User Requirement Specification (URS)

For Eyedrops Filling Machine

Document Code:

☛This document is under control and unalterable.

Revision History:

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Prepared By	Technical Department Project Department Quality Assurance	F.GH	12/18/2023
Project manager	Eng. Khaje		12/18/2023
QA Manager	Dr. Keshavarz		12/18/2023
Production Manager	Dr. Yousefy		12/18/2023
Technical Manager	Eng. Mohammadshahi	M.SHAHI 23 DEC 2023	12/18/2023
Responsible Pharmacist	Dr. Torabi		12/18/2023

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2. Purpose and Scope

This document defines the User Requirement Specification (URS) for Eye Drop filling 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 requirements for the design, manufacturing, FAT, supply, inspection, delivery, installation, commissioning, SAT, documentation, and qualification activities of Eye Drop filling for production department.

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

The Eye Drop filling machine is required to fill Eye Drop solution to the bottles and put Dropper top of the bottles and wrap of Capping. This process should be fully automated. The Eye Drop filling machine is located in Grade B Clean room on the first floor of the production at the new building.

This document is applicable on Specification at SINA DAROU Pharmaceutical site.

This machine used for:

Eye Drop Filling Machine

5. Operational Requirements

Technical specification

5.1The speed of machine must be adjustable up to 200 bottle per/min with min 2% accuracy..

5.2 The volume of eye drop solution must be 10 cc with high tolerance and ability to changeover to 5 and 20 cc.

5.3 The filling machine must be connected to the existing CIP & SIP systems.

5.4 The machine must have all the size parts that are needed for different volumes. (5-10-20 cc size parts).

5.5 All equipment requirements of the machine must be sent by vendor.

5.6 All contacts or noncontact materials with product must comply with cGMP.

5.7 The machine must be equipped with unscrambler for capping station , Dropper and bottle station.

5.8 Capacity of bottle, dropper and capping storage should be 2500 bottles at least.

5.9 The machine must be equipped with Laminar Air Flow and H14 Hepa filter.

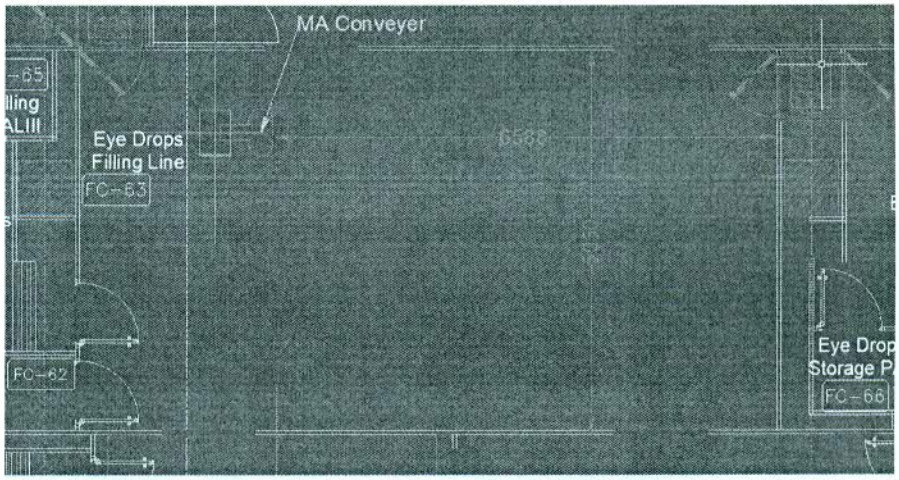
5.10 The machine must work under Laminar Air Flow.

5.11 Laminar Air flow should have the ability to disassemble and enough space for the filling machine.

5.12 Total height room dimension is 2700 mm.

5.13 Dimension of the machine must be approved by SINA DAROU Company.

5.14 The machine location in the room is shown in the below drawing.



5.15 The outlet Product of the machine must be delivered to the MA Conveyor which is indicated in the picture.

5.16 The machine must be able to work with 3 type of bottles (5-10-20 cc). The bottle, cap and dropper dimensions are attached to this document.

