

TENDER SPECIFICATION FOR THE SUPPLY OF ULTRA PERFORMANCE LIQUID CHROMATOGRAPH TANDEM QUADRUPOLE MASS SPECTROMETER (LC-MS/MS) SYSTEM

The LC-MS/MS system must be able to comply with the following requirements:

- A. The configurations and requirement of the LC-MS/MS system:
 - 1. Ultra performance liquid chromatography
 - 2. Quadrupole mass spectrometer
 - 3. Data management system
 - 4. Miscellaneous
 - B. The ability to perform the drugs analysis required by the laboratory using test samples given. Please refer to Section E.
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Section A – ULTRA PERFORMANCE LIQUID CHROMATOGRAPHY

A.1 Binary gradient solvent delivery system

- 1. The system must be equipped with two solvent selection valves to enable the choice of 4 different mobile phase solvents.
- 2. There must be a switching valve to divert the mobile phase flow to waste, without going through the analytical column, for regular flushing of the system.
- 3. It must have a flow rate range of at least 0.1 – 2 ml/min.
- 4. Flow rate accuracy shall be within $\pm 1\%$.
- 5. Flow rate precision shall be $< 0.1\%$ RSD or < 0.02 min SD, whichever is greater.
- 6. The operational pressure range should be up to at least 1,000 bar.
- 7. Solvent composition must be settable from 0-100%.
- 8. Solvent composition precision must be $< 0.3\%$ RSD or 0.05 min SD, whichever is greater, and with accuracy $\leq 0.5\%$.
- 9. Solvent resistant materials must be used in all areas which have contact with the mobile phases.
- 10. There must be a real-time monitoring system and electronic log for the purpose of diagnostics/troubleshooting. For safety and maintenance, it must have leak detectors and voltage low enough for safe handling during routine maintenance areas.
- 11. The system must be equipped with automatic purge and seal wash.

A.2 Solvent rack with degasser

- 1. The solvent rack must have capacity for at least four (4) 1-L bottles.
- 2. It must have four (4) internal degassers with flow rate per channel of at least 2 ml/min.

A.3 Autosampler/injector

- 1. The sample injection shall have design such that there is zero loss injection.
- 2. Injection volume shall be settable from at least 0.1 – 10 μ l.
- 3. Injection volume accuracy should be within $\pm 1\%$, and precision should be $< 0.5\%$ RSD at 5 μ l.
- 4. The injector should have function for user to set the speed and the needle depth for drawing sample.
- 5. There shall be a feature for external and internal needle wash to prevent contamination.
- 6. Carryover must be no more than 0.005%.
- 7. The autosampler must be able to accommodate at least 100 positions for 2-ml vials.
- 8. It must be able to process samples automatically in any (random) sequence.
- 9. The autosampler shall be thermostatted; the temperature should be settable from at least 4°C to ambient temperature.
- 10. Solvent resistant materials must be used in all areas which have contact with the mobile phases.

11. It must have leak detectors, autosampler (rack/tray) detector and electronic log.
12. It must have a safety feature when replacing the injection needle.

A.4 Thermostatted column compartment

1. The operational temperature should range from at least 25-60°C.
2. It must provide precise and homogenous column thermostat within the operational temperature range.
3. The temperature shall have accuracy within $\pm 0.5^\circ\text{C}$, stability/precision within $\pm 0.1^\circ\text{C}$.
4. It should have the capacity of holding at least 4 analytical columns with 2.1 mm ID and column length of at least 10 cm, and each with guard columns.
5. It must come with automatic column switching valve to at least 4 different analytical columns according to user setting, without the need to remove and re-attach the columns.
6. It must have solvent leak sensor and real time temperature monitoring.
7. Good and easy-to-use column fitting which does not require the need to use wrench or tools.

A.5 Built-in or external infusion system/syringe pump

1. Must have a built-in or external mechanical infusion system/syringe pump to support real-time data acquisition for MS method optimization.
2. Infusion flow rate must range from a minimum of 10 $\mu\text{L}/\text{min}$.

