INNOVATION PROJECT SUOG (20062)

Final Report

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EXECUTIVE SUMMARY

This report is intended to provide market and business development support services implemented for an innovation project SUOG by an independent consultancy company Civitta. More specifically, this report is intended to provide answers to the following requests:

1. Refine the business model and market strategy;
2. Refine the regulatory strategy.

To ensure that SUOG reaches its full potential, Civitta consultants executed market and regulatory analyses and evaluated the existing models and frameworks of SUOG.

Civitta experts provided recommendations on the unique selling proposition, product acceleration plan outline, and performed a regulatory strategy assessment.

BUSINESS MODEL

First, Civitta experts conducted market and competitor analysis in terms of possible benefits for developing countries without access to ultrasound experts on the one hand, and experts who want to improve the sensitivity of their ultrasound exams on the other. EU MSs were classified into three categories according to identified criteria and further researched. Moreover, the closest indirect competitors were identified together with potential future competitors by consulting with the consortium and performing in-depth desk research. Thereafter, dashboard analysis and categorisations were carried out in order to better determine the competitive advantage of SUOG. As a result, a communication concept that highlights the competitive advantage of the SUOG solution with regard to the different target markets was identified.

Thus, Civitta experts came up with the following recommendations:

- SUOG, even though unique and with no direct competitors, should be careful of potential competition and catching up from the other major market shareholders;
- Try to position itself with a unique selling point that highlights its unique features, such as guided ultrasound image analysis, adaptability, semantic- and AI-rendered knowledge base, user-Friendliness, and ontology;
- GE Healthcare's strengths should also be stressed with its excellent reputation and market share.

MARKET STRATEGY

Second, to fine-tune the market strategy, the product acceleration plan outline was devised. This entails the identification of possibilities for acceleration, whereby eight main recommendations are drawn. Following this, the main risks of such acceleration are determined, quantified, and mitigation measures for them strategised.

Notably, all are low risk and would not require immediate action—if at all.

Thus, Civitta experts came up with the following recommendations:

- In order to accelerate its development or to determine whether such an acceleration would be worth it, SUOG should consider the following elements: ensuring continued management involvement, maintaining a strong team, ascertaining continual communication, following limited product objectives, drawing up joint product specification, building comparative models, minimising procedures and controls.

REGULATORY STRATEGY

Third, the regulatory strategy is reassessed by considering the regulatory landscape of the EU as well as national reimbursement and financing measures of the selected countries, i.e. Poland, Germany, The Netherlands, France, Italy, and Spain. Further delving into policy analysis, EU-wide, as well as national

policies and recommendations, are outlined, which fall in line with SUOG's goals, creating a suitable environment for its commercialisation in these markets.

The comparative analysis that follows shows that there are a lot of similarities among EU MSs which would allow SUOG a more general approach to the European market, although these markets are still distinct enough to require additional time and resources for efficient entry. Similarly to the market strategy, the main regulatory risks are determined, quantified, and mitigation measures for them strategised. For this, risks range from low to high and, thus, would require more attention to detail and planning.

Thus, Civitta experts came up with the following recommendations:

- Consider the regulatory aspects and the device risk classes that determine the regulatory pathway and the whole supply chain;
- Fully anonymise data, used only as an encrypted knowledge base in its common repository of de-identified DICOM cases;
- Closely follow possible developments in the legislation and proactively update its risks and mitigation strategies.

CONTENTS

RECOMMENDATIONS

SERVICE REQUESTED	METHODOLOGY, ANALYSIS AND KEY FINDINGS	CONCLUSIONS	RECOMMENDATION	ANNEXE
Refine the business model and market strategy	**PART 1. BUSINESS MODEL** **METHODOLOGY |** Analysis of evaluator feedback report and Q&A sessions with consortium management personnel to better understand the developed technology and its application possibilities. Comparative analysis involving competitors in order to design a communication concept that highlights the competitive advantage of the SUOG **solution with regard to the different target markets.** **ANALYSIS | First, to distinguish global competitors that might impact the market capture of SUOG, the absence or presence of the following technical specifications of the competitors and their products are considered:** • **Guided image analysis– actual images integrated into the ultrasound systems on which the differential diagnosis tools are based;** • **Keywords–keywords search on which the differential diagnosis tools are further based;** • **Semantic reasoning/ontology–decision-support system with the ability to provide broad explanations about the ultrasound image findings, potential disorder origins, and outcomes. The system is an expert-validated knowledge base that improves the diagnostic performance of nonexpert examiners;** • **Adaptability–the software can adapt to unusual or abnormal findings;** • **On-premises software–installed and runs on computers on the premises of the person or**	**PART 1** **SUOG definitely possesses a competitive advantage as well as the potential advantage of the first mover.** **No competitors are direct, only indirect.** **Even then, the global market players are substantial and should be taken into consideration with caution in terms of the speed of the technology uptake after SUOG is commercialised.** **PART 2** **SUOG's acceleration plan is still in its infancy. With no clinical trial endpoints due to the lack of the CE mark, the outline of the acceleration plan is suggested in order to guide SUOG towards entering the market at its earliest capability with an optimal balance among time, quality, and money.**	**PART 1** To competitively position itself, SUOG should adopt USPs that focus on the following: • **Guided ultrasound image analysis;** • **Adaptability to unusual and abnormal findings;** • **Semantic- and AI-rendered knowledge base;** • **Friendly for any level of operator expertise;** • **Ontology-enabled automated reasoning and dynamically-derived personalised protocols.** **PART 2** **As a recommendation, in order to quantify the necessary steps needed to accelerate SUOG, several steps should be taken:** 1. **Determine the value of SUOG's development time by:**	Annexe 2 & Annexe 3

SERVICE REQUESTED	METHODOLOGY, ANALYSIS AND KEY FINDINGS	CONCLUSIONS	RECOMMENDATION	ANNEXE
	organization using the software, rather than at a remote facility such as a server farm or cloud. Second, for the identification of the two types of markets as mentioned by the consortium, solely EU MSs are considered in order to remain within the scope of the project. The three levels of a country's need for ultrasound range from 1 (the most in need) to 3 (the least in need), and are defined in Figure 1. To classify the countries accordingly, three criteria are used: • Physicians, obstetric and gynaecological group of specialities (pp), per 100 000, EU, 2018–to help identify countries where ultrasound machine technicians and/or OB/GYN experts are lacking and, thus, could have a higher demand for SUOG; • Practising midwives, per 100 000, EU, 2016–to help identify countries where ultrasound machine technicians and/or OB/GYN experts are lacking and, thus, could have a higher demand for SUOG; • Radiologists, per 100 000, EU, 2019–to help identify countries where ultrasound machine technicians and/or OB/GYN experts are lacking and, thus, could have a higher demand for SUOG. **KEY FINDINGS |** After analysing the competitiveness in the market, it can be seen that there are not many similar solutions to the problem on the market yet, therefore, it is not difficult to stand out. SUOG has distinctive capabilities compared to provided potential challengers: • Guided ultrasound image analysis, • Adaptability to unusual and abnormal findings, • Semantic- and AI-rendered knowledge base,		– Reviewing project product costs; – Develop alternative models. – Calculate trade-off rules. 2. Ensure continued management involvement; 3. Maintain a strong team; 4. Ascertain continual communication; 5. Follow limited product objectives; 6. Draw up joint product specification; 7. Build models; 8. Minimise procedures and controls. Moreover, to mitigate the potential risks that arise from product acceleration, SUOG should: • Consider the calculated profits in light of the trade-off rules/conversion rates when designing the product timeline so as to accelerate product development only	

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	• Friendly for any level of operator expertise, • Ontology-enabled automated reasoning and dynamically-derived personalised protocols. Moreover, the women's health ultrasound business of GE healthcare is uniquely positioned as the leader in the women's health segment with its • Continued innovation, • Unmatched image quality, • User-friendly devices, • Co-development with leading KOL's in the world, • External partnerships to augment and accelerate brand awareness. **PART 2. MARKET STRATEGY** **METHODOLOGY |** Analysis of the background materials from the consortium and Q&A sessions with the consortium management personnel were used to better understand what the starting position of SUOG is. Business and technology aspects of the project, as well as its organisational structure, product development cycle and strategy, the timeline, and the processes that it entails, were taken into account to the extent that such information as provided/existent. **ANALYSIS |** After outlining the main acceleratory elements, acceleration risks and mitigation measures are identified; they are evaluated on a two-dimensional matrix using a qualitative rating of the likelihood of the event occurring and the scale of the possible impact. As a result of evaluating the likelihood and impact risk, scores were set. In the risk matrix, there are three types of risks: low,		when the projected profits outweigh the projected costs; • Consider market-entry timing apropos political climate and business environment; • Stress very frequent, informal peer review to monitor and control progress; • Co-locate the team to enhance communication and commitment.	

SERVICE REQUESTED	METHODOLOGY, ANALYSIS AND KEY FINDINGS	CONCLUSIONS	RECOMMENDATION	ANNEXE
	medium, and high. The risk analysis provides information critical to determining what risks need to be treated and what risks are accepted. **KEY FINDINGS |** Acceleration risks vary depending on the medical device, however, those presented below are applicable beyond SUOG as well. The identified risks fall across risk categories, from low to medium to high. Taking this into consideration, those risks with the higher/highest risk scores should be emphasised and the mitigation measures prioritised.			
Refine the regulatory strategy	**METHODOLOGY |** Analysis of the background materials from the consortium and Q&A sessions with the consortium management personnel were used to better understand what the starting position of SUOG is. Additional research on various regulatory frameworks was conducted, thereby identifying best practices, and developing the pathways to ensure regulatory approval with their accompanying risks and mitigation strategies. Through desk research and policy analysis of the regulatory landscape, information about the requirements associated with certification were gleaned. Moreover, a comparative analysis of best practices was carried out in order to formulate the steps and pathways that SUOG should take to tackle potential regulatory barriers. **ANALYSIS |** In order to provide a snapshot of the regulatory processes in the EU, the countries that satisfy the following are analysed more in-depth: • Represent the diversity of legal processes pertaining to medical devices;	Routine ultrasound scans in OB/GYN are recognized both on the supranational level as well as on national levels. With most of the EU MSs having a specific policy or a recommendation in connection with the number of scans, SUOG seems to have a favourable regulatory landscape for entering these markets. Despite diagnostic device purchasing decision in the public sector in all countries belongs to each individual provider or at least to local authorities, the purchasing procedure is usually taking the form of public tenders. Moreover, financing and reimbursement decisions are centralized and regulated by laws and other acts.	As a recommendation, in order to tackle potential regulatory barriers, SUOG should: 1. Consider the regulatory aspects and the device risk classes that determine the regulatory pathway and the whole supply chain; 2. Fully anonymise data, used only as an encrypted knowledge base in its common repository of de-identified DICOM cases; 3. Closely follow possible developments in the legislation and proactively update its risks and mitigation strategies.	Annexe 4

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	• Have sufficient data available to determine the legalities; • Are not the UK, since the medical device market is subject to substantial changes due to Brexit; • Possess a considerable potential market. Thence, taking into account the four criteria mentioned above, the following countries are considered for in-depth analysis: Poland, Germany, The Netherlands, France, Italy, Spain. After the in-depth analysis, policy analysis of the EU regulatory landscape is performed together with an illustration of national policies. In line with this, regulatory risks and mitigation measures are identified; they are evaluated on a two-dimensional matrix using a qualitative rating of the likelihood of the event occurring and the scale of the possible impact. As a result of evaluating the likelihood and impact risk, scores were set. In the risk matrix, there are three types of risks: low, medium, and high. The risk analysis provides information critical to determining what risks need to be treated and what risks are accepted. **KEY FINDINGS |** EU-wide, the most relevant regulations on medical devices that apply to SUOG are the following: • Medical Devices Regulation (Regulation (EU) 2017/745); • Manufacturers of medical devices have to draw up the EU declaration of conformity (the CE mark);			

