SC1-PHE-CORONAVIRUS-2B

ENVISION

Intelligent plug-and-play digital tool for real-time surveillance of COVID-19 patients and smart decision-making in Intensive Care Units

Project No. 101015930

Deliverable Number	D5.4
Deliverable Title	Guidelines on ethical, social, legal and psychological aspects of ENVISION
Work Package Number	5
Work Package Title	Health Technology Assessment (HTA) and Ethical, Legal and Social Implications (ELSI)
Lead Participant	GUF
Contributors	GUF: Lea Grebe (LG), Markus Ketomäki (MK), Jan Kloka (JK), Benjamin Friedrichson (BF) UMCG: Thea van Asselt (TvA)
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Abstract

Within only six months, over 7.4 million people have been diagnosed with SARS-CoV-2. In the most severely hit countries, more than 10% of infected patients have received treatment in Intensive Care Units (ICUs). Insufficient data and limited knowledge on the disease as well as the lack of tools to support the intensivist in making accurate, timely and informed decisions have led to high mortality rates.

Continuous surveillance, the collection and intelligent analysis of data from many sources, including ventilators and electrical impedance tomography, would allow intensivists to decide on the best suitable treatment to accelerate the recovery of the often comorbid COVID-19 patients, while reducing the burden on clinical staff and healthcare costs. This information would also increase our understanding of the yet unknown course of disease, supporting other stakeholders in the quest for new therapies.

In ENVISION, our multidisciplinary public-private consortium will advance an innovative digital tool, Sandman.MD, a real-time and plug-and-play monitoring app, to an intelligent decision-support system for monitoring, prediction and treatment of COVID-19 patients in ICUs – the Sandman.ICU – reaching Technology Readiness Level 9 and ready for CE marking by the end of the project. The app has been developed by our SME partner app@work and was successfully introduced by several hospitals in Germany for use during the perioperative period. Sandman.ICU will be integrated into an AI-driven data analytics suite with predictive modelling tools and enhanced with a smart alert functionality. The digital tool will be validated and demonstrated in 13 hospitals across Europe. Our Health Technology Assessment expert partner will demonstrate the economic and societal value of Sandman.ICU, while an experienced SME will manage the innovation process in view of an immediate market uptake. The rollout will be supported by the European Society of Anaesthesiology and Intensive Care (ESAIC).

Revision history

Date	Authors	Revision
18.05.2021	Markus Ketomäki (GUF), Lea Grebe (GUF), Benjamin Friedrichson (GUF), Jan Kloka (GUF)	Draft version
19.05.2021	Thea van Asselt (UMCG)	Revision 1
27.05.2021	Thea van Asselt (UMCG), Markus Ketomäki (GUF)	Final version

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Partner short names

AAW	app@work GmbH
accelCH	accelopment Schweiz AG
accelDE	accelopment Deutschland GmbH
CCHT	Spitalul Clinic Judetan De Urgenta Pius Brinzeu Timisoara
CHUC	Centro Hospitalar e Universitario de Coimbra E.P.E.
DPT	Central Hospital of Southern Pest National Institute of Hematology and Infectious Disease
ESAIC	European Society of Anaesthesiology and Intensive Care
GUF	Johann Wolfgang Goethe Universität Frankfurt am Main
ICS-HUB	Institut Catala de la Salut – Bellvitge University Hospital
iDA	Intelligent Data Analytics GmbH & Co. KG
KC	Lietuvos Sveikatos Mokslu Universiteto Ligonine Kauno Klinikos
LMI	Löwenstein Medical Innovation GmbH & Co. KG
SE	Semmelweis Egyetem
TAU	Tampereen Korkeakoulusaatio SR
UCL	University College London
UMCG	Universitair Medisch Centrum Groningen
UMCL	Univerzitetni Klinicni Center Ljubljana
UMCM	Univerzitetni Klinicni Center Maribor
UMFCD	Universitatea de Medicina si Farmacie Carol Davila din Bucuresti
UNIPG	Università degli Studi di Perugia
UNITO	Università degli Studi di Torino

Abbreviations

D	Deliverable
EC	European Commission
EEA	European Economic Area
GDPR	General Data Protection Regulation
DSGVO	Datenschutz-Grundverordnung (German for GDPR)
H2020	Horizon 2020
M	Month
MS	Milestone
MDR	Medical Device Regulation
TLR	Technology readiness level
WP	Work Package

