D6.3 1st Report on dissemination and exploitation plans including communication activities

Project Information

Project name:	**A Multiplexed plasmo-photonic Biosensing platfoRm fOr rapid and intelligent Sepsis dIAgnosis at the point of care**
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Project coordinator:	Nikolaos Pleros / AUTH
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1 Executive Summary

This deliverable provides the dissemination and communication activities as well as the initial exploitation plan and strategies for market entry of the AMBROSIA technology including management of IPR. Regarding the objective of the dissemination activities, the focus is to identify and organize the actions to be performed in order the project to gain visibility and to promote the results both to the scientific community and the general public. Furthermore, dissemination material is presented and the dissemination actions are described. Regarding the exploitation plan, the initial market and competition analysis, the initial market cost analysis and exploitation strategies are described.

2 Introduction

2.1 Purpose of this document

The objective of this deliverable is to provide insight into the dissemination and communication activities of the project, and to provide the roadmap for AMBROSIA market entry.

2.2 Document structure

The present deliverable is split into the following two major parts:

1 Dissemination and communication activities
2 Initial exploitation plan
3 Protection and management of IPR

2.3 Audience

This content of this document is public.

3 Dissemination and Communication activities

The purpose of the dissemination and communication activities has been to make the results and the knowledge obtained during the AMBROSIA project available to parties outside the consortium, which includes the definition of the essential marketing characteristics and the elaboration of an effective plan for disseminating project results. Activities to ensure wide visibility and identification of the project have been identified and are being executed. In this way, the scientific community including universities, research centers, companies and individual organizations will have the benefit to access the theoretical and experimental results that have been achieved during the project. In addition, the general public ("the European tax-payer") is targeted. What has been done during the first reporting period (M01-M18) of the project is given in the next sub-sections.

3.1 Communication kit

The communication kit includes a set of project promotional material that has been developed and distributed through various mass media channels for public use to allow the project Consortium to reach large audiences in a short period of time and communicate the mission, vision and objectives of the project. Below, a brief description of the communication is given. More details can be found in D6.1.2024

- **Project Website**

The AMBROSIA website was developed and released during the first months of the project and it is constantly maintained and updated ever since. The website of the project is http://ambrosia-h2022.eu/.

- **Social media accounts**

With social media becoming more and more relevant, the AMBROSIA Consortium has decided to create visibility for the project at the major platforms: LinkedIN and Facebook and Twitter

- ✓ https://www.linkedin.com/groups/9307372/: the group had 75 followers on 03/07/2024.
- ✓ https://www.facebook.com/ambrosia.h2022/: the group had 27 followers on 03/07/2024.
- ✓ https://twitter.com/ambrosia_h2022: the group had 30 followers on 03/07/2024.

More followers are expected during the project duration when more announcements (e.g. regarding participation in more conferences) continue to be disseminated through the above channels.

- **Project Factsheet**

The project factsheet includes a clear overview of the project: the logo, the title of the project, general information about the project's duration, funding details and the Consortium. It summarizes the challenges the project is aiming to address as well as the mission statement detailing the aims of the project. The factsheet is available online at the AMBROSIA website (http://ambrosia-h2022.eu/docs/%CE%91MBROSIA_factsheet.pdf) and has been promoted through its social media channels.

- **Short project presentation**

The short project presentation contains the basic information about the project and the Consortium, Ambrosia's overall concept, objectives and work packages. It is intended to be used by the partners for

promoting the project and increasing its visibility. The presentation is available online at the Ambrosia website (http://ambrosia-h2022.eu/index.php/dissemination/communication-kit#home).

- **Press release**

The kick-off of the project was announced in a press release that was distributed by BIOPIX-T in the following channels:

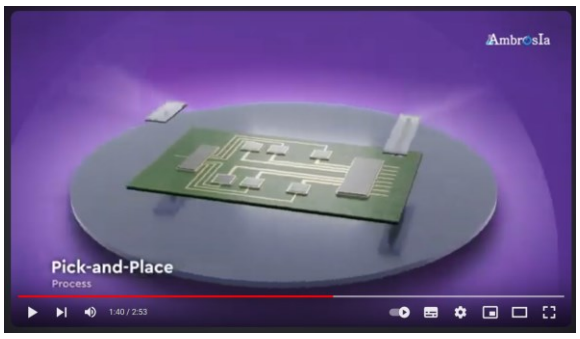
- ✓ https://biopix-t.com/news/biopix-t-to-participate-in-a-h2020-ria-project-granted-for-the-early-detection-of-sepsis-at-the-point-of-care/
- ✓ https://news.europawire.eu/ambrosia/eu-press-release/2023/05/09/11/28/55/116721/

