Clotime
Impedance-based point of care blood coagulation monitoring device

Risk Management

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Change history

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V01	Created	12/11/22	Dawn
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V03	Further modifications	23/11/22	Dawn, Walid, Alireza, Sadan
V04	Modifications in response to instructor feedback (revision of scope; risk index calculation; definitions for severity of harm and probability of occurrence; hazards 8-9 and 11-15; risk assessment; residual risk statement; and summary).	06/12/22	Dawn, Walid, Alireza, Sadan

Approvals

Title/Function	Signature	Scope of Approval	Date
Dawn Lo		Primary author	07/12/22
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Abbreviations

ALARP - as low as reasonably practicable
P - probability of occurrence
PHA - preliminary hazard analysis
RI - risk index
RS - requirement specification
S - severity of harm

1. Purpose

The purpose of this Risk Management document is to identify and control risks associated with the use of Clotime (see **P04D01** [1] and **P04D02a** [2] for more information on the design and use of Clotime). Following the identification and control of risks, the requirement specifications of Clotime (**P04D02b** [3]) and parts of the architectural design (**P04D02a**) were updated accordingly. The residual risks were clearly stated at the end of this document.

Clotime is a medical device indicated for measuring blood coagulation time in individuals who are at high risk of internal clotting or excessive blood loss. The device is intended to monitor blood coagulation time in patients. Users can be laymen, medical professionals, or caregivers. Clotime is intended for home use.

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”; and
- The Strips: Referred to as “Clotime strips”, “test strips”, and “strips”.

2. Scope

This document evaluates risks foreseen in the early design stage. A method for calculating risk index from severity of harm and probability of occurrence is provided, along with suitable actions based on the resulting level of risk (**Section 3. Risk management plan**). It assesses and addresses risks that may arise due to both the characteristics of Clotime, as well as use scenarios, both normal and abnormal (**Section 4.1. Hazard identification**). Information about the device and steps taken to mitigate risks are documented (**Section 4.2. Risk assessment**), as well as the residual overall risk of the device after the mitigations have been implemented (**Section 5. Residual risk statement**).

Please note that because this analysis was conducted in the early stage of design, the following hazard analysis is a Preliminary Hazard Analysis (PHA). Throughout the design and development of Clotime, this document will be revisited and updated.

This document was written following the guidance of ISO 14971 and CAN/CSA-ISO/TR 24971:21 [4-5]. It is part of a series of documents about CarePoint's device Clotime. Please see document **P04D01** [1] for information on the intended use of the device. See **P04D02a** [2] for the architectural design of the device, and **P04D02b** [3] for requirement specifications.

3. Risk management plan

The risk index algorithm is chosen to be additive because both the severity (S:1-4) and the probability (P:1-3) are linear values. Both severity and probability are important for coagulation time measuring devices, as such a device may have frequent but non-severe consequences, and vice versa. The severity is given slightly more weight in the algorithm as some of the more serious issues such as battery ingestion can easily lead to physical harm or death.

The risk index can be calculated from severity and probability using the following equation:
$risk\ index\ =\ 2.5\ \times\ severity\ +\ 1.5\ \times\ probability$.

Tables 3.1 to **3.4** describe the levels of severity and probability, their corresponding risk indices, and the action required for different risk indices. **Tables 3.1** and **3.2** were created with reference to Tables 2-4 of [5]

Table 3.1 Definitions for severity of harm.

Severity of harm	**Description**
Catastrophic	Death
Significant	Severe irreversible injury
Moderate	Reversible or minor injury
Negligible	No injury or slight injury

Table 3.2 Definitions for probability of occurrence.

Probability of occurrence	**Description**
High	Likely to happen several times during lifetime of device
Medium	Likely to occur a few times during lifetime of device
Low	Unlikely to occur during lifetime of device

Table 3.3 Severity, probability, and corresponding risk indices. Created with reference to Annex C.4 of [5].

