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RISK MANAGEMENT PLAN

WP8, TASK 8.2

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AUTHOR:

Ana Valkama (HUS)

ENDOTARGET

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EXECUTIVE SUMMARY

The objective of this deliverable is to provide a risk management work methodology for the ENDOTARGET project to manage and control those events that could have a negative impact on it.

It exposes the risk management approach for the project to manage and monitor all project risks in order to keep an eye on the day-to-day project management and detect potential or foreseeable risks as early as possible, thus implementing the needed mitigation measures to avoid their possible impact on the project.

This plan addresses the relevant roles and responsibilities for risk identification and assessment, the processes, tools, and procedures to be used for that, as well as the project risk control and mitigation response plan.

This deliverable contains the results of the first review and the update of the internal risk register tables.

The plan will be updated throughout the project in case it is needed.

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LIST OF ABBREVIATIONS

ACRONYM	DESCRIPTION
AI	Artificial Intelligence
D&C	Dissemination and Communication
EC	European Commission
ELISA	Enzyme linked immunosorbent assay
EU	European Union
F2F	Face to Face
GA	Grant Agreement
HUS	Helsinki University Hospital
iMM	Instituto de Medicina Molecular João Lobo Antunes
ISO	International Organization for Standardization
LPS	Lipopolysaccharides
PM	Project Management
RA	Rheumatoid arthritis

RDPT	Rheumatic disease prediction tool
SWOT analysis	Strengths, Weaknesses, Opportunities, Treats analysis
UNICAM	Università degli studi della Campania Luigi Vanvitelli
WP	Work Package
WP No(s)	Work Package Number(s)

1. INTRODUCTION

“Risk is a measure of the probability and consequence of not achieving a defined project goal.” (Kerzner 2017, 601)¹

Project risks refer to those that produce a negative effect on our project, so their identification and control are key pieces in the management of any project.

ENDOTARGET Work Package 8 is the Project Management Package, and one of its main objectives is to ensure the quality control of project results and risk management of the project.

WP8 contains task 8.2: Day-to-day management, which includes "risk management, i.e., preparing a risk management plan (with regular updates) and managing the risks under the whole project duration".

To comply with this important task, this risk management plan was developed, and its primary objective is to provide a management framework for the ENDOTARGET project to handle and control those events that could have a negative impact on it, namely, the risks that may appear and cause some or total damage to our project and to all the effort that all involved staff are putting into it.

ENDOTARGET is a complex project where multicentre clinical research, laboratory research, multiple cohort collaborations, organ on a chip and animal model, and data mining, among others, are carried out, so it requires clear processes and tools to execute a good risk management throughout the entire useful life of the project.

For that reason, this plan addresses the roles and responsibilities for their identification and assessment, includes the processes, tools, and procedures to be used for their mitigation and as well as the mechanisms for the possible mitigation measures implementation and control.

¹ Risk mitigation in Project Management: Case Horizon 2020. Hanna Kivisaari, Master Thesis, Tampere University of Applied Sciences:

https://www.theseus.fi/bitstream/handle/10024/226363/Kivisaari_Hanna.pdf?sequence=2

This plan reveals the risk management approach for the entire project and all project risks, providing a systematic approach from risk identification of potential risks to the control of the strategies or mitigation measures to be implemented.

This deliverable will be updated throughout the project in case it is needed.

2. RISK MANAGEMENT

2.1 RISK MANAGEMENT ROLES AND RESPONSABILITIES

Due to the multidisciplinary aspect of ENDOTARGET, the project handbook included the creation of a multidisciplinary HUS Coordinator Team for discussing the project process and controlling the risks during the 4 years.

The HUS Coordinator Team consists of ENDOTARGET members from HUS, the ENDOTARGET Coordinator.

The team is already actively functioning from the beginning of the project, and it will be ultimately responsible for the oversight of the entire project, controlling the deliverables and milestones, and applying the procedures established in this risk management process.