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	• **Manufacturers have to have in their organisation at least one person responsible for regulatory compliance;** • **Manufacturers have to plan, establish, document, implement, maintain and update a post-market surveillance system.** **Other regulations to take into account include:** • **Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community Code Relating to Medicinal Products for Human Use;** • **Standard ISO 14971 "Application of Risk Management for Medical Devices";** • **General Data Protection Regulation (GDPR) (Regulation (EU) 2016/679 of the European Parliament and of the Council of 27 April 2016 on the protection of natural persons with regard to the processing of personal data and on the free movement of such data and repealing Directive 95/46/EC).** **On the country level:** • In Poland, requirements for medical equipment in the primary care sector are regulated in a centralized way by the order of the President of the National Health Fund (NFZ). Procurement of medical equipment usually takes the form of open tenders. The main source of funding for medical equipment contracts with the NFZ, but in practice, other sources are needed such as the Ministry of Health, hospital owners, external sources or from individual and institutional donations. • **In Germany,**			

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	• **In the Netherlands, planning, purchasing and maintenance of medical devices are the responsibility of individual health care providers and institutions and there are no strict rules about it as long as they are achieving quality care standards.** • In France, the decision if a medical device will be admitted to reimbursement is centralised in the authority of the Health Minister and the decision to purchase medical device is decentralised and belongs to Regional Health Agencies (in both private and public sectors). • In Italy Diagnosis Related Groups Tariff determines if the medical device is reimbursed or not (in both public and private sectors). If it is – costs are fully covered by the National Healthcare System (SSN) and purchases take the form of public tenders if it is not – additional funding can be obtained at the regional level. • In Spain, official tenders are used for most public health care sector purchases and in the private sector, direct purchases are usually made. **Policy analysis reveals the following:** • **"Standards of Care for Women's Health in Europe" by The European Board and College of Obstetrics and Gynaecology. Standard 7 of the document is predicated on the rationale that Ultrasound scanning is an integral part of the investigation for a wide range of gynaecological conditions such as early pregnancy monitoring, management of infertility as well as diagnosis of benign and malignant gynaecological conditions.** • **European strategic approach for making pregnancy safer: Improving maternal and**			

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	perinatal health" by the WHO Regional Office for Europe also makes a point and emphasises the importance of organising and strengthening health service delivery through better infrastructure and medical equipment. On the country level: • Even though this was not the case before, there are no national scan policies in place in Croatia, but usually, three scans are performed. On the other hand, the Netherlands and Spain switched from not having an official policy to having one. Regulatory risks: • All identified risks are medium, forming a combination of unlikely events with tolerable or generally unacceptable negative impact.			

ANNEXES

ANNEXE 1. Q&A

#	QUESTION	ANSWER
1	Who are the main market competitors and how do they compare?	The most relevant competitors, though indirect, are Phenomizer, Phenotip Beta, Open-i. All these devices/software, have keywords as a feature, but only one other has semantic reasoning/ontology. As such, none of the others possesses guided image analysis, adaptability, and on-premises software as features/abilities, making SUOG a unique medical device. Other potential competitors include Siemens Healthineers, Koninklijke Philips MV, Esaote, Hitachi Medical Corporation, Samsung, Toshiba Medical Systems Corporation, Anlogic Corporation, Mindray Medical International LTD, Fujifilm Holdings Corporation, Hologic INC., Canon Medical Systems Corporation, Sonacare Medical LLC.
2	What should the communication concept highlight as SUOG's competitive advantage for countries without access to ultrasound experts on the one hand, and those with experts who want to improve the sensitivity of their ultrasound exams on the other?	For the first identified segment, the following features should be emphasised: • Guided ultrasound image analysis, • Semantic- and AI-rendered knowledge base, • Friendly for any level of operator expertise, • Ontology-enabled automated reasoning and dynamically-derived personalised protocols. For the second identified segment, the following features should be emphasised: • Adaptability to unusual and abnormal findings, • Semantic- and AI-rendered knowledge base, • Ontology-enabled automated reasoning and dynamically-derived personalised protocols.

#	QUESTION	ANSWER
3	**What are the possibilities for product acceleration?**	**To initiate the product acceleration plan development, SUOG should:** 1. Determine the value of SUOG's development time by: a. Reviewing project product costs; b. Develop alternative models. c. Calculate trade-off rules. 2. Ensure continued management involvement; 3. Maintain a strong team; 4. Ascertain continual communication; 5. Follow limited product objectives; 6. Draw up joint product specification; 7. Build models; 8. Minimise procedures and controls.
4	**What are the potential risks and their respective mitigation strategies related to the acceleration?**	**1. Speedy development can increase R&D expense, inflate the product costs and degrade SUOG's performance and quality:** **a. Considering the calculated profits in light of the trade-off rules/conversion rates, the product timeline will be accelerated only when the projected profits outweigh the projected costs. This takes into consideration performance and quality in light of maintenance costs, etc;** **b. Market-entry timing, in view of the market window, is contingent upon the completion of the new product's development cycle.** **2. Team members may be under work stress not only because of divided loyalties between their functional area and the development team but also because of the increase in their workload as a consequence of being a part of the development team:** **a. Stress very frequent, informal peer review to monitor and control progress;** **b. Co-locate the team to enhance communication and commitment.** **3. Launching a new product too early, particularly when the product is qualitatively not ready for the market:**

#	QUESTION	ANSWER
		a. **Upon the assessment of the various models and the subsequent alterations to the processes, whether pertaining to additional testing, contract services, incentives or travel costs, the product will be launched timely, rather than in the shortest period possible.**
5	**What steps should SUOG take to ensure certification and regulatory approval?**	Regardless of the national system, the first step of the regulatory strategy always constitutes the obtaining of the CE Mark. Thereafter, various national agencies need to be contacted. Despite the fact that diagnostic device purchasing decision in public sector in all countries belongs to each individual provider or at least to local authorities, the purchasing procedure is usually carried out in the form of public tenders. Moreover, financing and reimbursement decisions are centralised and regulated by laws and other acts. On the other hand, financing and purchasing decisions are less regulated in private sectors in all countries and, thus, it should be easier, and it would take less time to enter the private sector.
6	**What are the potential risks and their respective mitigation strategies related to the regulation?**	1. **Additional procedures and time needed in case the device falls under a higher risk category (invasive device, medical software):** a. **Development phase decisions should consider the regulatory aspects and the device risk classes that determine the regulatory pathway and the whole supply chain.** 2. **The use of patient data to build a reference annotated ultrasound images database might not be fully synchronised with the privacy and cybersecurity laws:** a. **The consortium should fully anonymise data, used only as an encrypted knowledge base in its common repository of de-identified DICOM cases, ensuring compliance with the following:** i. **GDPR;** ii. **Software as medical device regulations (sensitive patient data, conditions for consent, the security of processing);** iii. **EU Agency for Network and Information Security (ENISA) recommendations.**

#	QUESTION	ANSWER
		b. Due to the changes that are yet to be implemented in 2020, the consortium should closely follow possible developments in the legislation and proactively update its risks and mitigation strategies. 3. The ultrasound market is particularly susceptible to political unrest because most ultrasound tenders are controlled by state governments; the budget squeeze would also affect the private sector: a. SUOG is solving a problem of a highly unmet need within the society. Following the commercialisation plan and market capture estimates, the political environment should not have a substantial effect on SUOG's entry.

ANNEXE 2. REFINEMENT OF THE UNIQUE SELLING POINT (USP)

CONTEXT

Currently, GE is preparing to penetrate the European market with the SUOG system. During a discovery interview with the consortium, it was identified that a refinement of the USP is needed in order to better convey SUOG to its target markets. In order to find environments suitable for expansion of SUOG, several steps were taken. First, a general overview of the ultrasound market by application is outlined in order to gain an understanding of the global trends and better assess SUOG's unique points. Second, competitor analysis is necessary to apply appropriate market-penetrating strategies, combined with an emphasis on SUOG's distinctive features. Third, the consortium expressed interest in product-differentiating strategies between the countries with a lack of experts and countries with experts but willingness to increase ultrasound sensitivity. Therefore, such countries were classified according to relevant criteria. Finally, taking into account grouped countries, the USP was refined in regard to the communication concept that highlights the competitive advantage of SUOG considering the different target markets.

METHODOLOGY

Analysis of background materials from the consortium and Q&A sessions with consortium management personnel were used to better understand the technical specifications are other.

In order to identify potential and promising markets/countries, it is necessary to find suitable environments for the successful expansion of SUOG. Appropriate dilation domains can be acquired through the chain of methods explained below.

First, by distinguishing global competitors that might impact the market capture of SUOG. This is done by considering the absence or presence of the following technical specifications of the competitors and their products:

- Guided image analysis— actual images integrated into the ultrasound systems on which the differential diagnosis tools are based;
- Keywords—keywords search on which the differential diagnosis tools are further based;
- Semantic reasoning/ontology—decision-support system with the ability to provide broad explanations about the ultrasound image findings, potential disorder origins, and outcomes. The system is an expert-validated knowledge base that improves the diagnostic performance of nonexpert examiners;
- Adaptability—the software can adapt to unusual or abnormal findings;
- On-premises software—installed and runs on computers on the premises of the person or organization using the software, rather than at a remote facility such as a server farm or cloud.

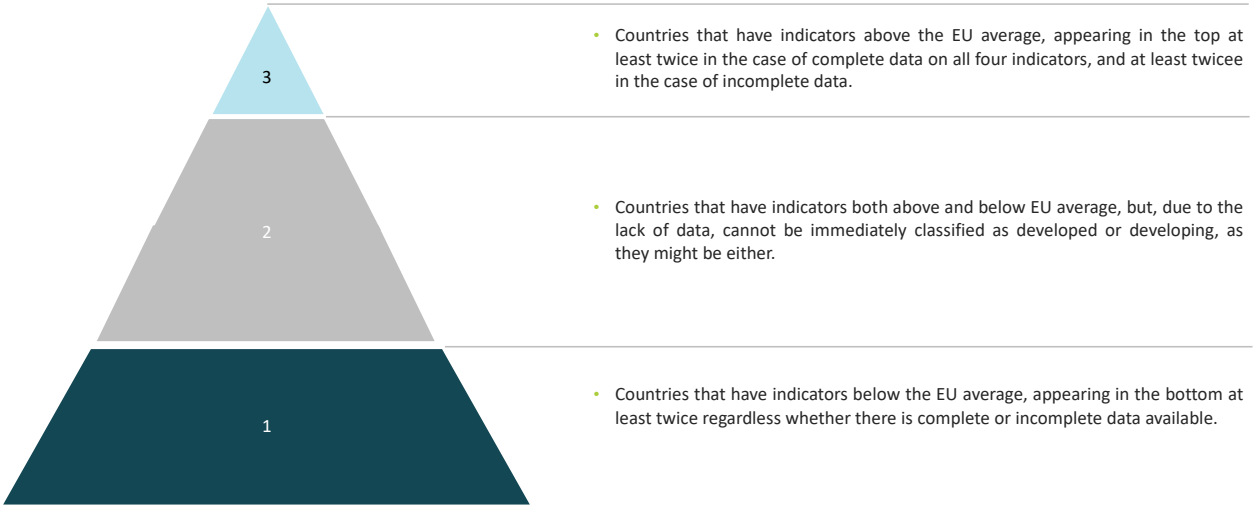
Additionally, it vital to evaluate not only the current competitiveness in the market but also the potential companies that may become direct competitors in the future, due to the high competition and fast-paced catching up of competitors in the ultrasound market. In order to do so, the latest data on market shares in the OB/GYN ultrasound industry are used.