	Qualitative severity levels (S)			
Probability (P)	1. Negligible	2. Moderate	3. Significant	4. Catastrophic
3. High	7	9.5	12	14.5
2. Medium	5.5	8	10.5	13
1. Low	4	6.5	9	11.5

Table 3.4 Risk indices, level of acceptability, and action required

Risk index	**Acceptability**	**Action required**
$RI \leq 5.5$	Insignificant	No need for further risk reduction
$5.5 < RI \leq 11.5$	Acceptable	Reduce risk as low as reasonably practicable (ALARP); risks should not outweigh benefits
$RI > 11.5$	Unacceptable	Implement controls to reduce risk

4. Hazard Analysis

4.1. Hazard identification

Annex C of [4] was referenced when identifying potential hazards. Predicate devices were also referenced when identifying potential hazards of Clotime [6-7]. This section contains potential sequences of events leading to hazards and harms, described in **Tables 4.1** to **4.15**.

4.1.1. Device characteristics related to safety

Annex A.2 of [5] was referenced when evaluating the nature of the device and identifying device characteristics that may be related to safety.

Since the device is not intended to be implanted, and any contact with the patient is non-invasive and short in nature (see **P04D02a Section 2.1** [2]), the device is not expected to pose many risks for the users. Though the device is intended to be used in informing care, it is not directly responsible for sustaining or supporting life. While the device is electrical in nature, no energy is delivered to or extracted from the patient. Any biological materials extracted from the patient is done by a separate, already commercially-available device (see **P04D02a Section 2.1** [2]), and biological materials are not intended to be reused nor transfused. Therefore, the risks of biological material extraction are not relevant to the following hazard analysis.

The risks associated with the device arise mainly from the lithium battery (see **P04D02a Section 2.3.2** [2]), faulty measurements, and inappropriate maintenance of the device. As the product is developed further, information regarding the confidence limits of Clotime's measurements and the recommended frequency of maintenance will be determined.

Tables 4.1 to **4.11** in this section describe hazards arising from device characteristics in greater detail.

Table 4.1. H01 - exposed lithium battery.

Hazard	H01 - exposed lithium battery
Sequence of events	Device opened either manually or through device degradation, exposing lithium battery
Hazardous situation	User touches lithium battery terminals
Harm	Electric shock resulting in injury or death

Table 4.2. H02 - damaged lithium battery.

Hazard	H02 - damaged lithium battery
Sequence of events	Degradation of product battery due to overcharging, over discharging, short circuiting, overheating, and more
Hazardous situation	Leaking lithium battery that may be touched or prone to explosion
Harm	Explosion leading to burns and other injuries; environmental damages due to leakage; corrosion of skin if battery contents touched or ingested

Table 4.3. H03 - physical blunt force contact between device and person.

Hazard	H03 - physical blunt force contact between device and person.
Sequence of events	Device stored or held above ground
Hazardous situation	Device dropped
Harm	Injury such as bruising

Table 4.4. H04 - broken screen.

Hazard	H04 - broken screen.
Sequence of events	Device stored or held above ground is dropped or is met with force of other kind
Hazardous situation	Screen shatters, shards of glass scatter
Harm	Injury such as cuts, inflammation and irritation due to micro glass fragments in skin

Table 4.5. H05 - Ingestion of test strips.

Hazard	H05 - ingestion of test strips.
Sequence of events	Child gains access to test strips
Hazardous situation	Child attempts to ingest test strips
Harm	Choking, abrasions in throat

Table 4.6. H06 - improper disposal of test strips.

Hazard	H06 - improper disposal of test strips.
Sequence of events	Test strips improperly disposed of
Hazardous situation	Test strips in nature's waterways and more; accessible to wild animals and people
Harm	Environmental harm or biohazard

Table 4.7. H07 - ingestion of batteries.

Hazard	H07 - ingestion of batteries.
Sequence of events	Device opened and batteries exposed and accessible
Hazardous situation	Batteries swallowed and/or punctured by teeth by child or other persons
Harm	Choking; abrasions to throat; severe poisoning; corrosive material ingested

Table 4.8. H08 - incorrect measurement.