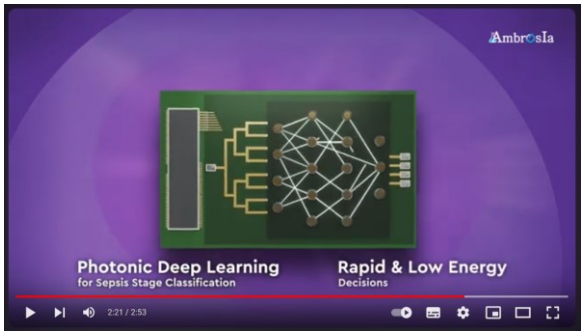
- **Project brochure**

A brochure has been generated for illustrative dissemination of the Ambrosia project in meetings, workshops, conferences, exhibitions and open public events. The brochure can be found at http://ambrosia-h2022.eu/docs/AMBROSIA-brochure1.png and http://ambrosia-h2022.eu/docs/AMBROSIA-brochure2.png.

- **Project video**

A short AMBROSIA video has been created to promote its vision, objections and challenges to the general public. Apart from the project's website, the video has been uploaded on YouTube and can be found at https://www.youtube.com/watch?v=GSyXR0-G1MI. Some screenshots from the video are shown below:





- **1st Project newsletter**

The first newsletter of the project has been created. The newsletter includes main project features (objectives, expected outcome) and recent news from the project. A second newsletter will be created with news from fabrication activities. The project newsletter can be downloaded from the project website.

3.2 Participation in relevant events, exhibitions, workshops, specialized international meetings, etc.

AUTH presented the AMBROSIA project at:

- ✓ **Photonics Partnership annual meeting, 26-27 April 2023, Brussels.**
  AMBROSIA was presented by AUTH at the Photonics Partnership annual meeting, 26-27 April 2023, in Brussels at the Workshop 'Health'. AUTH had the opportunity not only to present the project, but also to learn about similar EU project efforts that have also commenced and discuss future collaborations between projects.
- ✓ **20th International Conference on Nanosciences and Nanotexnology, 04-07 July 2023, Thessaloniki.**

  AUTH gave an invited talk at the 20th International Conference on Nanosciences and Nanotexnology, 04-07 July 2023, in Thessaloniki.
- ✓ **Conference on Lasers and Electro-Optics (CLEO), 2024, Charlotte, NC, USA.**

  AUTH had presence at CLEO 2024 conference in Charlotte, USA with an oral presentation where AUTH researchers communicated AMBROSIA and its recent outcomes to the global scientific community involved in optical sensing.

ICN2 presented the AMBROSIA project at:

- ✓ **Gordon Research Conference, 2023 Lasers in Micro, Nano and Bio Systems. 4-9 June , 2023, Mount Snow, Vermont (USA).**

ICN2 presented an invited talk at Gordon Research Conference, 2023 Lasers in Micro, Nano and Bio Systems on 4-9 June 2023, in Vermont, USA entitled "Nanophotonics Biosensors for Ultrasensitive Label-free Bioanalysis". ICN2 had the opportunity to present and increase visibility of the project.

X-Celeprint presented or mentioned the AMBROSIA project at:

- ✓ **Photonics West, San Francisco (US), January 2024.**
- ✓ **Semicon EU 23, EPIC Technology Meeting on Microelectronics & Photonics – Two Sides of One Coin, Frankfurt, November 2023.**
- ✓ **PIC-EU Summit 23 + IPSRI, Eindhoven, October 2023.**
- ✓ **ECOC 2023, Glasgow, September 2023.**
- ✓ **EPIC Online Technology Meeting on Hybrid Photonics Integration, September 2023.**
- ✓ **Laser World of Photonics 2023, Frankfurt, June 2023.**

LIGENTEC acknowledged the AMBROSIA project at:

- ✓ **PIC International conference 2023, 18-19 April 2023, Brussels.**

- ✓ **Photonics North 2023, 12-15 June 2023, Montréal.**
- ✓ **Laser World of Photonics, 27-30 June 2023, Munich.**
- ✓ **Optica Photonic-Enabled Cloud Computing Summit, 24-25 October 2023, CA (USA).**
- ✓ **PIC International conference 2024, 16-17 April 2024, Brussels.**

LIGENTEC presented the AMBROSIA project at:

- ✓ **MicroNano-Fabrication Annual Review Meeting , 14 May 2024, Lausanne.**

BIOPIX-T presented the AMBROSIA project at the two following capital funds:

- ✓ **11 VC (https://www.11.vc/)**
- ✓ **Metavallon (https://metavallon.vc/)**

In addition, **BIOPIX-T** exhibited at the booth of the

- ✓ **'SusHi Tech Tokyo 2024 Global Startup Program' held at Tokyo Big Sight from May 15th (Wednesday) to 16th (Thursday), 2024 (https://sushitech-startup.metro.tokyo.lg.jp/).**

Planned events

AUTH will present research outcomes related to AMBROSIA **at:**

- ✓ **14th International Conference on Metamaterials, Photonics Crystalls and Plasmonics, 2024, Toyama, Japan**

AUTH will organize a workshop on "Lithographic Mask Design" at its premises in Thessaloniki, Greece on 1-10 July 2024. The announcement can be found here.