Second, for the identification of the two types of markets as mentioned by the consortium, solely EU MSs are considered in order to remain within the scope of the project. The three levels of a country's need for ultrasound range from 1 (the most in need) to 3 (the least in need), and are defined in Figure 1. To classify the countries accordingly, three criteria are used:

- Physicians, obstetric and gynaecological group of specialities (pp), per 100 000, EU, 2018—to help identify countries where ultrasound machine technicians and/or OB/GYN experts are lacking and, thus, could have a higher demand for SUOG;
- Practising midwives, per 100 000, EU, 2016—to help identify countries where ultrasound machine technicians and/or OB/GYN experts are lacking and, thus, could have a higher demand for SUOG;

- Radiologists, per 100 000, EU, 2019—to help identify countries where ultrasound machine technicians and/or OB/GYN experts are lacking and, thus, could have a higher demand for SUOG.

FIGURE 1. METHODOLOGY FOR COUNTRY CLASSIFICATION



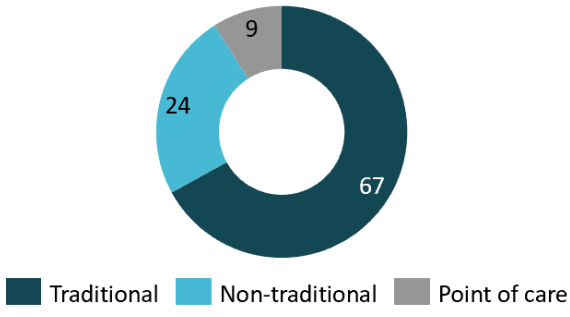
Lastly, given the customer segment of SUOG, as relayed by the consortium, the USP will reflect the appropriate stakeholders. More particularly, these are primary customers, i.e. private or public hospital or clinic, or OB/GYN or ultrasound clinics.

RESULTS

Ultrasound Market Overview

GENERAL | The global ultrasound market is one of the fastest-growing markets in the medical equipment area, showing promising returns. In 2015, it was estimated that the ultrasound market value had reached approximately €5.6 billion. Based on the clinical application, the global ultrasound industry is segmented into three broad categories: traditional, non-traditional, and point of care (see Figure 2).

FIGURE 2. WORLD MARKET FOR ULTRASOUND BY APPLICATION REVENUES, 2015, PERCENT



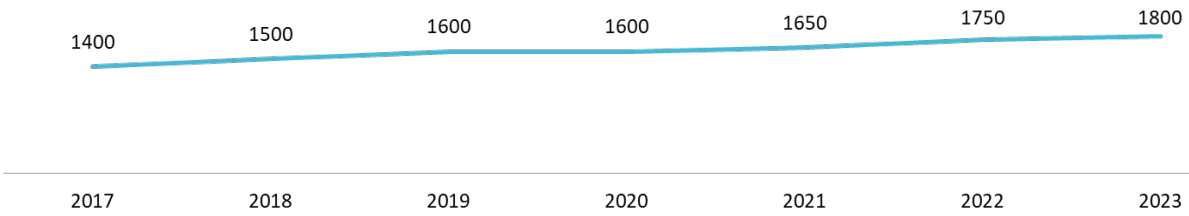
- Traditional segment—contains radiology/general imaging, obstetrics/gynaecology, cardiologic applications, which contains the majority of the ultrasound market applications;
- The non-traditional segment—includes ultrasound used for applications such as surgery, vascular, and veterinary imaging;
- Point of care applications—include anaesthesia, critical care, emergency medicine, and musculoskeletal ultrasound.

Regardless of the major traditional segment revenue share in 2018, healthcare providers continued to predominantly purchase traditional equipment, which accounted for more than 70% of global ultrasound unit shipments in 2018. Therefore, traditional revenues totalled €4.5 billion of the €6.4 billion ultrasound market.

OB/GYN | On of the key users of the ultrasound application is obstetrics/gynaecologists. In 2018, OB/GYN ultrasound unit shipments increased by over 10% YoY, making it the fastest-growing traditional ultrasound application. Despite that, one of the most substantial OB/GYN markets was in mainland China, where relaxed child-limiting policies have led to a rise in birth rates; however, during the past year, they have seen a decrease.

Conversely, OB/GYN revenues declined in countries with low birth rates, like Japan and South Korea. In other mature markets, an emphasis on improving women's healthcare drove OB/GYN growth in North American and Western European markets as governments and healthcare providers aimed to improve access to quality care. Despite shrinking childbirth numbers, global market revenues for ultrasounds application in 2017 reached approximately €1.3 billion with the forecasted growth of 23% within five years (see Figure 1).

FIGURE 3. APPROXIMATE GLOBAL MARKET REVENUES FOR ULTRASOUND OB/GYN APPLICATION, 2018, $ MLN.



Therefore, traditional ultrasound is strongly predicted to maintain its stronghold of the ultrasound market during the next five years presenting large opportunities for ultrasound manufacturers.

Competitor Analysis

In order to better understand the industry landscape, it is essential to analyse the competitors—be they direct, indirect, or substitute. Notably, at this stage, no direct competitors to SUOG can be identified through desk research. Therefore, all competitors are indirect, as can be seen in Table 1 below.

TABLE 1. COMPETITOR ANALYSIS

COMPANY	DEVICE	GUIDED IMAGE ANALYSIS	KEYWORDS	SEMANTIC REASONING/ ONTOLOGY	ADAPTABLE	ON-PREMISES SOFTWARE
SUOG PROJECT CONSORTIUM	SUOG	✓	✓	✓	✓	✓
PHENOMICS	PHENOMIZER[1]	✗	✓	✓	✗	✗
PHENOTIP	PHENOTIP BETA[2]	✗	✓	✗	✗	✗
U.S. NATIONAL LIBRARY OF MEDICINE	OPEN-I[3]	✗	✓	✗	✗	✗

PHENOMICS | At Phenomics AI, they are leveraging computer vision and high-content screening to develop the next wave of therapeutic antibodies against cancer and fibrosis. Specifically, they use deep neural networks to screen and analyse physiologically relevant disease models. The company's device Phenomizer is a published differential diagnosis tool for human genetics based on semantic reasoning.

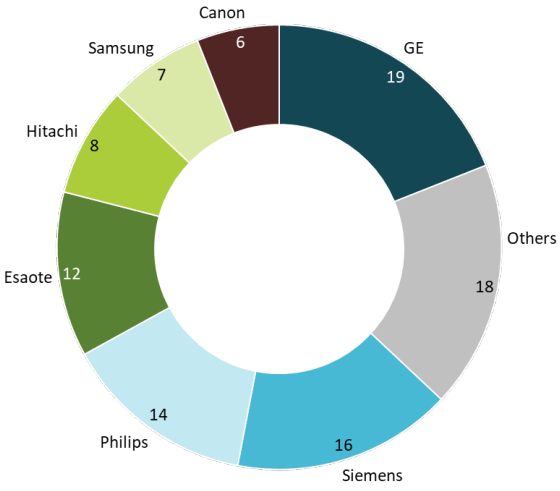
PHENOTIP | The Phenotip collaboration is an independent international association between maternal-foetal medicine specialists with an interest in prenatal diagnosis and an experienced software engineer. The prime purpose of the association is to promote accurate and rapid antenatal diagnosis of syndromes. The Phenotip collaboration is not externally funded and relies on the input of its volunteers. The Website offers an image-less search engine for foetal disorders based on ultrasound markers keywords.

U.S. NATIONAL LIBRARY OF MEDICINE | The National Library of Medicine supports and conducts research, development, and training in biomedical informatics and health information technology. In addition, the Library coordinates a 6,500-member National Network of Libraries of Medicine. Their device, Open-i, is a biomedical image search engine which contains 3.7 million images, including series of ultrasound fetal cases.

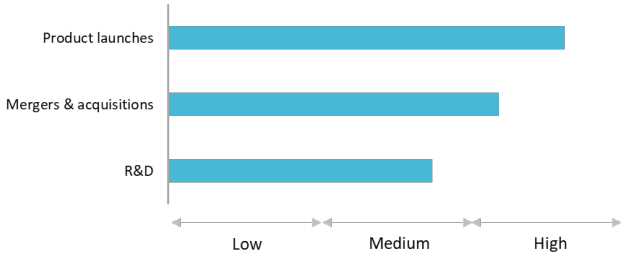
POTENTIAL FUTURE COMPETITORS | The global market of ultrasound devices is highly competitive with the presence of a large number of global as well as local players. The advancement in technology, such as cloud and software, to connect ultrasound devices to smartphones and tablets are factors spurting the adoption of these devices. Although no solution such as SUOG has been identified at the moment, due to competition, the following companies might pose a threat in the future, bearing in mind that they are some of the biggest players in the ultrasound device industry:

FIGURE 4. MARKET PARTICIPANT OVERVIEW

GLOBAL ULTRASOUND MARKET SHARES, 2015, PERCENTAGE



COMPETITIVE DASHBOARD ANALYSIS



STRATEGY	SPEARHEADS
R&D	• Mindray Medical International LTD
Product launch	• **GE Healthcare** • Canon • Koninklijke Philips NV
Mergers & acquisitions	• Koninklijke Philips NV

From the competitive dashboard analysis, some of the main strategies of several potential competitors can be identified, which should be taken into consideration when evaluating market capture, uptake, and penetration.

Moreover, for a better understanding of competitor strategies and comparative competitive edges and weaknesses, they were categorised into mature players and emerging players as per their market share, according to the available information.

TABLE 2. POTENTIAL FUTURE COMPETITOR CATEGORISATION

	COMPANY	OPERATING STRATEGIES	COMPETITIVE EDGE	WEAKNESSES
Mature players	• **GE Healthcare** • Koninklijke Philips NV • Anlogic Corporation • Mindray Medical International LTD • Fujifilm Holdings Corporation • Hitachi Medical Corporation • Hologic INC. • Siemens Healthineers • Canon Medical Systems Corporation • Samsung	• Integrating advanced technologies for ultrasound imaging in the field of OB/GYN, radiology, and others. • Growing participation in various exhibitions and medical trade fairs to increase reach of their products.	• Acquisitions of various distributors to strengthen the distribution network for ultrasound products. • In September 2013, Mndray acquired Ulco Medical for the distribution of its innovative products. Growing	• Due to the relative maturity and history of corporations, to launch a new product, its compatibility and complementarity with the company portfolio should be approved so as to be in line with overall business direction and profitability.
Emerging players	• SonaCare Medical LLC	• The company is incorporating various advance technologies such as remote monitoring for the development of various products.	• The company launches remote monitoring platform Sonalink, which helps in remote monitoring HIFU process.	–

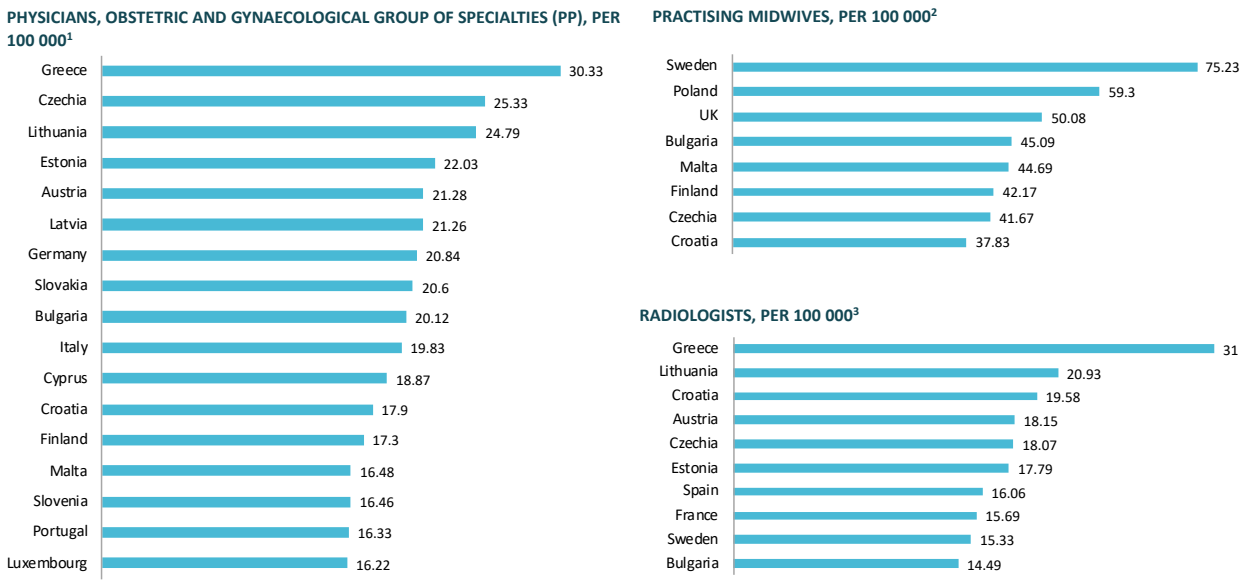
As such, GE is both a mature player with the largest chunk of the market pie and thus, is ahead of its competition at the moment. However, the competitive environment should not be neglected.

