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Manual Syringe Filler Application Cell

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Abstract

This document contains the preliminary design documentation and project aspects of the manual syringe filler application cell, which is entirely theoretical but is based on current automation technologies.

The intent is to build a new process development platform for already operational assembly machines. A new process can be built and implemented with little to no downtime for the assembly machines while under validation and approval. This document is an outline of the preliminary design process and defines the design process at each step. The general basis of content will follow a detailed procedure of the steps as if a company is designing and building the application cell under contract from some manufacturer customer. The document goes through the necessary specifications and will be outlined in this document. A general goal was that three sized syringes would be tested on the new equipment. A customer team will have to identify essential areas that will require some development work and will be discussed throughout the System design and build.

Keywords: *Application Cell, Sars-COVID-19, Assembly machines, Design.*

1. Introduction

Looking at the current world social climate as inspiration, it became clear that a medical device company would have an immediate need to fast track any new process validation when getting a drug to market. At current market paces, typical process development and validation can take months before a product can be manufactured and sold to the public. In current government guidance, it is recommended that medical manufacturers have teams allocated preform many critical tasks that allow for a high-quality safe product to be distributed (FDA, 2011). The application test cell could provide a parallel path during the process development. A team responsible with building the process can use the test cell while equipment is allocated for manufacturing can be kept online while the validation is underway. This will free up valuable manufacturing time while completing the necessary tasks involved in the process development aspect of taking a new product to market.

The preliminary design aspects of the system are described to some detail in the article and while based on real world technologies and current manufacturing technologies, are meant to be theoretical in nature.

2. Problem Definition and Identification of Need

The Manual Syringe Filler Application Cell is a single syringe semi-automated filling machine designed to support the process development for more extensive, fully automated assembly machines of the same vaccine filled products. The fundamental purpose will be that the machine is flexible enough to build a process that can be approved by all respective governing agencies. The process can be transferred to the mass production machines such that it does not need re-approval, which will substantially reduce the validation time requirements.

The test cell development will eliminate downtime caused by the process development process and subsequent approval on the larger dedicated assembly machines while a new process is developed and tested. The immediate short-term functionality will be used to prebuild the process that will dispense the vaccine for the Sars-COVID-19 virus. Since dispense process variables are still largely unknown, this machine will be flexible enough to build a process for three currently

operating assembly machines that will eventually be dedicated to the vaccine's mass production. If the vaccine demand falls, the test cell can be used to develop the main assembly machine's new process function.

The test cell will fulfill the current demand for a mass-produced vaccine that is on a short time to market schedule. According to USA TODAY, the US hopes to ship 2.4 Million doses just 24 hours after the FDA approves the Vaccine (Weise, 2020). It will accelerate the development and validation process required to safely distribute the vaccine filled product when it becomes available to the public.

The test cell's primary design specification will be to accept three size syringe barrels with interchangeable tooling. The tooling will use a manually operated fixture to support the parts while in process. The fixtures will be identical to the tooling used on the more extensive line. The machine will use the same automated dispense apparatus, the same transfer tubing materials, and be programmable for a varying array of variables that can affect the process. The test cell will require no more than one operator and fit inside a small lab with standard ceiling height. The material dispense apparatus or pump will be able to fill a 3mL, 5mL, and 7mL size syringe. All assembly materials shall be food grade or approved for food contact by the NSF/ANSI 51-2019. All construction materials shall be non-shedding and non-corrosive. The dispense process time will need to be at a minimum of 5% faster than the assembly line dispenses time to ensure the process can be performed without an effect on the larger machine speed.

As with any medical device equipment being installed and validated in a production facility, is it important the OEM follows proper IQ, OQ, and PQ techniques (The FDA Group LLC., 2019). When designing a production machine this is important for not only the customer but also the builder to adhere to.

3. Management Planning

3.1 Group Organization

The following table outlines the department and associated roles and responsibilities that will be required of each department. Each department will require to maintain their respective roles and meet their responsibilities outline in the action item lists.

Table 1: Group Organization Outline

Role	***Responsible For***
Systems Engineering	❖ Authoring the PMP, SEMP, and System Specification documents (This Document) with guided input from all departments. ❖ Making sure that the plan stays on schedule and defines roles and responsibilities for the duration of the project. ❖ Reviewing design documents are specific, unambiguous and can be validated.
Process Development Engineering	❖ Reviewing and approving the System Specifications to make sure it correctly describes the manufacturing process to be automated. ❖ Managing outside suppliers and contractors. ❖ Final validation of the project ❖ Perform Market analysis and data collection
Automation Engineering	❖ Reviewing and approving the System Specifications to make sure it adequately describes the controls aspect of the manufacturing process to be automated. ❖ Carry out the design aspects of the controls system design and implementation.