This team will be responsible for ensuring that the risks do not escalate. Once a WP leader or a member of ENDOTARGET informs them that a risk probability is advancing, the HUS Coordinator Team must jointly assess the risk with the risk owners and see if the risk owner can mitigate that risk alone or not.

Each partner must report to the WP leader and the HUS Coordinator Team as soon as it detects any risk situation that may impact ENDOTARGET, putting at risk delays or problems in some of its parts or its completion.

HUS Coordinator Team will monitor and control the risks during the project lifetime, and as a general rule, the risk owner is the WP leader of the WP affected by the risk.

In the case of actions and risks that include several work packages, the leaders of those WPs will have a shared risk responsibility.

The ENDOTARGET risk management will be performed by the **HUS Coordinator Team**, and it must:

- Overall responsibility for project success.
- Control the quality of the deliverables and the achievement of the milestones.
- Oversight of risk management activities.

- Monitor the project to identify possible risks that may impact the project.
- Control the risks identified and mentioned in the GA by the different WP leaders.
- Support the identification, assessment, and mitigation of risks.
- Collaborate, if it is necessary, with other WP leaders in the containment and implementation of possible mythification measures that are necessary to avoid an imminent risk.
- Make decisions on risk response strategies. The HUS Coordinator Team will have the final say on risk management and the measures to be taken, always trying to coordinate with the WP /WPs leaders appropriately.
- Report imminent risks to the Consortium and discuss possible risk strategies and mitigation measures with them.
- Compilation and maintenance of the Risk Register. The HUS Coordinator Team will carry out a constant assessment of the real-risk situation of the project.

Work Package leaders: They are responsible for the correct implementation of their WP, thereby, assume the risks responsibility of their WP; therefore, they will:

- Be the responsible for the correct development of the WP tasks and send the deliverables on time.
- Be responsible for the performance and progress of the WP with regards to the planned milestones.
- Be the risk owner for their own WP, the tasks, deliverables, and milestones within their own WP.
- Actively participate in risk identification and assessment.
- Report potential risks promptly to the HUS Coordinator Team. WP leaders are responsible for identifying and communicating any risk that occurs in their WP.
- Provide input on potential risks within their areas of expertise.
- Be responsible for the impact of the risk on their WP, and for implementing specific risk response strategies.
- Provide updates on the status of risk response actions.
- Help other risk owners create and control risk strategies.
- WP leaders must inform the HUS Coordinator Team without delay in case the risk leader is going to need help from other WP leaders or task leaders to control the situation risk.

All ENDOTARGET members must be attentive and notify their immediate superior or WP leader of any detected risk as soon as possible, and it must be communicated to the HUS Coordinator Team.

2.2 RISK MANAGEMENT PROCESS DESCRIPTION

The literature related to the risk management process², establishes that this risk management process entails a series of steps and actions that have been adapted to the ENDOTARGET project based on the type of project, its WPs, and the potential and foreseeable risks recognized by the ENDOTARGET partners.

ENDOTARGET risk management process considers the following steps:

- To identify potential risks that could impact the project.
- To assess and prioritize identified risks based on their likelihood and impact.
- To develop effective risk mitigation and response strategies.
- To establish a framework for ongoing monitoring and control of risks.



Figure 1: Risk Management Process Description

² Risk mitigation in Project Management: Case Horizon 2020. Hanna Kivisaari, Master Thesis, Tampere University of Applied Sciences:

https://www.theseus.fi/bitstream/handle/10024/226363/Kivisaari_Hanna.pdf?sequence=2

Gestión de riesgos en proyectos de investigación, Fernando Ubieta Romero, trabajo de fin de Grado, Universidad Politécnica de Madrid:

https://oa.upm.es/68567/1/TFG_FERNANDO_UBIETA_ROMERO.pdf

OpenPM², and European Academy Resources:

<https://www.europeanacademy.com/templates-guides/>

ISO 31000:2018 Risk management -- Guidelines, International Organization for Standardization

<https://www.iso.org/obp/ui/#iso:std:iso:31000:ed-2:vl:en>

Project Management

<https://www.projectmanager.com/blog/risk-management-process-steps>

Risk Identification:

The objective of this step is the identification and documentation of a risk that may occur throughout the entire life of the ENDOTARGET.