Target Countries for the USP

It was proposed to analyse EU MSs that have indicators above or below the EU average (refer to Figure 1. Methodology for country classification). Therefore, the criteria mentioned above are proxies that are used to infer the potential demand for SUOG. The gathered data are presented in the figures below.

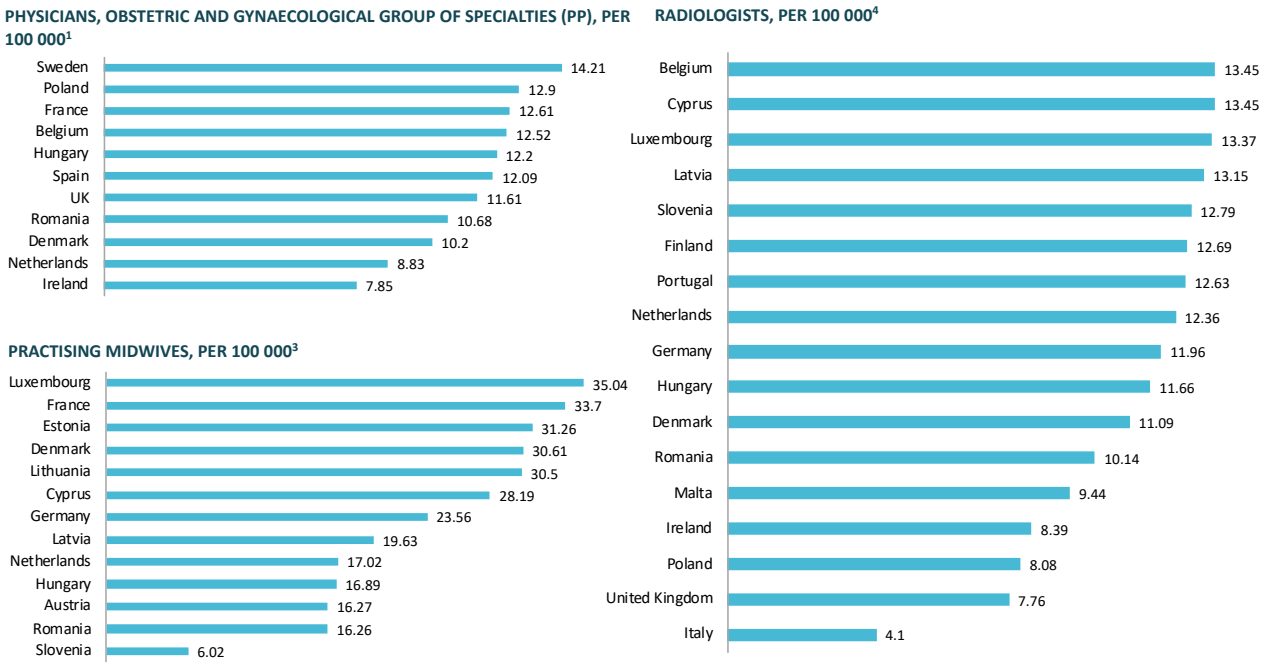
The first presents the top EU countries, i.e. those above the EU average in the indicated criteria.

FIGURE 5. TOP EU COUNTRIES IDENTIFIED ACCORDING TO THE SELECTED CRITERIA



Conversely, the second set of figures presents the bottom EU countries, i.e. those below the EU average in the indicated criteria.

FIGURE 6. BOTTOM EU COUNTRIES IDENTIFIED ACCORDING TO THE SELECTED CRITERIA



As surmised in Figure 5 and Figure 6, Figure 7 shows the classification of the countries as per the methodology.

FIGURE 7. CLASSIFICATION ACCORDING TO THE PROPOSED CRITERIA AND METHODOLOGY

THE MOST IN NEED	THE LEAST IN NEED	UNDETERMINED/MODERATELY IN NEED
• Denmark	• Czechia	• Italy
• Romania	• Sweden	• Portugal
• Hungary	• Finland	• Slovakia
• The United Kingdom	• Croatia	• Spain
• Poland	• Bulgaria	
• Germany	• Estonia	
• Latvia	• Lithuania	
• Ireland	• Malta	
• The Netherlands	• Austria	
• France	• Greece	
• Luxembourg		
• Slovenia		
• Malta		
• Cyprus		

CONCLUSIONS AND RECOMMENDATIONS

The key players are highly focusing on innovation in production technologies to improve efficiency and shelf life. The best long-term growth opportunities for this sector can be captured by ensuring ongoing process improvements and financial flexibility to invest in optimal strategies.

After analysing the competitiveness in the market, it can be seen that there are not many similar solutions to the problem on the market yet, therefore, it is not difficult to stand out. SUOG has distinctive capabilities compared to provided potential challengers (see Table 1).

SUOG's main advantages are the following:

FIGURE 8. THE MAIN ELEMENTS OF THE REFINED USP FOR SUOG

COMPETITIVE ADVANTAGE

- There are not many similar solutions on the market yet, therefore, it is not difficult to stand out.
- SUOG's unique features include:
  - Guided ultrasound image analysis,
  - Adaptability to unusual and abnormal findings,
  - Semantic- and AI-rendered knowledge base,
  - Friendly for any level of operator expertise,
  - Ontology-enabled automated reasoning and dynamically-derived personalised protocols.

STRENGTHS DERIVING FROM GE

- The women's health ultrasound business of GE healthcare is uniquely positioned as the leader in the women's health segment with its
  - Continued innovation,
  - Unmatched image quality,
  - User-friendly devices,
  - Co-development with leading KOL's in the world,
  - External partnerships to augment and accelerate brand awareness.

These intangible assets favour SUOG, giving it unique features with high potential of growth and penetrating the market. Hence, the two value propositions suggested for the two different target markets (as per the classification) are as follows:

FIGURE 9. POSITIONING SUOG IN THE TARGET MARKETS

COUNTRIES THE MOST IN NEED OF SUOG

The only intelligent assistant for ultrasound in pregnancy that helps you achieve expert-level image documentation and diagnosis. Team up with SUOG—your friendly neighbourhood assistant.

COUNTRIES THE LEAST IN NEED OF SUOG

One scan away from happiness! Harnessing the power of real-world data, SUOG brings precision to your diagnosis and security to the mothers and their children.

ANNEXE 3. REFINEMENT OF THE MARKET STRATEGY

CONTEXT

During a discovery interview with the consortium, it was identified that an outline of a product acceleration plan would add value to the project. The consortium has a preliminary commercialisation plan and a general timeline, but strategies for acceleration are yet to be explored.

In order to achieve this, several steps were taken. First, the importance of the awareness of development time is emphasised. Thereafter, the main elements of product acceleration are presented for SUOG. Lastly, acceleration risks and mitigation measures are identified.

METHODOLOGY

Analysis of the background materials from the consortium and Q&A sessions with the consortium management personnel were used to better understand what the starting position of SUOG is. Business and technology aspects of the project, as well as its organisational structure, product development cycle and strategy, the timeline, and the processes that it entails, were taken into account to the extent that such information as provided/existent.

After outlining the main acceleratory elements, acceleration risks and mitigation measures are identified; they are evaluated on a two-dimensional matrix using a qualitative rating of the likelihood of the event occurring and the scale of the possible impact. As a result of evaluating the likelihood and impact risk, scores were set. In the risk matrix, there are three types of risks: low, medium, and high. The risk analysis provides information critical to determining what risks need to be treated and what risks are accepted.

TABLE 3. ACCELERATION RISK MATRIX

		SCALE OF IMPACT		
		ACCEPTABLE	TOLERABLE	GENERALLY UNACCEPTABLE
SCALE OF LIKELIHOOD	NOT LIKELY	LOW RISK	MEDIUM RISK	MEDIUM RISK
	POSSIBLE	LOW RISK	MEDIUM RISK	HIGH RISK
	PROBABLE	MEDIUM RISK	HIGH RISK	HIGH RISK

RESULTS

Development Time

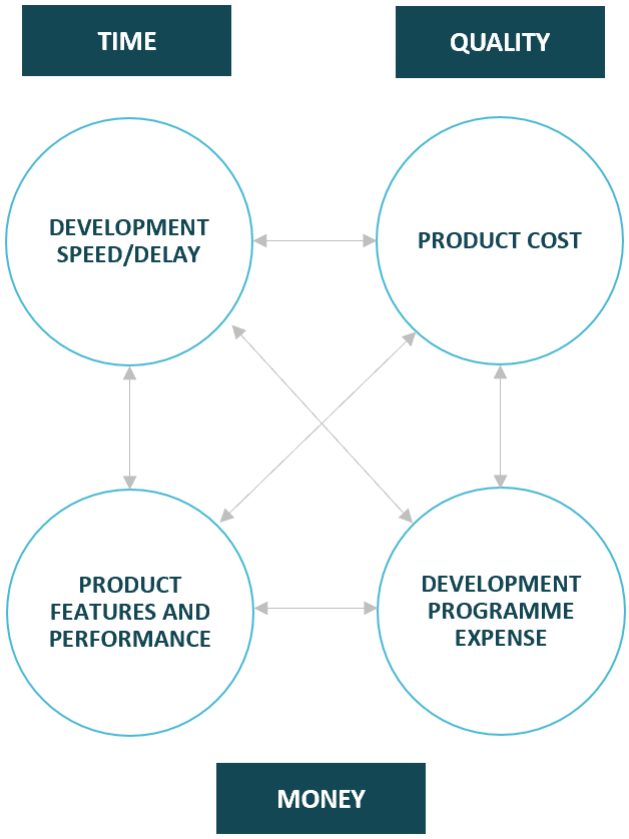
Determining the value of SUOG's development time not only helps understand how the product development process can be accelerated but also offers insights about its main objectives that in turn help accelerate the process.

First, the value of the development time can be calculated by building a financial model for SUOG. This means modelling and projecting the revenue generated, which the consortium has already preliminarily done up until 2032.

Second, in contrast to this baseline model, other models as variations from this baseline should be developed. The key is for each variation to model a change in one development objective. Particularly, the four objectives that could prove to be useful for SUOG are development delay, product cost, product performance, and development expense.

