Clotime
Impedance-based point of care blood coagulation monitoring device

Architectural design

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Change history

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Approvals

Title/Function	Signature	Scope of Approval	Date
Alireza Bahari		Primary author and “Concept and mechanical design”	08/12/2022
Dawn Lo		“Software Design”	08/12/2022
Sadan Wani	Sadan	“Regulations”	08/12/2022
Walid AlChamaa		“Electrical Design”	08/12/2022

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LCD - liquid crystal display
PCB - printed circuit board
PT - prothrombin time
RS - requirement specifications. See **P04D02b** [1] and **P04D03** [2] for more information.

1. General Information

1.1. Device name

The device and its components are named as follows:

- The Device: Referred to as “Clotime”, derived from the combination and truncation of the words Clot and time, or “the device”.
- The Strips: Referred to as “Clotime strips”, “test strips”, and “strips”

1.2. Scope

This document is intended to illustrate Clotime’s device design by conceptually dividing it into functional sections. In each section, the main commercial components and the custom components to be designed are identified. Sections include concept, software design, electrical hardware design, mechanical design and labeling. Based on the architectural design, each section is captured in different subsystem design requirements. This document outlines design requirements that are accessible and practical at the highest level and will serve as a basis for developing detailed design, fabrication, software and firmware, verification, evaluation and validation, and risk analysis.

This document is part of a series of documents on CarePoint’s medical device Clotime. Please see **P04D01** [3] for the product’s initial concept, **P04D02b** [1] for requirement specifications, and **P04D03** [2] for risk management. Any mentions of RS can be traced back to **P04D02b** and **P04D03** for more information on the hazard analysis which gave rise to the requirement specifications and changes to the architectural design in this document.

1.3. Indications for use

Clotime is indicated for measuring blood coagulation time in patients with health conditions such as liver disease, hemophilia and thrombophilia [4]. These individuals are often at high risk of internal clotting or excessive blood loss.

1.4. Intended use

The device is intended for use in monitoring blood coagulation time in patients. The user is any adult, including medical professionals, patients, or patients’ caregivers. The system is intended for home use.

2. Architectural design

2.1. Concept

Clotime measures the prothrombin time (PT) by monitoring the global impedance of clotting blood samples; the changes in conductivity associated with clot formation are measured. To evaluate instrument performance, the clotting time determined from the data was correlated to a "gold-standard" clinical measurement of prothrombin time. Clotime includes three key functional modules: 1- Test strip containing electrodes and a microfluidic channel that collects the patient's blood drop, 2- measurement unit that processes the signals sent and received by the test strip, and 3- display unit that shows the current and previous measurements. Clotime uses existing finger prick lancing modules approved by healthcare professionals, such as the Accu-Chek Safe-TPro or Safe-T-Pro Plus lancing devices [5]. **Figure 1** demonstrates key functional modules and how they are connected. The measurement routine is started after inserting the test strip into Clotime; then, the user obtains a small (around 15 µL) drop of blood from the fingertip with the lancing device. The user must place the drop onto the test strip reservoir within 15 seconds. Blood will reach the electrodes in less than 1 second; impedance measurement starts as soon as electrodes touch the blood. Within 1 minute the user can read the current prothrombin time.

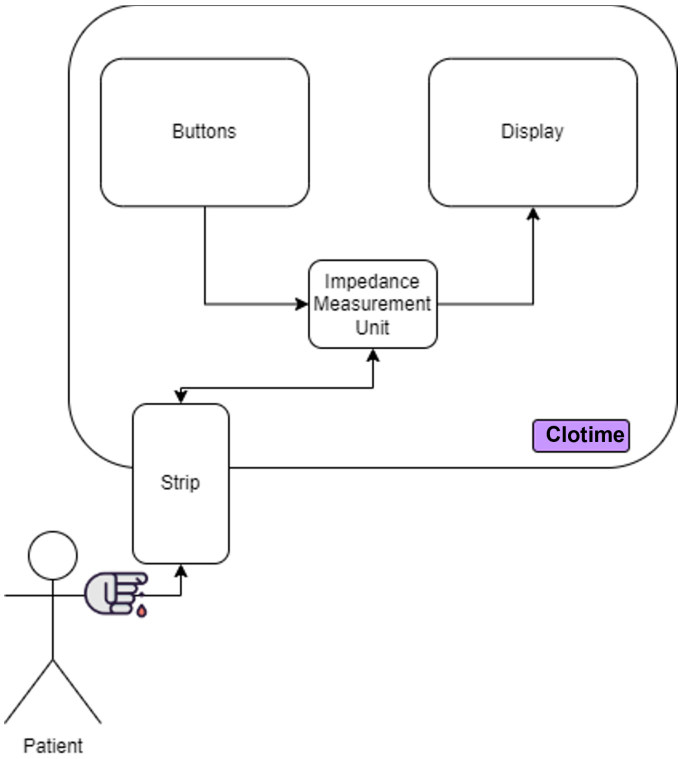


Figure 1. Concept of Clotime and the key functional modules and their connection inside Clotime.

