APPROVAL

Role	Name	Function	Signature
Author	Eva Kilimtzidi	QA	
Review	Julien Finci	CTO	
Approval	Mauro Rinaldi	RAQM	

PURPOSE

This document describes the Risk Management process and risk record creation applicable for medical devices developed at ASPIVIX and for their entire lifecycle. It is based on the applicable EN ISO 14971 and IEC 62366-1 standards. The objective of the Risk Management and usability process is to:

- Identify and document possible hazards and hazardous situations that might lead to adverse events and/or associated risks to patients, operators, and other.
- estimate and evaluate the associated risks
- identify and implement risk controls to prevent or reduce risk to a level where residual risks and overall residual risks are acceptable without adversely affecting the benefit-risk ratio
- describe and ensure documentation of the Risk Management process related to product development, design changes, new hazardous situations, and new or updated manufacturing processes in accordance with EN ISO 14971.

SCOPE

In the scope are the Risk Management activities related to a product. Risk Management activities are conducted throughout all phases of the product lifecycle, such as design and development, production and post-production phases including but not limited to storage, transport, use and disposal. The usability engineering process is integrated in the Risk Management process to assess use related risks associated to a working product.
Third party (e.g., Contract Manufacturing Organization and Suppliers) contracted by ASPIVIX for the development, supply, storage, and transportation of the products perform Risk Management activities according to their internal process and procedures. The output of that assessment shall be approved by ASPIVIX before its use as input for the ASPIVIX's Risk Management activities.

RESPONSIBILITIES

The responsible for the application of this SOP is the Quality and Regulatory Affairs Manager.
Responsibilities related to document creation, review and approval are defined in the Appendix 1 to this SOP. The deliverables of the Risk Management and usability process are documented as a team effort that involves the

appropriate representative Subject Matter Experts (SME). The SME must be competent for the tasks of the deliverable and have appropriate training, knowledge, and experience within their representative area of expertise. A clinical advisor expert in the field of the product intended use must be involved in the Risk Management and usability process. Whether appropriate, qualified subcontractors shall be part of the Risk Management team and contribute to the risk assessment.

For each deliverable the team is established by the Author who leads the Risk Management document creation and is responsible for involving co-authors (also external), reviewers and approvers, informing the stakeholders of all applicable document updates and releases.

DOCUMENT HISTORY

Description of Changes	Version
Initial version	A
General review and revamping of the core text to comply with EN ISO 14971:2019 and to clarify the Risk Management and usability processes and interconnections, define responsibilities. Amendment of figures 1 and figure 2; introduction of the detectability (PRN) and correction of the RPN with numeric value. Description of the usability process with reference to the IEC 62366-1 2015	B
Update by including the newly created Usability Test Protocol T-302-8A and Usability Test Report T-302-8B	C
Update by including the Usability Test Protocol/Report List T-302-9	D
Update by removing the T-302-9 and adding that the Usability Test Protocol and Report will be recorded in the T-200-18 (Test Report List)	E
Update to include changes of the Hazard assessment template (T-302-3)	F
Update with references to software lifecycle procedures & update PRN table	G

TABLE OF CONTENT

1 DEFINITIONS

Term	Definition
Benefit	Positive impact or desirable outcome of the use of a medical device on the health of an individual, or a positive impact on patient management or public health Note: Benefits can include positive impact on clinical outcome, the patient's quality of life, outcomes related to diagnosis, positive impact from diagnostic devices on clinical outcomes, or positive impact on public health
Harm	Injury or damage to the health of people, or damage to property or the environment
Hazard	Potential source of harm
Hazardous situation	Circumstance in which people, property or the environment is/are exposed to one or more hazards
Intended use	Use for which a product, process or service is intended according to the specifications, instructions and information provided by the manufacturer Note: The intended medical indication, patient population, part of the body or type of tissue interacted with, user profile, use environment and operating principle are typical elements of the intended use
Reasonably foreseeable misuse	Use of a product or system in a way not intended by the manufacturer, but which can result from readily predictable human behavior Note: Readily predictable human behavior includes the behavior of all types of users, e.g., lay and professional users. Reasonably foreseeable misuse can be intentional or unintentional
Residual risk	
Risk	Combination of the probability of occurrence of harm and the severity of that harm
Risk control	Process in which decisions are made and measures implemented by which risks are reduced to,

	or maintained within, specified levels
Safety	Freedom from unacceptable risk

2 PROCEDURE

2.1 GENERAL

The Risk Management and usability engineering process applies during the entire lifecycle of a product, from project start until delivery of the last product or batch, as well as the post market phase.

The procedure for Risk Management and usability engineering consists of the following steps that are explained in the corresponding sections:

- Risk Management Planning
- Risk Assessment
- Risk Control
- Evaluation of Overall Residual Risk
- Risk Management Review
- Production and Post-Production activities

The Risk Management process follows the schematic representation illustrated in figure 1 and with more detailed information in figure 2.

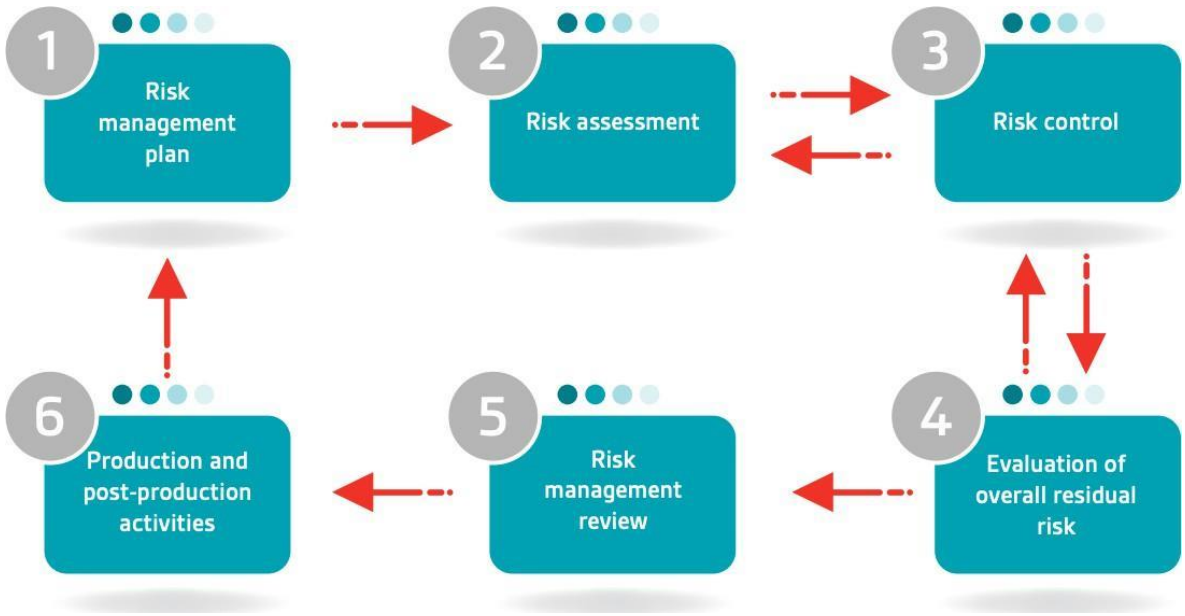


Figure 1 – The six process steps of the risk management process following EN ISO 14971