5.17 The machine Outlet must be connected and synchronized with the MA Conveyor which is indicated in the picture.

5.18 Sufficient space for maintenance operation must be considered.

5.19 The machine doors must be electro-polished with high quality.

5.20 The machine should be equipped with hopper.

5.21 Vendor must provide a guarantee for main components of the machine for 2 years.

5.22 Vendor must provide after sale services for 10 years.

5.23 Vendor must send spare parts for 2 years.

5.24 The machine must have minimum vibration.

5.25 The outlet Products mustn't have any leakage.

5.26 All steps of the CIP, SIP and production process and etc. must be shown in the HMI.

5.27 The machine shall have the ability to changeover 5cc to 10cc and 20cc eyedrop molds and conversely.

5.28 All the required spare parts for 2 years should be sent by vendor.

5.29 The machine must be able to work in both automatic and manual modes. (jog).

5.30 Level of each filling product must be adjustable.

5.31 All pipe connections must be installed with tri-clamp Stainless Steel 316L.

5.32 The machine shall have a filter housing before filling step.

Material / General

5.33 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

5.34 Certificates for all the stainless steel components and materials in direct or non-direct contact with the product should be available and signed by vendor. All material of construction should have certificates which must be sent by vendor.

5.35 Welding Quality – Orbital welds must be passivized (mirror) with suitable product thatre-establishes the material surface intact state with no discoloration at the site of weld.

CONTROL SYSTEM

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

5.37 All parts have to be grounded.

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

5.39 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.

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

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

5.42 All data lines have to be shielded.

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

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

5.45 Control voltage 24 V DC

5.46 The Filling machine should be able to work slowly and under control . (jogging mode)

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

5.48 The filling machine must be able to work with two separate systems (channel 1 and 2) without problems.

5.49 The machine inlet feed should be done by the container sorting bowl and stare wheel .

5.50 The filling machine must have safety covers that stop as soon as the machine door is opened.

5.51 All electrical equipment, including PLC, HMI, SERVO DRIVE, SERVO MOTOR must be of prominent European brands.

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

5.53 Drive: Protection class: at least IP54

5.54 Items that should be displayed in the control panel:

1- INFEED OPTIC SENSOR

2- MISSING PRODUCT CONFIRM

3- MISSING GOOD PRODUCT CONFIRM

4- FAULTY SIDE OPTICAL SENSOR

5- MISSING FAULTY PRODUCT CONFIRM

6- INFEED STARWHEEL OVER TORQUE

7- LOW AIR PRESSURE

8- PRODUCT SIZE

9- PRODUCT NAME

10- INVERTER COMMUNICATION

11- DISCHARGE STARWHEEL SERVO MOTOR

12- MAIN POWER FAILURE

13- Number of approved products

6. Required components

6.1 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.

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

Protection class: at least IP 54 according to DIN 40065

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

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

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

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

6.5 Protection against overload is required.

6.6 Protection against short circuit is required.

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

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

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

6.10 Residual voltage test according to EN 60204.

6.11 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.

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

6.13 0-voltage connections of the devices with low voltage outlet have to be established.

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

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

6.16 Safety devices operate directly in the circuit.

6.17 The line must be adjustable.

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

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

6.20 The password must be changed periodically.

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

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

6.22.1 Date and time of the alarm.

6.22.2 Description of alarm.

6.22.3 Date and time of alarm acknowledgement

6.22.4 Date and time of alarm end / confirmation.

6.23 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.

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

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

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.

7.4 The machine should be connected to the existing CIP and SIP units.

8. Calibration

8.1 A calibration certificate from an accredited institute with traceable references for all instruments 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 B and shall be compliant to the foresaid class.Room temperature: 18 to 28 °C, Relative humidity: 45 ± 5%

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

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

Eye Drop Filling machine should comply with cGMP CFR parts 11, 21, 210, 211, 600, 610 and EU guide toGMP.
The Machine must have the ability to work with 5-10-20 cc bottles.

It is the responsibility of the supplier to ensure that the equipment complies with all relevantnational and international requirements and regulations.

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.

10-5- Access Level

Different access levels for users:

10,5.1 operator,
10.5.2 supervisor,
10.5.3 administrator,

10.5.4 maintenance

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 site.

Equipment shall be qualified for design phase, installation phase, operational phase and the performance phase.

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	

11.3 Support and training

List of training option with technical support should be available.

12. References

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

12.2 EU Guide to Good Manufacturing Practices, volume 4

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

12.4 PICS

13. 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
MA = modular automation

14.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

15. Attachments

Date:12.18.2023	URS for	سینادارو Sina Darou
Version:01	Eyedrops Filling Machine	

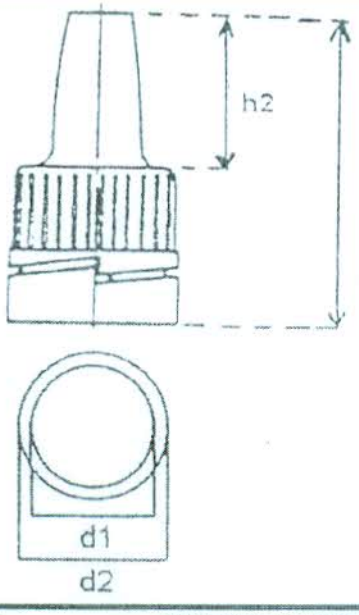
PACKAGING MATERIALS SPECIFICATIONS AND TEST NOTE