Quality Engineering	❖ Reviewing and approving the System Specifications to make sure it is following regulatory requirements. ❖ Carrying out quality build verification and subsequent quality validations of the machine.
Operations	❖ Reviewing and approving the System Specifications to make sure it correctly addresses all Operational requirements. ❖ To detail and fill in operational aspects of the machine build and final design.
Design and Mechanical Engineering	❖ Ensure compliance with all aspects of the System Specifications during the development of the machine during its development life cycle. ❖ Prompt notification of issues related to machine development. ❖ Facilitation of design reviews. ❖ Facilitation of Final testing and provision of engineering support. ❖ Adherence to change control system and prompt notification of any requested changes to the system specification requirements/design constraints before implementation.

3.2 Project action items lists

The following table outlines the proposed action items list and verification for the duration of the project. The table is a living section and will change as the project develops based on the project's requirements. As the project is approved for a full system design and implementation, due dates will be assigned.

Table 2: Group Organization Outline

Owner	***Detail***
SYS Eng.	Role Responsibility
SYS Eng.	System Design and Feasibility Analysis
SYS Eng.	System Requirements
Design Eng.	Design approaches or alternatives
All Eng.	Evaluate the feasibility of alternative designs
Op, Automation Eng.	System Operational Requirements
All Eng.	System Maintenance and Support
Op Eng.	Technical Performance Measures
Automation and Design	Data Collection
PD Eng.	Functional Analysis
Quality Eng.	Update Type A System Specification
PD Eng.	Project review
PD Eng.	Project submission
All	Role Responsibility

3.3 Resource Requirements

All design teams will utilize the latest design software to develop the system, Such as CAD, CAM, Hardware specific IDEs, and other such development platforms for R&D.

4. System Design and Feasibility Analysis.

4.1 System Requirements: (see Table 3)

4.2 Design Approach and Alternatives

First, the design is to define spatial requirements and a detailed layout of the location where the machine is to be installed, taking into consideration any entryway the machine must pass through, as well as ceiling heights. The Volume must be adhered to during design. An initial design approach would be the cellular design, a uniform shape such as a rectangle, without protrusions or irregular shapes so that other equipment can be positioned next to the machine. Another option is to customize the machine into the existing space with a footprint that molds into space, with considerations for doors or cabinetry that need to open.

The next design feature would be to implement interchangeable tooling that must also match the existing machinery. The machinery currently in use may not have tooling that can be fit seamlessly on top of another's footprint. Consider adapter plates that go along with the tooling or consider retrofitting tooling on a larger in use machine.

4.3 Feasibility of Design Alternatives

The customer must ultimately decide the layout that fits their needs. The cellular approach is better for manufacturing but may be cumbersome to the customer. Cost benefits are held with cellular design.

Interchangeable tooling. The customer application requires the same tooling to be used. Because it is uncertain which tooling will be in regular use, three tools must be adapted to fit on the machine and workk. Adapter plates add additional setup and will take time in adjustments but are by far more cost-effective than the alternative of a retrofit with newly designed tooling on other equipment.

Table 3: System Requirements

Name	***Description***	***Tangible***	***Metric***
Interchangeable tooling	Accept three size syringe barrels	Tangible	Tooling System Designed and Tested
Manual Operation	Machine Easy to use	Tangible	Performance Testing
Tooling Currently in use	Use Existing Designs from Previous machines	Tangible	Review, evaluate and approve for use
Dispense equipment	Validate Equipment Suggest Possible Upgrades to current equipment	Intangible	
One Operator	Design for use by a single person	Tangible	Verification
Volume Specification	Market Research for Variable precision dispense equipment	Tangible	Product selection
Food Grade	Market research for material selection	Tangible	Product selection
construction materials	non-shedding and non-corrosive	Intangible	
Dispense Time restriction	5% Faster than Existing equipment	Tangible	Measure output

5. System Operational Requirements

The System Operational Requirements are summarized in Table 4.

