Syringe Filling System for New Born Injections

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Submitted for the degree of Master of Science in Biomedical Engineering

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August 2016

Acknowledgements

I wish to express my sincere gratitude to Mr. Patrick Carena, my supervisor, for providing me the opportunity to do such an interesting project at Ninewells hospital.

I also thank Dr. Shetty Bhushan consultant Neonatologist from the Neonatal department, for the time he gave me to explain the procedures for new-born injections.

I sincerely thank Mr. Duncan Kirkcaldy from the mechanical workshop and Mr. Cheng Wei from the Division of Cancer Research, for the time they accorded me for advising and manufacturing the parts I needed.

Abstract

Every year, 50 000 babies are born at Ninewells hospital. According to the weight of the baby a specific amount of vitamin K needs to be administrated to each of them.

The aim of this project is to demonstrate the feasibility of a system, that can automatically prepare a syringe ready for injection, with the correct volume of drug according to an input weight. During this project, an innovative device was designed, that not only calculates the appropriate amount of drug that needs to be used, but also serves to the user a ready-to-use syringe.

In the market, there are already some syringe filling systems. What makes this project special, is the requirement of using two needles, as that is necessary for ensuring safety of neonatal. Vitamin K comes in an ampoule made from glass. A filter containing needle is firstly used, to avoid glass particles penetrating the syringe, then a very fine needle is used to inject the drug to the baby.

The technical specifications of the device were determined, combining information from literature and consulting with a clinician specialised on that field. During the prosecution of the project, a 3D model of the system was designed on SolidWorks, which was then realised through 3D printing and conventional manufacturing. The project was completed with a reliability evaluation, to make apparent the safety of the system and its potential future improvements.

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I. Background

There are four drugs that are normally administered to neonatal facing difficulties at birth. The volume of the drugs that needs to be administrated to the baby depends on their body weight. It would be helpful for the clinical staff in the labour ward and the neonatal intensive care unit, to have a way to assist them to estimate and prepare a syringe that contains the correct amount of medication. That would not only be of convenience but also would minimise the possibility of human mistake.

Initially, the aim of the project was to find a solution to fill a syringe with the four drugs that are included in the emergency box. After discussing with the clinician, it was realized that they never mix different drugs in the same syringe, they always proceed with separate injections by using different syringe each time. It would be more useful for the clinical personal to have a vitamin K syringe filing system than the emergency drugs because of the higher rate of use. Moreover, if the system is working for the vitamin K, it could also be used to fill syringes with the emergency drugs.

Because this project aims to improve the efficiency in the neonatal ward, the project has been redefined in order to fit as well as possible with the needs of the ward.

This project is concentrated in producing a system regarding the administration of Vitamin K specifically. That would facilitate in demonstrating the feasibility of a system like this, using Vitamin K administration system, as a prototype.

II. Method

This project is composed in two main parts: literature review and design & development of a prototype.

The literature review covers:

- Specifications definition with the clinicians
- Market review for related devices
- Review of international standards of medical devices
- Technologies research
- Review and implement drug protocol
- Risk assessment

The design & development of the prototype covers:

- Mechanical design/manufacture
- Electronical design/manufacture
- Software design
- Integration/Testing

(A detailed Gant chart is available in appendix □1.)

III. Specifications definition

1. Meeting with the clinician

In order to identify and clarify the needs of this project, a consultation with a specialist from the neonatal department unit of the hospital, Doctor Shetty Bhushan a consultant Neonatologist was completed. During this meeting, current procedures regarding neonatal recovery were discussed, about premature and “on time” babies. Procedures included drug administration choice, volume, time and other related factors affecting these procedures.

For babies with weight superior to 2.5Kg, the amount of vitamin K to be administrated, is the same. Bellow this weight, the amount is reduced proportionally to body weight.

For premature babies in emergency situation, four drugs (that are stored in an emergency box) are injected to the babies. The amount of these medications, also depends to their body weight (see picture below).

The emergency drugs are:

- Epinephrine (Adrenaline) 2 bottles of 10ml
- Glucose Injection 2 bottles of 10ml
- Naloxone HCI 2 bottles of 1ml
- Sodium Bicarbonate 2 bottles of 10ml

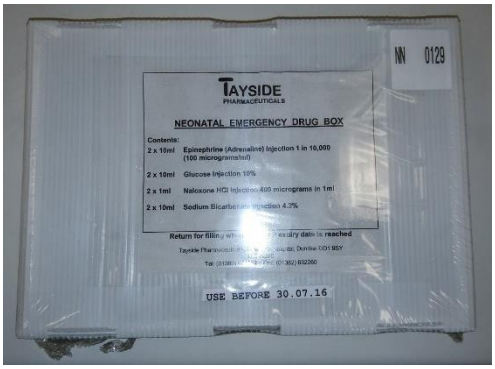


Figure 1: Emergency box

For each injection, the amount injected into the baby has to reach optimal accuracy, with a very small margin error. During the administration process, the needle of each syringe has to be changed twice before every injection. Firstly, a needle with a filter is used to take the drug from the glass container. The filter is there to ensure that no glass

dust will penetrate inside the syringe, which can be harmful for the baby. Then, the filter needle is replaced with a smaller needle suitable for baby injections.

These injection procedures are all very precise and always checked by two people to eliminate the error. However, despite high attention from the clinicians, human error can still occur because of factors such as exhaustion or due to high pressure environment.

IV. Literature review

1. Vitamin K Protocol

1.1. General use

Vitamin K prophylaxis is offered for all new-born babies in the early postnatal period to prevent Vitamin K Deficiency Bleeding (VKDB). Neonates are relatively deficient in vitamin K and those who do not receive supplements are at risk of VKDB, including intracranial haemorrhage. VKDB is a rare but very serious disease. It affects about 1 in 10,000 babies if they are not given vitamin K at birth. [1] The vitamin K can be administrated orally or intramuscularly, to healthy babies. The intramuscular way is recommended and consists of a single dose injection. [2]

1.2. Toxic effects

It has been shown that for new-born, large intake of vitamin K can induce, an increase hemolysis (rupturing of red blood cell), hyperbilirubinemia that can lead to kernicterus (brain dysfunction caused by excess of bilirubin) especially for premature baby. [3] However, vitamin K toxicity highly depends of the dose administrated when superior to 1mg/d. [4]

1.3. Vitamin K injection guidelines

For healthy babies, greater than 36 weeks' gestation [2]:

- 1mg Konakion MM Paediatric (Vitamin K) 2mg/0.2ml = 0.1ml (1/2 ampoule)
- Care will be required when giving Konakion MM Paediatric (Vitamin K) to ensure that only 1/2 the contents of the vial are drawn up and administered
- A vial breaker should be used to break the glass vial of Konakion MM Paediatric and a filter needle must be used to draw up Konakion MM Paediatric into the syringe. The needle should then be changed prior to a ensuring correct dose and administering

For babies under 2.5kg or less than 36weeks gestation [2]:

- A dose of **0.4mg/kg** intramuscular must be prescribe up to a maximum of a 1mg dose
- Care must be taken to accurately measure small dose volumes

- Intramuscular administration is strongly recommended in this group.

2. Technology review

Before starting the design of the product, it is important to carry out a review to determine if there are any existing products in the market which carry out the required function.

2.1.AddedPharma

Added Pharma is a flexible organization that delivers medical products and solutions for hospital pharmacies and commercial compounding companies. [5]

2.1.1. ***SmartFiller & Capper***

Smartfiller & Capper is a syringe filling machine for oral and sterile syringes. The machine has the ability to fill a syringe of every kind and use caps of every kind. [6]

Figure 2: Picture of the SmartFiller & Capper

Plus:

- Fast filling
- Syringe closed at the end
- precise

Cons

- No needles
- Not easy to clean

2.1.2. Smartfiller

The SmartFiller is an automated syringe filling machine that accurately fills syringes with drugs at a speed of about 5 syringes per minute. It enables small scale aseptic batch filling of syringes in hospital pharmacy and pharmaceutical compounding environments. [6]

Figure 3: Pictures of the SmartFiller

Plus

- Small size
- GUI with touch screen
- Fast
- precise
- Caps

Cons

- Only one needle
- Not easy to clean

2.1.3. SmartCompounder MibMix

The SmartCompounder MibMix is an automated bag filling machine that can mix up to 12 different substances for total parenteral nutrition (TPN). It is a flexible machine, which can be used as a 4, 8 or 12 channel compounder, due to its modular construction. The combination of different equipment, smart features and easy operating software makes the machine an efficient tool in safe aseptic TPN compounding. [6]

Figure 4: SmartCompounder MibMix

Plus:

- Different drugs available (4 to 8)
- Fast
- Precise
- Easy to clean

Cons:

- Manual manipulation
- No double needle

2.2.Bosh

2.2.1. FXS 2020 Syringe Filling and Sealing

A fully automatic filling and sealing machine for pre-sterilized nested syringes in a tube.

The FXS 2020 performs up to 80 syringes per minute and is specifically designed for filling syringes with volumes between 0.5 ml up to 50 ml. [7]

Figure 5: FXS 2020 Syringe Filling and Sealing

Features

- A fully automatic filling and sealing machine for pre-sterilized nested syringes in a tub such as BD Hypak SCF™
- Performance goes up to 4800 syringes per hour
- Specifically designed for filling syringes with volumes between 0,5 ml up to 50 ml
- All product contacting parts are made out of AISI 316L
- Operated by means of a touch panel
- Transportation system and each pump are individually controlled by servo motors
- Only one type of drug at a time

2.2.2. FXS 5100 Syringe Filling Machine

The FXS 5100 filling and closing machine has been specifically designed for the processing of pre-sterilized, nested syringes. It has been developed to meet current pharmaceutical industry requirements and address the needs of the end user. The very compact design reduces expensive sterile area space – whether this is within a conventional clean room or within an isolator system. Additionally, the FXS 5100 has been designed to be serviced exclusively from one side. This reduces the time and effort during servicing and also minimizes the installation space requirements by allowing the unit to be wall mounted with no required rear access. [8]

Figure 6: FXS 5100 Syringe Filling Machine

Features

- Slim Design: space-saving and easily to clean, optimal for inline placement.
- Entire machine is operated from one side: optimal for inline and wall installation.
- The transport system is precise and adaptable to all process steps.

- Continuous filling and closing even during the nest change
- Flexible and adaptable filling needle movement
- Stopper supply without interferences: optimal for free airflow around the syringes during the entire process
- Only one type of drug at a time

2.2.3. MLD Multi-Function Filling Machine with Built-in Checkweigher

The MLD is a flexible filling machine that can be configured to handle a wide variety of syringes, cartridges and related containers. Its wide processing spectrum ranges from dental or insulin cartridges right up to contrast medium cartridges. Filling is accomplished either by rotary piston pumps or Bosch Smart FillTM time pressure filling and fills at rates up to 600 units per minute. The MLD is the only commercial syringe filler available with built-in checkweighing.

With its narrow 800 mm width, the MLD offers a small footprint and easy access to all areas of the machine, even in the optional barrier isolator configuration. [9]

Figure 7: MLD Multi-Function Filling Machine

Features

- GMP-compliant construction
- Linear transportation system, continuous and synchronised (continuous towing in the infeed and outfeed, filling, overseal caps areas, synchronised with precision movements such as, for instance, oversealing)
- Prism-clip system for container transportation, no sliding. Containers are free at the top and bottom (patented special design), optimum flow ratios in laminar flow
- Filling system: with rotary slide piston pumps or oder Time/pressure filling

- No double needle supported

All the Bosh solutions seems to be designed for industrial production purpose seeing the high rate of syringe per hour.

1.2.Tridak LLC

Tridak LLC, originally founded in the early 1970's, specializes in the manufacture of easy-to-use, cost-effective systems for filling cartridges and syringes. Entry-level systems like the Model 1000 are perfect for initial users who may be filling syringes by hand now. At the same time these systems offer quick, repeatable filling. [10]

1.2.1. Model 1050 Syringe Filling System

The Tridak Model 1050 is a semi-automated, bench-top syringe filling system. This system is manually loaded and unloaded, making it ideal for low volume production or as an alternative to filling syringes manually. Each syringe is filled through the tip, allowing this system to be compatible with a number of different syringe types including Luer Lock syringes, Luer Slip syringes, and Oral syringes.

The Model 1050 is recommended for use with fluids having a viscosity up to 60,000 cP and can be paired with a number of different material reservoirs to accommodate different material package sizes. The system utilizes a Model 830 disposable fluid path valve to make material changeover fast and easy while eliminating material contamination. This valve also features adjustable suck-back for accurate, clean cut-off of stringy or tacky materials. [11]

Figure 8: Model 1050 Syringe Filling System

System Features

- Dispensing valve features adjustable suck-back for a clean dispense of stringy and tacky materials
- System fills 1-60 mL syringes with pre-inserted pistons. Tooling nozzles are available for both Luer Lock and Oral tips
- Adjustable, pneumatic stop assures accurate fills
- Utilizes disposable wetted components, eliminating messy clean-up and minimizing maintenance
- This system's fluid path can be capped and remain attached to the material cartridge for storage
- Foot switch for hands-free fill cycle activation
- Smooth, easy-to-clean surface

Cons

- No precise
- Drug injected with pressure
- No double needle supported

Other model available from this company, but based on the same technology (pressure)

1.3.Beverage application

The solutions above show various technology possibility. They are not designed for medical purpose but they show a system with multiple drugs filling. Despite a very different application field, these products could be adapted for biomedical purpose.

1.3.1. The Inebriator

This system is a cocktail dispenser where a glass jogs below different bottles to receive an amount of liquid. The soft drinks are dispensed from a tube driven by pumps and the alcohol drinks with pressure valves. [12]

Figure 9: The Inebriator

Plus

- Different liquids available
- GUI
- Fast

Cons

- Not sterile
- No precise
- Not for medical purpose

1.3.2. BlendBow barmate Infinite

Barmate Infinite is a machine design by BlenBow company, it is a cocktail maker. [13]

Figure 10: BlendBow barmate Infinite

The different drinks are put in a glasses, interesting option as pilling and shaking are available and can be useful for our medical application.

2. Technologies review Conclusion

The addedPharma solutions seems to share a lot of similar characteristics with the device that is attempted to be designed. However, these solutions don’t seem to achieve high precision of filling.

