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QUALIFICATION OF EQUIPMENT ANNEX 7: QUALIFICATION OF MASS SPECTROMETERS

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**ANNEX 7 OF THE OMCL NETWORK GUIDELINE
“QUALIFICATION OF EQUIPMENT”**

**7.1: QUALIFICATION OF GAS CHROMATOGRAPHY-MASS SPECTROMETERS
WITH ELECTRON IMPACT IONIZATION (GC-EI-MS)**

Introduction

The present document is the first part of the 7th Annex of the core document “Qualification of Equipment”, and it should be used in combination with it when planning, performing and documenting the qualification process of GC-EI-MS.

The core document contains the Introduction and general forms for Level I and II of qualification, which are common to all type of instruments.

The present annex contains instrument-related recommendations on parameters to be checked at Level III and IV of qualification and the corresponding typical acceptance limits, as well as practical examples on the methodology that can be used to carry out these checks.

TABLE III**Level III. Periodic and motivated instrument checks****Minimum requirements for GC-EI-MS (examples)**

Parameter to be checked	Typical tolerance limits
Mass accuracy PFTBA (FC-43) ^{*)} or internal calibration gas	$m/z = 69 \pm 0.5$ $m/z = 219 \pm 0.5$ $m/z = 502 \pm 0.5$ or defined masses of internal calibration gas ± 0.5
Linearity ^{**)}	$r^2 \geq 0.995$
System/instrument precision ^{**)}	$\leq 10.0\%$

^{*)} PFTBA (FC-43): Perfluoro-tributyl-amine (CAS NO.: 311-89-7)

^{**)} In case of quantification purposes, these parameters have to be checked.

TABLE IV

Level IV. In-use instrument checks

Requirements for GC-EI-MS

Parameter to be checked	Typical tolerance limits
As defined by the specific analysis method or according to the Ph. Eur. or the MAH dossier (see examples in Level IV, Annex II)	Identified by library or with reference standard

ANNEX I

Level III. Periodic and motivated instrument checks

This Annex contains **practical examples** of tests and their associated tolerance limits for several parameters related to the performance of GC-EI-MS.

These **examples** can be considered by the OMCLs as possible approaches to perform the Level III of the equipment qualification process: “Periodic and motivated instrument checks”.

GENERAL CONSIDERATIONS

- GC-MS is mainly used for the identification of unknown substances or quantification of low concentrated substances where high specificity is needed.

MASS ACCURACY

Materials:

PFTBA (FC-43) or internal calibration gas

Method:

Internal instrument check or spectrum of PFTBA (FC-43) in full scan mode

Limits:

$$m/z = 69 \pm 0.5$$

$$m/z = 219 \pm 0.5$$

$$m/z = 502 \pm 0.5$$

Note: the tolerance limits for mass accuracy are only valid for quadrupole and ion trap mass spectrometers. Instruments like Time-of-Flight (TOF) or hybrid instruments like quadrupole-Time-of-Flight (QTOF) have a much better mass accuracy and adequate requirements should be applied by the laboratory.

LINEARITY

Materials:

Stock solutions: 1-Octanol in dichloromethane 0.2, 0.4, 0.6, 0.8, 1.0 $\mu\text{L}/\text{mL}$

Method:

2 injections of each level (injection volume: 1.0 μL)

Limits:

$$r^2 \geq 0.995$$

SYSTEM/INSTRUMENT PRECISION

Materials:

Stock solution: 1-Octanol in dichloromethane 1.0 $\mu\text{L}/\text{mL}$

Method:

6 injections (injection volume: 1.0 μL)

Limits (minimum requirement):

$$\text{RSD} \leq 10.0\% \text{ (without internal standard)}$$

ANNEX II

Level IV. In-use instrument checks

This Annex contains **practical examples** of tests and their associated tolerance limits for several parameters related to the performance of GC-EI-MS.

These **examples** can be considered by the OMCLs as possible approaches to perform the Level IV of the equipment qualification process: “In-use instrument checks”.

