

REQUIREMENT SPECIFICATIONS

ITEM :	High Performance Liquid Chromatography-Mass Spectrometer (HPLC-MS) System and control software
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QUANTITY :	One (1) Complete System
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1. Scope of Tender

To tender for the Supply, Installation and Commissioning of one (1) complete system that consists of two (2) sub-systems and one (1) computer with control and deconvolution software: (A) High Performance Liquid Chromatography (HPLC) system with one set of HPLC columns, a (B) single quadrupole mass spectrometer (MS) and a (C) control and deconvolution software to manage the two sub-systems (line A to B). The complete system will be installed and commissioned in the Division of Physics and Applied Physics, School of Physical and Mathematical Science, Nanyang Technological University.

2. General Description

The Nanyang Technological University (NTU) invites tenders for the Supply and Commissioning of a High Performance Liquid Chromatography-Mass Spectrometer (HPLC-MS) system for the chromatographic purification and mass characterization of biomolecules.

This is one (1) complete system that consists of two (2) sub-systems and one (1) computer with control and deconvolution software: (A) High Performance Liquid Chromatography (HPLC) system with HPLC columns, a (B) single quadrupole mass spectrometer (MS) and a (C) computer with control and deconvolution software to manage the two sub-systems (line A to B). End-user training must be provided on-site in NTU to ensure long-term sustained operation and good maintenance of the system by the operators. The system will be delivered and installed in the Division of Physics and Applied Physics, School of Physical and Mathematical Science, Nanyang Technological University.

- i. The complete system must be configured to perform mass-based or wavelength-based analytical-scale analysis to preparative scale purification (accommodating column size from i.d.= 4.6 mm up to i.d.= 50 mm) as well as in-situ mass detection of all fractions. The (A) High Performance Liquid Chromatography (HPLC) system with HPLC columns should be configured with the following modules: a high-pressure solvent delivery system that should perform with flow rate of 0.50 to at least 100.00 mL/min; an autosampler/fraction collector that should accommodate injection volumes from at least 5 μ L to at least 8 mL while the several options for fraction collection modes should be available; an auxiliary flow controller that should be equipped with independent control analytical and preparative flow paths; a wavelength detector that should monitor at least 2 specific wavelengths in the range of 190 nm to 600 nm simultaneously; one set of HPLC columns that should consist of at least two analytical scale reversed-phase columns and one reversed-phase preparative scale column. The (B) single quadrupole mass spectrometer should be of Electrospray Ionization (ESI) source and compatible with the liquid chromatography system above, with mass range of at least 30 – 1200 m/z. Together, the (A) HPLC system with HPLC columns, with a (B) single quadrupole mass spectrometer, and a (C) computer with control/deconvolution software

- should be able to manage all 2 sub-systems, including processing/deconvoluting the data generated by both sub-systems, to form the complete system sought in this tender.
- ii. The complete system must be fully self-contained with all the necessary support components such as tubings, fittings, sample loops, sample and collection racks, flow splitter, flow cell to the HPLC-MS system.

3. Technical Specifications

It is critical that the footprint of the complete system including the HPLC system, the MS system and the computer must be at most 750 mm wide to fit the laboratory bench, but not in exceeding 2250 mm in length.

It is critical that the HPLC system can integrate seamlessly with the MS system for in-situ mass detection of all fractions separated in the HPLC system and/or to trigger the mass-based separation in HPLC.

The technical specifications of: (A) HPLC system with HPLC columns, with a (B) single quadrupole mass spectrometer and a (C) computer with control/deconvolution software are given below:

(A) High Performance Liquid Chromatography (HPLC) system with HPLC columns

- i. The unit should be fully automated while being fully compatible and seamlessly integrable with other units (B) to (C) to make up the HPLC-MS system.
- ii. The system must allow for analytical to preparative scalability with low delay volume and high-pressure mixing.
- iii. The HPLC system with one set of HPLC columns should meet the conditions in the subsequent sections:
 - a. High-pressure solvent delivery system
 - b. Autosampler/Fraction collector
 - c. Auxiliary flow controller
 - d. Wavelength Detector
 - e. HPLC columns

a. High-pressure solvent delivery system

1 to 4 are critical requirements.

- 1. It should be equipped with a high-pressure mixing binary pump that allows concurrent use of two solvent lines from analytical to preparative scale.
- 2. The flow rate deliverable should range from 0.50 to at least 100.00 mL/min with a minimum of 0.01 mL/min flow rate increment.
- 3. The pump should be able to support solvent flow into HPLC columns of up to 50 mm in diameter.
- 4. The operable pump pressure should fall in the range of 0 – 400 bar.
- 5. The flow accuracy should be at least of $\pm 1.0\%$.
- 6. Number of solvent lines accommodable should be at least four.
- 7. The delay volume should be less than 350 μL .