Bosh solutions seems to be quite reliable regarding to the standards conformity, but it is designed for production purposes.

The solution from TRIDAK LLC is original, as it is applying pressure to the drug, instead of moving the plunger of the syringe. However, this technical solution cannot be applied in our case as it is not suitable for the medical syringe use.

The beverage product offers the possibility to put more than only one drug, but these design is too distant from biomedical purpose.

3. Standards Review

Because the product will be a biomedical device, standards have to be respected in order to guaranty security and efficiency of the product for the patients as defined by the standards. It is important to consider the standards before the design of the product, to achieve product design that is reliable without time waste.

It is important to make the standards review before thinking of the system design, to be able consider and implement the standards directives during the design process. That will prevent future design modification and save some time.

In function of the market range chosen, there are different standards. For instance, if the chosen market is only the United Kingdom, the product will have to be conformed to British Standards (BS), for Europe, it will be Europe standards (CE). (because UK is part of the European Union, the product has to follow European standards as well).

For biomedical devices, EU directives 92/42/CEE has to be followed. These directives mainly define some basic design requirements, how to classify a medical device and describe conformity procedure validation. According to the Eu directives, the classification of the syringe filling system is IIa.

For each kind of biomedical device, there are specific standards. For this case the directive used is the BS EN 60601-2-24:2015 part 2-24, which define Particular requirements for the basic safety, essential performance and tests protocol for infusion pumps and controllers. This document defines general requirements for pump and infusion devices and procedures to test the performances.

V. Design

1. Objectives

For vitamin K administration, the drug is contained in an ampoule made of glass. (see Figure 11) To open the ampoule, its tip is broken, putting some glass dust into the drug. To avoid any glass dust injection into the baby, a first special needle with a filter is used to fill the syringe. Then the first needle is replaced by a thin needle suitable for baby's injections. (see Figure 12)

Figure 11: Picture of a vitamin K glass ampoule

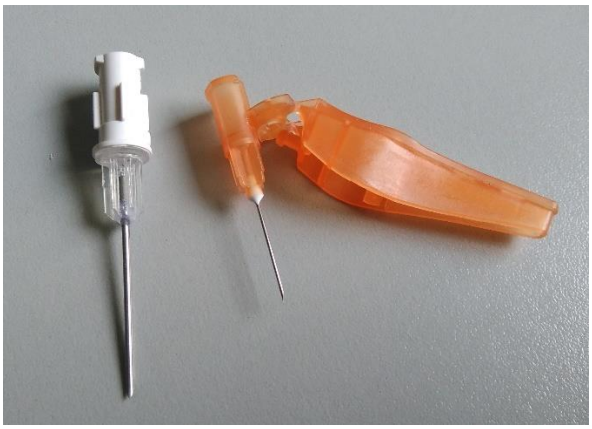


Figure 12: Picture of the needles, filtered needle on the left, micro needle on the right

The system has to perform the same tasks as a normal syringe filling procedure which are:

1. Installation of the first needle (filter needle)
2. Draw the medication from the ampoule
3. Installation of the second needle
4. Remove the air bubbles
5. Adjust the amount of medication

2. Mechanical Design

2.1.Cinematic

- Setup the needles:

The syringe and the needles are connected with a system called Luer lock. This system is similar to a screwing between the syringe and the needles. The screwing motion is obtained by the combination of a translation and a rotation motion, two motors are necessary for this operation (one for the translation and another one for the rotation). The first idea that comes in mind, is to screw the needle to the syringe by making the needle rotate. However, because there are two needles, making the syringe rotate and translate for both needles makes more sense in order to save some motors. Moreover, the second needle is equipped of a plastic protection, (see Figure 12) used after the injection to prevent any injuries and to avoid the ripping of a bin plastic bag. This protection makes the shape of the needle non-symmetric and makes any operation of rotation difficult. The needles are so static and picked by the syringe. (see Figure 13)

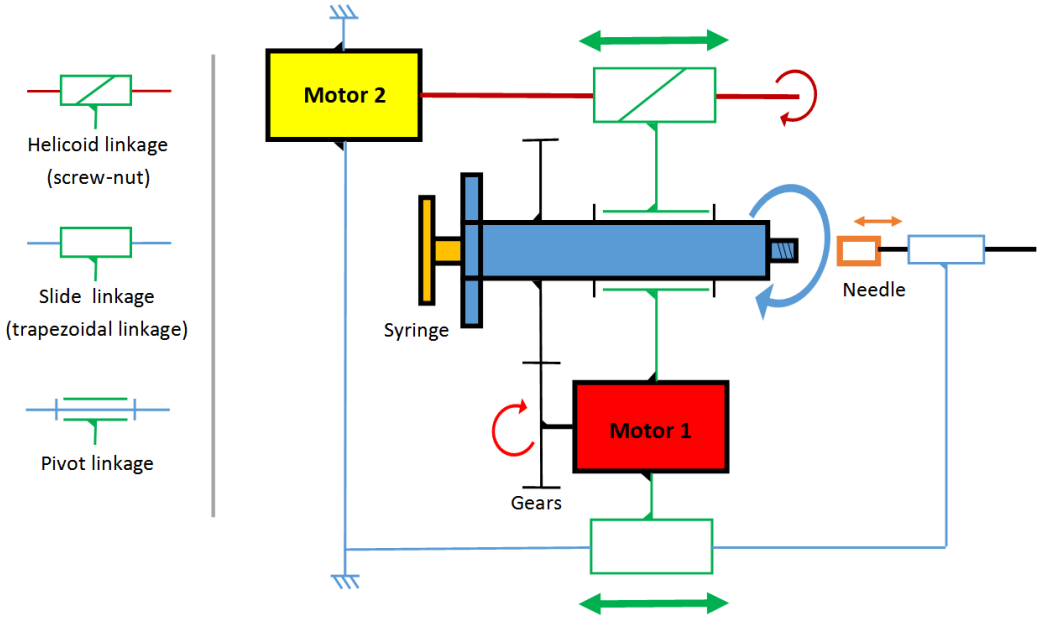


Figure 13: Cinematic diagram of the needle setup system

On this diagram is represented the mechanical system to install the needle to the syringe. The syringe is drawn in blue and yellow and the syringe in orange and black. The motor 1 makes the syringe rotate while the motor 2 makes the syringe translate.

To pick the second needle, a third motor is used to rotate the syringe and all its "screwing system" described above. (See Figure 14)

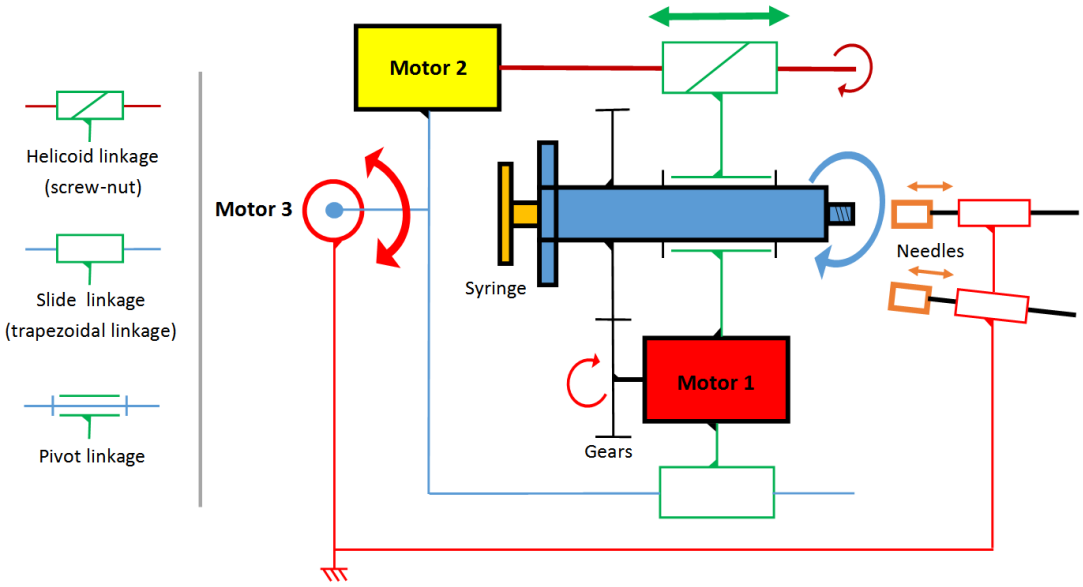


Figure 14: Cinematic diagram of needles setup system

- Draw the medication:

To fill the syringe, two translation motions have to be used, a translation to plunge the syringe equipped with the first needles inside the ampoule, and the second one is motion of translation of the syringe's plunger to draw the medication. The first translation motion can be done with the same translation motion used to setup the needles and the second motion have its own motor for this operation. (see Figure 15)

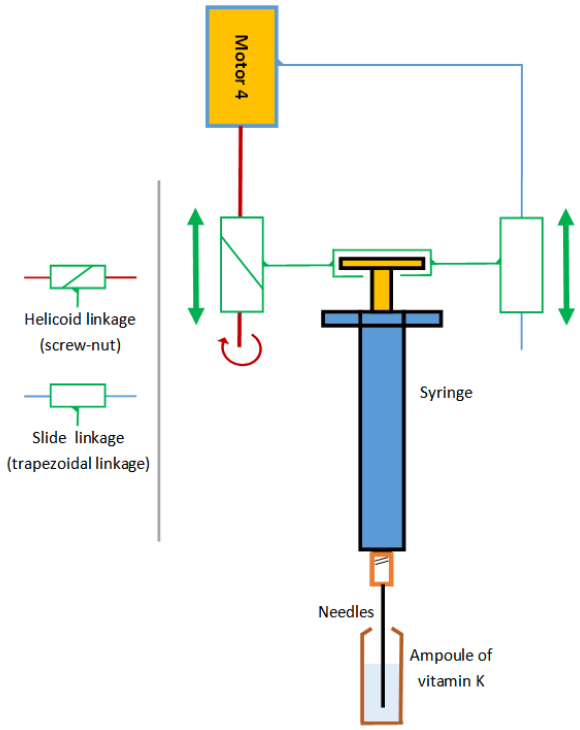


Figure 15: Cinematic diagram of the drug drawing system

- Remove the air bubbles:

To remove the air bubbles, the syringe has to be pointed up and the plunger has to be pressed in order to push the air bubbles outside. Some tap can be applied to the tip of the syringe to help the air bubbles to move out. To push the air bubbles outside, the same motor used to draw the medication is used, but in the other direction (motor 4). The "tap" motion is made by a vibrator (see Figure 17), it is the same kind of vibrator found on a cell phones (see Figure 16). To point the syringe up, a rotation motion is made from another motor. This motor also makes the syringe point to the two needles and the ampoule (motor 3).

Figure 16: Micro Vibrator

Here is a diagram of the complete cinematic:

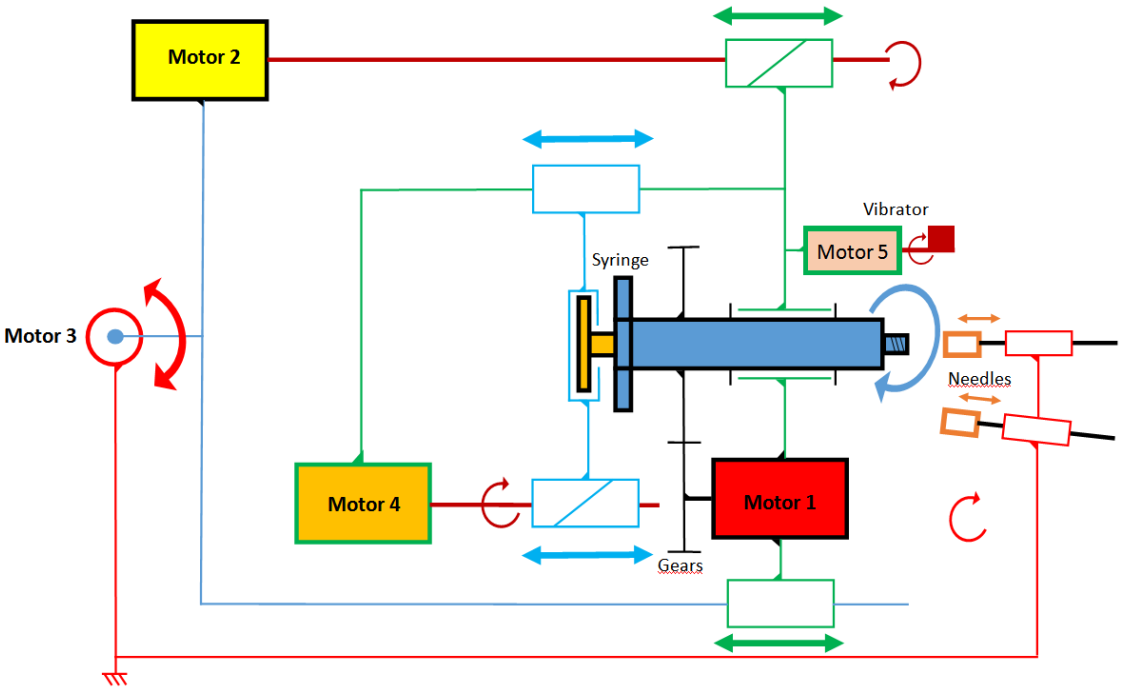


Figure 17: Complete cinematic diagram

2.2.Motors Types

There are two kinds of motors that are generally used, DC motor and Stepper motor. The DC motor is the most common motor; it is a device that converts a continuous electric current power to a mechanical rotation power. The position or the speed cannot be known precisely without any additional device, a sensor such as an encoder is necessary to measure these parameters. [14]

The stepper motor, is a motor that also convert an electrical power to a mechanical rotation power, but it doesn't work continuously. Indeed, a full rotation of the stepper motor is divided by a number of steps and a step is "passed" with an electrical impulsion. Stepper motors have commonly a resolution of a couple hundreds of steps per rotation, and because they are controlled with electrical impulsions, the rotation of the axis can be highly accurate from a known position without adding any additional device like encoders. However, because stepper motors are mechanically more complex than DC motor they are also more expensive and require a complex system to drive it. [15]

For the system only one motion requires a high accuracy, it is the motion when the medication is drawn and then adjusted inside the syringe (motor 4 in Figure 17). The accuracy of the amount of drug injected into the new born has to be high. That's why a stepper motor is used for this motion.