Executive Summary

The purpose of the deliverable D5.4 is to discuss the ethical, societal, legal and psychological aspects of the project ENVISION. As these four aspects can greatly influence the approval and acceptance of clinical projects, it is important to address them early on. The obligation for ethical reviews of clinical projects is also rooted in the European legislation. In this context, the legal frameworks relevant to ENVISION are the GDPR and the Medical Device Regulation. Sandman.ICU is planned to reach technology readiness level 9 (TRL) and be ready for CE marking by the end of the project. Thus, ISO 13485:2016 (requirements for a quality management system in the medical device industry) as well as the requirements for the CE marking constitute further relevant regulations to ENVISION. Potential legal obstacles to the deployment of Sandman.ICU may arise from the aforementioned regulations concerning medical products and CE marking, and in regard to the GDPR legal obstacles may arise from any potential country-specific derogations from the regulations on data protection. To aid the clinical partners in fulfilling the legal obligations in regard to ethics and data protection, templates and example documents, as well as a user guide with detailed explanations, were produced and provided to the clinical partners. The psychological and societal impacts of ENVISION were assessed using interviews (SPOTLIGHT) with professionals and end users.

Related deliverables:

D7.1: Templates of the informed consent/assent forms and information sheets (in language and terms intelligible to the participants) must be kept on file.

D7.2: Copies of approvals by ethics committees and/or competent authorities for the research with humans must be kept on file.

D7.3: Description of the anonymisation /pseudonymisation techniques that will be implemented must be submitted as a deliverable.

D7.5: A description of the technical and organisational measures that will be implemented to safeguard the rights and freedoms of the data subjects/research participants must be submitted as a deliverable.

D7.6: A description of the security measures that will be implemented to prevent unauthorised access to personal data or the equipment used for processing must be submitted as a deliverable.

1 Introduction

Sandman.ICU, the software to be developed in the ENVISION project, is intended to assist healthcare personnel in accurate and timely decision-making when treating COVID-19 patients in ICUs. Due to its intended purpose in healthcare setting and usage of personal data, apart from ethical and societal acceptance of the project, also an analysis of relevant European laws as well as identification of potential legal obstacles to the deployment of the solution developed in the ENVISION project are crucial to the project's success.

The deliverable 5.4 constitutes a part of the Work Package 5 (WP5), which overall deals with the health technology assessment and ethical, legal and societal implications of the project ENVISION. The success of Sandman.ICU depends both on its economic viability (established via economic assessment within WP5) as well as compliance with the relevant legal frameworks. This document focuses

foremost on the ethical, societal, legal and psychological aspects of ENVISION, leaving economic considerations out of scope.

1.1 Purpose of the deliverable

The purpose of this deliverable is to discuss the ethical, societal, legal and psychological aspects of the project ENVISION. Chapter 2 reviews the relevant European laws to the expected output from the ENVISION project, especially focusing on the relevance of the laws pertaining to medical devices and protection of personal data.. Further, the analysis will be used to identify any potential legal obstacles to the deployment of the solution developed during the ENVISION project. Following this, Chapter 0 focuses on the ethics approval process and describes the tools provided to the project partners to deal with the hurdles arising therefrom. Finally, Chapter 4 discusses the potential psychological and societal impacts of the project ENVISION and, thus, addresses the acceptance of using AI in a clinical setting among professionals and end-users. Further information on these topics is also available in the related deliverables listed in the executive summary and in the data protection concept of the project ENVISION.

2 European laws relevant to ENVISION

The General Data Protection Regulation (GDPR) and the Medical Device Regulation (MDR) are identified as the main relevant legal frameworks to the ENVISION project. The former aims to ensure data protection for all EU citizens and those living in EU countries. Country-specific derogations from the GDPR are allowed though in certain situations. The latter framework ensures the safety and efficacy of medical devices.

2.1 General Data Protection Regulation

The GDPR is the relevant legal framework on data protection and privacy in the European Union and the European Economic Area. According to Art. 4 No. 15 GDPR, health data is personal data which relates to the physical or mental health of a natural person, including the provision of health services, and from which information about his or her state of health is derived. Thus, the personal medical data to be processed in a research project belongs to the health data, which contains special categories of personal data according to Art. 9 GDPR. In this context it bears mentioning that Sandman.ICU will work solely on pseudonymised data. Further information on this is available in Deliverable 7.3 (POPD – Requirement No. 3).

