User Requirement Specification (URS)

For High Voltage Leakage Test

Document Code:

☞This document is under control and unalterable.

Revision History:

Change from previous version	Date

Prepared By	Technical Department Project Department Quality Assurance		12/18/2023
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1. Table of contents

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2. Purpose and Scope

This document defines the User Requirement Specification (URS) of HVLT (High Voltage Leakage Test) for sterile finish product of BFS machine, to be installed in Sina Darou Pharmaceutical Company. This document clearly defines the user requirements to ensure compliance of the system with current Good Manufacturing Practices (cGMP) and all applicable regulations.

Scope of this specification is to describe the minimum requirements for the design, manufacturing, FAT, supply, inspection, delivery, installation, commissioning, SAT, documentation, IQ, OQ and qualification activities of HVLT for sterile finish product of BFS machine accordance with the cGMP-guidelines, EU-guidelines, FDA-guidelines, the current WHO regulations and local regulations.

3. Responsibility

The Supplier of the system is required to adhere to the content of this document; any deviations proposed must be clearly identified and justified by the Supplier

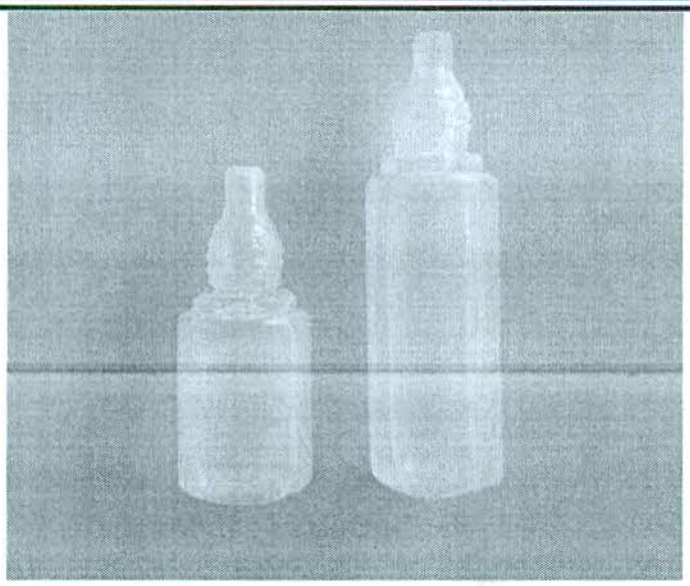
4. Overview

In the production unit of Sina Darou, 5 or 10 cc eye drops are produced by a filling machine. This process should be fully automatic, which should be 5 or 10 cc product in the conveyor, the speed should be 140 bottles per minute. All should be leak tested for pinholes, leaks and defects.