Material Code: 11211102 — **PLASTIC CAPS, WHITE, PILFERPROOF, STERILIZED**

Ref : USP 41/ In House

Manufacturer	*No Of Sample Checked*	*QC No*	*Release Date*
Quantity	*No of Containers*	*Receiving Report No*	*Analyst*
Batch No / Lot No	*Exp Date / Shelf Life*	*Receiving Report Date*	*Chief Analyst*

Tests	*Specifications*	*Results*
Appearance:	Well-formed sterile plastic caps free of visible defects inside and outside of caps.	
Color:	Should be white as the standard.	
Cleanliness:	Should be clean inside and outside.	
Dimensions:	d1: Between 16.9 and 17.5 mm.	
	d2: Between 19.4 and 19.8 mm.	
	h1: Between 35.9 and 36.7 mm.	
	h2: Between 17.2 and 17.8 mm.	
	Weight: Between 1.9 and 2.3 g.	
Integrity of moulding:	Should be well-formed caps with no hole on the top, indent or cracks.	
Cap fit and removal:	Cap should be sealed on the bottle properly and should be removed easily without sealing ring	
Leak test:	Identifying site of leakage if exist.	
Sterility:	Should be sterile and meet the USP requirement for sterility.	



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Date:12.18.2023	URS for	سینادارو Sina Darou
Version:01	Eyedrops Filling Machine	

PACKAGING MATERIALS SPECIFICATIONS AND TEST NOTE

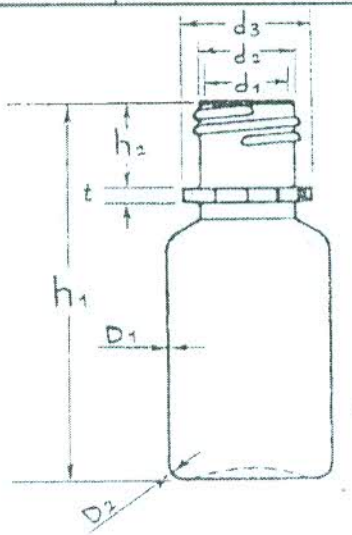
Material Code: 11211106

10 mL PLASTIC BOTTLES, PILFERPROOF, STERILIZED

Ref : USP 41/ In House

Manufacturer	*No Of Sample Checked*	*QC No*	*Release Date*
Quantity	*No of Containers*	*Receiving Report No*	*Analyst*
Batch No / Lot No	*Exp Date / Shelf Life*	*Receiving Report Date*	*Chief Analyst*

Tests	*Specifications*	*Results*
Appearance:	Well-formed sterile plastic bottles free of visible defects inside and outside of bottles.	
Color:	Should be white as standard.	
Cleanliness:	Should be clean inside and outside.	
Dimensions:	d1: Between 8.95 and 9.20 mm.	
	d2: Between 12.75 and 13.05 mm.	
	d3: Between 16.9 and 17.3 mm.	
	h1: Between 51.2 and 51.6 mm.	
	h2: Between 11.8 and 12.2 mm.	
	t: Between 1.6 and 2 mm.	
	D1: Between 0.8 and 1.1 mm.	
	D2: Between 0.7 and 1.1 mm.	
	Weight: Between 3.3 and 3.9 mm.	
Sterility:	Should be sterile and meet the USP requirement for sterility.	
Leak test:	Should meet leak test.	



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PACKAGING MATERIALS SPECIFICATIONS AND TEST NOTE

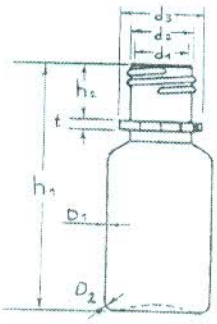
Material Code: 11211108

20 mL PLASTIC BOTTLES, COLORLESS, PILFERPROOF
Rinosaltin Nasal Drops, 20 mL

Ref : USP41,In House

Manufacturer	No Of Sample Checked	QC No	Release Date
Quantity	No of Containers	Receiving Report No	Analyst
Batch No / Lot No	Exp Date / Shelf Life	Receiving Report Date	Chief Analyst

