

# General European OMCL Network (GEON) QUALITY MANAGEMENT DOCUMENT

**PA/PH/OMCL (10) 86 R6**

## QUALIFICATION OF EQUIPMENT ANNEX 7: QUALIFICATION OF MASS SPECTROMETERS

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<b>Concerned Network</b>	GEON

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

**QUALIFICATION OF MASS SPECTROMETERS**

*Note: Mandatory requirements in this guideline and its annexes are defined using the terms «shall» or «must». The use of «should» indicates a recommendation. For these parts of the text other appropriately justified approaches are acceptable. The term «can» indicates a possibility or an example with non-binding character.*

**Introduction**

The present document is the 7<sup>th</sup> Annex of the core document “Qualification of Equipment” and it shall be used in combination with it when planning, performing and documenting the qualification process of Mass Spectrometers coupled with Chromatographic equipment.

The core document “Qualification of Equipment” contains the introduction and general forms for Level I and II of qualification, which are common to all type of instruments.

The present Annex 7 contains a general introduction and requirements for GC-EI-MS and LC-ESI-MS.

Level III and IV qualifications must be carried out being an ISO 17025 requirement.

Requirements and (if applicable) corresponding typical acceptance limits given in bold should be applied, however other appropriately justified deviations are acceptable provided they are traceable.

Exemplary procedures provided in Annexes have non-binding character. They can be helpful to carry out the required qualification. Nevertheless, other procedures can be applied depending on the model of the MS equipment.

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

TABLE I

### Level III. Periodic and motivated instrument checks

#### GC-EI-MS

Requirements and related typical acceptance limits are indicated in bold.

Parameter to be checked	Typical acceptance limits*
<b>Mass accuracy</b> (PFTBA ** (FC-43) or internal calibration gas)	$m/z = 69.0 \pm 0.5$ $m/z = 219.0 \pm 0.5$ $m/z = 502.0 \pm 0.5$
<b>Linearity</b> ***	Limit to be set up based on OMCL experience/service provider instructions and type of regression mode chosen
<b>System/instrument precision</b> ***	<b>RSD <math>\leq 10.0</math> %</b>

\*Other figures given under column of “typical acceptance limits” are typical values obtained when applying the exemplary procedures provided in annexes, therefore these values are not binding.

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

\*\*\* To be checked when quantification is requested.

**TABLE II**

**Level IV. In-use instrument checks**

**GC-EI-MS**

**Requirements and related typical acceptance limits are indicated in bold.**

<i>Parameter to be checked/ Typical acceptance limits</i>
According to specific analysis method or Ph. Eur. monograph or MAH dossier (see examples in Level IV, Annex II)

### Level III. Periodic and motivated instrument checks

This Annex contains practical exemplary procedures for several parameters related to the qualification 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”.

However, alternative procedures can be applied.

GENERAL CONSIDERATION: 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:*

As defined in Table I

#### LINEARITY

*Materials:*

Stock solutions: 1-Octanol in methanol at concentrations of 0.2, 0.4, 0.6, 0.8, 1.0 µL/mL

*Method:*

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

*Limits:*

Limit to be set up by OMCL based on experience and type of regression mode chosen

NOTE: Linearity is typically performed in SIM/MRM, since this mode is normally applied for quantification of analytes in low concentration.

#### SYSTEM/INSTRUMENT PRECISION

*Materials:*

Stock solution: 1-Octanol in methanol at concentration of 1.0 µL/mL

*Method:*

Injection volume: 1.0 µL (6 injections)

*Limits:*

RSD ≤ 10.0 % on peak area (without internal standard)

**Level IV. In-use instrument checks**

IDENTIFICATION (by mass spectral library)

*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 mass spectral library

*Limits:*

Match reference spectra

SYSTEM/INSTRUMENT PRECISION \*\*

*Materials:*

See identification

*Method:*

Injection volume: 1.0 µL (6 injections)

*Limits:*

RSD ≤ 10.0 % on peak area

\*\* to be checked when performing quantification testing

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

Ionisation sources of Mass Spectrometry include:

ESI: Electrospray Ionisation

APCI: Atmospheric Pressure Chemical Ionisation

APPI: Atmospheric Pressure Photo-Ionisation

**TABLE III**

### Level III. Periodic and motivated instrument checks

#### LC-ESI-MS

Requirements and related typical acceptance limits are indicated in bold.

