S to 5 ml with *water R*. Add 0.3 ml of *barium hydroxide solution R*. A greenish-blue precipitate is formed.

TESTS

Solution S. Dissolve 4.0 g in *carbon dioxide-free water R* and dilute to 20 ml with the same solvent.

Appearance of solution. Solution S is not more opalescent than reference suspension II (*2.2.1*).

Dextrins, gum, salts, sugars. To 2 ml of solution S, add 2 ml of *alcohol R*. The solution is clear. Add 1 ml of *ether R*. The solution remains clear for at least 10 min.

Resins. To 5 ml of solution S, add 5 ml of *water R*. The mixture remains clear for at least 15 min (*2.2.1*).

Loss on drying (*2.2.32*). Not more than 12.0 per cent, determined on 0.200 g by drying at 100 °C to 105 °C.

Sulphated ash (*2.4.14*). Not more than 0.1 per cent, determined on 1.0 g.

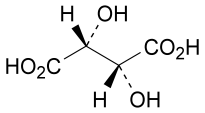
STORAGE

Store protected from light.

01/2005:0460

TARTARIC ACID

Acidum tartaricum



$C_4H_6O_6$ M_r 150.1

DEFINITION

Tartaric acid contains not less than 99.5 per cent and not more than the equivalent of 101.0 per cent of (2*R*,3*R*)-2,3-dihydroxybutanedioic acid, calculated with reference to the dried substance.

CHARACTERS

A white or almost white, crystalline powder or colourless crystals, very soluble in water, freely soluble in alcohol.

IDENTIFICATION

A. Solution S (see Tests) is strongly acid (*2.2.4*).

B. It gives the reactions of tartrates (*2.3.1*).

TESTS

Solution S. Dissolve 5.0 g in *distilled water R* and dilute to 50 ml with the same solvent.

Appearance of solution. Solution S is clear (*2.2.1*) and not more intensely coloured than reference solution Y_6 (*2.2.2, Method II*).

Specific optical rotation (*2.2.7*). Dissolve 5.00 g in *water R* and dilute to 25.0 ml with the same solvent. The specific optical rotation is + 12.0 to + 12.8.

Oxalic acid. Dissolve 0.80 g in 4 ml of *water R*. Add 3 ml of *hydrochloric acid R* and 1 g of *zinc R* in granules and boil for 1 min. Allow to stand for 2 min. Collect the liquid in a test-tube containing 0.25 ml of a 10 g/l solution of *phenylhydrazine hydrochloride R* and heat to boiling. Cool rapidly, transfer to a graduated cylinder and add an equal volume of *hydrochloric acid R* and 0.25 ml of a 50 g/l solution of *potassium ferricyanide R*. Shake and allow to stand for 30 min. Any pink colour in the solution is not more intense than that in a standard prepared at the same time in the same manner using 4 ml of a 0.1 g/l solution of *oxalic acid R* (350 ppm calculated as anhydrous oxalic acid).

Chlorides (*2.4.4*). 5 ml of solution S diluted to 15 ml with *water R* complies with the limit test for chlorides (100 ppm).

Sulphates (*2.4.13*). 10 ml of solution S diluted to 15 ml with *distilled water R* complies with the limit test for sulphates (150 ppm).

Calcium (*2.4.3*). To 5 ml of solution S add 10 ml of a 50 g/l solution of *sodium acetate R* in *distilled water R*. The solution complies with the limit test for calcium (200 ppm).

Heavy metals (*2.4.8*). 2.0 g complies with limit test C for heavy metals (10 ppm). Prepare the standard using 2 ml of *lead standard solution (10 ppm Pb) R*.

Loss on drying (*2.2.32*). Not more than 0.2 per cent, determined on 1.000 g by drying in an oven at 100 °C to 105 °C.

Sulphated ash (*2.4.14*). Not more than 0.1 per cent, determined on 1.0 g.

ASSAY

Dissolve 0.650 g in 25 ml of *water R*. Titrate with *1 M sodium hydroxide* using 0.5 ml of *phenolphthalein solution R* as indicator, until a pink colour is obtained.

1 ml of *1 M sodium hydroxide* is equivalent to 75.05 mg of $C_4H_6O_6$.

01/2005:1837

TEA TREE OIL

Melaleucae aetheroleum

DEFINITION

Essential oil obtained by steam distillation from the foliage and terminal branchlets of *Melaleuca alternifolia* (Maiden and Betch) Cheel, *M. linariifolia* Smith, *M. dissitiflora* F. Mueller and/or other species of *Melaleuca*.

CHARACTERS

Appearance: clear, mobile, colourless to pale yellow liquid with a characteristic odour.

IDENTIFICATION

First identification: *B.*

Second identification: *A.*

A. Thin-layer chromatography (*2.2.27*).

Test solution. Dissolve 0.1 ml of the substance to be examined in 5 ml of *heptane R.*

Reference solution. Dissolve 30 µl of *cineole R*, 60 µl of *terpinen-4-ol R* and 10 mg of *α-terpineol R* in 10 ml of *heptane R.*

Plate: *TLC silica gel plate R.*

Mobile phase: *ethyl acetate R, heptane R* (20:80 *V/V*).

Application: 10 µl, as bands.

Development: over a path of 10 cm.

Drying: in air.

Detection: spray with *anisaldehyde solution R.* Heat at 100-105 °C for 5-10 min while observing. Examine in daylight.

Results: see below the sequence of the zones present in the chromatograms obtained with the reference solution and the test solution. Furthermore, other zones are present in the chromatogram obtained with the test solution.

Top of the plate	
Cineole: a violet-brown zone	A violet-brown zone, less intense (cineole)
Terpinen-4-ol: a brownish-violet zone	A brownish-violet zone terpinen-4-ol)
α-terpineol: a violet or brownish-violet zone	A violet or brownish-violet zone (α-terpineol)
Reference solution	**Test solution**

B. Examine the chromatograms obtained in the test for chromatographic profile.

Results: the characteristic peaks in the chromatogram obtained with the test solution are similar in retention time to those in the chromatogram obtained with the reference solution.

TESTS

Relative density (*2.2.5*): 0.885 to 0.906.

Refractive index (*2.2.6*): 1.475 to 1.482.

Optical rotation (*2.2.7*): + 5° to + 15°.

Chromatographic profile. Gas chromatography (*2.2.28*): use the normalisation procedure.

