Grant Agreement no.:	**688878**
Project acronym:	**ANTI-SUPERBUGS PCP**
Funding Scheme:	**Pre-Commercial Procurement**
Project Start:	**01/09/2016**
Project Duration:	**48 months**

D2.1 - Needs Elicitation through questionnaires and WIBGIs events with end users

Due date:	31/08/2017
Actual submission date:	16/07/2018
Deliverable type:	Report
Responsible partner:	SBE
Version:	[1.2]
Dissemination level:	Public
Status:	Final version

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 688878

Deliverable Description
Report on the results and activities performed for the needs elicitation through questionnaires and WIBGIs events with end users.

Revision History			
Version	**Date**	**Comments**	**Partner**
0.1	01/03/2017	First draft sent to Partners (methodology)	SBE
0.2	20/05/2017	Second Draft (complete document)	SBE
0.3	31/07/2017	Integrated version sent to Partners for review.	SBE
0.3.1	31/07/2017	Format updated to new Deiverable template	AQuAS
0.4	14/12/2017	Third Draft	SBE
0.5	05/03/2018	Revised version sent to Coordinator	SBE
0.6	15/03/2018	Draft sent to WP co-leaders (ICO, PAT) for reciew	AQuAS
0.6	19/03/2018	Draft sent to Partners for review	AQuAS
1.0	26/03/2018	Feedback from partners incorporated. Document sent to Project Officer for review.	AQuAS
1.1-1.2	16/07/2018	Update of the document considering Project Review Report	AQuAS

Authors	
Name	**Partner**
Sara Bedin	SBE
Rossana Alessandrello	AQuAS
Esther Arévalo	AQuAS

Contributors	
Name	**Partner**
E. Limon, G. de Carvalho Rodrigues	ICO
E. Torri, G. Nollo, F. Tessarolo	PAT
JP Mathieu	AQuAS
M. C. Heissler, B. Ghebremedhin	HELIOS
S. Dumanli	MOH
K. J. Ward, D. Partridge	STH
L. Buguñá, J. Trenado Alvarez	FMT
A. Peine, D. Dahms	UKA
U. Elofsson, D. Ilver	ACREO and RISE

ABBREVIATIONS AND ACRONYMS

A. baumannii	*Acinetobacter baumannii*
AMR	Antimicrobial Resistance
APSS	Azienda Provinciale per i Servizi Sanitari (Healthcare Trust of the Autonomous Province of Trento)
AQuAS	Agencia de Qualitat i Avaluació Sanitàries de Catalunya (Agency for Health Quality and Assessment of Catalonia)
ASB	ANTI-SUPERBUGS
ATPase	Microbiology test able to detect different MDROS
BSI	Blood Stream Infection
CAUTI	Catheter associated urinary tract infection
CDC	Centers for Disease Control and Prevention (USA)
CDI	*Clostridium difficile* Infection
C. diff.; C. difficile	*Clostridium difficile*
CLabsi	Central Line-associated blood Stream infection
CP	Carbapenemase-producing
CPE	Carbapenemase-producing Enterobacteriaceae
CRE	Carbapenem-resistant Enterobacteriaceae
D4D	Devices for Dignity
DALYs	Disability Adjusted Life Years
DGKL e.V.	German Society of Clinical Chemistry and Laboratory Medicine
DoA	Description of the Action
EARS-Net	European Antimicrobial Resistance Surveillance Network
EC	European Commission
ECDC	European Centre for Disease Prevention and Control
E. coli	*Escherichia coli*
ESBLs	Extended-spectrum beta-lactamases
ESCMID	European Society of Clinical Microbiology and Infectious Diseases
EU	European Union
EU/EEA	European Union and European Economic Area
FMT	Fundació Mútua de Terrassa per a la Docencia i Recerca Biomèdica i Social, Fundació privada catalana, (Research Foundation of Mútua Terrassa)
G+	Gram positive
G-	Gram negative
GA	Grant Agreement
GNB	Gram negative bacilli
HAI	Healthcare-Associated Infection
HAP	Healthcare-Associated Pneumonia
HELIOS	Helios' Wuppertal Clinical University (HELIOS Universitätsklinikum Wuppertal)
HELIOS D.I.R.	HELIOS Department of Innovation of Research Support
HELIOS IML	HELIOS Institute for Medical Laboratory Diagnostics
HER	Hospital Electronic Record
HIS	Hospital Information System
HUMT	Hospital Universitari Mutua Terrassa (University Hospital of Mutua Terrassa)
HW	Hardware

ICO	Institut Català d'Oncologia (Catalan Institute of Oncology)
ICT	Information and Communication Technologies
IC	Infection Control
ICU	Intensive Care Unit
IPC	Infection prevention and control
KPC	Klebsiella pneumoniae carbapenemase
KPI	Key Process Indicator
K. pneumonia	*Klebsiella pneumoniae*
LIS	Laboratory Information System
LOS	Length of stay
LTCFs	Long-term care facilities
LT-TLC	Long-term and total life-cycle
MD	Medical Doctor
MDROs	Multidrug-resistant organisms
MOH	Ministry of Health of Turkey
MRSA	Methicillin-resistant Staphylococcus aureus
MSSA	Methicillin-sensitive Staphylococcus aureus
NGT	Nominal Group Technique
NI	Nosocomial infection
OECD	Organization for Economic Cooperation and Development
OMC	Open Market Consultation
OR	Operating Room
OVC / VOC	Organic Volatile Compound(s)
P. aeruginosa	*Pseudomonas aeruginosa*
PAT	Provincia autonoma di Trento (Autonomous Province of Trento)
PCP	Pre-Commercial Procurement
PCR	Polymerase Chain Reaction
PHE	Public Health England
PN	Parenteral Nutrition
QALYs	Quality Adjusted Life Years
S. aureus	*Staphylococcus aureus*
SBE	Sara Bedin
SISCat	Catalan Health System
SSI	Surgical Site infection
STH	Sheffield Teaching Hospitals NHS Foundation Trust
SW	Software
UKA	Clinical university of Aachen
VAP	Ventilator-Associated Pneumonia
VINCat	Vigilància d'Infeccions Nosocomials a Catalunya (Nosocomial Infection surveillance Program in the Catalan Hospitals)
VRE	Vancomycin-resistant enterococcal
WHO	World Health Organisation
WIBGI	"Wouldn't It Be Good If...?"
XHUP	Xarxa Hospitalària d'Utilització Pública (Public-use Hospital Netwok)