Tests	Specifications	Results
Appearance:	Well-formed plastic bottles free of visible defects inside and outside of bottles.	
Color:	Colorless as standard.	
Cleanliness:	Should be clean inside and outside.	
Dimensions:	d1: Between 9.0 and 9.2 mm.	
	d2: Between 12.65 and 12.95 mm.	
	d3: Between 17.1 and 17.5 mm	
	h1: Between 63.5 and 64.1 mm	
	h2: Between 11.5 and 11.9 mm	
	t: Between 1.7 and 2.1 mm	
	D1: Between 0.7 and 1.0 mm	
	D2: Between 0.7 and 1.1 mm	
	Weight: Between 4.2 and 4.5 g	
Leak test:	Should meet leak test.	
Microbiological quality:	TAMC: Not more than 1000 CFU/g.	
	TYMC: Not more than 100 CFU/g.	



Remarks

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Approved Date: 1400/08/15

QUALITY CONTROL DEPARTMENT
SINA DAROU PHARMACEUTICAL COMPANY

FM-10-0-052-2

PACKAGING MATERIALS SPECIFICATIONS AND TEST NOTE

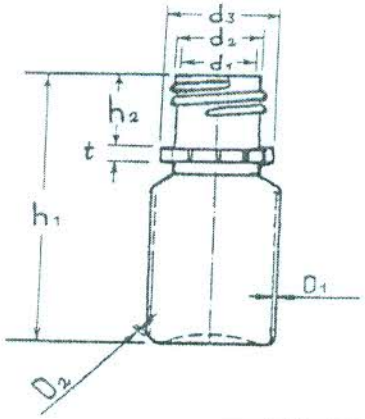
Material Code: 11211118

5 mL PLASTIC BOTTLES, PILFERPROOF, STERILIZED

Ref: USP41,In House

Manufacturer	*No Of Sample Checked*	*QC No*	*Release Date*
Quantity	*No of Containers*	*Receiving Report No*	*Analyst*
Batch No / Lot No	*Exp Date / Shelf Life*	*Receiving Report Date*	*Chief Analyst*

Tests	*Specifications*	*Results*
Appearance:	Well-formed sterile plastic bottles free of visible defects inside and outside of bottles.	
Color:	Should be Colorless as standard.	
Cleanliness:	Should be clean inside and outside.	
Dimensions:	d1: Between 8.9 and 9.1 mm.	
	d2: Bwtween 12.75 and 13.05 mm.	
	d3: Between 17.1 and 17.5 mm	
	h1: Between 43.2 and 43.8 mm	
	h2: Between 11.8 and 12.2 mm	
	t: Between 1.8 and 2.2 mm	
	D1: Between 0.7 and 1.1 mm	
	D2: Between 0.5 and 1.0 mm	
	Weight: Between 2.5 and 2.7 g	
Sterility:	Should be sterile and meet the USP requirements for sterility.	
Leak test:	Should meet leak test.	



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PACKAGING MATERIALS SPECIFICATIONS AND TEST NOTE

Material Code: 11211110

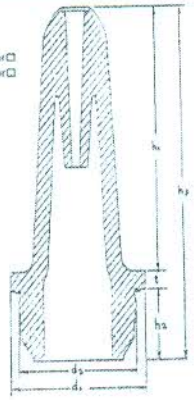
PLASTIC DROPPERS, OPHTHALMIC, STERILIZED

Ref : In House

Manufacturer	*No Of Sample Checked*	*QC No*	*Release Date*
Quantity	*No of Containers*	*Receiving Report No*	*Analyst*
Batch No / Lot No	*Exp Date / Shelf Life*	*Receiving Report Date*	*Chief Analyst*

Tests	*Specifications*	*Results*
Appearance:	Well-formed sterile plastic bottles free of visible defects inside and outside of bottles.	
Color:	Should be white as standard.	
Cleanliness:	Should be clean inside and outside.	
Dimensions:	d1: Between 11.25 and 11.4 mm.	
	d2: Type A: Between 9.60 and 9.80 mm.	
	d2: Type B: Between 9.39 and 9.55 mm.	
	h1: Between 17.6 and 17.8 mm.	
	h2: Between 4.40 and 4.75 mm.	
	h3: Between 23.45 and 23.75 mm.	
	t: Between 1.3 and 1.6 mm.	
	Weight: Between 0.55 and 0.65 g.	
Sterility:	Should be sterile and meet the USP requirement for sterility	
Drop size & number of drops/mL:	Should be performed on 5 droppers Number of drops for 1 mL of P.W.: 20-25 drops	
	Weight of each drop: 30-50 mg.	

Type A: English Mould of Dropper☐
Type B: Wire Mould of Dropper☐



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