Third, results from each variation are compared with the baseline to calculate trade-off rules, such as cumulative profit lost due to a 1-month delay or the profit impact of a 1% increase in product cost.

FIGURE 10. DETERMINING THE VALUE OF SUOG'S DEVELOPMENT TIME AND TRADE-OFF RULES



Such analysis provides two types of useful information: guidance as to which product development objectives, i.e. cost, time, performance, expense, warrant the greatest emphasis, and trade-off rules among these objectives, as illustrated above.

Main Elements for SUOG's Acceleration

TOP MANAGEMENT INVOLVEMENT | The consortium already ascertains that there is continuous communication with the leadership team—product managers are aware of the milestones and communicate it to the product development team.

A STRONG TEAM | The strong teams of SUOG form one of the most important elements in getting a new product to market quickly. Specifically, the global product team is responsible to share a general guidance of expectation and offers a buffet of possible configurations, hardware features, AI features and others that are catalogued with unique identifiable part numbers to the region; the global marketing team takes responsibility for the commercial aspects of the product, while the R&D team ensures SUOG stays competitive in the industry and aids with technological development.

CONTINUAL COMMUNICATION | Although the teams are strong and coordinated, it is still advisable to keep teams as small as possible (through the use of full-time workers, for example), and physically locate them within talking distance in order to facilitate face-to-face conversation to facilitate the transmission of information quickly and reliably without slowing down the decision-making process, especially if the team is moving quickly—the reports/reviews prepared beforehand might be out-of-date by that time.

LIMITED PRODUCT OBJECTIVES | Although SUOG is a high-complexity product, development complexity often manifests itself in development time, because this is the least tangible development variable. It is imperative to ascertain that product advances are worthwhile and that their combined effect on development effort is multiplicative rather than additive. If the latter is the case when deciding what features should become a part of the default configuration of SUOG, then an advantageous strategy is to limit the feature options and defer them to the next generation product with fast-paced incremental innovation.

JOINT PRODUCT SPECIFICATIONS | Product features, performance, cost, and development schedule, i.e. product specification creates a basis of communication among the various functions involved in the product development cycle.

MODEL BUILDING | In order to accelerate the product development, building and testing of models needs to be carried out continuously without building elaborate models that look or function as the ultimate product; instead, building several functional models and testing basic concepts helps identify failures quickly which has a major effect on a team's willingness to move ahead quickly. The key is not to avoid failure.

PROCEDURES AND CONTROLS | Keeping in mind the corporate structure behind SUOG, the control systems in place might stretch the development time. This needs to be balanced with the thicket of procedures used to protect financial resources by considering the time-based thinking (as illustrated on the previous slide) and cut out controls that no longer seem appropriate.

Acceleration Risks and Mitigation Measures

Acceleration risks vary depending on the medical device, however, those presented below are applicable beyond SUOG as well. Potential consequences and mitigation measures were identified for every risk event in the following table:

TABLE 4. IDENTIFIED REGULATORY RISKS AND MITIGATION MEASURES FOR SUOG

RISK	LIKELIHOOD	IMPACT	RISK SCORE	MITIGATION MEASURES
A.1. Speedy development can increase R&D expense, inflate the product costs and degrade SUOG's performance and quality.	2	3	6	• Considering the calculated profits in light of the trade-off rules/conversion rates, the product timeline will be accelerated only when the projected profits outweigh the projected costs. This takes into consideration performance and quality in light of maintenance costs, etc. • Market-entry timing, in view of the market window is contingent upon the completion of the new product's development cycle.
A.2. Team members may be under work stress not only because of divided loyalties between their functional area and the development team, but also because of the increase in their workload as a consequence of being a part of the development team.	2	1	2	• Stress very frequent, informal peer review to monitor and control progress. • Co-locate the team to enhance communication and commitment.
A.3. Launching a new product too early, particularly when the product is qualitatively not ready for the market.	1	3	3	• Upon the assessment of the various models and the subsequent alterations to the processes, whether pertaining to additional testing, contract services, incentives or travel costs, the product will be launched timely, rather than in the shortest period possible.

Note. Scale: 1 (low), 2 (medium), 3 (high)
Risk score: likelihood x impact

As per the methodology, the risk scores can be found classified in the table below:

TABLE 5. ACCELERATION RISK MATRIX (IDENTIFIED)

SCALE OF LIKELIHOOD	SCALE OF IMPACT: ACCEPTABLE	TOLERABLE	GENERALLY UNACCEPTABLE
NOT LIKELY	LOW RISK	MEDIUM RISK	A.3. MEDIUM RISK
POSSIBLE	A.2. LOW RISK	MEDIUM RISK	A.1. HIGH RISK
PROBABLE	MEDIUM RISK	HIGH RISK	HIGH RISK

Low risk Medium risk High risk

It can be seen that the identified risks fall across risk categories, from low to medium to high. Taking this into consideration, those risks with the higher/highest risk scores should be emphasised and the mitigation measures prioritised.

CONCLUSIONS AND RECOMMENDATIONS

SUOG's acceleration plan is still in its infancy. With no clinical trial endpoints due to the lack of the CE mark, the outline of the acceleration plan is suggested in order to guide SUOG towards entering the market at its earliest capability with an optimal balance among time, quality, and money.

As a recommendation, in order to quantify the necessary steps needed to accelerate SUOG, several steps should be taken:

1. Determine the value of SUOG's development time by:
   - Reviewing project product costs;
   - Develop alternative models;
   - Calculate trade-off rules.
2. Ensure continued management involvement;
3. Maintain a strong team;
4. Ascertain continual communication;
5. Follow limited product objectives;
6. Draw up joint product specification;
7. Build models;
8. Minimise procedures and controls.

ANNEXE 4. REFINEMENT OF THE REGULATORY STRATEGY

CONTEXT

Currently, SUOG is preparing to penetrate the European market, among others. During the discovery interview, the consortium pointed out the need for advice on financing mechanisms and reimbursement procedures. make these recommendations, a thorough investigation and validation of research results need to be carried out.

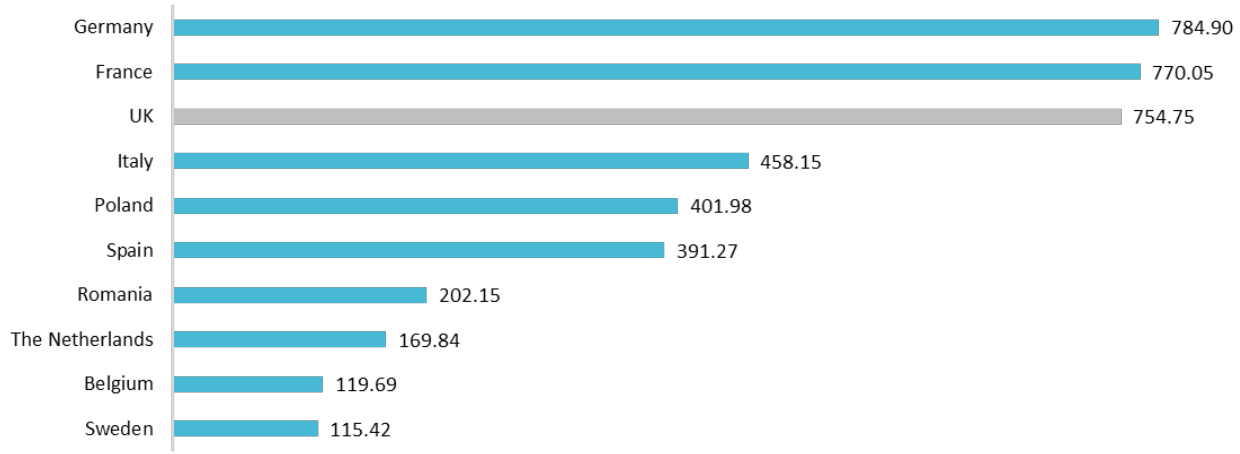
METHODOLOGY

Analysis of the background materials from the consortium and Q&A sessions with the consortium management personnel were used to better understand what the starting position of SUOG is. Additional research on various regulatory frameworks was conducted, thereby identifying best practices, and developing the pathways to ensure regulatory approval with their accompanying risks and mitigation strategies. Through desk research and policy analysis of the regulatory landscape, information about the requirements associated with certification were gleaned. Moreover, a comparative analysis of best practices was carried out in order to formulate the steps and pathways that SUOG should take to tackle potential regulatory barriers.

In order to provide a snapshot of the regulatory processes in the EU, the countries that satisfy the following are analysed more in-depth:

- Represent the diversity of legal processes pertaining to medical devices;
- Have sufficient data available to determine the legalities;
- Are not the UK, since the medical device market is subject to substantial changes due to Brexit;
- Possess a considerable potential market (see the figure below).

FIGURE 11. TOP 10 EU MS'S ACCORDING TO LIVE BIRTHS, 2017, TOTAL



Thence, taking into account the four criteria mentioned above, the countries highlighted in green have been chosen for in-depth analysis:

FIGURE 12. IDENTIFIED EU MS'S FOR REGULATORY ANALYSIS IN EACH CATEGORY

THE MOST IN NEED

- Denmark
- Romania
- Hungary
- The United Kingdom
- Poland
- Germany
- Latvia
- Ireland
- The Netherlands
- France
- Luxembourg
- Slovenia
- Malta
- Cyprus

THE LEAST IN NEED

- Czechia
- Sweden
- Finland
- Croatia
- Bulgaria
- Estonia
- Lithuania
- Malta
- Austria
- Greece

UNDETERMINED/MODERATELY IN NEED

- Italy
- Portugal
- Slovakia
- Spain

After the in-depth analysis, policy analysis of the EU regulatory landscape is performed together with an illustration of national policies. In line with this, regulatory risks and mitigation measures are identified; they are evaluated on a two-dimensional matrix using a qualitative rating of the likelihood of the event occurring and the scale of the possible impact. As a result of evaluating the likelihood and impact risk, scores were set. In the risk matrix, there are three types of risks: low, medium, and high. The risk analysis provides information critical to determining what risks need to be treated and what risks are accepted.

TABLE 6. REGULATORY RISK MATRIX

		SCALE OF IMPACT		
		ACCEPTABLE	TOLERABLE	GENERALLY UNACCEPTABLE
SCALE OF LIKELIHOOD	NOT LIKELY	LOW RISK	MEDIUM RISK	MEDIUM RISK
	POSSIBLE	LOW RISK	MEDIUM RISK	HIGH RISK
	PROBABLE	MEDIUM RISK	HIGH RISK	HIGH RISK

RESULTS

Overview

EU | Overall, there are four main features of market entry in the EU. First, the legal pathway is dependent on the risk level or device class of the medical device. Second, the regulations cover actions needed in pre-market, placing on market and post-market phase. Third, post-market surveillance focuses on safety and performance. Lastly, depending on the device, there might be a need to consider privacy and cybersecurity laws.

In terms of regulations, the most relevant regulations on medical devices that apply to SUOG are the following:

- Medical Devices Regulation (Regulation (EU) 2017/745) will be legally binding to all EU Member States and automatically applying across the EU from May 26th, 2020:
  - "Software which drives a device or influences the use of a device shall fall within the same class as the device";
  - "If the software is independent of any other device, it shall be classified in its own right";
  - "Software intended to provide information which is used to make decisions with diagnosis or therapeutic purposes is classified as Class IIa". European Database on Medical Devices (EUDAMED) will be created.
- Manufacturers of medical devices have to draw up the EU declaration of conformity (the CE mark);
- Manufacturers have to have in their organisation at least one person responsible for regulatory compliance;
- Manufacturers have to plan, establish, document, implement, maintain and update a post-market surveillance system.