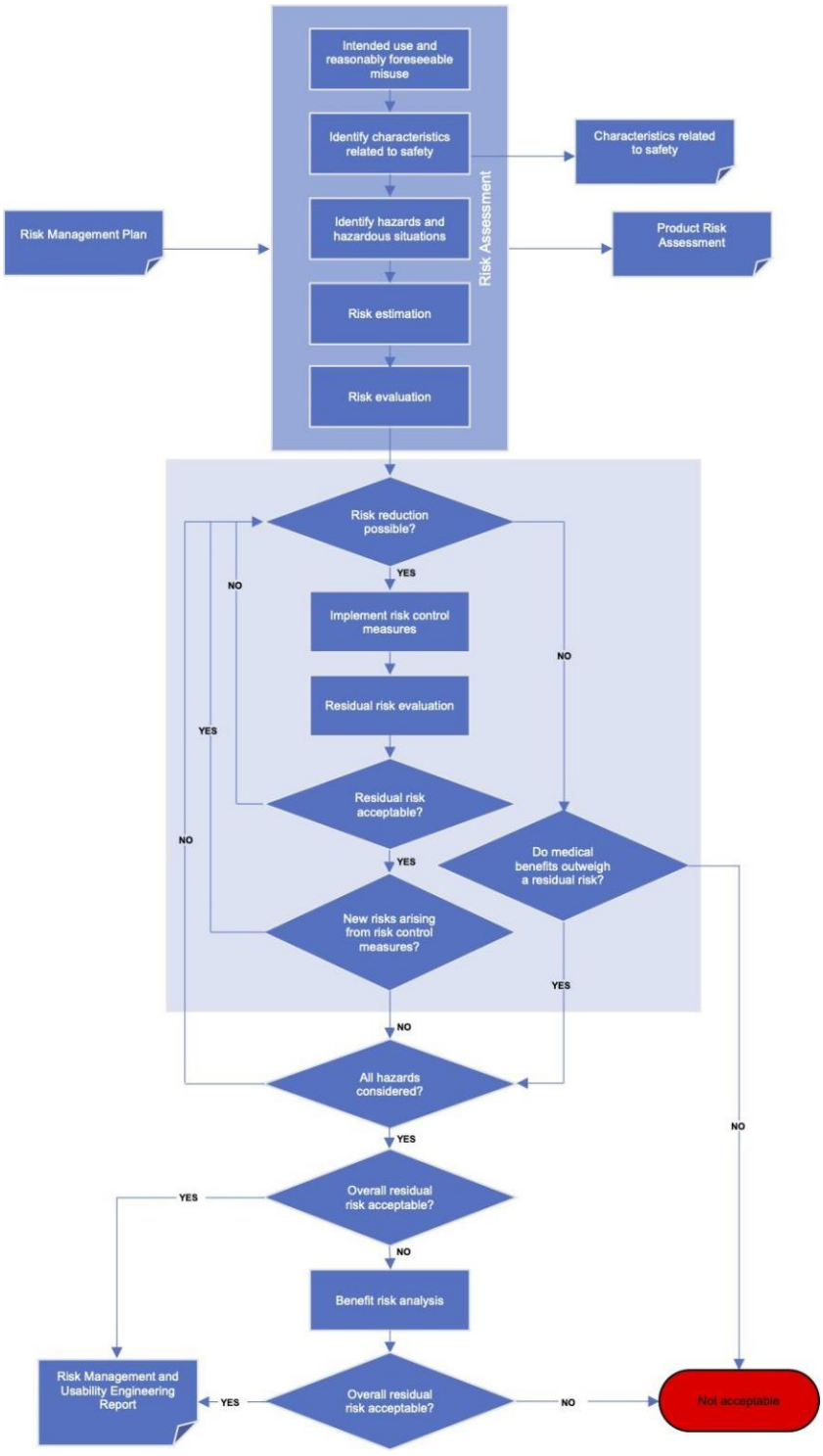


Figure 2: Risk Management Process

2.2 RISK MANAGEMENT FILE (RMF)

The RMF is constituted of a set of documents for each product:

- Risk Management Plan T-302-1
- Product risk assessment T-302-4 (it includes the Task Analysis)
- Hazards Assessment T-302-3
- Design & Process FMEA T-302-5 (it includes transportation assessment)
- Biological Evaluation Plan & Report T-302-6
- Risk Management Report T-302-2, including the Benefit-Risk Assessment, the evaluation of the overall residual risk, and the Risk Management review

All documents of the Risk Management File (RMF) are part of the product's Design History File (DHF). During the entire lifecycle of a product, every change and every review of the Risk Management File documents shall be documented.

3 RISK MANAGEMENT

3.1 RISK MANAGEMENT PLAN

The Risk Management process is initiated with the planning activities documented in the Risk Management Plan (T-302-1). It contains:

- Scope and date of the planned Risk Management activities, identifying and describing the product and its lifecycle phases for which the plan is applicable
- Assignment of responsibilities and authorities including identification of persons and organizations who are carrying out risk analysis
- Requirements for the review of the Risk Management activities
- Criteria for risk acceptability based on the management policy described in this SOP (section 3.2.3.2)
- Evaluation method of the overall risk and criteria for acceptability of overall residual risk
- Requirements for the verification for implementation and effectiveness of risk control measures
- Requirements for the collection and review of production and post-production information

Whether the plan changes during the lifecycle of the medical device, a record of the changes shall be maintained in the Risk Management File.

