User Requirements
Pen Assembly Machine

1.0 Purpose
To specify the user requirements for automated equipment used to assemble the Disposable Pen in accordance with product specifications and of cGMP.

2.0 System Description
A fully automated assembly machine capable to assemble the Pens, the pen assembly machine will consist of the following systems as a minimum:

- An automated feeding system to drive the pen components to the assembly station.
- An automated conveyor system to move the assemblies from station to station based on a pre-defined assembly workflow.
- Automated testing mechanisms to inspect pre-defined critical features of the pen assembly and labeling.
  - Cartridge vision system
  - Label print-out vision system
  - Label alignment vision system
- Automatic Laser label printer/applicator.
- Close loop automated rejection systems for defective components and/or assemblies.
- Label rework station.
- In-process sampling port
- Assembly Machine – Packaging Machine transfer conveyor
- Built-in statistical process control system to measure machine and manufacturing metrics.

3.0 Specification Documentation

3.1 Products
The machine must be able to manufacture the two different disposable pen configurations:

(Low Dose 1.5 ml cartridge)
(High Dose 2.7 ml cartridge)

The disposable pen consists of the following main components:

<table>
<thead>
<tr>
<th>Component</th>
<th>Pen high dose</th>
<th>Pen low dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dosing Mechanic</td>
<td>Pen Size Specific</td>
<td>Pen Size Specific</td>
</tr>
<tr>
<td>Cartridge Holder</td>
<td>Pen Size Specific</td>
<td>Pen Size Specific</td>
</tr>
<tr>
<td>Drug Filled Cartridge</td>
<td>Pen Size Specific</td>
<td>Pen Size Specific</td>
</tr>
<tr>
<td>Pen Label</td>
<td>Pen Size Specific</td>
<td>Pen Size Specific</td>
</tr>
<tr>
<td>Retention Spring</td>
<td>Generic for both pen sizes</td>
<td></td>
</tr>
</tbody>
</table>
3.1.1 The following diagram depicts the assembly of the disposable pens:

![Diagram of pen assembly](image)

3.2 Theory of Operation

3.2.1 These are the basic steps and requirements involved in the pen assembly:

a) Cartridge holder and Dosing Mechanic shall be automatically extracted out of their shipping trays. The Cartridge Holder must be automatically inspected to confirm it is the correct internal diameter for the pen being assembled. Dosing Mechanic must be confirmed as the correct color for the pen being assembled.

b) Cartridges shall be loaded into the machine from their handling trays in a direct and simple way, oriented, and placed into the cartridge holder automatically. Cartridges shall be inspected to confirm correct combi-seal color and correct diameter of cartridge for the specific pen size being assembled.

c) The machine shall place cartridge into cartridge holder. No damage should be imparted to the cartridge by the handling process. An inspection should confirm that the cartridge is inserted and present for the next operation.

d) Retention springs shall be loaded into the machine from bulk boxes, oriented using a coated vibratory bowl, and placed into the cartridge holder in correct
orientation. An inspection should confirm that the retention spring is inserted and oriented in the right position. A sound hood shall be installed on the vibrating bowl to further minimize the noise from the bowl.
e) The dosing mechanism shall be aligned and placed onto the cartridge holder/cartridge assembly; the machine shall retract the injection mechanism’s injection knob. The assembly is snapped fit together by applying sufficient pressure to the shoulder of the Dose Selection Ring.
f) The pen assembly shall be transferred to the label station.
g) The label shall laser printed with Lot and Expiration Date, and inspected using a vision system to confirm legibility and accuracy of variable printed data (Lot and Expiry), and to confirm correct label through verification of unique identifying aspect (typically pharmacode or 2D matrix code). If these characteristics are acceptable the label shall be applied to the pen assembly. A vision system shall be used to inspect the correct alignment of the label on the pen assembly.
h) The Pen Cap shall be fed and oriented utilizing a coated vibratory bowl and shall be applied to the pen automatically. Clip of pen cap must be in alignment with the pen dose window. A sound hood shall be installed on the vibrating bowl to further minimize noise from the bowl.
i) The Injection Knob shall be depressed automatically during the snap-fit of pen cap.
j) The Machine shall be able to load single or double cartridge onto the transfer conveyor’s racks.
k) Completed pen is placed into a single or double thermoformed plastic tray and discharged from machine. The Machine must have capability to load either 1 or 2 pens into the trays.