2.2 Software Design

2.2.1 State diagram

To power on and power off the device, the user must long-press the center button. In order to measure blood coagulation, the device requires time and impedance inputs. It will then use an equation to output coagulation time, display it, and save the data. If the impedance cannot be measured or, for some other reason, the coagulation time cannot be calculated, and an error message will be displayed with an option to access troubleshooting pointers on the device's "Help" page. The device also has other functions to supplement its main function. The device will monitor the battery level and display an appropriate percentage and battery sign on the top. Should the memory space run low, the device will also display a sign at the top of its display to notify the user. The device can also detect connections at its ports and act accordingly to transfer memory, charge, or measure impedance. **Figure 2** demonstrates the software state diagram of Clotime.

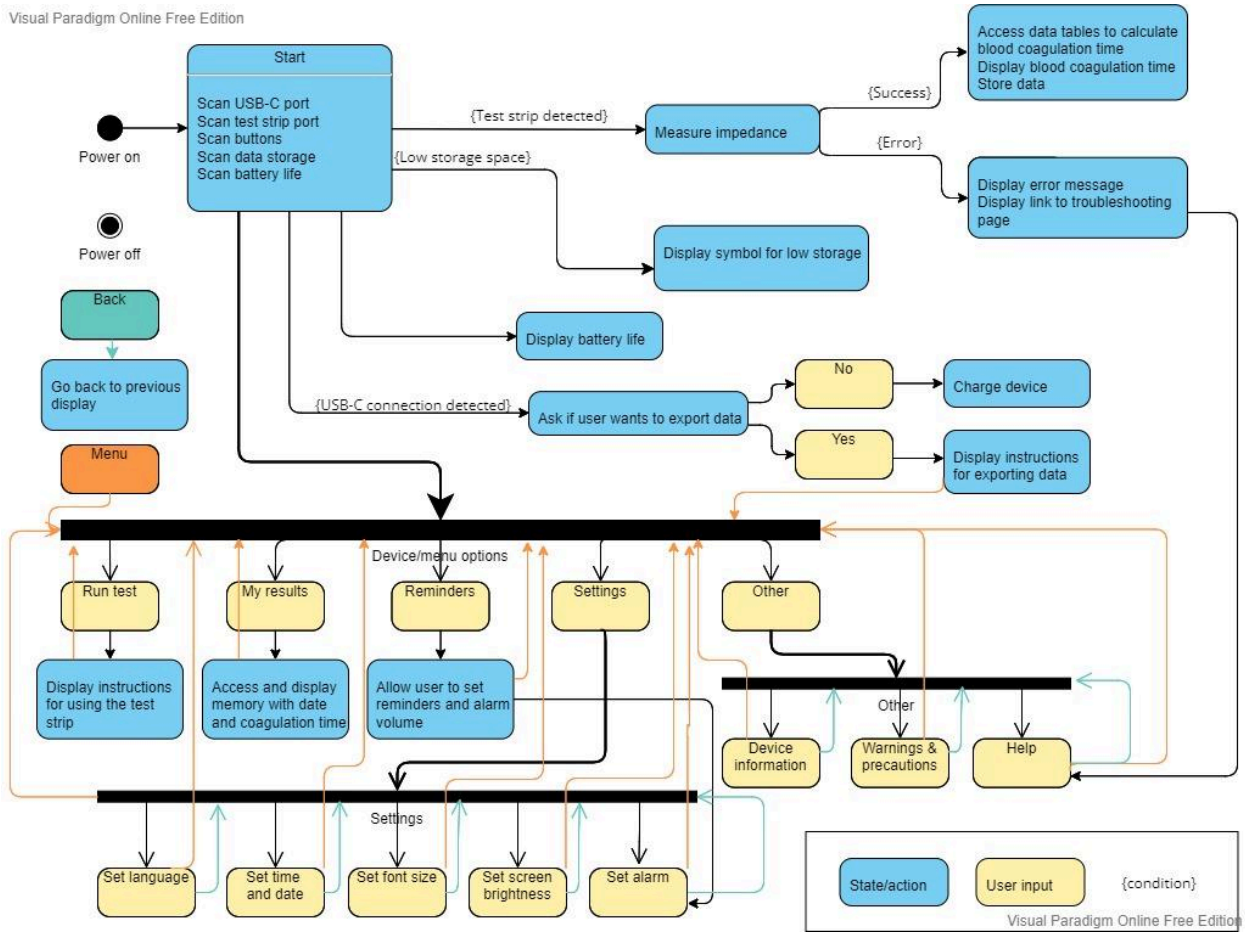


Figure 2. Software state diagram for Clotime.

