Certificate of Analysis

Reference Material

Ibuprofen EP Impurity F
Part.Number: CB3002.32
Lot.Number: XXV-IV00042

Certificate of Analysis

Reference Material

Product name
Ibuprofen EP Impurity F

IUPAC / Chemical name
3-[4-(2-methylpropyl)phenyl]propanoic acid

Catalogue number
CB3002.32

Long-term storage
+5°C, dark and dry (slightly hygroscopic)

CAS number
65322-85-2

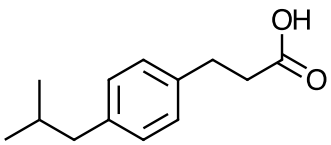
Shipping conditions
Room Temperature

Appearance
White, Solid

Lot number
XXV-IV00042

Molecular weight
206.28 g/mol

Molecular formula
$C_{13}H_{18}O_2$



Analytical Information

Test description		Specifications	Results
Identity	(^{1}H, ^{13}C) NMR	Conforms to Structure	Structure confirmed
	FTIR	Conforms to Structure	Structure confirmed
	HRMS	Conforms to Structure	Structure confirmed
Purity	HPLC (214 nm)	>97%	99.44%
Others	Elemental Analysis (EA)	Conforms	Conforms
Assay (Mass Balance)	100% - Formula	>95%	99,34%

Release date 06/2025

Retest date 04/2028

Prepared by
Analytical Services

Approved by
Quality Assurance

Klivon Scientific
Avenida Jacques Delors, 411, Taguspark, Edifício Inovação 2
2740-122, Oeiras, Portugal

