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| Coating Machine | URS No.: | Supersedes: | N/A |
| Rev: 00 | Effective Date: |  |
| **USER REQUIREMENT**  **SPECIFICATION**  **OF**  **COATING MACHINE** | | | |

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| **1.0** | APPROVAL PAGE The User requirement specifications for Coating Machine have been prepared, reviewed, and approved by concerns from the following area | | | |
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| 2.0 | INTRODUCTION | | | | | |
|  | The URS has been initiated by Novugen Oncology Sdn Bhd., and pertains to procurement of Coating Machine.  Being end user of proposed equipment, user department has initiated the document, which has been reviewed by Engineering / Project, Quality Assurance and approved by Quality assurance.  This document is prepared to help suppliers to understand the user requirement for developing the functional specification and design specification. Each with approval from Novugen Oncology Sdn Bhd. will become a contractual agreement between suppliers and Novugen Oncology Sdn Bhd. | | | | | |
| **3.0** | **OVERVIEW** | | | | | |
| 3.1 | Name of  System/Equipment/  Instrument/ Software | | | **:** | | Coating Machine |
| 3.2 | Desired/ Suggested Capacity | | | **:** | | 250L Mention capacity |
| 3.3 | Number of System/Equipment/  Instrument/ Software | | | **:** | | 6 units of equipment together with an integrated system and software related.   * Tablet Coating Machine * Solution Preparation Tank and Stirrer * Lifting and positioning device (similar to existing LPD) * Auto Discharge Station with split butterfly valve assembly (to fit existing buck valve design) * Air handling unit, dust collector and scrubber unit * CIP Unit |
| **4.0** | | **STATUTORY REGULATIONS** | | | | |
| 4.1 | | General Regulations | | | | |
| 4.2 | | GMP standards | **:** | | The equipment should be designed and manufactured in accordance with the latest editions and subsequent amendments of all relevant USFDA and EU as listed below.   1. EU: The Rules Governing Medicinal Products in European Union – Eudralex, volume IV ‘Good Manufacturing Practice’ Part 1 2. EU GMP Guide, Annex 15 (Qualification and Validation) 3. US FDA: 21 CFR Parts 210 and 211 – cGMP in Manufacturing, Processing, Packing or Holding of Drugs and Finished Pharmaceuticals. 4. US FDA: 21 CFR Part 11 – Electronic Records; Electronic Signatures. | |
| 4.3 | | Local Regulations | **:** | | 1. Environmental Quality Act 1974 (Act 127) and all related regulations 2. Occupational Safety and Health Act 1994 (Act 514) and all related regulations. 3. Factories and Machineries Act 1976 (Act 139) and all related regulations. 4. Electricity Supply Act 1990 (Act 447) and all related regulations. | |
| 4.4 | | EC directives and declarations | **:** | | EC directives and declarations to be followed / issued in general. The vendor must ensure that all relevant directives are adhered to / for a given delivery.  ATEX certified flame proof declaration should be provided where flame proof design is considered in manufacturing equipment. | |
| 4.5 | | Guidelines | **:** | | The following guidelines for design should be consulted to help satisfy the cGMP’s. It should also comply with regulations of USFDA, EU standards, ISPE BASELINE GUIDE, VOLUME 2, PIC/S Guide to Good Manufacturing Practice for Medicinal Products and ISPE Good Practice Guide, Assessing the Particulate Containment Performance of Pharmaceutical Equipment. | |
| 4.6 | | GAMP  requirements | **:** | | The system should meet the standard requirement GAMP 5, Good Automated Manufacturing Practice - Guide for Validation of Automated Systems in Pharmaceutical Manufacture. | |
| 4.7 | | Any other specific GMP requirement | **:** | | N/A | |
| **5.0** | | **PROCESS** | | | | |
| 5.1 | | Process description:  Charging tablets into coater shall be ensured by integrated system proposed by supplier within contained condition.  The following coating steps can be applied by campaign of multiple batches   1. Charging tablets in coater using split butterfly valve through auto charging method which shall be similar to existing design. 2. Pre-heating the core tablets with a controller flow of heated air with the tablet bed continuously mixed to improve the heat transfer 3. Sub-coating the core tablets uniformly by mixing the tablet bed and controlled spraying of a aqueous or solvent based coating solution. Spray rate with a controlled flow of process air. 4. Drying of the coated tablets by controlling flow of heated air. 5. Sampling of tablets on intervals 6. Cooling of the coated tablets by a controlled flow of air at ambient temperature. 7. Discharging of coated tablets by rotating the coater drum in opposite direction, which shall start the discharging of tablets automatically. 8. Charging a new lot / batch of core tablets and applying here above steps 1 to 6 9. Repeat step 7 for the next lot / batch. 10. Automatic cleaning and drying of the coater drum by using CIP system. Cleaning of supply and return duct shall be in place.   On the HMI a recipe for the product is selected with validated parameters. For example, spray rate, airflow temperature, air flow, spray rate, spray pump speed and coating pan rotation speed. The operation, recipe and process control screen and controls shall be able to configured as per client’s request.   |  |  | | --- | --- | | **Process Module** | **Description** | | Tablet Coating | - Tablet coating machine with containment to handle OEB 1 – 5 product.  - The system should be able to handle both film and functional coating process.  - The system and other assemblies shall be designed for both aqueous (water based) and organic solvent based processes.  - The peristaltic pump shall be able to be controlled through system.  - Contains suitable number of Schlick gun for spraying coating solution  - Sampling port shall be fitted with a collection bottle / container for handling of samples. | | Solution Preparation Tank and stirrer | - To stir and store the coating solution for spraying with pneumatic supply and peddle type mechanism.  - Suppliers provide solution transfer assembly which shall be used to supply spray liquid to coater nozzle. | | Lifting and positioning device (LPD) | To support feeding of tablets into the coater and shall be capable of docking IBC of existing design.  Vendor should provide suitable capacity. | | Auto Discharge Station with split butterfly valve assembly | Active split butterfly valve on coater discharge station. Closed transfer of tablets for loading and unloading/ discharge of coated tablets. Split butterfly valve assembly and transfer into coating machine shall be in scope of work. | | Air handling unit, dust collector and scrubber unit | Inlet and exhaust air requirements shall be fulfilled by this unit and the dust could be collected in the BIBO unit. The organic vapor traces should be entrapped in wet scrubber. Scrubber, dust collector and air handling unit shall be in vendor’s scope of work. | | CIP Unit | To clean the Coating Machine, Coating gun and its hose pipes, auto discharge station and other assemblies.  CIP unit should be able to supply Portable Water ( Hot and Ambient) , Purified Water, and Cleaning Solution with Sodium Lauryl Sulfate.  To clean the supply and return duct through HMI operation. | | | | | |
| 5.2 | | Process Flow Diagram: | | | | |
|  | | The sequence diagram is intended as a principle drawing, this means that not all details are shown. | | | | |
| 5.3 | | Process Parameters and Aspects | | | | |
|  | | Critical Process Parameters, CPP’s | **:** | | 1. Inlet air temperature and humidity 2. Exhaust air temperature 3. Product temperature 4. Coater drum differential pressure 5. Inlet airflow 6. Spray rate of coating solution 7. Atomization air pressure 8. Pattern air 9. Rotation speed of coating drum | |
|  | | Critical Design Attributes, CDA’s | **:** | | 1. The equipment and its parts must be easily cleanable. 2. Electrical, cables, pneumatic hydraulic and instrumentation equipment shall be identified and correspond with Electrical and Instrumentation drawings. | |
|  | | Critical Material Attributes, CMA’s | **:** | | 1. Coater housing and pan should be of pharmaceutical grade stainless steel AISI 316L with a suitable surface roughness (Ra <= 1.2 μm). 2. The inside surface (product contacting) should be mirror polished with a lower surface roughness (Ra <= 0.5 μm) 3. Other product contacting surface should be made up of stainless steel AISI 316L, mirror polished and with a surface roughness of Ra <= 0.5 μm. 4. Non-contact part should be of pharmaceutical grade like non-rusting, non-shedding, non-corrosive, or SS 304. 5. Process materials should not react with equipment, product contact parts and MOC certificates required for all contact parts. | |
| 5.4 | | User Requirement | | | | |
| **5.4.1**  1. | | **Tablet Coating Machine**  1. Coating pan should be made up of Stainless Steel AISI 316L material. It should be in a Cantilever design, where the front bearing housing are smooth and easily cleanable.  2. Coating chamber must be in negative pressure with respect to process room and shall be suitable up till OEB 5 products. The chamber shall be fitted with monochromatic lamp.  3. Coating pan drive unit should be adjusted from the HMI to control the speed of rotation.  4. Smooth surface baffles for homogenous mixing of product during process.  5. The occupancy of coating pan should accommodate a minimum of 30% of filled volume and a maximum of 100% of filled volume. The required filled volume should be considered as more or equals to 250 L.  6. The spray system (highly recommended Schlick) should be suitable for both film and functional coating with a aqueous or solvent based coating solution.  7. The angle of positioning coating guns shall be controllable from outside the coating pan. A specific scale should be kept to control the gun to bed distance, without stopping the process.  8. The spray arm (gun holding device) should be designed with scale to indicate the gun to gun distance.  9. The hoses connected to the spray gun should be designed within the spray arm and it is able to be retracted out of the coater for cleaning purpose.  10. Automatic self-cleaning circuit for each spray nozzles during spraying phase. Actuation of needle to remove any deposit present in nozzle inserts should be available.  11. Each gun should be equipped with integrated pressure transmitter that can monitor individual pressure gun chocking and provide a warning when a potential obstruction is expected.  12. The cleaning of guns shall be part of the CIP cycle.  13. The peristaltic spray pump (recommended Watson Marlow) should be installed on the room / equipment wall.  14. A suitable flowmeter should be provided between the peristaltic pump and spray gun where the spray rate are displayed on screen of Coating Machine.  15. Charging tablets into coater is via the auto discharge system, connected to the HMI of coater.  16. The auto discharge shall be designed to operate upon introduction of IBC bin buck valve (existing containment valve).  17. 100% automatic discharging of coated tablets should be in design with an integration of manual valve.  18. The discharge containment manual valve is positioned at height of more than 800 mm from ground level.  19. Suitable solution preparation tank and stirrer should be equipped with pneumatic agitation, grounded on wheels and with an outlet fitting for 100% coating solution discharge. The interior and exterior should be easily cleanable.  20. Loading of tablets shall be via Tablet IBC bin. The lifting and positioning device (LPD) shall be supplied similar to fit the handling of existing tablet IBC bin.  21. LPD shall have a defined angle of movement to enable smooth operation for docking the IBC bin on Auro Discharge station.  22. The Auto Discharge Station shall fit the Buck Valve of existing Tablet IBC bin and shall be operated via HMI.  23. A stainless-steel chute should be provided to transfer the tablets from IBC bin to Coater Pan via the Auto Discharge station.  24. For process steps of pre-heating and drying operations the air shall be supplied through the air handling unit for the coater.  