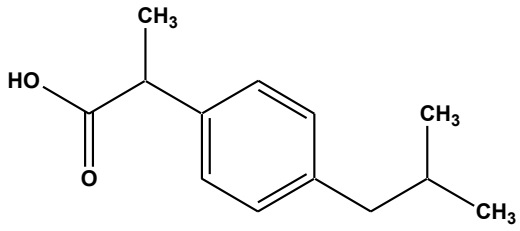
Certificate of Analysis

ISO GUIDE 34
ACLASS Cert# AR-1470

ISO/IEC 17025
ACLASS Cert# AT-1467

IBUPROFEN

CERTIFIED REFERENCE MATERIAL



CERTIFIED PURITY: 99.9%, U_{crm} = ±0.1% k = 2
(Mass Balance/as is basis)

NOMINAL PACKAGE SIZE: 1g

CATALOG #: PHR1004 **LOT #:** P500004

CERTIFICATE VERSION: 500004.10 **ISSUE DATE:** 17 April 2012

Note: Certificates may be updated due to Pharmacopeial Lot changes or the availability of new data. Check our website at: www.RT-Corp.com or 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 at Room Temperature, keep container tightly closed. Attachment of a 20 mm aluminum crimp seal recommended for unused portions.

CHEMICAL FORMULA: $C_{13}H_{18}O_2$ **MW:** 206.29

PHYSICAL DESCRIPTION: White Powder in amber vial. **CAS #:** 15687-27-1

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 as is. 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

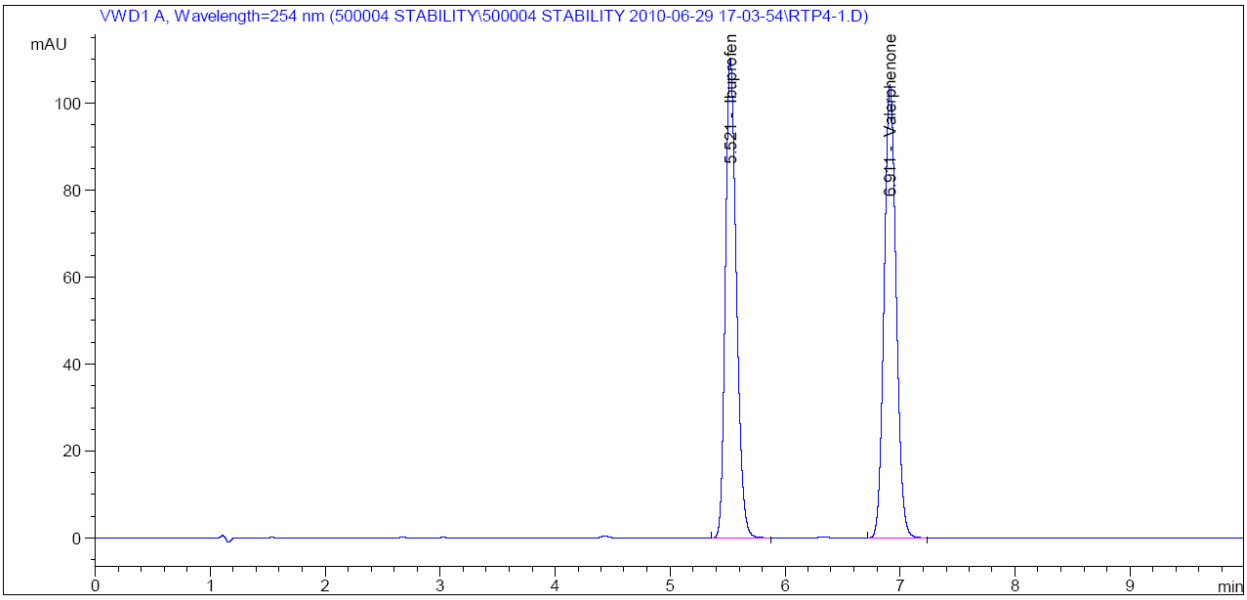
Comparative assay demonstrates direct traceability to Pharmacopeial Standards
Specification: 97.0-103.0 % (anhydrous, USP)

ASSAY vs. USP REFERENCE STANDARD (as is basis)

ASSAY VALUE	vs. USP LOT
99.5%	**K0J008**
	Labeled Content = 0.999mg/mg

METHOD: HPLC (ref.: Ibuprofen; USP32)
Column: ProteCol-GP C18 125, 4.6 x 250mm, 5µm
Mobile Phase: Acetonitrile/Water/chloroacetic acid (600:400:4)
Column Temperature: 30°C
Flow Rate: 2 mL/min
Injection: 5µl
Detector Wavelength: 254 nm