Test solution. Dissolve 0.15 ml of the substance to be examined in 10 ml of *hexane R.*

Reference solution. Dissolve 5 µl of *α-pinene R*, 5 µl of *sabinene R*, 15 µl of *α-terpinene R*, 5 µl of *limonene R*, 5 µl of *cineole R*, 30 µl of *γ-terpinene R*, 5 µl of *p-cymene R*, 5 µl of *terpinolene R*, 60 µl of *terpinen-4-ol R*, 5 µl of *aromadendrene R* and 5 mg of *α-terpineol R* in 10 ml of *hexane R.*

Column:

– *material*: fused silica,
– *size*: *l* = 30 m (a film thickness of 1 µm may be used) to 60 m (a film thickness of 0.2 µm may be used), Ø = 0.25-0.53 mm,
– *stationary phase*: *macrogol 20 000 R.*

Carrier gas: *helium for chromatography R.*

Flow rate: 1.3 ml/min.

Split ratio: 1:50.

Temperature:

	Time (min)	**Temperature (°C)**
Column	0 - 1	50
	1 - 37	50 → 230
	37 - 45	230
Injection port		240
Detector		240

Detection: flame ionisation.

Injection: 1 µl.

Elution order: order indicated in the composition of the reference solution. Record the retention times of these substances.

System suitability: reference solution:

– *resolution*: minimum 2.7 between the peaks due to terpinen-4-ol and aromadendrene.

Using the retention times determined from the chromatogram obtained with the reference solution, locate the components of the reference solution in the chromatogram obtained with the test solution. Disregard the peak due to hexane.

Determine the percentage content of these components. The percentages are within the following ranges:

– *α-pinene*: 1.0 per cent to 6.0 per cent,
– *sabinene*: less than 3.5 per cent,
– *α-terpinene*: 5.0 per cent to 13.0 per cent,
– *limonene*: 0.5 per cent to 4.0 per cent,
– *cineole*: less than 15.0 per cent,
– *γ-terpinene*: 10.0 per cent to 28.0 per cent,
– *p-cymene*: 0.5 per cent to 12.0 per cent,
– *terpinolene*: 1.5 per cent to 5.0 per cent,
– *terpinen-4-ol*: minimum 30.0 per cent,
– *aromadendrene*: less than 7.0 per cent,
– *α-terpineol*: 1.5 per cent to 8.0 per cent.

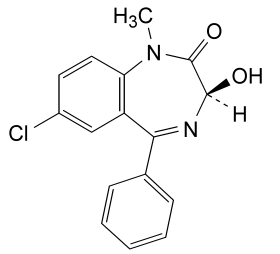
STORAGE

In an airtight, well-filled container, protected from light, at a temperature not exceeding 25 °C.

01/2005:0954

TEMAZEPAM

Temazepamum



and enantiomer

$C_{16}H_{13}ClN_2O_2$ M_r 300.7

DEFINITION

(3*RS*)-7-Chloro-3-hydroxy-1-methyl-5-phenyl-1,3-dihydro-2*H*-1,4-benzodiazepin-2-one.

Content: 99.0 per cent to 101.0 per cent (dried substance).

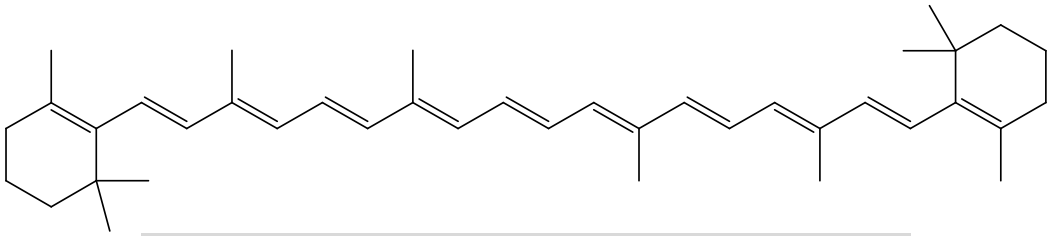
Certificate of Analysis

ISO GUIDE 34
ACLASS Cert# AR-1470

ISO/IEC 17025
ACLASS Cert# AT-1467

BETA CAROTENE

CERTIFIED REFERENCE MATERIAL



CERTIFIED PURITY: 94.9%, U_{crm} = ±0.3% k = 2.09
(Mass Balance as all-*trans*-Beta Carotene/as is basis)

NOMINAL PACKAGE SIZE: 1g

CATALOG #: PHR1239 **LOT #:** LRAA4126

CERTIFICATE VERSION: LRAA4126.1 **ISSUE DATE:** 27 October 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 in a Freezer/Protect from Light. Discard unused portions.

CHEMICAL FORMULA: $C_{40}H_{56}$ **MW:** 536.9

PHYSICAL DESCRIPTION: Red powder in amber vial **CAS #:** 7235-40-7

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: UV (ref.: Beta Carotene, USP37)
Solvent: Cyclohexane
Cell Pathlength: 1cm
Wavelength: 457nm

ASSAY vs. USP REFERENCE STANDARD (as is basis)

ASSAY VALUE	vs. USP LOT
95.1%	**F0J240**
	Labeled Content = None, calculated= 94.2%*

*Note: The USP designates its standard content to be calculated at the time of use using the coefficient of extinction of 2505

PURITY DETERMINATION BY MASS BALANCE

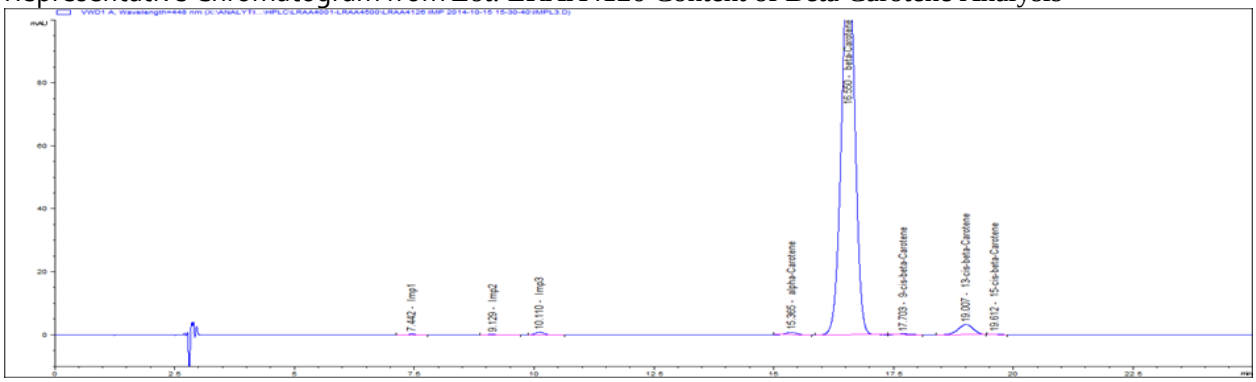
CHROMATOGRAPHIC IMPURITY ANALYSIS
METHOD: HPLC (ref.: Beta Carotene, USP37)
Column: Supelcosil Suplex pkb-100, 4.6 x 250mm, 5µm
Mobile Phase: 50mg/L Butylated Hydroxytolune, 20mL/L 2-propanol, 0.2mL/L Triethylamine, 25mL/L 0.2% Ammonium Acetate in Water, 455mL/L Acetonitrile, 460mL/L Methanol
Flow Rate: 0.6mL/min
Column Temperature: 30ºC
Injection: 20µL
Detector: 448nm

