**PRILOG I. –** *ATTACHMENT I.*

TEHNIČKE SPECIFIKACIJE /

*USER REQUIREMENT SPECIFICATION*

Automatic monoblock filling and capping machine for sterile pharmaceutical products

# INTRODUCTION

The scope of this document is:

* To define the requirements for the equipment
* To indicate product type
* To define services to be rendered by the supplier
* To specify documentation that must be included with equipment

# OVERVIEW

Machine will cover application in pharmaceutical area, installed in cleanroom classified as “A/B” area following current EU GMP regulations. Area will be located in Pilot Plant, not yet constructed. Machine will be used for production of non-GMP and GMP products.

All cleanroom conditions regarding class “A/B” area will be provided by JGL.

Machine will be used for filling sterile liquids into plastic or glass bottles and closing it with snap-on or screw on plastic closures in aseptic environment with operating speed, optimally, up to 60 pcs/min.

Products may consist of screw neck bottle with dropper and cap, screw neck bottle with dropper and cap as one piece, or snap-on bottle with spray pump/dropper pump. Pumps may or may not have dip tubes that enter bottles during closing phase.

# REQUIREMENTS

## 3.1. Directives and standards compliance

The machine must be designed, manufactured, and tested following current EU GMP requirements, applicable FDA and CE Guidelines.

It is necessary to differentiate the requirements according to the keywords:

* mandatory = a strict requirement with critical impact – no deviation is allowed
* must = a strict requirement, without the possibility of deviation
* need = a request that is necessary to follow, but variation in the solution is allowed
* may = optional request, allows deviation or non-performance

## 3.2. General requirements

| **URS ID** | **Required specification** | **YES** (if offered specification is equal to one required) / or **WRITE OFFERED SPECIFICATION DETAILS** | **Notes, remarks, references** |
| --- | --- | --- | --- |
|  | All parts in contact with the product and/or packaging material must be designed to ensure that there is no possibility of defect on product and/or packaging material due to line processing |  |  |
|  | Machine must be designed to operate in class “A” following current EU GMP regulations. Laminar airflow must be ensured in all parts of the machine to avoid contamination of product |  |  |
|  | Machine must be designed to operate in passive/open “RABS” (Restricted Area Barrier System) mode. During production run, access to the restricted area is possible only through gloves.  Laminar air flow (LAF) inside room where machine will be installed will be provided by JGL. |  |  |
|  | Machine must have prearranged positions for onboard particle counters, active microbial sampler and settle plates in critical areas |  |  |
|  | Machine must have as small as possible footprint |  |  |
|  | Machine base must be made of aluminium and/or stainless steel, and top plate must be made of AISI 316L |  |  |
|  | All parts that are in contact with any part of the product must be made of materials which have no impact on product quality |  |  |
|  | Machine drive must be infinitely variable via servo motor |  |  |
|  | Machine guards must be from tempered glass |  |  |
|  | Machine must have internet connectivity to allow remote assistance |  |  |
|  | Automation architecture must be based on Siemens PLC S7 or equivalent[[1]](#footnote-2) |  |  |
|  | PLC backup program must be supplied with the machine to allow future maintenance |  |  |
|  | Machine must be equipped with all safety devices required by the current CE standard |  |  |
|  | Each removable part must be marked with a unified mark in order to avoid mixing |  |  |

# MACHINE DESIGN REQUIREMENTS

* 1. **BOTTLE UNSCRAMBLER/TURNTABLE**

| **URS ID** | **Request specification** | **YES** (if offered specification is equal to one required) / or **WRITE OFFERED SPECIFICATION DETAILS** | **Notes, remarks, references** |
| --- | --- | --- | --- |
|  | Machine must be designed to process containers within the following size range:  Unscrambler for plastic bottles (containers):  Ø: min. 20 mm – max 35 mm  H: min 30 mm – max 75 mm  Turntable for glass bottles (containers):  Ø: min. 30 mm – max 40 mm  H: min 60 mm – max 75 mm |  |  |
|  | Plastic bottles are supplied to the machine in steri-dual™ or LDPE bags with each bag containing a minimum of 100 bottles. |  |  |
|  | Plastic bottles must be processed in a sorting unit to ensure correct orientation |  |  |
|  | Glass bottles will be supplied to the turntable in a tray upside down. Table must be equipped with a turning device which will rotate the bottle tray by 180° |  |  |
|  | Sorting unit must be easily accessible for installation and removal during changeover and cleaning |  |  |
|  | Unscrambler / turntable performance must be at least 10% above the filling / capping machine |  |  |
|  | It is mandatory that no physical damage is allowed on the containers after the unscrambling process |  |  |
|  | Machine operation must not disturb the laminar flow |  |  |
|  | Unscrambler for plastic bottles must be outside open/passive RABS system |  |  |