For risk identification, we can use, for example, checklists, brainstorming, and SWOT analysis.

As tools and techniques, the most appropriate for ENDOTARGET will be the risk register, information gathering, and expert judgment.

Any ENDOTARGET member or partner can identify a risk and is responsible for reporting the potential risk by informing the task leader, WP leader, or project coordinator.

The remote monthly WP meetings, as well as the biannual general assemblies and biannual meetings of the consortium, will be very important events where identify and anticipate risks.

Also, the analysis of the management, quality, and delivery of the project deliverables by the project partners, and the achievement or not of the milestones on time, can also help give some indication to the HUS Coordinator Team about possible risks that are coming and may affect the smoothness and good work of the project in general.

All ENDOTARGET members must be alert and report any detected risk as soon as possible.

Risk Assessment:

The second step in this process is the risk assessment. This evaluation is a very important step to carry out before implementing any plan or mitigation measure because the assessment requires a quantitative analysis (timeline, budget, risk owner, WP, or WPs involved) and also an objective qualitative analysis regarding the probability of its occurrence and the scope of the impact to finally be consistent with the proposal of mitigation measures to be taken.

The qualitative risk analysis will be carried out by the Risk Likelihood and Impact Matrix, whose main variables are the Likelihood, which measures the chance of occurrence, and the magnitude of the Impact, which measures the level of the impact in case it comes real.

The literature related to the risk management process³ has a varied range of proposals as a risk matrix, and for ENDOTARGET the following has been selected:

Likelihood	High	Medium	High	High
	Medium	Low	Medium	High
	Low	Low	Low	Medium
		High	Medium	Low
		Impact		

Figure 2. Risk Likelihood Impact Matrix

The risk matrix presents the risk visually, with likelihood and impact on the axes.

Likelihood represents the probability of a risk event occurring.

Impact represents the effect of a risk event on project / WP objectives.

Risk Response Planning:

The purpose of this step is to select the best response strategy for the risks once identified and evaluated in the previous steps.

Mitigation measures are the actions planned to reduce the likelihood or impact of a risk.

³ 3 Risk mitigation in Project Management: Case Horizon 2020. Hanna Kivisaari, Master Thesis, Tampere University of Applied Sciences:

https://www.theseus.fi/bitstream/handle/10024/226363/Kivisaari_Hanna.pdf?sequence=2

Gestión de riesgos en proyectos de investigación, Fernando Ubieta Romero, trabajo de fin de Grado, Universidad Politécnica de Madrid:

https://oa.upm.es/68567/1/TFG_FERNANDO_UBIETA_ROMERO.pdf

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Project Management

<https://www.projectmanager.com/blog/risk-management-process-steps>

This step mainly consists of the development of strategies and the establishment of the mitigation actions for its containment, as well as a possible reprogramming of some sub-tasks or planned actions to reduce the probability of the occurrence of a high project impact.

The literature on risk management mentioned above says that we can make a response plan for a risk based on four strategies: avoid or eliminate the risk, reduce or mitigate it, transfer or share it, or accept the risk.

Depending on the risk in question and its level of impact, we will select one strategy response plan or other.

During this response planning, actions will have to be prioritized according to the repercussions of the risk to be solved, acting a priori on the factors that could transform the risk into a real event, and if it is not possible to modify or eliminate those causal factors from the risk, then a plan with possible mitigation measures will be adopted in the event that the risk increases its possibility of occurrence and/or the severity of its impact.

We must take into account in this planning the possibility of scalability of the risk and also if other WPs, which at first do not seem to be, may be affected.

Risk Control.