Impurities Detected:

Impurity 1:	0.2%
Impurity 2:	0.2%
Impurity 3:	0.5%
alpha Carotene:	0.7%
9-cis-beta Carotene:	0.3%
13-cis-beta Carotene:	3.2%
15-cis-beta-Carotene:	0.1%

Total Impurities: **5.1%**

Representative Chromatogram from Lot: LRAA4126 Content of Beta Carotene Analysis



RESIDUAL SOLVENTS

Method: GC-MS Headspace (ref.: Residual Solvents <467>, USP34)
Column: DB-1301
Carrier gas: He
Flow: 1.2mL/min
Split Ratio: 1:5
Injection/Temperature: 1µl/250°C
Temperature Program: 40°C for 20min, 10°C/min to 240°C, hold 20min

Solvents Detected: None

LOSS ON DRYING/VOLATILES

Method: Oven at 105°C
Mean of three measurements, Loss = **0.03%**

RESIDUE ANALYSIS

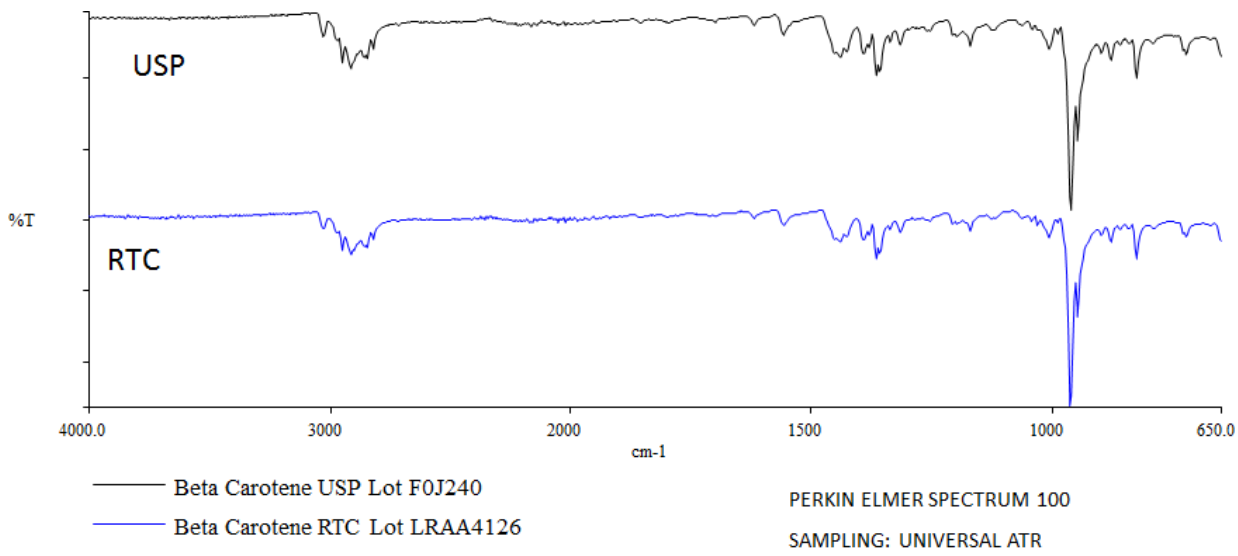
Method: Sulfated Ash
Sample Size: ~1g
Mean of three measurements, Residue = **0.01%**

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

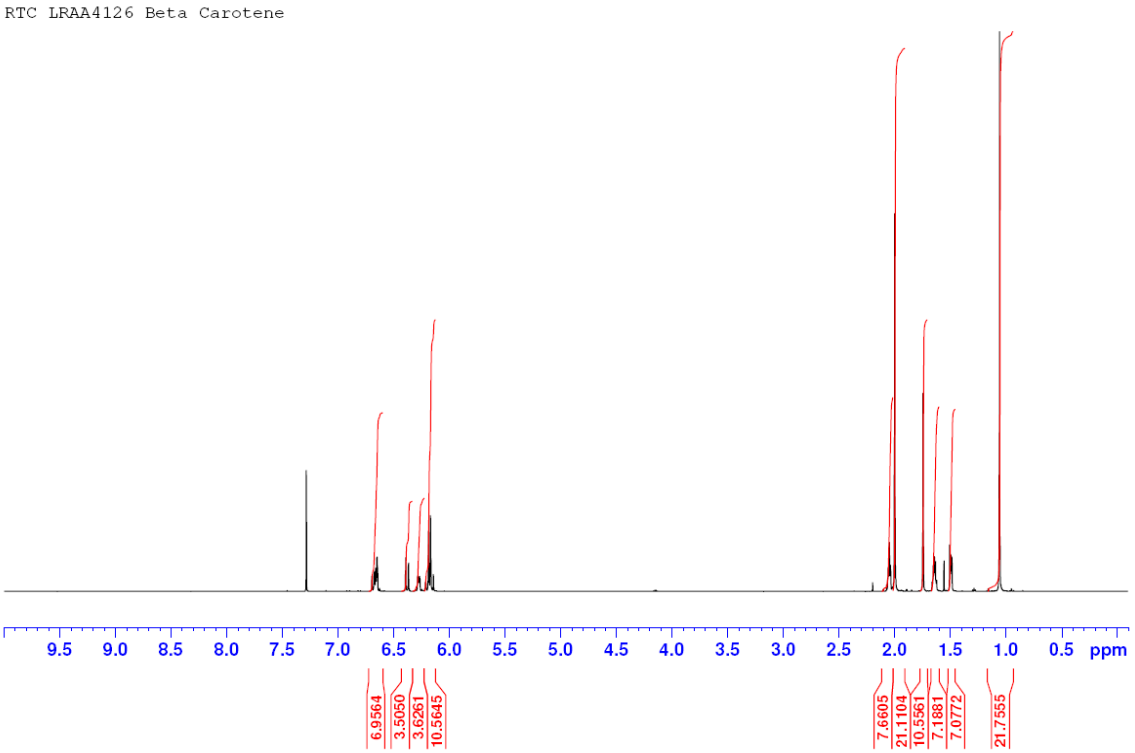
94.9% U_{crm} = ±0.3%, k = 2.09
(all-*trans*-Beta Carotene, as is basis)