* 1. **PRODUCT BUFFER VESSEL**

| **URS ID** | **Request specification** | **YES** (if offered specification is equal to one required) / or **WRITE OFFERED SPECIFICATION DETAILS** | **Notes, remarks, references** |
| --- | --- | --- | --- |
|  | Filling machine must be equipped with a buffer vessel without overpressure (vented to room pressure) |  |  |
|  | Buffer vessel must be made of AISI 316L or AISI 316Ti |  |  |
|  | Buffer vessel volume must be adequate to ensure there is no influence of product level to the filling system precision.  Product will be transferred to the buffer vessel pressurized to approx. + 0,5 barg |  |  |
|  | Product may be transferred to the buffer vessel in inert atmosphere |  |  |
|  | Buffer vessel must be equipped with a level monitoring system which will indicate the minimum and maximum level |  |  |
|  | Buffer vessel must be equipped with a sanitary membrane valve (Gemü or similar) which will be controlled with before mentioned level probe. Valve should open when the level reaches low position and close when the vessel is full |  |  |
|  | Buffer vessel must have a magnetic mixer installed on the bottom |  |  |
|  | Buffer vessel must be easily removable for offline cleaning |  |  |
|  | Filling line must be equipped with two (2) buffer vessels. One vessel will be used on the line, second for spare. |  |  |
|  | All parts in contact with the product must be sterilizable in autoclave. Equipment must be built to withstand steam sterilization process at at least 121°C |  |  |

* 1. **FILLING STATION**

| **URS ID** | **Request specification** | **YES** (if offered specification is equal to one required) / or **WRITE OFFERED SPECIFICATION DETAILS** | **Notes, remarks, references** |
| --- | --- | --- | --- |
|  | Dosing system technology must be volumetric piston pump |  |  |
|  | Pump stroke must be controlled via servo motor |  |  |
|  | Pump volume must be controlled via HMI. Central volume adjustment is mandatory |  |  |
|  | System must be equipped with drip retraction technology |  |  |
|  | Filling needle stroke must be controlled via servo motor |  |  |
|  | Filling system dosing range:  **Min. volume: 2.0 ml**  **Max. volume: 40.0 ml**  Volume range can be supplied with different dosing sets |  |  |
|  | All parts of the filling system in contact with the product must be sterilizable in autoclave |  |  |
|  | Dosing system must support any of the following water like liquids: solutions, suspensions, emulsions and viscous products. Some products may have foaming behaviour during filling, and the machine must be adjustable to such products |  |  |

* 1. **SPRAY PUMP / DROPPER FEEDING AND CLOSING SYSTEM**

| **URS ID** | **Request specification** | **YES** (if offered specification is equal to one required) / or **WRITE OFFERED SPECIFICATION DETAILS** | **Notes, remarks, references** |
| --- | --- | --- | --- |
|  | System will be used to sort and supply either spray pumps or droppers, depending on the product type |  |  |
|  | Spray pumps or droppers are supplied to the machine in steri-dual™ or LDPE bags with each bag containing a minimum of 100 pumps. |  |  |
|  | Spray pumps or droppers must be processed in a sorting unit to ensure correct orientation. |  |  |
|  | Sorting unit must be easily accessible for installation and removal during changeover and cleaning |  |  |
|  | All parts in contact with the pumps or droppers must be sterilized in autoclave. Equipment must be built to withstand steam sterilization process |  |  |
|  | In case of spray pumps, a centring device for dip tubes is mandatory. Centring device must ensure that dip tubes which are off centre from the pump are securely centred and positioned in the bottle without any damage to the dip tube, spray pump or bottle |  |  |
|  | In case of spray pumps with dip tubes, dip tube presence verification device is mandatory. Device must ensure that the dip tube was present and integral part of the spray pump assembly at the moment of closing dip the tube with the bottle. Spray pumps with inadequate dip tubes must be rejected |  |  |
|  | Before closing, a N2 gassing system must be installed to create inert atmosphere in the bottle. If the machine has different dropper / pump closing station, gassing system must be installed on each one. |  |  |
|  | After the bottle top and bottle are closed, a height inspection system must confirm correct placement. Objects which are too high or too low must be rejected |  |  |
|  | Format change must be quick and easy. No special tools should be required (If special tools are required, they must be supplied by supplier) |  |  |