Representative Chromatogram from Lot: P500004 USP Analysis



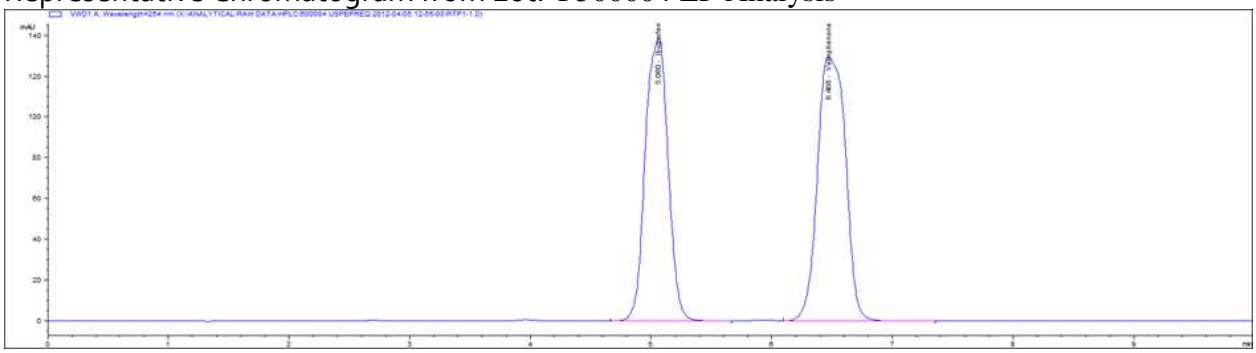
ASSAY vs. EP CRS (as is basis)

ASSAY VALUE	vs. EP BATCH
99.8%	**5.0**
	Labeled Content = None
	Assigned Content = 99.8% *

METHOD: HPLC (ref.: Ibuprofen; USP34)
Column: Ascentis C18, 4.6 x 250mm, 5µm
Mobile Phase: Acetonitrile/Water/chloroacetic acid (600:400:4)
Column Temperature: 30°C
Flow Rate: 2 mL/min
Injection: 10µl
Detector Wavelength: 254 nm

*The assigned content of the EP CRS was determined by assay against the USP Reference Standard

Representative Chromatogram from Lot: P500004 EP Analysis

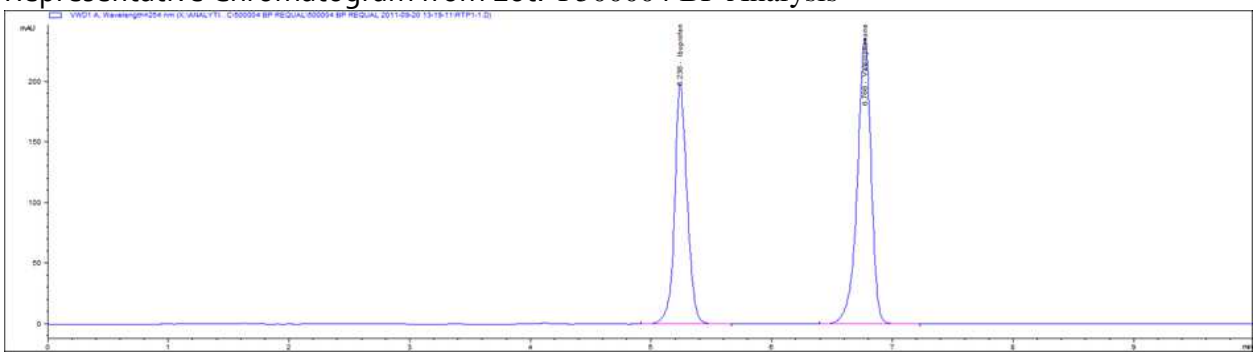


ASSAY vs. BP CRS (as is basis)

ASSAY VALUE	vs. BP BATCH
101.2%	**3309**
	Labeled Content = 99.9%

METHOD: HPLC (ref.: Ibuprofen; USP34)
Column: Ascentis C18, 4.6 x 250mm, 5µm
Mobile Phase: Acetonitrile/Water/chloroacetic acid (600:400:4)
Column Temperature: 30°C
Flow Rate: 2 mL/min
Injection: 10µl
Detector Wavelength: 254 nm

Representative Chromatogram from Lot: P500004 BP Analysis



ASSAY BY TITRATION

Method: Dissolve in MeOH. Titrate with 0.1 M NaOH to phenolphthalein end point.
Ref.: Ibuprofen; EP6