TABLE OF CONTENTS

1. EXECUTIVE SUMMARY

This document refers to ANTI-SUPERBUGS PCP Grant Agreement, Work Package 2, **Deliverable *D2.1 'Needs Elicitation through questionnaires and WIBGIs events with end users'***. The deliverable provides a report on the results and activities performed for the needs elicitation through questionnaires and WIBGIs events with end users, and is the first step for the definition of the ANTI-SUPERBUGS PCP Common Challenge.

The document presents the main phases implemented and resulting outcomes for the ANTI-SUPERBUGS PCP **common unconvered innovation needs elicitation and validation**, and offers an overview of the problem faced by the PCP Buyers'Group.

The core outcome of this phase, illustrated in the last section (§ 6.2) of the deliverable, is the common list of **functional requirements** that the new solutions shall comply with. The requirements have been defined and validated by the ANTI-SUPERBUGS PCP procurers, with the support of the innovation procurement partners. A **preliminary list of indicators** to assess how the desired novel solutions could satisfy the emerged common requirements is also an outcome of the methodology presented here.

2. INTRODUCTION

A pre-commercial procurement has to start from a **genuine and real need** that concern a public service delivered and that impact negatively on the quality and/or cost of health-care public services offered.

The activities and evidences reported have been aimed to assure a collective need elicitation and description.

The document describes the outcomes of activities performed to carry out task 2.1, represented as the first step of the methodology, consisting of a cross-border contextual inquiry aimed at problem and need elicitation and analysis in the domain of Health care-associated infections (HAIs), or "nosocomial" and "hospital" infections. HAIs are defined as infections acquired in hospital by a patient who was admitted for a reason other than that infection (see ***Annex 7.1*** – Glossary).

The coordinated investigation has involved two main categories of stakeholders who are knowledgeable about the domain, namely: 1) the professionals operating in infection control teams and hospital clinical services (e.g.Surgical services; ICUs; Emergency rooms, oncology services), who helped in the analysis of the current practices and of the extent to which ICT related detection system of colonisation by MDROs are being adopted and of the issues that are worth to be explored; and 2) technical experts in the field of technology development and assessment, whose feedback was considered paramount.

This deliverable refers to the first step of the following methodology to come up with the appropriate need elicitation.

We recommend the reader to consider WP2 deliverables in an integrated way, because they have been designed, developed, updated, integrated and reviewed in two phases, also to incorporate the contributions provided by the additional buyers that joined the project from December 2017 and recommendations provided during first project review.

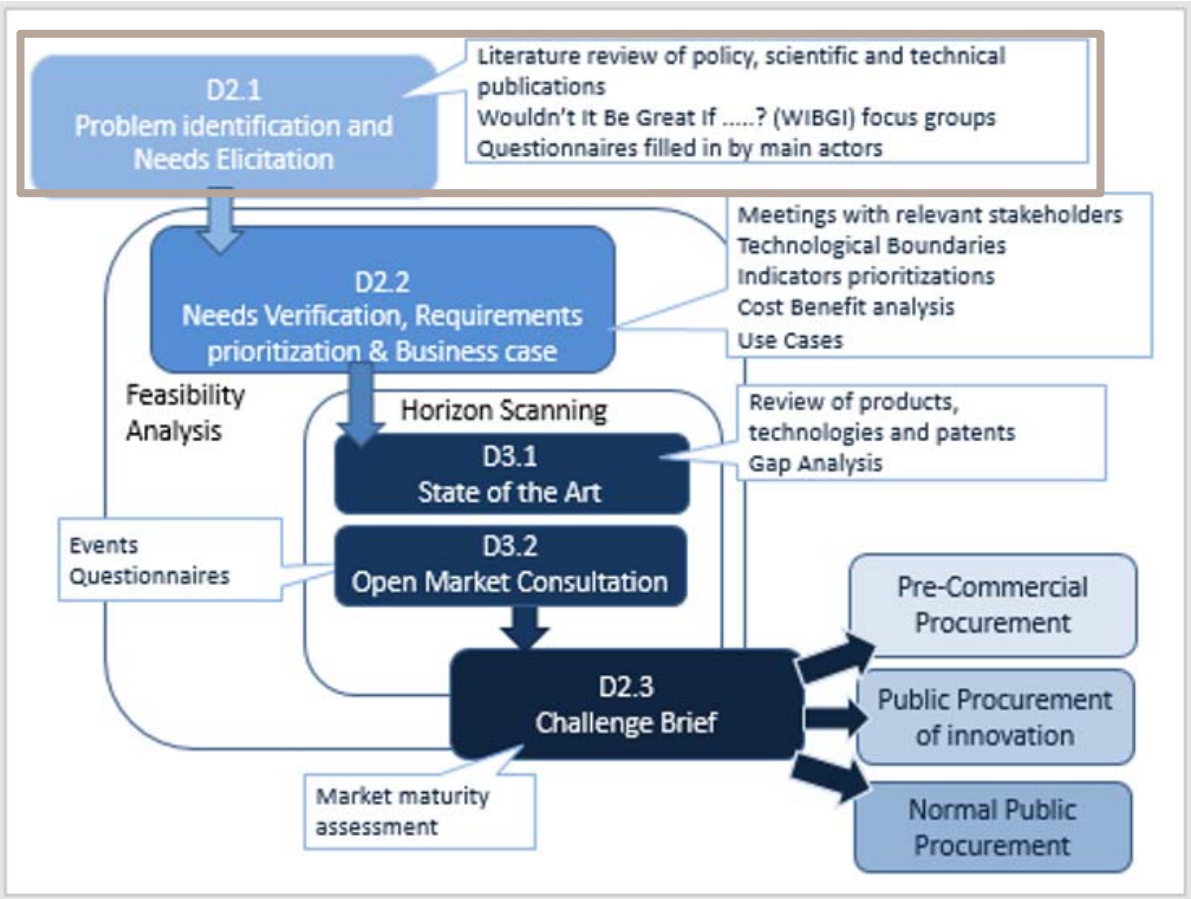

Figure 1 - ANTI-SUPERBUGS PCP Framework
(Elaborated from DECIPHER Innovation Management Framework;
Source: DECIPHER D2.1 Phase 0: Needs Assessment report)

The process defined in this methodology ensures that all the key steps are present and at the same time adds overlapping temporal windows among the different stages, allowing a major efficiency in the PCP scope definition.