Section B – QUADRUPOLE MASS SPECTROMETER (MS/MS)

B.1 Ion Source

1. The system must be equipped with Electrospray Ionization (ESI) source as the standard, operable at both positive and negative polarity.
2. The ion source must come with grounded and fixed nebulizer needle for safety and easy/optimized alignment.
3. The ion source design must be able to increase the efficiency of ion transfer from the ion source to the quadrupole MS analyser and eliminate undesirable neutral contaminants for improved robustness.
4. Capable of handling LC mobile phase flow rate from 5 $\mu\text{L}/\text{min}$ to at least 2000 $\mu\text{L}/\text{min}$, with gradient from 100% aqueous to 100% organic, with complete vaporization of solvent and good ionization.
5. Changing or maintaining the ion source must be possible without braking the vacuum and simple for the user to perform (without specific tools).
6. Opening/removing the ion source chamber should shut down the gas and power supply automatically, otherwise other safety measure must be demonstrated for safe routine maintenance.
7. The ESI source must be able to allow effective optimization of ionization with minimal adduct formation.

B.2 Mass Spectrometer

1. The system must be able to perform full scan MS and selected ion monitoring for both Q1 and Q3, Product Ion Scan, Precursor Ion Scan, Neutral Loss or Gain Scan, and Multiple Reaction Monitoring (MRM) scan modes.
2. The system must be capable of rapidly switching between positive and negative ion detection. The detector polarity must be able to switch between alternate scans in not more than 50 msec.
3. The system must have a mass range (m/z) of at least 5-2000 Da in triple quadrupole mode.
4. The system must have scan speed of 10,000 Da/sec or higher in triple quadrupole mode.
5. The system must have a dynamic range of at least 5 orders of magnitude

6. The system must have a mass stability of 0.1 Da over 24 hrs with normal operating temperature and after it has reached vacuum and electronics equilibrium.
7. The MRM dwell time must be at least 1 msec.
8. ESI Positive Mode MRM Sensitivity Signal-to-Noise ratio: The S/N must be higher than 40,000:1 for 1 pg reserpine injection on column.

Section C – DATA MANAGEMENT SYSTEM**C.1 Computer and Accessories**

1. At least Intel Core i5 3.2 GHz processor or equivalent.
2. At least 8 GB RAM.
3. At least 1 TB hard disk.
4. Pre-installed Windows 7 (64-bit) professional or higher with MS Word and MS Excel, and antivirus software which is compatible with the data management software system of the proposed system
5. Computer must have at least 3 years' warranty.
6. At least a 22" LCD colour monitor, a 101-key keyboard, and an optical mouse
7. At least 2 Ethernet for the installation of LAN.
8. One black and white laser printer with the capability to print duplex and capacity of 500 sheets of paper or better.

C.2 Software

1. The software must include full digital instrument control, automatic tuning, automated MRM optimizer, data acquisition, qualitative and quantitative analysis, report creation and diagnostics.
2. Must be able to perform automated MRM optimization for at least 5 analytes.
3. The software must have the ability of working with Multiple Reaction Monitoring (MRM), Full scan MS, selected ion monitoring for both MS1 and MS2, product ion scan and precursor ion scan modes.
4. Data acquisition, peak integration, calibration, quantification and QC calculation must be fully automated.
5. The software must update ion ratios and retention times automatically.
6. Software should have user-defined flags for different parameters.
7. The system control software should have at least user and administrator access rights.
8. It should be able to acquire data, integrate, review and report on an actively running sample
9. It should be able to save the acquisition parameters and data analysis method (if any) together with every data file.
10. Should be able to import/export sample sequence or calibration information minimally to Excel.
11. Quantification must be possible by using historical calibration data or calibration from different sequences.
12. Quantification software must allow for multiple internal standards to be processed in a single data analysis method.
13. The software should be able to auto calculate the MRM ratio.
14. Audit trail must be available.
15. Output for importation to LIMS system must be possible for result uploading.
16. Online help should be available for users in each of the software.

C.3 Information/ Details to be included in the report

1. Tenderer must provide the initial report for qualitative and quantitative analysis as required by the user.
2. The software must be available for user to customize or modify the report format.

3. The report must include information such as XIC chromatogram, m/z, retention time, relative retention time, MRM ion ratio, expected MRM ratio, MRM ratio pass or fail indication, area of analyte, area of internal standard, area ratio, calculated concentration, calibration curve, calibration type and equation, S/N and method name in one report.
4. In general, the report must include basic sample information such as sample name, operator, acquisition date and time, sample vial position, injection volume, data file name/path, acquisition and data analysis method as well as any user comment.