Table 4: Operational Requirements

Item	*Detail*
1	The machine shall be set up for operation by a single operator
2	The cell must fit through a standard 36-inch door frame
3	The cell must not take up more than 15 Square Feet
4	The cell must be programmable to dispense at minimum 2.6mL, as well as up to 12mL of vaccine
5	The cell must include a recipe management system where parameters can be stored
6	The cell must have interchangeable tooling or adaptors that take no longer than 5 minutes to change
7	All control electronics must be kept contained in a cabinet with a minimum of IP67 rating.
8	Any parts that touch the vaccine must meet food safe specifications
9	Any storage containers of the vaccine product must be made of 18/8 Stainless Steel
10	Framing must be constructed of anodized aluminum or painted mild steel, where applicable
11	The machine must be designed to run in a cleanroom
12	Any compressed air exhaust must be filtered and be positioned where it will not affect vaccine dispense.
13	All Safety Hazard must be identified and labeled. Safety hazards must also have reasonable protection.
14	The cell must dispense vaccine within 425mS, which is 5% faster than the mainline
15	The cell must be engineered for at least a 5-year service life
16	The system must not cause abnormal recycling requirements to post-normal service life, such as require special disposal processes.

6. System Maintenance and Support

The System Maintenance and Support Requirements are summarized in Table 5.

Table 5: Maintenance and Support outline

Onsite /Offsite	*Detail*	*Corrective /Preventative*	*Skill Level*[1]
Onsite	General Cleaning	Preventative	Unskilled
Onsite	Tooling Change over	Corrective	Unskilled
Onsite	Fine Adjustments	Corrective	Entry Technician
Onsite	Pump Cleaning	Preventative	Skilled Technician
Onsite	Leak Repairs	Corrective	Skilled Technician
Off-site	Overhaul	Corrective	Seasoned builder/Vender
Onsite	Lube of moving parts	Preventative	Entry Technician
Onsite	Electrical repairs	Corrective	Skilled Technician
Onsite	Electronic re-programming Firmware updating	Preventative	Engineer

1. Definition of Skills:
   Unskilled - Operator, no training
   Entry Technician - Entry-level Technician with less than 2 years' experience.
   Skilled Technician - Technician with more than 2 years of experience.
   Seasoned builder or Vendor - Original equipment manufacture or outside source

7. Technical Performance Measures

The Technical Performance Measures (TPM) are summarized in Table 6.

Table 6: TPM Outline

TPM	*Metric*	*Benchmark*	*Importance %*
Design Release	8 Weeks	15 Weeks	30
Manufacturing Components	4 Weeks	8 Weeks	20
Long Lead Procurement	2 Weeks	6 Weeks	10
10% Overhead of dispense speed spec	425mS	<400mS dispense speed	10
Successful fill rate before a fault	98%	98%	20
Smaller footprint then specification	<15 Sq Ft	15 Sq Ft	10
			100