During the installation of the needles on the syringe, a synchronised motion of the translation and the rotation to screw the needles is necessary. For instance, according to the screw thread, a complete rotation corresponds to a specific distance of translation. Moreover, because the "screwing" requires some torque to be correctly connected, it is complicated and not necessary to drive this operation with high accuracy. That is why the current solution uses a stepper motor to make the translation motion (motor 2 on the Figure 17) and a DC motor is used to make the rotation of the syringe (motor 1 on the diagram). By using a DC motor for the rotation, it allows the system more flexibility at the end of the screwing, to tighten the needle to the syringe. The synchronisation between the two motors will be adjusted empirically: first a fixed rotation speed will be set on the stepper motor (motor 2, translation) and the voltage supply of the DC motor (motor 1, rotation) will be adjusted to obtain a satisfying screwing.

The motor 3, which allows the syringe to point to different positions (pick the needles, draw the drug and point up to remove the air bubbles), has to move with accuracy, a heavy system composed of three motors with a variable centre of gravity. A stepper motor, in addition with a reduction gear box is the most logic solution. However, the current motor 3 is a DC motor, this motor was already own by the hospital and its characteristics are suitable for this purpose.

2.3.Contamination prevention:

To prevent contamination, the needles have to treated in a way that remain sterile. To achieve that, it is vital that the needles do not come in direct contact with any parts of the system. For that reason, it is important to consider how the needles are preinstalled on the system and how the syringe is removed from the system after the cycle.

Figure 18: Picture of the Needle preinstalled on their Supports

As shown on the picture, the current solution respects this requirement. To achieve the conservation of sterilisation, the needle support is featured with an opening, so direct contact between the needle and the needle support part of the system, can be avoided easily (Figure 18, Figure 19).

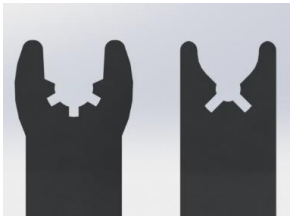


Figure 19: Needle Support Footprints

Another way to facilitate the contamination avoidance, is that the syringe is installed and removed in the system, with a holding system that can be opened and closed. (Figure 20)

Although these considerations especially for the solution of the openable system that holds the syringe and makes it turn, are making the design of the system more complicated (Figure 20). No matter how complicates the deign can become if that serves to assure the first priority; patient safety.

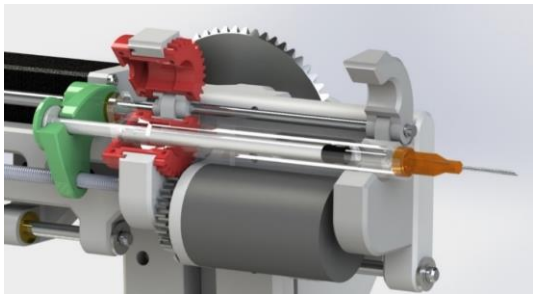


Figure 20: Syringe Holding System

2.4.Numeric Model

The system is designed by the CAD (Computer-Aided Design) software Solidworks from Dassault Systemes. Each part is drawn in 3D then assembled between each other. Solidworks allows to simulate the cinematic, check if there are any unwanted collision and also verify if the system is mountable before manufacturing any parts.

The Figure 21 below is a rendering of the system:

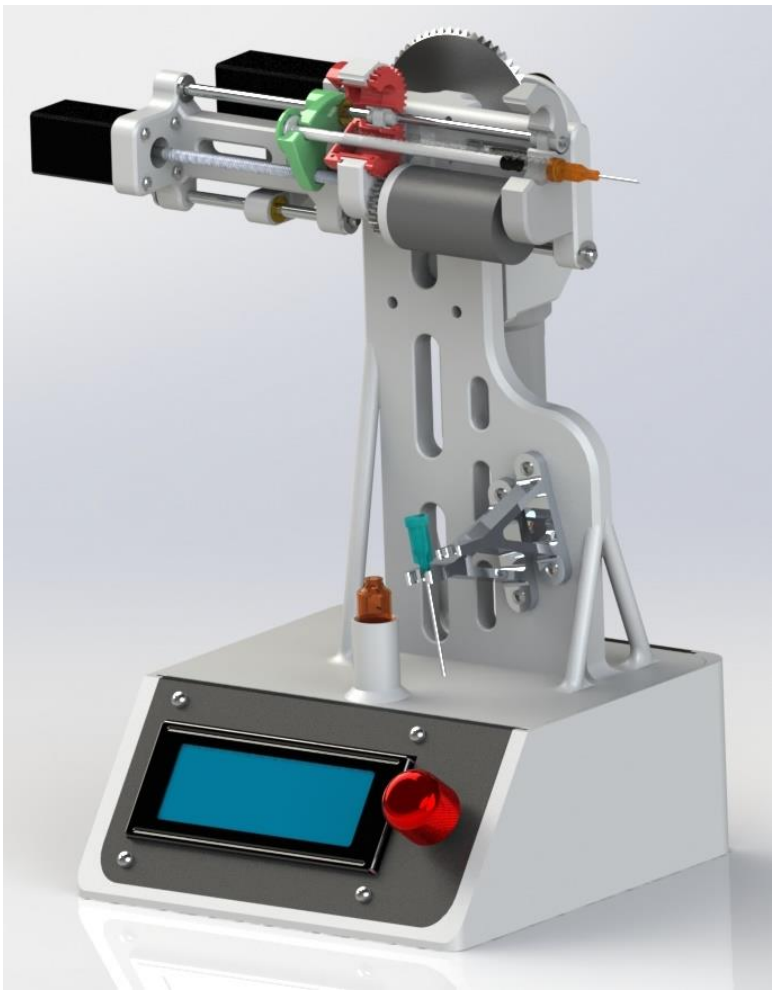


Figure 21: Rendering of the system on Solidworks

All the CAD parts and other numeric resources are available on the CD attached or at:

https://drive.google.com/folderview?id=0BzNA4W-Aisa4T2wxRm5uTDlzN0E&usp=sharing

2.5.Prototype realisation

2.5.1. Manufacturing

The medical physics department has its own mechanical workshop, some parts such as shafts and bronze guide bearings were manufactured at this place. Because the communication was very efficient with the technician, the parts were manufactured with high quality and efficiency. (see Figure 22)

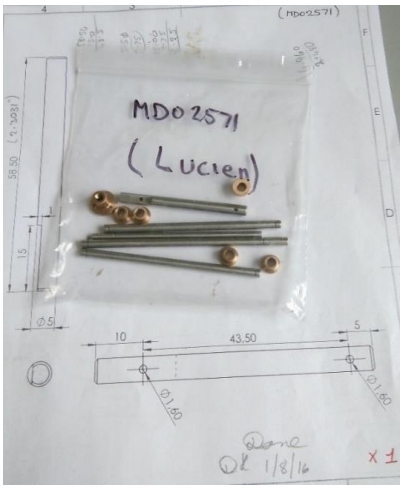


Figure 22: Parts manufactured

Most of the parts were manufactured by two 3D printers, an Ultimaker[2] owned by the Division of Cancer Research and managed by Mr. Cheng Wei, that was used for small parts that require high precision (Figure 24). The second 3D printer, my own one, that was used for bigger parts that did not require high precision. (Figure 23)

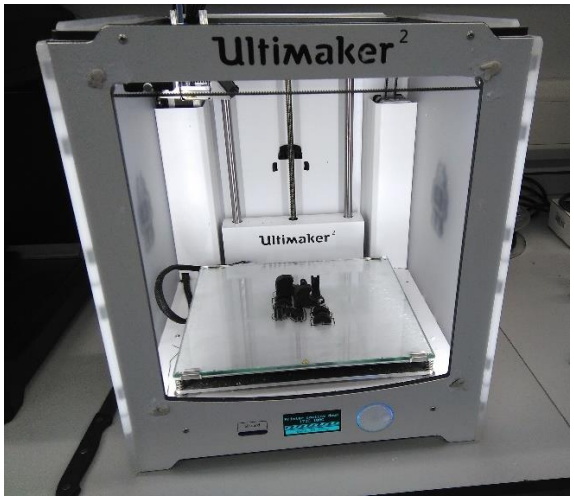


Figure 24: 3D printer of the division of cancer research

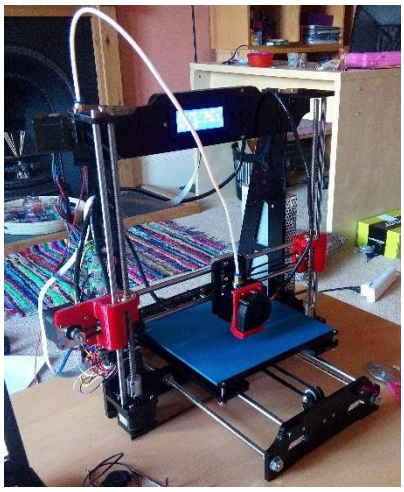


Figure 23: 3D printer

3D printing is less restrictive than conventional manufacturing (milling, turning…), indeed by using additive technology manufacturing, there are no preoccupation with

tool paths and it allows to make more complex parts. Moreover, the process to print a part from its 3D model is very fast and easy: first the 3D model from the Solidworks is exported into the STL format. Then this STL file is imported into a software, that will generate all the paths for the 3D printer in the GCode format. Finally, this gcode is sent to the 3D printer thanks an SD card and the printing begins.

The time that is required to print a part mostly depends of its volume, bigger is the volume of the part longer the printing will take. The longest printing time for the system was about 10 hours, (Figure 25) this duration may seem long, but if conventional manufacturing was used to make the prototype, it would probably take more than a week to get a physical part (time to find the appropriate manufacturing method, find the tool, talk with the workshop, modify the original design after feedback etc.).

Figure 25: Picture of the main Support 3D printed

2.1.1. Ordering

All the parts that were not available at the medical physics department or not makeable (motors, circlips, bar etc.) were ordered from two suppliers, RS component and CPC. The list of the ordered parts can be saw on the Appendix □2.

3. Electronic Design

The electronic of the system is design so it controls all the motors, in function of the sensors and the weight of the baby set by the user.

3.1.Human-Machine Interface (HMI)

3.1.1. Input

The main purpose of the HMI (Human Machine Interface) is to allow the user to set the weight of the baby in order to prepare the syringe with the appropriate amount of drug. The weight is a numerical information, that can be communicated to the machine thanks two hardware solutions; a numeric keypad or a Clickable Rotary Encoder (Figure 26).

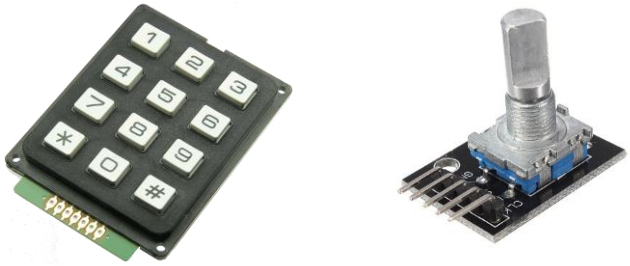


Figure 26: Picture of a Keypad (left) / Clickable Rotary Encoder Ky-040 (right)

Using a keypad is the most natural solution, it is fast and easy to use, the weight is directly typed like people are used to in the everyday life (typing a phone number, a card password etc.) However, the Clickable Rotary Encoder has more advantages:

- No mistyping: Mistyping can happen because of stress or tiredness that the user may press a wrong button, not realize his mistake and validate a wrong weight. That is less likely to happen by using the rotary encoder, because, to input the number the user has to increment or decrement the current number displayed on a screen. This way requires a constant attention of the user and so reduces the risk of inputting the wrong weight.
- Intuitive Menu Navigation: The rotary encoder feels intuitive to navigate in the menu; the selections can be selected by going up or down the menu, which is done by rotating in clockwise or anticlockwise the button. The rotary encoder is also clickable; it means that a switch is integrated so a short press on it can validate a choice. (Figure 27)

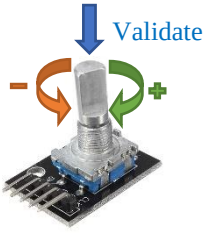


Figure 27: Rotary Encoder Functionalities

- Less pins used (I/O): The rotary encoder only requires three pins from the microcontroller, two for the increment/decrement and one for the switch. Whereas the keypad needs at least 7 inputs.
- Easy to clean: The knob can be removed from the rotary encoder and easily cleaned.

3.1.2. Output

An LCD display is used to display menus and communicates the states of the system to the user. (Figure 28). The LCD display requires six outputs from the microcontroller.

Figure 28: LCD Display 204A-GC-BC-3LP

3.2.Drive the motors

3.2.1. DC motors

To drive the DC motors an H-bridge is necessary, it allows to control the speed of the motor and the rotation direction. The H-bridge is power supplied in 12V. It requires two signals from the microcontroller, one for the rotation direction (high/low) and the second for the speed. The second signal is a PWM (Pulse Width Modulation) signal, for example, a pulse with a duty cycle of 50% causes the motor to rotate in half speed, full speed for 100% etc.

The H-bridge board used is dual, so it allows to control the two motors (motor 1 and motor 3) within the same board. The output maximum voltage is 48V and the maximum current 2A, these values are higher than what will be required to drive the motor 1 and 3 (12V and 1A max) so this board is suitable. (Figure 29)

Figure 29: Dual DC motor driver L293

The angle feedback for the motor 3 is done by a single turn rotary potentiometer. Usually, the feedback for a DC motor is done by an incremental or absolute encoder. However, because the rotation doesn't exceed more than 180° and the rotation range of a single turn potentiometer is around 220°, the solution of using a single turn potentiometer is mechanically possible.

(Figure 30) Moreover, a potentiometer is very cheap, only uses one analogue input and is easy to use with the Arduino. The voltage red from the potentiometer corresponds to a specific angular position, when the angle increases the voltage increases proportionally. A PID (Proportional-Integral-Derivative) controller will be implemented in order to drive efficiently the motor. This method to get feedback from a rotation thanks to a potentiometer, is generally used inside servomotor for robotics that have an angle range smaller than 360°.

If it is concluded on the prototype that this method is not satisfying, the potentiometer will be replaced by an absolute encoder.