The review of the Risk Management process suitability is planned once a year to ensure continuing effectiveness of the Risk Management process and document any decisions and actions taken (section 3.7).

3.2 RISK ASSESSMENT

The Risk Assessment is executed by the established Team in accordance with the Risk Management Plan and follows the schematic representation of the Risk Management process illustrated in figure 1.

3.2.1 RISK ASSESSMENT PROCESS

The risk assessment process consists of:

- Identification and description of the product
- Identification of the intended use
- Identification of characteristics related to safety and performance
- Identification of hazards and hazardous situations
- Risk estimation

Relevant information from the state of the art such as clinical data and post-market data available for equivalent or similar products shall be identified and investigated. Available information shall be referenced and used as a starting point for the Risk Assessment. The degree of relevance of available data will depend on the differences between the device designs, their intended use and whether a new hazard or significant differences in outputs,

characteristics, performance, or results are introduced. If such data is not available, the team establishing the

Risk Assessment will provide a best estimate regarding the probability of occurrence based on experience and common sense.
ASPIVIX SA shall assign a software safety class (A, B, or C) according to the possible effects on the patient, or other people resulting from a hazard to which the software system can contribute, according to the procedure SOP-208 Software Development.

The risk assessment process has the following deliverables:

- Hazards Assessment T-302-3
- Product risk assessment T-302-4, top-down assessment (it includes the Task Analysis),
- Design & Process FMEA T-302-5, bottom-up assessment (it includes transportation assessment)
- Biological Evaluation Plan & Report T-302-6
- Benefit – Risk Assessment T-302-7

3.2.1.1 Identification and description of the product

Based on available information from the User Requirement Specifications and available technical and clinical knowledge in the field of the product use, the team defines an early description of the product. This description is refined during the product development process. Any change shall be assessed trough ought the Risk Management process as a source of new risks. Description of the product is established in the Hazards Assessment T-302-3 and referenced in the Design and Development plan T-200-1 and the other design control documents.

3.2.1.2 Identification of the intended use

The intended use of the product is established in the User Requirement Specification document (T-200-3) from which any reasonably foreseeable misuse is formulated, assessed, and recorded in the Risk Assessment process deliverables mentioned in 3.2.1. The intended use is the starting point for Risk Assessment as identifies the use application, user, user environment and potential known related hazards identified and listed in T-302-4.

3.2.1.3 Identification of characteristics related to safety and performance

Qualitative and quantitative product characteristics, such as e.g., sterility, re-use, device operations, materials, energy sources, and user interface characteristics that could affect product safety and performance (including packaging, IFU and labels), shall be identified, and listed in T-302-4.

3.2.1.4 Identification of Hazards and hazardous situations

Known and foreseeable hazards and hazardous situations generated by reasonably foreseeable sequences or combinations of events linked to the intended use and foreseeable misuse associated with the product in both normal and fault conditions, shall be identified and listed in the Hazards Assessment (T-302-3).

Information from the identified hazards and hazardous situations is used as input for the Product Risk Assessment T-302-4 concerning usability and for Design and Process in T-302-5.

3.2.2 Estimation of Risk(s)

A risk is the probability of harm occurring under defined circumstances, considering how severe the harm could be. Following that definition, reasonably foreseeable sequences, or combinations of events, including misuse, that can result in a hazardous situation leading to a harm shall be considered and assessed. For each identified hazardous situation, the associated risk(s) shall be estimated using applicable information or data (if available) or a best estimate shall be made by the team of experts. Information or data to estimate risks can be obtained, from published standards, scientific data, field data from similar marketed products, including published reported incidents; usability tests employing typical users, clinical evidence, results of appropriate investigations, expert opinion, external quality assessment schemes. For hazardous situations for which the probability of the occurrence of harm is unknown, the possible consequences shall be listed for the correct estimation and use in

the risk evaluation and risk control.

3.2.2.1 Severity of a harm

Severity is the measure of the possible consequences of a hazard. A severity rating is based on the probable outcome of a single instance of the harm inflicted. The severity levels are listed in the table below.

Score	Classification	Quality Criteria	Harm
5	Catastrophic	Effects may cause a Health Authority to suspend the Manufacturing/Marketing Authorization	Death or life-threatening serious adverse event
4	Critical	Effects may lead to serious/critical regulatory observations and/or lead to a product recall	Serious adverse event requiring medical attention / Results in permanent impairment or irreversible injury
3	Major	Effects may lead to major regulatory observations or non-conformance with internal quality standards, procedures or regulatory requirements leading to product quality impact	Non-serious adverse event requiring medical attention / Results in injury or impairment requiring medical or surgical attention
2	Moderate / Minor	Effects may lead to only minor observations or recommendations in regulatory inspections, or minor non-conformance with internal quality standards, procedures or regulatory requirements and no product quality impact	Results in temporary injury or impairment not requiring surgical attention or minor medical care
1	Negligible	Effects will not lead to non-conformance with internal quality standards, procedures, or regulatory requirements	Customer dissatisfaction / User experiences negligible non-medical event

When the severity of harm is unknown, for the estimation, the highest severity score should be considered.

3.2.2.2 Probability of Occurrence of a Hazardous Situation

Following the identification of each hazard, the probability of occurrence of the corresponding hazardous situation shall be estimated based on the available data with reference to the estimated annual production volumes:

Score	Probability of occurrence of harm	Value
5	Frequent	≥ 1/10
4	Probable	1/100
3	Occasional	1/1'000
2	Remote	1/10'000
1	Exceptional / Improbable	< 1/100'000

When the probability of occurrence of a hazardous situation is unknown, the related risk estimate shall be based on a reasonable worst-case estimate of probability.

3.2.2.3 Detectability

The probability of detection specifies how likely it is that a hazard is discovered when it occurs before the product is used. The detectability is calculated with reference to the estimated annual production volumes:

Score	Quality Criteria	Probability of detection	Value
5	There is no established inspection, testing, or monitoring in place to detect the failure	Remote	< 1/100'000
4	There is limited inspection, testing, or monitoring in place. Detection is delayed and multiple failures may go undetected between consecutive steps	Low	1/10'000
3	Some inspection, testing, or monitoring is in place. Detection is delayed and single failure could go undetected between consecutive steps	Moderate	1/1'000
2	Inspection, testing, or monitoring is in place. There is a high probability that the failure will be detected within the step	High	1/100
1	Consistent inspection, testing, or monitoring is in place to immediately and consistently detect the failure	Very High	≥ 1/10

Ratings for detectability (design and process risk assessments only) might be aligned with the development or manufacturing partner respectively and documented in the Risk Management & Usability Engineering Plan.