5. Operational Requirements

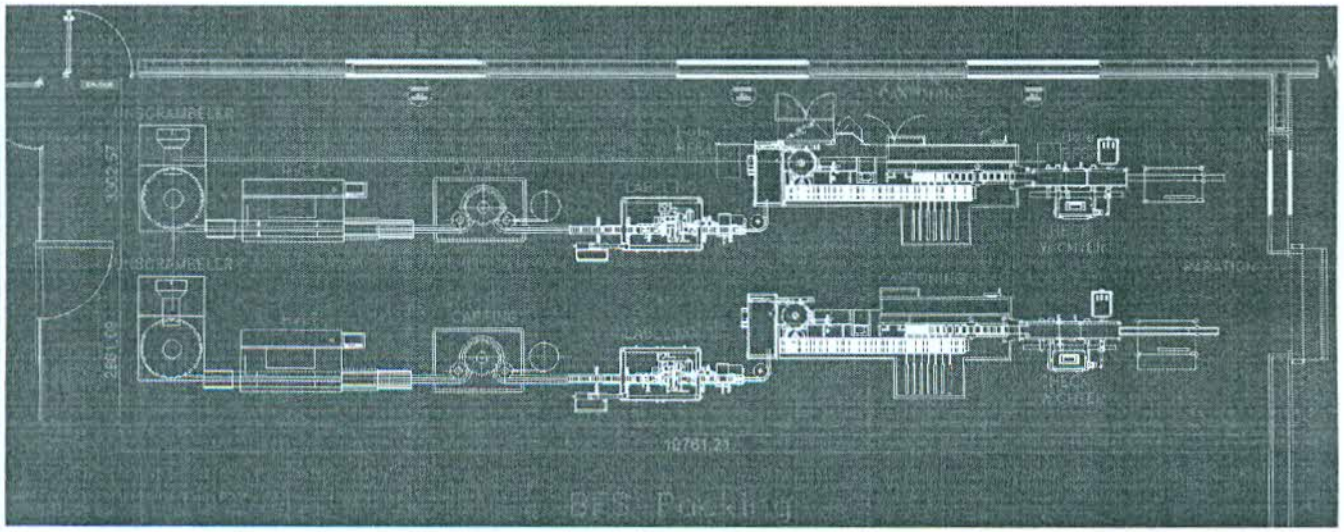
Technical specification

5.1 The actual speed of machine must be 140 eyes drop bottle/min at least and adjustable.
5.2 The volume of liquid is 5cc and 10cc.
5.3 The machine must be worked with 2 types of eyes drops as in below picture.



5.4 The machine should be ability to worked with 2 types of eyes drop Bottle

5.5 This machine must be line with conveyor as extend to filling machine as below drawing. Dimension of place UNSCRAMBALER, HVLT, CAPPING, LABELING, CARTONHNG and CHECKWIGHTER machine located in below drawing.



5.6 All the equipment's the HVLT machine needs must be prepare by vendor.

5.7 The machine must have a separate parts size for 5cc and 10 cc eyes drop Bottle.

5.8 Sina Darou Company must approve dimension of machine.

5.9 Vendor must be guaranteed this machine for 2 years.

5.10 Vendor must be warrantied for this machine 10 years.

5.11 Vendor must be sent spare parts for 2 years.

5.12 The machine must have minimum vibration.

5.13 The machine should be easy maintenance and user-friendly working.

5.14 Output of machine must be product at the same direction on the conveyor.

5.15 The machine shall be designed to ability changeover 5cc and 10cc and conversely.

5.16 The machine must be worked with automatically and manual.

5.17 The unit shall be marked with a stainless-steel nameplate

5.18 Infeed process: the products are typically fed from a conveyor into the in feed of the HVLT, and can be integrated to provide a steady flow of properly oriented objects.

5.19

Material / General

5.20 All material-contact part must be Stainless Steel 316L and the other non-contact partcould be Stainless Steel 304 and should properly polished Ra ≤1.2 µm

5.32.a Material Certificates

5.21 All components and parts used must be long term corrosion free.

5.22 Surfaces of the unit which are in clean zone are not painted. Frame is of stainless steel. Only vacuum pump is painted.

CONTROL SYSTEM

5.23 All components and materials have to be listed and approved by the customer.

5.24 All parts have to be grounded.

5.25 In the control-cabinet at least 30% of spare place has to be left over.

5.26 The control-cabinet has to be designed so that the part for the power supply and the part for the controller devices are kept separate.

5.27 Allowed temperature of the components within the control-cabinet from +5°C to 35°C (EN 60204) has to be ensured.

5.28 All wires have to be numbered on both sides, external from connector block inside the control cabinet.

5.29 All data lines have to be shielded.

5.30 Free access to the connectors and devices in the control-cabinet.

5.31 Separate laying of the data line and the line for the power supply.

5.32 Control voltage 24 V DC

5.33 Two supply connections have to be foreseen, one for UPS and one for direct power connection with emergency power.

5.34 The control cabinets are either integrated in the equipment or above on the suspended ceiling in the technical area.

5.35 The system must unify upstream and downstream machines to work simultaneously Pre-set maximum and minimum values in the parameter setting to prevent user settings over the range.

5.36 Equipment failure can be analyzed by failure analysis system comes with equipment diagnostic functions

5.37 Suppliers can archive remote diagnosis through the network for the production line

5.38 Drive: Protection class: at least IP54

6. Required components

6.1 Industrial PC for process control and data acquisition. Operating panels of this equipment will be mounted in the technical area and switch panel in the hygienic class D area.

6.2 The controller has to be connected to a UPS-system. In case of power supply failure of the machine has to stop in a safe condition. The needed UPS-capacity for this step has to be specified, backup time at least 1h.