IDENTIFICATION TESTS

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



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



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	89.49	88.82	88.67	88.75
H	10.51	10.48	10.55	10.52

MELTING RANGE

Specification: 176-182ºC (with decomposition, USP35)
Mettler Toledo FP900 Thermosystem with FP81 Measuring Cell
Mean of three measurements = **177.7-180.1ºC**

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: UV-Vis Sample size: ~50mg

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: 27 October 2014

Manufactured and certified by Sigma-Aldrich RTC, Inc.
2931 Soldier Springs Rd, Laramie WY, USA 82070
(Phone): 1-307-742-5452 (Fax): 1-855-831-9212
email: RTCTechGroup@sial.com

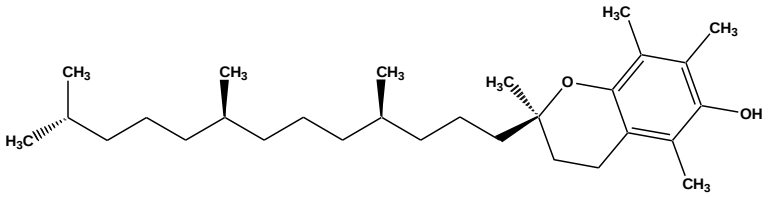
Certificate of Analysis

ISO GUIDE 34
ACLASS Cert# AR-1470

ISO/IEC 17025
ACLASS Cert# AT-1467

α-TOCOPHEROL

CERTIFIED REFERENCE MATERIAL



CERTIFIED PURITY: 98.6%, U_{crm} = ±0.2% k = 2
(Mass Balance/as is basis)

NOMINAL PACKAGE SIZE: 500mg

CATALOG #: PHR1031 **LOT #:** P500031

CERTIFICATE VERSION: 500031.5 **ISSUE DATE:** 31 December 2013
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: 12 Months from Receipt (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/Protect from Light, transfer unused portion to a tightly closed container, blanket with inert gas.

CHEMICAL FORMULA: $C_{29}H_{50}O_2$ **MW:** 430.71

PHYSICAL DESCRIPTION: Pale yellow liquid in amber ampule **CAS #:** 10191-41-0

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. This is the dl- form of α-Tocopherol. 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

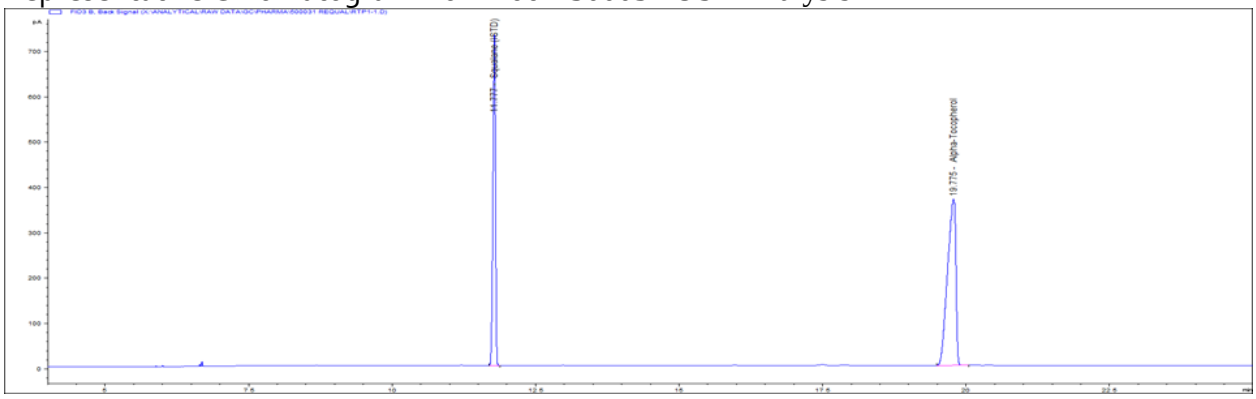
Comparative assay demonstrates direct traceability to Pharmacopeial Standards
Specification: 96.0% to 102.0% (USP)

ASSAY vs. USP REFERENCE STANDARD (as is basis)

ASSAY VALUE	vs. USP LOT
98.6%	**O0K291**
	Labeled Content = 0.985 mg/mg

METHOD: GC (ref.: all-rac-α-Tocopherol, EP6)
Column: Equity-1, 30m x 0.25mm, 0.25µm
Carrier gas: H_2
Flow: 1.4mL/min
Split Ratio: 1:20
Injection/Temperature: 1µl, 280°C
Temperature Program: 80ºC for 1 min, 40ºC/min to 300ºC, hold 9 min
Detector/Temperature: FID, 280°C
Internal Standard: Squalane

Representative Chromatogram from Lot: P500031 USP Analysis

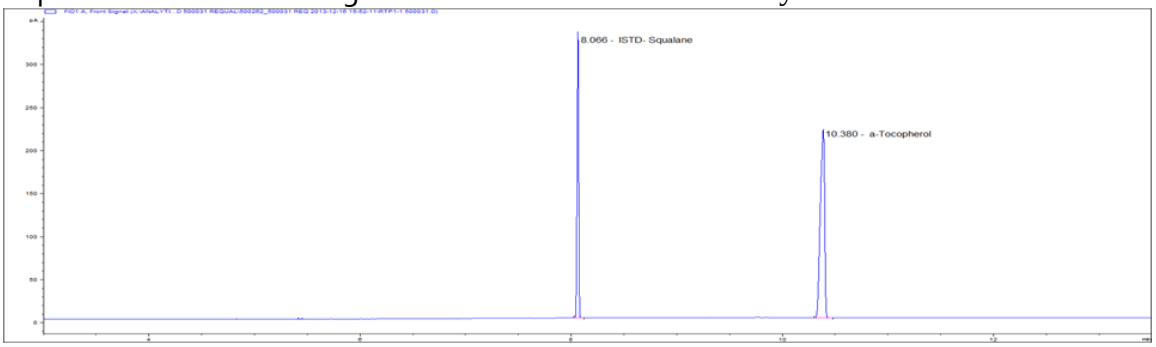


ASSAY vs. EP CRS (as is basis)