Other regulations to take into account include:

- Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community Code Relating to Medicinal Products for Human Use;
- Standard ISO 14971 "Application of Risk Management for Medical Devices", which will be harmonized and replaced by ISO/FDIS 14971 and ISO/DTR24971. However, the changes will be minor;
- General Data Protection Regulation (GDPR) (Regulation (EU) 2016/679 of the European Parliament and of the Council of 27 April 2016 on the protection of natural persons with regard to the processing of personal data and on the free movement of such data, and repealing Directive 95/46/EC)— recognises data concerning health as a special category of data and provides a definition for health data for data protection purposes.

Poland

The registration of medicinal product is granted either by the EMA or the Office for Registration of Medicinal Products, Medical Devices and Biocidal Products of Poland. The reimbursement approval process is performed by the Ministry of Health and requires companies to complete a reimbursement submission form; the submission form can be sent to the Ministry during the first seven days of each quarter. The reimbursement decision should be granted in no longer than 90 days, if together with price application, in no longer than 180 days. According to the law on health benefits financed from public means reimbursement criteria are the following:

- The necessity to provide health care for society.
- Making medicines accessible.
- Safety.
- Importance of a drug in the treatment of conditions associated with the high epidemiological threat.
- Influence of a drug on direct medical costs.
- Affordability for the public payer obliged to finance healthcare services.

Furthermore, there are four levels of reimbursement: 0% (non-reimbursed), 50%, 70% ,and 100%.

An important stakeholder is the AOTM, which is an advisory body to the Ministry of Health. Its opinion is crucial, though the decisions in practice are not always consistent. The pricing and reimbursement process should not take longer than 180 days. However, past experiences clearly indicate that it takes longer to make a reimbursement decision.

Thereafter, the pricing approval process begins with the price for the product being set through negotiation with the Ministry of Health. The following criteria are taken into account:

- Production cost (provided by the manufacturer).
- Cost of daily treatment.
- Cost of standardized therapy.
- Risk-benefit ratio compared to alternatives.
- Therapy costs per day in comparison to products with the same efficacy.
- Evaluation of the economic impact on the national health system.
- Estimated sales of the new medical equipment.
- Prices in countries with similar GDP.

As a final note, pricing and reimbursement decisions are made on the national level and published in the official journal (Dziennik Ustaw).

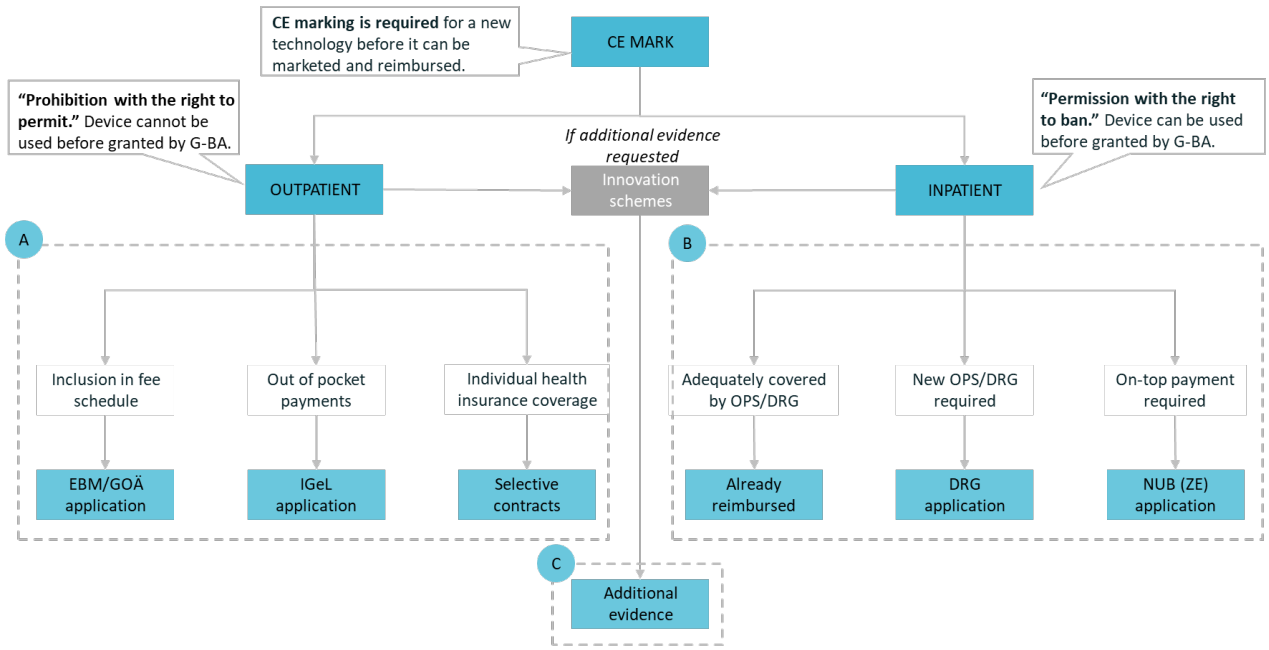
Germany

In order to start the process of reimbursement, the CE marking must first be obtained (see Figure 13). Then, the manufacturer must decide either they want to pursue outpatient or inpatient care pathway. In outpatient care, the application of a new diagnostic or treatment method can only be done and is only reimbursed if the G-BA has explicitly approved the new method. In inpatient care, the device may be used before the approval of G-BA. The approval of G-BA means that the medical device will be listed in the medical technical aids' reimbursement list. Products are initially listed or adjusted at the request of the manufacturer (or by third parties authorised by them). The listing considers the relevant statutory requirements imposed by the Federal Association of SHI funds. The products available on the market are classified into different product groups according to their applications.

The preconditions for the listing of a device in the medical technical aids' reimbursement list are:

- The efficacy & functionality of the product;
- Safety and the fulfilment of the already stipulated requirements for the product group to which the device belongs;
- If the product introduces a new diagnostic or treatment method into the German outpatient care, a further precondition for the listing is that the G-BA needs to assess this new diagnostic or treatment method and approve it for the outpatient care.

FIGURE 13. REIMBURSEMENT SYSTEM IN GERMANY



Considering SUOG's use, it can be assumed that it would qualify as inpatient care. Although the information is provided about outpatient care as well, the former will be discussed in more detail. As such, for the application of a new medical device in the inpatient sector, only a CE mark is required. Then an OPS application must be placed with DIMDI unless there is already an existing OPS code available. After that, the DRG application must be sent to InEK and if the DRG fee is reasonable the reimbursement will be available. If the DRG fee does not seem to be reasonable a NUB (ZE) application must be filed with the InEK who decides whether an 'on-top payment' can be negotiated.

If there is a request for additional clinical evidence, the manufacturer can partake in innovation schemes. Co-funding for clinical studies is induced through direct applications by manufacturers or in the process of a method evaluation by the G-BA. From the manufacturer perspective, this strategy is only valuable for medical devices in outpatient care as there is currently no strict evidence requirements for inpatient care.

The G-BA decides on whether a medical device is suitable for the Experimental Coverage programme. An Experimental Coverage application needs to point out a strong innovative potential and a high unmet need. The manufacturer must bear a specific part of the clinical research costs. Medical device manufacturers can apply for such experimental coverage using specific forms provided by the G-BA and many reimbursement consultancies specialize in these applications.

To directly apply for a co-funded study:

- Manufacturers file an application form including a systematic literature review, outline of a suggested study and a letter of intent of cost-contribution
- The G-BA then tests if the method in question is eligible for a co-funded study and develops a study directive specifying the key characteristics of the study including indication, intervention and comparison intervention, endpoints, study type, observation period as well as material, personnel and other requirements
- The G-BA collaborates with the IQWiG. Before releasing the study directive, the G-BA calls hospitals that are using the method to provide additional information and then invites interested parties to make comments or suggestions
- In the next step, an independent research institute is contracted via public tender. The institute is responsible for the development of the study protocol, scientific supervision of the study conduction and analysis of the data

- Based on the results of the co-funded study the G-BA with the support of IQWiG decides upon inclusion or exclusion of the method as a benefit in the statutory health insurance. Evaluation results only apply to the sector defined in the scope of the evidence creation.

In cases where a co-funded study is induced through a direct application by the manufacturer, the manufacturer must cover the main costs of the study, including administrative costs as well as costs for conduction and evaluation of the study. The amount depends on the scope (size and complexity) of the study and is between €600,000 and €3,300,000 with a cost per patient of €1,500 to €9,000. Treatment costs are completely covered by sickness funds. This includes material, medical staff, infrastructural costs for both, the studied intervention and comparative treatment. In case a co-funded study is induced through the G-BA during the process of a method evaluation, a cost-contribution from manufacturers is only required if the method is essentially based on a specific medical device. The amount of contribution is then determined in each case.

Methods need to fulfil the following criteria to qualify for evidence creation through a co-sponsored study:

- The method is expected to be less complex, less invasive or have fewer side effects than existing methods or to optimize the current treatment or make it more efficient in any other way;
- Enough scientific evidence exists as a basis to plan a study that will create significant outcomes for a subsequent method evaluation and reimbursement decision;
- The method is not included as a benefit in the outpatient catalogue called EBM.

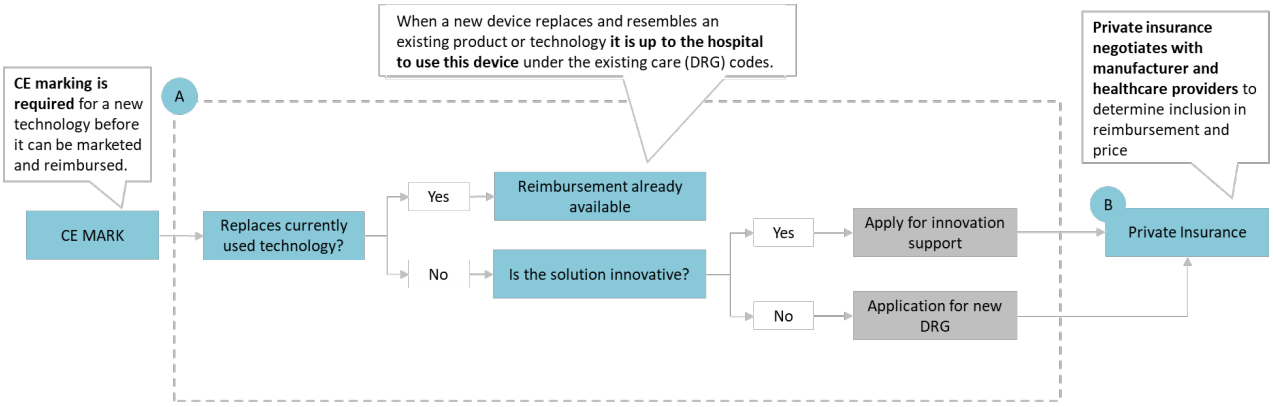
Note that the innovation schemes might not be applicable to SUOG as they are typically given to discover new treatment pathways, not specific products. However, this route should be explored further by SUOG to see if they can qualify for the innovation schemes. If so, this can potentially shorten the pathway to reimbursement and gain additional financing.

The Netherlands

To start the reimbursement process, the CE marking must first be obtained. Moreover, in order to market a medical device, each device must obtain national approval, i.e., a performance code. In the Netherlands, it is only allowed to invoice types of healthcare for which the NZa has created a performance description.

The NZa and the ZIN each play a role during the decision-making process regarding the reimbursement of a new healthcare product. For obtaining a new performance description there are several possibilities, as shown in the figure below.

FIGURE 14. THE REIMBURSEMENT SYSTEM IN THE NETHERLANDS



The first possibility is to submit a change request. This involves the following:

- The submission of the request at NZa. NZa maps and outlines the request. In addition, political and technical aspects play a role. This phase lasts six to eight weeks.