Going through each of the steps:

- ***Needs elicitation*****:** this activity is being described in this deliverable, *D2.1 Needs Elicitation through questionnaires and WIBGIs events with end users.* Its main outcome is the identification of the common needs of all the ANTI-SUPERBUGS PCP buyers and uncovered by current off the shelf technologies.
- ***Verification and Prioritization of Needs, Indicators and Functionalities*****:** this activity is being described in this deliverable and in the deliverable *D2.2 'Business case(s) and prioritized list of common uncovered innovation needs'*. The main relevant outcome of this deliverable is the list of needs, indicators and functionalities identified, defined and prioritized by the buyers and lately verified by different stakeholders and experts.

- ***Feasibility Analysis*:** this step consists of different stages aimed to support ANTI-SUPERBUGS PCP consortium to validate the feasibility of the procurement procedure:
  - **Business case:** this activity is being described in deliverable *D2.2 Business case(s) and prioritized list of common uncovered innovation needs.* The main relevant outcome of this deliverable is the feasibility study of the procedure as a whole (taking into consideration from one side the expected impact to the buyers and the benefits that the development of new technologies would bring, from the other side the costs that the overall procedure and the ones entailed by deployment of the developed technologies).
  - **Horizon scanning**
  - **Analysis of the State of the Art and regulatory requirement:** through the analysis of the state of the art, ANTI-SUPERBUGS consortium wants to assess the market readiness and ensures that the novel technologies expected to address its needs can be developed during the procedure life and, finally are susceptible to be protected and exploited as expected. The outcomes of this phase are the knowledge of the market and technology readiness, plus and initial identification of eventual regulatory requirements and certifications that ANTI-SUPERBUGS PCP novel technologies should one day satisfy. These activities are reported under Deliberable 3.1.
- ***Market Consultation*:** this activity is being described in the deliverable *D3.2 Open market consultation and EU-level meet-the-market events report.* ANTI-SUPERBUGS PCP consortium considers this activity as one of the most critical for the success of the project since it will support the buyers to:
  - Provide a pre-information to the market in order to give a congruous time for the preparation of fit-for-purpose proposals.
  - Find out whether technologies are commercially available and acquire information about the advantage and disadvantages and the level of coverage of the desired functionalities, in order to confirm the assumption for PCP.
  - Identify market risks potentially able to endanger business goals and supplier performance,
  - Enable and increase the opportunities for industry to form fit-for-purpose consortia.

3. OBJECTIVES

The initial objective of the **task T.2.1. 'Needs assessment and description'** has been to allow ANTI-SUPERBUGS procuring authorities to validate a common, shared background regarding health care associated infections prevention and detection, as well as the pre-commercial public procurement scope and assumptions. This effort has been considered as vital from the project proposal, due to the different nature and background of the procurers.

The **pre-commercial public procurement (PCP)** is a procurement contract aimed to steer the development of solutions towards concrete public sector needs, whilst comparing / validating alternative solution approaches from various vendors (possibly new comers). Pre-commercial procurement is a preparation exercise which enables public purchasers to filter out technological R&D risks of potential alternative solutions, before committing to procuring a large scale commercial roll-out.

Table 1 – PCP definition

The aim of this document is to describe how the need assessment phase has been conducted, and on how focus group discussions with procurers and end-users have been organized.

Conducting the activities, ANTI-SUPERBUGS Consortium answered to the following questions:

- What are the needs and problem faced in health-care associated infections control and reduction?
- How many diseases and infections are affecting patients during the process of care in hospital or other healthcare facility in EU?
- What are the extreme or typical environments to use the new (desired) solutions?
- What functions do the users need from the innovative solutions?
- How do users think the (desired) solutions should work and do?
- Is the challenge description detailed enough to enable a comparability of the solutions?
- Is the challenge description formulated to enable the elaboration of novel and potentially disruptive solutions?

4. THE ANTI-SUPERBUGS NEED ASSESSMENT METHODOLOGY AND TOOLS

The ANTI-SUPERBUGS need assessment and elicitation process has been articulated in two phases: the first with the initial Buyers' Group (i.e. partners ICO, UKA, STH, PAT) and the second with the enlarged group of procurers (ICO, UKA, STH, PAT, HELIOS, MOH and FMT). Indeed, the subsequent enlargement of the consortium has imposed the repetition and the deepening of the analysis in order to enable the representativeness of all in the identification of common, cross-border and genuine uncovered needs. An additional iteration was implemented to address the recommendations provided by the EC reviewers and the Project Officer during the project review and with the final group of procurers (ICO, UKA, STH, PAT, HELIOS and FMT).

In terms of the methodology for the assessment and elicitation, we realized it was not sufficient to structure a series of questions through a questionnaire, but it had to go on focusing the group discussion. It was decided a combination of the "WIBGI Brainstorming", the "Nominal Group Technique" and "semi-structured and structured questionnaire" methodologies, integrated with the TCP-PE approach to create associations (described in Table 3).

The **WIBGI method** adopted to investigate innovation needs is a collective exercise to complete the sentence "*Wouldn't be great/good if...*".