UOI will present research outcomes related to AMBROSIA **at:**

- ✓ **18th International Congress on Artificial Materials for Novel Wave Phenomena – Metamaterials 2024 Crete, Greece, Sep. 9th –14th, 2024**
  - ***"Enhancement of plasmo-photonic index sensor sensitivity by slow-light effects"***, E. Lampadariou, E. Chatzianagnostou, D.V. Bellas, D. Spasopoulos, J.-C. Weeber, N. Pleros, E. Lidorikis

X-CELEPRINT will present and acknowledge AMBROSIA **at:**

- ✓ **Epic online meeting, September 2024.**
- ✓ **ECOC 24, Frankfurt, September 2024.**
- ✓ **MedPhab symposium in Zurich on September 2024.**

3.3 Publications in scientific journals and conference proceedings

Scientific publication in journals is also one of the main dissemination mechanisms. Until now AMBROSIA project has been acknowledged in the following paper by **AUTH**:

- ✓ Konstantinos Fotiadis, et al., "A High-Sensitivity Bi-modal Plasmo-photonic Refractive Index Sensor", ACS Photonics Journal, vol 10, no 8, pp 2580-2588, August 2023.
- ✓ Konstantinos Fotiadis, et al., "Theoretical and Experimental Analysis of Single-Arm Bimodal Plasmo-Photonic Refractive Index Sensors", Sensors, vol. 24, no. 12, 2024.

Additionally, **UOI** is preparing a theoretical publication detailing the key design principles and the performance metrics of Bragg-assisted plasmo-photonic sensors.

- ✓ Eleftheria Lampadariou, et al., "Slow-light enhanced integrated plasmo-photonic index sensor", under preparation.

4 Initial exploitation plan

The AMBROSIA project aims to exploit a new technologically advanced platform for sepsis diagnosis and classification. The exploitation & business strategy for the AMBROSIA solution, including market & competitor analysis, supply chains, revenue forecast, and regulatory/financial requirements will be gradually developed until its final version which will be delivered by the end of the project.

4.1 Market Drivers, Needs, and Restraints for Sepsis Diagnosis

The prevalence of sepsis has increased significantly over the last decade; the condition has the highest mortality rates of any disease. The major factors responsible for the rising prevalence of sepsis include the growing geriatric population, the development of drug resistance among individuals, and the rise in increasingly virulent infections. Approximately 30 million people develop sepsis globally every year. In the US, more than 1.7 million people are diagnosed with sepsis every year, and the incidence rate is expected to grow by 8% each year.

The chances of developing sepsis are very **high in infants**, due to their weak immune systems. The incidence of sepsis is also **high among the elderly** due to various factors, such as coexisting comorbidities (such as cancer, diabetes, obesity, and HIV infections), weakened immune response, and prolonged and repeated hospitalizations. **Patients undergoing surgical procedures** are prone to developing sepsis infections and complications. Globally, surgical procedures have increased significantly in the last few decades. The incidence of **hospital-acquired infections is increasing worldwide**, with an increase in hospitalizations.

The window of opportunity for sepsis management is in hours: the chance of survival drops by 7.6% each hour of disease progression until an appropriate treatment is started. **Early and accurate sepsis detection and stratification are essential for enhancing survival rates.**

For the AMBROSIA technology, the market needs are predefined by the unmet clinical needs professional healthcare environments are facing in the field of diagnosing and treatment of Sepsis, in combination with cost-efficiency and health economics.

Such needs include:

- Rapid technology (short time to result within minutes)
- High accuracy, sensitivity, and specificity (multiple measurements)
- User-friendly technology (limited manual handling required)
- Affordable technology (cost-efficiency and health economics)

Companies focus on developing automated diagnostic devices based on advanced technologies, such as molecular diagnostics, for detecting sepsis. These devices are easy to use, fast, and boast advanced features, owing to **which they cost more than conventional blood culture tests**. For instance, the cost of molecular diagnostic tests is between USD 300 and USD 3,000, which is very high compared to the cost of blood culture tests, priced as low as ~USD 28–35. Thus, due to limited budgets, government hospitals (especially in emerging nations) and academic research laboratories **cannot afford such systems**. In addition, maintenance costs, and several other indirect expenses increase the total cost of ownership of these instruments, thereby further limiting their adoption, especially among small-scale end users.