3.2.2 The machine must supply sufficient force to complete the snapping operation of the Dosing Mechanic to the Cartridge Holder, and Pen Cap to finished pen without imparting damage to any component. Table below indicates the approximate forces expected in the pens.

<table>
<thead>
<tr>
<th>Items Being Assembled</th>
<th>Amount of Force</th>
</tr>
</thead>
<tbody>
<tr>
<td>Retract Injection Knob</td>
<td>10-15 N</td>
</tr>
<tr>
<td>Cartridge Holder to Dosing Mechanic</td>
<td>Less than 230 N</td>
</tr>
<tr>
<td>Depress Injection Knob</td>
<td>10-15 N</td>
</tr>
<tr>
<td>Pen Cap to Cartridge Holder</td>
<td>5-20 N</td>
</tr>
</tbody>
</table>

3.2.3 The machine must possess a station that will consistently apply a printed label to the assembled pen. Printing of Lot and Expiration Date on the label should be accomplished using a laser printing process. In addition, the machine will be installed with a system to verify Lot and Expiration Date have been printed correctly and legibly. If an incorrect label is detected or the print quality is not acceptable then the label is rejected and not placed on a pen. The machine must also inspect the pen label
on the pen for skewness. If the pen label is not straight according to the specification, the machine must place the rejected pen into a reject location to allow for reconciliation.

3.2.4 Label dimensions will be approximately 40 mm by 49 mm.

3.2.5 Labels will be supplied on rolls with 3” core ID and up to 355 mm (14 inch) in outside diameter, and in whatever copy position is necessary to facilitate application.

3.2.6 The label must be applied in the same position relative to the dosage window within a defined specification. The label must be inspected for correct label placement (location on pen and skewness). This should be done using an automated vision system.

3.2.7 The finished pen will be automatically placed from the machine into a finished pen tray (either 1 pen or 2 pens per tray) for “Good” units or into a “Reject” chute if the machine detected a defect during assembly. A “Reject” is defined as failing any of the inspections discussed in 3.2.1. These are summarized below:

- Too much or too little force to snap the Dosing Mechanic to the Cartridge Holder
- Too much force to press pen into Pen Cap
- Incorrect label as detected by camera
- Incorrect or illegible print of Lot and Expiration Date
- Incorrect pen label placement
- Incorrect or missing components (cartridge, Cartridge Spring, Cartridge Holder or Dosing Mechanic)

3.2.8 The machine must be designed for each component (cartridge holder, cartridge, spring, dose mechanic, label, pen cap, and pen trays) to allow for a minimum of 20 minutes operation without reloading – Reference Only.

3.2.9 A rework station must be fitted on the machine. This station will allow for pens to be relabeled if they were rejected for labeling defects. Station must be equipped with appropriate safety features for operator protection.

3.2.10 The pen assembly machine shall include an automatic pen sampling port for in-process inspection including an alarm for sample removal.

3.3 Machine Performance

3.3.1 The machine must assemble a minimum of 25 acceptable pens per minute.

3.3.2 The machine is expected to run up to 24 hours a day, 5 days a week.

3.3.3 The machine must have an uptime of 95% when in production mode assuming all components are within specification. Any vibratory bowls installed on the machine must have an uptime of 95%.

3.3.4 The machine must be designed such that critical components (e.g. servo motors) are not damaged due to a jam situation.

3.3.5 Pens must be assembled without physical damage or cosmetic defects.

3.3.6 Machine must be designed to be capable of manufacturing a minimum of 50 million disposable pens over its lifetime. Replacing wear parts may extend the lifetime of the machine.
3.4 **Machine Safety**

3.4.1 Machine access points are to be completely guarded with interlocked doors utilizing lexan or similar panels. Doors must contain interlocks that prevent opening the doors without a controlled machine stop.