The **Nominal Group Technique (NGT)** adopted to investigate innovation needs is a group process involving problem identification, functional requirements elicitation and decision-making. It has been used to make decision quickly, but assuring everyone's opinions taken into account (as opposed to traditional voting, where only the largest group is considered). The method of tallying has been the difference. Every member of the group have given their view of the problem and need, with a short explanation. Then, duplicated ideas have been eliminated from the list of all requirements and the members have proceeded to select the options. AQuAS and Sara Bedin, as facilitators, have encouraged the sharing and discussion of reasons for the choices made by each procurer, thereby identifying common ground and a plurality of requirements. This diversity often allowed the creation of a hybrid requirements (combining parts of two or more ideas), often found to be even better than those ideas being initially considered.

The **semi-structured questionnaire** enables open answers to be used in focus group discussions, and **structured questionnaire** allows to compile qualitative responses which you tick off such 'Yes' or 'No' or select from a limited list of options. These questionnaires have been adopted to focus and prioritize the key elements of the emerged needs, assuring a common terminology.

Table 2 - Need assessment methodologies and tools (S. Bedin, 2012)

- Continues on previous page –

The **method TLC-PE** (Bedin, 2012) **(long-term and total life-cycle performance description)** adopted to create associations between descriptive functions and quantified performance targets and to classify functions and related performances along the solution life-cycle phases (installation, use, management, maintenance and disposal), in order to address high long-term performance and (total life-cycle) costs as low as possible.

Table 3 - Need assessment methodologies and tools (S. Bedin, 2012)

- Continues from previous page -

Initially, the activity with the procurers has been conducted through several conference calls and through a semi-structured questionnaire (please refer to ***Annex 7.2***) to guide local focus groups. The aim was to introduce the need assessment methodology and tools, and enable a discussion between peers and multi-disciplinary professional profiles within each procuring authority (experts from the infection control teams, microbiologists, infectious disease specialists, cleaning staff, maintenance staff, etc.)

After that, we decided to implement joint discussion among procurers to understand and bring out real elements of convergence and create a common ground of analysis, through WIBGI sessions and NGT approach. In conducting the preliminary focus group and WIBGI brainstorming sessions, we have evidences that it is important to involve together similar staff groups from multiple locations affected by the same problem. This diversity is needed in order to avoid that a perceived inefficiency or need can be related to local habits and practices, and in this way could adversely affect the economies of scale that are the basis of the innovation procurement.

A series of buyers group WIBGI brainstorming and NGT meetings have been managed to collectively identify common problems and uncovered innovation needs. In this way, we assured that requirements elicitation followed naturally and authentically the analysis of the problems faced by the procurers involved and based on sound common ground of scientific evidence and professional expertise.

With the proposed approaches, procurers were allowed to add value because from the first moment they had to discuss their points of view (after viewing the presentation by the facilitator and being aware of the proposed examples).

We extended the NGT approach to the added procurers, to assure a convergence before the conduction of open market consultations.

At a later time, a structured questionnaire has been applied at the level of each participating public procurer, based on the analysis of their own procurement strategy. In this process we had a confirmation that procurers aggregated in ANTI-SUPERBUGS contractual group -

delivering the same services of public interest in multiple locations -, are struggling with the same problem and that the need is shared by multiple potential buyers/end-users. This confirmation shall enable the development of solutions that are scalable, interoperable and more cost-effective.

In case of ANTI-SUPERBUGS, the **challenge** that is used for the PCP has emerged and is shared by all procurers composing the enlarged group (as joint procurement aims to share the cost of the PCP procurement among procurers and aims to create a market of suppliers that are able to address the shared need).

Innovation procurement refers to the entire product life-cycle and concerns the total cost of ownership and not the lowest price per piece. Thus, the structured questionnaire has been crucial to identify innovation requirements towards the entire life-cycle of the solution. In this regards, the method TLC-PE (Bedin, 2012)[1] has been useful to classify functions and related performances along the solution life-cycle phases - installation, use, management, maintenance and disposal - in order to address high long-term performance and (total life-cycle) costs as low as possible.

The use of functional and performance based requirements offered the opportunity not to pre-define the technical solution and to be open to alternative technical ways to address the needs. However, this does not mean that needs definition has been short and general. We considered that the only way in which solutions will meet performance targets and impact is when those expected outcomes are specified upfront, clearly, unambiguously and exhaustively. It is a simple fact that if functions and performances are not stated as requirements then suppliers will generally not (strictly) consider them.

At the same time, in order to create a wide potential market (public and private) for the new solutions and to enable the desired economies of scale and cost savings, we haven't fallen into an hyper-description of the desired solution (i.e. exceeding customization and personalization).

For the purpose of this document, the **ANTI-SUPERBUGS procurement challenge** addresses the need of end-users and can be itemised in two elements (**Figure 2** – Procurement challenge elements:

- **Functional requirements**, that are the basic elements of needed solutions, and describe the original intent, purpose, operation that a solution must be able to perform. These requirements are mapped to the different solution life cycle phases.
- **Performance requirements**, that include the measurable KPIs or targets to be achieved implementing a specific function.

[1] S.Bedin, 2012. TLC-PE method developed and implemented in Lombardy Region for PCP and PPI projects.

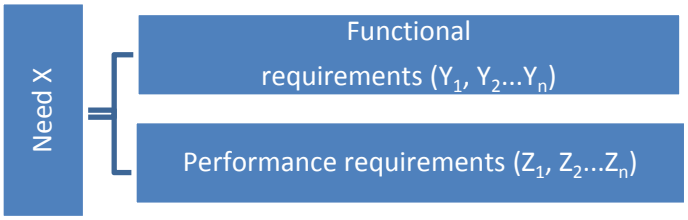

Figure 2 – Procurement challenge elements

With the support of AQuAS, the assessment tools have been defined and provided by Sara Bedin (SBE). SBE has been also in charge of instructing partners to the ANTI-SUPERBUGS need assessment approach and tools, as well as for moderating the focus groups and panel meetings.