* 1. **SCREW CAP FEEDING AND CLOSING SYSTEM**

| **URS ID** | **Request specification** | **YES** (if offered specification is equal to one required) / or **WRITE OFFERED SPECIFICATION DETAILS** | **Notes, remarks, references** |
| --- | --- | --- | --- |
|  | Caps are supplied to the machine in steri-dual™ or LDPE bags with each bag containing a minimum of 100 pieces. |  |  |
|  | Caps must be processed in a sorting unit to ensure correct orientation |  |  |
|  | Sorting unit must be easily accessible for installation and removal during changeover and cleaning |  |  |
|  | All parts in contact with the caps must be sterilizable in autoclave. Equipment must be built to withstand steam sterilization process |  |  |
|  | System must be equipped with gripper closing heads |  |  |
|  | Each closing head must be individually controlled via servo motor |  |  |
|  | Each closing head must control the closing torque |  |  |
|  | During closing, bottle must be held in place using grippers |  |  |
|  | Capping unit should have consistent cap torque, the torque is adjustable according to the container closure system requirements |  |  |
|  | In case the torque is too high or too low, product must be rejected |  |  |
|  | In case the cap is too high or too low after closing, product must be rejected |  |  |

* 1. **REJECT STATION**

| **URS ID** | **Request specification** | **YES** (if offered specification is equal to one required) / or **WRITE OFFERED SPECIFICATION DETAILS** | **Notes, remarks, references** |
| --- | --- | --- | --- |
|  | Reject station must be equipped with a removable tray to ensure easy takeout of faulty objects |  |  |
|  | Removable tray and bottles must be removed without interrupting the open/passive RABS process |  |  |
|  | Reject process must not influence the line speed |  |  |
|  | Reject process must be controlled and verified. In case the rejected bottle is not confirmed machine must stop immediately |  |  |

* 1. **TRANSPORT SYSTEM**

| **URS ID** | **Request specification** | **YES** (if offered specification is equal to one required) / or **WRITE OFFERED SPECIFICATION DETAILS** | **Notes, remarks, references** |
| --- | --- | --- | --- |
|  | Bottle, bottle top and closed product transport system must be designed to transport the objects without damaging the parts or altering them in any way |  |  |
|  | Transport system must not generate any measurable particles |  |  |

* 1. **QUALITY INSPECTION**

| **URS ID** | **Request specification** | **YES** (if offered specification is equal to one required) / or **WRITE OFFERED SPECIFICATION DETAILS** | **Notes, remarks, references** |
| --- | --- | --- | --- |
|  | Machine must be equipped with safety control devices to ensure each phase of product processing did not damage the product in any way. These systems must include:   * Spray pump dip tube presence right before closing the bottle with spray pump * Spray pump/dropper pump presence on bottle after closing * Spray pump/dropper pump height on bottle after closing * Defined cap torque applied to the bottle * Confirmation in case of reject |  |  |

* 1. **PARTICLE COUNTERS**

| **URS ID** | **Request specification** | **YES** (if offered specification is equal to one required) / or **WRITE OFFERED SPECIFICATION DETAILS** | **Notes, remarks, references** |
| --- | --- | --- | --- |
|  | Particle counter must be supplied with the machine. Particle counter must be placed at the position of product filling |  |  |

* 1. **SETTLE PLATES**

| **URS ID** | **Request specification** | **YES** (if offered specification is equal to one required) / or **WRITE OFFERED SPECIFICATION DETAILS** | **Notes, remarks, references** |
| --- | --- | --- | --- |
|  | Settle plate holders must be positioned on the line. Position must contain two settle plate holders. One holder will be used for the settle plate, other for the holder. Settle plate holder must be placed on position of product filling |  |  |
|  | Settle plates must be placed and removed of their respective holders without opening the open/passive RABS system. This must be ensured for each settle plate position |  |  |

* 1. **ACTIVE MICROBIAL COLLECTOR**

| **URS ID** | **Request specification** | **YES** (if offered specification is equal to one required) / or **WRITE OFFERED SPECIFICATION DETAILS** | **Notes, remarks, references** |
| --- | --- | --- | --- |
|  | Active microbial collector must be supplied with the machine. Active microbial collector must be placed on position of product filling to ensure that the product was not contaminated by any possible operator intervention |  |  |