Hazard	H08 - incorrect measurement.
Sequence of events	User handles fingerstick and test strip with wet hands; removal of test strip during test; performs test with old test strip or blood from previous puncture; other improper use of test
Hazardous situation	Incorrect measurement leading to unsuitable diagnosis and actions
Harm	Unsuitable actions include taking medications that may be contraindicated for patients with conditions related to blood coagulation time, or inaction due to failure to detect dangerous blood coagulation times. This could result in severe injury or death.

Table 4.9. H09 - deviation from calibration.

Hazard	H09 - deviation from calibration.
Sequence of events	Device is not calibrated after a specified time frame and number of uses (TBD) by an authorized specialist
Hazardous situation	Incorrect measurements leading to unsuitable diagnosis and actions
Harm	Unsuitable actions include taking medications that may be contraindicated for patients with conditions related to blood coagulation time, or inaction due to failure to detect dangerous blood coagulation times. This could result in severe injury or death.

Table 4.10. H10 - device dropped in water or cleaned while battery on.

Hazard	H10 - device dropped in water or cleaned while battery on.
Sequence of events	User forgets to turn device off before cleaning Accidental submersion in water
Hazardous situation	Device battery on while in contact with water
Harm	Electric shock or injury

Table 4.11. H11 - out-of-date software.

Hazard	H11 - out-of-date software.
Sequence of events	Users do not update software
Hazardous situation	Updates related to safety missed; software updates crucial to processing of data also missed
Harm	Incorrect measurements and out-of-date safety information could misinform users about the safety of the device and blood coagulation time of the sample. This could then lead to inappropriate actions being taken, which could result in life-threatening situations (for instance, ingestion of unsuitable medications that result in blood thinning or coagulation).

4.1.2. Use scenarios leading to hazards

Normal and abnormal use cases were considered when identifying the following hazards, described in **Tables 4.12** to **4.15**.

Table 4.12. H12 - device used to take non-indicated measurements.

Hazard	H12 - device used to take non-indicated measurements.
Sequence of events	User uses test strip to test blood of others, old blood, or other bodily fluids
Hazardous situation	Measurements lead to incorrect conclusions and and unsuitable actions
Harm	Unsuitable actions include taking medications that may be contraindicated for patients with conditions related to blood coagulation time, or inaction due to failure to detect dangerous blood coagulation times. This could result in severe injury or death.

Table 4.13 H13 - unsuitable analysis of results for patient condition.

Hazard	H13 - unsuitable analysis of results for patient condition.
Sequence of events	Patient with pre-existing condition that results in higher or lower than average coagulation times, regardless of the condition they are being treated for
Hazardous situation	Correct measurement but incorrect conclusion due to patient's unique condition.
Harm	Unsuitable actions taken, including taking medications that may be contraindicated for patients with conditions related to blood coagulation time, or inaction due to failure to detect dangerous blood coagulation times. This could result in severe injury or death.

Table 4.14. H14 - use of device without consulting healthcare practitioner.

Hazard	H14 - use of device without consulting healthcare practitioner.
Sequence of events	User uses device and takes action based on measurements without first consulting healthcare practitioner
Hazardous situation	Uneducated interpretation of results and unsuitable actions taken
Harm	Unsuitable actions include taking medications that may be contraindicated for patients with conditions related to blood coagulation time, or inaction due to failure to detect dangerous blood coagulation times. This could result in severe injury or death.

Table 4.15. H15 - use of unsuitable test strips.

Hazard	H15 - use of unsuitable test strips.
Sequence of events	Users source test strips from unauthorized third parties. Test strips cause erroneous measurements or be unsuitable for use in some other way.
Hazardous situation	Erroneous measurements
Harm	Unsuitable actions taken, including taking medications that may be contraindicated for patients with conditions related to blood coagulation time, or inaction due to failure to detect dangerous blood coagulation times. This could result in severe injury or death.

4.2. Risk assessment

The risk assessment in this section (**Table 4.16**) was conducted with reference to the information provided in **Section 3. Risk Management Plan**, as well as the hazards identified in **Section 4.1. Hazard identification** (**Tables 4.1** to **4.15**). Suitable requirement specifications were then added to **P04D02b** [3]; where necessary, **P04D02a** [2] was updated.