6.3 Emergency-stop buttons has to be provided in all dangerous zones

6.4 Protection class: at least IP 54 according to DIN 40065

6.5 System / equipment suitable for nominal voltage 400 V (three phases) according to DIN IEC 38.

System / equipment suitable for rated frequency 50 Hz ± 10%.

6.6 All drives will be switched on directly (without delta-wyes).

6.7 The system has to be designed and built in accordance to the Low Voltage Directive (LVD) 73/23/EEC

6.8 Protection against overload is required.

6.9 Protection against short circuit is required.

6.10 Cross-sectional areas and connections of the protective conductor according to EN 61010-1.

6.11 Insulating resistance according to EN 60204-1 and VDE 0100 T610.

6.12 Voltage test according to EN 60204 and VDE 0100 T610.

6.13 Residual voltage test according to EN 60204.

6.14 Every electric circuit, that has to be grounded, has to be connected to one central grounding point. The connection to the 0-potential will be provided on site.

6.15 Solvable 0-voltage connections of the control low voltage to the grounding system have to be established.

6.16 0-voltage connections of the devices with low voltage outlet have to be established.

6.17 An emergency-stop has to be at every dangerous place.

6.18 Safety devices cannot be circumvented on an easy basis or be disabled.

6.19 Safety devices operate directly in the circuit.

6.20 An emergency-stop should be within the reach for the operation personnel (inside and outside of RABS/Isolator)

6.21 The software of the automation has to accomplish the following functional requirements:

- 6.21.1 Automated process execution and visualization
- 6.21.2 Automated registration of the measured process values, including a graphical analysis of these data
- 6.21.3 Monitoring of the critical process values within limits (warning and action limit)
- 6.21.4 Automatic alarm in case of an overstepping of a critical value and in case of failure
- 6.21.5 Reporting
- 6.21.6 Calibration
- 6.21.7 User administration
- 6.21.8 Archiving, backup of acquired data online via external system

6.22 Consecutively the requirements for the individual functional requirements are specified. The following data should be documented:

- 6.22.1 Extruder screw cooling water temperature at the inlet / outlet

6.22.2 Inlet pressure of cooling water

6.22.3 Inlet temperature of cooling water

6.22.4 Extruder temperature

6.22.5 Extruder speed

6.22.6 Pressure at the compressed air inlet

6.23 The software for the process execution, data acquisition, data processing and reporting has to be projected, created, tested and documented according to GAMP Vol.5.

6.24 The software of the automation for the process execution, data acquisition, data processing and data archiving has to be compliant to 21 CFR Part 11 and has to be validated.

6.25 The software has to be organized in at least three levels:

6.25.1 Field level (Standard signals: 24 V DC for I/O-signals; 4 - 20 mA for analogue signals; Field bus Profibus DP for valves)).

6.25.2 Controller-level (continuous and sequential functions in the controller).

6.25.3 Recipe level for operation and monitoring (Recipe level in the PC-System).

6.26 The analogy signals are directly wired to the field bus.

6.27 Standard sequence structure:

The standard sequence structure (typical) must have, according to the state transition diagram, the following branches:

6.27.1 RUN

6.27.2 ABORT

6.27.3 HOLD

6.27.4 S-HOLD

HOLD means that the sequence remains in the actual step and the transition to the next step is blocked.

S-HOLD means that in case of equipment failure a safe mode of operation has to be ensured at all times by proper means. The machine has to stay in safe operation mode without taking any damage or inflict damage on other systems in case of equipment failure.

If the HOLD status is not directly managed by the supervision, other solutions included in the freeze-drying cycle can be accepted. This point will be studied during DQ.

6.28 *Data integrity:* New or changed raw data sets are not allowed to overwrite existing data.

6.29 In case of instrument air failure, safe mode of operation has to be assured at all times. In case of electrical power failure, safe mode of operation has to be assured at all times.

6.30 In case of electrical power failure, safe mode of operation has to be assured at all times.

6.31 In case of electrical power failure, the requested UPS must buffer and safe all relevant process data and must assure secure and reliable system shut down after a certain period of power failure. Valve positions after pneumatic or electric utility failure according to the PID's.