2.2.2 Algorithms

Alg-1 Input to output

The device will start impedance measurement upon detection of a test strip. The measurement will then undergo data processing and error handling. If the impedance cannot be measured, an error message will display along with the option to look at the device's troubleshooting page. If the impedance can be measured with a satisfactory signal-to-noise ratio, the impedance, along with the temperature detected by the device, will be used to compute blood coagulation time. The measurement will then be displayed and stored with the respective time at which the test strip was inserted.

$$coagulation\ time\ =\ f([impedance\ 1,\ time\ 1],\ [impedance\ 2,\ time\ 2],\ \ldots)$$

Equation 1. The formula used to calculate blood coagulation time based on impedance measurements.

Alg-2 Communication:

Upon detection of a USB-C connection, the device will ask the user if they would like to export their data. The user can then select the data to be exported.

2.2.3 Data storage

The device will be capable of storing 8GB of data. When no more room is present, data will be removed, starting from the oldest data. The user will also be alerted when memory space is low. **Tables 1** and **2** detail how data will be stored. “yymmdd” stands for year, month, and date; “hh:mm:ss” stand for hour, minute, and second; “sss” stands for seconds; “imp” stands for impedance; “T” stands for temperature; “mm:ss” stands for minutes and seconds.

Table 1. Data storage table for impedance measurements with their respective storage formats.

Date and time	**Impedance measurements**	**Temperature**	**Coagulation time**
yymmdd-hh:mm:ss	{[sss, imp], [sss, imp], [sss, imp], …}	T	mm:ss

Table 2. Data storage display for user’s easy viewing.

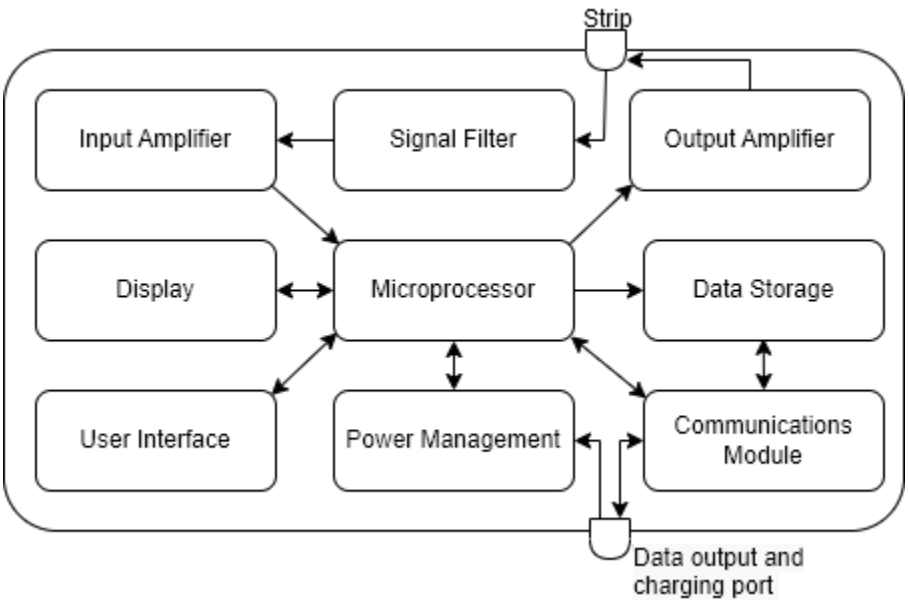
Date and time	**Coagulation time**
yymmdd-hh:mm:ss	mm:ss

2.3 Electrical hardware design

2.3.1 Functional section

All electrical modules are integrated into one PCB. **Figure 3** demonstrates the components of the main PCB and the connection between its modules.

Figure 3. Main PCB components and their connections.