AMBROSIA aims to provide an **affordable disruptive solution for sepsis diagnosis at the point of care** that will offer **multiplexed** (within a single test) quantification of multiple protein biomarkers and bacteria **within minutes**, also providing real-time disease-stage classification and enable **rapid and precise decision-making** for therapy and medical actuation. The AMBROSIA solution will be the first photonic AI-enabled sepsis point-of-care diagnostic unit on the market.

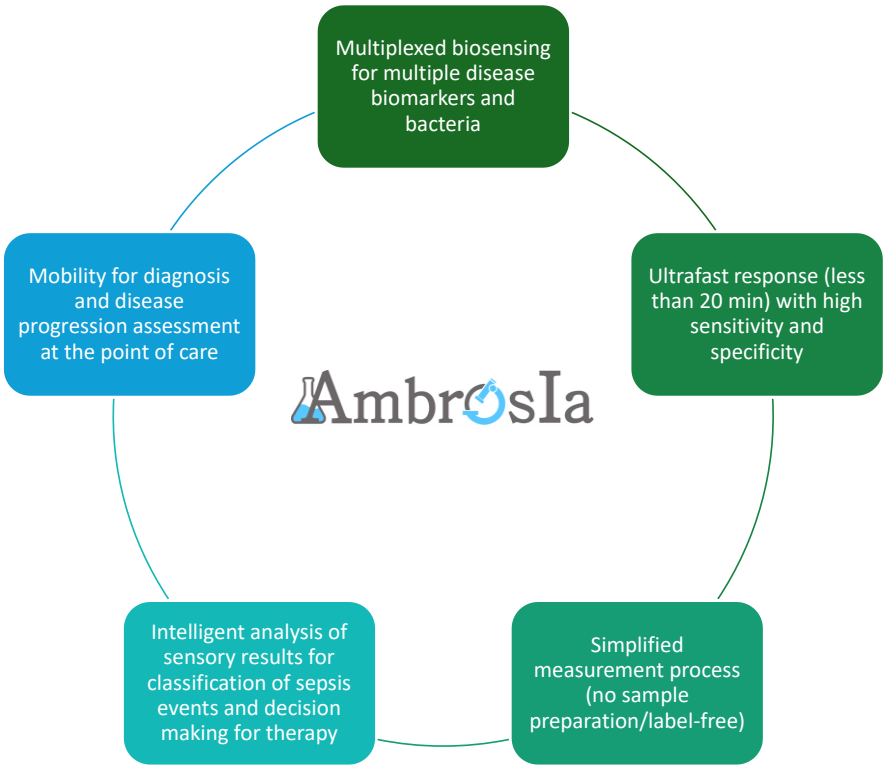


Fig. 1: The concept of the AMBROSIA unique solution

4.2 Market Size & Segmentation

The sepsis diagnostics market is projected to reach **USD 771.6 million by 2026** from USD 503.3 million in 2021, at a **CAGR of 8.9%**.

In Europe it is projected to reach USD 232.3 million by 2026, growing at a CAGR of 8.4%. Europe accounts for the second-largest share of 30.9% of the global sepsis diagnostics market. Germany, the UK, France, Italy, and Spain are the major contributors to the European sepsis diagnostics market. According to the European Centre for Disease Control and Prevention (ECDC), ~9 million cases of healthcare-associated infections occur across Europe each year.

By product, the sepsis diagnostics market is segmented into:

- blood culture media,
- assays & reagent kits,
- instruments,

The blood culture media segment is estimated to account for a larger **share of 45.1%** in the global sepsis diagnostics market, by product, in 2020. The growth of the blood culture media segment can be attributed to the growing utilization of blood culture media by hospitals & pathology laboratories for the diagnosis of sepsis coupled with the increase in the availability of blood culture media in the market.

Based on technology, the market is segmented into:

- blood culture,
- molecular diagnostics,
- immunoassays,
- flow cytometry,
- microfluidics,
- biomarkers,

In 2020, **the blood culture segment held 56.2%** of the sepsis diagnostics market share. This can be attributed to the low cost and the wide use of blood culture methods to diagnose sepsis.

Based on the method, the sepsis diagnostics market is categorized into conventional and automated diagnostics. The conventional diagnostics segment commands the largest share of the global sepsis diagnostics market. The growth of this segment can be attributed to the high adoption of this method for sepsis diagnosis and clinical evidence for its efficacy. **The automated diagnostics segment is expected to grow at the highest CAGR of 10.7%** due to its accuracy, rapidity, and user-friendliness.