6.32 In case of no sufficient utilities the operation has to stop in a second way.

6.33 Ventilator (control cabinet) failure must be indicated by an alarm. Not included in control system.

6.34 In case of ventilator (control cabinet) failure process start is interlocked.

6.35 Active processes must not be aborted.

6.36 High temperature in the control cabinet must be indicated by an alarm message. A thermostat in the control cabinet and the contact will be added to the GTC (GTC) signal.

6.37 In case of high temperature in the control cabinet process start is interlocked. No report of the signal to POLARIS 2 supervision (only hardware contact).

6.38 Active processes must not be aborted.

6.39 Motor protection failure must be indicated.

6.40 Line safety switch failure must be indicated.

6.41 Remote assistance, maintenance must be documented in a readable log-file.

6.42 System and application access are only allowed with user-ID and password.

6.43 The password must be changed periodically.

6.44 An alarm has to provoke the following: Coloured identification at the visualization.

Acoustic signal

6.45 Alarm messages, warning messages and user notifications have to differ from each other and have different priorities which need to be visualized accordingly.

6.45.1 Priority 1: System messages (system failure).

6.45.2 Priority 2: Malfunction message (motor protection switch, sensor breakage etc.)

6.45.3 Priority 3: Alarm messages (action limit)

6.45.4 Priority 4: Warning messages (warning limit)

6.45.5 Priority 5: Operation notification (information for the operator)

6.46 2 alarms levels can be proposed with the use of GTC contact relayed on the supervision, with for example a flash lamp. Details to be approved during the DQ.

6.47 System, malfunction, alarm and warning messages must be classified in different categories. According to the category the system reacts different:

6.47.1 Category 1: System returns in initial safe state.

6.47.2 Category 2: Active processes are aborted.

6.47.3 Category 3: Non-influence on the active process.

6.48 According to the alarm, the system will react according to the 3 mentioned categories but alarms are not classified in categories.

6.49 All alarm notifications have to be documented with the following information:

6.49.1 Date and time of the alarm.

6.49.2 Description of alarm.

6.49.3 Date and time of alarm acknowledgement.

6.49.4 Date and time of alarm end / confirmation.

6.49.5 Who has confirmed the alarm?

6.50 Critical alarm stops the machine

6.51 Alerting and failure: As a minimum following alarm messages must be configured and displayed:

6.51.1 Power failure

6.51.2 Emergency button actuated

6.51.3 Motor safe guard

6.51.4 Run time error valve

6.51.5 PLC failure

6.51.6 Utility failure (Temp. pressure etc.)

6.51.7 Error peristaltic pump

6.51.8 Program aborted

6.51.9 Program run time error

6.51.10 Sensor status not valid

7. Cleaning

7.1 The equipment must be designed for easy cleaning according to DS/EN 1672-2 and DS/EN 1672-2/AC and hygienic design consideration.

7.2 All parts of the machine must be designed for easy access for cleaning. There mustn't be any places that can't get cleaning.

7.3 All parts of the machine must be designed for easy visual cleaning inspection.

8. Calibration

8.1 A calibration certificate from an accredited institute with traceable references for all pressure and calibration devices must be available.

8.2 The pressure, temperature, volume (Scaled measure), RPM and RPM measuring devices must be accessible for calibration.

8.3 It must be possible to remove pressure, temperature, volume, and RPM measuring devices for calibration.

8.4 Note: All instruments must be mounted in such a way that visual inspection can be performed as part of maintenance and monitoring.

9. Environment

The equipment will be installed in class D and shall be compliant to the foresaid class.Room temperature: 18 to 32 °C.

10. Constraints

10.1 Milestones and Timelines

The eyedrops filling machine shall be installed, commissioned and ready for operation till **September 2024**

10.2 Equipment Constraints

The noise Generated by the machine shall be below 60dB at 1-meter distance from the machine for all normal operating conditions

10.3 Compatibility and Support

HVLT should comply with cGMP CFR 21 parts 11, 210, 211, 600, 610 and EU guide to GMP.

The must comply with the Safety Directive.

It is the responsibility of the supplier to ensure that the equipment complies with all relevant national and international requirements and regulations of sterile production.