3.2.3 Risk Evaluation

3.2.3.1 Classification

The criteria for risk classification are defined in the tables below.

- (PRN) Primary Risk Number matrix, used for the Product Risk Assessment (T-302-4)
- (RPN) Risk Priority Number matrix, used for the Design and Process Risk Assessment (T-302-5)

Using that tables, the risk will be classified under one of the three categories, i.e., High, Medium, or Low:

High	control, risk is not acceptable, risk control action required
Medium	investigate, risk control actions must be investigated to determine if risk can be reduced
Low	acceptable, no further risk control action required

Primary Risk Number Matrix (PRN)

		Probability of Occurrence				
		Exceptional	Remote	Occasional	Probable	Frequent
		1	2	3	4	5
Severity	5	5	10	15	20	25
	4	4	8	12	16	20
	3	3	6	9	12	15
	2	2	4	6	8	10
	1	1	2	3	4	5

PRN = Severity x probability of occurrence	
13-25	**High:** risk control action required
5-12	**Medium:** risk control actions must be investigated to determine if risk can be reduced
1-4	**Low:** no further risk control action required

Risk Priority Number Matrix (RPN)

		Probability of Detection				
		Very High	High	Moderate	Low	Remote
		1	2	3	4	5
Primary Risk Number	25	25	50	75	100	125
	20	20	40	60	80	100
	16	16	32	48	64	80
	15	15	30	45	60	75
	12	12	24	36	48	60
	10	10	20	30	40	50
	9	9	18	27	36	45
	8	8	16	24	32	40
	6	6	12	18	24	30
	5	5	10	15	20	25
	4	4	8	12	16	20
	3	3	6	9	12	15
	2	2	4	6	8	10
	1	1	2	3	4	5

RPN = PRN x probability of detection	
24-125	**High:** risk control action required
9-20	**Medium:** risk control actions must be investigated to determine if risk can be reduced
1-8	**Low:** no further risk control action required

The evaluation of the estimated risk and the result of the risk acceptability is recorded in the Risk Assessment process deliverables mentioned in section 3.2.1.

Any deviations from these criteria shall be specified in the Risk Management Plan T-302-1.

In case of one or more risk assessments are outsourced, the criteria for risk classification shall be communicated to the subcontractor.

3.2.3.2 Risk Management Policy

ASPIVIX SA shall define a Policy (according to annex C of ISO TR 24971) that provides a framework for establishing the criteria for risk acceptability. The policy will address the following elements:

- Purpose - which describes the goals for establishing criteria for risk acceptability;
- Scope – specifies to whom, where, and when the policy applies;
- Factors and considerations or determining acceptable risk – the following factors and considerations should be considered:
    - Relevant international standards for the particular type of medical device, including standards for testing of specific properties with approval/rejection limits;
    - Generally acknowledged state of art;
    - Validated concerns from stakeholders;
- Approaches to risk control
- Requirement for approval and review.

3.2.3.3 Risk Acceptance Criteria

For each identified and classified risk, the SMEs, see Appendix 1, evaluates, and estimates the risk acceptability following the risk acceptance criteria defined in the Risk Management plan. The policy to determine criteria for risk acceptability must be appropriate for the product under assessment. These criteria are based upon applicable national or regional regulations and relevant International Standards and consider available information such as the generally accepted state of the art and known SME's concerns. The criteria should include criteria for accepting risks when the probability of occurrence of a harm cannot be estimated and should be defined before the actual Risk Assessment begins. The review of the risk acceptance criteria is made from a Team of experts including a SME and it's based on the review of information from post-market surveillance for each product such as production and post-production information, complaints and adverse events reports, feedback from the users and marketing surveys, information from similar products on the market, review of available scientific information (see SOP-105 Post Market Surveillance and section 6 of this document for more details). Such a review is performed together and with the same frequency of the PMS activities.

3.3 RISK CONTROL

All risks shall be reduced to the lowest practicable level possible. When a risk mitigation is required, risk control measures shall be identified by the SME and implemented for each of the Risk Assessment process deliverables mentioned in section 3.2.1. Risk control shall be documented in T-302-4 Product Risk Assessment and T-302-5 design and process risk assessment as appropriate.

3.3.1 IMPLEMENTATION OF RISK CONTROL MEASURES

The measures for risk reduction must be implemented in a way the residual risk(s) associated with each hazard are judged as low or medium and reduced to the lowest practicable level possible. Economic reasons are not appropriate regarding risk acceptability. Information alone is not adequate and suitable to reduce the probability of occurrence.

Risk reduction shall follow an integrated approach in which one or more of the following in the priority order listed shall be used:

- Inherent safety by design
- Protective measures in the medical device itself or in the manufacturing process
- Information for safety and, where appropriate, training to users

The effectiveness of all defined risk control measures must be verified and recorded (i.e., usability/design/process verification or validation as appropriate).

Relevant standards shall be applied as part of the risk control option analysis.

3.3.2 RESIDUAL RISK EVALUATION

Following implementation of the selected risk control measures, each residual risk is evaluated for risk

acceptability against the risk acceptance criteria defined in the RMP. The residual risk evaluation is conducted by the appropriate SMEs and follows the process described in Section 3.2.3

Low risks	Low risks cannot be reduced any further or additional control measures would not further increase safety. They must be balanced against benefit.
Medium risks	Medium risks shall be analyzed accurately regarding possible risk control measures and shall be reduced to the lowest practicable level possible. If no further risk reduction is possible, a justification for the acceptability of the risk based on a benefit-Risk Assessment must be provided.
High risks	High risks are not acceptable and must be reduced to an acceptable level.

3.3.3 Benefit-Risk Assessment

If there are still risks in the medium range after implementation of risk control measures, the SME shall evaluate them individually, justify and document why the remaining risk is acceptable and why it can't be reduced any further.

If the residual risk is judged unacceptable to the risk acceptance criteria defined in the RMP, and further risk control is not practicable, data and literature, provided by SMEs, can be used to determine if the benefits of the intended use outweigh the residual risks:

- If data and literature evidence cannot provide rationale for the conclusion that the benefits outweigh the residual risks, then this risk remains unacceptable.
- If the benefits outweigh the residual risks, then this risk is acceptable.