ASSAY VALUE	vs. EP BATCH
100.3%	**7.0**
	Labeled Content = 97.7%

METHOD: GC (ref.: all-rac-α-Tocopherol, EP7)
Column: Equity-1, 30m x 0.25mm, 0.25µm
Carrier gas: H_2
Flow: 1.4mL/min
Split Ratio: 20:1
Injection/Temperature: 1µl, 290°C
Temperature Program: 80ºC for 1 min, 40ºC/min to 300ºC, hold 9 min
Detector/Temperature: FID, 280°C
Internal Standard: Squalane

Representative Chromatogram from Lot: P500031 EP Analysis

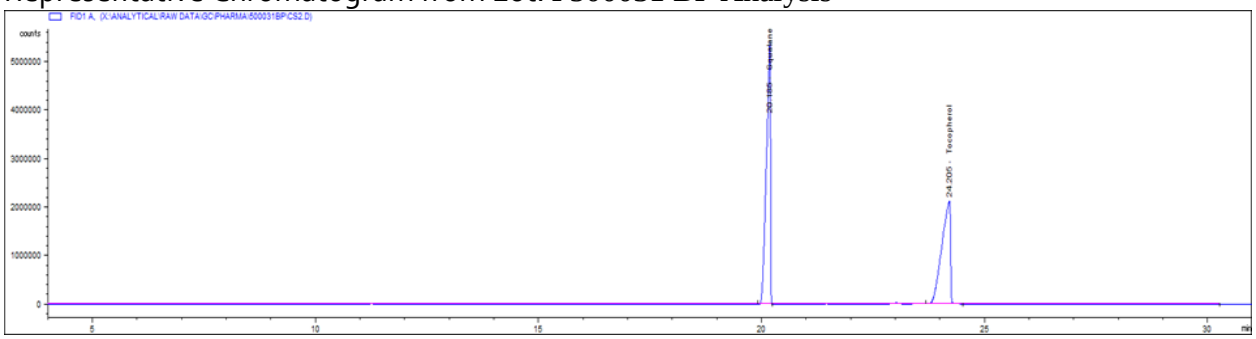


ASSAY vs. BP CRS (as is basis)

ASSAY VALUE	vs. BP BATCH
99.4%	**3129**
	Labeled Content = 99.8%

METHOD: GC (ref.: all-rac-α-Tocopherol, EP7)
Column: Equity-1, 15m x 0.53mm, 1.5µm
Carrier gas: He
Flow: 4.1mL/min
Split Ratio: 1:20
Injection/Temperature: 1µl, 280°C
Temperature Program: 80°C for 1 min, increase 10°C/min to 280°C, hold 10 min
Detector/Temperature: FID, 280°C
Internal Standard: Squalane

Representative Chromatogram from Lot: P500031 BP Analysis



PURITY DETERMINATION BY MASS BALANCE

CHROMATOGRAPHIC IMPURITY ANALYSIS

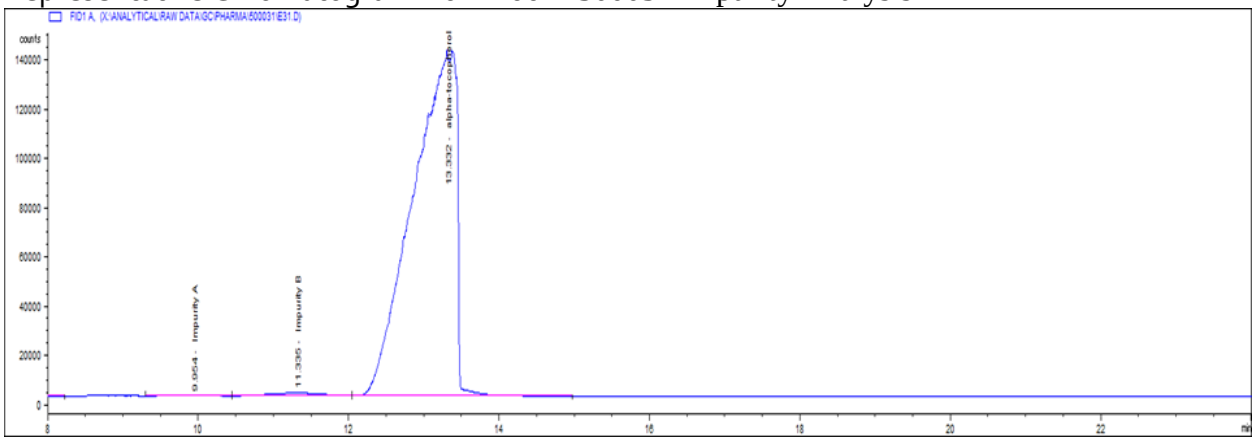
METHOD: GC (ref.: all-rac-α-Tocopherol, EP6)
Column: EC-1, 30m x 0.25mm, 0.25µm
Carrier gas: He
Flow: 2mL/min
Split Ratio: 1:100
Injection/Temperature: 1µl, 290°C
Temperature Program: Hold oven at 280°C
Detector/Temperature: FID, 290°C

Impurities Detected:

Impurity A:	**0.3%**
Impurity B:	**1.1%**

Total Impurities: **1.4%**

Representative Chromatogram from Lot: P500031 Impurity Analysis



RESIDUAL SOLVENTS

Method: GC-MS Headspace (ref.: Residual Solvents <467>, USP34)
Column: DB-1301
Carrier gas: He
Flow: 1.2mL/min
Split Ratio: 1:5
Injection/Temperature: 1µl/250°C
Temperature Program: 40°C for 20min, 10°C/min to 240°C, hold 20min

Solvents Detected: None

WATER DETERMINATION

Method: Karl Fisher titration
Mean of three measurements, Water Content = **0.02%**

