LTQ LC/MS Performance Monitoring and Maintenance

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1 INTRODUCTION

This document addresses the performance monitoring and maintenance of the LTQ LC/MS system consisting of a Thermo Electron LTQ Mass Spectrometer (MS) and a Liquid Chromatograph (LC). The LTQ system is comprised of a Shimadzu LC and a Thermo Electron Linear Ion Trap LTQ MS. The instrument is configured with an API source that is capable of electrospray ionization (ESI), atmospheric pressure chemical ionization (APCI), or atmospheric pressure photoionization (APPI). The instrument is primarily used in ESI mode. However, it can be used for APCI or APPI provided the method of ionization is clearly labeled in the resulting data and documentation. Definitions and guidelines are outlined in IOSS-701.

2 SCOPE

This document applies to personnel using the associated instrument(s)/equipment in the following disciplines/subdisciplines: General Chemistry, Explosives Chemistry, and Seized Drugs.

3 EQUIPMENT

- Instrumentation
  - Thermo Electron LTQ MS, API Source, and Xcalibur software (or equivalent)
  - Shimadzu Prominence LC (or equivalent)
- Materials
  - Nitrogen, 99.99% (high purity or equivalent)
  - Helium, 99.99% (high purity or equivalent)
  - Methanol (Optima grade or equivalent)
  - Deionized Water, 18.2 MΩ·cm (Milli-Q or equivalent)
  - Acetone (HPLC grade or equivalent)
  - Ammonium Nitrate (NH_4NO_3) (reagent grade or equivalent)
  - Ammonium Hydroxide (NH_4OH) (reagent grade or equivalent)
  - Caffeine (Sigma or equivalent)
  - Codeine (Sigma or equivalent)
  - Brucine (Sigma or equivalent)
  - Reserpine (Sigma or equivalent)

Redacted

  - 10 µL LC syringe (Hamilton or equivalent)
  - 100, 250 or 500 µL LC syringe (Hamilton or equivalent)
  - Basic LC Mobile Phase (95:5:0.03 Methanol:Water:Ammonium Hydroxide) (or appropriate discipline/subdiscipline specific mobile phase)
  - C-18 Column (Grace Altima or equivalent)
  - Pierce LTQ ESI Positive Ion Calibration Solution (Thermo or equivalent)
  - Pierce ESI Negative Ion Calibration Solution (Thermo or equivalent)
  - General laboratory supplies

4 STANDARDS AND CONTROLS

4.1 Testmix (General Chemistry, Seized Drugs)

The testmix is used to assess daily operating performance, mass assignment, and continued integrity of the system. Alternatively, a procedure-specific positive control (e.g., insulin, HGH) may be used to assess instrument performance. Record preparations in the appropriate discipline/subdiscipline reagent log.

- Stock Solution
  Weigh 5.0 mg caffeine, 1.0 mg codeine, 1.0 mg brucine, and 1.0 mg reserpine into a 100-mL volumetric flask. Bring to the mark with methanol and mix well. Shelf life is three years when stored refrigerated in brown glass. This preparation may be appropriately scaled.
- Testmix Solution
  Pipette 4.0 mL of the Stock Solution into a 100-mL volumetric flask. Dilute to the mark with methanol and mix well. Shelf life is three years when stored refrigerated in brown glass. This preparation may be appropriately scaled.

4.2 Testmix (Explosives Chemistry)

The testmix is used to assess daily operating performance, mass assignment, and continued integrity of the system. Record preparations in the appropriate discipline/subdiscipline reagent log.

4.2.1 ESI Testmix

- Stock Solution
  Place 1 mL of each Redacted standards in a separate 10 mL volumetric flask and dilute to the mark with acetone to achieve a final concentration of 100 µg/mL. Shelf life is two years when stored refrigerated in colored glass. This preparation may be appropriately scaled.
- Testmix Solution
  Pipette 1.0 mL of each Redacted into a 10 mL volumetric flask and dilute to the mark with a 60/40 methanol/water solution to achieve a final concentration of 10 µg/mL. Shelf life is two years when stored refrigerated in colored glass. This preparation may be appropriately scaled.

4.2.2 APCI Testmix

- Testmix Solution
  The APCI Testmix is a Redacted in deionized water. This solution must be prepared fresh each day. To prepare the testmix, add 10 µL Redacted to an autosampler vial, then add 990 µL of 18.2 MΩ·cm deionized water. This preparation may be appropriately scaled.

4.3 Calibration Solutions

The calibration solutions are used for coarse tuning and calibrating the mass spectrometer over the entire mass range. This procedure only needs to be performed when the instrument has been moved, down for a long period of time, undergone a major repair, or warranted based on system performance. The calibration solutions are purchased from Thermo Fisher Scientific or equivalent.