The results of the benefit-risk assessment shall be recorded in the T-302-7 and referenced in the Risk Management Report T-302-2. The benefit risk assessment shall be agreed and approved by at list one (1) SME having clinical experience in the field of the product's intended use.

3.3.4 Risks arising from risk control measures

Risk control measures implemented shall be reviewed by appropriate SMEs for effects regarding whether:

- New risks, hazards or hazardous situations are introduced.
- Estimated risks for previously identified risk and hazardous situations are affected by the introduction of the risk control measures.

Any new or increased risks shall be managed in accordance with section 3.2.2 Estimation of Risk(s) and section 3.3.3 Benefit-Risk Assessment of this SOP.

3.3.5 Completeness of risk control

Risk control activities shall be reviewed to ensure that risks from all identified hazardous situations have been considered, and all risk control activities are completed.

The result of the risk control review shall be recorded in the Risk Management report, T-302-2.

3.4 Overall Residual Risk Evaluation

The overall residual risk evaluation is executed in accordance with the Risk Management Plan T-302-1 and documented in the Risk Management report, T-302-2.

All risk control measures implemented and verified shall be evaluated for the overall residual risk posed by the product, considering the contributions of all residual risks, in relation to the benefits of the product, using the risk acceptance criteria defined in the Risk Management Plan T-302-1.

If the overall residual risks are judged acceptable in relation to the benefits of the intended use, users must be informed of any significant residual risks. To disclose those residual risks, that information must be included in the product's accompanying documentation, such as but not limited to instructions for use (IFU).

If the overall residual risks are judged unacceptable in relation to the benefits of the intended use, it may be considered to:

- implement additional risk control measures
- modify the product
- change the intended use

The Risk Management process shall be repeated if any of the three conditions above is applicable (iterative process). Otherwise, the overall residual risk remains unacceptable, and the design shall be abandoned.

3.5 Risk Management Review

Once the overall residual risks assessment is completed, the outcome of the deliverables mentioned in section 3.2.1 is reviewed. That review must at least ensure that:

- the Risk Management plan has been appropriately implemented
- the overall residual risk is acceptable, e.g., either thought risk control actions or benefit-Risk Assessment. Favorable / unfavorable elements, limitation, and incertitude must be noticed. These incertitude & limitation will be considered to define the Post Market Surveillance plan.
- appropriate methods are in place to collect and review information during production and post-production.

The Risk Management review is executed in accordance with the Risk Management Plan T-302-1 and the result of this review shall be recorded and maintained as the Risk Management Report T-302-2.
Risk Management review participants are defined in Appendix 1: Roles and Responsibilities.
Risk review by management is ensured by the review from the CTO and the approval of the Risk Management Report T-302-2 by RAQM.
Risk Management Review can also be conducted ad hoc to review the residual risks, for instance, prior to clinical studies or to support any submission data to health authorities. In such cases, reviewed and documented data may be partial (e.g., postproduction control not applicable at such stage). The outcome of such review will be documented in an (interim) Risk Management Report using the same T-302-2 but with limited available information.

3.6 Post-Market Surveillance Information

ASPIVIX SA is responsible for gathering and assessing post-market surveillance information related to the identification of possible new or changed hazards, hazardous situations, or risks (SOP-105). Methods to obtain and analyze production and post-production information is defined in the Quality Management System processes such as, but not limited to:

- SOP-103 Complaints Handling
- SOP-104 CAPA, and
- SOP-106 NC Product Handling,

The results of the evaluation of the information from post market surveillance must be fed back as inputs into the Risk Management process if one of the following conditions is satisfied:

- previously unrecognized hazards or hazardous situations are present
- estimated risk(s) arising from a hazard or hazardous situations is no longer acceptable
- the overall residual risk is no longer acceptable in relation to the benefits of the intended use; or
- the generally acknowledged state of the art has changed

3.7 Re-Evaluation of Risk Management File

The Risk Management File shall be reviewed following inputs from the Post Market Surveillance activities defined in a product specific Post Market Surveillance Plan. The Risk Management Report T-302-2 shall be updated if one or more deliverables mentioned in section 3.2.1 are reviewed with information from the Post Market Surveillance. In cases where residual risk is no longer acceptable, the impact on previously implemented risk control measures shall be evaluated and should be considered as an input for modification of the medical device.

ASPIVIX SA shall consider the need for actions regarding medical devices already on the market. Any actions shall be recorded in the risk management file.

ASPIVIX SA shall evaluate the impact on previously implemented risk management activities and the result of this evaluation shall be considered as an input for the review of the suitability of the risk management process by top management (during management review).

Even if the Post Market Surveillance information does not lead to new information regarding Risk Management, the Risk Management File is to be re-evaluated on a regular basis (once a year). The review of the Risk Management File shall be noted in the Risk Management Report T-302-2 even if there are no changes to the reviewed documents of the Risk Management File.

4 USABILITY ENGINEERING

The Usability Engineering (Human Factors Evaluation) process is used during the development of a new product or changes to an existing one to address:

- user interface safety concerns, where a user interface[1] includes all points of interaction between the product and the user

[1] A User Interface definition, includes, the size and shape of the product; Elements that provide information to the user, such as indicator lights, displays, auditory and visual alarms; Graphic user interfaces of device software systems; The logic of overall user-system interaction, including how, when, and in what form information (i.e., feedback) is provided to the user; Components that the operator connects, positions, configures or manipulates; Hardware components the user handles to control device operation such as switches, buttons, and knobs, Components or accessories that are applied or connected to the patient, and Packaging and labeling, including operating instructions, training materials, and other materials (https://www.fda.gov/medical-devices/human-factors-and-medical-devices/human-factors-considerations).

- risks related to the user's tasks to use a working product under its intended use.

The flowchart in figure 3 shows the Risk Management and Usability Engineering interactions.