25. Inlet air handling unit (AHU) shall be equipped with Pre filter (G4 filter), Fine filter (F7 filter), and a final HEPA filter (H13 filter).  26. The relative humidity of the process air is measured and displayed on HMI.  27. The AHU body should be insulated with double-walled, incorporating glass wool insulation. The outer wall is made of galvanized and painted carbon steel, while the inner surface are made up of stainless steel 304.  28. Heated air supply are through steam with a maximum of 80 ℃ achievable at the inlet of machine.  29. The steam control valve, steam trap, drain piping and insulation design shall be provided by the vendor.  30. Analog pressure measurement sensor should display the differential pressure on HMI.  31. The dehumidification system should be designed for an ambient air condition of close to 37 ℃ and 80% RH. The position of control valve, temperature of inlet and outlet line shall be displayed on HMI.  32. The GA drawing for connecting ductwork and insulation between Coater and exhaust air system shall be provided.  33. The exhaust air system should be designed with deduster, wet scrubber, blower, ducting and filters.   |  |  | | --- | --- | | 5.4.1.11 | Cleaning of the system shall be through Wash-in- place unit with option for one detergent dosing shall be planned. | | 5.4.1.12 | The WIP time shall be registered. The cleaning process must be documentable. | | 5.4.1.13 | Typical WIP cycle with peak loads shall be suggested by the supplier for this process module. | | 5.4.1.14 | Prior to launch the WIP cycle, some utility connections could be done manually by the operator | | 5.4.1.15 | The WIP unit shall provide connections and spray nozzles in locations as needed to effectively clean the different equipment | | 5.4.1.16 | The WIP unit includes the WIP media supply and return | | 5.4.1.17 | The WIP unit will clean all product contact areas automatically. The supplier will provide solutions for all parts which cannot be cleaned by the WIP unit to ensure wash down or wetting with WIP cycle before dismantling. | | 5.4.1.18 | WIP media shall be supplied with controlled and registered Temperature | | 5.4.1.19 | After the last rinse, the equipment will be completely dried using the preparation air group. | | 5.4.1.20 | After WIP process is ended, the equipment must be clean and dry and will be controlled visually. | | 5.4.1.21 | The full WIP system shall be designed in a sanitary way (easy to clean, no dead-legs). |   5.4.2 Control Functions for Critical and Operational Parameters   |  |  |  | | --- | --- | --- | | **Req. No.** | **Description** | **Equipment operating range/ value** | | **Tablet Coater:**  The below stated functions are the minimum, but not limited to, required functions to be controlled via the HMI | | | | 5.4.2.1 | Inlet air temperature | 20 - 80°C | | 5.4.2.2 | Exhaust air temperature | NMT 80°C | | 5.4.2.3 | Inlet air absolute humidity | STS in gm/kg | | 5.4.2.4 | Dehumidification Temperature | STS in °C | | 5.4.2.5 | Exhaust air absolute temperature | STS in gm/kg | | 5.4.2.6 | Pan Motor Speed | STS in rpm | | 5.4.2.7 | DP Pan | STS in mmWC | | 5.4.2.8 | Air Flow Inlet | STS in cfm | | 5.4.2.9 | Spray Pump Speed | STS in rpm | | 5.4.2.10 | Atomisation Air Pressure | STS in bar | | 5.4.2.11 | Atomisation Air Flow | STS in cfm | | 5.4.2.12 | Pattern air pressure | STS in bar | | 5.4.2.13 | Compressed Air Supply Pressure | STS in bar | | 5.4.2.14 | Front Door Sealing Pressure | STS in bar | | 5.4.2.15 | Spray Solution Flow | STS in gm/min | | 5.4.2.16 | Phase Time | STS in min | | **Solution Preparation Tank and Stirrer:**  The below stated functions are the minimum, but not limited to, required functions to be controlled via the operating panel of the assembly | | | | 5.4.2.13 | Stirrer speed | STS rpm | | **Clean in Place (CIP):**  The below stated functions are the minimum, but not limited to, required functions to be controlled via the HMI | | | | 5.4.2.20 | CIP media pressure | 2 — 6 bar/ STS | | 5.4.2.21 | CIP media flow | STS m3/h | | 5.4.2.22 | CIP media temperature (inlet) | 20 - 60°C | | 5.4.2.23 | CIP media concentration | TBD | | 5.4.2.24 | Drying air (inlet air) | 20 - 85°C | | 5.4.2.25 | Dosing pump | STS |   5.4.3 Alarms, Warnings and Messages –  Only process related alarms are defined. All alarm ranges shall be set through PLC as per process requirements.  Note: The supplier shall evaluate the alarms mentioned and consider all necessary alarms for trouble-free operations.   |  |  |  |  | | --- | --- | --- | --- | | **Req. No.** | **Description** | **Range (Min-Max)** | **Action** | | **Alarms:** | | | | | 5.4.3.1 | Spray rate | STS in g/min | Alarm | | 5.4.3.2 | Spray pump tripped and error |  | Alarm | | 5.4.3.3 | Spray pressure | STS bar(g) | Alarm | | 5.4.3.4 | Pattern air pressure | STS bar(g) | Alarm | | 5.4.3.5 | Inlet air flow | STS m3/h | Alarm | | 5.4.3.6 | Inlet air blower tripped and error |  | Alarm | | 5.4.3.7 | Inlet air temperature | STS | Alarm | | 5.4.3.8 | Exhaust air flow | STS m3/h | Alarm | | 5.4.3.9 | Exhaust air temperature | STS | Alarm | | 5.4.3.10 | Exhaust air blower tripped and error |  | Alarm | | 5.4.3.11 | Inlet air temperature | 20 - 85°C | Alarm | | 5.4.3.12 | Inlet air humidity content | TBD g/kg | Alarm | | 5.4.3.13 | Outlet air temperature | NMT 80°C | Alarm | | 5.4.3.14 | Dosing pump reactions | STS rpm | Alarm | | 5.4.3.15 | Spray pressure in the tube before spray guns | STS bar (g) | Alarm | | 5.4.3.16 | WIP media pressure | 2 - 6 bar (g)/ STS | Alarm | | 5.4.3.17 | WIP media flow | STS m3/h | Alarm | | 5.4.3.18 | WIP media low level |  | Alarm | | 5.4.3.19 | WIP media temperature (inlet) | 20 - 85°C | Alarm | | 5.4.3.20 | WIP media concentration | 1 -200 mS | Alarm | | 5.4.3.21 | WIP cycle - Drying air (inlet air) | 20 -85°C | Alarm | | 5.4.3.22 | Conductivity of final rinse | TBD µS | Alarm | | 5.4.3.23 | Coater pan front door open |  | Alarm | | 5.4.3.24 | Drain valve not open / open |  | Alarm | | 5.4.3.25 | Scrubber pump motor tripped |  | Alarm | | 5.4.3.26 | Scrubber water level and pressure low |  | Alarm | | 5.4.3.27 | Coater pan motor tripped and error |  | Alarm | | 5.4.3.28 | Coater pan is not moving |  | Alarm | | **Warnings:**  Only process related warnings are defined | | | | | 5.4.3.29 | Exhaust Humidity (Optional) | 5% - 40% | Warning – flash on screen | | **Messages:**  Only process related messages are defined | | | | | 5.4.3.30 | Differential pressure — inlet air filter | TBD | Display | | 5.4.3.31 | Differential pressure — outlet air filter | TBD | Display | | 5.4.3.32 | Spraying liquid — maximum set pressure is exceeded or line burst | TBD | Display | | 5.4.3.33 | **Spraying liquid — minimum limit or under-run** | TBD | Display |   5.4.4 Control Systems  **General Control System Functions:**  Coating machine should have its own PLC with HMI and also to be integrated with third party PLC on industrial ethernet TCP/IP over fibre optic transmission on multi-mode fibre optic cable.   |  |  |  | | --- | --- | --- | | **Req. No.** | **Requirements** | **Comments** | | 5.4.4.1 | Control System :   * PLC Siemens * PC-based control system with Windows Professional * Touch panel operation (min 15inch, IP65)   MS SQL database to store the production and audit data | | | 5.4.4.2 | Control Functional Specification (FS):  Required a customizable control operation similar with existing Coater | | | 5.4.4.3 | The system should limit access to authorized individuals. | | | 5.4.4.4 | Passwords shall be constructed using both numeric and alphabetic characters and have a length of minimum 6 characters | | | 5.4.4.5 | Login + password for system access shall be changed regularly (pt. after 90 days). The computer system should enforce automatic expiration of passwords (optional).  Auto Alarm or pop up to be display at least 15 days before expiration | | | 5.4.4.6 | It shall be possible for a system administrator to change a user's password in case the user forgets it or in case the password has been compromised. The change of date and time option is available for admin only | | | 5.4.4.7 | The system should have a password protected screensaver or similar safeguards after a specified period of inactivity. HMI shall be programmed for auto logout | | | 5.4.4.8 | Each attempt at unauthorized access to the system shall be logged by the computer system | | | 5.4.4.9 | The system shall ensure that only authorized individuals can:   * Use the system * Access the operation or computer system input or output device   Perform the operation at hand | | | 5.4.4.10 | The minimum security and access system shall be configured with the following user groups:   * Operator * Supervisor * Engineer / Manager * Maintenance * Administrator   **Note** : The quantity of users should not be limited. | | | 5.4.4.11 | A default “user” (not included in a user group) shall be created. This “user” is logged in at start up and must only have visualization rights to all pictures | | | 5.4.4.12 | **The system shall contain a recipe handling tool, changes in recipes must be logged by user with username and password** | | | 5.4.4.13 | The system shall comply with GAMP 5.0 methodology at a minimum, validated that supplier provides this customer with the functionality, process and technical controls it needs to help comply with regulatory standards including US FDA 21 CFR Part11. | | | 5.4.4.14 | IP Address Configuration and setting of Baud Rate | | | 5.4.4.15 | Design Parameters:  Ambient temperature: 25 +5 °C  Maximum operating temperature: 80°C  Relative Humidity: 3 to 95% | | | 5.4.4.16 | The system shall have Fibre Optic Ports (for Tx/Rx) suitable for ST type connectors. | | | 5.4.4.17 | The system shall be OPC compatible to transfer data via LAN / RJ45. Auto back up feature should be available. | | | 5.4.4.18 | It should have an Industrial Ethernet TCP/IP communication module along with the required Optical Converter of Multi-Mode Transmission. For end connections following shall be provided:   * LIU Unit for 6 core unarmoured fibre optic cable. * Patch Cords for ST type connectors from LIU Unit to Ethernet TCP/IP Converter Modules. * Cable channel and gland plate to be provided in PLC Panel for third party FO cable interfacing.   Splicing of FO cable and jointing at LIU shall be done by others; however necessary coordination to complete the integration work is under the scope of this supply. | | | **Monitoring and Control:**  All controlling shall be based on recipes. High level user interface/ software interface shall be provided. In case of power failure, parameters cannot be changed, but operator interference is required to restart the machine without interfering into parameter. All measurements, actions and valve settings shall be logged to document the executed process. But suppliers should also provide manual run options without any pre-set value along with monitoring and logging of all identified run parameters.  The screen layout must have following information:   * Logo * Current date and time * Current user / operator name and ID * Batch Number * Command-button for login / logout * PFD * Batch run time * All process Parameters (pressure, temperature, flow rates, levels, all log in log out details should be in / part of printout etc.) * Warnings and alarms indication (visual and audio) | | | | **Req. No.