The main purpose of the GDPR is to allow individuals control over their personal data and to unify the related regulations within the EU. The regulation contains provisions and requirements related to the processing of personal data of individuals located in the European Economic Area (EEA) and applies to any organisation processing this information inside the EEA, regardless of the location of the organisation and the citizenship or residence of the concerned individuals. However, it should be mentioned that the GDPR allows the Member States to introduce derogations to the regulations on data protection. Thus, country-specific regulations have to be observed where necessary.

The GDPR defines several obligations that organisations dealing with personal data must fulfil. The ENVISION project fulfils these requirements with its data protection concept, data protection impact assessment, and role and authorisation concept (see Chapter 3.2 for more details on these

documents). Of these three documents, the latter two constitute annexes to the data protection concept and all three documents are mandated by the GDPR. These documents were prepared in close dialogue with the data protection officer of Gutenberg University Frankfurt (GUF) starting from the beginning of the project. The initial draft of the data protection concept, including annexes, was completed and submitted to the ethics committee at GUF in January 2021 for approval. Following this, the ENVISION project was approved by the local ethics committee in Frankfurt on 15 February 2021 (see also D7.1 and D7.2 for further information). The data protection concept, data protection impact assessment, and the role and authorisation concepts were finalised in cooperation with the local data protection officer following the approval. The indication of the partner responsible for the data hosting was excluded from the data protection concept until now as the evaluation and the selection process is planned to be finished only in May / June 2021. After the selection process, the data protection concept will be updated in close communication with the data protection officer to contain the relevant information on the data hosting partner. After the update, the data protection concept will be reviewed again by the data protection officer at GUF to ensure compliance with the GDPR.

The submission of these documents is also required for the approval process by the local ethics committees of the participating clinical partners. A positive vote by the ethics committees of the participating clinical partners is necessary for the ENVISION project. For this purpose, the original documents submitted to the ethics committee at GUF, including the ethics approval, were uploaded to the project cloud to assist the clinical partners in their own respective approval processes. The data protection documents from GUF were also used to prepare templates and a user guide to further assist the clinical partners in receiving the respective local ethics approval for their participation in the ENVISION project. Further information on this and the training of the project partners on the ethical and legal implications is offered in Chapter 0.

2.2 Laws and regulations pertaining to medical devices

Sandman.ICU is planned to achieve technological readiness level (TRL) 9 and to be ready for CE marking by the end of the ENVISION project (currently TRL 7). Thus, the Regulation (EU) 2017/745 on medical devices constitutes a relevant legal framework for ENVISION. Potential country-specific regulations on medical products, such as the German Act on Medical Devices, are also expected to be relevant.

The market launch of Sandman.ICU is planned to be implemented by Löwenstein Medical Innovation after the ENVISION project. Thus, Löwenstein Medical Innovation is required to comply with ISO 13485:2016 (requirements for a quality management system in the medical device industry) as well as with the requirements for the CE marking.

2.3 Potential legal obstacles to the deployment of the solution developed in ENVISION

Based on the review of the relevant regulations to ENVISION, potential legal obstacles to the deployment of Sandman.ICU may arise from regulations concerning medical products and CE marking as discussed in Chapter 2.2. Further potential legal obstacles may arise from country-specific derogations to the GDPR as mentioned in Chapter 2.1. In addition, potential legal obstacles in the context of GDPR may arise later through the involvement of organisations from other Member States currently not represented in ENVISION.