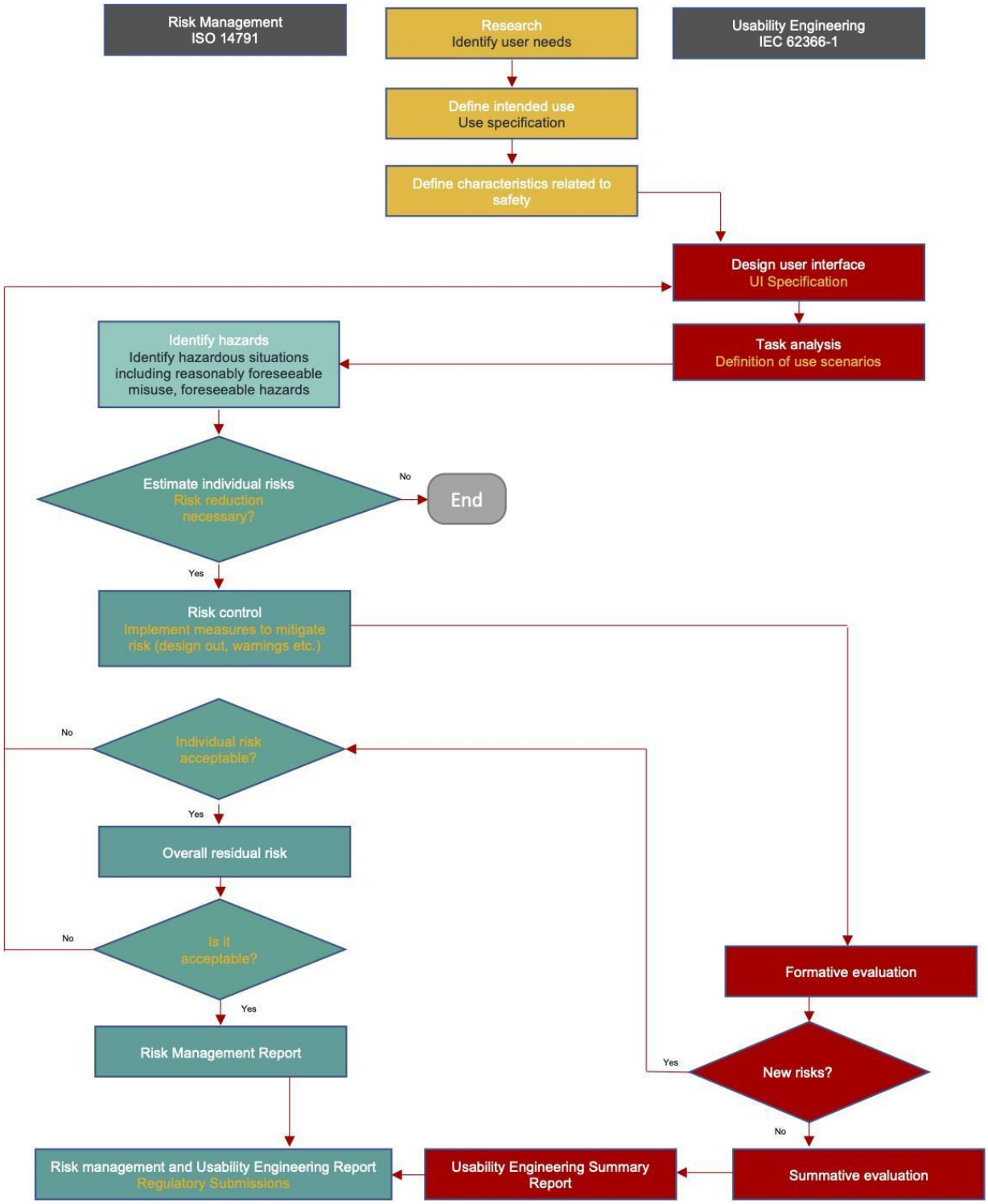


Figure 3: Risk Management and Usability Engineering interactions

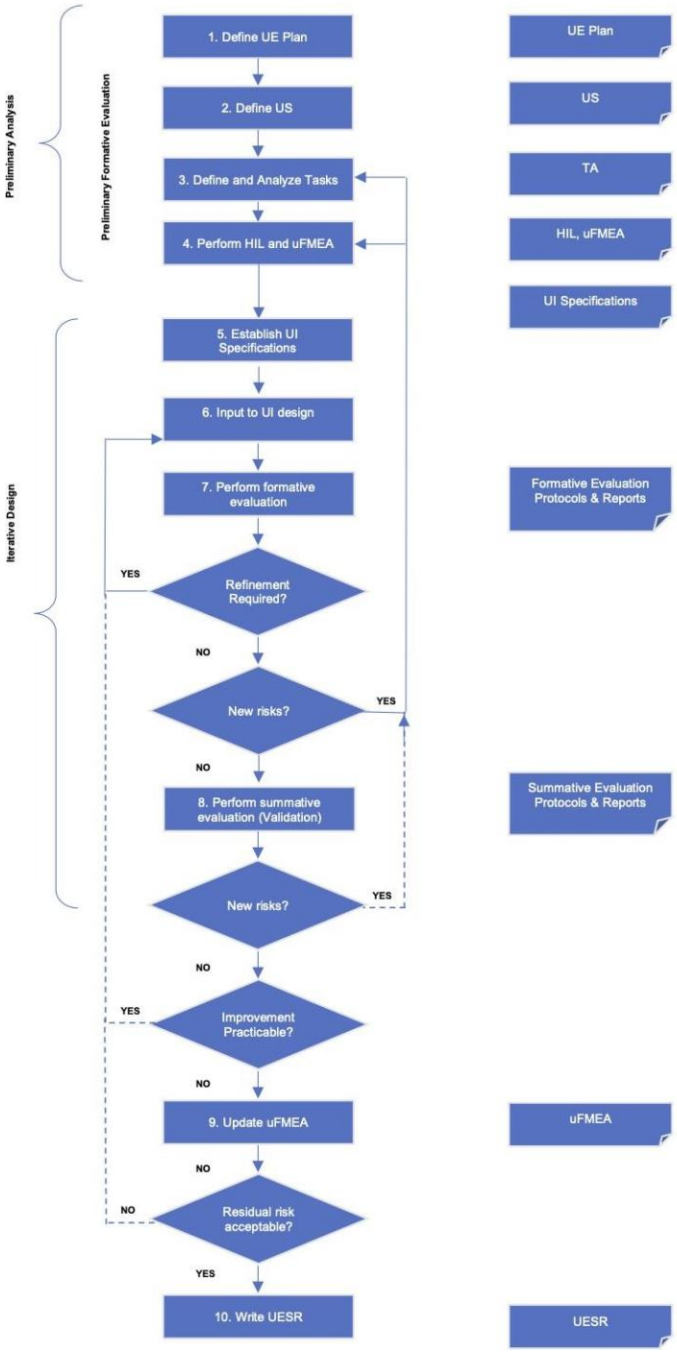
The Usability Engineering process shall be based upon an explicit understanding of the intended use and products interfaces and operations and focus on (1) device users, (2) device use environments and (3) device user interfaces. The Usability Engineering is an iterative process that drives the product development and its refinement through user-centered evaluation. The purpose is to ensure safe and effective use and, at the same time, get information regarding use errors that could compromise medical care or patient or user safety.