** | **Description** | | | 5.4.4.20 | The screen layout shall have process pictures/ PFD, these pictures shall contain information about the running process, and it must show an overview of the skid. | | | 5.4.4.21 | The screen layout shall have parameter pictures present all critical product, equipment and non-recipe parameters. It must be possible to change parameter settings with log to record the change with username and date | | | 5.4.4.22 | The screen layout shall have alarm summary list. | | | 5.4.4.23 | The operation panel shall have emergency stop button to handle emergency event and designed to stop all physical movements of the equipment immediately. All devices shall go to their “original" state after emergency stop button pushed | | | 5.4.4.24 | When activated, the emergency stop shall shut the system down immediately in accordance with the following requirements:   * No damage to the machine or product shall occur as a result of an emergency stop * In case of emergency stop, batch ID, batch status and sequence information can't be lost. * Emergency stop shall take action to prevent product contamination * The machine shall not be allowed to restart without operator intervention. It shall be necessary to restore the emergency stop button to the original state before restarting. | | | 5.4.4.25 | A printer connection shall be available, standard PC interface (Ethernet RJ 45/LAN and USB, to print documents illustrating production data and pre-set regulation parameters for each product.Furthermore, the possibility to equip the printer with the Ethernet web connection allows the location of the printer on a desk or table i.e. PAMs. | | | 5.4.4.26 | **The system shall have provision to communicate to Central PLCUSCADA on Industrial Ethernet TCP/IP (multi-mode FO cable). The list of signals exchanged between Equipment PLC and Central PLC/SCADA shall be detailed later.** | | | **Batch report:**  The system shall be able to create a batch report saved locally in a storage space available with machine; after each cycle to document the executed process. The batch processing report shall be created with the following minimum requirements but could be elaborated by the supplier: | | | | 5.4.4.27 | Date | | | 5.4.4.28 | Start and stop time for the recipe | | | 5.4.4.29 | Product name | | | 5.4.4.30 | Batch number | | | 5.4.4.31 | All recipe values | | | 5.4.4.32 | All executed values (Process data- table with actual set point for all minimum and maximum values)  All control functions and measured values | | | 5.4.4.33 | All Login interactions/interventions | | | 5.4.4.34 | All events | | | 5.4.4.35 | All messages | | | 5.4.4.36 | All measurements & graph (the set point of measured parameter needs to be displayed on the graph) | | | 5.4.4.37 | AII Alarms | | | 5.4.4.38 | Operator ID | | | 5.4.4.39 | PDF batch record shall be generated at batch end and shaft not be modifiable. | | | **Back up and data management:**  The system shall be able to take back up after each batch and cleaning cycle | | | | 5.4.4.40 | The historical data of the system shall be stored in dedicated server/ suppliers control system at least for 6 months. Historical data should be accessible and available for trending and analyzing. | | | 5.4.4.41 | System shall be able to make data backup automatically or manually. The data backup includes all raw data, configurations and audit trail records. | | | 5.4.4.42 | System shall be able to support to archive backup database to external storage. | | | 5.4.4.43 | System shall be able to retrieve and restore data from the backup database. | | | 5.4.4.44 | The supplier shall design the system to include a “safe state” in which the likelihood of injury to personnel and damage to the equipment is minimized. | | | 5.4.4.45 | On power failure the system shall be positioned in a safe state. On power restoration, the system shall be able to start by itself and recall all controlling parameters.  A “safe state" shall be defined as:  All motion stopped on the machine  Valves and actuating devices go to safe state and to keep containment intact (TBD by supplier) | | | 5.4.4.46 | In the event of a power failure, the system shall protect in the following priority:   1. **Personnel** 2. **Equipment** 3. **Product** | | | 5.4.4.47 | Manually re-start based on Operator / Supervisor's inputs (Operator / Supervisor initiates power recovery sequence). | | | 5.4.4.48 | All equipment shall be designed to retain the Programmable Logic Controller (PLC) program in case of power loss and be able to recover with minimal operator actions. | | | 5.4.4.49 | System's controller, such as PLC, shall be controlled by Uninterrupted Power Supply (UPS) system provision which is provided by the client. The control power specification is 1KVA, 230VAC, 50Hz | | | 5.4.4.50 | The information in the batch reporting system shall be retained in the event of a power failure. | | | 5.4.4.51 | The seller shall provide PLC source code hard copy and electronic version to facilitate reprogram or program updating in the future. | | | 5.4.4.52 | Furthermore, the possibility to equip the printer with the Ethernet web connection allows the location of the printer on a desk or table. | | | 5.4.4.53 | The system shall have a maintenance mode, which will allow troubleshooting of the equipment without an excess of constraining interlocks | | | 5.4.4.54 | The system shall have an automated mode utilizing recipes for typical batch process operations having minimal operation interaction. | | | | | | |
| 5.5 | | Material of Construction | | | | |
|  | | All product contact parts | **:** | | SS316L with Mirror Finish | |
| Other non-product contact | **:** | | SS304 with Matt Finish | |
| Elastomers in contact with product | **:** | | Silicon | |
| Elastomers not in contact with product | **:** | | Food Grade | |
| **6.0** | | **CLEANING REQUIREMENTS** | | | | |
|  | | 1. In accordance with cGMP guidelines the units must be easy to clean, disinfect and sterilize when necessary. 2. The design should be such as to allow mechanical cleaning of the surface, and that the cleanliness of the surface can be checked easily. 3. All machine parts, in particular instrumentation, should be constructed so that they can be easily removed and calibrated 4. All special tools required for running and maintenance should be adequate. 5. Adequate rotating jet spray balls design for all CIP ports with suitable water pressure. 6. The cleaning cycle includes    1. Wetting with Portable Water (Hot / Ambient)    2. Dosing with detergent (SLS)    3. Washing with Portable Water (Ambient)    4. Rinsing with Purified Water 7. The entire cleaning should be completed in less than 1 hour. | | | | |
| 6.1 | | Recommended cleaning and / or sanitization agent and its chemical nature | **:** | | 1. Potable Water 2. Purified Water 3. Sodium Lauryl Sulfate | |
| **7.0** | | **GENERAL REQUIREMENT** | | | | |