In **Table 4.16**, "Hazard ID" contains the identification number of the hazard, which links back to **Tables 4.1** to **4.15** in **Section 4.1. Hazard identification**. The "Hazard" is the same as the hazards listed in the aforementioned tables. "P", "S", and "RI" stand for probability, severity, and risk index respectively; this is assessed before the risk control and after risk control. "Outcome" contains the ruling of the risk as "Insignificant", "Acceptable", and "Unacceptable" (see **Section 3. Risk Management Plan**). "Risk control" contains the controls to mitigate the risks, and "RS#" contains the corresponding requirement specification identification (see **P04D02b** [3]).

Table 4.16 Risk assessment and controls implemented for Clotime.

Hazard ID	Hazard	P	S	RI	Outcome	Risk control	RS#	P	S	RI	Outcome
H01	Exposed lithium battery	2	4	13	Unacceptable	Design device to not be openable unless by manufacturer or other authorized persons.	21	1	4	11.5	Acceptable (ALARP)
						Provide clear instructions to not touch lithium battery under any circumstances.	22				
H02	Damaged lithium battery	2	4	13	Unacceptable	Protection circuits against overcharging, over discharging and short circuiting (see **Section 2.3.2** of [2]).	23	1	4	11.5	Acceptable (ALARP)
						Thermal probes at battery to maintain a suitable battery temperature and thermal cutoff for battery when it reaches critical temperature.	24				
H03	Physical blunt force contact between device and person	3	1	7	Acceptable	Add wrist strap to device to prevent user from dropping device (see **Section 2.4.3** of [2]).	25	1	1	4	Insignificant
						Provide instructions and warnings to store device out of reach of small children and in secure location where it will not fall.	26				

						Suggestions to use device while seated at table or desk.	27				

Hazard ID	Hazard	P	S	RI	Outcome	Risk control	RS#	P	S	RI	Outcome
H04	Broken screen	3	2	9.5	Acceptable	Use an acrylic plastic screen to reduce risk of screen breaking (see **Section 2.3.1** of [2]).	28	1	2	5.5	Insignificant
						Add wrist strap to device to prevent user from dropping device.					
H05	Ingestion of test strips	3	4	14.5	Unacceptable	Add child safety lock to test strip container.	29	1	4	11.5	Acceptable (ALARP)
						Coat nonfunctional parts of strips with Bitrex (see **Section 2.4.2** of [2]).	30				
						Instructions and warnings to store test strips out of reach of small children.	31				
H06	Improper disposal of test strips	3	3	12	Unacceptable	Provide suitable and accessible disposal methods based on the region the device is sold in.	32	1	3	9	Acceptable (ALARP)
						Provide secure container for storing used test strips before disposal.	33				
H07	Ingestion of batteries	2	4	13	Unacceptable	Design the device to not be openable unless by manufacturer or other authorized persons	21	1	4	11.5	Acceptable (ALARP)
						Provide instructions and warnings to store device out of reach of small children and in secure location where it will not fall.	26				
H08	Incorrect measurement	3	4	14.5	Unacceptable	Link to instructional video	34	1	4	11.5	Acceptable (ALARP)
						Thorough instructions for use, reagents to be used, etc. with illustrations where suitable	35				
						Provide contact information of specialists or help	36				