- Advice by NZa. In this phase, NZa looks further into the details of the request. These results end in the "change request advice". Positive advice also contains the functional specifications for admission into the system.
- The Board of Directors of the NZa subsequently decides about all detailed change requests and informs about these decisions (second go or no-go). This decision still holds reservations regarding the technical implementation of the request. After the decision of the Board of Directors, NZa elaborates on the change request in a product description. After this technical elaboration, the NZa comes to a final decision about the total package extradition. Ultimately the Healthcare Institute is asked to pass judgment about whether the performance should be part of the basic insurance package.

The second option is to submit a request at NZa to get a so-called DOT-registration code (=Innovation DOT). Based on a completed Quick Scan this procedure starts at NZa. The Medical Scientific Advisory Board (MWAR) assesses the request based on various criteria and the KEEPS test: quality, economical aspects, ethical aspects, patients' preferences, and system consequences. If all this is obtained and the new medical device replaces a current technology, then it means that reimbursement is already available. If not, the reimbursement depends on whether the solution is innovative or not. When a new device replaces and resembles an existing product it is up to the hospital to use this product under the existing care codes if it fits within a predefined budget constraint.

Finally, the third – and, arguably, the most relevant – possibility is that for innovative solutions. If the solution is innovative, then the manufacturer can apply for the Experimental Coverage Programme which offers two schemes.

The first scheme is aimed at experimenting with short-term and small-scale innovative healthcare performances. For this experiment, a care provider, together with a health insurance company, submits a request with the NZa. This request should be about improving healthcare that is already covered by basic health insurance. There should also be a research proposal including information on how the funding will be organized and where the money should come from. If the NZa approves the proposal, the experiment can start with the intended target group. The research period initially has a maximum of three years, however, as it turned out, this can be too short to conduct a good experiment. Therefore, the experiment can be extended for a maximum of two years since 1st January 2017. While conducting the experiments, ongoing consultations are provided by the Institute.

The second scheme is a subsidy scheme for quicker availability of promising healthcare products aimed at promoting cost-effectiveness. Through this scheme, parties involved can apply for financing of both the costs for care as the research costs during the research period (up to EUR 2.5m). After the research period, judgment is passed by ZIN, which states whether the healthcare product can be taken into the basic insurance package. The scheme aims at new treatments, medical technology, medical devices and specific groups of pharmaceuticals.

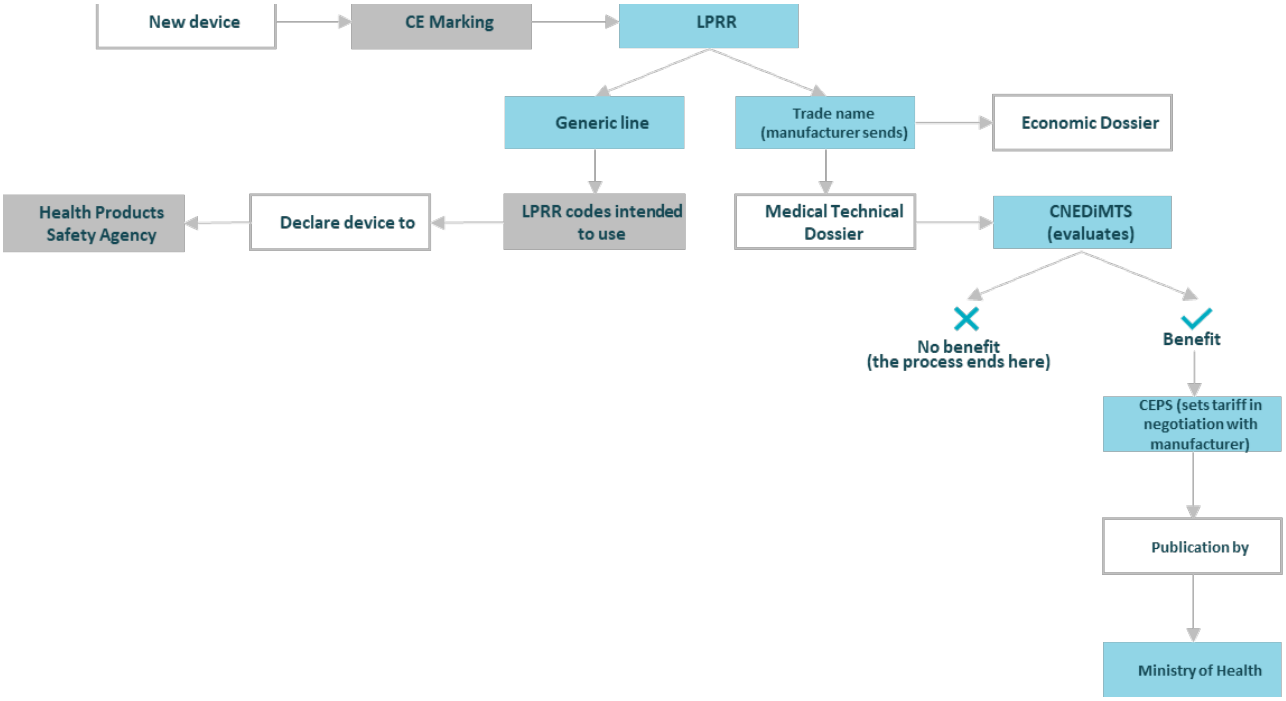
Lastly, applying for the performance code is a lengthy procedure which can take up to three years, depending on how much clinical data is already collected, and how supportive the key opinion leaders are. As such, the more efficient process would be applying for the innovation scheme straight away. But even then, when it comes to negotiating with insurance companies, it might be a big bottle-neck—each insurance company needs to be approached independently, and the reimbursement amounts differ throughout.

France

The first step in the reimbursement procedure of medical equipment in France is DRG Funding. The DRG Funding is a scheme of reimbursement applied to both public and private sectors. Most devices are included in this tariff and are funded by the National Health Insurance. The role of COMEDIMS, a subcommittee set in every hospital/group of hospitals, is to enlist and decide which devices to buy for their respective hospitals. The devices not included in this funding are usually considered as innovative and/or costly devices.

The second step is the enlistment on the positive list, i.e. LPPR, which is where a device is enlisted if the reimbursement for a device in ambulatory care or for a device is too expensive for the DRG tariff. As visualised below, there are two pathways to be enlisted: generic line, and trade name.

FIGURE 15. THE REIMBURSEMENT SYSTEM IN FRANCE



The generic line represents a class of products, their use, and technical characteristics without mentioning any company or brand name. If a medical device conforms with the LPRR generic line description, it does not need to go through a CNEDiMTS evaluation. The manufacturer only needs to label the products with an LPRR code and declare it to the Health Products Safety Agency for future monitoring. This means the device will be reimbursed by at the existing tariff.

On the other hand, to obtain a trade name and enter this list the device has to be innovative. This listing is also recommended when the device needs a specific follow-up due to associated safety issues. Additionally, CNEDiMTS requires the manufacturer to submit two dossiers: a technical dossier, and an economic dossier. The technical dossier includes a technical description of the technology and its use, the severity of the condition, clinical benefits and alternatives; the economic dossier includes the price or tariff required for reimbursement, sale forecasts and price justification, as well as a breakdown of costs, from manufacturing to distribution. A cost/effectiveness analysis may be submitted in both dossiers.

Lastly, a two-step process is implemented. First, the technical assessment by CNEDiMTS will verify:

- If a trade name listing is appropriate according to their characteristics.
- If the service provided by the device is sufficient to guarantee reimbursement.
- The added value for the patient.
- The number of patients who might get benefits from the device.

Second, CEPS, in negotiation with the manufacturer, sets a tariff for reimbursement. If there are many trademark devices with similarities, the CEPS can consider creating a new generic description to set a common tariff. Eventually, reimbursement is submitted to set up a registry and produce further clinical evidence. The time for the process should be 180 days but could also take longer.

Italy

Devices appear largely unregulated and purchase decisions are in practice left to individual providers (hospital Committees and managers). Because public and private healthcare providers are remunerated through a fee-for-service system based on the Rate Nomenclature for Outpatient Services and Rate Nomenclature for Hospital Benefits, three possible pathways may apply for both hospital and ambulatory care; the only difference is that in the case of in-patient treatment the hospital-DRG Tariff is used, whilst ambulatory (out-patient care) providers are remunerated through the relevant ambulatory Tariff. Notably, as the use of services in the out-patient setting is very limited, this path occurs less frequently.

Importantly, medical devices which are not registered on the special register—Repertorio dei Dispositivi Medici—may not be sold to hospitals and other public institutions within the NHS.

The willingness of purchasers to fully adopt the new technology will ultimately rest on its price level; in fact, depending on the weight of the price, versus the DRG or Ambulatory tariff, two funding mechanisms would eventually apply.

First, the DRG Hospital Tariff System, which has been applied in Italy since 1994, in both the public and private hospital sectors. Most devices are included in the DRG tariffs and thus, fully covered by the SSN. In such a case, hospitals are purchasers in the context of public tender regulation. It is the role of hospital drug committees to run the assessment for the enlistment on the hospital formulary and/or the decision of purchase. Hospitals and ASLs are increasingly grouping in procurement organizations to obtain better prices and prompted to do so by the Regions.

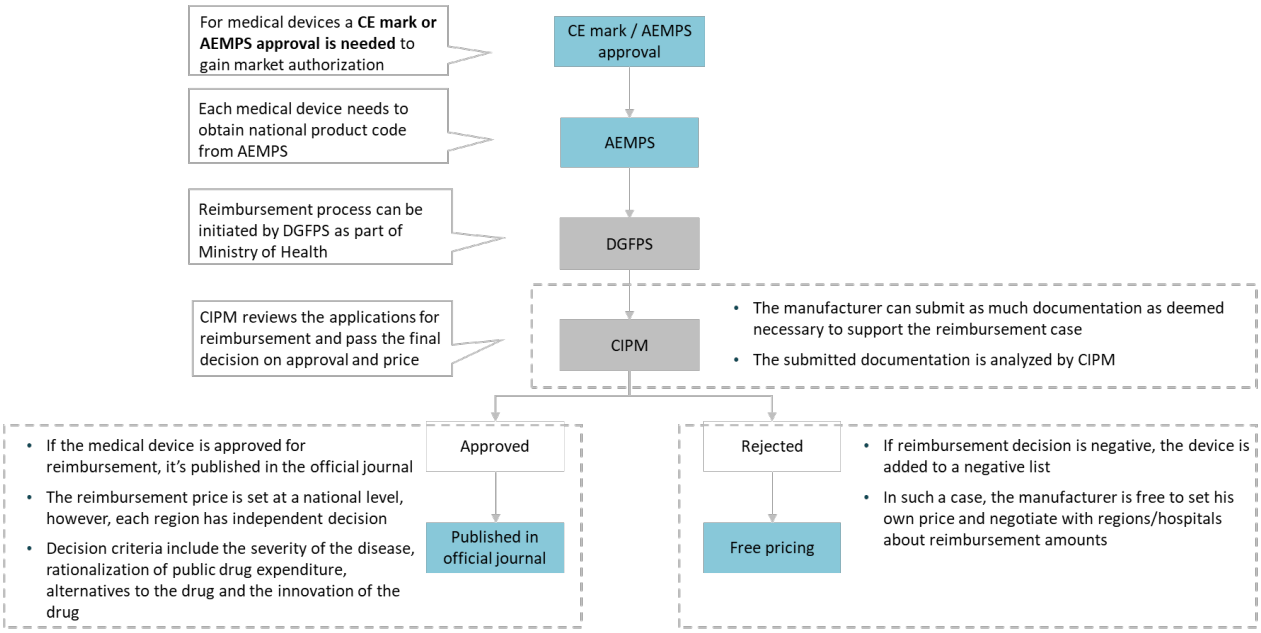
Second, some innovative and/or costly devices are not included in DRG funding and may be reimbursed separately from a specific Regional budget. In that case, prices or extra-tariff-funding is to be negotiated at the Regional level. The Regions who are mostly active in enlisting and updating extra-payments are Piemonte, Lombardia, Veneto, Emilia-Romagna, FriuliVG, and Sicilia. The extra-payment may be set as a precise figure, specifically set to fund the device, or as a percentage of the cost of the device; in this latter case, reimbursement will be given to the hospital upon presentation of the purchase invoice.

