ANTISUPERBUGS

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Contactors

1. Main Results: The innovative solution *(mark parts that are not suitable for publication purposes).*

The innovative solution (in its current form):

The CULTURE project involves the development of a comprehensive platform and highly modular solution to support healthcare professionals in their efforts to minimize the pace of Antibiotics resistance. This should be done not only by studying emergent microorganisms and resistance mechanisms, but also through diagnostic technologies like advanced sensing devices and information systems with capacities to gather information from different clinical datasets and to monitor and prevent infectious episodes in a connected and interoperable way. The solution is the result of a combination of different technologies.

1) A real time detection system, called the CULTURE sensing device, with capacities to detect the pathogens identified in the ANTISUPERBUGS health challenge. CULTURE sensing device is based on Photoionization detection, a technology with high sensitivity and that allows miniaturization, low energy consumption and that it has all attributes to become a real-time and portable technology.
2) A digital solution, called CULTURE ICT solution that can integrate, in a single point and with high interoperability, the data obtained from the CULTURE sensing device as well as from other relevant hospital datasets.
3) The CULTURE ICT solution also incorporates a Local Control and surveillance system, able to exploit the combined data gathered from the different sources and to support healthcare professionals on how to manage patients, infectious episodes, and Antimicrobial Stewardship programs.

Where exactly lies the innovativeness in the solution: In which ways and to which extent does the solution go beyond what existing solutions can achieve?

The first radical and perhaps more important innovation is the overall proposal of the CULTURE platform. Phase 2 main R&D activities were concentrated on the development of the sensing device. These R&D activities involved the study of a combination of PID lamps for the ionization and detection of the complex mixture of VOCs that are released by bacteria in real hospital environments as well as all developments necessary for the engineering and assembly of a real prototype. The design and engineering of the Sensing device is focused on the end user and it is compatible with different sampling procedures already in the market. As a result, the CULTURE sensing device has been designed to analyse Volatile Organic Compounds from the patient exhaled breath and from urine or faeces samples. Finally, the CULTURE sensing device also offers capabilities to monitor bacteria VOcs in the room air.

Additionally, the CULTURE project also explored the application of the latest computational methods and mathematical algorithms to improve the performance indicators of the CULTURE sensing device. Concretely, the CULTURE team investigated the potential exploitation of machine learning algorithms to improve the sensing device. The proposed work intended to automatically interpret all the VOC complex data released by bacteria and detected by a PID sensor based on a combination of single lamps. We have investigated the application of Machine Learning algorithms to help researchers in the interpretation of the complex data that could be generated. The algorithms significantly contribute to solve the selectivity issues related to the detection of similar VOCs released from several bacteria in real hospital environments.

The level of innovativeness of the CULTURE solution increased through the development of a software platform that integrates both the data form the CULTURE sensing device and relevant information related to Hospital infectious episodes. This information not only includes hospital datasets but also the data that will be obtained by the CULTURE sensing device. The CULTURE ICT solution follows international standards like HL7, IHE or SNOMED and it incorporates an interoperability engine to facilitate its integration with Electronic Health Records across Europe. As far as we know nobody has developed or combined similar technologies in a single solution.

The degree of innovation: indicate if your innovative solution is (a) a totally new product / service / process / method; (b) an improvement to an existing product / service / process / method; (c) a new combination of existing products / services / processes / methods (d) a new use for existing products / services / processes / methods), (e) otherwise

The CULTURE project intends the development of a comprehensive solution to offer a unique value proposition to patients, health professionals and hospital managers. The comprehensive solution is a totally new product that is the result of a combination of existing technologies (mostly open-source technologies integrated in the ICT solution) and radical new technologies (mostly integrated in the sensing device). Therefore, we are working on a totally new product. This new product can open new services. For instance, the combination of the PID

sensing technologies and the computational models developed under the ANTISUPERBUGS project could also be commercialised through new surveillance services for the anticipation of infectious episodes in hospitals. The technology can also contribute to support Antimicrobial stewardship programs, providing more information and facilitating training programs or the deployment of alerts for healthcare professionals.

2. Main Results: Benefits obtained

Provide a short description (mark parts that are not suitable for publication purposes) of any benefits that you obtained from participating in the procurement.