| 7.1 | | |  |  | | --- | --- | | **Req. No.** | **Specification** | | 1. | The contractor must specify for each piece of equipment the Guaranteed performance and the guaranteed system performance. The values will be tested on the acceptance test. | | 2. | In addition, the functionality described in the user requirements and details in the system specifications will be tested. | | | | | |

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| **8.0** | | **INSTALLATION** |
| 8.1 | | |  |  | | --- | --- | | Positioning and Dimensions | | | **Req. No.** | **Requirements** | | 8.1.1. | **Room Conditions:**  NMT 25°C  NMT 60% RH  **Room Classification:**  Grade D  ATEX classification of the process room: Zone 21  The HMI panel will be installed to Ex Zone of the process room | | 8.1.2. | The supplier will provide with the quotation general arrangement layout of the coater including technical equipment and critical dimensions for the equipment entrance and maintenance | |
| 8.2 | | Installation Requirements  Below the requirements are separated into general requirements and requirements for each process module or unit.   |  |  | | --- | --- | | **Req. No.** | **Requirements** | | 8.2.1 | General installation requirement specification describes the requirements for process systems, process support and utility systems | | 8.2.2 | Installations shall follow all government regulations | | 8.2.3 | All major components shall be CE compliant and in accordance with the relevant directives | | 8.2.4 | Framework and carriages shall be made of stainless steel AISI SS304L or better. | | 8.2.5 | All labeling shall be long-lasting, scratch and abrasion-resistant, well readable and resistant to solvent based cleaning agents | | 8.2.6 | In general, the equipment has to be designed in a way to get easy and quick access to all necessary maintenance points e.g. pumps, motors, filters, valves, instruments etc. | | 8.2.7 | Plug-in type format parts with centering rings and quick connections are provided for all format parts to secure minimum change over time. | | 8.2.8 | ATEX classification. The supplier shall provide the ATEX classification of its equipment | | 8.2.9 | All product contact parts must be made of stainless steel, AISI 316L with surface grade Ra ≤ 0.4 mm and mirror polished.  Material certificates will be supplied for all parts that are exposed to product EN 10204-3.1 The vendor will deliver certificates of roughness for all product contact parts. | |
| 8.3 | | Special Installation Requirements |
| 8.3 | |  |  | | --- | --- | | **Req. No.** | **Requirements** | | 8.3.1 | **Tablet coater**:   1. Pan / Drum diameter and pan / drum mouth diameter and Length of pan 2. Pan sizes shall be suggested for different batch sizes by the supplier. 3. MOC of Pan shall be SS 316/ SS316L 4. Perforated Pan shall be provided 5. Area of perforations to be mentioned 6. Size of perforations to be mentioned 7. Coating drum and baffles (or spirals): surfaces in contact with product must be smooth, without sharp edges (edges must be chamfered smoothened, and the moving part of the equipment shall not damage the product which could be a possible reason for product rejection 8. Reproducible adjustment of the spraying arm, angle, nozzle locations, angle and distance to core-bed. 9. These positions should be clearly marked to allow reproducible adjustments 10. The number of spray nozzles shall guarantee the equal distribution of coating solution to the product bed 11. The spraying device shall be mobile (STS) and removable from the pan for cleaning 12. Spray nozzle shall be closed as soon as the spray process is stopped. 13. Vibrations shall be avoided; the system shall be supplied with anti-vibration feet 14. Contained sampling options shall be provided   Discharging of coated tablets using split butterfly valves by rotating the coater drum in opposite direction, which shall start the discharging of tablets automatically  **Solution Preparation tank and stirrer** :   1. Capacity to be suggested with dosing pump, top mounted variable drive pneumatic agitator. 2. Zero hold-up design to be provided for the tank system 3. Minimum stirring volume to be indicated by the supplier 4. The range of viscosity of solution to be indicated by the supplier 5. Temperature and agitator pneumatic controller and indicator with display shall be provided 6. All manual valves in the system shall be in accessible positions 7. Tank shall be mounted on legs with antistatic caster wheels 8. The flexible hose connection from the tank, transfer pump to coater spray nozzle is in the scope of supplier 9. Temperature and pressure rating of the system and instruments installed on the tank shall be specified by the supplied 10. Coating solution spray rate shall be adjustable and measurable. | | |
|  | |  |  | | --- | --- | | **Req. No.** | **Requirements** | | 8.3.1 | 1. Coating solution spray rate shall be adjustable and measurable. 2. Coating suspension recirculation in case spraying is stopped. 3. Flow rate of coating solution to the spray guns needs to be controlled and monitored by means of the dosing pump and a mass flow meter. Mass flow sensor to be provided (Supplier to check & confirm) 4. Each solution line from the pump head is fitted with a pressure switch, with ensures that a spray gun become blocked then the pump system will stop before the connecting pipe burst out 5. The mass flow meter shall be able to control and shut off the pump if air bubbles are in the solution or definite amount of coating solution is dosed 6. The cleanability of the equipment to be ensured by manually disassembling the system   **Washing-in-place (WIP) system:** Tank with pump skid can be planned by the supplier  The system shall have two option of recipes to have the following:  Washing-in-place:   * Wash down of valve assembly * Wash-off of spray nozzles   After dismantling the spray nozzles for manual cleaning  Wetting-in-place:   * Automatic cleaning of drum and internals of the coater  1. Control of the WIP system shall be performed through PLC of the coater and the key process parameters shall be monitored and trended from the HMI 2. All inlet utility isolation auto valves shall be