5 PROCEDURE

5.1 Daily Checks

The following steps will be performed daily. Enter the appropriate information in the instrument log.

A. Record the remaining disk space on the hard drive. Verify that the hard disk has at least 100 MB of free disk space. Do not use if less than 100 MB remain.
B. Record the line pressure of the building nitrogen supply (API gas). The regulator should read between 70 and 100 psi. If it cannot maintain this pressure, contact appropriate instrument support personnel. If the nitrogen is supplied by a gas cylinder, record the tank pressure. Change the tank if less than 250 psi remaining.
C. Record the line pressure of the building helium supply (ion trap gas). The regulator should read between 20 and 40 psi (30 - 60 psi if two instruments are to be run off the same regulator). If it cannot maintain this pressure, contact appropriate instrument support personnel. If the helium is supplied by a gas cylinder, record the tank pressure. Change the tank if less than 100 psi remaining.
D. Check the vacuum pressure to ensure that no significant leaks are present in the system. Do not use if the convectron gauge reads above 2 torr, or the ion gauge (if present) reads above 20 microtorr.
E. If using a Shimadzu LC System, prime each LC solvent line to be used that day. Open the prime valve on the front of each pump module to be used by turning the valve handle ninety degrees and press the "PURGE" button on the module. If the pump does not start priming, disengage remote control by pressing the "PUMP" button and then pressing the "PURGE" button again. After the prime cycle finishes (about three minutes), close the prime valves.
F. If using the Shimadzu LC System, the autosampler solvent wash can be primed by pressing the "PURGE" button on the front of the autosampler module.
G. Prepare the instrument for analysis of testmix. Verify that the instrument has the correct source probe installed, the correct tune file loaded (esi_tune, exp_tune or equivalent), positive ion or negative ion mode selected, and centroid data being collected.
H. Analyzed the testmix:
    - General Chemistry, Seized Drugs
        - If a column is installed, remove it from that system and replace it with a zero-dead-volume union. Perform an analysis of the appropriate testmix prior to the analysis of case samples. Use parameters listed in the 'Instrumental Conditions' section. Select the appropriate mobile

phase. Start the HPLC pump. Engage the ESI probe and turn on the MS. Start an acquisition using a filename such as 'TMyymmdd' (or equivalent). Make three 5 µL injections of the testmix solution at least 10 seconds apart by using the manual loop injector, and then stop the data collection. Evaluate the results using the 'Acceptance Criteria' section. If the results are acceptable, print the TIC, RICs, and spectra for components in the testmix.

- For targeted analytes, a procedure-specific positive control can be substituted for the testmix. Use the appropriate column, mobile phase and instrument conditions as specified in the discipline/subdiscipline procedure. Print the TIC, RICs, and spectra for target analytes.

- Explosives
  Conduct a performance verification of the appropriate testmix through the column. Evaluate the results using the 'Acceptance Criteria' section. If the results are acceptable, print the TIC, RICs, and spectra for components in the testmix.

I. If all requirements are within specification, prepare the documentation as outlined in IOSS-701. If any requirements fail, contact appropriate instrument support personnel.

5.2 As Needed Maintenance/Checks

The following steps are to be performed as needed. Enter the information in the appropriate instrument log to indicate completion. Refer to IOSS-701 for more information on instrument maintenance and documentation.

A. Check the faceplate for debris, clean as needed.
B. Replace the capillary as needed.
C. Check level and color of rough pump oil. Top off or change oil as needed.

5.3 Mass Calibration

The mass calibration procedure should be performed as needed, when the instrument has been moved, down for a long period of time, undergone a major repair, or warranted based on system performance.

A. Load a 100, 250 or 500 µL syringe with the appropriate calibration solution.
B. Connect the infusion syringe to the ESI probe assembly, and place in the syringe pump.
C. Set the syringe pump to the correct syringe type and set the pump rate to 10 µL/minute. The pump rate can be adjusted as needed.
D. Load the tune file "esi_tune" (or equivalent).
E. Check that instrument is in the appropriate ionization mode (positive or negative) and collecting centroid data.
F. Set the detector using the parameters listed in the 'Instrumental Conditions' section.
G. Turn on the syringe pump and verify that the solution is flowing out the ESI needle.
H. Engage the ESI probe and turn on the MS.