The ANTISUPERBUGS Phase 2 gave us several benefits

i) During the phase 2, we have developed the prototype that has demonstrated its capacity to detect bacteria at early stages of outbreak in a controlled laboratory environment. We have also had the opportunity to develop the necessary software to improve the capacities of the sensor and to connect the solution to real hospital ICT infrastructures. This first version of the prototype and the first results obtained were critical to reduce future development risks and technology uncertainties.

ii) Phase 2 also gave us the possibility to test and abandon the development of a technology based on a wavelength-tuneable light source (SIPS technology): The preparations for practical implementations carried out at the beginning of phase 2 were not satisfactory. The information gathered served us to focus our progress on a CULTURE sensing device based on a combination of lamps and coupled to a Machine Learning module.

iii) We also have investigated the current limitations of the available commercial products that are also based on PID detection technologies, developing a new R&D line to attain higher sensitivity and selectivity limits.

iv) Phase 2 also served us to generate the first data. The data was related to the outputs of the sensing device and several KPIs related to the hospital activity that can have influence on bacteria outbreaks. Due to the Covid19 pandemic, we could not obtain these KPIs from Buyers Groups or form subcontracting parties. We have therefore created artificial data from other Antimicrobial Stewardship initiatives in Europe. The data gathered during phase 2 served to develop our first models for the Local Control and Surveillance System that will be improved and validated in Phase 3 with real data from hospitals.

v) Phase 2 also gave us the opportunity to develop the first prototype of the ICT software platform.

vi) During Phase 2, we have also gathered significant knowledge about clinical validation methodologies and particularly about clinical research in humans. We presented two versions of a comprehensive research protocol and we have significantly improved our protocols to manage effectively and under strict protection measures the data that can be obtained in phase 3.

vii) We have also increased our knowledge about the healthcare market and about similar solutions to fight antimicrobial resistance. As a result, we have identified interesting business opportunities and partnerships.

viii) ANTISUPERBUGS also served us to identify potential competitors. The knowledge gained also served us to redefine our business strategy.

Other benefits: complete if applicable

Finally, the ANTISUPERBUGS Phase 2 helped us to build the first prototype of a technology with a great potential thanks to the unique combination of modular components, functionalities, and services. The design considered not only technical aspects but also the requirements defined by the ASB team as well as an analysis of its market potential.

3. Lessons learned

Provide a short description (mark parts that are not suitable for publication purposes) of any lessons learned from participating in the procurement.

PCP methodology in three phases significantly reduces development risks and increases the feeling of competition. In our case, the feeling of competition increased the commitment level of our team (three very

different organizations). We believe that the PCP methodology has helped us to attain better results when compared with other R&D funding mechanisms.

Based on our experience, during the two phases of the ANTISUPERBUGS procurement, PCP also helps companies to get a good understanding of public and private market at European level. On the one hand, public procurers identified a health challenge that is not well covered with the existing technologies. This challenge is the result of a deep analysis, discussions and consensus (mostly from medical experts and users of similar technologies) and it clearly represents and inspiration to develop high risk- high reward projects.

We also appreciated that PCP demands real R&D and disruptive technologies. On the one hand, the companies are forced to carry out an extensive literature review, get a deep knowledge of the latest scientific discoveries in the field and enter in contact with experts, R&D groups or specialized start-ups. On the other hand, the R&D teams of pure research organizations are also challenged buy the procedures of a public tender. Besides the fruitful collaborations already established during the phase 1 and Phase 2 can be extended to other innovation projects and challenges beyond ANTISUPERBUGS.

In our vision, PCP also served to rethink how R&D and product development is currently executed in companies and research centres. Usually, SMEs like BAHIA SOFTWARE or research centres like GRADIANT or INL initiate R&D activities with internal resources or through a R&D national or European grant without clear orientations to healthcare professionals and patient's needs. In most of these projects, participants also do not address IPR strategies, regulatory issues or quality protocols during the first stages of the R&D activities. PCP definitively requires a different approach. Since the very beginning, PCP procurement projects like ANTISUPERBUGS force contractors to think about the commercialisation strategy, IPR management, clinical validations, data management policies and regulations and to reach agreements among project partners on future exploitation strategies, even before the collaboration starts. Besides, companies must rethink important aspects like ethics, data security, busines and impact strategy, clinical research in humans, etc. In our view and comparing PCP calls with national or European grants, the level of exigency is higher in PCP calls, but the rewards for contractors can be also higher.

Finally, one key aspect in the development process is related to the validation of the technology following the indications of ethics committees and clinical research in humans' policies. The knowledge gained about how to implement validation studies in real clinical environments (through multicentre studies in different European countries) is highly useful for SMES. The possibility of performing a clinical study at European level is also very relevant for further commercialisation activities. Usually, these clinical validation studies are out of the technical and financial capacities of European SMEs (particularly technology companies).

4. Final remarks *(not for publication purposes, to assess how further EU support could best help you)*

What are remaining bottlenecks to commercialise your solution (e.g. certification, legislation etc.)