Mean of nine measurements: **99.7%**

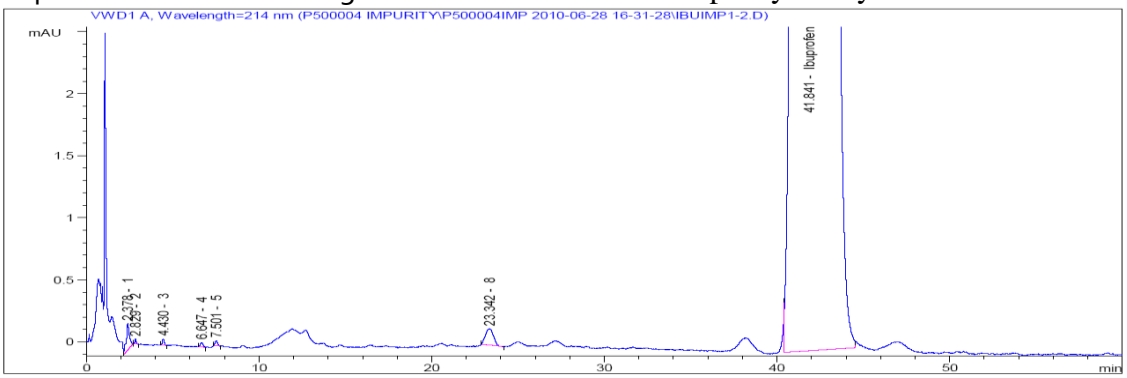
PURITY DETERMINATION BY MASS BALANCE

CHROMATOGRAPHIC IMPURITY ANALYSIS

METHOD: HPLC (ref.: Ibuprofen USP32)
Column: Wakosil 5C18 RS, 4.6 x 150mm, 5µm
Mobile Phase: Water/Acetonitrile (1340:680) pH 2.5
Column Temperature: 30°C
Flow Rate: 2 mL/min
Injection: 5µl
Detector Wavelength: 214 nm

Six individual impurities detected
Total Detected Impurities: **0.03%**

Representative Chromatogram from Lot: P500004 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 after drying over P_2O_5
Mean of three samples, Water Content = **0.04 %**

LOSS ON DRYING/VOLATILES

Method: Dry in vacuum over P_2O_5
Mean of three samples, Loss = **0.008 %**

RESIDUE ANALYSIS

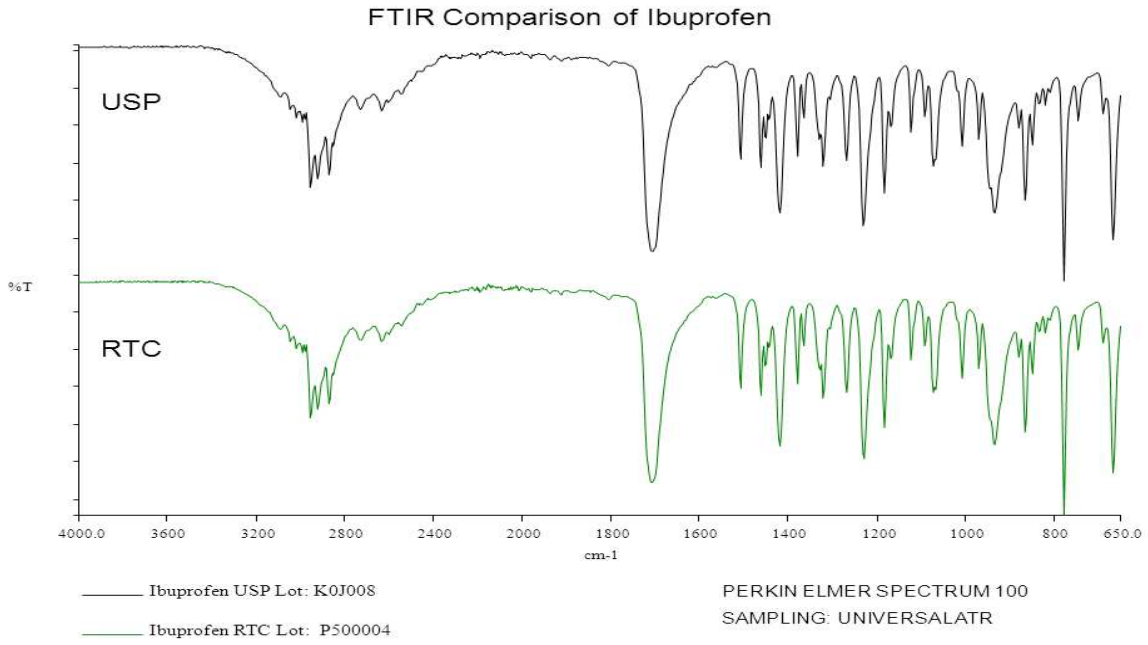
Method: Sulfated Ash
Sample Size: ~ 1 g
Mean of three determinations: **0.02%**