IDENTIFICATION^{*)}

Materials:

Papaverine 20.0 µg/mL in methanol, Caffeine 10.0 µg/mL in methanol or another compound chosen according to the specific method

Method:

Identification by library

Limits:

Positive

^{*)} only in case of use of library identification

SYSTEM/INSTRUMENT PRECISION ^{**)}

Materials:

Any of the above-mentioned reference standard solutions used for the identification

Method:

6 injections (injection volume: 1.0 µL)

Limits (minimum requirement):

RSD ≤ 10.0%

^{**)} in case of use for quantification

Other tests according to the system suitability of the analysis method in use.

7.2 QUALIFICATION OF LIQUID CHROMATOGRAPHY-MASS SPECTROMETERS (LC-MS)*

Introduction

The present document is the second part of the 7th Annex of the core document “Qualification of Equipment”, and it should be used in combination with it when planning, performing and documenting the qualification process of LC-MS*.

The core document contains the Introduction and general forms for Level I and II of qualification, which are common to all type of instruments.

The present annex contains instrument-related recommendations on parameters to be checked at Level III and IV of qualification and the corresponding typical acceptance limits, as well as practical examples on the methodology that can be used to carry out these checks.

* Ionisation sources include:

ESI: Electrospray Ionisation

APCI: Atmospheric Pressure Chemical Ionisation

APPI: Atmospheric Pressure Photo-Ionisation

TABLE III**Level III. Periodic and motivated instrument checks****Minimum requirements for LC-MS (examples)****For positive mode:**

Parameter to be checked	Typical tolerance limits
Mass accuracy Reserpine	$m/z = 609 \pm 0.5$
Fragmentation of $m/z = 609$ without fragmentation energy ^{*)}	$m/z = 609 \pm 0.5$
Fragmentation of $m/z = 609$ with fragmentation energy ^{*)}	$m/z = 448 \pm 0.5$ (most intense fragment)

^{*)} only for instruments with MS/MS capabilities.

For negative mode:

Parameter to be checked	Typical tolerance limits
Mass accuracy Acid Red 4 ^{**)}	$m/z = 357 \pm 0.5$
Fragmentation of $m/z = 357$ without fragmentation energy ^{*)}	$m/z = 357 \pm 0.5$
Fragmentation of $m/z = 357$ with fragmentation energy ^{*)}	$m/z = 170 \pm 0.5$ (most intense fragment)

^{*)} only for instruments with MS/MS capabilities.

^{**)} Acid Red 4, CAS NO.: 5858-39-9.

Note: The minimum requirements must correspond to the ionisation source used.

TABLE IV

Level IV. In-use instrument checks

Requirements for LC-MS

Parameter to be checked	Typical tolerance limits
As defined by the specific analysis method or according to the Ph. Eur. or the MAH dossier	As defined in the used analysis method

The tests to be performed in Level IV are those in accordance with the system suitability of the analysis method in use.

ANNEX I

Level III. Periodic and motivated instrument checks

This Annex contains **practical examples** of tests and their associated tolerance limits for several parameters related to the performance of LC-MS.

These **examples** can be considered by the OMCLs as possible approaches to perform the Level III of the equipment qualification process: “Periodic and motivated instrument checks”.

GENERAL CONSIDERATIONS

- LC-MS is widely used for the identification of unknown substances or quantification of low concentrated substances where high specificity is needed.

MASS ACCURACY

Materials:

Reserpine

Note: the selected concentration will depend on the instrument and experimental conditions. The laboratory should define the appropriate concentration. The following concentration may be used: 0.01mg/mL in methanol/water = 60/40

Method:

Direct infusion or flow injection

Limits:

As defined in Table III: “Minimum requirements for LC-MS”

Note: the tolerance limits for mass accuracy are only valid for quadrupole and ion trap mass spectrometers. Instruments like Time-of-Flight (TOF) or hybrid instruments like quadrupole-Time-of-Flight (QTOF) have a much better mass accuracy and adequate requirements should be applied by the laboratory.

ANNEX II

Level IV. In-use instrument checks

As defined by the specific analysis method or according to the Ph. Eur. or the MAH dossier.

REFERENCES

(For all references, the latest version applies)

- 1) Ph. Eur. (2.2.43. MASS SPECTROMETRY).