* 1. **USER INTERFACE & OPERATING SYSTEM**

| **URS ID** | **Request specification** | **YES** (if offered specification is equal to one required) / or **WRITE OFFERED SPECIFICATION DETAILS** | **Notes, remarks, references** |
| --- | --- | --- | --- |
|  | Machine must be equipped with a PLC combined with touch-screen easy to use with protective equipment through which all commands, real-time cycle data, program data and alarms will be inputted and displayed |  |  |
|  | Machine must be designed to follow GAMP5 requirements |  |  |
|  | All parameters must be kept in the Audit trail. Audit trail data must be stored locally on the machine and must have possibility of a transfer to another system |  |  |
|  | Logging on to the system must precede entering the operator’s ID and password |  |  |
|  | Machine must have domain based user authentication |  |  |
|  | HMI must be in accordance with 21 CFR Part 11 and Annex 11 EU GMP |  |  |
|  | User right levels must be defined at least as:   * Guest (read only, basic access) * Operator * Maintenance * Administrator |  |  |
|  | Machine must be equipped with an Emergency Stop push-button key lock, mounted on the control panel. It switches OFF the power for electrical control system, stopping instantly all electrical, pneumatical and mechanical operations of the machine. The purpose of this feature is to prevent human hazards, accidents or equipment breakdown |  |  |
|  | Operating system and all functions of machine must be in Croatian language |  |  |

1. **PRODUCT DETAILS**

All products that will be processed on the line belong in below groups:

|  |
| --- |
| Screw on system – bottle assembled with dropper and corresponding cap (3 pcs container closure configuration) |
| Screw on system – dropper with cap assembled with bottle (2 pcs container closure configuration) |
| Snap on system – dropper with cap assembled with bottle (2 pcs container closure configuration) |
| Snap on system – bottle assembled with dropper pump without dip tube (2 pcs container closure configuration) |
| Snap on system – bottle assembled with spray pump with dip tube (2 pcs container closure configuration) |

Machine must be designed to process:

* plastic and glass bottles within the following size range:

Plastic bottles (containers):

Ø: min. 20 mm – max 35 mm

H: min 30 mm – max 75 mm

Glass bottles (containers):

Ø: min. 30 mm – max 40 mm

H: min 60 mm – max 75 mm

* plastic spray pumps within the following size range:

Ø: min. 20 mm – max 35 mm

H: min 50 mm – max 85 mm

* plastic droppers within the following size range:

Ø: min. 10 mm – max 30 mm

H: min 15 mm – max 75 mm

* plastic screw caps within the following size range:

Ø: min. 18 mm – max 22 mm

H: min 30 mm – max 33 mm

Initially machine must be equipped with formats to process following products:

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **PRODUCT NAME** | **JGL BOTTLE code** | **JGL BOTTLE name** | **JGL SPRAY PUMP / DROPPER code** | **JGL SPRAY PUMP / DROPPER name** | **CAP code** | **JGL CAP name** |
| Product A | 130002904 | BOTTLE HDPE 30 ML SNAP ON APT INDEN | 130000338 | SPP APF 64mm 140mg SGama | / | / |
| Product B | 130002651 | BOTTLE HDPE 15 ML SNAP ON SGAMA INDEN | 130003345 | SPP APF 51MM 140MG SGAMA | / | / |
| Product C | 130000187 | BOTTLE LDPE 5ml SGama (Ger) | 130000317 | DROPPER LDPE SGm Brimo (Ger) | 130000415 | CAP HDPE SGama Brimo (Ger) |
| Product D | 130003400 | OSD BOTTLE 10ML SOFT SGAMA | 130003396 | DROPPER OSD PURECAP 37.5% FPV SGAMA | / | / |

# MACHINE PERFORMANCE

Optimally, line should deliver the output up to **60** **pcs/min** or **3600 pcs/h** following standard DIN 8743 for all formats. Output of the line must not be below 40 pcs/min or 2400 pcs/h for any format or product on the line.

|  |  |
| --- | --- |
| **PRODUCT NAME** | **Write expected output (production speed) for formats initially supplied with machine** |
| Product A  (Format 1) |  |
| Product B  (Format 2) |  |
| Product C  (Format 3) |  |
| Product D  (Format 4) |  |

# 7. ENVIROMENTAL CLASSIFICATION

Line will be installed in a room classified as EU GMP class “A”.

All defined room conditions for EU GMP class “A” will be provided by JGL.

Room temperature: 18 – 24 °C

Room height: 2800 mm

Relative room humidity: 30-65% rH

Laminar flow: 0.45 m/s

Other dimensions of room are not defined.

# 8. AVAILABILITY

Line will be used in one shift, 5 working days. Total weekly use 40 hrs.