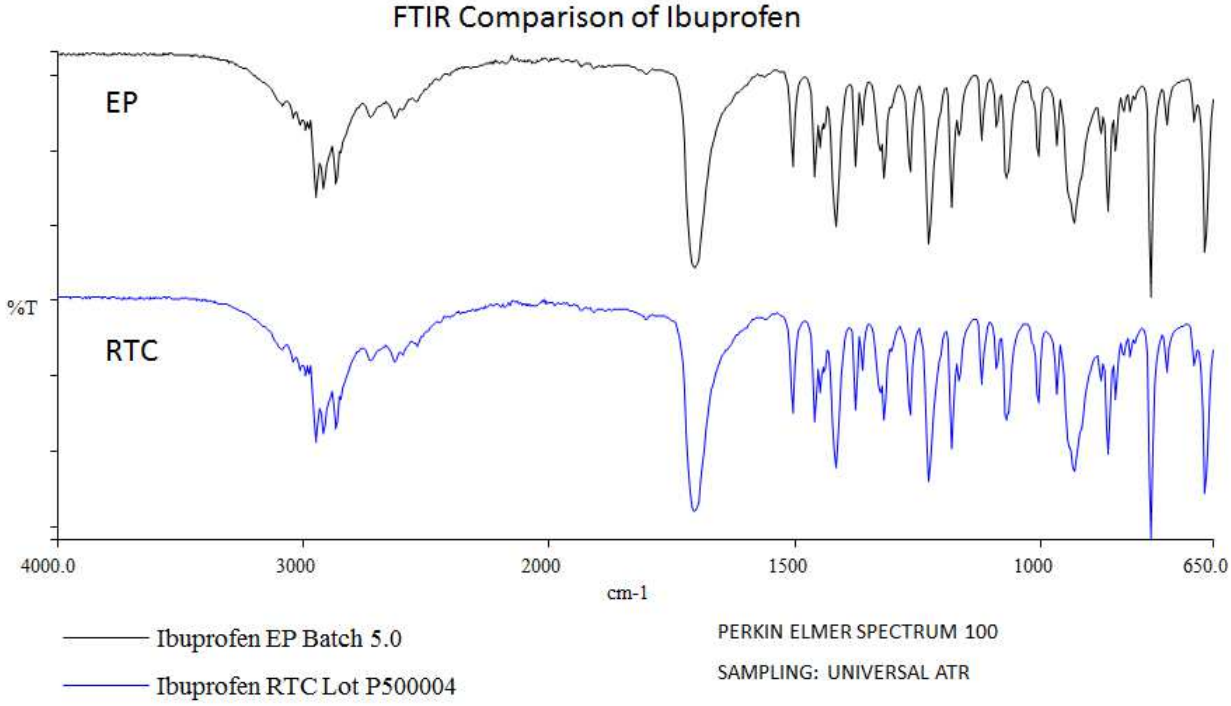
CERTIFIED PURITY BY MASS BALANCE [100% - Impurities (normalized)]

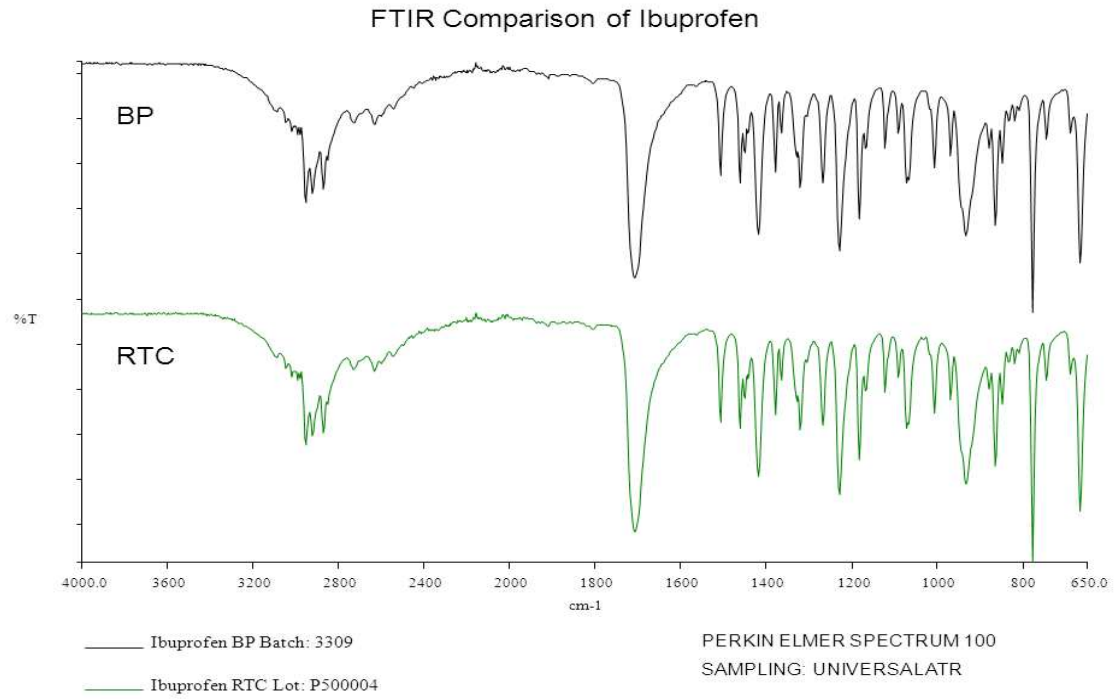
99.9% U_{crm} = ±0.1%, k = 2
(as is basis)