3 Training of project partners on the ethical and legal implications inherent to ENVISION

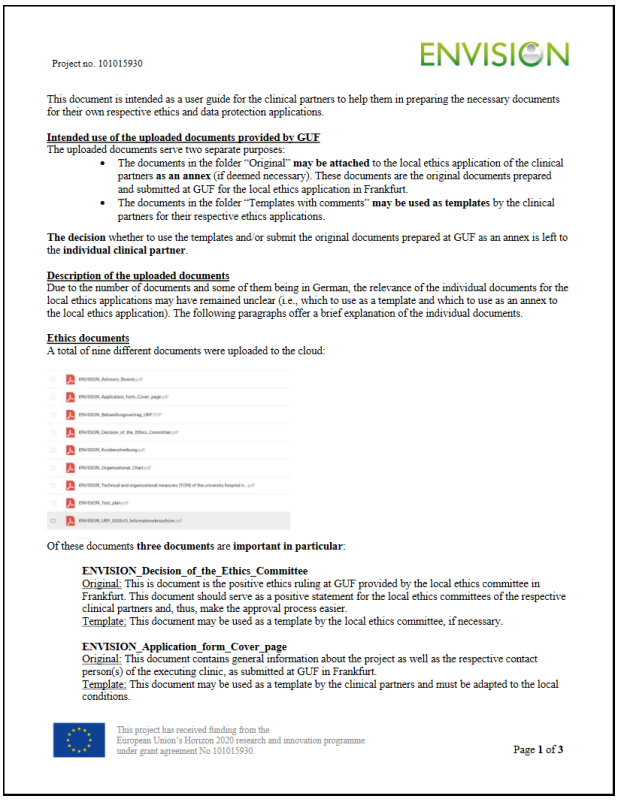
The following chapter addresses the topics related to the training of the clinical partners on the ethical and legal implications inherent to ENVISION. Other documents relevant to the training of the partners have also been prepared in the context of WP7. These include:

- D7.1: Templates of the informed consent/assent forms and information sheets (in language and terms intelligible to the participants).
- D7.2: Copies of approvals by ethics committees and/or competent authorities for the research with humans.
- D7.3: Description of the anonymisation /pseudonymisation techniques that will be implemented.
- D7.5: A description of the technical and organisational measures that will be implemented to safeguard the rights and freedoms of the data subjects/research participants.
- D7.6: A description of the security measures that will be implemented to prevent unauthorised access to personal data or the equipment used for processing.

3.1 Ethics approval process

By February 15, the ENVISION project was approved by the local ethics committee at GUF. To simplify the approval process, there has to be a second ethics vote received by the local ethics committees of the clinical partners. The relevant documents for the GUF ethics vote were provided to the clinical partners by 12 March 2021 after they were uniformly translated into English. Prior to data acquisition, the clinical partners must receive an approval from their respective local ethics committees. As of Milestone 13 (D4.2) “Clinical partners ready to start data collection”, this is expected to be achieved at the end of July 2021. Some of the documents provided by GUF could be directly attached to the respective ethics application of the individual partner clinics in their current form; others could be used as templates by the partner clinics. The documents provided by GUF also included a user guide (see Figure 1), which explained the provided documents in detail as well as offered further assistance to the clinical partners in compiling their own applications.

The templates must be adapted to local conditions by each clinical partner. On the part of GUF, comments were attached to indicate the points to be adjusted.



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ENVISION

This document is intended as a user guide for the clinical partners to help them in preparing the necessary documents for their own respective ethics and data protection applications.

Intended use of the uploaded documents provided by GUF
The uploaded documents serve two separate purposes:

- The documents in the folder "Original" **may be attached** to the local ethics application of the clinical partners **as an annex** (if deemed necessary). These documents are the original documents prepared and submitted at GUF for the local ethics application in Frankfurt.
- The documents in the folder "Templates with comments" **may be used as templates** by the clinical partners for their respective ethics applications.

The decision whether to use the templates and/or submit the original documents prepared at GUF as an annex is left to the **individual clinical partner**.

Description of the uploaded documents
Due to the number of documents and some of them being in German, the relevance of the individual documents for the local ethics applications may have remained unclear (i.e., which to use as a template and which to use as an annex to the local ethics application). The following paragraphs offer a brief explanation of the individual documents.

Ethics documents
A total of nine different documents were uploaded to the cloud:

Of these documents **three documents** are **important in particular**:

ENVISION_Decision_of_the_Ethics_Committee
Original: This is document is the positive ethics ruling at GUF provided by the local ethics committee in Frankfurt. This document should serve as a positive statement for the local ethics committees of the respective clinical partners and, thus, make the approval process easier.
Template: This document may be used as a template by the local ethics committee, if necessary.

ENVISION_Application_form_Cover_page
Original: This document contains general information about the project as well as the respective contact person(s) of the executing clinic, as submitted at GUF in Frankfurt.
Template: This document may be used as a template by the clinical partners and must be adapted to the local conditions.

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 101015930.

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Figure 1: A user guide for the templates and documents provided to the clinical partners.