The purpose of this step is to monitor and control the implementation of risk response activities while continuously monitoring the project environment for new risks or changes (probability and/or impact) to already identified risks. The monitoring and control process is a continuous process that must be carried out throughout the life of ENDOTARGET, with the aim of ensuring the correct development of the project at all times. This control process requires keeping our risk matrix updated at all times and considering the inclusion of new measures and actions when necessary. Risk control also involves the implementation of mitigation measures provided in risk response planning in order to keep potential risks under control.

At ENDOTARGET, risk control will be carried out constantly through the daily management of the project (delivers, milestones, wp meetings, consortium meetings, etc), and the WP leaders will be contacted with a certain periodicity for the qualitative analysis of the risks in order to reassess the probability and degree of impact of their previously recognized risks.

In the case of the periodic risk assessment, if the HUS Coordinator Team sees that a risk drastically increases its level of probability and/or severity of its impact on several WPs, or if several WP leaders report its severity and need for control, the HUS Coordinator Team may create a management and control team for a specific risk with the affected WPs or task leaders. The Risk Team will be dissolved as soon as the degree of tension over that specific risk is minimized or disappears.

2.3 RISK REGISTER TEMPLATE

The risk register template will be an important tool to be used for risk management.

In the case of a positive detection and identification of a risk for an ENDOTARGET member, a risk register will be created.

This risk register will include at least the following sections:

- Identification and description: all ENDOTARGET members can identify a risk. On the template, we should recognize the risk with:
 - o Number: All risks will be given a number.
 - o Description: A brief but concise description of the risk will be given.
 - o WP No(s): The WP that would be affected will be identified.
- Assessment: The risk assessment must be done by the WP leader(s) responsible for the risk:
 - o Level of Likelihood: low, medium, or high
 - o Level of severity in case of Impact: low, medium, or high
 - o In cases of high probability or impact, the risk should also be evaluated quantitatively (timeline, budget, personnel for the WP and also at project level).
- Response planning: The Proposed Mitigation Measures: The WP risk owner will propose a series of mitigation measures for each specific risk and, if necessary, will be responsible for their implementation once the risk has been communicated and the execution of the measures has been agreed upon with the HUS Coordinator Team and/or other affected WPs and partners.

Risk Register Template

Risk Register Level of Likelihood: Low, Medium, High Severity of the Impact: Low, Medium, High					
Risk number	Description	WP No(s)	Likelihood	Impact	Proposed Mitigation Measures

Table 1: Risk Register template

3. ENDOTARGET RISK REGISTER

During the preparation stage of the Grant Agreement, the coordinator has collected the project risks with the active participation of all ENDOTARGET WP leaders.

At that time, the main risk areas were identified and mitigation measures were proposed to avoid, or at least mitigate, the impact of foreseeable risks for the successful completion of the project. (GA, part A of the “Description of the Action”)

To carry out this risk management plan and subsequent control work, the risk register was sent again in December 2023 to the WP leaders, a year after the project started, to be qualitatively re-evaluated and reanalyzed according to the level of probability and severity of the impact in case the risk turns into a real issue.

The Risk Register will be regularly updated throughout the project lifecycle. Updates may include newly identified risks, changes in risk status, or modifications to risk response strategies from our WP leaders.