# 9. MAINTENANCE

| **URS ID** | **Request specification** | **YES** (if offered specification is equal to one required) / or **WRITE OFFERED SPECIFICATION DETAILS** | **Notes, remarks, references** |
| --- | --- | --- | --- |
|  | Supplier must provide at minimum the following maintenance instructions:   * All sub-systems provided (Maintenance and operation manuals of vendor equipment); * A comprehensive lubrication list and recommended lubrication schedule; * A comprehensive recommended maintenance (regular recommended inspection intervals, wear points, recommended spare parts list); * Supplier shall supply two copies of Operation, Installation, Maintenance and de-commissioning manuals as well as electronic copy of those documents |  |  |
|  | Supplier must provide a list with total cost of wear and tear spare parts needed for two year operation |  |  |
|  | Supplier must provide a budgetary annual fee for regular yearly maintenance |  |  |

# 10.LIFE CYCLE

## Development

The supplier shall provide a Quality and Project Plan as a part of their proposal. The project shall utilize the GAMP methodology when developing the system and documentation.

## Factory Acceptance Test (FAT)

In order to verify system performance, the User shall witness the execution of the Factory Acceptance Test procedures at Supplier’s premises. The Factory Acceptance Test Specification shall be submitted to the User for review and approval prior to execution. A minimum of two weeks shall be allowed for the User to review and to comment and/or approve the Factory Acceptance Test Specification. According to FAT outputs, it will be decided if the equipment could be shipped to JGL or some additional modifications should be carried out.

## Qualification

The supplier is responsible for preparation of qualification protocols including Design Qualification (DQ); Installation Qualification (IQ); Operation Qualification (OQ), Hardware design specification (HDS), Software design specification (SDS) and Functional specification (FS). These protocols must cover all design and safety aspects as well as complete functionality of the equipment according to JGL’s User Requirement Specification (URS) and other relevant specifications and guidelines. The supplier must provide the qualification protocols for preliminary review to JGL before the delivery of the equipment. The protocols must be approved by JGL before the qualification activities commence. The Supplier is responsible for the execution of the qualification activities together with JGL employees. Final results and qualification reports also have to be approved by JGL before final commissioning of the equipment.

All qualification documentation must be in English language.

## Site Acceptance Test (SAT)

Upon delivery of the equipment, the selected Supplier must perform all required commissioning activities to ensured expected performance. The supplier must supply document templates for SAT and also assure its availability for SAT performance.

## Training

Selected Supplier must provide appropriate training for personnel from R&D and Maintenance department (aprox. 4 persons selected by JGL). Training duration shall be at least 8 hours. The training shall include practical workshops directly on supplied equipment or other equipment of equal design, purpose and function. Upon the training, the Supplier shall grant the Certificate of Attendance for each participant.

## Other documentation (mandatory)

Additionally to FAT, SAT and qualification protocols, the Supplier shall supply the following documentation:

* Material and surface finish certificates for all parts in contact with liquid product
* Operator, Maintenance and Service manual
* List of materials and components (with ID tagging)
* Data sheets and certificates for components and subsystems
* Certification of calibration
* Conformity certification
* Instrument Listing
* Control Schematics
* Spare Parts List with exploded view of components
* Component Cut Sheets
* Control Platform Program
* A listing of utility connections

The supplier shall briefly describe the following capabilities of the control system on a separate sheet and append to the report:

* Response on power failure;
* Response on utility failure;
* Critical alarm conditions and system response [identify all];
* Informational alarm conditions and system response [identify all].

Operator and user manual including maintenance must be supplied in hard copies and electronic backup in Croatian language. Electric diagram sheets can be supplied in English.

1. The Contracting Authority notes that the management and supervision of its automated industrial production line systems is based on Siemens PLC S7 controllers and related operating system, and for the management and programming of which it has trained professional staff in production.

   Therefore, the request of the Contracting Authority is justified that the purchased machine has a controller equivalent to the technical characteristics of Siemens PLC S7 controllers so that, without spending additional time and money, by the Contracting Authority, controllers can use all systems of the Contracting Authority to automate the production process. If the bidder offers an equivalent controller for machine automation, the equivalence is measured in such way that all software tools and systems currently used by the Contracting Authority in production automation are compatible with the offered controller, i.e., that the offered controller enables compatibility, normal operation and full functionality of all existing and new software tools and hardware for automation of the Contracting Authority’s production. By signing offered URS (User Requirement Specification) document, the bidder guarantees full compatibility of the offered controller with the existing production automation system of the Contracting Authority and undertakes to maintain training at its own expense to train Contracting Authority’s staff to use and manage the offered production automation system. [↑](#footnote-ref-2)