Based on test type, the market is segmented into laboratory tests and point-of-care tests. The laboratory tests segment accounts for the largest **share of 92.7%** due to the high use of conventional blood culture tests for sepsis diagnosis, lack of awareness about POC tests, and the low cost of laboratory testing services.

4.3 Competition Analysis

A lot of competition in the Point-of-Care (PoC) market for sepsis detection is expected in the coming years. The market potential for diagnostic tests to detect sepsis is considered high. The leading companies in IVD and sepsis diagnostics are expected to offer more sensitive and specific PoC solutions that are extremely rapid in providing patient results. **These companies also have the power and budgets to offer package deals with lower instrument and/or reagent costs.** This will challenge the AMBROSIA solution to also offer cost-efficient solutions to be competitive without affecting the accuracy of the provided results. In addition, smaller companies are also expected to develop into strong competitors when providing similar technologies.

The prominent players operating in the global sepsis diagnostics market include bioMérieux (France), Becton Dickinson and Company (US), Danaher Corporation (US), T2 Biosystems (US), Luminex (US), Roche Diagnostics (Switzerland), Thermo Fisher Scientific (US), Bruker Corporation (US), Abbott Laboratories (US), Immunexpress (Australia), Axis-Shield Diagnostics (UK), Quidel Corporation (US), Siemens Healthineers (Germany), EKF Diagnostics (UK), Seegene Inc., (South Korea), Boditech Med (South Korea),

Alifax S.r.l. (Italy), and AdvanDx (US). The key growth strategies adopted by the top players in this market are new product launches, collaborations, partnerships, acquisitions, and expansions.

The total market share of the Top 5 Players (bioMérieux, Becton Dickinson and Company, Danaher Corporation, Roche Diagnostics, and Abbott Laboratories) is between 85–88%. All five of them have a strong and established product portfolio, a strong market presence, and provide innovative and reputable products in the sepsis diagnostics market.

Additional competitors include established vendors with very strong business strategies, but they provide limited offerings and focus on a specific type of technology instead of a diversified product range. These are T2 Biosystems (US), Thermo Fisher Scientific (US), Bruker Corporation (US), and Luminex (US).

Some vendors including Immunexpress (Australia), Quidel Corporation (US), Siemens Healthineers (Germany), and EKF Diagnostics (UK), have broad product portfolios, but they do not have yet established their presence in the market. Other vendors with niche product offerings might be new entrants in the market and may require time to gain traction. The participants in this market are, for example, Axis-Shield Diagnostics (UK) and Seegene Inc. (South Korea).

Finally, the competitive landscape also includes start-ups/SMEs developing products for the sepsis diagnostics market including Abionic SA (Switzerland), Qvella Corporation (Canada), Cube Dx GmbH (Austria), Q-linea (Sweden), Alpha laboratories (UK), Inflammatix, Inc (US), Nanōmix, Inc (US), Molzym GmbH & Co. KG (Germany), Miacom diagnostics GmbH (Germany), Spectral Medical (Canada), Novus Diagnostics Ltd (Ireland) , Cytovale Inc (US), Resistell AG (Switzerland), and Presymptom Health (UK).

Table 1: Product footprint of companies

COMPANY NAME	BLOOD CULTURE	IMMUNOASSAY	MOLECULAR DIAGNOSTICS
bioMérieux (France)	Yes	Yes	Yes
Becton, Dickinson, and Company (US)	Yes	Yes	Yes
Danaher Corporation (US)	No	No	Yes
T2 Biosystems (US)	Yes	Yes	Yes
Luminex (US)	Yes	No	No
Roche Diagnostics (Switzerland)	No	Yes	Yes
Thermo Fisher Scientific (US)	Yes	No	Yes
Bruker Corporation (US)	Yes	Yes	No
Abbott Laboratories (US)	Yes	No	No
Immunexpress (Australia)	Yes	Yes	Yes
Axis-Shield Diagnostics (UK)	Yes	No	No
Quidel Corporation (US)	Yes	No	No
Siemens Healthineers (Germany)	Yes	No	No
EKF diagnostics (UK)	Yes	No	No
Seegene Inc., (South Korea)	Yes	No	No
BODITECH MED INC., (South Korea)	Yes	No	No
Alifax S.r.l., (Italy)	No	No	No
AdvanDx (US)	No	No	No
CytoSorbents (US)	No	No	Yes
Sysmex Corporation (Japan)	No	No	No

4.4 Pricing Trend Analysis

Cost and quality are the most important parameters for purchasing sepsis diagnostics products. The cost of sepsis diagnostics equipment, media, and accessories depends on various factors—manufacturing expenses, brand, purchase type (bulk or single), and reimbursement scenario. Based on all these factors, the price of sepsis diagnostics systems and consumables varies from region to region.