RESIDUE ANALYSIS

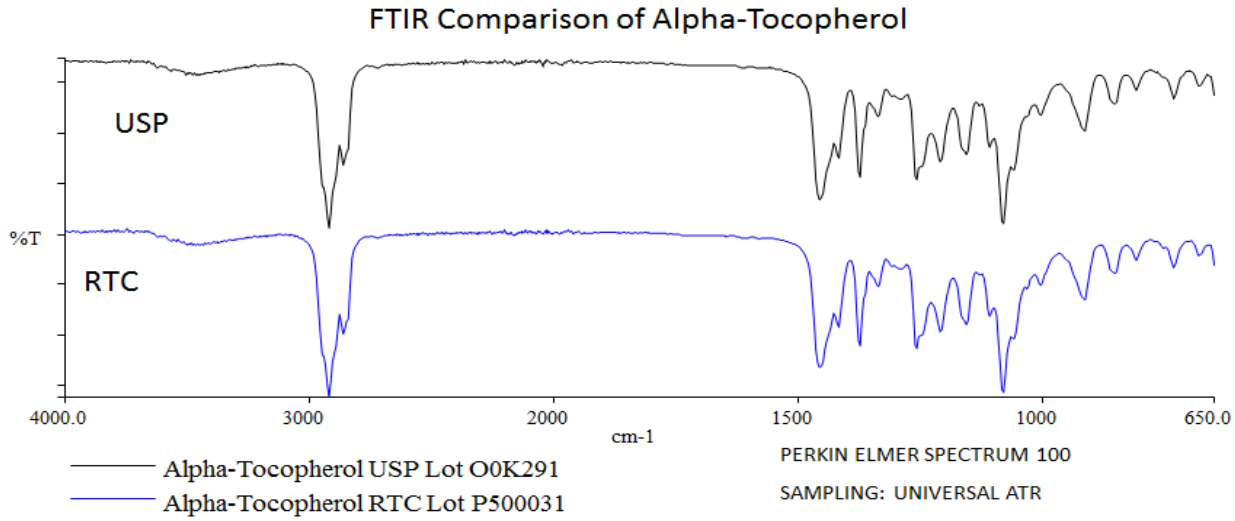
Method: Sulfated Ash
Sample Size: ~1g
Mean of three measurements, Residue = **0.04%**

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

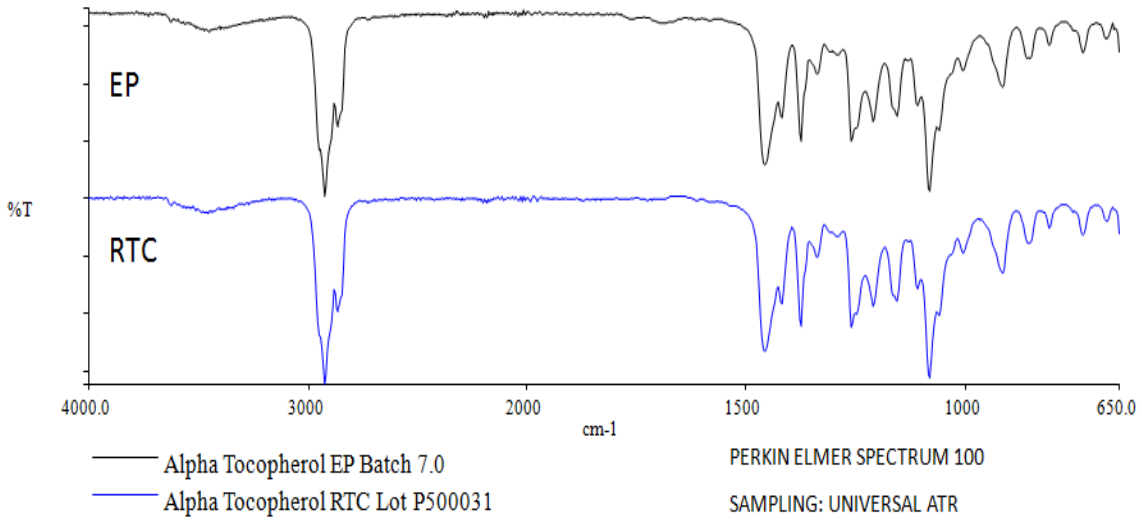
98.6% U_{crm} = ±0.2%, k = 2
(as is basis)

IDENTIFICATION TESTS

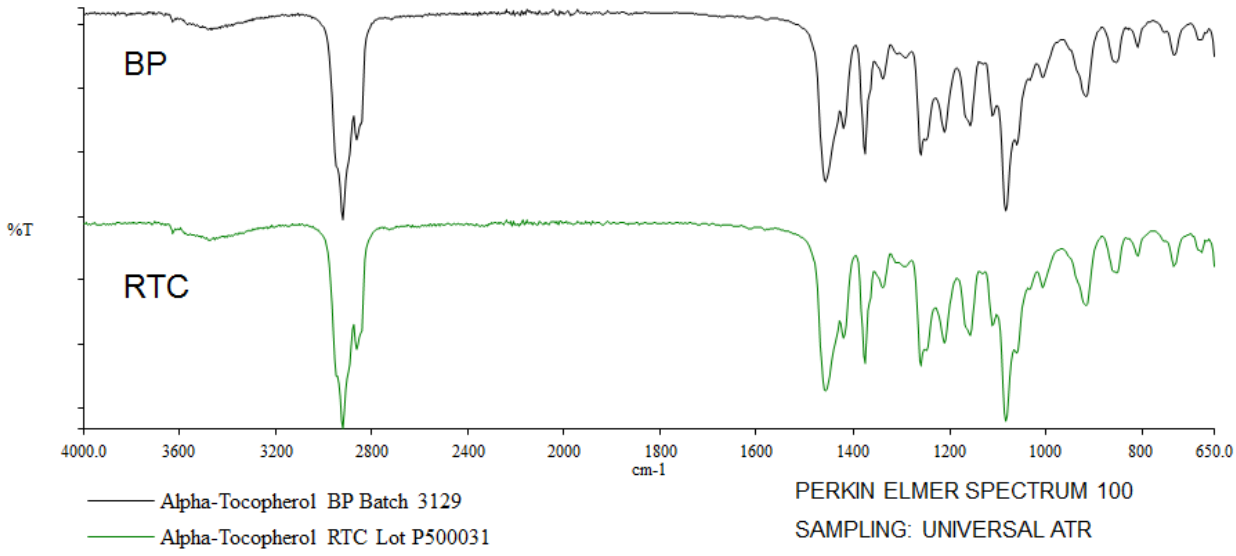
INFRARED SPECTROPHOTOMETRY (Comparative identification analysis demonstrates direct traceability to Pharmacopeial standards)