FM-1: Key Commercial Modules:

- 32-bit ARM microprocessor (part of a custom PCB)
- Step-down inverting output amplifier
- Step-up inverting input amplifier
- Signal Filter: Bandpass filter of 10th order (part of a custom PCB)
- Power Management: DC to DC conversion (part of a custom PCB)
- Non-Volatile Memory 512 MB solid-state drive for data storage (part of a custom PCB)

FM-2: User Interface Components:

- 480 x 320 LCD Display (commercial component)
  Note: LCD Display is featured with an acrylic plastic screen to reduce risk of screen breaking (**RS28**).

- Large and spaced out buttons (commercial component)

FM-3: Custom Interfaces Between Commercial Modules:

- 10 Gbit/s USB-C communication module (part of a custom PCB)

FM-4: Safety Isolation Plan

There is no need for a specific isolation plan as the working voltage is low and conventional/built-in wire insulation techniques are sufficient.

2.3.2 Power section

Power requirements for each functional module presented in **Figure 3** are noted in **Table 3**. The main power functional block is the Power Management unit which has an input voltage of 12V and will generate the required input for other functional blocks. Input voltage in the Power Management unit will charge the 12V commercially available lithium-ion battery. The Power Management unit also protects the device from overcharging to avoid damaging and overheating the battery and to mitigate other risks (**RS23**).

Table 3. Input and Output voltage of each functional block for future reference.

Functional Block	**Input voltage**	**Output voltage**
Input amplifier	0.5V	5V
Signal Filter	0.5V	0.5V
Output amplifier	5V	0.5V
Display	5V	5V
Microprocessor	5V	5V
Data storage	5V	3.6V
User Interface	5V	5V
Power Management	12V	0.5-5V
Battery	12V	12V
Communication module	5V	5V
Strip	0.5V	0.5V
Data output and charging port	12V at 1.2 amps (15 W)	12V

2.4 Mechanical design

Clotime includes one general printed circuit board (PCB) (see **Section 2.3**), the strip as a support structure, and an enclosure.

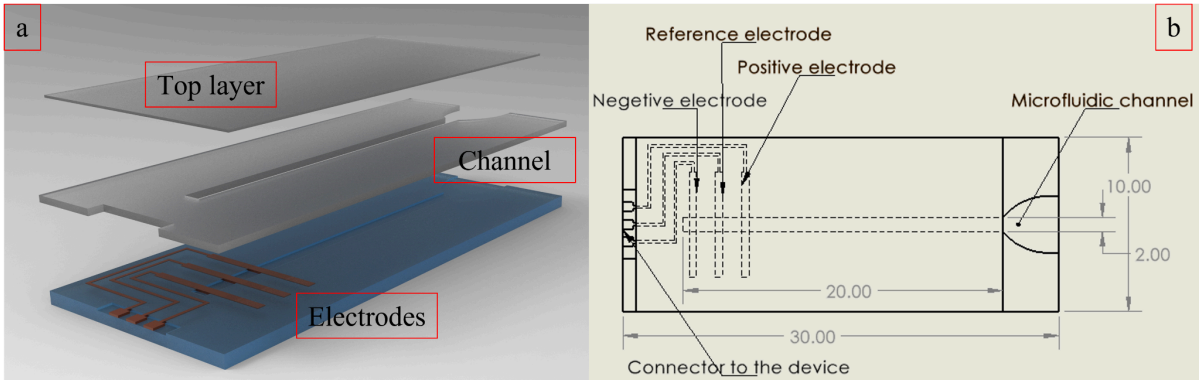
2.4.1 PCB

The size of the PCB influences the mechanical design. Based on the commercial modules and other modules demonstrated in **Section 2.3**, the PCB size will be 40mm * 70 mm. PCB will be screwed to the enclosure. There is a 5 mm gap between PCB and enclosure walls.

2.4.2 Strip

Test strip is a microfluidics chip containing three electrodes that serve as a reference, positive and negative electrodes. A microfluidic channel draws blood from the reservoir onto the electrodes. **Figure 4** shows the layers of the microfluidic strip. The microfluidic channel is 25 mm long and 2 mm wide. To maintain capillary flow inside the strip, channel height and reservoir radius are set to 450 µm and 5mm, respectively [6]. So for 35 uL blood, it takes about 1s (894ms) to reach the electrodes (located at 20 cm of the reservoir). The top layer is added to isolate the channel and the blood from the environment. The strip is made out of Polyamide (PA), and the electrode material is gold to improve the accuracy of the results. Fabrication of the strip is similar to glucose strips. For safety reasons, non-functional parts (i.e. parts that are not in contact with the blood) are coated with Bitrex (the bitterest substance in the world) (**RS30**) to avoid ingestion of the strip. Also, to prevent the use of unsuitable test strips, a notch is designed at the connector of part of the strip, which only allows the connection of approved test strips (**RS47**).