Section D – MISCELLANEOUS

D.1 Training, Warranty and Support

1. In-house training for at least 4 staffs must be provided that shall minimally include routine hardware maintenance and troubleshooting, software to operate the system and basic and advance data analysis.
2. The system shall come with at least one-year warranty upon successful commissioning. The warranty must include the following:
 - (a) At least 1 preventive maintenance (PM) inclusive of PM kit;
 - (b) Provision of unlimited breakdown calls, on-site services, troubleshooting and repairs during Office Hours i.e. 8am to 5:30pm from Monday to Friday excluding Saturday, Sunday and Public Holidays. Please refer to **Section D – Miscellaneous: Clause D.2-1(d)** for the response time;
 - (c) Supply of all replacement and wear & tear parts; and
 - (d) Provide system update or upgrade of software version.
3. The Contractor shall guarantee that the spare parts, consumables and services for the system will be available for a period of 7 years from the date of discontinuation of the system.
4. Option to purchase comprehensive maintenance contract for 3 years after the warranty period must be quoted. The price quoted must include:
 - (a) At least 1 preventive maintenance (PM) inclusive of PM kit,
 - (b) Provision of unlimited breakdown calls, on-site services, troubleshooting and repairs during Office Hours. Please refer to **Section D – Miscellaneous: Clause D.2-1(d)** for the response time;
 - (c) Supply of all replacement parts and wear & tear parts; and
 - (d) Provide system update or upgrade of software version.
5. The Contractor must have at least 2 hardware engineers and 2 application chemists locally for the provision of technical support of the proposed system. Please provide the list of trained engineers & chemists of the proposed system in **Annex E Performance Summary** for reference.

D.2 Performance of Services

1. The Services to be performed by the Contractor shall consist of Preventive Maintenance and Corrective Maintenance as described below.

Preventive Maintenance

- a) The Preventive Maintenance shall consist of:

Routine maintenance of the System, including but not limited to the testing of functions and inspecting of the condition of the System in order to keep the System safe for use and in Good Working Order; and Adjustment and/or repair of any defect in or malfunction of the System discovered by the Contractor's representatives during the course of routine maintenance checks.

- b) The Preventive Maintenance performed shall be in compliance with the maintenance procedures and safety tests specified by the manufacturer.
- c) The Preventive Maintenance shall be carried out and completed during Office Hours from 8:00 am to 5:30 pm Monday to Friday excluding Saturday, Sunday and Public Holidays.

Corrective Maintenance

- d) Upon receipt of oral or written notice from the Authority, the Contractor shall use its best endeavours to ensure that the Contractor's suitably qualified and duly authorised representatives attends to the Authority, within the response time of not more than 24 hours upon receipt of oral/written notification if the request is made on a Working Day. If the request is made on a non-Working Day, the Contractor shall respond within the first 24 hours of the beginning of the next Working Day.
- e) The Contractor shall complete any repair, or replacement or adjustment of components within 2 working days if there is no need to order parts from overseas or within 5 working days if the parts are not available locally and needed to be ordered from overseas from and including the date on which the Contractor was given notice pursuant to **Section D – Miscellaneous: Clause D.2-1(d)** unless the Authority had agreed in writing to have the time period extended.

D.3 Replacement and Purchase of Components

- a) The Contractor shall inform the Authority of any part or component of the System that needs to be replaced. Prior written approval must be issued by the Authority before the replacement may be effected unless the replacement required is deemed urgent by the Authority in which case a verbal approval (which shall subsequently be confirmed in writing) obtained from an authorised officer of the Authority shall suffice.
- b) The Contractor shall use all reasonable endeavours to supply only original or genuine replacement components, which are required to maintain the System in Good Working Order. All replacement components shall not be chargeable during the period of warranty period and post warranty comprehensive maintenance contract

D.4 Guarantee

1. The Contractor hereby warrants that all the System and every part or unit thereof serviced by the Contractor shall conform to the requirements of this Contract and be free from any defect or deficiency in their performance or workmanship for a period of six (6) months from the date of acceptance of the Services by the Authority (hereinafter referred to as "the System Guarantee Period"). The Contractor hereby also warrants that all materials and every part or unit thereof, used for the Services shall be free from any defect in manufacture or any defect arising out of design, workmanship or materials used or any failure or malfunction due to quality of material, workmanship, design, assembly, installation or integration for a period of six (6) months from the date of acceptance of the materials by the Authority (hereinafter referred to as "the Materials Guarantee Period"). The System Guarantee Period and the Materials Guarantee Period shall collectively be known as the "Guarantee Period".