10.4 Availability/Maintenance

10.4.1 The machine is intended to be operated continuously, 24 hours per day, 7 days per week.

10.4.2 The machine shall be maintained on a schedule as indicated by the supplier. Supplier should provide (at minimum) the following maintenance instructions:

10.4.2.1 A comprehensive recommended maintenance (regular recommended inspectionintervals, wear points, recommended spare parts list)

10.4.2.2 Supplier shall supply 2 (two) copies of Operation, Installation, Maintenance andcommissioning manuals in English.

11 Lifecycle

11.1 Testing

Factory Acceptance Test (FAT) is performed at the supplier site prior to shipping.Site Acceptance Test (SAT) is performed and approved at the manufacturer s i t e .

11.2 Delivery/ Documentation

Documentation includes:

#	Document title	Format
1	Electrical components lists	
2	Electrical documents lists	
3	Electrical diagrams	
4	Fault finding (troubleshooting	
5	Parts List / Mechanical & Electrical	All documents shall be in the English language and supplied with hard copies and electronic versions (pdf)
6	Tag number must be key to the list.	
7	Component list	
8	Function of component	
9	Supplier parts number	
10	Manuals, Maintenance, Drawings & Descriptions / Mechanical & Electrical	
11	Manufacturer part number	
12	installation, operation, and maintenance instruction	
13	Cleaning SOP and Check list	
14	Calibration certificates of each component	
15	IQ/OQ/PQ protocols	
16	FAT protocols	
17	SAT protocols	
18	Material & test certificate	
19	Alarm list	

11.2.1 The documentation requirements describe all technical, GMP and Quality documentation, which covers the needs of Sina Darou and has to be delivered by the supplier.

11.2.2 The documentation requirements are part of the technical specification and part of the basis for quotation.

11.2.3 The time schedule for document submission follows GEP and is linked with the schedule for the preparation of the qualification documentation through Sina Darou.

11.2.4 The supplier has to deliver cGMP and EMEA, FDA compliant standards and local regulations and procedures for the areas described below. These standards might be demonstrated and documented or they might be verified by means of an audit by the customer (see chapter 6.1).

11.2.5 The quality assurance system has to include the following aspects: design methods, change control, system configuration management, computerized systems validation compliant documentation.

11.2.5.1 All documents must be signed by authorized persons according to "organogram" of the company.

11.2.5.2 Every document of the documentation is part of the system specification and therefore basis of

the qualification.

11.2.5.3 Where possible, all documents should be generated with Microsoft™ software products (exception drawings: dxf-format).

11.2.5.4 The whole documentation needs to be presented in triplicate on paper and a single dispatch as data carrier. All deviations must be listed up documented and solutions must be accepted or refused by responsible persons with written agreement.

11.2.5.5 Instruction manuals have to be in English language.

11.2.5.6 Units of measure: Metric system

11.2.5.7 Every abbreviation used by the supplier must be listed in a dedicated section (list of abbreviation).

11.2.6 As long as it is not part of standard documentation, the cover page of each document needs to have the following information:

11.2.6.1 Title of document.

11.2.6.2 Document number and version / revision level.

11.2.6.3 Date of issue.

11.2.6.4 Name of computer file.

11.2.6.5 Name of project.

11.2.6.6 Project number.

11.2.6.7 Name of company preparing the document.

11.2.6.8 Signature of person(s) preparing the document.

11.2.6.8 Signature of an authorized person within the company preparing the document approving all contents of the document.

11.3 Support and training

List of training option with technical support should be available.

11 References

11.1 CFR11, 21, 210, 211, 600 & 610

11.2 EU Guide to Good Manufacturing Practices, volume 4

11.3 ASTM A 380-99 "Standard Practice for Cleaning, Descaling, and Passivation of Stainless Steel Parts, Equipment's and System

11.4 PICS

12 Definitions, Acronyms and Abbreviations

DQ = Design Qualification
FAT = Factory Acceptance Test
SAT = Site Acceptance Test
USP = United States Pharmacopoeia
HMI = Human-Machine Interface
P&ID = Piping and Instrumentation Diagram
cGMP = Current Good Manufacturing Practice
IQ = Installation Qualification
OQ = Operational Qualification
PICS = Pharmaceutical Inspection Co-operation Scheme