I. Open the calibration dialog box, choose the 'Automatic' tab and check the individual tests or 'Select All' and then 'Start.'
J. When the calibration is complete, it will display whether or not the calibration was successful.
    - If the procedure fails, repeat the calibration.
    - When the procedure passes, save the report and evaluate the calibration solution spectrum using the 'Acceptance Criteria' section.
    - If all requirements are within specification, prepare the documentation as outlined in IOSS-701. If any requirements fail, contact appropriate instrument support personnel.

6 INSTRUMENTAL CONDITIONS

6.1 Testmix (General Chemistry, Seized Drugs)

6.1.1 Liquid Chromatograph

Mobile Phase:	Basic LC Mobile Phase
Flow Rate:	0.3 mL/min
Column:	N/A
Injection Volume:	5 µL
Number of Injections:	3

6.1.2 Mass Spectrometer

Ionization:	ESI
Polarity:	Positive
Tune File:	esi_tune (or equivalent)
Sheath Gas Flow:	6 (arb)
Aux Gas Flow:	3 (arb)
Sweep Gas Flow:	3 (arb)
Scan Mode:	Full Scan
Scan Range:	100–650 m/z

6.2 Testmix (Explosives Chemistry – ESI)

6.2.1 Liquid Chromatograph

Mobile Phase:	60% Methanol : 40% 3.125 mM NH_4NO_3
Flow Rate:	0.3 mL/min
Column:	C-18
Injection Volume:	5 µL

6.2.2 Mass Spectrometer

Ionization:	ESI
Polarity:	Negative
Tune File:	exp_tune (or equivalent)
Sheath Gas Flow:	20 (arb)
Aux Gas Flow:	5 (arb)
Sweep Gas Flow:	0 (arb)
Scan Mode:	Full Scan

Scan Range:	200-400 m/z (minimum)

6.3 Testmix (Explosives Chemistry – APCI)

6.3.1 Liquid Chromatograph

Mobile Phase 1:	Methanol with 1.25 mM NH_4NO_3
Mobile Phase 2:	DI Water with 1.25 mM NH_4NO_3
Flow Rate:	0.3 mL/min
Gradient:	0-2 min 90% Mobile Phase 2
	12-14 min 50% Mobile Phase 2
	17-20 min 90% Mobile Phase 2
Column:	C-18
Injection Volume:	10 µL

6.3.2 Mass Spectrometer

Ionization:	APCI
Polarity:	Positive Ion
Tune File:	hmtd_tune (or equivalent)
Vaporizer Temp	150°C
Sheath Gas Flow:	35 (arb)
Aux Gas Flow:	15 (arb)
Sweep Gas Flow:	0 (arb)
Scan Mode:	Full Scan
Scan Range:	150-250 m/z (minimum)

6.4 Mass Calibration

6.4.1 Mass Spectrometer

Ionization:	ESI
Polarity:	Positive or Negative (select as appropriate)
Tune File:	esi_tune (or equivalent)
Scan Mode:	Full Scan
Scan Range:	100-2000 m/z

7 ACCEPTANCE CRITERIA

7.1 Testmix

7.1.1 General Chemistry, Seized Drugs

Verify the results of the testmix. RICs should show contemporaneous signals for components at the following masses:

- Caffeine 195 m/z
- Codeine 300 m/z
- Brucine 395 m/z
- Reserpine 609 m/z

7.1.2 Explosives Chemistry - ESI

Redacted

7.1.3 Explosives Chemistry – APCI

Redacted

7.2 Mass Calibration

Verify the results of the calibration. The calibration will indicate if the procedure was successful. For reference, the individual ions for the calibration solution are:

- Caffeine 195 m/z
- MRFA 524 m/z
- Ultramark 1022 m/z
  1122 m/z
  1222 m/z
  1322 m/z
  1422 m/z
  1522 m/z
  1622 m/z
  1722 m/z
  1822 m/z
  1922 m/z

8 LIMITATIONS

Only properly trained personnel will perform duties involved in the operation, maintenance, or troubleshooting of this instrument.

9 SAFETY

Many instrument components are held at temperatures of 250°C and higher. Precautions should be taken to prevent the contact of skin with heated surfaces and areas.

10 REVISION HISTORY

Revision	Issued	Changes
06	06/01/2023	Section 4- Changed Explosives Chemistry ESI Testmix dilution from acetone to 60/40 methanol/water.
07	11/15/2023	Section 3- Removed GABA and Ammonium Nitrate Mobile Phase from materials. Section 4- Removed GABA from General Chemistry, Seized Drugs Testmix. Section 6- Updated LC gradient and gas flows and added vaporizer temp for Explosives Chemistry – APCI.
08	02/18/2025	Section 5.3 – Changed Calibration section from print to save report. Section 6.3 – Updated sheath and aux gas flows.