8. The accuracy of solvent composition should be of $\pm 1.0\%$ while the precision should be of $<0.3\%$ Relative Standard Deviation (RSD) or 0.1 min Standard Deviation (SD), whichever is greater.
9. The pump should be equipped with leak sensing ability.

b. Autosampler/Fraction collector

The autosampler

1 to 4 are critical requirements.

1. The analytical and preparative injection valves must be independent.
2. The syringe delivery accuracy of more than 99.0 % at full stroke.
3. The module should be able to accommodate sample loops with injection volumes from at least 5 μL to at least 8 mL.
4. The module should be able to withstand pressure of at least 400 bar.
5. Injection reproducibility should be less than 0.75 % Relative Standard Deviation (RSD).
6. At least two sample loops of 20 μL and 1 mL should be included.
7. The wash cycle should complete in less than 30 s.
8. The wash station should support at least two wash solvent ports.

The fraction collector

1 to 2 are critical requirements.

1. Sample and collection rack must be independent.
2. The users should be able to control the fraction collection mode, which could be time-based, threshold-based, slope-based, mass-based or of a mixed trigger.
3. Unit should at least include 2 mL vial injection rack capable of holding at least 100 x 2 mL vials as well as 13 mm falcon tube collection rack capable of holding at least 100 tubes.
4. Injections can be made from any location on the bed and from any racks.

c. Auxiliary flow controller

1 to 3 are critical requirements.

1. The unit must support control of at least 2 analytical and 2 preparative columns.
2. The unit must support flow splitting for mass spectrometer.
3. The unit must be equipped with analytical or preparative switching valves and must provide full automation to allow for automated switching between analytical and preparative flow paths
4. Options should be provided for upgrade to automatic injection of solvent modifiers.
5. Options should be provided for upgrade to column dilution to diminish effects of mixing organics with aqueous phase.
6. The unit should be accompanied by optional system leak sensing capability.

d. Wavelength Detector

1 to 2 are critical requirements.

1. A single analysis should allow for simultaneous detection and monitoring of at least 2 specific wavelengths in the range of 190 nm to 600 nm without loss in sensitivity.
2. The unit should possess wavelength accuracy of at least ± 1 nm.

3. With a 10 mm path length cartridge cell, the short-term noise allowed should be of $< \pm 7 \mu\text{AU/cm}$.
4. The linear range should not deviate by more than five percent (5 %) up to 2.5 AU.
5. This unit should deliver sensitive detection of major and minor components in both analytical and preparative scale runs with linear dynamic range.
6. The unit should at least include:
 - 10 mm path length analytical flow cell that can withstand up to 100 mL/min flow rate.
 - 3 mm path length semi-preparative flow cell that can withstand up to 100 mL/min flow rate.
 - 1mm path length preparative flow cell that can withstand up to 100 mL/min flow rate.

e) High Performance Liquid Chromatography Columns

1 to 3 are critical requirements.

1. This lot should consist of at least two analytical scale reversed-phase columns.
2. This lot should consist of at least one reversed-phase preparative scale column with respective guard cartridge and cartridge holder.
3. The packing materials and length of the columns should allow for maximum method development flexibility so as to enable seamless method transfer of analytical to preparative liquid chromatography (direct scalability).
4. The length of all three columns should be identical and less than 120 mm.
5. The internal diameter (i.d.) of the analytical columns should be 4.6 mm while that of the preparative column should be within 19-22 mm.
6. The packing materials of all columns and preparative guard cartridge should be identical, with the following features:
 - The particle size (dp) should be 5 μm .
 - The pore size should be 130 Å.
 - The column particles should be of C18 chemistry and able to withstand pH 1 – 12.
 - The guard cartridge for preparative scale column should be 10 mm in length.
 - The cartridge holder should fit the internal diameter of preparative column and length of the guard cartridge.
 - The column must be fully compatible for the purification of biomolecules (peptides, proteins, oligonucleotides and the peptide-oligonucleotide conjugates).

(B) Single quadrupole mass spectrometer

- i. The system should be fully automated while being fully compatible and must integrate seamlessly with other components (A) to (C) that make up the HPLC system.
- ii. The mass spectrometer should be a bench top model with Electrospray Ionization (ESI) source and requires only tool-free maintenance.
- iii. Mass identification of biomolecules (peptides, proteins, oligonucleotides and the peptide-oligonucleotide conjugates) must be viable and accurate with or without the aid of deconvolution software.
- iv. It should complete the HPLC system with mass spectral data, complementing quantitative optical data of individual peaks that possess or do not possess UV response or at levels not accessible by optical detection.

v. The single quadrupole mass spectrometer should meet the conditions in the subsequent conditions:

1 to 4, 8, 13, 15 are critical requirements.