**IDENTIFICATION** - Positive mode:

<b>Parameter to be checked</b>	<b>Typical acceptance limits (Low Resolution MS)*</b>	<b>Typical acceptance limits (High Resolution MS)*</b>
<b>Mass accuracy (Reserpine)</b>	$m/z = 609.3 \pm 0.5$	<b><math>\pm 5.0</math> ppm</b>
<b>Mass accuracy of fragments** (Reserpine)</b>	$m/z = 448.2 \pm 0.5$ $m/z = 195.1 \pm 0.5$	<b><math>\pm 5.0</math> ppm</b> <b><math>\pm 5.0</math> ppm</b>
<b>Resolution</b>	See Annex III	See Annex III

\*\* only for instruments with MS/MS capabilities.

**IDENTIFICATION** - Negative mode:

<b>Parameter to be checked</b>	<b>Typical acceptance limits (Low Resolution MS)*</b>	<b>Typical acceptance limits (High Resolution MS)*</b>
<b>Mass accuracy</b> (Chloramphenicol <sup>**</sup> )	m/z = 321.0 ± 0.5	± 5.0 ppm
<b>Mass accuracy of fragments</b> <sup>***</sup> (Chloramphenicol)	m/z = 152.0 ± 0.5	± 5.0 ppm
<b>Resolution</b>	See Annex III	See Annex III

\* Other figures given under column of “typical acceptance limits” are typical values obtained when applying the exemplary procedures provided in annexes, therefore these values are not binding.

\*\* Chloramphenicol, CAS NO.: 56-75-7.

\*\*\* only for instruments with MS/MS capabilities.

**QUANTIFICATION:**

Check following parameters both in positive and negative modes:

<b>Parameter to be checked</b>	<b>Typical acceptance limits</b>
<b>Linearity</b>	Limit to be set up based on OMCL experience/service provider instructions and type of regression mode chosen
<b>System/instrument precision</b>	<b>RSD ≤ 5.0 %</b>
<b>Carry over:</b>	<b>≤ 1.0 %</b>



**TABLE IV**

**Level IV. In-use instrument checks**

**Requirements for LC-ESI-MS**

<i>Parameter to be checked/ Typical acceptance limits</i>
According to specific analysis method or Ph. Eur. monograph or MAH dossier

## ANNEX III

### Level III. Periodic and motivated instrument checks

This Annex contains practical exemplary procedures for several parameters related to the performance of LC-ESI-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”.

However, alternative procedures can be applied.

GENERAL CONSIDERATION: 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:*

ESI positive: Reserpine at concentration of 0.01 mg/mL in methanol/water (60/40 V/V)\*

ESI negative: Chloramphenicol at concentration of 0.01 mg/mL in methanol containing 0.1% of formic acid\*.

\*Note: concentrations should be selected depending on the instrument and experimental conditions to be applied

##### *Method:*

Direct infusion or flow injection

##### *Limits:*

As defined in Table III.

#### RESOLUTION:

Procedure to be followed depends on the instrument. Instructions to check resolution can be provided by service supplier/ instrument manual.

#### LINEARITY

##### *Materials:*

Solutions as mixture of betamethasone-17,21-dipropionate and betamethasone-17-valerate in methanol at concentrations of 0.002, 0.004, 0.006, 0.008, 0.01 mg/mL

##### *Method:*

Column: BEH-C18 1.7  $\mu$ m 50 x 2.1 mm or equivalent  
Suitable gradient of acetonitrile/water containing 0.1 % formic acid

Injection volume: 1.0  $\mu$ L (2 injections at each concentration)

*Limits:*

Limit to be set up based on OMCL experience/service provider specifications and type of regression mode chosen

SYSTEM/INSTRUMENT PRECISION

*Materials:*

Solution as mixture of betamethasone-17, 21-dipropionate and betamethasone-17-valerate in methanol at concentration of 0.006 mg/mL.

*Method:*

Injection volume: 1.0 µL (6 injections)

*Limits:*

RSD ≤ 5.0 % on peak area

CARRY OVER

*Materials:*

- Solution as mixture of betamethasone 17, 21-dipropionate and betamethasone 17-valerate in methanol at concentration of 0.002 mg/mL.
- Methanol (blank)

*Method:*

Injection volume: 1.0 µL

*Limits:*

The percentage of the peaks corresponding to betamethasone-17,21-dipropionate and betamethasone 17-valerate in the blank (injected after 0.002 mg/mL solution) does not exceed 1.0 % of the area of said peaks in the chromatogram obtained injecting 0.002 mg/mL solution of betamethasone-17,21-dipropionate and betamethasone 17-valerate.

## REFERENCES

(For all references, the latest version applies)

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