AOAC SMPR® 2019.002

Standard Method Performance Requirements (SMPRs®) for Identification and Quantitation of Selected Residual Solvents in Cannabis-Derived Materials

Intended Use: Consensus-Based Reference Method

1 Purpose

AOAC SMPRs describe the minimum recommended performance characteristics to be used during the evaluation of a method. The evaluation may be an on-site verification, a single-laboratory validation, or a multi-site collaborative study. SMPRs are written and adopted by AOAC composed of representatives from the industry, regulatory organizations, contract laboratories, test kit manufacturers, and academic institutions. AOAC SMPRs are used by AOAC expert review panels in their evaluation of validation study data for method being considered for *Performance Tested Methods*℠ certification or AOAC *Official Methods of Analysis*℠ adoption and can be used as acceptance criteria for verification at user laboratories.

2 Applicability

Method, or a suite of methods, to identify and quantify selected residual solvents (Table 1) in cannabis derivatives.

3 Analytical Technique

Any analytical technique(s) that measures the analytes of interest and meets the following method performance requirements is/are acceptable. More than one analytical technique may be needed.

4 Definitions

Cannabis plant material.—Plant material from *Cannabis* spp. and its chemical varieties or "chemovars."

Cannabis derivatives.—Products or extracts derived from cannabis plant material.

Limit of detection (LOD).—Minimum concentration or mass of analyte in a given matrix that can be detected. A minimum 3 to 1 signal to background noise ratio (S/N).

Limit of quantitation (LOQ).—Minimum concentration or mass of analyte in a given matrix that can be reported as a quantitative result. A minimum 10 to 1 S/N.

Parts per million (ppm).—mg of analyte per kg of cannabis derivatives.

Quantitative method.—Method of analysis where response is the amount of the analyte measured either directly (enumeration in a mass or a volume), or indirectly (color, absorbance, impedance, etc.) in a certain amount of sample.

Recovery.—Fraction or percentage of spiked analyte that is recovered when the test sample is analyzed using the entire method.

Repeatability.—Variation arising when all efforts are made to keep conditions constant by using the same instrument and operator and repeated on individually prepared sample/test portions. Expressed as the repeatability standard deviation (SD_r); or % repeatability relative standard deviation (%RSD_r).

Reproducibility.—Standard deviation or relative standard deviation calculated from among-laboratory data. Expressed as the reproducibility standard deviation (SD_R); or % reproducibility relative standard deviation (% RSD_R).

5 Method Performance Requirements

See Table 2.

6 System Suitability Tests and/or Analytical Quality Control

Suitable methods will include blank check samples, and check standards at the lowest point and midrange point of the analytical range.

7 Reference Material(s)

Refer to Annex F: *Development and Use of In-House Reference Materials* in Appendix F: *Guidelines for Standard Method Performance Requirements*, *Official Methods of Analysis of AOAC INTERNATIONAL* (2019) 21st Ed., AOAC INTERNATIONAL, Rockville, MD, USA. Available at: http://www.eoma.aoac.org/app_f.pdf

8 Validation Guidance

<467> Residual Solvents, USP Dietary Supplements (2016)

International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use. Impurities: Guideline for Residual Solvents Q3C (R6) (2016). Available at www.ich.org

Appendix D: *Guidelines for Collaborative Study Procedures to Validate Characteristics of a Method of Analysis, Official Methods of Analysis of AOAC INTERNATIONAL* (2019) 21st Ed., AOAC INTERNATIONAL, Rockville, MD, USA. Available at: http://www.eoma.aoac.org/app_d.pdf

Appendix F: *Guidelines for Standard Method Performance Requirements, Official Methods of Analysis of AOAC INTERNATIONAL* (2019) 21st Ed., AOAC INTERNATIONAL, Rockville, MD, USA. Available at: http://www.eoma.aoac.org/app_f.pdf

Appendix K: *Guidelines for Dietary Supplements and Botanicals, Official Methods of Analysis of AOAC INTERNATIONAL* (2019) 21st Ed., AOAC INTERNATIONAL, Rockville, MD, USA. Available on line at: http://www.eoma.aoac.org/app_k.pdf

U.S. Food and Drug Administration (May 2018) *Bioanalytical Method Validation Guidance for Industry*

9 Maximum Time-to-Result

None

Approved by attending stakeholders of the AOAC Cannabis Analytical Science Program (CASP) meeting on September 7, 2019. Final Version Date: October 3, 2019.