1. The mass range should at least be 30 – 1200 m/z.
2. The scan speed should be of at least up to 10,000 Da/s.
3. The spectrometer must be able to perform full-scan mass analysis or selected ion monitoring.
4. The mass drift must not exceed 0.1Da over a 24 hr period.
5. The mass accuracy must be better than +/- 0.2 Da over full mass range.
6. The scan speed should be automatically-optimized for enhanced data quality for acquisition rates up to 20 Hz.
7. The linearity of range of response relative to sample concentration for a specific compound is up to four magnitude from the limit of detection.
8. The ion polarity switching time must be 30 ms or shorter between positive and negative ion modes.
9. The acquisition rate for single ion monitoring mode should be automatically-optimized for enhanced data quality for acquisition rates up to 100 Hz.
10. There must be at least up to 1024 single ion recording (SIR) channels which can be monitored in a single acquisition.
11. There must be automated mass resolution control of less than 0.9 Da for constant data quality.
12. The spectrometer must possess the ability to run functions in a single experiment with varying cone (or equivalent) voltages.
13. The instrument must have a single method file where all parameters are set.
14. The system should come with facile shut down option when needed for power saving/maintenance, the off to ready time should be less than an hour after switching on.
15. There must be automated mass calibration and resolution verification.
16. It should have a pre-filter to maximize resolution and transmission while preventing contamination of mass analyzer.
17. The size must be smaller than or equivalent to 40 cm (width) x 20 cm (height) x 80 cm (depth).

(C) Computer and control/deconvolution software

- i. The computer and control software should provide one-stop monitoring and control of HPLC system and MS system. The computer should be fully compatible with the software package.
- ii. The MS system must come with a deconvolution software.
- iii. The computer and software should meet the conditions in the subsequent conditions:

1 to 12 are critical requirements.

1. The software should allow automated fraction collection based on desired parameters as well as tracking of samples and fractions in an easy-to-view format.
2. The software should allow collection of peaks that are not of primary concern but that are not classified as waste.
3. The software should provide waste collection option.
4. The software must allow automatic sample screening to determine the preparative strategy in an analytical-scale separation. Subsequently, the appropriate method for each sample in a batch should be chosen for purification and the fractions collected should be screened to determine the next process step.

5. The software must be able to perform mass spectrometry data review through fractions tracked and tube purity determination.
6. The software must give the flexibility in data acquisition to provide manual review and override.
7. The software package must include deconvolution software to perform automatic rationalization of MS spectra of multiply-charged species such as peptides, containing product ions in a range of different charge states.
8. The software must possess the ability to plot complex peptide MS spectra containing fragment ions in multiple charge states into homogenous (virtual $Z=1$) charge state representation.
9. The software must enable control across multiple columns.
10. The software should allow monitoring solvent levels and gives solvent level alarms.
11. The software should allow automated mass calibration and mass resolution.
12. The software should allow automated diagnostics, checks and alerts.
13. The computer should be supplied with minimum specification of at least 17" LCD monitor, DVD-RW, Windows 7 Professional Operating System, 64-bit, 2 TB hard disk, 2 GB RAM.

Note: Any proposal that fails to meet any critical requirement listed will not be considered. In the cases where all proposals fail, the proposal offering the best specifications will be considered first.

4. Safety Features

- i. Protection features against power surges must be provided.
- ii. The system must be operable on the PUB main electric power supply available in Singapore which is 220 – 240 V, 50 Hz for single phase and 415 V, 50 Hz for three phases.

5. Installation and Commissioning

- i. The complete system must be tested to be in a good working condition prior to leaving the factory.
- ii. The complete system must be delivered, installed, tested and commissioned at the specified site in NTU.
- iii. System installation must be carried out by professionally trained engineers.
- iv. A full set of operator instruction manuals must be provided.
- v. A fully documented commissioning is to be conducted by the supplier.

6. Training and Support

i is Critical Requirement.

- i. Comprehensive training on the operation and maintenance of the complete system by experienced and qualified engineers (certification to be attached in the tender response) must be provided. Tenderers should also include a tentative training curriculum, and the training will be provided for a minimum of four (4) users over a period of at least two (2) days.
- ii. Tenderers must have a good track record of the availability of a strong and competent local support team by demonstrating they have installed at least three (3) identical/similar system afore-described.

7. Warranty

The tenderer must provide no less than twelve (12) months warranty for manufacturing defects of the system including parts and labor upon acceptance test.

8. Other Critical Requirements

- i. The proposed HPLC-MS system must have a proven track record for mass-direction purification of biomolecules (oligonucleotides, peptides, proteins).
- ii. A compilation of customer testimonials must be provided prior to evaluation.

9. After-sales Service

- i. Tenderers response time to our support requests must be by next working day from report in the case of equipment failure/maintenance by (list separately) email, phone, or attendance by local service personnel (if applicable).
- ii. Delivery times for spare parts should not exceed one (1) month to acknowledge our order and four (4) months to deliver after receipt of order.

10. Submission of Tender

- i. Tenderers are required to submit brochures, datasheets, and relevant reports for evaluation.