+351 300-305-540

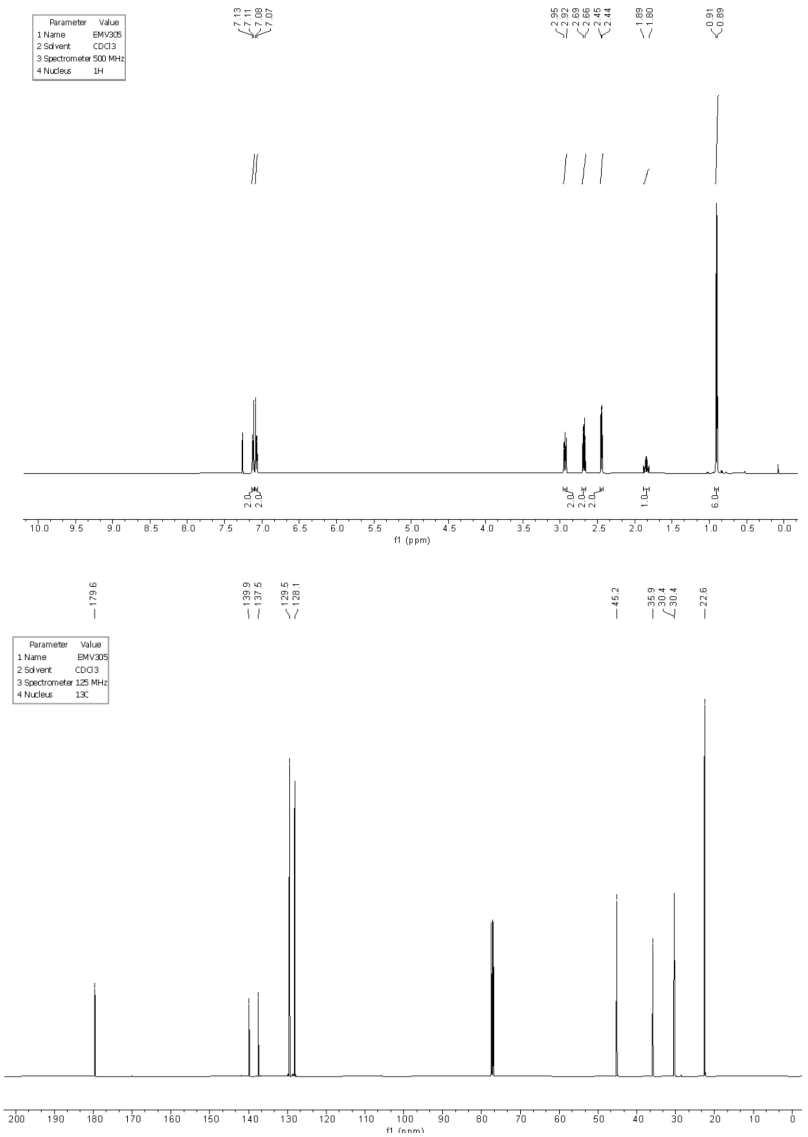
www.klivon.com

Identity Assessment

The structure of the Ibuprofen EP Impurity F sample under analysis was confirmed by (^{1}H, ^{13}C) NMR, FTIR and HRMS.

(^{1}H, ^{13}C) NMR

Equipment	Bruker AVANCE 500 Nuclear Magnetic Resonance Spectrometer
^{1}H and ^{13}C NMR conditions	500 MHz, $CDCl_3$

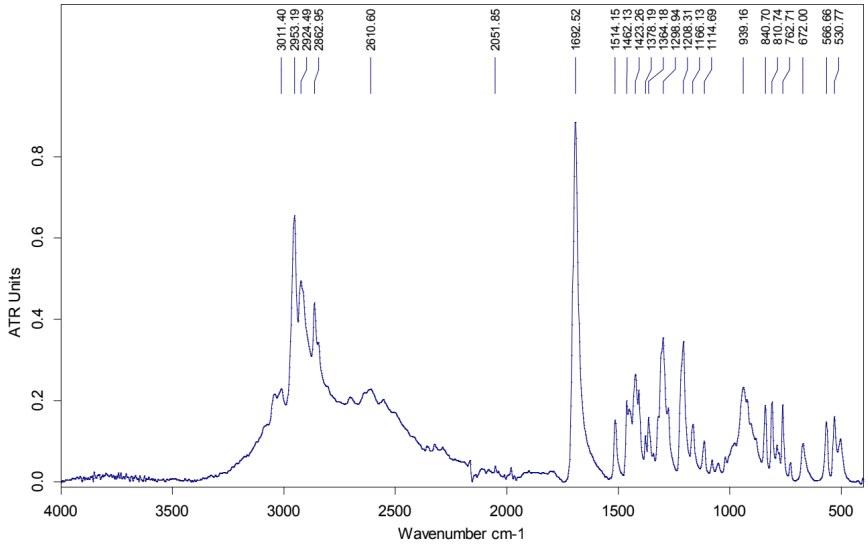


Remarks

^{1}H-NMR (500 MHz) and ^{13}C-NMR/DEPT-135 (125 MHz) in CDCl3: confirm structure. No residual solvents are detected by NMR (no volatile contents are present).