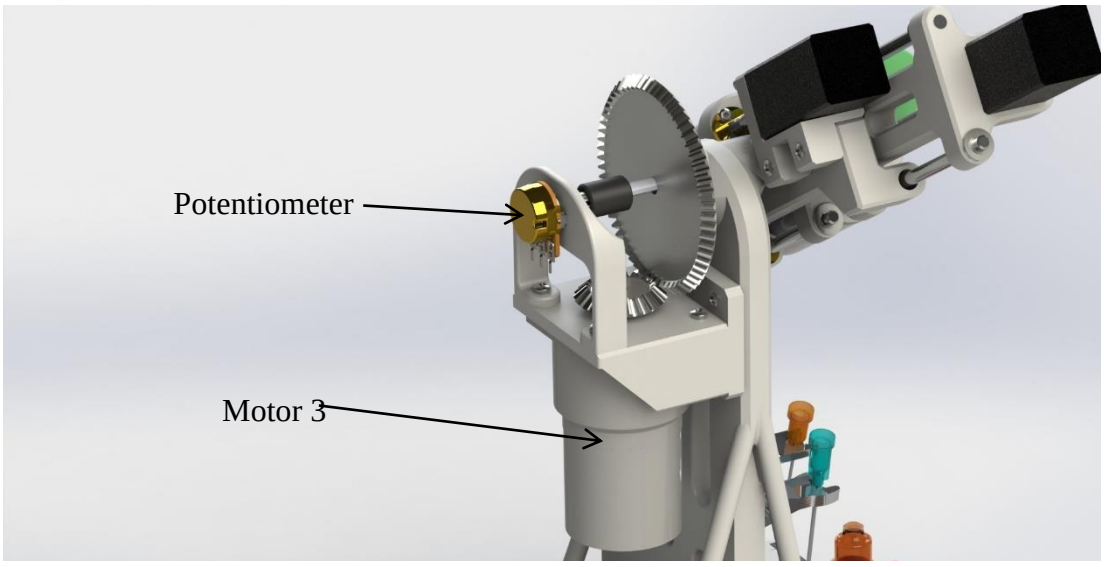


Figure 30: Picture of the Motor 3 feedback control

To drive the motor 1, only one position is necessary, this position is where the gears are aligned to be open (see Figure 32). A simple sensor such as a contact sensor can be used (Figure 31). Later, in order to respect medical standards, an optic switch can be used instead.

Figure 31: Contact sensor (left) / Optical switch (right)

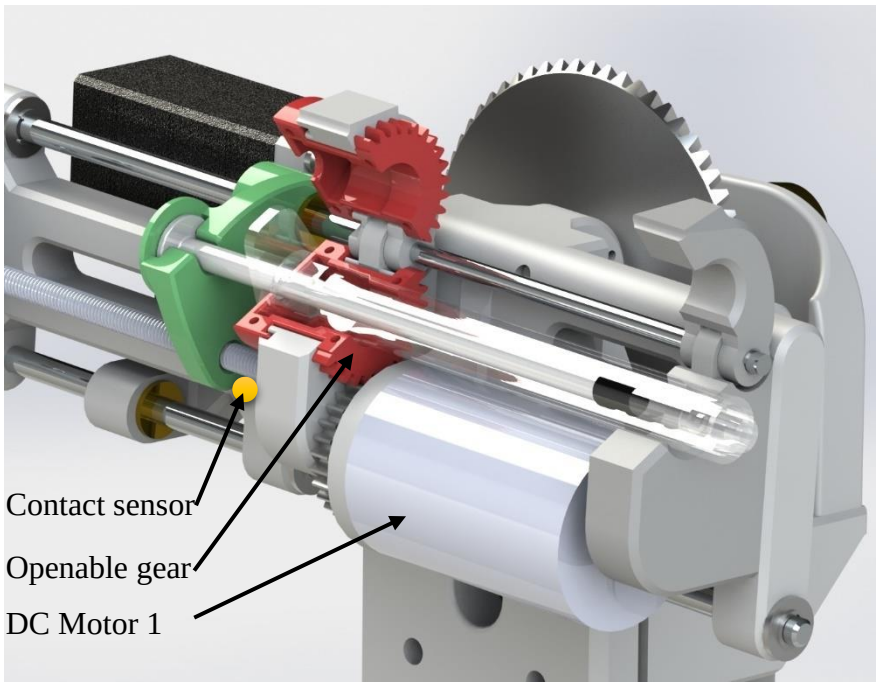


Figure 32: Motor 1 control (with gears in position to be opened and closed)

3.2.2. Stepper motors

Stepper motors are driven by a stepper motor driver A4988 (see picture Figure 33). As with the H-bridge, it requires two signals, one for the direction (low/high) and the second for the steps (for each rise the motor will turn of a single step).

Figure 33: Stepper Motor Driver A4988

Because the motor 2 is a stepper motor, no feedback is necessary to control the speed or its current position. However, the starting position has to be known, that is why a sensor is necessary at the beginning, to return the motor into home position. Once the home position is reached, the position of the motor will be known as long as the system is on. The sensor can be a contact sensor, but the best choice according to medical standards would be an optic switch.

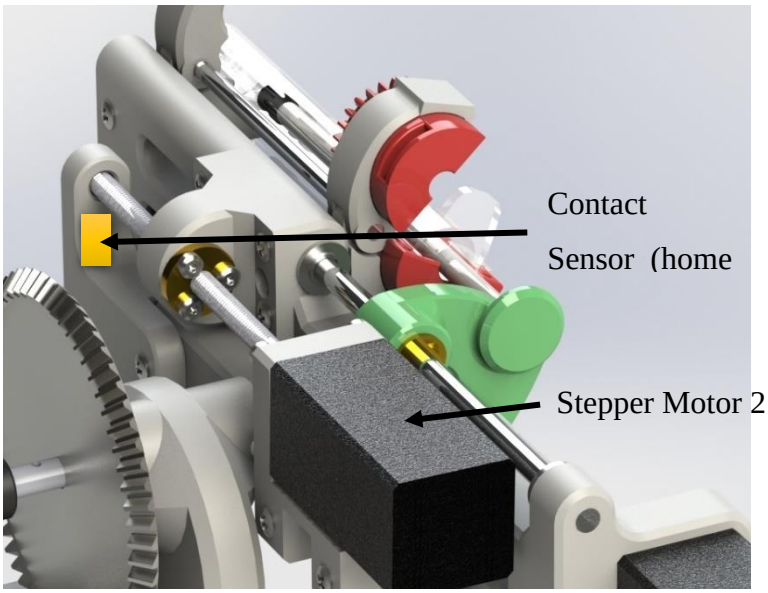


Figure 34: Motor 2 control

The stepper motor 4 works in the same way as the motor 2 (with a home sensor that can be tactile or optic)

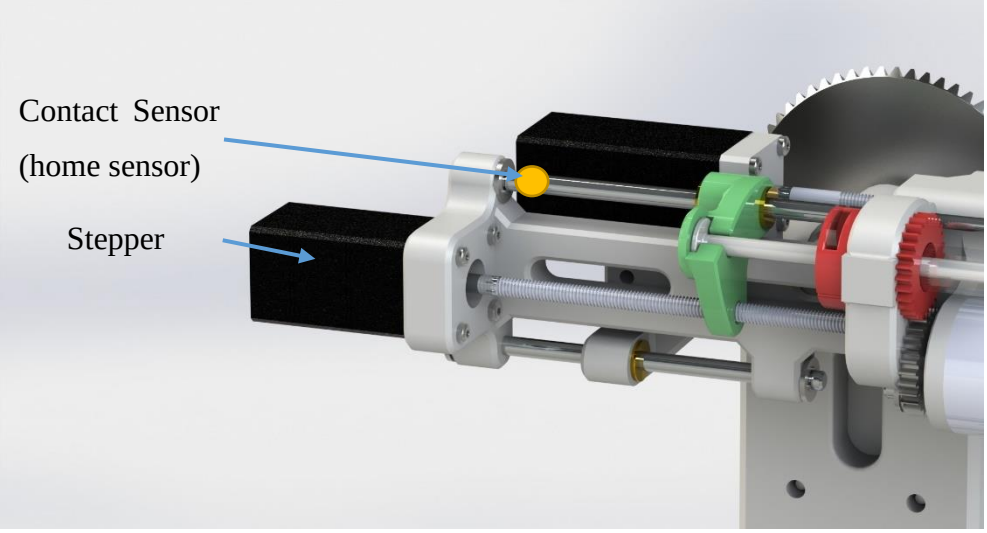


Figure 35: Motor 4 control

The vibrator (motor 5), does not change the position of any part of the system, it just has to rotate to produce vibrations in order to help the air bubbles to go out, that is why it does not need any feedback. Moreover, this motor is very small and does not need any high power in comparison of the other motors used for the system (only 3Volts and 200mA). A simple NPN transistor can be used to control it.

3.3.Microcontroller

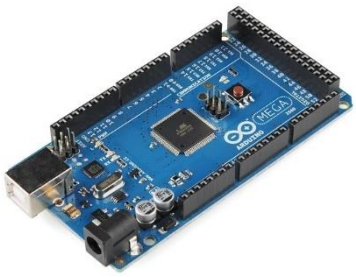


Figure 36: Arduino Mega

The choice for the microcontroller has been made for an Arduino, because of the low price to get the development board, and for the big and active community behind it. Indeed, because Arduino is popular, it is easier to get external help and a large choice of library is already available making the development of the code faster and easier. The number of input/output (I/O) is around 19, so an Arduino Uno that have 20 I/O could be used for the system. However, because the system will evolve and probably get additional devices such as sensors or actuators, only one extra (I/O) is not enough to guaranty the future evolving process. That is why the microcontroller used is an Arduino Mega, which has 60 I/O. (Figure 36)

3.4.Electronic Functional Diagram

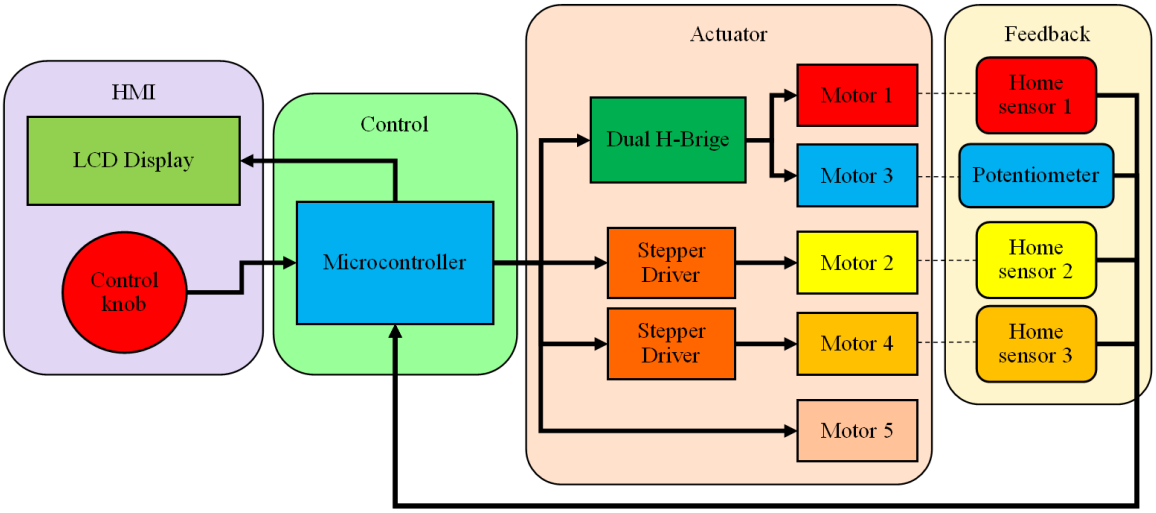


Figure 37: Electronic Function Diagram

Components:

- Microcontroller: Arduino Mega (Figure 36)
- LCD Display: 204A-GC-BC-3LP (Figure 28)
- Control knob: ky-040 (Figure 26)
- Dual H-bridge: L293 (Figure 29)
- Stepper Driver: A4988 (Figure 33)
- Motor1: L149-12-90
- Motor2: RS 892-8726
- Motor3: RS 9904 120 52605
- Motor4: RS 535-0338

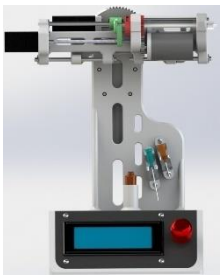
4. Programing

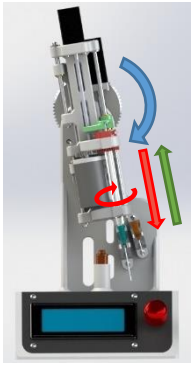
The method used to program the microcontroller is; design the state machine of the movements then a second state machine of the HMI and finally implement it on the microcontroller by using C language.

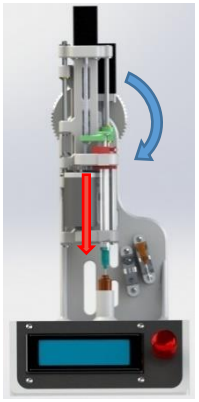
Machine state is a way of describing the behaviour of a system by using states and transitions. The state machine is always at one state at a time and evolve to the next state when the conditions for the transition are validated. [16]

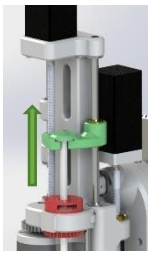
Using a state machine to program the system allows to produce a well-structured and non-blocking program. Indeed, the code is a direct translation of the state machine diagram which easier to understand than just code lines.