considered for fully automatic cleaning cycle. All inlet utility isolation auto valves shall be considered for fully automatic cleaning cycle 3. Installation with automatic isolation valves on drain line to be provided to collect high contaminated and low contaminated liquid drains separately 4. Cleaning in place recipe shall be built as per the product characteristics 5. Detergent addition station with pump for dosing shall be provided (one detergent to be planned) 6. Final rinse cycle shall be complete with conductivity measurement (online / manual sampling option to be finalized by customer) 7. Process Compressed air to purge pipes before drying cycle 8. The WIP system should be designed for the cleaning of all internal surfaces of the equipment including the exhaust air duct   Installation with automatic isolation valves on drain line to be provided to collect high contaminated and low contaminated liquid drains separately. | | |
|  | |  |  | | --- | --- | | **Req. No.** | **Requirements** | | 8.3.2 | All motors shall be FLP designed | | 8.3.3 | All product contact surfaces shall be stainless steel 316Lwith Ra ≤ 0.4 um finish with mirror polish | | 8.3.4 | All non-metallic materials shall be FDA compliant materials | | 8.3.5 | Dual drain philosophy with diverter valve to collect / divert high and low contaminated liquid waste shall be considered for coater and WIP unit. The integration with the drain system shall be further discussed during the later phase. | | 8.3.6 | Dust collector with Bag-in Bag-out system safe change technology shall be provided by the supplier | | 8.3.12 | Inlet air handler:   * Filter step I (pre-filter) G4 required * Design criteria for dehumidification system shall be indicated * Heater required * Filter step Il (fine-dust filter) F7 required * Filter step Ill (HEPA) H13 required * Filters shall be delivered with certificate and tested for integrity * Vibrations shall be avoided; the system shall be supplied with anti-vibration feet * Fan mounted on a frame with vibration absorbers shall be provided * Differential pressure sensor with switch / transmitter for the inlet air pre-filters, current values shall be indicated (local pressure measurement)   Inlet and exhaust air piping diameter to be mentioned | | 8.3.13 | Exhaust/ Outlet air handler:   * Double HEPA Filter H13 + H14 with bag-in & bag-out functionality is required * The exhaust from the air handling unit shall be terminated in wet scrubber unit, which shall be in the scope of supplier * Scrubber installation shall be part of the system to suppress solvent vapors apart from dust * Wet scrubber shall be delivered with certificate for the solvents handled as listed in this URS   Inlet and outlet explosion protection valve shall be provided with safety interlocks and earth continuity | | |
| 8.4 | |  |  |  | | --- | --- | --- | | Requirements for Buildings | | | | **Req. No.** | **Requirements** | **Comments** | | Process module comprises of Coater with air handling unit, dust collector and WIP unit to be installed at ground floor processing area in this manufacturing building. | | | | 8.4.1 | Tablet coater to be installed in clean room (Grade D area) | N/A | | 8.4.2 | Air handling unit and WIP unit to be installed in non-classified areas (NC) | N/A | | 8.4.3 | Free fresh air supply is considered in the technical area where the air handling unit is located. | Supplier shall specify the quantity of air to be supplied in m³/h | | 8.4.4 | Supplier shall specify the dimension of the exhaust air of the following: Dust extractor, air handling unit. | N/A | | 8.4.5 | Wall portioning shall be installed after the installation of the equipment (especially with installation through the wall).  Finishing (silicone, airtightness) shall be ensured by Novugen Oncology. | N/A | | |
| 8.5 | |  |  |  |  | | --- | --- | --- | --- | | Utility Connections | | | | | Connection of utilities from header to the process equipment and auxiliary equipment shall be in Novugen Oncology scope of work.  Supplier to provide suitable endtraining connections to connect utilities.  Electric cable delivery near the electrical cabinet is done by Novugen Oncology. The connection of the cable from the cabinet to the equipment shall be in the scope of Vendor.  The layout / design shall be provided by Vendor after discussing with Novugen Oncology engineering and production teams, ensuring all equipment physical integrations requirements are planned beforehand and delivered before the equipment delivery at Novugen site.  Vendor to consider the exhaust air piping, electrical wiring, and piping length in actuals during the installation from main to auxiliary equipment. The scope of supply to be clearly mentioned in the P&ID and all relevant drawings submitted for approvals. | | | | | **Service** | **Supply Conditions** | **Average Operating Load** | **Peak Load** | | Electricity | 3 Phase | 415 Volts ± 10%,  Frequency: 50Hz | To be advised | | Compressed Air | Process air  Pressure: 3.5 bar  Instrumentation air: 6 bars | Operating pressure required: STS  Operating temperature required: STS | STS | | Process inlet and exhaust air from air handling unit | Inlet air volume: STS m3/hr  Inlet air pressure: STS bar | Inlet air volume: STS m3/hr  Inlet air pressure: STS bar | STS | | Outlet air volume:  STS m3/hr  Outlet air pressure: STS bar | Outlet air volume:  STS m3/hr  Outlet air pressure: STS bar | STS | | Chilled water for air handling unit | Supply Pressure: 2 - 4 bar  Supply temperature: 7oC | Operating pressure required: STS  Operating temperature required: STS | STS | | Steam | Supply Pressure: 3.5 bar  Supply temperature: 120 - 130oC | Operating pressure required: STS  Operating temperature required: STS | STS | | Steam condensate | NA | Pressure & Temperature - STS | STS | | |
|  | |  |  |  |  | | --- | --- | --- | --- | | **Service** | **Supply Conditions** | **Average Operating Load** | **Peak Load** | | Potable water ambient | Pressure: 1-3 bar  Temperature: Ambient | Operating pressure required: STS  Operating temperature required: STS | STS | | Potable hot water | Pressure: 1 -3 bar  Temperature: 60 oC | Operating pressure required: STS  Operating temperature required: STS | STS | | Purified water | Pressure: 1 -3 bar  Temperature: Ambient | Operating pressure required: STS  Operating temperature required: STS | STS | | |