FTIR

Description	Bruker Vector 22
Spectral Range	4000-400 cm^{-1}
Number of scans	100

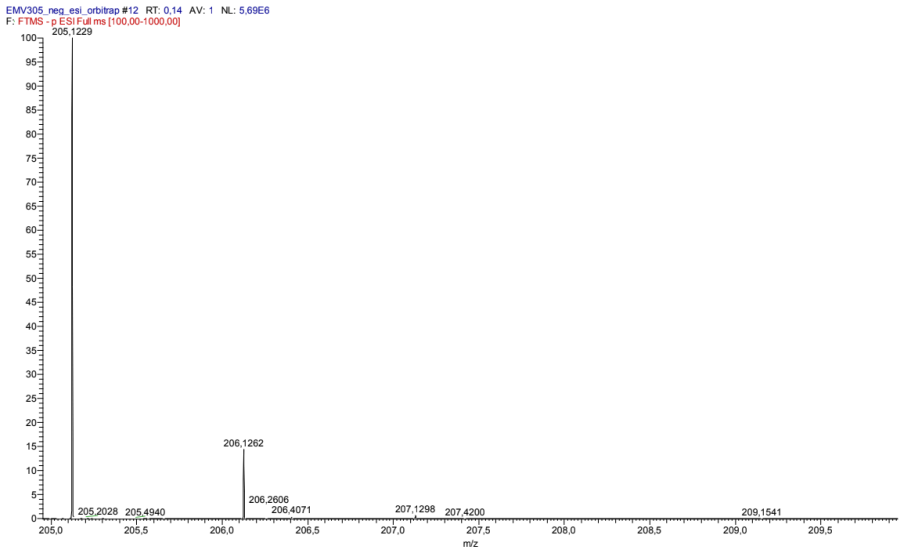


Band (cm^{-1})	Assignment	Comments
2953	–CH3	C–H symmetrical and asymmetrical stretch (methyl –CH3 groups
1693	–C=O	–C=O stretch (carboxylic acid)
1423	–C=C (aromatic)	C=C stretch (benzene ring)
1299	–C=C (aromatic)	C=C stretch (benzene ring)
1208	–C=C (aromatic)	C–H in-plane bend (benzene ring)
939	–C=C (aromatic)	C–H out-of-plane bend (benzene ring)
811	–C=C (aromatic)	C–H out-of-plane bend (benzene ring)

Remarks
The bands obtained in the FTIR spectrum are compatible with the main functional groups present in the molecule.

HRMS

Equipment	LTQ-Orbitrap Discovery Mass Spectrometer
Conditions	ESI-, Ion Spray Voltage 4.5 kV, Dry Heater 200 ºC



Expected mass (m/z)	Observed monoisotopic mass (m/z)	For. Mol.	Ion type	Error (ppm)
205.1234	205.1229	$C_{13}H_{17}O_2$	$[M - H]^-$	-0.503

Remarks

Negative HRMS-ESI spectrum exhibits a major signal at m/z = 205.1229, that is compatible with the expected structure of the compound.

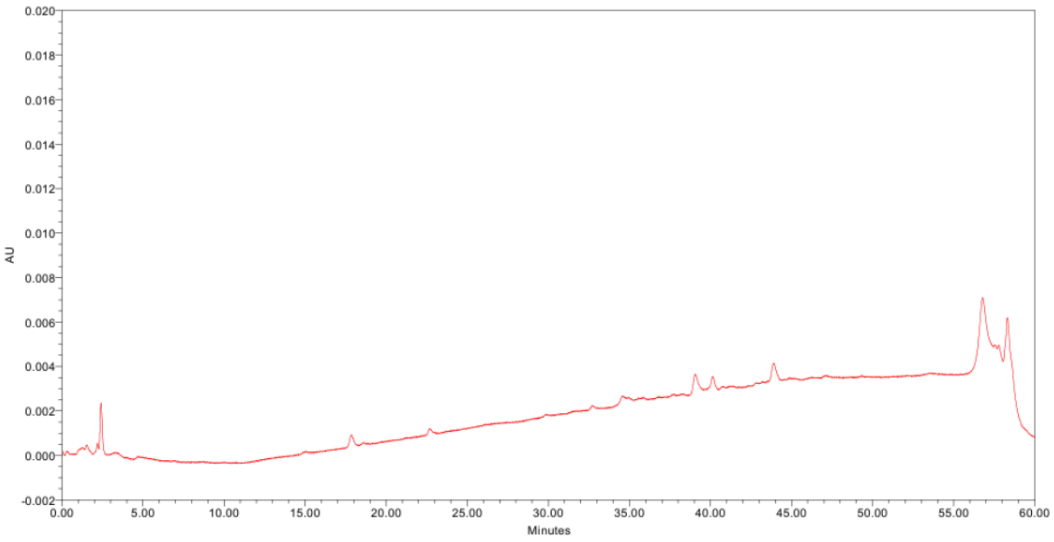
Purity Confirmation

The purity of the analyte was confirmed by HPLC (214 nm).