In short, the need assessment and elicitation process, consisting in two main phases, can be illustrated as a converging funnel. It started with a broad range of innovation driven requirements and gradually refines and selects from among them, and has been integrated by additional requirements emerged by the new procurers, creating a project that can be managed through PCP and open new markets.

4.1 PHASE 1: Need assessment with original buyers group

This paragraph describes how has been conducted the phase 1 of the need assessment and how NGT sessions and WIBGI focus group with initial procurers (ICO, STH, PAT and UKA) and end-users have been organized.

Two main meetings where organized in this Phase:

- a focus group in Barcelona (May 04th and 05th, 2017) with the participation of procurers ICO, STH and PAT plus SBE, RISE and AQuAS; and
- a panel meeting in Trento (June 28th and 29th, 2017), with the participation of all initial partners (ICO, PAT, STH, UKA – as procurers – and RISE, SBE and AQuAS).

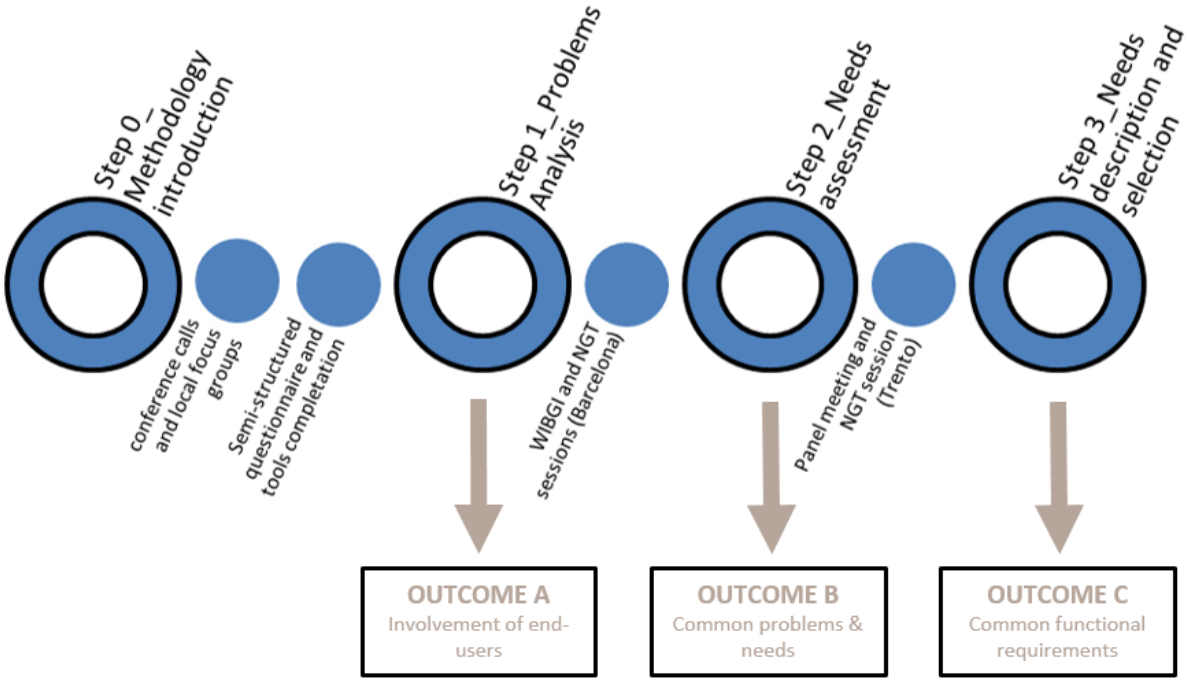

Figure 3 – Phase 1 ANTI-SUPERBUGS Need assessment

4.1.1 STEP 1 – Problems Analysis

Responsible partners:

- Methodological definition: SBE
- Facilitator role: AQuAS
- Contributors: Initial ANTI-SUPERBUGS Buyers' group (ICO, UKA, STH, PAT)
- Period of execution: October 2016 - March 2017

Step description:

- The description of the problem has to be thorough and include constraint descriptions, without attempt to prescribe the solution and should concern:
    - what is the issue,
    - when does it happen,
    - where does it happen (what is the process /service affected)
    - who is impacted,
    - how often does it happen,
    - what is the actual and long-term potential problem dimension.
- The described 'problem' has to be "genuine", real, not itself questionable and not a just a symptom of a more fundamental issue. In other terms, it is important to determine if the problem is 'big' enough to justify devoting resources to solve it.

- The problem statement enables the correct identification of the end-users to be involved in the next phase.
- It identifies the areas where there are issues that need to be addressed, such as inefficiencies, missed solutions, unacceptable market price and performance or unfavourable consumer response to a product or service already available on the market.
- To address a PCP, the problem may be predictive or anticipatory as it lies in the future, in this sense trend data are important to show the persistence and evolution of the problem.

The activity has been conducted through several conference calls, a semi-structured questionnaire (***Annex 7.2***) and local focus groups, aimed to introduce the need assessment methodology and tools and enable a discussion between peers and key professional and staff in each procuring authority.

OUTCOME A: Involvement of end-users interacting with the critical process/service on a daily basis.

4.1.2 STEP 2 – Need assessment and statement

Responsible partners:

- Methodological definition: SBE
- Conduction and facilitator role: SBE
- Contributors: Initial ANTI-SUPERBUGS Buyers' group (ICO, UKA, STH, PAT)
- Period of execution: March - May 2017

Step description:

- The preferred method to identify innovation needs and validate them against their relevance has been the WIBGI methodology developed by the (NHS UK). It uses collective brainstorm exercises with end-users to complete the sentence "*Wouldn't It Be Great or useful If...*".
- In this setting, focus groups ought to be made by end-users or beneficiaries of innovation: as they work and interact with a process on a daily basis, they are best-placed to see its problems or inefficiencies and identify possible areas of improvements.
- WIBGI's basic concept is to make time to take key actors in out of their usual environment, group them and ask them to finish the sentence *"Wouldn't It Be Good If...?"*.
- In conducting such session, it has been necessary to bring together stakeholders from multiple locations, since a perceived inefficiency or need can be simply due to local customs and practices at one site. We had experienced facilitators (SBE and AQuAS) to conduct the session, to enliven it and to draw out issues and ideas, as well as a subject domain expert (ICO) who guided the facilitator with respect to the subject's technicalities.