Figure 4. Test Strip. a) different layers and b) dimensions of the test strip.



2.4.3 Enclosures:

Clotime enclosure is made out of medical grade ABS that contains: (1) Five buttons (four arrow keys and one main button), (2) USB-C port (charging and data transfer), and (3) Strip port that guides the strip into the connector. **Figure 5** shows the enclosure of the device. The trapezoidal shape provides a better grip for the user and maintains the universal design. Clotime also is featured with a wrist strap to prevent the user from dropping the device (**RS25)**. **Figure 6** shows the drawing of the device and its dimensions.

Figure 5. Enclosure for a) Clotime and b) Clotime in the user's hand.

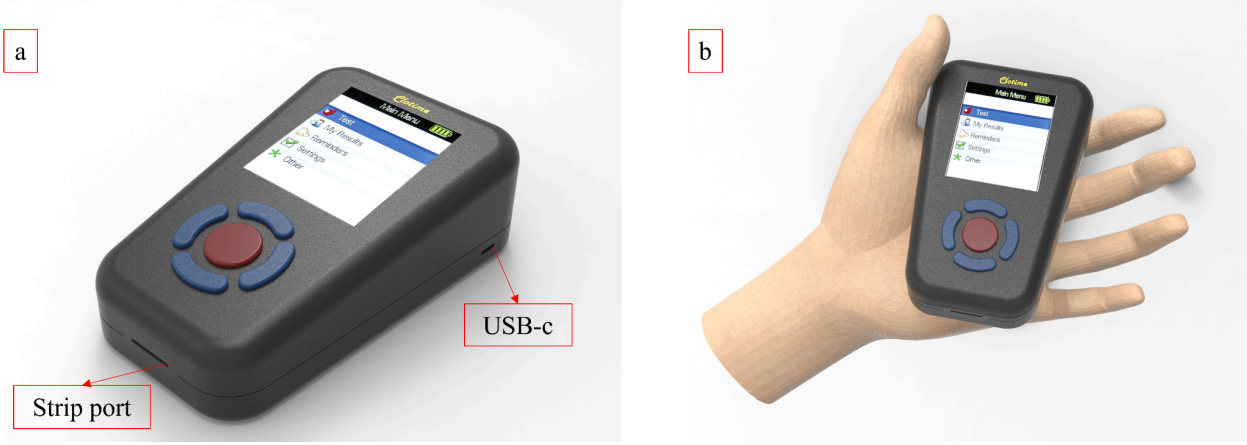
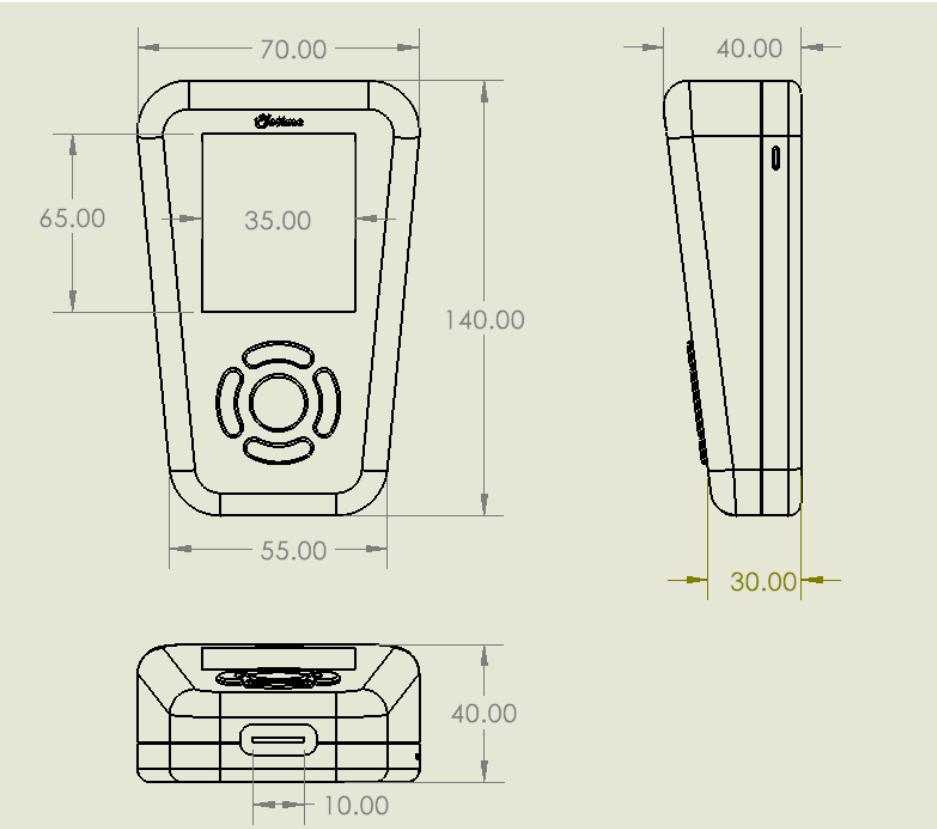