Table 2: Average price of sepsis diagnostics products by country

COUNTRY	BLOOD CULTURE MEDIA (USD)	ASSAYS & REAGENT KITS (USD)	INSTRUMENTS (USD)
US	25-30	35-40	~250,000
Germany	20-25	30-33	235,000-240,000
UK	~18	~25	~225000
France	~20	28-30	~230000
Italy	18-20	~26	225,000-230,000
Spain	~21	26-28	230,000-235,000
Japan	12-15	15-18	~175,000
China	~10	~12	~125,000
India	~8	~10	~100,000

The pricing of the AMBROSIA solution should follow the trend for assays and instruments to be on par with the competition.

The target price for the market entry of the AMBROSIA product will be in the order of $30,000 - $50,000. This estimation is based on the current costs for manufacturing and assembly of the components into the envisaged instrument without considering any manufacturing agreements for specific production volumes.

Concerning the pricing of the consumables including the sensors and the reagents for surface functionalization and detection, the estimated price per test will be not more than $50. It should be noted that the sensing element can accommodate multiple sample analyses which significantly reduces the cost per sample test.

Based on the above, it is apparent that the AMBROSIA system will be competitive in terms of pricing compared to other commercially available solutions, while at the same time allowing for a considerable margin for the company that will commercialize it. Cost analysis will become more detailed and accurate as the project evolves and is expected to be completed after all necessary technical steps for the AMBROSIA diagnostic system have been experimentally validated.

4.5 Conclusions and next steps

According to the market analysis, the blood culture segment (traditional microbiology) commands the largest share of 56.2% of the global sepsis diagnostic market, by technology. This is mainly because of the lower cost of blood culture tests. The microbiological evaluation of sepsis includes direct culture tests - blood culture bottles (aerobic and anaerobic) are inoculated with blood and incubated for **six to seven days** - and tests using body fluids (urine, feces, and secretions), to identify the causative agent of sepsis for further treatment. However, this method has a prolonged turnaround time. To satisfy the need for faster responses and improved healthcare outcomes, the molecular diagnostics segment is estimated to grow at a CAGR of 10.7%, the immunoassays segment at a CAGR of 8.9%, and the biomarkers segment at the highest CAGR of 11.6%. The AMBROSIA project will capitalize on these trends by offering a complete solution for multiplexed (7 biomarkers, molecular detection combined with immunoassays) and AI-enhanced rapid diagnosis of sepsis. At the same time, the pricing of the AMBROSIA solution should follow the trend for assays and instruments to be on par with the competition.

As for the next steps:

i. The potential of the AMBROSIA solution will be investigated further to strengthen the market position and the usability of the platform. This technology implementation analysis will focus on stakeholders including patients and healthcare professionals. AMBROSIA aims to target customers where its technological solution can provide additional benefits. This could generally

be the case for acute clinical settings (emergency departments, wards, intensive care units), and primary or ambulatory care. The targeted user group would be clinical users like physicians, nurses, and clinical laboratory technicians. Patients shall benefit from the implementation of the technology. In addition, the implementation analysis will help to identify potential improvements to the AMBROSIA technology for integrating into clinical workflows.

ii. A technology assessment study will be performed focused on cost analysis versus previous workflow, integration into workflows, and impact on patient care. Such a study will strengthen the value proposition of the product with economic arguments.

iii. An analysis of the key manufacturing challenges will be performed to maximize and secure the manufacturing capabilities for the hardware and wet chemistry products with respect to yield, reliability, and cost efficiency.

iv. A gap analysis toward the regulatory approval and CE marking.

v. The AMBROSIA project aims to generate a prototype platform that will be validated in a laboratory setting using clinical samples. Afterward, commercial product developments including industrial design, trial productions, clinical studies, and regulatory approval will follow toward the commercialization of the technology (from TRL 6 to TRL 9). The amount of the further required investment for the activities will be assessed for the partners to plan early the next day of the AMBROSIA technology.

In addition to all the above, throughout the project, we will keep monitoring for other exploitable results from any of the partners as well as exploring opportunities for additional application areas. For each novel development or new application, we will evaluate the market potential, the benefits it brings, the size of the targeted market, the time-to-market, and the investment costs until exploitation.