- When describing the unmet needs it has been important to take care to be clear, simple, unambiguous and comprehensive in the description.
- Focus on describing the problem to be solved and defining clear and measurable outcomes and targets that are required and to be achieved within a mid-to-long period (performance & efficiency improvements) rather than focusing on how the solution for the problem should be built.

OUTCOME B: Agreement on a (initial list) of common problems and needs to be addressed through PCP, as result of the 1st WIBGI session and NGT session in Barcelona on May 5th, 2017.

4.1.3 STEP 3 – Need description and selection

Responsible partners:

- Methodological definition: SBE
- Contributors: Initial ANTI-SUPERBUGS Buyers' group (ICO, UKA, STH, PAT)
- Period of execution: May - July 2017

Step description:

- It was required a straightforward articulation of the problem/needs that a procurement action is supposed to solve.
- When identified a need, a methodology has been used to elicit the functional specifications to describe the original intent or purpose that a product, process or service expected to be performed.

  The description of a Function is restricted to a two words format: 'Active Verb + Measurable Name'. The Verb is used to answer to the question: '*What does it do?'* While the Name is used to answer to the question: *'What does the Verb apply to?'*
- When describing the unmet need we have taken care to:
  - describe the specific context where the innovation was needed;
  - focus on describing the problem to be solved, clearly defining target outcomes, performances and functionalities and improvements to be achieved, rather than prescribing technologically how the solution for the problem should be built;
  - express the requirements in a technology neutral way (e.g. avoid reference to proprietary production methods);
  - be clear and simple in the description;
  - provide measurable requirements against which solutions can be evaluated and offers uncompliant could be objectively rejected;

- don't over specify the desired solution allowing the market to be creative, enabling the desired economies of scale and cost savings,
- avoid customization and personalization requests for and support scalability,
- do not use requirements that are not directly needed to fulfil the need, but may restrict competition.

OUTCOME C: Agreement on a (list) of **minimum common functional requirements** (Table 4, Table 5, Table 6) that the new solution should have, as result of the 2nd NGT session and focus group in Trento (June 28th and 29th, 2017). The focus group has not been oriented to find nor to discuss on potential inventive solutions, but to identify needed functionalities, main dilemma or trade-off between contradictory elements which needs to be resolved.

Clinical:

Early detection of superbugs on patients and on surfaces (including colonized individuals)

- ***In situ* test** that rapidly detects:
  - ✓ carbapenem-resistant producing gram-negative bacilli +/- extended-spectrum beta-lactamases (ESBLs) production and,
  - ✓ either *E. coli* or *Clostridium difficile* or both
    (All to be confirmed later by the microbiology service)
  - ✓ Flexibility to integrate detection capabilities for additional MDROs or future proofing
  - ✓ Flexibility to integrate detection capabilities for additional clinically relevant HAIs microorganism and vectors
  - ✓ Continuous or high frequency detection
  - ✓ 99,9% of sensitivity (also in adverse environments) and specificity of micro-organism identification.
  - ✓ Sensitivity at least of PCR test (low false negatives)
  - ✓ Acceptable to patients
  - ✓ Minimally invasive
- Continuous or high frequency surveillance system for contamination by MDROs (including colonized individuals) and potentially other healthcare associated pathogens on high contact surfaces
- Ability to sense all the places at more risk of either to be colonized or to be HAIs vectors (e.g.: flush handles, commodes, sinks, bed rails, remote controls, bed linen, curtains, door handles, keyboards, tablets)
- To be deployed/installed into existing healthcare environments
- Possibility to be used in crowded areas
- Availability of remote alert system
- Availability of alert system to be triggered where the contamination is detected
- Inform in real time the hospital information system of the risks of infection

- Integration with electronic patient health record and the hospital information system (linking the infection with the place of detection) using interoperability standards (HL7, etc.)
- *(nice to have)* destroy specific superbugs

Table 4 - Minimum common clinical requirements

Economic:

- In case of ***patients screening***: **cost effective** compared to common practice (e.g. weekly screening by PCR or culture, estimated to be 40-50 Euros/per each PCR test per person, requiring 1 day and half)
- In case of ***surface screening:*** **cost effective** compared to existing screening practices (e.g.: such as ATPase testing)

Table 5 - Minimum common economic requirements

Life cycle:

Installation and replacement:

- Allows to be integrated in the regular health care or support staff routines
- Easy to be integrated into different hospital facilities and architectures
- Appropriate supply integrated into existing systems

Use and management:

- Comfortable for users (inpatients and health & support staff)
- Easy and risk-free to use, minimally demanding human interaction for early detection
- Continuously working system (24 hours) with high frequency sensing the system should provide highly interoperable data
- The system must have a self-diagnostic function
- Highly usable user interfaces

Maintenance, scalability and renewal:

- Easy to maintain – Self-manageable by the responsible maintenance staff
- Easy to upgrade and renew
- Easy to deploy throughout the system
- Minimal or no recalibration required
- Minimum or no consumables
- Cheap consumables (if any)
- The covering material (if any) of the sensing components should be cleanable

Disposal:

- No toxic material to be handled by the personnel
- Using existing disposal routes
- Environmentally friendly, limited amount of single-use material

Table 6 - Minimum common life cycle requirements

4.2 PHASE 2 _ Need assessment with the enlarged ANTI-SUPERBUGS Buyers' Group

This paragraph describe how has been conducted the Phase 2 of the need assessment with all the procurers (ICO, UKA, STH, PAT, HELIOS, MOH and FMT).