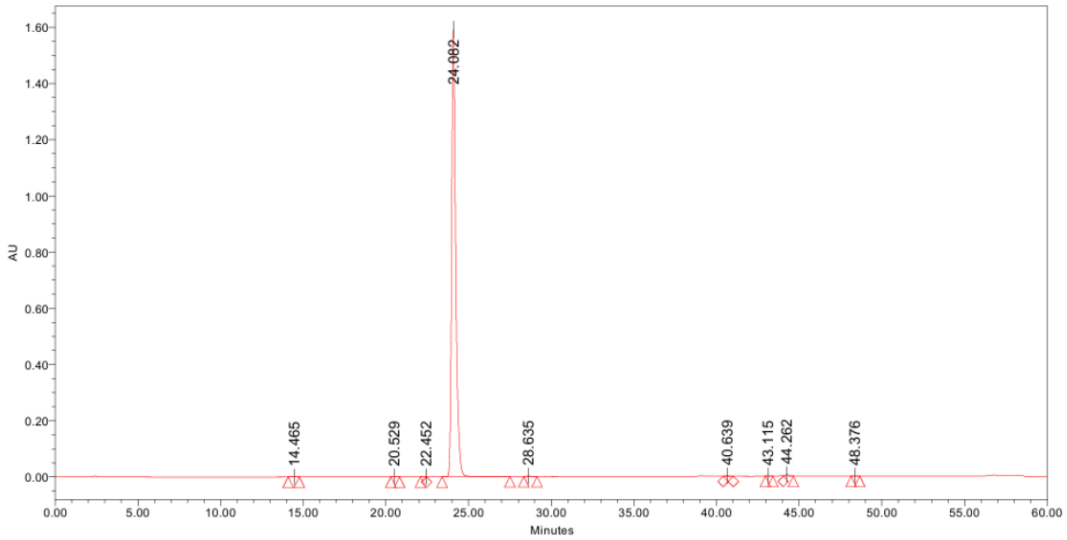
HPLC (214 nm)

Sample Preparation	0.4mg/ml dissolved in H2O:ACN (1:1) mixture
Column	XSelect HSS T3, 150 x 2.1 mm, 3.5 µm
Column Temperature	25 °C
Detector	UV, 245nm
Injection Volume	5 µL
Flow rate	0.2 mL/min
Mobile Phase A	H_3PO_4 0.05% in Water
Mobile Phase B	Acetonitrile
Gradient Program	0-5 min (Phase A/Phase B - (65:35); 5-40 min (Phase A/Phase B) (10:90); 40-50 min (Phase A/Phase B) (10:90); 50-51 min (Phase A/Phase B) (65:35); 51-60 min (Phase A/Phase) B (65:35)

Blank Chromatogram



Analyte Chromatogram



Sample name	RT (min)	Area (AU.min.)	% Area
Ibuprofen EP Impurity F	24.08	-	99.44

Result (n=3)	99%; SD=0%

Remarks
The HPLC purity by relative integration obtained for Ibuprofen impurity F is 99.44%

Others

This section encompasses a set of analytical techniques that support the analysis that were performed for identification and purity of the compound under evaluation.

Elemental Analysis (EA)

	% C	% H
calculated	75.69	8.80
Found	75.67	8.56

Remarks
The sample Ibuprofen impurity F meets the elemental analysis. All deviations are less than 0.4% (maximum permissible). Therefore, the analyzed sample does not contain water, solvents or inorganic impurities (salts), which would lead to a breach of the theoretical percentages of CH.

100% - Formula

The Mass Balance (100% Formula) has been applied to determine the assay value of the compound and was calculated using the following formula:

$$\text{Assay (\%)} = (100\,\% - \text{volatile contents (\%)}) \times \frac{\text{Purity (\%)}}{100}$$

Analytical technique	Result
HPLC	99.44
KF	0.10
Assay (%)	99.34

Remarks
The result of assay (Mass Balance method) is 99.34% considering the amount of water obtained in KF analysis - 0.1%, that was subtracted to the HPLC purity value.

Final Remarks
All analytical data are consistent with the structure of the expected compound. The HPLC purity by relative integration obtained for Ibuprofen impurity F (batch EMV305) is 99.44%. The result of assay (Mass Balance method) is 99.34% and the result of Carbon Titration method is 99.97%. The verified result lies inside the acceptance criteria, i.e. less than 1.0 % difference to the Mass Balance method and Carbon Titration method.