8. Functional Analysis

8.1 Functional Allocation Breakdown Diagram: See Fig. 1.

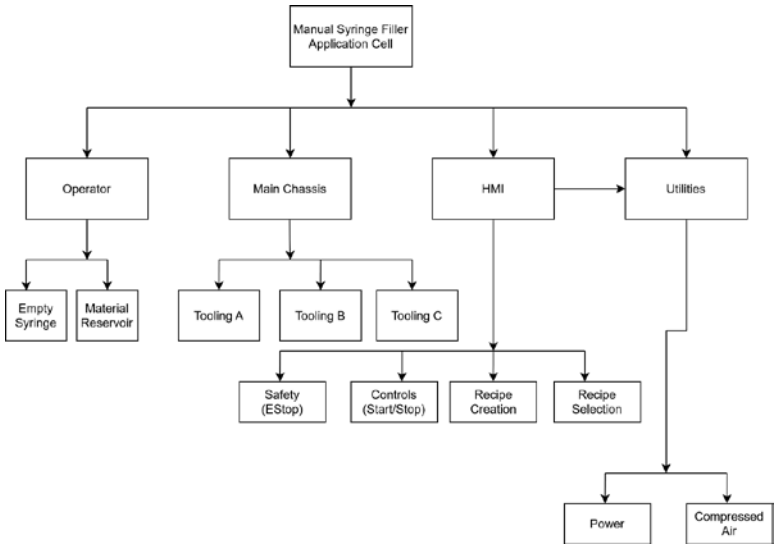

Fig. 1 Functional Allocation

8.2 Functional Flow Diagram; System As a whole: See Fig. 2.

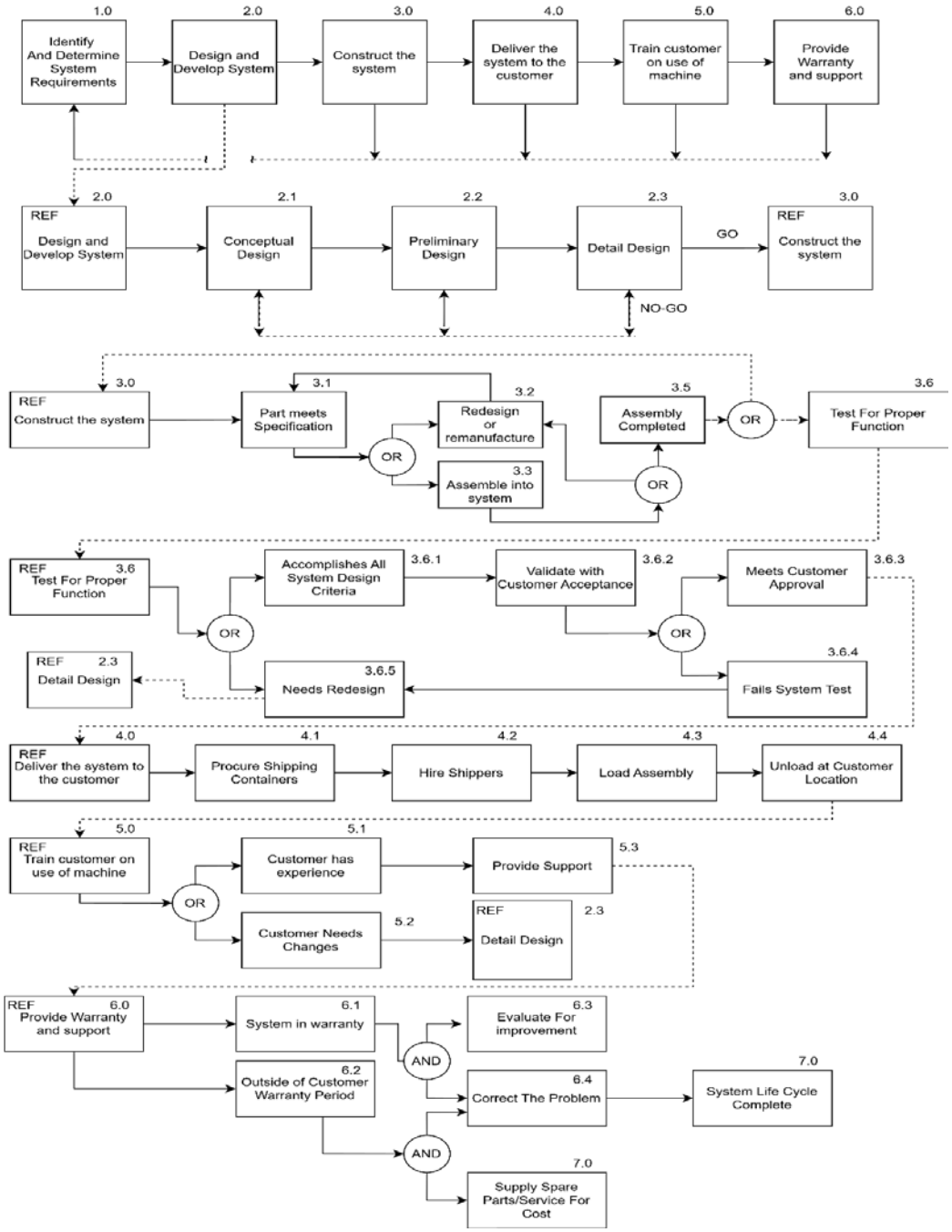

Fig. 2 System Functional Flow Diagram.

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8.3 Functional Flow Diagram; Operational Details breakdown: See Fig. 3.