D5. Site preparation

1. The complete system includes computer, printer, LC and MS shall be placed on existing bench with the available space of 250 cm (width) x 84 cm (depth) x 200 cm (height). Additional or customized bench with the additional of not more than 10cm for the depth shall be provided if it is required.
2. Any other modification cost of existing cabinet in order to accommodate the system shall be borne by the Contractor.

3. The Contractor shall ensure the proposed system can be installed and connected to existing facility such as power and gas lines.
4. A vacuum pump stand with adjustable legs and non-vibration isolators should also be provided to avoid vibration to the bench.
5. Tenderer is required to attend mandatory site-show that will be held on **ddmmyy (day) at 10am**.

Section E – SAMPLE EVALUATION

E1. Sample Collection

1. Tenderer is required to perform sample evaluation using the system proposed in this tender. The sample must be evaluated locally and not to be sent overseas.
All participating tenders shall collect the sample and instructions for sample evaluation on the site-show or between 2pm to 4.30pm from **ddmmyy (day) to ddmmyy (day) <3 working days>** at:

Health Sciences Authority
11 Outram Road
Singapore 169078
Contact number: 6213 0856

2. Tenderer shall write in to HSA to request for alternative collection dates if they are unable to collect on the stipulated date. Please email Ms Elin Tan at Tan_Siew_Hoon@hsa.gov.sg for arrangement.
3. All samples for evaluation will be provided only once and request for additional sample is not allowed.
4. The following sample will be provided for evaluation:
 - (a) Neat standard solutions for the analytes and internal standards.
 - (b) unknown samples
5. Tenderers are not allowed to concentrate the samples provided by HSA.

E2. Sample Testing Result

1. All participating Tenderers shall submit the sample testing results with the required details of report as stated in **Clause C.3 by tender closing date** via email to Nadia_wong@hsa.gov.sg and Tan_Siew_Hoon@hsa.gov.sg unless an extension is sought. For extension of sample results submission, Tenderer shall write in to Tan_Siew_Hoon@hsa.gov.sg to request for extension of maximum of 5 working days before the tender is closed.
2. The result of the sample analysis must comprise of the information as stated in **Clause C.3**.
3. In addition to the report, Tenderer is required to submit the following information:
 - (a) Method parameters for the chromatographic system including mobile phase, column, injection volume, column temperature, pump flow rate, LC gradient elution programme, date of analysis; and
 - (b) Method parameters for the MS conditions including MRM transitions, dwell time, voltage setting.
4. Tenderer who does not participate in the sample evaluation test or fail to follow the stipulated instructions to perform the test or fail to submit the test results by the stipulated deadline shall be disqualified from the evaluation.

5. The analysis result shall minimally meet all the criteria that required in the tender as follow:

- (a) Linearity: linear relationship between analyte signal and concentration in the sample
- (b) $R \geq 0.99$ or $R^2 \geq 0.98$
- (c) Signal to Noise – $S/N \geq 10$
- (d) Accuracy: not more than $\pm 20\%$ of spiked concentration
- (e) Must have at least 2 MRM transitions per analyte (1 transition for quantitation and the 1 for qualifier)
- (f) The MRM ion ratio shall satisfy the following criteria when compared with the calibrator:
 - i) Within $\pm 20\%$ if relative intensity $> 20\%$ of base peak; or
 - ii) Within $\pm 30\%$ if relative intensity $\leq 20\%$ of base peak
- (g) The retention time of unknown must be $\pm 2\%$ of the calibrator
- (h) The peak shape must be in gaussian peak or symmetrical

5. The area of analyte will be evaluated. Please refer to evaluation criteria stated in **Annex C**.

COMPLIANCE OF REQUIREMENT SPECIFICATIONS

I hereby confirm that I can meet all the Requirement
Specifications as stated above.

Yes/ No*

Please indicate any non-compliance to requirement specifications here should there be any.

Reference To	Remarks