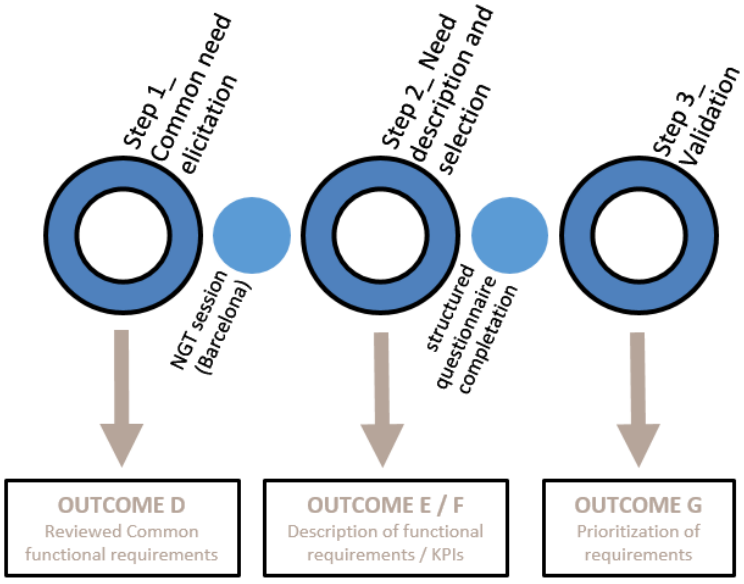

Figure 4 - Phase 2 ANTI-SUPERBUGS Need assessment

4.2.1 STEP 1 – Common need elicitation through an enlarged panel meeting.

Responsible partners:

- Methodological definition: SBE and AQuAS
- Contributors: enlarged ANTI-SUPERBUGS Buyers' Group
- Deadline: September 2017 – December 2017

Step description:

- It was required a straightforward articulation of the problem/needs that a procurement action is supposed to solve, before launching the open market consultation process.

- It has been necessary in this phase to evaluate the actual and historic past-performance of the process or service under consideration, using key performance indicators (KPI) as a measure.
- Based in the list obtained in Phase 1 (Outcome C), it has been required particular attention to create associations between descriptive functions and quantified performance targets. All solution life-cycle phases (production, delivery, installation, use, management, maintenance and disposal) have been considered in order to encourage suppliers to propose solutions with higher long-term performance and lower (total life-cycle) costs (LT-TLC, long-term and total life-cycle performance description method by Sara Bedin, 2009).

OUTCOME D: Agreement on a set of **reviewed minimum common functional requirements** that the new solution should have, as result of the list generated in Phase 1 and the 3rd NGT session and focus group in Barcelona, on December 14th, 2017. The focus group has not been oriented to discuss on potential trade-offs between contradictory elements, which need to be resolved, and assume decisions on these contradictions.

4.2.2 STEP 2 – Functional requirements description and selection

Responsible partners:

- Methodological definition: AQuAS (with the support of SBE, PAT and ICO).
- Contributors: enlarged ANTI-SUPERBUGS Buyers' Group
- Deadline: December 2017 – April 2018

Step description:

- Following the methodology described in ***Section 4.1.3***, **OUTCOME D** is used as a base to detail the description of functional requirements.
- This extended description is used to create a structured questionnaire to facilitate the validation and prioritization of an extended refined list of requirements and functionalities that the innovation solution(s) has to comply in order to meet the described needs. First draft of the questionnaire is provided by AQuAS and final version is issued with the support of ICO, PAT and SBE.
- This extended list ensures the inclusion of inputs received by the new procurers and allows the partners to classify the requirements according to 3 categories: "MUST HAVE", "NICE TO HAVE" and "NOT RELEVANT".

OUTCOME E: Refined list with description of functional requirements identified by the enlarged ANTI-SUPERBUGS buyers' group and to be validated with internal stakeholders. The

description of the requirements considers the entire life cycle of the solution(s) and performance terms. (Table 7; Table 8; Table 9)

*Questionnaire for Requirements validation is provided as **Annex 7.3.** Main results of the compiled inputs received from the partners (Outcome G of PHASE 2 - Step 3) are summarized in **Section 6.2** and full details are presented as **Annex 7.4.***

Clinical use requirements (extended list):

The 'ASB' ICT solutions shall be designed as:

- Stand-alone medical device (HW & SW)
- Environmental/surface sensor (remote detection of colonization/infection) triggering alerts to be confirmed by a point-of-care test/microbiology lab (HW & SW)

***In situ* alert system that rapidly detects:**

- Carbapenem-resistant producing gram-negative bacilli +/- extended-spectrum beta-lactamases (ESBLs) production
- Either *E. coli* or *Clostridium difficile* or both

Any positive detection by the 'ASB' ICT solutions shall be confirmed later by the microbiology service

The 'ASB' ICT solutions shall be:

- Acceptable to patients
- Non-invasive
- Minimally intrusive technology

The 'ASB' ICT solutions shall provide:

- Flexibility to integrate detection capabilities for additional MDROs or future proofing
- Flexibility to integrate detection capabilities for additional clinically relevant HAIs microorganism and vectors
- Continuous or high frequency detection
- 99,9% of sensitivity (also in adverse environments) and specificity of micro-organism identification
- Sensitivity at least of PCR test (low false negatives)
- Continuous or high frequency surveillance system for contamination by MDROs (including colonized individuals) and potentially other healthcare associated pathogens on high contact surfaces
- Ability to sense all the places at more risk of either to be colonized or to be HAIs vectors (e.g.: flush handles, commodes, sinks, bed rails, remote controls, bed linen, curtains, door handles, keyboards, tablets)
- Deployment/installation into existing healthcare environments
- The possibility to be used in crowded areas

- Availability of remote alert system
- Availability of alert system to be triggered where the contamination is detected
- Inform in real time the hospital information system of the risks of infection
- Integration with electronic patient health record and the hospital information system (linking the infection with the place of detection) using interoperability standards (HL7, etc.)
- Destruction of specific superbugs

Sensing components of the ASB ICT solution shall include:

- Sensors with proven accuracy levels comparable to medical grade devices with similar functions
- the possibility to operate without line power supply (e.g. battery operated)
- Compact dimensions to be fitted on desktops with portable design.