						services upon sale or transfer of device					

Hazard ID	Hazard	P	S	RI	Outcome	Risk control	RS#	P	S	RI	Outcome
H09	Deviation from calibration	3	4	14.5	Unacceptable	Implement reminders for calibration directly into the device software.	37	1	4	11.5	Acceptable (ALARP)
						The user manual shall instruct users to bring device to specialists for calibration at regular intervals (TBD).	38				
						Provide access to specialists during visits to clinicians.	39				
						Provide contact information of specialists or help services upon sale or transfer of device.	36				
H10	Device dropped in water or cleaned while battery on	3	3	12	Acceptable	Instruct users to not clean test dock.	40	1	3	9	Acceptable (ALARP)
						Instructions for cleaning exterior of device.	41				
						The device manual shall instruct users to bring device to specialists for cleaning and inspection of test dock at suitable intervals (TBD).	42				
						Provide contact information of specialists or help services upon sale or transfer of device.	36				
						Suggestions to use device while seated at table or desk.	27				
						Warn against dangers of electric shock.	43				
H11	Out-of-date software	2	4	13	Unacceptable	The device shall have reminders for users to bring device to specialists for software updates at regular intervals (TBD) should they be unable to do so themselves.	44	1	4	11.5	Acceptable (ALARP)
						Provide access to specialists during visits to clinicians	39				

						Provide contact information of specialists or help services upon sale or transfer of device	36				

Hazard ID	Hazard	P	S	RI	Outcome	Risk control	RS#	P	S	RI	Outcome
H12	Device used to take non-indicated measurements	1	4	11.5	Acceptable	Provide clear instructions for indications of the device to both clinicians and users	45	1	4	11.5	Acceptable (ALARP)
H13	Unsuitable analysis of results for patient condition	2	4	13	Unacceptable	Provide clear instructions for indications of the device to both clinicians and users	45	1	4	11.5	Acceptable (ALARP)
						Direct users to consult their healthcare practitioner before use and when interpreting results	14				
H14	Use of device without consulting healthcare practitioner	3	3	12	Unacceptable	Limit over-the-counter sale of device without supervision or approval of clinicians	46	1	3	9	Acceptable (ALARP)
						Direct users to consult their healthcare practitioner before use and when interpreting results	14				
H15	Use of unsuitable test strips	3	4	14.5	Unacceptable	Use proprietary test strip docks that are only compatible with approved test strips (see **Section 2.4.2** of [2]).	47	1	4	11.5	Acceptable (ALARP)

5. Residual risk statement

Appropriate controls were taken to mitigate the risks identified during this preliminary hazard analysis. The remaining risks of this device have been reduced to be insignificant or ALARP through design changes, instructional manuals, and warning messages.

Many of the risk controls involve periodic maintenance on the device by specialists. Significant residual risks include damaged or exposed lithium batteries (**H01-02**); ingestion of batteries or test strips (**H05**, **H07**); improper disposal of test strips (**H06**); failure to maintain upkeep of the device including cleaning, calibration, and software updates (**H09-11**); or use scenarios that may lead to faulty measurements or incorrect conclusions from the results (**H08**, **H12-15**).

The risks do not outweigh the benefits of the device. It is expected that, by following instructions and using the device reasonably, users will not be subject to any serious harm. Therefore, at this stage further development of Clotime can progress.

6. Risk management report summary

This report contains instructions for calculating and evaluating risk indices based on severity and probability of incidents (**Section 3. Risk management**).

A preliminary hazard analysis was conducted with regards to the device characteristics and use scenarios (both normal and abnormal). A total of 15 hazards were identified (**Section 4.1. Hazard identification**). The risk indices were then calculated for each hazard using the methods described in **Section 3. Risk Management**. In total, 30 appropriate risk controls were implemented to reduce the risks to ALARP levels (**Section 4.2. Risk assessment**). **P04D02b**'s requirement specifications [3] were updated according to the risks foreseen in this exercise, and **P04D02a** [2] was also updated where necessary.

It was determined that the benefits outweigh the risks of this device, and further work related to Clotime may proceed (**Section 5. Residual risk statement**).

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] ISO 14971:2019, *Medical devices - Application of risk management to medical devices*, 2019.

[5] CAN/CSA-ISO/TR 24971:21, *Medical devices - Guidance on the application of ISO 14971*, 2021.

[6] Roche. *CoaguChek XS Pro Operator's Manual Version 5.0* (2015). Accessed: Nov. 12, 2022. [Online]. Available: https://www.coaguchek.ca/build/assets/files/CoaguChek-XS-Pro-Operators-Manual-en.612fbda7.pdf

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