Fig. 2: Overview of AMBROSIA market entry activities roadmap

5 Protection and management of IPR

5.1 Freedom-to-operate analysis

Introduction

During the project preparation, the partners performed an IPR search on topics relevant to the project to ensure no patent infringement issues. Some relevant patents were found and analysed. It was concluded

that ***they do not pose any patent infringement limitations to the execution of AMBROSIA***, since they were either of a different scope or address complementary issues:
"Photonic sensor using a fixed wavelength laser", WO 2021207834A1, UBC, 2021.
"Implantable sensor", US 9532738B2, UGENT - IMEC, 2017.
"Integrated plasmo-photonic sensor and method of use", US20200003696A1, AUTH, 2020.
"Structure for a photonic integrated circuit", WO2021152143A1, SMART, 2021.
"Method and apparatus for performing a real-time colorimetric nucleic acid amplification assay", WO2020089399, BIOPIX-T, 2019.
"Interferometer and sensor based on bimodal optical waveguides, and detection method", US8279445B2, ICN2,2012.

During the first 18 months of the project, a full FTO search was conducted to identify whether the medical device or its intended use falls within the scope of the claims of patents and applications valid within the European market, in other words, if the device/use contain all the claimed features. If the device/use does not contain all the claimed features (i.e. there is overlap) then the device/use does not infringe literally. If the device/use differs in a few trivial features that are considered equivalent to the claimed features, then there may be infringement by equivalence. In case of partial overlap where there is at least one substantial difference compared to the claimed features then there is no infringement.

Codes and keywords

For the FTO search the following IPC/CPC codes and keywords were used:

IPC/CPC codes
G01N
G02B
B82Y
G02B2006/12159 Interferometer
G01B9/02051 Integrated design, e.g. on-chip or monolithic
G01N2021/7779 Measurement method of reaction-produced change in sensor interferometric
G01N21/45 Refractivity; Phase-affecting properties, e.g. optical path length using interferometric methods; using Schlieren methods
G02B6/1226 Basic optical elements, e.g. light-guiding paths involving surface plasmon interaction
G06N3/0675 Physical realisation, i.e. hardware implementation of neural networks, neurons or parts of neurons using optical means using electro-optical, acousto-optical or opto-electronic means
G01N2333/585 Calcitonins
G01N2800/26 Infectious diseases, e.g. generalised sepsis
G01N2800/52 Predicting or monitoring the response to treatment, e.g. for selection of therapy based on assay results in personalised medicine; Prognosis

Keywords
Photonic Integrated Circuit (PIC)
Photonic and plasmonic refractive index (RI) sensors
Plasmo-photonic sensors
Plasmo-photonic interferometers
Plasmo-photonic Mach-Zehnder Interferometric (MZI) refractometric sensor

Complementary Metal-Oxide-Semiconductor (CMOS)-compatible plasmonic waveguides integrated with silicon nitride photonic integrated circuits (PICs)
Single-arm bimodal interferometers
Aluminum plasmonic waveguides co-integrated with silicon nitride (Si_3N_4) photonic chips
Silicon photonics
Bragg-grating-decorated plasmonic stripe waveguides
Dielectric-loaded Bragg cavities
(Aluminum) Plasmonic transducer (Bragg-grating decorated thin films)
Periodic Bragg barrier structures
[Micro-transfer printing (uTP)]
Optically-enabled artificial intelligence-based Diagnosis Decision Support System
Photonic Deep Neural Network (DNN) inference engine
Detection of multiple sepsis biomarkers and bacteria [C-reactive protein (CRP), procalcitonin (PCT), interleukin 6 (IL-6), and the mid-regional pro-adrenomedullin (MR-proADM), Escherichia coli, Staphylococcus aureus, and Pseudomonas aeruginosa]
Photonic circuit crossbar architecture

Search results

A. Patents related to the device or its parts

EP3583406B1 Integrated plasmo-photonic biosensor and method of use
EP2214049B1 Integrated optical waveguide interferometric sensor
EP4097520A1 Semiconductor apparatus and semiconductor device, and method for producing
EP3931879A1 Waveguide integrated plasmon assisted field emission detector
EP3671187A1 Photonic sensor chip, packaged photonic sensor device and arrangement
EP2762858B1 Integrated interferometric optical sensor circuit
EP3944005A1 Photonic device
EP4264369A1 Balanced photonic architectures for matrix computations
EP4193306A1 Coherent photonic computing architectures
EP4127668A1/WO2021207834A1 Photonic sensor using a fixed-wavelength laser
EP2475294B1/US9532738B2 Implantable sensor
EP3854300A1/US9532738B2 Implantable sensor
EP4097517B1/WO2021152143A1 Structure for a photonic integrated circuit
EP2017602B1 Interferometer and sensor based on bimodal optical waveguide and sensing method

Other related but distinct inventions: **EP3754326B1** (Integrated optical circuit with encapsulated reference arm), **EP3364171B1** (Method for detecting a local change in the refractive index of a dielectric medium placed at the surface of an optical sensor)