A total of nine different ethics documents were created and provided to the clinical partners:

- Overview of the advisory boards
- Application form cover page
- Behandlungsvertrag UKF (treatment contract of university hospital Frankfurt (UKF) in German, translation not available)
- Decision of the ethics committee
- Kurzbeschreibung (project summary in German, translation not available)
- Organisational chart
- Technical and organisational measures (TOM) of the university hospital network
- Test plan
- UKF DSGVO Informationsbroschüre (data protection information brochure of universtiy hospital Frankfurt in German, translation not available)

The contents of the documents are as follows:

- The **Advisory boards document** lists the members of the external advisory boards of the ENVISION project.
- The **Application form cover page** contains general information about the project as well as the respective contact person(s) of the executing clinic, as submitted at GUF in Frankfurt. The clinical partners could use this document as a template after necessary adjustments to the local conditions.
- The document **Behandlungsvertrag UKF** represents the treatment contract used at the university hospital Frankfurt and it provides general facts about the treatment to the patients. This document was intended as an example and was to be substituted with the treatment contract of the respective clinical partner.

- The **Decision of the ethics committee** document is the positive ethics ruling at GUF provided by the local ethics committee in Frankfurt. This document was intended as a positive statement for the local ethics committees of the respective clinical partners and, thus, make the approval process easier. The local ethics committee, if necessary could also use this document as a template.
- The document **Kurzbeschreibung** offers a brief description / summary of the project contents in German.
- The **organisational chart** describes the distribution of roles of the parties in the project.
- The **Technical and organisational measures (TOM) of the university hospital network** document describes the appropriate technical and organizational measures to ensure the protection of the rights and freedoms of natural persons with regard to the processing of their personal data. This document is to be replaced by the TOM of the respective clinical partner.
- The **Test plan** (from German "Versuchsplanung", i.e. study plan or outline) describes the contents and the scope of the project more in detail (objectives, background, etc.) and lists the people participating in it at the hospital (here GUF). This document could be used as a template by the clinical partners and was to be adapted to the local conditions.
- The document **UKF DSGVO Informationsbroschüre** (the data protection information brochure of university hospital Frankfurt in German) describes the general rules of data collection and data processing of patients at university hospital Frankfurt. This document is to be replaced with the information booklet of the respective clinical partner.

3.2 Data protection

In addition to the ethics documents, further templates for the data protection were prepared and translated. A total of seven documents were made available to the clinical partners:

- D4.1 Study Protocol and SOP
- Data protection concept
- Data protection impact assessment
- Data protection impact assessment - risk analysis/treatment
- Participant contact list
- Data protection authorization concept
- Technical and organisational measures (TOM) of the university hospital network

The contents of the documents are as followed:

- The **D4.1 Study Protocol and SOP** provides method sheets to outline the processes and/or procedures required for this project in accordance with the study protocol and requirements as part of WP4.
- The **Data protection concept** contains the most important facts about data collection, as well as the measures and the regulations for compliance with the data protection laws in Germany. This document must be adapted to the local conditions of the respective clinical partner.
- The **Data protection impact assessment** document provides an overview of the data protection processes and an assessment of the existing risks for ensuring data security in the project at GUF.
- The **Data protection impact assessment - risk analysis / treatment** document provides an assessment of the existing risks for ensuring data security in the project ENVISION. This document must be adapted to the local conditions of the respective clinical partner.

- The **Participant contact list** contains the contact information of the project members and organisations.
- The **Data role and authorisation concept** describes the roles and their respective access rights as well as how the data protection requirements are implemented at ENVISION. This document must be adapted to the local conditions of the respective clinical partner.

3.3 Further documents

Other documents besides the templates and example documents relating to ethics and data protection were provided to the clinical partners as well. These consisted of an action plan for the clinical partners and a tracking list.

3.3.1 Action plan

The action plan for the clinical partners in obtaining an ethics approval consists of following points:

- Obtaining the local ethics vote
- Approval and establishment by MT/IT local clinic for the use of the Sandman.ICU (due to possible technical risks associated with new equipment)
- Approval and establishment by local clinic for the use of Elisa 600 (single ventilator type to be used initially due to the heterogeneity of clinical equipment at partner hospitals)
- Obtaining the local data protection vote

Hence, the clinical partners were also asked to pre-inform their local ethics committee on the ENVISION project and to adapt the templates/documents to local country-specific circumstances.