IDENTIFICATION TESTS

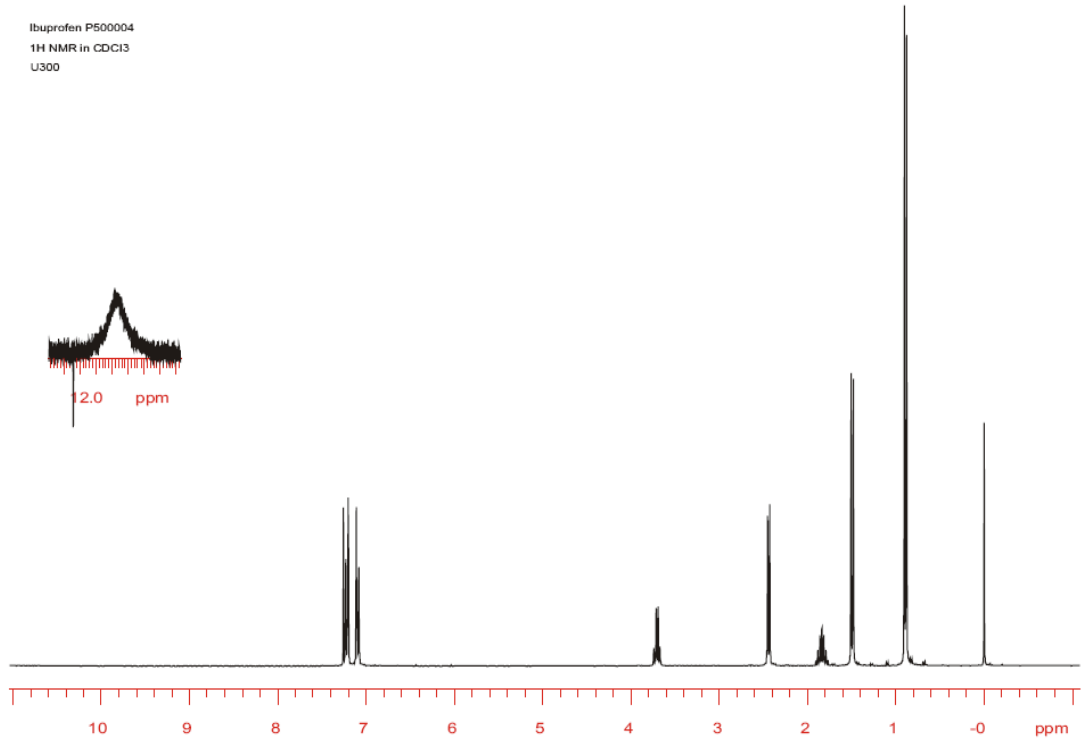
INFRARED SPECTROPHOTOMETRY (Comparative identification analysis demonstrates direct traceability to Pharmacopeial standards)







^{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	75.69	75.47	75.49	75.48
H	8.80	8.88	8.79	8.84

MELTING RANGE

Specification: 75-78°C (EP)
Mettler Toledo FP900 Thermosystem with FP81 Measuring Cell
Mean of nine measurements = **75.0 – 75.3 °C**

OPTICAL ROTATION

Specification: Specific Rotation: -0.05 to +0.05 (EP)
Perkin Elmer Polarimeter 343
Wavelength: 589 nm
Concentration: 0.025 g/mL
Cell Path: 100 mm
Mean of three Measurements, Specific Rotation = **-0.0137**

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: ~120mg

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.

General Manager, Pharmaceutical Standards Operations