The Usability Engineering process:

- Supports for defining the intended users, use environments, and user interface.
- Supports the identification of use-related hazards.
- Identifies and categorizes critical tasks.
- Supports the development and implementation of risk control measures.
- Validates use -related safety.
- Documents the Usability Engineering process.

The Usability Engineering process follows the steps defined in figure 4.

UE Process	UE Output	Purpose of the UE Process Step



[1]. Usability Engineering Plan (UEP) is a high-level description of the planned UE activities and responsibilities which can be documented

[2]. as part of the Risk Management Plan (RMP). The UEP describes at high-level how formative and summative evaluations will be conducted and the iteration process with the Risk Management and Design & Development activities.

[3]. Usability Specifications (US) describes the intended medical indications, users and context of use, and the knowledge gained on similar products.

[4]. Task Analysis (TA) defines the use of the product in terms of discrete steps and forms a basis for the identification of use errors and critical tasks. Note that the TA may be documented as part of the Product FMEA (uFMEA) instead of a separate document.

[5]. Hazard-related use scenarios are defined as part of the Hazard Identification List (HIL) and uFMEA.

[6]. Note that the UI Specification is typically documented as part of the Design Input Requirements (DIRs). DIRs for the User Interfaces (UIs) include:

- Testable requirements relating to the UI.
- Testable requirements for risk controls.

UE are input to UI design of product, labeling (including IFU), and packaging, and training. Typically, the UI design used in formative evaluation is documented within the formative evaluation protocol or as part of the technical documentation.

[7]. Formative evaluations provide input to the design of the UI and assess efficacy of risk controls. Such inputs are typically documented within the formative evaluation report. The Formative protocol describes the product and the UI under assessment, the purpose of test (including the analysis of the tasks to use it, and risks associated to the tasks), the methodology to execute the test (the test itself, participants, test environments, test materials), and the methodology to assess the results. The report includes all it is defined in the protocol in addition to any deviation from that, the results of the test, the discussion of the results, and the conclusion; The latter to be further referenced and analyzed in the uFMEA.

[8]. Summative evaluation (Validation) confirms that the intended users can use the product safely and effectively for its intended use environments, and that residual risks would not be reduced by further product modification.

[9]. Update uFMEA based on output from summative evaluation, as appropriate.

[10]. UESR summarizes the UE process and all UE deliverables.

Figure 4: Usability Engineering process

4.1 USABILITY ENGINEERING PLAN

The Usability Engineering plan is a high-level description of the planned Usability Engineering activities and responsibilities to ensure that a product's User Interface has been rigorously evaluated for user and patient safety. The Usability Engineering plan is documented as part of the Risk Management Plan T-302-1. The Usability Engineering process is a living document, and it is refined during product development. That plan includes the estimation of the required usability studies (Formative and Summative/validation studies), and searches on the state of the art, such as equivalent and similar products in the same field of application, similar products in other fields of application but with same or similar User Interfaces, similar technologies. That search aims to get knowledge of existing use-related risks and potential existing risk control measures that can be used for the product under assessment.

4.2 USE SPECIFICATIONS

The Use Specifications is a summary of important characteristics related to the device use. The use specification shall include:

- Intended medical indication (e.g., conditions or disease(s) to be screened, monitored, treated, diagnosed, or prevented)
- Intended patient population (e.g., age, sex, weight, health, condition)
- Intended part of the body and/or type of tissue applied to or interacted with
- Intended user profiles, i.e., mental, physical, and demographic traits of each intended user group (lay or professional user, handicaps e.g., impaired vision)
- Intended use environment (e.g., including hygienic requirements, frequency of use, location, lighting, noise, temperature, mobility)
- Product's operating principle (Primary operating functions, end-to-end from opening the packaging until disposal

The Use Specifications is aligned with the User Requirements Specifications and product's Intended Use (see SOP-200 Design Control). The Use Specifications can be refined over time while more knowledge is gained through user research.

4.2.1 USER INTERFACE SPECIFICATIONS

The User Interface Specifications is part of the design input requirements (DIR) and contains testable user interface requirements. It shall include those requirements associated with risk control measures. User Interface Requirements (UIR) are identified in the template T-302-3 and verified according to the verification and validation plan (see SOP-200 Design Control). The Traceability Matrix T-200-10 is used to verify the completion of each User Requirement Specification (URS), Design Input Requirement (DIR) and Interface User Requirement (UIR).

4.2.2 TASKS ANALYSIS

Tasks are the actions the user is expected to perform to correctly use the product as per its intended use. Out of the task definition are all tasks that are not directly related to the use of the product by the user for its intended use, such as: The self-recognition of a medical need to determine whether to use the product and any treatment of the patient after using the product. Hazards and Hazardous Situations are related to tasks. The task analysis is included in the Product Risk Assessment T302-4.

4.2.3 FORMATIVE EVALUATION OF THE USER INTERFACE

Usability tests, cognitive walkthroughs, expert reviews, or other evaluation techniques as part of the formative evaluation shall be planned and carried out throughout the design and implementation of the user interface. Results of these evaluations shall support refinement of the design. Formative evaluation can be performed on prototypes that only allow testing one or more specific functions but also on fully functioning prototypes. It can be performed in a laboratory setting (e.g., saw bone), in a simulated environment (e.g., wet lab), or in the actual environment of intended use. Test subjects are generally users (e.g., clinicians), but also engineers, experts, designers, ergonomists etc. (depending on what shall be tested).

4.2.4 Summative Evaluation

The summative evaluation provides evidence of the usability and safety of the user interface. It is part of the validation of the device design and shall be carried out during the validation phase of the design and development process (see SOP-200 Design Control). Summative evaluation, including the selection of hazard-related use scenarios to be included in the evaluation, shall be planned. This plan can be documented in the Verification and Validation Plan (based on T-200-6) or a separate user interface evaluation plan. A successful summative evaluation demonstrates that the user interface is not vulnerable to potentially harmful use errors. Summative evaluation generally involves performing a usability test under conditions of simulated use. Tests shall be performed with devices that represent a final or near final design (e.g., 0-series or initial production run) in the actual intended use environment or at least a simulated use environment with real users (e.g., wet lab with orthopedic surgeons). Labeling (including but not limited to instructions for use and product labels) shall be of final or near final design and are subject to summative studies.