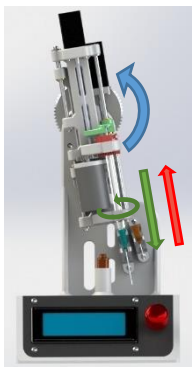
4.1.Motion State Machine











1 Initialisation

Actuators home

2 Wait

Start

3 Clockwise Motor3

Motor3 in front of the 1st

4 Clockwise Motor 1, Anti Clockwise Motor2 (setup the needle)

Motor2 X number of steps reached

5 Clockwise Motor2

Motor2 X number of steps reached

6 Clockwise Motor3

Motor3 in front of the

7 Clockwise Motor2 (plunge the needle in the

Motor2 X number of steps reached

8 Clockwise Motor4 (draw the drug)

Motor4 X number of steps reached (according to the

9 Anticlockwise Motor3

Motor3 in front of the 1st needle slot

10 Clockwise Motor1, Anticlockwise Motor2 (unset up the

Motor2 X number of steps

11 Clockwise Motor2

Motor2 X number of steps

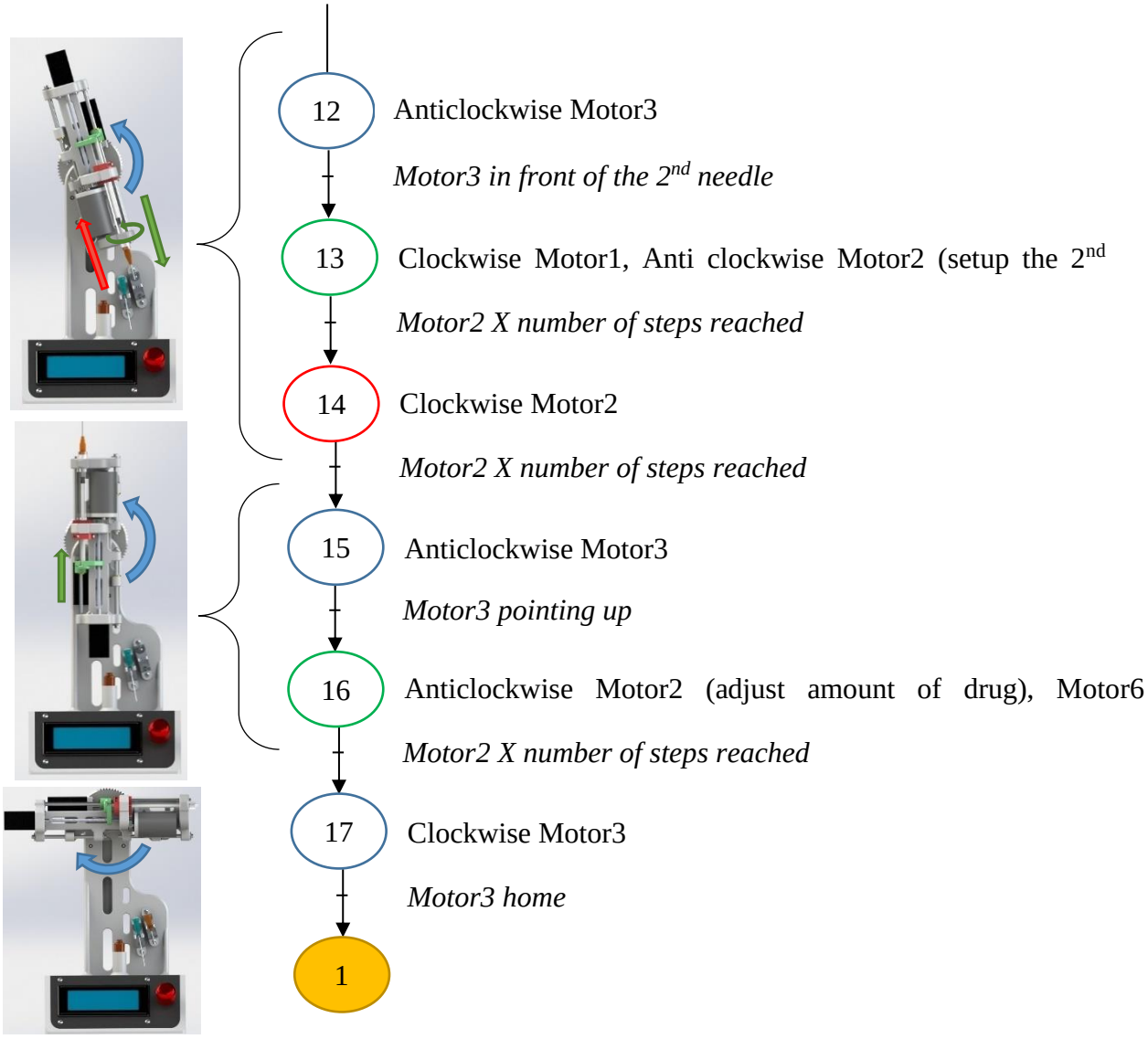


Figure 38: Motion State Machine Diagram

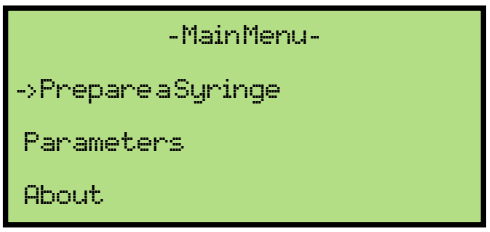
This state machine describes all the actions that have to be performed to fill the syringe. This machine state is not very complex because each state can only lead to one next state, and once the last state is reached it just loopback to the first state. The values "X" for the conditions will be defined after doing some measurements and tests directly on the system.

4.2.HMI State Machine

4.2.1. Menu design

Different menus will be used to control and get the feedback of the system. To navigate in the menu, the user can select one of the different options by turning the knob and validate the option by a press. (Figure 39)

0.

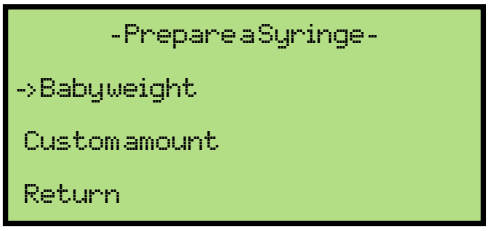


1: Start a new preparation

2: Open the parameters menu

3: Display information of the system

0.1.



1: Enter the baby weight

2: Enter a custom volume

3: Return to the main menu

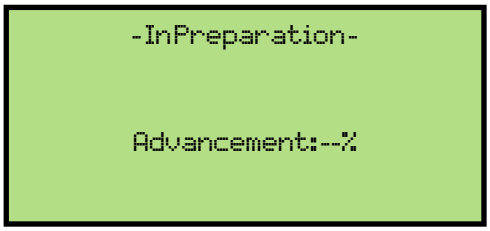
0.1.1

The user has to set the baby's weight by incrementing or decrementing the value, then validate by pressing the knob. The corresponding volume in mL is automatically computed and displayed.

0.1.2

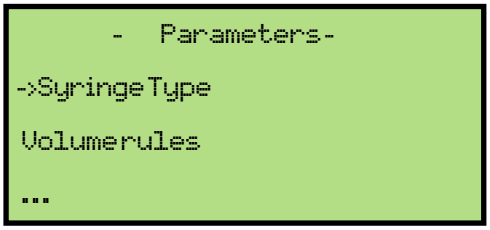
The user has to set the wanted volume by incrementing or decrementing the value, then validate by pressing the knob. When it is validated the next menu is displayed and the preparation begin.

0.1.1/2.1



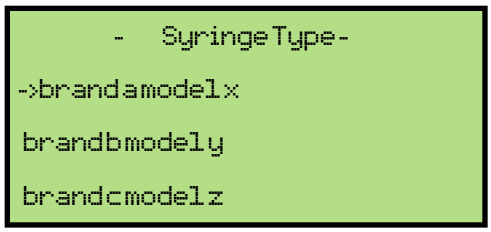
This menu is displayed during the preparation.

0.2



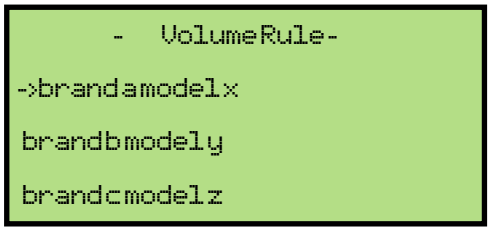
This menu displays the parameters that can be set. Further parameters will be added after performing some test.

0.2.1



The user can select the syringe used.

0.2.2



The user can modify the rule use to compute the volume injected according to the weight

0.3

This page displays main information about the system. Contact details to get support for technical issues, suggestion, question etc.

Figure 39: Menus Hierarchy

4.2.2. State Machine

The HMI state machine is designed from the menus hierarchy (Figure 40). The number of the state corresponds of the menu number from the Menus Hierarchy diagram (Figure 39).

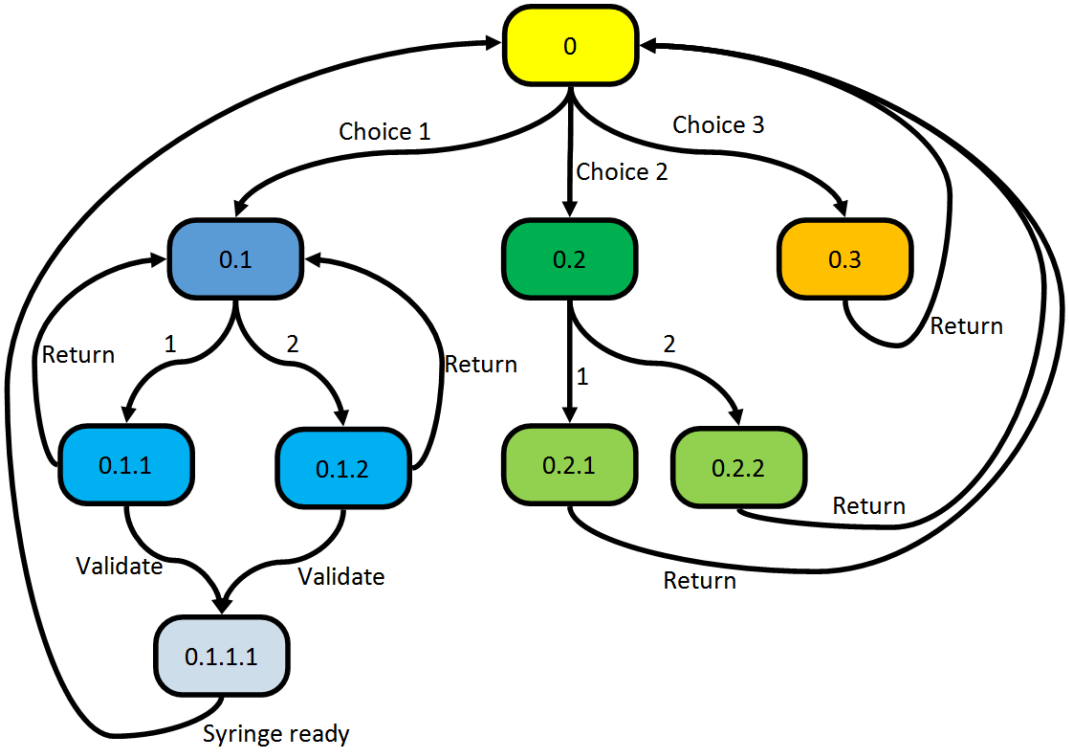


Figure 40: HMI State Machine

4.3.Coding

There are several methods to implement a state machine into a microcontroller by using the C language. The easier one is to use basic if-conditions and switch structures:

A variable that corresponds to the number of the current state machine. A switch structure implements the action according to the state variable. Then a second switch structure implements the conditions, to change the current state to the next one. (See the example bellow)

```
1.  int State = 0;
2.
3.    //Actions
4.  switch (State) {
5.     case 1: //action of the state 1
6.        break;
7.     case 2: //action of the state 2
8.        break;
9.     //etc.
10. }
11.
12.   //Conditions
13. switch (State) {
14.    case 1:
15.       if (/*Condition to go to the next step*/) State = 2;
16.       break;
17.    case 2:
18.       if (/*Condition to go to the next step*/) State = 3;
19.       break;
20.    case 3:
21.    //etc.
22. }
```

This method can be used to implement the two State Machines on the Arduino Mega.

VI. Results

1. Mechanical System

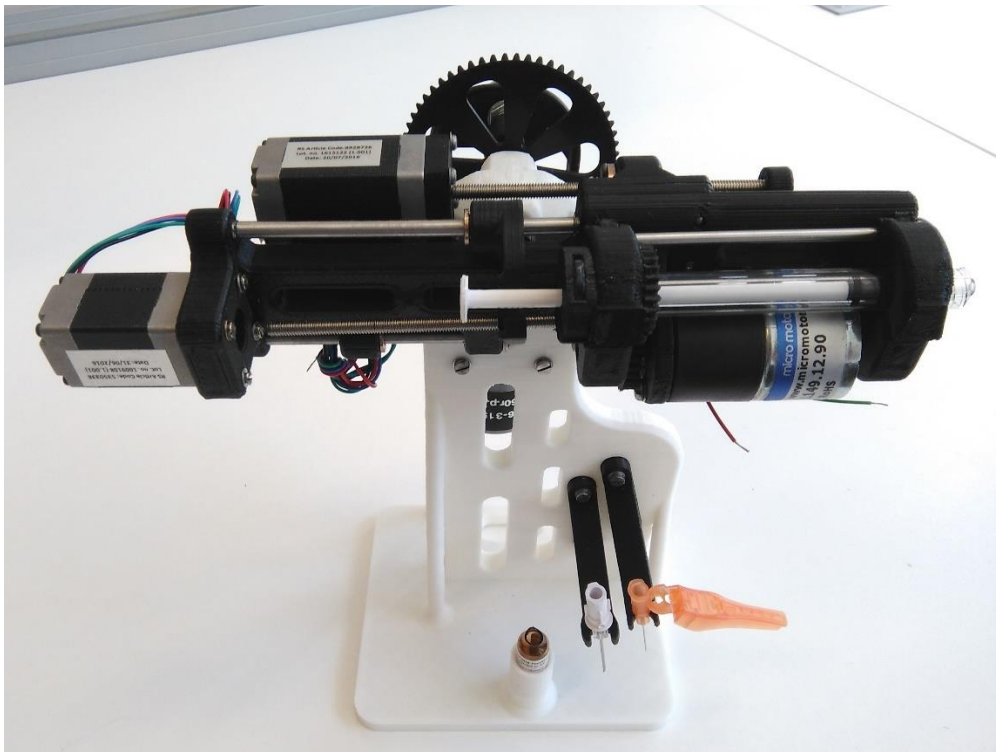


Figure 42: Picture of the Mechanical System

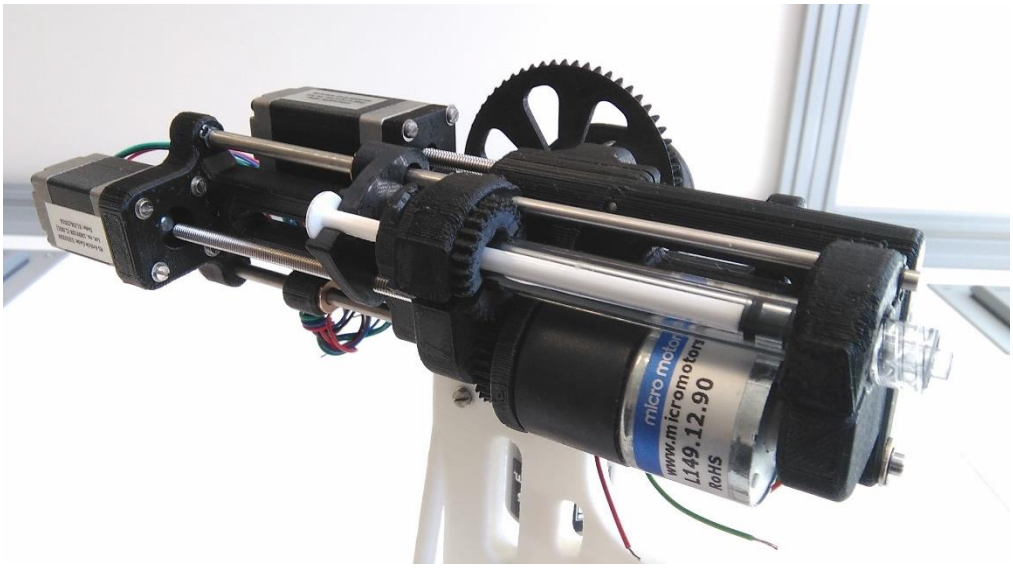


Figure 41: Picture of the Mechanical System (Syringe)