3.4.2 A minimum of two Emergency Stop buttons will be installed on the machine. One will be located within reach of the person operating the machine.

3.4.3 E-stop buttons will be a mushroom button design that must be manually reset before machine can resume functioning.

3.4.4 A message on the HMI will be displayed when any e-stop is depressed or interlocked door is open as well as the location that caused the stoppage.

3.4.5 Guarding must be installed at the discharge of the machine so that an operator cannot reach within arms length any heated components, pinch points or other potential causes of injury.

3.4.6 All e-stops and interlocked doors must be wired on the same safety circuit.

3.4.7 All pinch points, rollers, heated components, e-stops, and other inherent hazards shall be properly posted and/or labelled.

3.4.8 The sound level of the machine must not exceed 85 dB. Any vibratory bowls may utilize noise insulation to keep the decibel level down.

3.4.9 The machine must comply with all applicable safety standards.

3.4.10 The machine must be fitted with electrical lock off isolation.

3.4.11 It is acceptable to have an umbilical cable with function box which includes Start, Stop and Jog capabilities.

3.5 **Operating Environment**

3.5.1 The machine will be installed in a clean but unclassified working area. The machine must not generate any excess particulate matter.

3.5.2 Operating temperatures of the work area will be 60°F to 85°F.

3.5.3 Humidity in the work area is expected to be 30% to 70% RH.

3.5.4 The height of the machine should not exceed 2.5 meters.

3.6 **Electrical Requirements**

3.6.1 The machine is expected to run on 480VAC, three phase and 60Hz electrical power.

3.6.2 The machine must draw no more than 20 amps.

3.6.3 All major electrical components shall be CE marked.

3.6.4 Electrical enclosures must meet CE requirements.

3.7 **Air Requirements**

3.7.1 Incoming pressure will be 110 PSI. The machine must run on no more than 90 PSI.

3.7.2 Air supplied by the installation facility will be dry and non-lubricated.

3.7.3 The machine must be fitted with a minimum pressure alarm.

3.7.4 The preferred Pneumatic components supplier is Festo.
3.7.5 Critical stations may need to be fitted with individual pressure regulators

3.8 Control System

3.8.1 The machine will utilize an Allen-Bradley PLC controller.

3.8.2 The machine will come equipped with a Vision Automation system meeting the requirements of 21 CFR, Part 11. This vision system will be expected to perform the following inspections:
- Confirmation of combi-seal color
- Confirmation of Cartridge diameter
- Correct and legible printing of LOT and EXP
- Correct pharmacode on label
- Label placement on pen

3.8.3 If a labeling defect is detected, the affected pen must be discharged into a discreet chute to allow for rework.

3.8.4 The preferred Sensors supplier is SICK.

3.8.5 The preferred Servo controllers and motors supplier is Allen-Bradley.

3.8.6 Three-phase motors should be Baldor unless the motor is an integral part of another component of the machine (e.g. index boxes).

3.8.7 Human Machine Interface (HMI)

   a The machine will be equipped with an Allen-Bradley graphical color display HMI.

   b The HMI will include statistical data to track the following:

      Yield of good pens produced
      Number of rejects (segregated by cause of reject i.e. pen build, print error or label barcode reject)
      Total pens produced
      Cycle time (parts per minute)
      Track total hours of machine operation over the life of the machine
      Track hours between maintenance

3.8.8 The control system must allow for a manual jog of the machine as well as full semi-automated mode.

3.8.9 The machine must confirm that rejected parts have indeed been dispensed into an appropriate location.

3.8.10 The control system will allow for two Stop modes. One will be an Emergency Stop and discontinue all functions of the machine immediately. The second mode will be a Cycle Stop in which the machine will finish whatever cycle it is in and then cease operating.

3.8.11 The control system must allow for individual stations on the machine to be jogged via the HMI or umbilical cord control box and it should prompt the operator to return the station to its original station.

3.8.12 An umbilical control box with Start/Stop/Jog capability is required for the machine.
3.8.13 The control system must be able to detect a jammed condition at the appropriate location on the machine. This location must be indicated to the operator via the HMI.