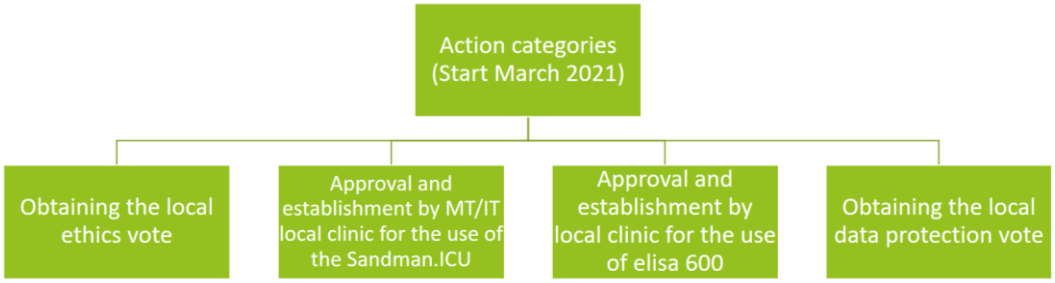

Figure 2: Action plan provided to the clinical partners.

3.3.2 Tracking list

A tracking list for all progress categories was uploaded in March 2021. Each clinical partner was required to check if the data entered has been presented correctly and adjust the information if necessary.

			Data Protection					
Organisation name	Short name	Country	Documents on data protection concepts sent to partners	Feedback on documents	Involvement of local data protection	Adaptation of documents to local requirements	Local approval of the data protection concept	Loc a
Semmelweis Egyetem	SE	HU						
Central Hospital of Southern Pest National	DPC	HU						
Universita degli Studi di Perugia	UNIPG	IT						
Universita degli Studi di Torino	UNITO	IT						
Lietuvos Sveikatos Mokslu Universiteto Ligonine Kauno Klinikos	KC	LT						
Centro Hospitalar e Universitario de Coimbra E.P.E.	CHUC	PT						
Universitatea de Medicina si Farmacie Carol Davila din Bucuresti	UMFCD	RO						
Univerzitetni Klinicni Center Ljubljana	UMCL	SI						
Univerzitetni Klinicni Center Maribor	UMCM	SI						
Institut Catala de la Salut	ICS-HUB	ES						
University College London	UCL	UK						
Spitalul Clinic Judetan De Urgenta Pius Brinzeu Timisoara	CCHT	RO						
x = done								
= open								
"-" = No								
"+" = Yes								

Figure 3: Tracking list for overall progress monitoring in preparation of the ethics applications and data protection documents.

4 Potential psychological and societal impacts of ENVISION

The analysis of potential psychological and societal impact of technologies developed in ENVISION was conducted using interviews with professionals and end users.

4.1 Analysis of psychological and societal impacts using interviews

The use of artificial intelligence (AI) assistance systems in medicine is becoming increasingly important and can offer great opportunities for clinical users. However, there is hardly any data on acceptance, experience and concern regarding AI support systems in hospitals (especially in the high-risk area of intensive care units). For this purpose, a Europe-wide questionnaire was developed to assess the acceptance of AI systems in medicine (SPOTLIGHT). SPOTLIGHT intends to measure the use of artificial intelligence and its acceptance among medical professionals at hospitals. Due to the lack of scientific data that addresses this topic at the European level, a high-impact publication based on these results is expected.

Additionally, a close and continuous contact will be maintained with the individual project partners in order to be able to respond in the best possible way to the interests, concerns and ideas of the individual stakeholders.

The individual interested parties also have the opportunity to directly interact with app@work. Telephone conferences are planned at regular intervals for this purpose.

4.2 Methodology of interviews

The survey is completely anonymous; data will be treated confidentially and will only be evaluated for scientific purposes. Participation in the survey is voluntary. The design is based on the Rogers et al. question model (Rogers, E. M. (2003). Diffusion of Innovations (5th ed.). New York: Free Press.) and is a validated survey design. To minimize the burden on the participants, the survey can be completed in under 5min. A number of 100 participants per country would be desirable for a country-specific

evaluation. To date, more than 800 people have taken part in the survey. As can be seen in Figure 4, medical professionals from all over Europe have participated in the interviews. Figure 5 and Figure 6 offer further insights into the distribution of the participants. A large number of participants we either specialists or senior consultants (as shown in Figure 5), and the participants mainly came from anaesthesiology and critical care departments (see Figure 6). A detailed statistical evaluation of the data will follow as the survey period has now ended. To ensure good scientific practice, the results are planned to be published in peer-reviewed journals.