When the acceptance criteria of the summative evaluation are met, the usability engineering process will join the Risk Management process to evaluate residual risk.

4.2.5 Usability Engineering File

Formative and summative test protocols and reports shall be written according to the templates T-302-8A and T-302-8B, respectively, and recorded in the T-200-18 Test Report List.

All documents in the Usability Engineering File are part of the product's Design History File. During the entire lifecycle of a product, every change and every review of the Usability Engineering File documents shall be documented.

4.2.6 Usability Engineering Summary Report

The Usability Engineering Summary Report is documented as part of the Risk Management Report T-302-2

5 REFERENCES

Procedures, instructions, and guidelines
EN ISO 14971: 2019 Medical devices – Application of Risk Management to medical devices
ISO/TR 24971:2020 Medical devices — Guidance on the application of ISO 14971
IEC 62304:2006/A1:2015 - Medical device software – Software life cycle processes
IEC 62366-1: 2015 Medical devices - Part 1: Application of usability engineering to medical devices
EU Medical Device Regulation 2017/745
21 CFR 820, Quality System Regulations
FDA Guidance: Factors to Consider When Making Benefit-Risk Determinations in Medical Device Premarket Approval and De Novo Classifications
FDA Guidance: Consideration of Uncertainty in Making Benefit-Risk Determinations in Medical Device Premarket Approvals, De Novo Classifications, and Humanitarian Device Exemptions
FDA Guidance: Applying Human Factors and Usability Engineering to Medical Devices
FDA Guidance: Medical Device Use-Safety Incorporating Human Factors Engineering into Risk Management
SOP-100 Management
SOP-102 Clinical Evaluation
SOP-103 Complaint Hanlding
SOP-104 CAPA
SOP-105 PMS
SOP-106 NC handling
SOP-200 Design Control
SOP-208 Software Development

5.1 Templates and Forms

[1] T-105-2 PMS report

[2] T-200-6 Verification & Validation Plan
[3] T-200-7 Verification & Validation Summary Report
[4] T-302-1 Risk Management and Usability Engineering Plan
[5] T-302-2 Risk Management and Usability Engineering Report
[6] T-302-3 Hazards Assessment (Characteristics related to Safety)
[7] T-302-4 Product risk Assessment
[8] T-302-5 Design & Process FMEA
[9] T-302-6 Biological Evaluation Plan & Report
[10] T-302-7 Benefit-Risk Assessment
[11] T-302-8A Usability Test Protocol
[12] T-302-8B Usability Test Report

Appendix 1: ROLES AND RESPONSIBILITIES

Author is responsible for leading the document creation, for contacting and informing all stake holders through the risk record creation process.

The authoring of a Risk Management and usability document can be outsourced. In that case the ASPIVIX author shall coordinate the external provider, ensuring the availability of all inputs. The outsourced Risk Management and usability document shall be reviewed and approved as per the table below. Additional subject matter experts can be involved in the creation or review of the document as appropriate.

	Document	**R&D Representative, or Project Manager**	**CTO**	**Clinical Subject Matter expert**	**Commercial Representative**	**RAQM**
Risk Evaluation	T-302-1 Risk Management and Usability Engineering Plan	Author	Review	-	-	Approve
	T-302-3 Hazards Assessment	Author	Review	Review	-	Approve
	T-302-4 Product risk assessment	Author	Review	Review	Review	Approve
	T-302-5 Design and process risk assessment	Author	Review	-	-	Approve
	T-302-6 Biological Evaluation Plan & Report	Author	Review	-	-	Approve
	T-302-7 Benefit risk assessment	Author	Review	Approve	Review	Approve
	T-302-2 Risk Management and Usability Engineering Report	Author	Review	Approve	Review	Approve
Human Factors Evaluation	T-302-1 Risk Management and Usability Engineering Plan	Author	Review	-	-	Approve
	T-302-8A Usability test protocol	Author	Review	Review	-	Approve
	T-302-8B Usability test report	Author	Review	Review	-	Approve
	T-302-2 Risk Management and Usability Engineering Report	Author	Review	Review	-	Approve

Aspivix SA | Route de la Corniche 8 | Bureau 10 | 1066 Epalinges | Switzerland

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Participants

Signatory	Email	Email Verification
Eva Kilimtzidi	eva.kilimtzidi@aspivix.com	☑
	Signatory's hash: 5c82ba48970ca2c8f4cdea81ab2f5fe95d4c71c4d1f26c05a5d383489c3cb064	
Julien FINCI	julien.finci@aspivix.com	☑
	Signatory's hash: 79a0931948a72f84aa0ac74abf56ed20b30f3369a15ceb8c5e8374e9158130ba	
Mauro Rinaldi	mauro.rinaldi@aspivix.com	☑
	Signatory's hash: 6b9921bea42aa332590bce216bd2c0b312f057d3f3d842f63729ba00ea23a8f8	

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Aspivix
Route de la Corniche 8
1066 Epalinges | Switzerland
contact@aspivix.com
https://aspivix.com
Tax ID CHE-347.247.288 TVA

Action	By	Date (UTC)
Creation	Aspivix SA, Eva Kilimtzidi eva.kilimtzidi@aspivix.com	03/26/2025 15:21:08
	Signature: f7d10ef2ca3740f718d99ebb6692b08daf0e237dbb19fdba95d879ed9f70d2ca	
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	Signature: 70fbedf48bd741e522261a9ac1498d3b278fb4192ede943ace6098407a92249f	
Signature 	Aspivix SA, Mauro Rinaldi mauro.rinaldi@aspivix.com	03/27/2025 15:46:22
	Signature: 88145aa338e173ac9f24d48ba1d07dae3cb1896e0e993237798fd917f1c362ed	

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Aspivix SA, Mauro Rinaldi mauro.rinaldi@aspivix.com	03/27/2025 15:46:13	Before Signature

Aspivix
Route de la Corniche 8
1066 Epalinges | Switzerland
contact@aspivix.com
https://aspivix.com
Tax ID CHE-347.247.288 TVA