Withdrawn/Lapsed: ***EP3264070A1*** *(Waveguide-based system and method for biomarker detection),* ***EP2310806A2*** *(Enhanced sensitivity interferometric sensors),* ***EP1794573B1*** *(Photonic crystal interferometer),* ***EP3988970A1, EP0852715B1, EP1182445B1, EP2496930A1, GR1006491B*** *(Monolithically integrated physical chemical and biological sensor arrays based on broad-band mech-zehnder interferometry; not valid),* ***GB2437543A, EP1766369B1, EP3264070A1*** *(Waveguide-based system and method for biomarker detection).*

B. Patents related to sepsis biomarkers

EP3577465B1 Proadm as marker indicating an adverse event

EP3682241B1 Pct and pro-adm as markers for monitoring antibiotic treatment

EP4027145A1 [Divisional of EP3682241B1] Pro-adm for therapy monitoring of intensive care unit patients

EP3662289A1 Diagnosis and risk stratification of fungal infections

EP3833979A1 Pro-adm for prognosing the risk of a medical condition requiring hospitalization in patients with symptoms of infectious disease

EP3729101A1 Workflow for risk assessment and patient management using procalcitonin and midregional-proadrenomedullin

EP3729082A1 Antibiotic therapy guidance based on procalcitonin in patients with comorbidities

EP3682245A1 Pro-ADM as a therapy monitoring marker for critically ill patients

Expired patents related to sepsis biomarkers (for reference purposes): EP1121600B1, EP2028493B1, EP1770397B1, EP1408334B1, EP2545379B1, EP2320237B1

Conclusions

The patent search and analysis verified the initial conclusion that ***no patents pose any infringement limitation to the execution of AMBROSIA concerning the device or its components***, since they are either of a different scope or address complementary issues.

Concerning the sepsis biomarkers:

- The method of using pro-ADM or a partial peptide to determine the presence of sepsis, its severity and/or the success of a therapeutic treatment is not per se patent protected. The same holds true for the use of PCT and CRP in the diagnosis of sepsis.
- The search has identified two follow-on patents and five applications owned by Brahms GmbH that claim the use of MR-proADM and/or procalcitonin (in some cases optionally also CRP and IL-6) in particular patient sub-populations.
- EP3577465B1 is under opposition and the outcome should be watched.
- EP3682241B1 was maintained in amended form during opposition with claims that are very similar to the granted ones. As long as EP3682241B1 remains valid, it should be avoided to making medical claims directed to the “antibiotic therapy guidance, stratification and/or control in a patient suffering from an infectious disease and receiving treatment with one or more antibiotic agents”.
- The five applications have to overcome inventive step, and in some cases also novelty and clarity, objections before they can be granted. Therefore, the claims are bound to change, and it is quite likely that eventually the scope of their claims will be limited to methods for risk stratification of specific sub-populations based on specific MR-proADM and/or procalcitonin cutoff levels.

This was an initial FTO analysis; the full confidential report is available upon request for all the consortium partners. The European patent landscape will be closely monitored throughout the project duration.

5.2 IPR committee activities

Given the strong exploitation potential that AMBROSIA presents, consortium partners have agreed on a series of steps to ensure the protection of the newly generated IP, as well as their background, and the

respective exploitation strategy. An agreement has been achieved on confidentiality measures, data management, IPR management, and joint ownership. IPR management is defined in detail in the "Consortium Agreement," (CA) with rules to identify and protect results and innovations, aligned with Commission-policy, with two mechanisms: a) Monitor newly generated knowledge globally to ensure results are not overhauled by other groups and decide whether they are worthy of patenting, b) protect IPR before publication, guaranteed by informing the consortium through emails or the project website, and each partner responsible of filing patents when needed.

Since the beginning of the project, an IPR council was established comprising one person appointed by each AMBROSIA member (Table 3) to continuously monitor the generated knowledge in the relevant AMBROSIA fields worldwide and ensure that IPR protection strategies will be activated before publishing. The IPR committee is responsible to:

- monitor the generated knowledge
- protect generated intellectual property (IP)
- ensure IP protection before publishing
- focus on post-project commercial exploitation
- ensure freedom to operate

The committee discusses the related matters every 6 months during the consortium meetings. Extraordinary meetings are also organized if an urgent matter arises.

Table 3: AMBROSIA IPR committee members

	PARTICIPANT	COUNTRY	ASSIGNED PERSON	email
1	AUTH	Greece	Dimosthenis Spasopoulos	dspa@auth.gr
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8	ARGO	Czech Republic	Michal Szaj	michal.szaj@argotech.cz
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