| 8.6 | |  |  |  |  | | --- | --- | --- | --- | | Maintenance and Calibration | | | | | **Sr. No.** | **Item** | **Requirement** | **Comment** | | 1. | Maintenance | Ensure that maintenance is performed in hygienic condition | N/A | | 2. | Calibration | Calibration procedure / manual shall be provided by the Vendor. Spare parts / accessories shall be readily available for easy purchase | | 3. | Service Contract | Together with the quotation Novugen Oncology would like to have a separate quotation for a service contract, including:   1. Price of maintenance once a year   Two years’ spare parts (if required) are in the inventory and to be delivered within 5 working days | Optional | | |

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| **9.0** | **HEALTH, SAFETY AND ENVIRONMENT** |
| 9.1 | |  |  | | --- | --- | | Noise level shall be less than 85 dB | All these must be provided by Vendor during equipment design | | Mechanical guards for all rotating parts | | Electrical panels shall be properly grounded with no unsecured parts | | All motors must be thermally protected | | All the installation must be in accordance with cGMP compliance | | Moving parts shall be guarded and secured with interlocking system | | Have an E-stop mechanism designed to stop all physical movement of the equipment | | Provide personnel training of operator and maintenance Engineer, validation execution, fast maintenance and guarantee against damage | | The ergonomic aspect of staff to handle | | Safety signages, Interlocks, flame proof electrical fittings and earth grounding shall be ensured. | | The cGMP concerning safety must be applied | |

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| **10.0** | **DOCUMENTATION / TRAINING** |
| 10.1 | Desired Documents**:** |
|  | |  |  |  | | --- | --- | --- | | Documents should provide by the Suppliers: | | | | **Sr. No.** | **Component/Features** | **Description** | | 1. | Material of construction Certificate (MOC) | MOC certificates are required for all major components. | | 2. | Calibration Certificates | As applicable | | 3. | Qualification Document (DQ/IQ/OQ) | Required. | | 4. | Hardware installation test | Required. | | 5. | Operation and Maintenance Manual | Required. | | 7. | Control panel assembly Drawings | Required. | | 8. | Equipment assembly Drawings | Required. | | 9. | Spare part list | Required. | | 10. | Electrical wiring / Control Panel Assembly Drawings | Required. | | 11. | Guarantee Certificate | Required. | | 12. | Mechanical Drawings   * Equipment / Systems electrical drawing * Point to point wiring diagram | Required. | |

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| 10.2 | Training**:** | | | |
|  | |  |  |  | | --- | --- | --- | | **Sr. No** | **Requirements** | **Comments** | | 1. | The machine shall be easily accessible to perform maintenance and service | NA | | 2. | All possible adjustments on mechanics and instrumentations shall be defined and described in the documentation | NA | | 3. | Proposal for service contract for periodic maintenance service shall be included as an option in the quotation | NA | | 4. | The maintenance personnel shall have the necessary training in operation and maintenance. A training program shall be included as an option in the quotation | NA | | 5. | A list of excepted service life and recommended service intervals of critical components shall be supplied | NA | | 6. | All training and documentation regarding training shall be done in the English language | NA | | 7. | Provide personnel training of operator and maintenance Engineer, validation execution, fast maintenance and guarantee against damage | NA | | 8. | Vendor to provide warranty from the date of installation as agreed with customer during order finalization | NA | | 9. | Accept on-site audit by Client | NA |   **Training:**  The Vendor shall provide a detailed and training for Operation and maintenance procedure. All equipment shall allow for a tool-less conversion wherever possible.  If any equipment requires special (un-common hand-tools) tools for changeover or common maintenance, these tools (two sets) shall be supplied with the equipment and cost shall be contained in the base price. | | | |
| **11.0** | **REFERENCES AND DEFINITIONS** | | | |
| 11.1 | Reference Documents**:** | | | |
|  | |  |  | | --- | --- | | QA Reference | Volume 4 of “The rules governing medicinal products in the European Union” Annex 11 Computerized Systems | | EHS Reference | Compliance with the Safety, Health, and Welfare at Work Act | | EHS Reference | EC Declaration of Conformity for equipment and machinery in accordance with EC Council Directive 98/37/EC | | EHS Reference | Compliance with the Low Voltage Directive 72/23/EEC | | | | |
| **12.0** | **ABBREVIATIONS:** | | | |
|  | | **Abbreviation** | **Full Form** | | --- | --- | | GA | General Arrangement | | GMP | Good Manufacturing Practice | | N/A | Not Applicable | | No. | Number | | MOC | Material of Construction | | FAT | Factory Acceptance Test | | SAT | Site Acceptance Test | | IQ | Installation Qualification | | OQ | Operational Qualification | | Sr No. | Serial Number | | URS | User Requirements Specification | | FS | Functional Specification | | OEM | Original equipment manufacturer | | QA | Quality Assurance | | GAMP | Good Automated Manufacturing Practice | | ATEX | Atmosphere Explosible | | cGMP | Current Good Manufacturing Practice | | STS | Supplier to Specify | | | | |
| **13.0** | **REVISION HISTORY:** | | | |
|  | **Rev. No:** | **Effective date:** | **Reason for revision** | |
| 00 |  | New URS | |
| **14.0** | **VENDOR ACCEPTANCE**  The User Requirement Specification has been discussed and agreed upon. We hereby declare that we will supply the System/Equipment/Instrument/Software as per above laid down specification. | | | |
| **Name of the Vendor** | | | **Signature / Date** |
|  | | | |