3.8.14 All wiring of the machine is to be legibly indicated with end-to-end markings or labels. These must exactly match the schematics provided in the documentation package for the machine and will be verified during FAT.

3.8.15 The machine will not be required to store or manipulate any cGMP information.

3.9 Changeover

3.9.1 The changeover from the Low Dose to High Dose (or vice versa) must take no longer than 30 minutes – Reference Only.

3.9.2 Changeover must be simple and require standard tools.

3.9.3 Changeovers must be easy enough to be completed by trained operators, not mechanics.

3.10 Machine Finish and Construction

3.10.1 The frame of the machine must be made of steel.

3.10.2 All product contact parts shall be made of stainless steel, hard anodized aluminum or POM. In addition, product contact parts should be designed to allow for cleaning in case of Cartridge breakage.

3.10.3 Exterior to be painted using Steel-It paint.

3.10.4 All welds, burrs, sharp edges or rough surfaces must be ground smooth. Any exterior edges or corners must be rounded off.

3.10.5 The use of asbestos or asbestos containing components is strictly prohibited.

3.10.6 Any lubricants used must be food grade if there is potential for the lubricant to come in contact with the pen components.

3.10.7 The machine must be stable, vibration free and mounted on lockable feet.

3.10.8 The machine should be designed such that as much mechanical equipment is installed below the top deck. Pneumatics should be covered whenever possible. Points where equipment or components meet on the top deck should be beveled or rounded to allow for cleaning. Care should be given to minimize small areas where dirt can accumulate.

3.11 Machine Maintenance and Calibration

3.11.1 Lubrication points must have an easy access.

3.11.2 Cleaning of the machine is expected to be done with isopropyl alcohol or mild cleaning detergents.

3.11.3 The machine must come with a resetttable timer to track hours between preventive maintenance routines. The machine must also possess a non-resettable timer to track hours of operation over the life of the machine.

3.11.4 Any gauges or measuring device utilized on the machine should be installed so as to allow for calibration to be completed without physical removal of the gauge or device.

3.12 Documentation

3.12.1 The machine must be CE marked for operation in the European Union.

3.12.2 A Certificate of Conformity must be provided upon delivery of the machine.
3.12.3 A Technical and Operational Manual for the machine must be provided. The manual must include:
- Equipment Setup
- Safety, Precautions and Control Mechanisms
- Startup and normal operating procedures including all Error messages that can be expected and means to deal with the error
- Shutdown procedures
- Examples and descriptions of all HMI screens
- Maintenance procedures and schedule
- Recommended spare parts list

3.12.4 Two (2) hard copies of the Technical and Operational Manual must be provided as well as on CD-ROM

3.12.5 An electronic and hard copy of any PLC ladder logic shall be provided.

3.12.6 Detailed assembly drawings of the “as built” machine will be provided in hard copy.

3.12.7 Detailed electrical schematic will be provided for the “as built” machine.

3.12.8 Any OEM manuals and/or certificates or quality documents for components or equipment installed on the machine will be provided.

3.12.9 The machine must be supplied with a 2 year recommended spare parts list.

3.12.10Material certifications must be provided for any machine part that comes in contact with the cartridge.

3.13 Factory Acceptance Test

3.13.1 Pen assembly machine vendor is responsible for preparing a Factory Acceptance Test (FAT) protocol. This will be reviewed and agreed upon by owner and installation facility personnel.

3.13.2 Owner agrees to supply ample quantities of materials (pen components and cartridges) to complete commissioning de-bugging and FAT activities.

3.13.3 Any gauges, controllers or other measuring devices installed on the machine must be calibrated prior to the FAT. Records of the calibration must be provided (if required).

3.13.4 There will be representatives from Owner and the installation facility present for the FAT.

3.13.5 Machine vendor agrees to have adequate technical support and personnel available to run the machine during the FAT.

3.13.6 Machine vendor agrees to provide support once machine is delivered to the manufacturing site for reassembly and IQ/OQ activities.

END OF DOCUMENT