Figure 6. Dimensions in mm for Clotime.



The main components that influence the enclosure size are (1)PCB, about 40mm * 70mm (2)LCD, 35 mm * 65 mm (2.6” LCD) (3)lithium Ion battery, which is about 60mm * 60mm.

2.5 Labeling

SOR/98-282 § 21(1) [4] regulates that the labeling of Clotime must include:

a) The name of the device - Clotime;
b) The name and the address of the manufacturer;
c) The identifier of the device - test strips and the device must have labels that identify them as separate parts of the Clotime coagulometer kit;
d) The expiry date of the device - specifically, the strips, which contain specific enzymes; and
e) Directions for use - Clotime must include all directions for use with a user manual as a separate document containing an introduction, safety instructions, overview of the device and user interface, setup and testing procedure, maintenance and care (e.g. calibration of the device), and troubleshooting.

All of the aforementioned labelings shall be in both French and English [7]. IEC 60601-1 Clause 7.2 [8] also regulates the markings on the surface of Clotime, including the serial number of each manufactured Clotime, the date of the manufacture or use, labeling the detachable accessories of Clotime (test strip) with the serial and batch number as well as manufacturing date, ISO 7000-1641 symbol **(Figure 7-1**). IEC 60601-1 Clause 7.2.6 specifically regulates the labeling for connections and ports, including the rated input supply voltage (5V) and nature of supply (Direct current - **Figure 7-2**). IEC 60601-1 Clause 7.2.9 specifies the labeling for IP classification on Clotime - Clotime is designed to have protection against solid foreign objects of 10mm diameter or greater and to have protection against temporary immersion in water which makes Clotime to be classified IP47.

Figure 7. Symbols for labeling Clotime.

#	Symbol	Reference	Description
1		ISO 7000:1641	Operator's manual; operating instructions
2		IEC 60417-5031	Direct current
3	IP47	IEC 60529	4 means Protected against solid foreign objects of 1,0 mm diameter and greater 8 means protected against the effects of temporary immersion in water
4		IEC 60417-5172	CLASS II equipment
5		ISO 7000-0434A	Caution
6		IEC 60417-5010	"ON" / "OFF" (push-push)
7		ISO 7000-1051	Do not reuse Note: This is only for the test strips
8		ISO 7010-M002	Refer to instruction manual/ booklet

References

[1] S. Wani *et al.*, *P04D01 "Clotime" Product Concept*, CarePoint, 2022.

[2] A. Bahari *et al.*, *P04D02a "Clotime" Architectural Design*, CarePoint, 2022.

[3] W. AlChamaa *et al.*, *P04D02b "Clotime" Requirements Specifications*, CarePoint, 2022.

[4] A. Pietrangelo, *Coagulation tests: Types, procedure, and results*, Healthline, 2018. Accessed: Oct. 14, 2022. [Online]. Available: https://www.healthline.com/health/coagulation-tests.

[5] *Accu-Chek® Safe-T Pro Uno*, Accu-Chek, n.d.. Accessed: Oct. 29, 2022. [Online]. Available: https://www.accu-chekcac.com/en/professional-lancing-devices/safe-t-pro-uno

[6] *Capillary flow in microfluidics channels*, Prof Steven Abbott, n.d.. Accessed: Oct. 29, 2022. [Online]. Available: https://www.stevenabbott.co.uk/practical-coatings/capillary-flow.php

[7] SOR/98-282 § 23(3), *Medical Devices Regulations*, "Labelling Requirements", Government of Canada. Accessed: Oct. 29, 2022. [Online]. Available: https://laws-lois.justice.gc.ca/eng/regulations/sor-98-282/

[8] IEC 60601-1:2015, *Medical electrical equipment*, 2015.