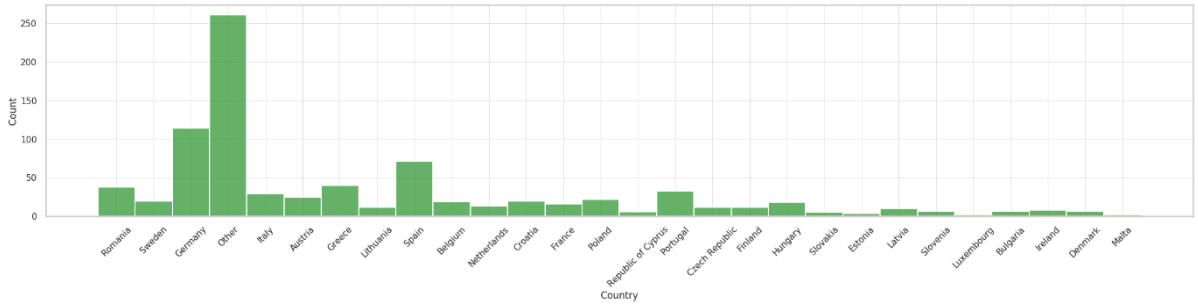

Figure 4: Distribution of respondents according to country.

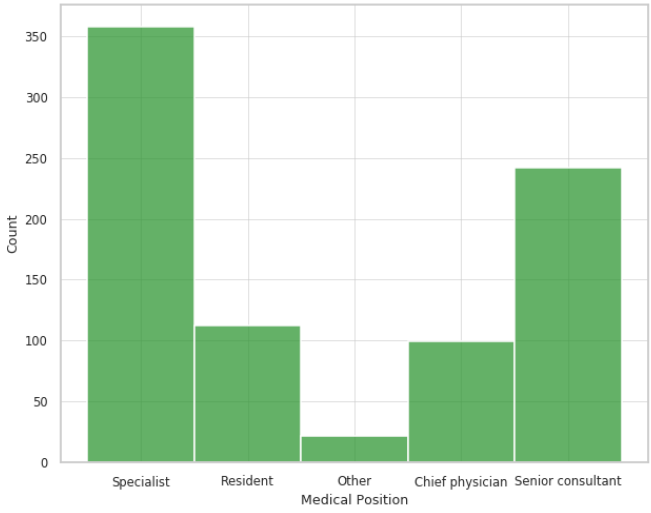

Figure 5: The distribution of the respondent according to the medical position.

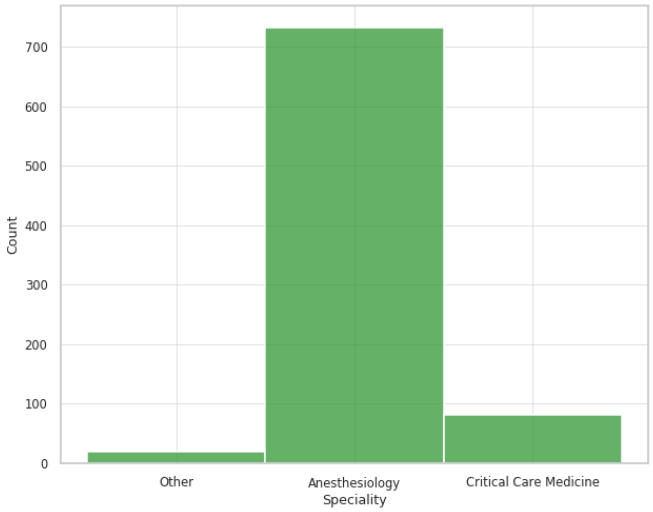

Figure 6: The distribution of the respondents according to departments.

5 Outlook

Matters relating to the ethics approvals and data protection matters have been addressed to since the beginning of the project ENVISION. One critical success factor for the ethics approval at GUF was the involvement of the data protection officer early on. Thus, in future projects, the data protection offices at local levels should be involved as early as possible to ensure rapid approval by the ethics committees.

The documents and the templates provided to the clinical partners have successfully aided the local ethics approval processes. At present, approximately a third of all clinical partners have received the approval of their local ethics committees and many of the pending approvals are scheduled for May to June 2021. This highlights the successful methodology implemented in the project ENVISION so far. The progress of the local approvals will be monitored, and supported where necessary, by the project coordination team.

At this stage, it is planned that all clinical partners will have their positive ethics vote in accordance with the deadline before reaching milestone MS13 (4.2 - "Clinical partners ready to start data collection") at the end of July 2021. The ENVISION project team is particularly proud that all clinical partners are expected to start collecting data before milestone 13 expires.