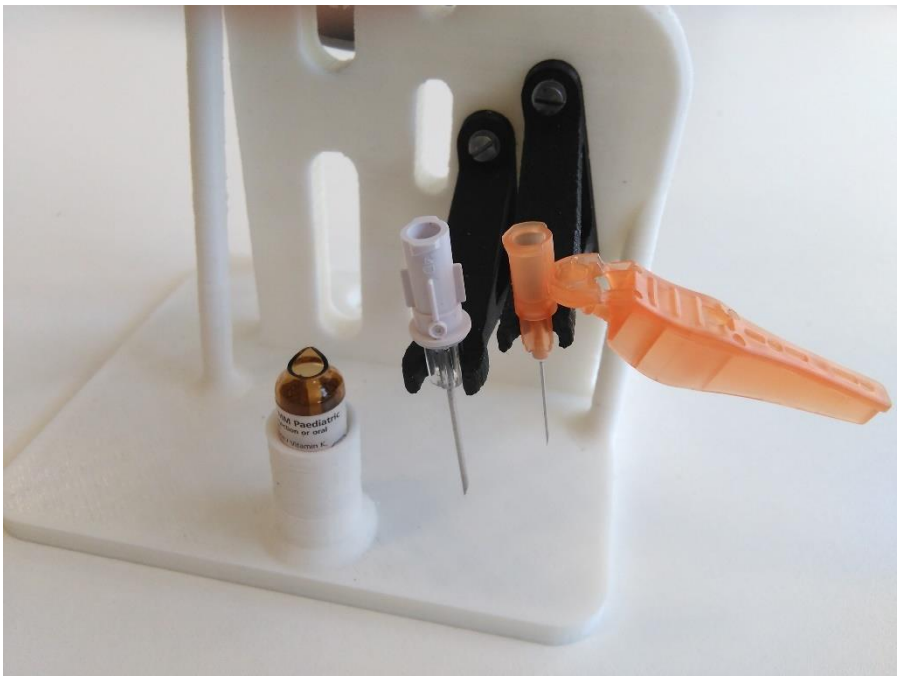


Figure 43: Needles and Ampoule installed in the System

2. HMI/Electronic Enclosure

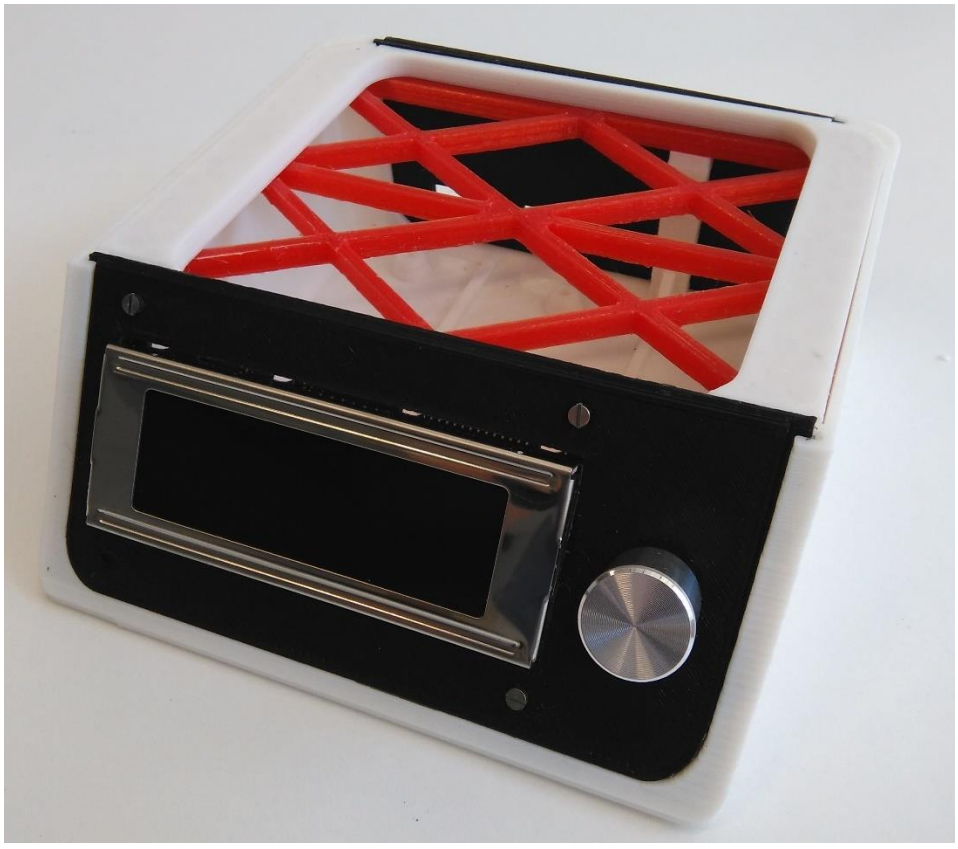


Figure 44: Picture of the HMI/Electronic enclosure

Figure 46: Picture of the Enclosure, Inside

3. Complete System

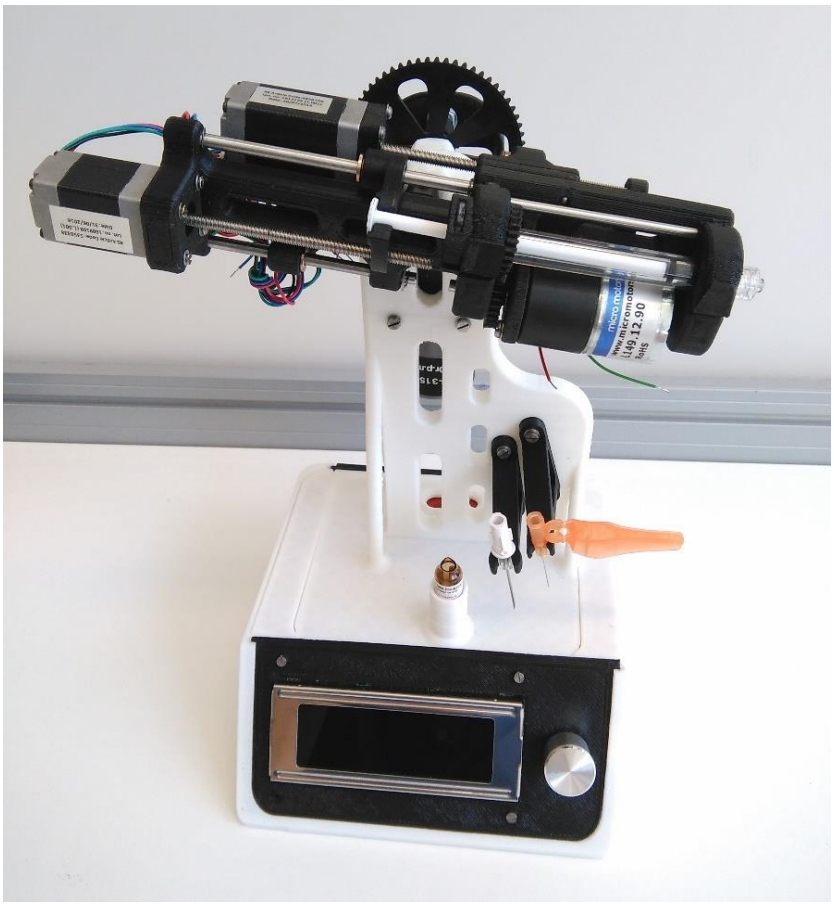


Figure 45: Front picture of the System

VII. Discussion/Analysis

1. Prototype discussion

The mechanical part of the prototype has been successfully made and can be so analysed. However, due to late delivery of the material, the electronic system has not yet been connected but once the connection would be finished, a prototype of the product will be fully created.

- The system is mainly manufactured from 3D printing, so most of the parts are made of plastic (ABS). The main disadvantage of 3D printing is the finishing of the parts; the surface quality is not good enough to make parts sliding between each other when it is required and need a hand finishing (with a knife or a file). This is especially a problem for the parts that hold the syringe and make it rotates. (Figure 47) Due to bad surface quality, the parts are not able to slide between each other.

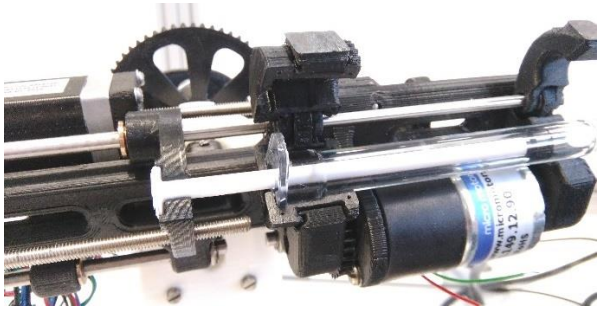


Figure 47: Holding Syringe System

This problem should be inhibited, if these parts are made of metal and get lubricated.

- The sliding by using shaft and bronze guide bearing gives very good results, the sliding is very smooth and easy, no alignment problem has been observed. (Figure 48)

Figure 48: Picture of the Sliding System

- The gears also seem to bring good results, despite the poor resolution of the 3D printing. (Figure 49) Moreover, the gears were not printed with the highest resolution that the 3D printer from the Division of Cancer Research can reach.

Figure 49: Printed Gears

Because the electronic system is currently not finished, it is not possible to evaluate the complete cinematic of the prototype. However, the prototype shows that the general mechanical design will work, and no main changes are required.

2. Risk/Reliability assessment (FMECA)

To ensure reliable operation of the system and to know its limitations, it is important to cover the main failures that can happen to the system. The Failure Mode, Effects and Criticality Analysis (FMECA) method is used for this purpose. [17][18] The aims of this method are:

- To evaluate the risks that a failure of a component can lead to
- Identify and prioritize the failures of a system.
- Provide the necessary correction actions to reduce the risks
- Make evolve the conception of the system or the maintenance to reduce the risks
- Prioritize the exploitation and maintenance rules

This method is performed to the filling system on a simplified version. However, this analysis is applied to a prototype and its results only have the purpose to help the improvement of new designs of the system. Moreover, to get the most exhaustive and reliable results, the FMECA required a specific team work with people from different background. That is why an additional full FMECA analysis will have to be performed by respecting all the rules.

The analysis consists of listing all components of the system and for each component analyse what failures can happen and the leading effects. Then a grade on 10 for the criticality is attributed according to the frequency, the gravity and how easy it is to detect the failure. And finally some correcting solutions are suggested to reduce the criticality. (Table 1)

Table 1: FMECA Analysis Table

FMECA				
Date: *August 2016* Version: *1* Analyst: *Lucien Renaud*				
Studied System: *Syringe Filling System*				
Component	**Failure Mode**	**Effects**	**Criticality**	**Correction**
Syringe	-Missing or badly installed	-Leaks due to bad needles attachment -Mechanical damages	8	Sensors to detect the syringe placement
Needles	-Missing or badly installed	-Leaks due to bad needles attachment -Mechanical damages	8	Sensors to detect the needles placement
Drug ampoule	-Missing or badly installed	-Wrong amount injected to the new born -Mechanical damages	7	Sensors to detect the ampoule placement
Mechanical linkages	-Stuck	-System unable to prepare the syringe -Mechanical damages -Wrong amount of drug in the syringe	6	-Maintenance: check and lubrication -Current sensor (to detect unusual current motor consumption)
Motor 1 (DC)	-Misconnection	-System unable to prepare the syringe	3	-Sensor to detect current faults -Maintenance: check
	-Stuck/Gripped	-System unable to prepare the syringe -Mechanical damages	4	-Sensor to detect current faults -Maintenance: check
Motor 2 (stepper)	-Misconnection	-System unable to prepare the syringe	3	-Sensor to detect missing step
	-Stuck/Gripped	-System unable to prepare the syringe -Mechanical damages	4	-Sensor to detect missing step -Maintenance: check
Motor 3 (DC)	-Misconnection	-System unable to prepare the syringe	3	-Sensor to detect current faults -Maintenance: check
	-Stuck/Gripped	-System unable to prepare the syringe -Mechanical damages	4	-Sensor to detect current faults -Maintenance: check