Posted: October 9, 2019

Table 1. Residual solvents and targeted LOQs

Residual solvents[a]	Proposed target LOQ, ppm	Analytical range Lower (≤ ppm)	Analytical range Upper (ppm)
	Class 1		
Benzene	2	1	60
Carbon tetrachloride	4	2	120
1,2-Dichloroethane	5	2.5	150
1,1-Dichloroethene	8	4	240
1,1,1-Trichloroethane	1500	750	45000
	Class 2		
Acetonitrile	6	3	180
Chlorobenzene	360	180	10800
Chloroform	60	30	1800
Cumene	70	35	2100
Cyclohexane	3880	1940	116400
1,2-Dichloroethene	1870	935	56100
1,2-Dimethoxyethane	100	50	3000
N,N-dimethylacetamide	1090	545	32700
N,N-dimethylformamide	880	440	26400
1,4-Dioxane	380	190	11400
2-Ethoxyethanol	160	80	4800
Ethylene glycol	620	310	18600
Formamide	220	110	6600
Hexane	290	145	8700
n-Hexane			
Methanol	400	200	12000
2-Methoxyethanol	50	25	1500
Methylbutylketone	50	25	1500
Methylcyclohexane	1180	590	35400
Methylene chloride	600	300	18000
N-Methylpyrrolidone	530	265	15900
Nitromethane	50	25	1500
Pyridine	200	100	6000
Sulfolane	160	80	4800
Tetrahydrofuran	720	360	21600
Tetralin	100	50	3000
Toluene	30	15	900
Trichloroethylene	80	40	2400
Xylene	2170	1085	65100
m,p-Xylenes			
	Class 3		
Acetic acid	5000	2500	150000
Acetone	1000	500	30000
Anisole	5000	2500	150000
1-Butanol	5000	2500	150000
2-Butanol	5000	2500	150000
Butyl acetate	5000	2500	150000
tert-Butylmethyl ether	5000	2500	150000
Dimethyl sulfoxide	5000	2500	150000
Ethanol	1000	500	30000
Ethyl acetate	5000	2500	150000
Ethyl ether	5000	2500	150000
Ethyl formate	5000	2500	150000
Formic acid	5000	2500	150000
Heptane	5000	2500	150000
Isobutyl acetate	5000	2500	150000
Isopropyl acetate	5000	2500	150000
Methyl acetate	5000	2500	150000
3-Methyl-1-butanol	5000	2500	150000
Methylethylketone	5000	2500	150000
Methylisobutylketone	5000	2500	150000
2-Methyl-1-propanol	5000	2500	150000
Pentane	5000	2500	150000
1-Pentanol	5000	2500	150000
1-Propanol	5000	2500	150000
2-Propanol	5000	2500	150000
Isopropanol (2-propanol)			
Propyl acetate	5000	2500	150000
	Additional		
Butane (sum of *n*- and iso-)	5000	2500	150000
Propane	12	6	360
2,2-Dimethylbutane	290	145	8700
2,3-Dimethylbutane	290	145	8700
2-Butanone	5000	2500	150000
2-Methylbutane	5000	2500	150000
2-Methylpentane	290	145	8700
3-Methylpentane	290	145	8700
Ethylbenzene	2170	1085	65100
Ethylene oxide	50	25	1500
Isobutane (methyl propane)	12	6	360
n-Butane	12	6	360
n-Heptane	1000	500	30000
n-Pentane	1000	500	30000
Nitrogen	0	0	
o-Xylene	10	5	300
Triethylamine	5000	2500	150000

[a] USP Guidance (467) Residual Solvents.

Table 2. Method performance requirements for residual solvents in Table 1

Parameter	Analytical range, ppm 1–100	100–500	500–1000	>1000
Recovery, %	60–120	90–107	95–105	97–103
RSD_r, %	≤20	≤5	≤4	≤3
RSD_R, %	≤30	≤8	≤6	≤4