Table 2: Risk Register

Risk Register					
Level of Likelihood: Low, Medium, High					
Severity of the Impact: Low, Medium, High					
Risk number	Description	WP No(s)	Likelihood	Impact	Proposed Mitigation Measures
1	Re-emergence of COVID-19 and risk of; i.) non- attainment of target number of patient samples in cohort studies (WP2) ii.) Difficulty to fulfil the clinical interventional study design (WP4) iii.) Challenges to participate in in-person F2F dissemination activities (WP7)	WP2	Low	Medium	i. WP2 will continue to perform analysis on previously collected samples. ii. Diet Intervention Study in RA (WP4) will transform the in-person activities to remote ones, including virtual culinary workshops, weekly online nutrition appointments and home- delivery of food baskets with recipes. The multicentre trial on larazotide in RA will provide the drug and the placebo at home (WP4). iii. All "in presence events" will be switched to an online-only format (WP7).
		WP4	Low	Low	
		WP7	Low	Low	
2	Methodologic Risk: Not recruiting the target number of patients for the clinical trial (Diet intervention study & Multicentre study on the efficacy of larazotide in RA).	WP4	Medium	Medium	iMM has vast experience in conducting translation studies and clinical trials and it follows a large group of RA patients. We will analyse recruitment rate monthly. If there is under enrolment, we will plan strategically in order to recruit a higher number of patients. HUS and UNICAM also have a track record of recruiting patients for interventional studies. If required, recruitment can be expanded to other local hospitals with rheumatology units and national patients' organizations.
3	Technology risk: Poor correlation between the high-throughput technologies and other diagnostic platforms used in the clinics.	WP2	Low	Medium	Lab testing shows good correlation in biomarker performance between standard ELISA, lipidprofiling and microbiome analysis. In addition, data obtained can be used immediately for development of new clinically useful tests.
		WP3	Low	Low	



Risk Register					
Level of Likelihood: Low, Medium, High					
Severity of the Impact: Low, Medium, High					
Risk number	Description	WP No(s)	Likelihood	Impact	Proposed Mitigation Measures
4	Clinical risk: Unknown whether new biomarker profiles will be discovered as the disease heterogeneity cannot be predicted – there is a risk of not finding clinically stratifying biomarkers.	WP1	Medium	High	Integration of data with genomic, lipidomic and microbiome data will lessen the risks of not providing clinically useful biomarkers. Consortium has experience in profiling many diseases with excellent results.
		WP5	Medium	High	
5	Statistical risk: Lack of power to identify risk factors that drive health to disease transition	WP1	Low	High	Our power calculations indicate that we should be successful. As the major aim is not to identify single risk factors for these outcomes this is not a major problem. We will use a relaxed significance level, aiming to a considerable enrichment of true risk factors for each measure being aware that some of the identified risk factors may be false positive.
		WP5	Low	High	
6	Methodology risk: Large variability of identified LPS origin from mass-spectroscopy and microbiome data.	WP2	High	Medium	Search for commonalities in LPS structures and use a common structures LPS for functional studies.
		WP3	Medium	Low	
7	Methodology risk: No clear profile of candidate cytokines/proteins to be involved in trained immunity or tolerance is identified through proteomic analysis.	WP3	Medium	Low	Select candidate cytokines/proteins based on previous literature.





Risk Register					
Level of Likelihood: Low, Medium, High					
Severity of the Impact: Low, Medium, High					
Risk number	Description	WP No(s)	Likelihood	Impact	Proposed Mitigation Measures
8	Technological risk: Technology risk: Unauthorized data access	WP5	Low	High	All precautions against automated attacks are used, most importantly performing data security upgrades and monitoring system log files regularly. The software has active safety features like enforcement of strong passwords, and account locking after multiple authentication failures
		WP6	Low	Medium	
9	Legal: Getting access to sufficient data to ensure robust and unbiased AI models.	WP6	Low	Medium	Sufficient and legal measures will be put in place to show that data is handled appropriately. Clinical partners will provide a contact person to help facilitate access to data.
10	Ethical risk: Potential resistance to use AI-based predictions in clinical practice making it hard to assess effectiveness.	WP6	Medium	Low	All AI models will be created in accordance with the EU Ethics Guidelines for Trustworthy AI. The project partners will ensure use of the RDPT in their own institutions.



4. CONCLUSIONS

ENDOTARGET's key risk control tools are the Risk Management Plan itself, the Risk Register, and the Risk Likelihood Impact Matrix.

It is essential that risk management be an iterative process that is developed continuously throughout the entire life cycle of the project to ensure its continued relevance and effectiveness in managing risks.

The HUS Coordinator Team will control the risk management throughout the life of ENDOTARGET and will send this plan and the Risk Register to our WP leaders to update the risk register periodically, adding or updating the risks present in it, updating the risk assessments, as well as the mitigation measures proposed by the WP risk owners.