Motor 4 (stepper)	-Misconnection	-System unable to prepare the syringe	3	-Sensor to detect missing step
	-Stuck/Gripped	-System unable to prepare the syringe -Mechanical damages	4	-Sensor to detect missing step -Maintenance: check
Motor 5 (DC)	-Misconnection	-System unable to remove the air bubbles	3	-Sensor to detect current faults -Maintenance: check
	-Stuck/Gripped	-System unable to remove the air bubbles	3	-Sensor to detect current faults -Maintenance: check
Micro-controller board	-Misconnection	-System unable to prepare the syringe	3	-Maintenance: check
	-Electromagnetic hypersensitivity	-System unstable	6	-Electromagnetic shield
	-Overheat	-System unstable -System unable to prepare the syringe	3	-Sensor for overheat detection
Dual H-bridge	-Misconnection	-System unable to prepare the syringe	3	-Maintenance: check
	-Electromagnetic hypersensitivity	-System unstable	4	-Electromagnetic shield
	-Overheat	-System unstable -System unable to prepare the syringe	6	-Sensor for overheat detection
Stepper Drivers	-Misconnection	-System unable to prepare the syringe	3	-Maintenance: check
	-Electromagnetic hypersensitivity	-System unstable	4	-Electromagnetic shield
	-Overheat	-System unstable -System unable to prepare the syringe	6	-Sensor for overheat detection
LCD Display	-Misconnection	-Unable to control the system	3	-Maintenance: check
	-Electromagnetic hypersensitivity	-Information hardly or not readable by the user -Display not stable	4	-Electromagnetic shield
	-Bad contrast	-Information hardly or not readable by the user	4	-Allow the user to change the contrast
Control Knob	-Misconnection	-Unable to control the system - Unable to prepare the syringe	3	-maintenance to check the knob
	-Wear	-Unable to control the system properly	4	-maintenance to check the knob
Contact sensors	-Misconnection	-Mechanical damages -System unable to prepare the syringe	3	-Maintenance to check the sensors
	-Wear (unstable information)	-Mechanical damages	6	-Use not mechanical sensor (optic sensor

		-System unable to prepare the syringe		to avoid mechanical wear)
	-Broken	-Mechanical damages -System unable to prepare the syringe	4	-Maintenance to check the sensors
Potentiometer (sensor)	-Misconnection	-Mechanical damages -System unable to prepare the syringe	3	-Maintenance: check -Use optic sensors
	-Wear	-Mechanical damages -System unable to prepare the syringe	6	-Maintenance: check and recalibrate the sensor
	- Broken	-Mechanical damages -System unable to prepare the syringe	4	-Maintenance: check

Synthesis of the FMECA analysis:

The simplified FMECA analysis leads to highlight 34 failure modes of the Syringe Filling System. The maximum criticality is 8 for the misplaced of the syringe and the needles, and the minimum criticality is 3 for the electrical misconnections. The misplacement failure can be corrected by adding sensors to detect the good placement of the syringe, the needles and the ampoule. Changing the technology of the contact sensors to optic will contribute to reduce the risk of mechanical failures due to wear and increase the reliability of the system.

3. Future work summary

3.1.Design

The design will have to be improved to fully integrate the electronic system such as the sensors location and fixations and the managements of the cables. An enclosure has also to be designed in order to protect the sensitive parts of the system and to improve the general esthetical aspect.

To increase the reliability of the system, it is recommended to add sensors. (syringe, needles and ampoule detection, electrical current monitoring…). The technology of the sensors has to be carefully chosen in order to find the best compromise between the quality of the detection, the respect of the standards, and the price.

An appropriate technical solution will have to be suggested to improve the accuracy and specially to control the volume in the syringe at the end of a cycle. A feedback of the amount drawn in the syringe can be controlled by a camera: the elongation of the plunger can be measured by image processing. However, this kind of process is too advanced for only a microcontroller. A Raspberry Pi can be used to do the image processing, in addition or instead the Arduino. The Raspberry Pi is a cheap credit card size computer working on a Linux distribution (or recently on windows 10).

3.2.Material

The choice of the final material that the system will be mainly made of, has to be defined to fulfil their function and the standards (sterilization, cleaning maintenance, longevity…). Then the manufacturing methods available will have to be clarified in order to design the parts in a way that they can be manufactured.

3.3.Assessment

The amount of drug inside the syringe after the filling process will have to be evaluated with a measurement procedure recommended by the British standards (BS EN 60601-2-24:2015). Then, in function of the results the design will have to be improved.

All along the development of the project, assessments of the risk and the reliability such as FMECA analysis have to be performed to improve the safety of the system. Standard assessments will also have to be done to assure the conformity and to anticipate the placing on the market.

VIII. Conclusion

The aim of this project is to demonstrate the feasibility of a system that can fill a syringe with vitamin K for new-born injections. This demonstration has been done by firstly defining with the clinicians the general technical requirements, then researching the market to find any related device, and finally the design of a prototype has been made in detail. The electronic part of the current prototype is currently not finished due to time limitation. However, all the design has been already thought, and only the connections between the components have to be made. For the programming, algorithms have been suggested and a method to implement it has also been described.

Concerning, the high standards required for every medical device, European standards have been studied and then pre-implemented to the design. Also a Failure Mode, Effects and Criticality Analysis has been made in order to evaluate the risks that can happen to the system and to suggest improvement solutions for the further design.

This system is expected to make a big difference inside the neonatal ward, by taking away some pressure carried by the clinicians and at the same time ensuring an accurate syringe preparation, especially for premature baby injections where the amount is variable.

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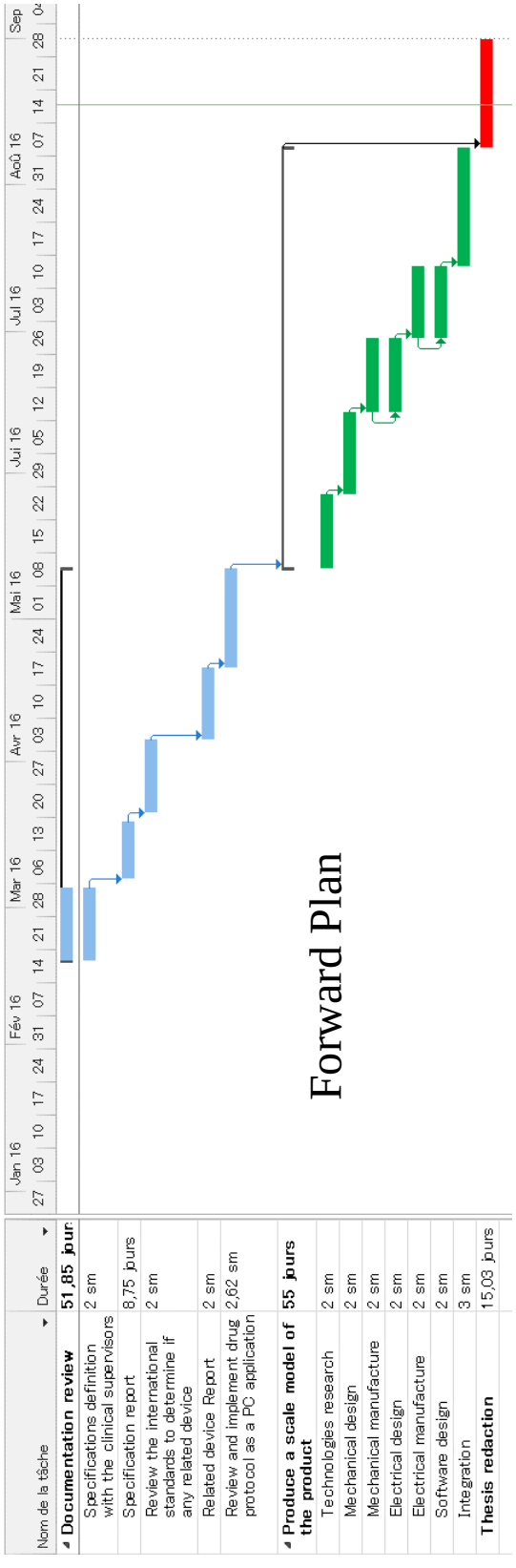
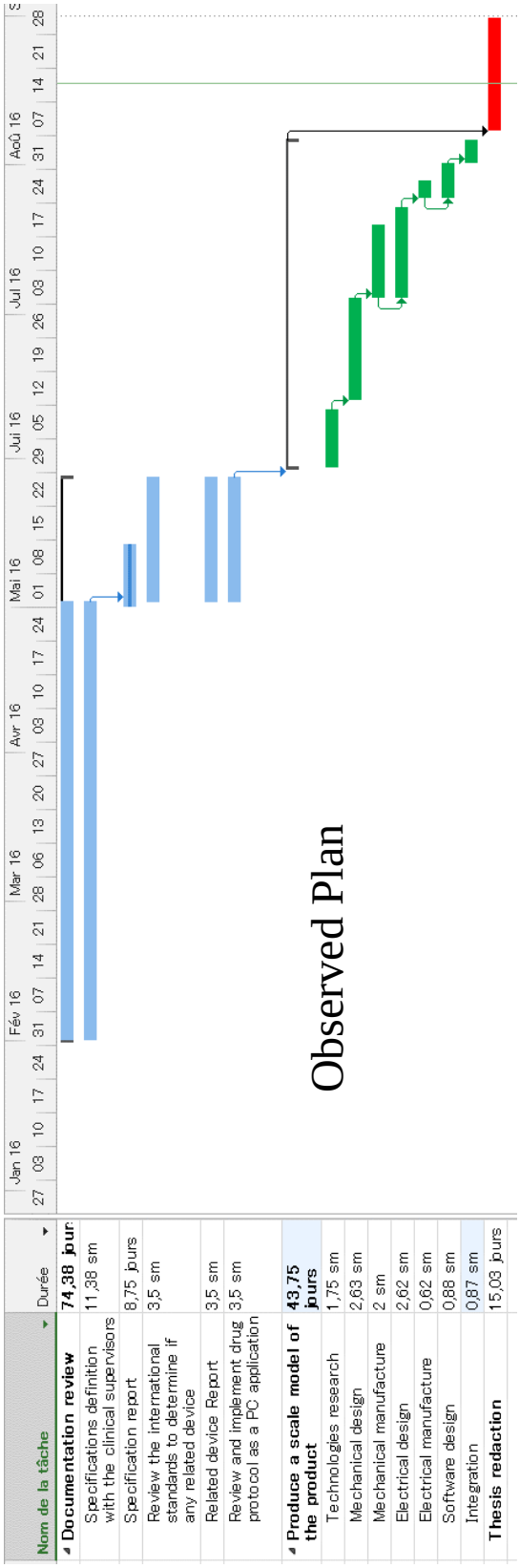
Appendix

1. Gant Charts





2. List of the parts to order

Name	Quantity	supplier link	Price
Stainless Steel bar 4mm diameters	300mm (1500mm pack of 10)	http://uk.rs-online.com/web/c/abrasives-engineering-materials/stainless-steel-tubes-sheets-angles/stainless-steel-rods-bars/?searchTerm=bar+4mm#esid=4294958745&applied-dimensions=4294883395	13,81 to 31,64£
Stainless Steel bar 3mm diameters	100mm (1500mm pack of 10)	http://uk.rs-online.com/web/c/abrasives-engineering-materials/stainless-steel-tubes-sheets-angles/stainless-steel-rods-bars/?searchTerm=bar+rod#esid=4294957213&applied-dimensions=4294851168	17012 to 23,74£
Stainless Steel bar 5mm diameters	50mm (1500mm pack of 10)	http://uk.rs-online.com/web/c/abrasives-engineering-materials/stainless-steel-tubes-sheets-angles/stainless-steel-rods-bars/#esid=4294957213&applied-dimensions=4294853377	27,43 to 42,87£
Ball bearing radial ID=5mm, OD=8mm	x2 (pack of 2)	http://uk.rs-online.com/web/p/ball-bearings/0138641/	3,10£
Ball bearing radial ID=3mm, OD=7mm	x2 (pack of 2)	http://uk.rs-online.com/web/p/ball-bearings/6125745/	4,45£
Circlip 4mm shaft diameter	x6 (pack of 100)	http://uk.rs-online.com/web/p/circlips/2096586/	7,79£
Circlip 3mm shaft diameter	x2 (pack of 100)	http://uk.rs-online.com/web/p/circlips/0289180/	2,49£
Stepper Motor (20x20x48,5m m)	x1	http://uk.rs-online.com/web/p/stepper-motors/8928726/	54,58£
Stepper Motor (20x20x33m m)	x1	http://uk.rs-online.com/web/p/stepper-motors/5350338/	41,58£
DC Motor 18rpm	x1	http://uk.rs-online.com/web/p/products/2985408/	23,55£
Arduino Mega	x1	http://uk.rs-online.com/web/p/processor-microcontroller-development-kits/7154084/	34,36£
Proto shield arduino mega	x1	http://uk.rs-online.com/web/p/processor-microcontroller-development-kits/7697399/	3,21£
Stepper Driver A4988	x2	http://cpc.farnell.com/velleman-kit/a4988-sp/spare-stepper-motor-driver-for/dp/HK01396?ost=A4988&selectedCategoryId=&categoryNameResp=All%2BCategories&searchView=table&iscrfnonsku=false	12,73£
LCD Display	x1	http://uk.rs-online.com/web/p/lcd-monochrome-displays/5326824/	10,69£
Dual DC motor driver L293	x1	http://cpc.farnell.com/webapp/wcs/stores/servlet/ProductDisplay?catalogId=15002&urlLangId=69&langId=69&productId=134809822&storeId=10180&MER=e-bb45-00001002	3,99£

3. Essential requirements from the European Council Directive 93/42/EEC

ANNEX I

ESSENTIAL REQUIREMENTS

I. GENERAL REQUIREMENTS

1. The devices must be designed and manufactured in such a way that, when used under the conditions and for the purposes intended, they will not compromise the clinical condition or the safety of patients, or the safety and health of users or, where applicable, other persons, provided that any risks which may be associated with their use constitute acceptable risks when weighed against the benefits to the patient and are compatible with a high level of protection of health and safety.

2. The solutions adopted by the manufacturer for the design and construction of the devices must conform to safety principles, taking account of the generally acknowledged state of the art.

In selecting the most appropriate solutions, the manufacturer must apply the following principles in the following order:

— eliminate or reduce risks as far as possible (inherently safe design and construction),

— where appropriate take adequate protection measures including alarms if necessary, in relation to risks that cannot be eliminated,

— inform users of the residual risks due to any shortcomings of the protection measures adopted.

3. The devices must achieve the performances intended by the manufacturer and be designed, manufactured and packaged in such a way that they are suitable for one or more of the functions referred to in Article 1 (2) (a), as specified by the manufacturer.

4. The characteristics and performances referred to in Sections 1, 2 and 3 must not be adversely affected to such a degree that the clinical conditions and safety of the patients and, where applicable, of other persons are compromised during the lifetime of the device as indicated by the manufacturer, when the device is subjected to the stresses which can occur during normal conditions of use.