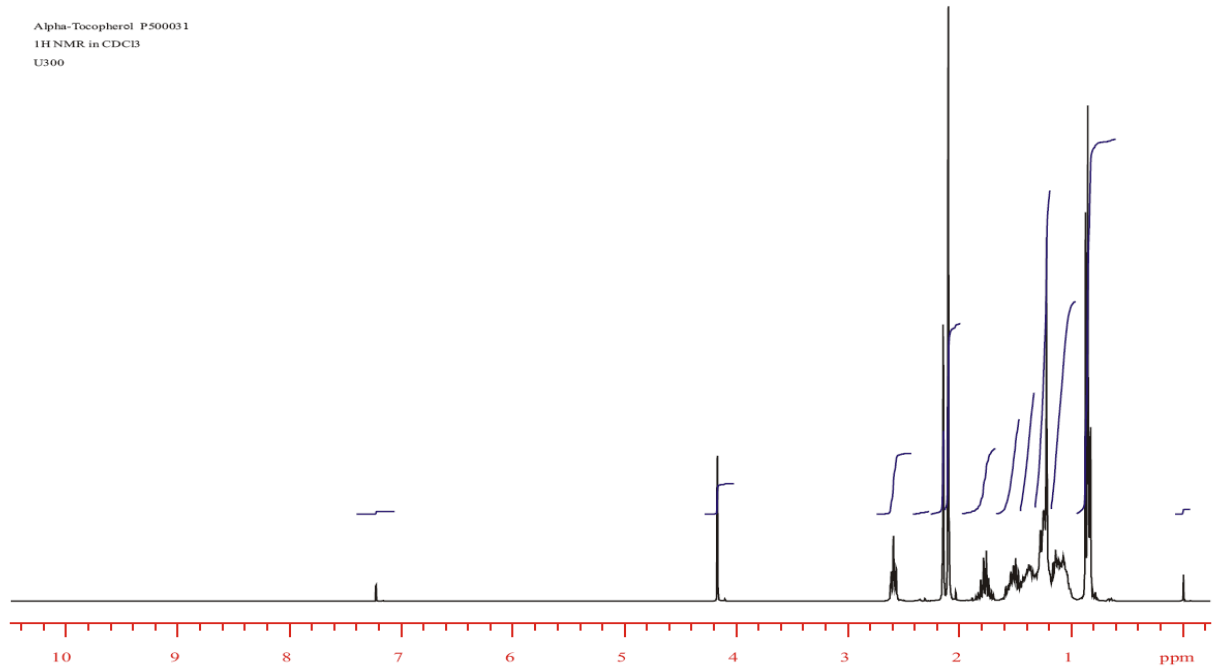
FTIR Comparison of Alpha Tocopherol



FTIR Comparison of α-Tocopherol



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



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	80.87	81.03	81.08	81.06
H	11.70	11.68	11.62	11.65

OPTICAL ROTATION

Specification: -0.01° to +0.01° (EP)
Perkin Elmer Polarimeter 343
Wavelength: 589nm
Concentration: 10g/100mL in EtOH
Cell Path: 100mm
Mean of three Measurements = **-0.004°**

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: ~100 mg

UNCERTAINTY STATEMENT

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Operations Manager

QA Supervisor

APPENDIX

Original Release Date:	17 September 2009
Stability Test Date:	22 November 2011
Requalification Test Date:	22 November 2011
Requalification Test Date:	17 December 2012
Requalification Test Date:	18 December 2013

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

SIGMA-ALDRICH®
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3050 Spruce Street, Saint Louis, MO 63103, USA
Website: www.sigmaaldrich.com
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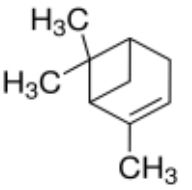
Outside USA: eurtechserv@sial.com

Certificate of Analysis

Product Name:
α-Pinene – 98%

Product Number:	**147524**
Batch Number:	**SHBD4790V**
Brand:	ALDRICH
CAS Number:	80-56-8
MDL Number:	MFCD00001339
Formula:	C10H16
Formula Weight:	136.23 g/mol
Quality Release Date:	06 FEB 2014



Test	Specification	Result
Appearance (Color)	Colorless	Colorless
Appearance (Form)	Liquid	Liquid
Infrared Spectrum	Conforms to Structure	Conforms
Purity (GC)	≥ 97.5 %	98.9 %
Optical Rotation Neat	-0.20 - 0.20 °	0.00 °

Jamie Gleason, Manager
Quality Control
Sheboygan Falls, WI US

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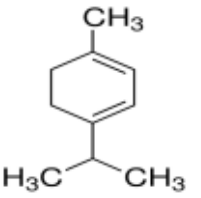
Certificate of Analysis

Product Name:
α-Terpinene - 85%

Product Number:	**223182**
Batch Number:	**MKBQ5088V**
Brand:	ALDRICH
CAS Number:	99-86-5
MDL Number:	MFCD00001534
Formula:	C10H16
Formula Weight:	136.23 g/mol
Quality Release Date:	22 NOV 2013



Test	Specification	Result
Appearance (Color)	Colorless	Colorless
Appearance (Form)	Liquid	Liquid
Infrared Spectrum	Conforms to Structure	Conforms
Purity (GC)	≥ 84.5 %	91.3 %
Solubility (Turbidity) 100mg/ml, Ethanol	Clear	Clear
Solubility (Color)	Colorless to Pale Yellow	Colorless

Jamie Gleason

Jamie Gleason, Manager
Quality Control
Milwaukee, Wisconsin US

SIGMA-ALDRICH®

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Certificate of Analysis

Product Name:	(+)-α-TERPINEOL analytical standard
Product Number:	83073
Batch Number:	BCBN0603V
Brand:	Fluka
CAS Number:	7785-53-7
Formula:	$C_{10}H_{18}O$
Formula Weight:	154.25
Storage Temperature:	2-8 C
Quality Release Date:	16 JUL 2014

TEST	SPECIFICATION	RESULT
APPEARANCE (COLOR)	COLORLESS TO VERY FAINT YELLOW AND COLORLESS TO VERY FAINT BROWN-YELLOW	COLORLESS
APPEARANCE (FORM)	CLEAR LIQUID OR SOLID	LIQUID
PURITY (GC AREA %)	≥ 97.0 %	97.1 %
SPECIFIC ROTATION (20/D)	84.0 ± 10.0 DEGREES	89.0 DEGREES
CONCENTRATION	NEAT	NEAT
PROTON NMR SPECTRUM	CONFORMS TO STRUCTURE	CONFORMS

Dr. Claudia Geitner
Manager Quality Control
Buchs, Switzerland

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Certificate of Analysis

Product Name:	(+)-AROMADENDRENE purum
Product Number:	11067
Batch Number:	435553/1
Brand:	Aldrich
CAS Number:	489-39-4
Formula:	C15H24
Formula Weight:	204.35
Storage Temperature:	2-8 C
Quality Release Date:	12 MAR 2002
Date retested:	30 JUL 2014