Spain

To start the reimbursement process, the CE marking must be obtained. After this, the manufacturer should contact AEMPS who is responsible for assigning the national product codes. The reimbursement process can be initiated by the DGFPS as a part of the Ministry of Health or it can be initiated by the manufacturer by sending an application to the CIPM.

Notably, in Spain, more than 85% of all procurement of medical devices go through big framework contracts and tendering regionals.

FIGURE 16. THE REIMBURSEMENT SYSTEM IN SPAIN



The inclusion of a medicinal product within the national reimbursement system is selective and based on the following criteria:

- The seriousness, duration and frequency of the illnesses to be treated with the medicinal product.
- The specific needs of certain groups.
- The therapeutic and social usefulness of the medicinal product.
- The rationalisation of public expenditure.
- The existence of alternative products or treatments for the same illness.
- The innovative character of the medicinal product.

Companies can submit as much documentation as they wish to support a case for reimbursement. The information is analysed by CIPM. As part of these documents it is mandatory for the company to determine the following (non-exhaustive list):

- Pricing strategy;
- Cost per day (compared to equivalent products in Spain);
- Price of product in other EU countries (if implemented somewhere else);
- Sales forecast;
- The overall cost of Research & Development;
- Production cost.

If the application is approved, the reimbursement is available, and the device is published in the official journal. This does not mean, however, that the reimbursement process is over. Each region in Spain has the power to individually decide whether to include this product to its reimbursement list. Therefore, it is necessary to negotiate with all the 17 regions separately. Decision criteria include the severity of the disease, rationalization of public drug expenditure, alternatives to the drug and the innovativeness of the drug. If the application is not approved, the device is added to a negative list. In such a case, the manufacturer is free to set his own price and negotiate with regions/hospitals about reimbursement amounts.

Policy Analysis of the Regulatory Landscape

OVERVIEW | There are several policies in the EU that deal with ultrasound scans. The first is "Standards of Care for Women's Health in Europe" by The European Board and College of Obstetrics and Gynaecology. Standard 7 of the document is predicated on the rationale that Ultrasound scanning is an integral part of

the investigation for a wide range of gynaecological conditions such as early pregnancy monitoring, management of infertility as well as diagnosis of benign and malignant gynaecological conditions. As such, the document aims to standardise scanning and its reporting. Within this standard about ultrasound scanning in gynaecological practice, several things that the organisation mentions are most notable:

- Protocols should be in place and relative to different gynaecological conditions;
- Accurate reporting of the findings is essential to inform the clinical interpretation and management;
- The result of the scan and its clinical interpretation should remain the responsibility of the referring doctor to avoid any misinterpretation or confusion to the patient.

Second, "European strategic approach for making pregnancy safer: Improving maternal and perinatal health" by the WHO Regional Office for Europe also makes a point and emphasises the importance of organising and strengthening health service delivery through better infrastructure and medical equipment.

Moreover, all EU Member States have signed the International Covenant on Economic, Social and Cultural Rights, which guarantees the "right to the highest attainable state of health" to everyone.

The EU also has an obligation to safeguard human health according to Article 168 of the Treaty on the Functioning of the European Union and Article 35 of its Charter of Fundamental Rights. However, Article 35 states that "everyone has the right to access preventive health care and the right to benefit from medical treatment under the conditions established by national laws and practices". This allows for national modification of the right to health.

Lastly, the EU has also subscribed to the UN Sustainable Development Goals, specifically Goal 3.8, which aims at "achieving universal health coverage, including risk protecting, access to quality essential health care services and access to safe effective, quality and affordable essential medicines and vaccines for all".

Thus, all the above is an indicator of the favourable policies and approach to ultrasound screening, and specifically to OB/GYN, in the European Union, creating an opportunity for SUOG.

NATIONAL POLICIES | Delving into the national policies of the EU MSs, it can be seen that prenatal screening policies vary widely across European countries but are mostly either about having one scan or three scans.

TABLE 7. NATIONAL POLICIES OR RECOMMENDATIONS FOR PRENATAL SCREENING FOR FOETAL ANOMALIES IN 16 EU MS'S, 2011

COUNTRY	PRENATAL SCREENING POLICY
Austria	Three scans
Belgium	Three scans
Croatia	No national policy
Denmark	One scan
England and Wales	Two scans
Finland	One scan
France	Three scans
Germany	Three scans
Ireland	One scan
Italy	Three scans
Lithuania	Two scans
Malta	One scan
The Netherlands	One scan
Poland	Three scans
Portugal	Three scans
Spain	Three scans
Sweden	One scan

Note: = countries that have no national policy/recommendations for routine ultrasound scans.

Notably, even though this was not the case before, there are no national scan policies in place in Croatia, but usually, three scans are performed. On the other hand, the Netherlands and Spain switched from not having an official policy to having one.

Such analysis provides useful insights about the frequency of ultrasound scans, and, therefore, their value to both the governments and the society, indicating rife opportunities for SUOG.

Regulatory Risks and Mitigation Measures

Regulatory requirements for medical devices might vary around the world, but within the EU, it is more harmonised. Even then, manufacturers´ efforts to comply with registration requirements are complex and involve additional resources.

Potential consequences and mitigation measures were identified for every risk event in the following table:

TABLE 8. IDENTIFIED REGULATORY RISKS AND MITIGATION MEASURES FOR SUOG

RISK	LIKELIHOOD	IMPACT	RISK SCORE	MITIGATION MEASURES
R.1. Additional procedures and time needed in case the device falls under higher risk category (invasive device, medical software).	1	2	2	• Development phase decisions should consider the regulatory aspects and the device risk classes that determine the regulatory pathway and the whole supply chain.

R.2. The use of patient data to build a reference annotated ultrasound images database might not be fully synchronised with the privacy and cybersecurity laws.	1	3	3	• The consortium should fully anonymise data, used only as an encrypted knowledge base in its common repository of de-identified DICOM cases, ensuring compliance with the following:
				  ◦ GDPR.
				  ◦ Software as medical device regulations (sensitive patient data, conditions for consent, security of processing).
				  ◦ EU Agency for Network and Information Security (ENISA) recommendations.
				• Due to the changes that are yet to be implemented in 2020, the consortium should closely follow possible developments in the legislation and proactively update its risks and mitigation strategies.

R.3. The ultrasound market is particularly susceptible to political unrest, because most ultrasound tenders are controlled by state governments; the budget squeeze would also affect the private sector.	1	2	2	• SUOG is solving a problem of a highly unmet need within the society. Following the commercialisation plan and market capture estimates, the political environment should not have a substantial effect on SUOG's entry.

Note. Scale: 1 (low), 2 (medium), 3 (high)
Risk score: likelihood x impact

As per the methodology, the risk scores can be found classified in the table below:

TABLE 9. REGULATORY RISK MATRIX (IDENTIFIED)

SCALE OF LIKELIHOOD	SCALE OF IMPACT: ACCEPTABLE	TOLERABLE	GENERALLY UNACCEPTABLE
NOT LIKELY	LOW RISK	R.1. MEDIUM RISK R.3.	R.2. MEDIUM RISK
POSSIBLE	LOW RISK	MEDIUM RISK	HIGH RISK
PROBABLE	MEDIUM RISK	HIGH RISK	HIGH RISK

Low risk Medium risk High risk

It can be seen that all identified risks are medium, forming a combination of unlikely events with tolerable or generally unacceptable negative impact.

CONCLUSIONS AND RECOMMENDATIONS

Routine ultrasound scans in OB/GYN are recognized both on the supranational level as well as on national levels. With most of the EU MSs having a specific policy or a recommendation in connection with the number of scans, SUOG seems to have a favourable regulatory landscape for entering these markets.

Despite diagnostic device purchasing decision in the public sector in all countries belongs to each individual provider or at least to local authorities, the purchasing procedure is usually taking the form of public tenders. Moreover, financing and reimbursement decisions are centralized and regulated by laws and other acts.

However, regardless of the national system, the first step of the regulatory strategy always constitutes the obtaining of the CE Mark. Thereafter, various national agencies need to be contacted. Despite the fact that diagnostic device purchasing decision in public sector in all countries belongs to each individual provider or at least to local authorities, the purchasing procedure is usually carried out in the form of public tenders.

Moreover, financing and reimbursement decisions are centralised and regulated by laws and other acts. On the other hand, financing and purchasing decisions are less regulated in private sectors in all countries and, thus, it should be easier, and it would take less time to enter the private sector.

In terms of regulatory risks and mitigation measures, identified risks do not fall under the critical category, though all of them are in the medium-risk category. Thus, mitigation measures for each risk are designed. SUOG should carefully plan and outline the medical device's technicalities so as to correctly identify its risk class, considering future advancements of SUOG as well. Additionally, full anonymity of data in compliance with the above-mentioned regulations and recommendations should be emphasised.

As a recommendation, in order to tackle potential regulatory barriers, SUOG should:

1. Consider the regulatory aspects and the device risk classes that determine the regulatory pathway and the whole supply chain;
2. Anonymise data, used only as an encrypted knowledge base in its common repository of de-identified DICOM cases;

3. Closely follow possible developments in the legislation and proactively update its risks and mitigation strategies.

ANNEXE 5. SOURCES

SOURCE	LINK(S)
Boyd PA, Devigan C, Khoshnood B, et al.	<link>
Demner-Fushman D, Antani S, Simpson M, and Thoma GR	<link>
EUROCAT	<link> <link>
European Commission	<link>
European Observatory on Health Systems and Policies	<link> <link> <link>
EUROSTAT	<link> <link>
Harvard Business School	<link>
IHS Market	<link> <link>
ISPOR	<link> <link> <link>
Köhler et al.	<link>
Phenotip	<link>
The European Board and College of Obstetrics and Gynaecology	<link>
The U.S. Department of Commerce's International Trade Administration	<link> <link>
UK Trade and Investment	<link>
WHO Regional Office for Europe	<link> <link> <link>

ANNEXE 6. ABBREVIATIONS

AEMPS	Spanish Agency of Medicines and Medical Products
AOTM	Health Technology Assessment Agency
CEPS	Economic Committee for Health Care Products
CIPM	Spanish Interministerial Medicinal Products Pricing Committee
CMEDiMTS	The Medical Device and Health Technology Evaluation Committee
COMEDIMS	Committee for Medicines and Sterile Medical Devices
DGFPS	Directorate-General for Pharmacy and Health Care Products
DIMDI	German Institute for Medical Documentation and Information
DRG	Diagnosis-Related Group
EU	European Union
G-BA	The Federal Joint Committee
GDP	Gross Domestic Product
GE	General Electric
InEK	Institute for the Hospital Remuneration System
IQWiG	Institute for Quality and Efficiency in Health Care
MSs	Member States
NZa	Dutch Healthcare Authority
OB/GYN	Obstetrics/Gynaecology
SUOG	Smart Ultrasound in Obstetrics and Gynaecology
USP	Unique Selling Proposition
YoY	Year-Over-Year
ZIN	National Healthcare Institute