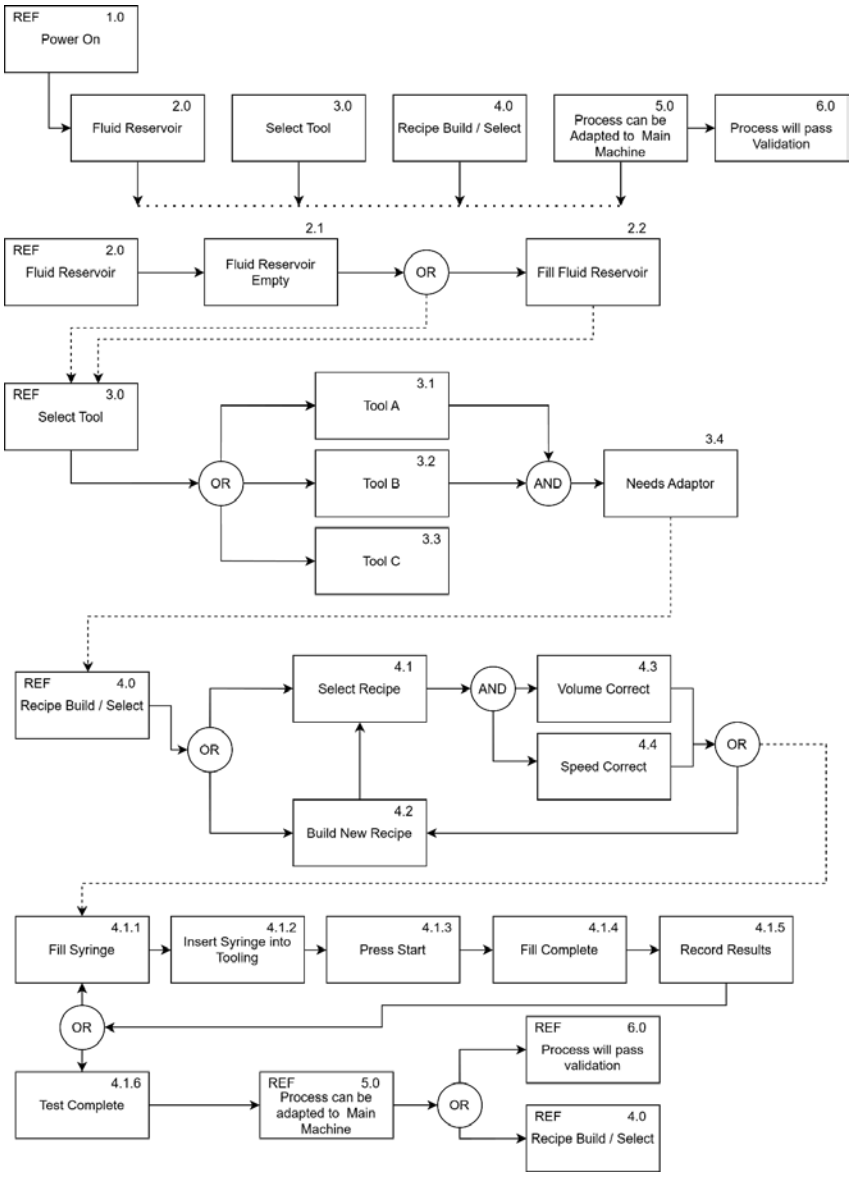

Fig. 3 Operational Details

9. Type A System Specifications

9.1 Scope Statement

This document contains the preliminary design documentation and project aspects of the manual syringe filler application cell one product line, with testing for three sizes of syringes. The intent is to build a new process for current successful technology (3 existing assembly machines). Where a new process can be built and implemented with little to no downtime for the assembly machines while under validation and approval by the customer.

9.2 Technical Documentation

This project will include – in addition to the tables and charts in this document – CAD drawings, electrical prints, pneumatic schematics, testing procedure Original SOW, and build contract for all equipment and floor space.

9.3 Requirements:

9.3.1 System Definition, Characteristics, Design, and Construction: (see Sections 2, and 4 through 8)

9.3.5 Reducibility/Manufacturability:

Parts will be purchased from local vendors and manufactured by local job shops. Each part will be first sourced from the vendor. If no parts are available that fill the requirements, they will be manufactured according to the design drawings. Control systems will be developed in house and be custom to the application.

9.3.6 Disposability

The machine will be recyclable for the most part. All construction materials will be made of recyclable metal and plastics. Any parts that may contain hazardous material will be subject to special recycling by the customer. The vendor will assume there are no hazardous materials used on the machine before delivery to the customer.

9.3.7 Affordability (estimation of relative cost)

An itemized breakdown of cost can be found in the original RFQ and Signed contract by the customer and us, the vendor. Barring any additional RFQ's, Add-ons, or Change requests, the final price of the line will be $250,000. (this is not to be assumed as a quote or final price).

9.4 Test and Evaluation

Testing and Evaluation will be addressed and performed by the manufacturer, the vendor, and by customer. The customer will provide the final testing procedures and metrics and will accept the line at the end of the build.

9.5 Quality Assurance Provisions

The customer will provide the final testing procedures and metrics. Testing results will be validated by the customer

9.6 Distribution and Customer Service

The vendor will provide a one-year support contract. After the year, we will inform the customer of any market sourced components used on the line that reaches the end of life and make attempts to replace the parts on an as-needed basis, for as long as 10 years.

9.7 Retirement and Material Recycling/Disposal

The vendor assumes that all construction materials are safe for disposal/recycling when the cell leaves the facility. Any special recycling will be the responsibility of the customer or the final user.

10. Conclusions

Building and implementing a test cell to validate a process on a new product that can be moved to another more efficient machine, can easily save a company months of downtime. This preliminary design study indicates that this project is feasible with the scope, details, and constraints outlined here. Upon buy-in, approval, and feedback provided by all stakeholders in this project, this preliminary design will be ready to expand into a complete system design.

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