TEST	SPECIFICATION	RESULT
APPEARANCE (COLOR)	COLORLESS TO VERY FAINTLY YELLOW	VERY FAINTLY YELLOW (Y6)
APPEARANCE (FORM)	CLEAR LIQUID	CLEAR LIQUID
PURITY (GC AREA %)	≥ 97.0 %	98.8 %
SPECIFIC ROTATION (20/D)	12.0 1 1.0 DEGREES	12.8 DEGREES
CONCENTRATION	NEAT	NEAT
REFRACTIVE INDEX N20/D	1.496 - 1.498	1.498

Dr. Claudia Geitner
Manager Quality Control
Buchs, Switzerland

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Certificate of Analysis

Product Name:	1,4-CINEOLE technical, mixture of isomers, >= 85 % GC
Product Number:	27395
Batch Number:	BCBM1534V
Brand:	Aldrich
CAS Number:	470-67-7
Formula:	$C_{10}H_{18}O$
Formula Weight:	154.25
Quality Release Date:	13 NOV 2013

TEST	SPECIFICATION	RESULT
APPEARANCE (COLOR)	COLORLESS TO VERY FAINT YELLOW	COLORLESS
APPEARANCE (FORM)	LIQUID	LIQUID
PURITY (GC AREA %)	≥ 70.0 %	92.5 %
GC MINOR COMPONENT 1 (AREA %)	≤ 20 %	1.2 %
MINOR COMPONENT 1	1,8-CINEOLE	1.8-CINEOLE
REFRACTIVE INDEX N20/D	1.447 - 1.455	1.447
PROTON NMR SPECTRUM	CONFORMS TO STRUCTURE	CONFORMS

Dr. Claudia Geitner
Manager Quality Control
Buchs, Switzerland

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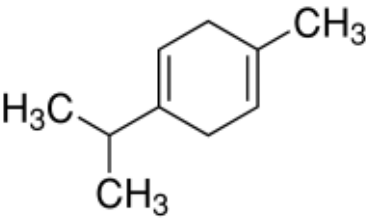
Certificate of Analysis

Product Name:
γ-Terpinene – 97%

Product Number:	**223190**
Batch Number:	**MKBN9731V**
Brand:	ALDRICH
CAS Number:	99-85-4
MDL Number:	MFCD00001537
Formula:	C10H16
Formula Weight:	136.23 g/mol
Quality Release Date:	11 MAR 2013



Test	Specification	Result
Appearance (Color)	Colorless	Colorless
Appearance (Form)	Liquid	Liquid
Infrared spectrum	Conforms to Structure	Conforms
Purity (GC)	≥ 96.5 %	99.3 %

Jamie Gleason, Manager
Quality Control
Milwaukee, Wisconsin US

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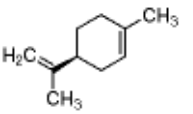
Outside USA: eurtechserv@sial.com

Certificate of Analysis

Product Name:
(S)-(−)-Limonene - 96%



Product Number:	**218367**
Lot Number:	**MKBH0284V**
Brand:	ALDRICH
CAS Number:	5989-54-8
MDL Number:	MFCD00001558
Formula:	C10H16
Formula Weight:	136.23 g/mol
Quality Release Date:	28 APR 2011

Test	Specification	Result
Appearance (Color)	Colorless	Colorless
Appearance (Form)	Liquid	Liquid
Infrared spectrum	Conforms to Structure	Conforms
Optical Rotation C= Neat	-90 - -61deg	-82deg
Purity (GC)	≥ 95.5%	97.9%

Jamie Gleason

Jamie Gleason, Manager
Quality Control
Milwaukee, Wisconsin US

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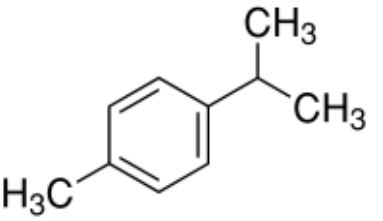
Outside USA: eurtechserv@sial.com

Certificate of Analysis

Product Name:
p-Cymene - 99%

Product Number:	**C121452**
Batch Number:	**MKBP8457V**
Brand:	ALDRICH
CAS Number:	99-87-6
MDL Number:	MFCD00008893
Formula:	C10H14
Formula Weight:	134.22 g/mol
Quality Release Date:	30 JUL 2013



Test	Specification	Result
Appearance (Color)	Colorless	Colorless
Appearance (Form)	Liquid	Liquid
Infrared spectrum	Conforms to Structure	Conforms
Purity (GC)	≥ 98.5 %	99.6 %

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Milwaukee, Wisconsin US

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Certificate of Analysis

Product Name:	(–)-TERPINEN-4-OL >= 95.0 % GC sum of enantiomers
Product Number:	11584
Batch Number:	BCBM5331V
Brand:	Aldrich
CAS Number:	
Formula:	$C_{10}H_{18}O$
Formula Weight:	154.25
Quality Release Date:	28 JAN 2014

TEST	SPECIFICATION	RESULT
APPEARANCE (COLOR)	COLORLESS TO VERY FAINT YELLOW AND COLORLESS TO VERY FAINT GREEN-YELLOW	COLORLESS
APPEARANCE (FORM)	LIQUID	LIQUID
PURITY (GC AREA %)	≥ 95.0 %	99.5 %
SPECIFIC ROTATION (20/D)	-25.0 ± 6.0 DEGREES	-20.5 DEGREES
CONCENTRATION	NEAT	NEAT
REFRACTIVE INDEX N20/D	1.478 - 1.480	1.479
PROTON NMR SPECTRUM	CONFORMS TO STRUCTURE	CONFORMS

Dr. Claudia Geitner
Manager Quality Control
Buchs, Switzerland

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Email USA: techserv@sial.com Outside USA: eurtechserv@sial.com

Certificate of Analysis

Product Name:	TERPINOLENE technical
Product Number:	86485
Batch Number:	BCBN2717V
Brand:	Fluka
CAS Number:	586-62-9
Formula:	$C_{10}H_{16}$
Formula Weight:	136.23
Quality Release Date:	17 JUN 2014

TEST	SPECIFICATION	RESULT
APPEARANCE (COLOR)	COLORLESS TO VERY FAINT YELLOW	COLORLESS
APPEARANCE (FORM)	LIQUID	LIQUID
PURITY (GC AREA %)	≥ 85.0 %	90.8 %
REFRACTIVE INDEX N20/D	1.489 - 1.493	1.489
PROTON NMR SPECTRUM	CONFORMS TO STRUCTURE	CONFORMS

Dr. Claudia Geitner
Manager Quality Control
Buchs, Switzerland