13 Document Distribution

Department	Version
Original version	Project Department
Copy No. 1	QA Department
Copy No. 2	QC Department
Copy No. 3	Technical Department
Copy No. 4	Production Department

14 Attachments

Attachment 1- dimension of bottles

The specifications of the bottles are in Appendix 1

Document Distribution

Department	Version
Original version	Project Department
Copy No. 1	QA Department
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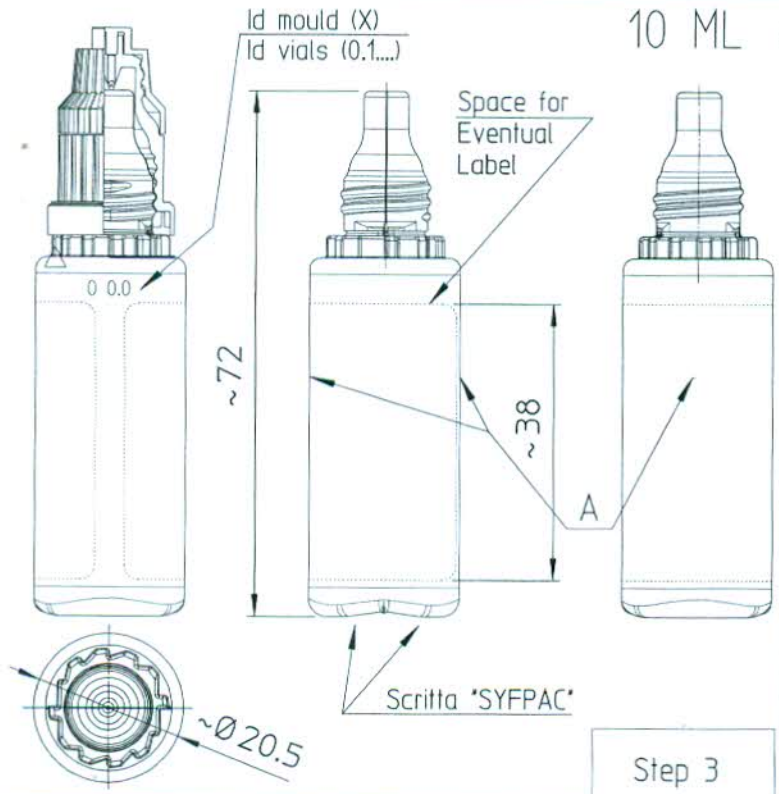
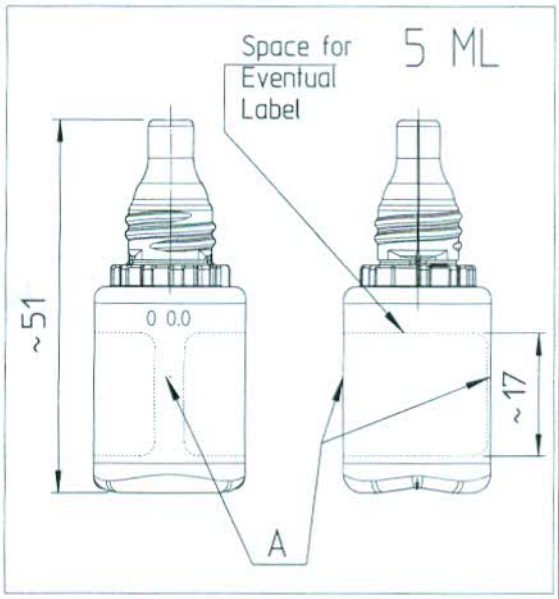
° DATI INDICATIVI CON RISERVA DI MODIFICHE SENZA PREAVVISO