5. The devices must be designed, manufactured and packed in such a way that their characteristics and performances during their intended use will not be adversely affected during transport and storage taking account of the instructions and information provided by the manufacturer.

6. Any undesirable side-effect must constitute an acceptable risk when weighed against the performances intended.

II. REQUIREMENTS REGARDING DESIGN AND CONSTRUCTION

7. **Chemical, physical and biological properties**

7.1. The devices must be designed and manufactured in such a way as to guarantee the characteristics and performances referred to in Section I on the 'General requirements'. Particular attention must be paid to:

— the choice of materials used, particularly as regards toxicity and, where appropriate, flammability,

— the compatibility between the materials used and biological tissues, cells and body fluids, taking account of the intended purpose of the device.

7.2. The devices must be designed, manufactured and packed in such a way as to minimize the risk posed by contaminants and residues to the persons involved in the transport, storage and use of the devices and to the patients, taking account of the intended purpose of the product. Particular attention must be paid to the tissues exposed and to the duration and frequency of exposure.

7.3. The devices must be designed and manufactured in such a way that they can be used safely with the materials, substances and gases with which they enter into contact during their normal use or during routine procedures; if the devices are intended to administer medicinal products they must be designed and manufactured in such a way as to be compatible with the medicinal products concerned according to the provisions and restrictions governing these products and that their performance is maintained in accordance with the intended use.

7.4. Where a device incorporates, as an integral part, a substance which, if used separately, may be considered to be a medicinal product as defined in Article 1 of Directive 65/65/EEC and which is liable to act upon the body with action ancillary to that of the device, the safety, quality and usefulness of the substance must be verified, taking account of the intended purpose of the device, by analogy with the appropriate methods specified in Directive 75/318/EEC.

7.5. The devices must be designed and manufactured in such a way as to reduce to a minimum the risks posed by substances leaking from the device.

7.6. Devices must be designed and manufactured in such a way as to reduce, as much as possible, risks posed by the unintentional ingress of substances into the device taking into account the device and the nature of the environment in which it is intended to be used.

8. **Infection and microbial contamination**

8.1. The devices and manufacturing processes must be designed in such a way as to eliminate or reduce as far as possible the risk of infection to the patient, user and third parties. The design must allow easy handling and, where necessary, minimize contamination of the device by the patient or vice versa during use.

8.2. Tissues of animal origin must originate from animals that have been subjected to veterinary controls and surveillance adapted to the intended use of the tissues.

Notified bodies shall retain information on the geographical origin of the animals.

Processing, preservation, testing and handling of tissues, cells and substances of animal origin must be carried out so as to provide optimal security. In particular safety with regard to viruses and other transferable agents must be addressed by implementation of validated methods of elimination or viral inactivation in the course of the manufacturing process.

8.3. Devices delivered in a sterile state must be designed, manufactured and packed in a non-reusable pack and/or according to appropriate procedures to ensure that they are sterile when placed on the market and remain sterile, under the storage and transport conditions laid down, until the protective packaging is damaged or opened.

8.4. Devices delivered in a sterile state must have been manufactured and sterilized by an appropriate, validated method.

8.5. Devices intended to be sterilized must be manufactured in appropriately controlled (e. g. environmental) conditions.

8.6. Packaging systems for non-sterile devices must keep the product without deterioration at the level of cleanliness stipulated and, if the devices are to be sterilized prior to use, minimize the risk of microbial contamination; the packaging system must be suitable taking account of the method of sterilization indicated by the manufacturer.

8.7. The packaging and/or label of the device must distinguish between identical or similar products sold in both sterile and non-sterile condition.

9. **Construction and environmental properties**

9.1. If the device is intended for use in combination with other devices or equipment, the whole combination, including the connection system must be safe and must not impair the specified performances of the devices. Any restrictions on use must be indicated on the label or in the instructions for use.

9.2. Devices must be designed and manufactured in such a way as to remove or minimize as far as is possible:

— the risk of injury, in connection with their physical features, including the volume/pressure ratio, dimensional and where appropriate ergonomic features,

— risks connected with reasonably foreseeable environmental conditions, such as magnetic fields, external electrical influences, electrostatic discharge, pressure, temperature or variations in pressure and acceleration,

— the risks of reciprocal interference with other devices normally used in the investigations or for the treatment given,

— risks arising where maintenance or calibration are not possible (as with implants), from ageing of materials used or loss of accuracy of any measuring or control mechanism.

9.3. Devices must be designed and manufactured in such a way as to minimize the risks of fire or explosion during normal use and in single fault condition. Particular attention must be paid to devices whose intended use includes exposure to flammable substances or to substances which could cause combustion.

10. **Devices with a measuring function**

10.1. Devices with a measuring function must be designed and manufactured in such a way as to provide sufficient accuracy and stability within appropriate limits of accuracy and taking account of the intended purpose of the device. The limits of accuracy must be indicated by the manufacturer.

10.2. The measurement, monitoring and display scale must be designed in line with ergonomic principles, taking account of the intended purpose of the device.

10.3. The measurements made by devices with a measuring function must be expressed in legal units conforming to the provisions of Council Directive 80/181/EEC [1].

11. **Protection against radiation**

11.1. *General*

11.1.1. Devices shall be designed and manufactured in such a way that exposure of patients, users and other persons to radiation shall be reduced as far as possible compatible with the intended purpose, whilst not restricting the application of appropriate specified levels for therapeutic and diagnostic purposes.

11.2. *Intended radiation*

11.2.1. Where devices are designed to emit hazardous levels of radiation necessary for a specific medical purpose the benefit of which is considered to outweigh the risks inherent in the emission, it must be possible for the user to control the emissions. Such devices shall be designed and manufactured to ensure reproducibility and tolerance of relevant variable parameters.

11.2.2. Where devices are intended to emit potentially hazardous, visible and/or invisible radiation, they must be fitted, where practicable, with visual displays and/or audible warnings of such emissions.

11.3. *Unintended radiation*

11.3.1. Devices shall be designed and manufactured in such a way that exposure of patients, users and other persons to the emission of unintended, stray or scattered radiation is reduced as far as possible.

11.4. *Instructions*

11.4.1. The operating instructions for devices emitting radiation must give detailed information as to the nature of the emitted radiation, means of protecting the patient and the user and on ways of avoiding misuse and of eliminating the risks inherent in installation.

11.5. *Ionizing radiation*

11.5.1. Devices intended to emit ionizing radiation must be designed and manufactured in such a way as to ensure that, where practicable, the quantity, geometry and quality of radiation emitted can be varied and controlled taking into account the intended use.

11.5.2. Devices emitting ionizing radiation intended for diagnostic radiology shall be designed and manufactured in such a way as to achieve appropriate image and/or output quality for the intended medical purpose whilst minimizing radiation exposure of the patient and user.

11.5.3. Devices emitting ionizing radiation, intended for therapeutic radiology shall be designed and manufactured in such a way as to enable reliable monitoring and control of the delivered dose, the beam type and energy and where appropriate the quality of radiation.

[1] OJ No L 39, 15. 2. 1980, p. 40. Directive as last amended by Directive 89/617/EEC (OJ No L 357, 7. 12. 1989, p. 28).

12. **Requirements for medical devices connected to or equipped with an energy source**

12.1. Devices incorporating electronic programmable systems must be designed to ensure the repeatability, reliability and performance of these systems according to the intended use. In the event of a single fault condition (in the system) appropriate means should be adopted to eliminate or reduce as far as possible consequent risks.

12.2. Devices where the safety of the patients depends on an internal power supply must be equipped with a means of determining the state of the power supply.

12.3. Devices where the safety of the patients depends on an external power supply must include an alarm system to signal any power failure.

12.4. Devices intended to monitor one or more clinical parameters of a patient must be equipped with appropriate alarm systems to alert the user of situations which could lead to death or severe deterioration of the patient's state of health.

12.5. Devices must be designed and manufactured in such a way as to minimize the risks of creating electromagnetic fields which could impair the operation of other devices or equipment in the usual environment.

12.6. *Protection against electrical risks*

Devices must be designed and manufactured in such a way as to avoid, as far as possible, the risk of accidental electric shocks during normal use and in single fault condition, provided the devices are installed correctly.

12.7. *Protection against mechanical and thermal risks*

12.7.1. Devices must be designed and manufactured in such a way as to protect the patient and user against mechanical risks connected with, for example, resistance, stability and moving parts.

12.7.2. Devices must be designed and manufactured in such a way as to reduce to the lowest possible level the risks arising from vibration generated by the devices, taking account of technical progress and of the means available for limiting vibrations, particularly at source, unless the vibrations are part of the specified performance.

12.7.3. Devices must be designed and manufactured in such a way as to reduce to the lowest possible level the risks arising from the noise emitted, taking account of technical progress and of the means available to reduce noise, particularly at source, unless the noise emitted is part of the specified performance.

12.7.4. Terminals and connectors to the electricity, gas or hydraulic and pneumatic energy supplies which the user has to handle must be designed and constructed in such a way as to minimize all possible risks.

12.7.5. Accessible parts of the devices (excluding the parts or areas intended to supply heat or reach given temperatures) and their surroundings must not attain potentially dangerous temperatures under normal use.

12.8. *Protection against the risks posed to the patient by energy supplies or substances*

12.8.1. Devices for supplying the patient with energy or substances must be designed and constructed in such a way that the flow-rate can be set and maintained accurately enough to guarantee the safety of the patient and of the user.

12.8.2. Devices must be fitted with the means of preventing and/or indicating any inadequacies in the flow-rate which could pose a danger.

Devices must incorporate suitable means to prevent, as far as possible, the accidental release of dangerous levels of energy from an energy and/or substance source.

12.9. The function of the controls and indicators must be clearly specified on the devices.

Where a device bears instructions required for its operation or indicates operating or adjustment parameters by means of a visual system, such information must be understandable to the user and, as appropriate, the patient.

13. **Information supplied by the manufacturer**

13.1. Each device must be accompanied by the information needed to use it safely and to identify the manufacturer, taking account of the training and knowledge of the potential users.

This information comprises the details on the label and the data in the instructions for use.

As far as practicable and appropriate, the information needed to use the device safely must be set out on the device itself and/or on the packaging for each unit or, where appropriate, on the sales packaging. If individual packaging of each unit is not practicable, the information must be set out in the leaflet supplied with one or more devices.

Instructions for use must be included in the packaging for every device. By way of exception, no such instructions for use are needed for devices in Class I or IIa if they can be used safely without any such instructions.

13.2. Where appropriate, this information should take the form of symbols. Any symbol or identification colour used must conform to the harmonized standards. In areas for which no standards exist, the symbols and colours must be described in the documentation supplied with the device.

13.3. *The label* must bear the following particulars:

(a) the name or trade name and address of the manufacturer. For devices imported into the Community, in view of their distribution in the Community, the label, or the outer packaging, or instructions for use, shall contain in addition the name and address of either the person responsible referred to in Article 14 (2) or of the authorized representative of the manufacturer established within the Community or of the importer established within the Community, as appropriate;

(b) the details strictly necessary for the user to identify the device and the contents of the packaging;

(c) where appropriate, the word 'STERILE';

(d) where appropriate, the batch code, preceded by the word 'LOT', or the serial number;

(e) where appropriate, an indication of the date by which the device should be used, in safety, expressed as the year and month;

(f) where appropriate, an indication that the device is for single use;

(g) if the device is costum-made, the words 'custom-made device';

(h) if the device is intended for clinical investigations, the words 'exclusively for clinical investigations';

(i) any special storage and/or handling conditions;

(j) any special operating instructions;

(k) any warnings and/or precautions to take;

(l) year of manufacture for active devices other than those covered by (e). This indication may be included in the batch or serial number;

(m) where applicable, method of sterilization.

13.4. If the intended purpose of the device is not obvious to the user, the manufacturer must clearly state it on the label and in the instructions for use.

13.5. Wherever reasonable and practicable, the devices and detachable components must be identified, where appropriate in terms of batches, to allow all appropriate action to detect any potential risk posed by the devices and detachable components.

13.6. Where appropriate, the instructions for use must contain the following particulars:

(a) the details referred to in Section 13.3, with the exception of (d) and (e);

(b) the performances referred to in Section 3 and any undesirable side-effects;

(c) if the device must be installed with or connected to other medical devices or equipment in order to operate as required for its intended purpose, sufficient details of its characteristics to identify the correct devices or equipment to use in order to obtain a safe combination;

(d) all the information needed to verify whether the device is properly installed and can operate correctly and safely, plus details of the nature and frequency of the maintenance and calibration needed to ensure that the devices operate properly and safely at all times;

(e) where appropriate, information to avoid certain risks in connection with implantation of the device;

(f) information regarding the risks of reciprocal interference posed by the presence of the device during specific investigations or treatment;

(g) the necessary instructions in the event of damage to the sterile packaging and, where appropriate, details of appropriate methods of resterilization;

(h) if the device is reusable, information on the appropriate processes to allow reuse, including cleaning, disinfection, packaging and, where appropriate, the method of sterilization of the device to be resterilized, and any restriction on the number of reuses.

Where devices are supplied with the intention that they be sterilized before use, the instructions for cleaning and sterilization must be such that, if correctly followed, the device will still comply with the requirements in Section I;

(i) details of any further treatment or handling needed before the device can be used (for example, sterilization, final assembly, etc.);

(j) in the case of devices emitting radiation for medical purposes, details of the nature, type, intensity and distribution of this radiation.

The instructions for use must also include details allowing the medical staff to brief the patient on any contra-indications and any precautions to be taken. These details should cover in particular:

(k) precautions to be taken in the event of changes in the performance of the device;

(l) precautions to be taken as regards exposure, in reasonably foreseeable environmental conditions, to magnetic fields, external electrical influences, electrostatic discharge, pressure or variations in pressure, acceleration, thermal ignition sources, etc.;

(m) adequate information regarding the medicinal product or products which the device in question is designed to administer, including any limitations in the choice of substances to be delivered;

(n) precautions to be taken against any special, unusual risks related to the disposal of the device;

(o) medicinal substances incorporated into the device as an integral part in accordance with Section 7.4;

(p) degree of accuracy claimed for devices with a measuring function.

14. Where conformity with the essential requirements must be based on clinical data, as in Section I (6), such data must be established in accordance with Annex X.