The development of health technologies is very complex, expensive and time-consuming. PCP is an outstanding innovation methodology that could significantly contribute to the development of health technologies by European SMEs. However, we would like to address some bottlenecks related to the execution of PCP projects. In our opinion, these execution-bottlenecks can also have a very direct impact on future commercialisation strategy.

Execution Bottleneck 1: Time constrains are very important in PCP projects. On the one hand, PCP calls demand breakthrough technologies but at the same time they expect results in 2-3 months to be presented in pre-prototype demonstrations of Phase 2. In our opinion contractors need longer period of times for the phase 2, which is critical to develop disruptive technologies with enough potential to transform markets.

Execution Bottleneck 2: Contractors need better definition of functional requirements for intermediate milestones. Contractors will really appreciate information about what Buyers really expect from a pre-prototype and from a prototype: Any information about the functional requirements of these important milestones can contribute to better results at the end of the project.

Execution Bottleneck 3: In order to develop health technologies, contractors need access to relevant data and ICT infrastructures during phase 2. In present times, all products and technologies are developed through iterative processes that are critical to incorporate user preferences. PCP procurement tenders should foster mechanisms to facilitate co-creation meetings. At the same time PCP should facilitate during phase 2 access to Buyer's infrastructure under equal and transparent methodologies during the development of the prototypes.

In addition to the execution Bottlenecks, we have also identified other commercialisation bottlenecks more related to policies and usual business practices of ehealth technologies:

Commercialisation Bottleneck 1: The certification of ehealth technologies is very complex, takes time and it is very expensive. In our opinion there is an explosion of ehealth technologies, and the regulatory bodies have not enough knowledgeable resources to speed up this process. European companies will need easier access to national and European bodies during the development phase of their technologies. We also believe that these public entities should create more and better services to support SMEs (from early phases) with the regulatory and certification aspects of their technologies.

Commercialisation Bottleneck 2: The acquisition of enough scientific evidence is also a significant bottleneck for many SMEs. The ANTISUPERBUGS-PCP will give us access to a few patients in Phase 3 but this number and the time to validate the technology is not enough. We will need longer projects and more ambitious clinical studies. PPI calls can cover partially this bottleneck. We believe that we need innovation mechanisms and specific calls for SMEs to execute clinical validations of ehealth technologies.

Commercialisation Bottleneck 3: Another important bottleneck is related with the introduction of innovate digital solutions in public health systems. The number of public health systems that launch PCP and PPI tenders in Europe is still extremely low. The commercialisation of innovative technologies is therefore very difficult because at the end of the PCP, we will compete with other providers and companies (in many cases large multinationals) with less efficient technologies that can win because they might offer a lower tender price and not necessarily better solution, neither a cheaper solution during the full technology lifecycle. Therefore it would be recommendable to promote more PPI calls as a natural continuation of PCP projects.

What type(s) of assistance do you need to address those bottlenecks and grow your business / commercialise your solution more widely (e.g. EU regulation on x, finding investors, IPR help etc.)

The PCP methodology, and particularly the Buyers group, should find mechanisms to interact more with contractors in Phase 2 in an equal and transparent methodology. During the implementation of Phase 1 and phase 2, we have interacted several times with the ANTISUPERBUGS Buyers group, but sometimes we needed more information to really develop a technology that targets their actual needs and that is compatible with their existing protocols and infrastructures.

At the same time, we believe that PCPs could increase dissemination activities with other key stakeholders related with the health challenge. In other words, the managers of the Buyers group could organise more dissemination meetings with external experts from other hospitals, investors, or large multinationals with technologies and commercialised products around the PCP health challenge. This feedback will be obviously non-binding and it will not affect the final result of Phase 2 but it could serve to better develop the technology and to better address some of the bottlenecks previously identified.

How important was the procurement for your business (could you have done it on your own?)

The ANTISUPERBUGS PCP gave us the opportunity to develop innovative technologies and more importantly, it helped us to identify an hospital need that can open new business opportunities. After internal discussion within the CULTURE consortium, it would be extremely difficult to develop such a technology without the financial support and the health challenge inspiration of the ANTISUPERBUGS procurement.

The ANTISUPERBUGS project also served to identify research lines of common interest for the three organizations involved in the CULTURE consortium. In essence the ASPB challenge was inspiring and opened new collaborations between the parties involved (SME and 2 R&D centres).

Finally, this is a European project and from the very beginning we have been working with a European ambition (even with a global ambition). We have designed a technology to compete in future times in the European market. During phase 1 and phase 2, we have analysed IPR factors, regulatory issues, standards, certifications processes and other important aspects like future scalability and relevant partnerships to deploy the technology across Europe and beyond. The organizations that participate in the CULTURE consortium would never have initiated or developed a such ambitious project like CULTURE without ANTISUPERBUGS.

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