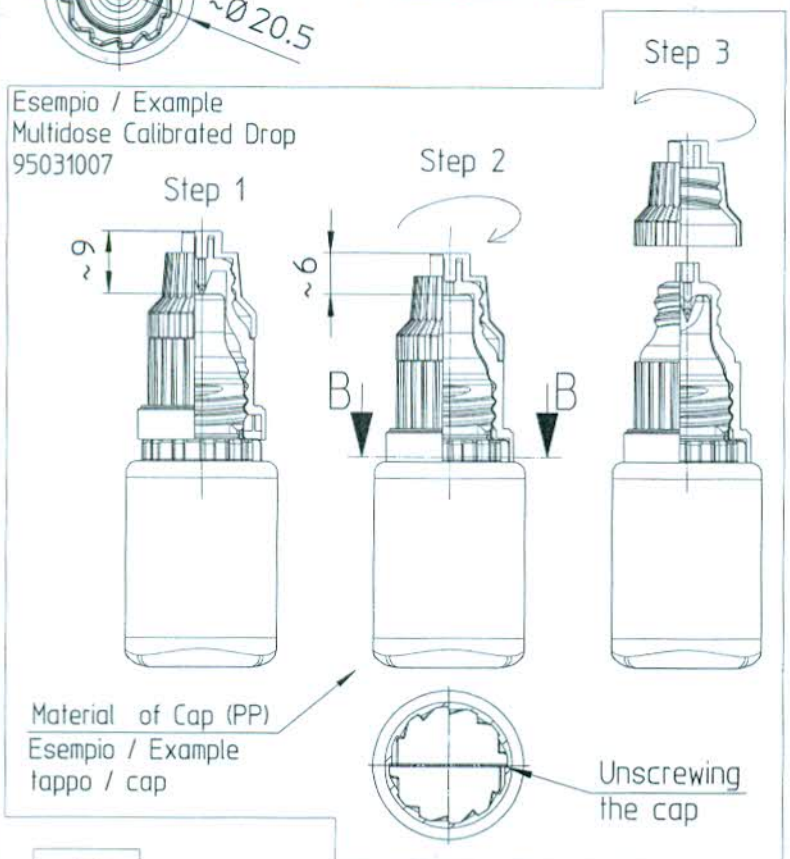
° DATA ARE INDICATIVE AND MAY BE REVISED WITHOUT NOTIFICATION.

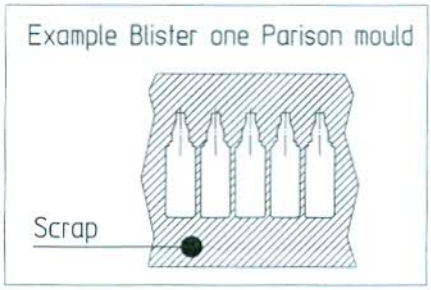
** The capacity mentioned are referred to the vials filled with aqueous solution having density and viscosity very near to water The filled volume tolerance and production are machine related, hence these are not applicable if only mould is purchased, without the machine.

10 ML Attachment 1- dimension of bottles









Controllo spessore
(Punto A)
A = 0.55 ± 0.15

**

Quote indicative Toll. ~ -2%
Approximate dimensions;
subject to shrinkage ~ - 2%

Volume (Teoretical)	** Toll.	** Production	Toll.	Working Range Scrap-Weight ± 15%	Toll. Repeatability	Working range Empty Weight ± 15%	Toll. Repeatability
5 ML	± 5 %	6.560	± 2 %	gr 5.7	± 3 %	gr 1.8	± 3 %
10 ML	± 3.5%	6.400	± 2 %	gr 6.2	± 3 %	gr 2.6	± 3 %

Notes internal technical office	MASEP	OPERAZIONE: (SEPARAZIONE IN FIALE SINGOLE A BORDO MACCHINA CON SMATEROZZATRICE)	Model - Modello	Type-Tipo	Material - Materiale
	NO	.	SVP 4.20	SYFPAC	PE / (EsBM)

Data Creazione	Disegnato da	Quote mm
25-01-17	Sartori S.	
Data Verifica	Verificato da	
06-07-18	Sartori S.	
Data Rilascio	Rilasciato da	Classe
06-07-18	Sartori S.	
Data Revisione	Revisionato da	Descrizione modifica
06-07-18	Sartori S.	Mod. cod. tappo da 13400498 a 95031007

ID: Part95_RC1wR06 | Data : 30-10-2008

BREVETTI ANGELA
Arzignano (VI)

Descrizione
FIALA STAMPO SCM91703

Description
VIAL MOULD SCM91703

Codice Elemento	Revisione	Versione
10491703	B1	01