SW components of the ASB solution:

- Ssecure authentication of users in accordance with the existing methods of the procurers
- Reading information about patient's infective events (current, historic) from the existing system infrastructure of the procurers
- Monitoring prioritized according to the patients infection histories and environment infection history
- Multiple user interface according to their professional profile (microbiologist, infectivologist, nurse, etc). Different users should have access to specific content.
- Notifications and alerting according to a prioritization scheme that could be updated according to local epidemiological data
- Report using collected data and visual (graph, tables). Reports should be available in different format (e.g. Pdf, HTML) and print friendly
- The possibility to share epidemiological data with national surveillance centres of the procurers
- The possibility to perform meaningful queries with the data (e.g. infected patients for a specific superbug in a certain area)
- Real time indication on the remaining time to superbug identification
- Clear differentiation in reporting data related to environment or to patients
- An on-line how-to manual with both a quick guide to appropriate sampling and instruction for use
- The possibility for integrating existing tools to enable communication between users when their status indicates availability (e.g. chat, voice message, video conferencing)
- Registration of the geographical location and time of bug detection for epidemiological purpose
- Wireless connectivity

- The possibility for integrating data about genetic bug profile for epidemiologic cluster analysis and disease mapping

Table 7 - Minimum clinical use requirements

Other life cycle requirements (extended list):

INSTALLATION AND REPLACEMENT: 'ASB' ICT solutions shall:

- Allow to be integrated in the regular health care and support staff routines
- Be easy to integrate into different hospital facilities and architectures
- Allow to be integrated into existing supply management channels

INSTALLATION AND REPLACEMENT: 'ASB' ICT solutions shall be installed/available in:

- In patient room(s)
- In Intensive care units (ICU)
- In Emergency rooms (ER)
- In common/public areas or the healthcare facility
- Operating theatres
- Microbiology labs
- Attached to other medical devices (e.g. mechanical ventilators)

USE AND MANAGEMENT: The 'ASB' ICT solutions shall be:

- Comfortable for users (inpatients and health & support staff) (HW & SW)
- Easy and risk-free to use, minimally demanding human interaction for early detection
- Continuously working system (24 hours) with high frequency sensing and providing highly interoperable data

USE AND MANAGEMENT: The 'ASB' ICT solutions shall have:

- A self-diagnostic function
- Highly usable user interfaces

MAINTENANCE, SCALABILITY AND RENEWAL: The 'ASB' ICT solutions shall be:

- Easy to maintain; self-manageable by the responsible maintenance staff
- Easy to upgrade and renew
- Easy to deploy throughout the system

MAINTENANCE, SCALABILITY AND RENEWAL: The 'ASB' ICT solutions shall have:

- Minimal or no recalibration required
- Minimum or no consumables
- Cheap consumables (if any)
- A cleanable covering material (if any) of the sensing components

DISPOSAL: The 'ASB' ICT solutions shall:

- Not include nor generate any toxic material to be handled by the personnel
- Use existing disposal routes
- Be environmentally friendly, limited amount of single-use material

Table 8 - Minimum common life cycle requirements

Economic requirements (extended list):

Considering the added functionalities to be provided by the 'ASB' ICT solutions:

- Would you consider acurate to compare its cost-effectiveness to your common practice for patient screening?
- Would you consider acurate to compare its cost-effectiveness to a weekly patient screening by PCR or culture?
- Would you consider acurate to compare its cost-effectiveness to your common practice for surface screening?
- Would you consider acurate to compare its cost-effectiveness to existing surface screening practices (e.g. ATPase testing)?

Table 9 - Minimum common economic requirements

- To streamline the process and involvement of stakeholders, the responsible partners for methodological definition decide to use the same approach for the validation and prioritization of indicators relevant for the Business case (Deliverable D2.2) and for the evaluation of the developed ANTI-SUPERBUGS solutions. Thus, a structured questionnaire is created so the buyers group express the level of importance ("relevant" or "not relevant") and the level of measurement feasibility ("already measured", "feasible measurement" and "non-feasible measurement").

OUTCOME F: To identify the **relevant set of KPIs for ANTI-SUPERBUGS** that are required, and to be achieved within a mid-to-long period (performance & efficiency improvements due to the desired innovations), a list of measures/indicators is created aimed to assess how the desired novel solutions could satisfy the emerged common users requirements. (Table 10; Table 11; Table 12; Table 13; Table 14)

Indicators for Prevalence/Incidence of the 'Superbugs'

- Overall Prevalence of Nosocomial Infections (given specific time-frame)
- Prevalence of Nosocomial Infections related to MDROs (given specific time-frame)

MRSA (Methicillin-resistant Staphylococcus aureus):

- No. of patients with MRSA

- No. of patients with *S. aureus*
- No. of episodes of bacteraemia due to MRSA
- No. of episodes of bacteraemia due to *S. aureus*

Extended-spectrum beta-lacatamase-producing Klebsiella pneumoniae (ESBL-producing K. pneumoniae)

- No. of patients with ESBL-producing *K. pneumoniae*
- No. of patients with *K. Pneumoniae*
- No. of patients with bacteraemia due to ESBL-producing *K. Pneumoniae*
- No. of patients with bacteraemia due to *K. Pneumoniae*

Carbapenemase-producing Klebsiella pneumoniae

- No. of patients with carbapenemase-producing *K. pneumoniae*
- No. of patients with *K. Pneumoniae* *(repated from above for structure coherence)*
- No. of patients with bacteraemia due to carbapenemase-producing *K. Pneumoniae*
- No. of patients with bacteraemia due to *K. Pneumoniae* *(repated from above for structure coherence)*

Carbapenemase-producing Escherichia coli

- No. of patients with carbapenemase-producing *E. coli*
- No. of patients with *E. coli*
- No. of patients with bacteraemia due to carbapenemase-producing *E. coli*
- No. of patients with bacteraemia due to *E. Coli*

Carbapenemase-producing Enterobacter cloacae

- No. of patients with carbapenemase-producing *E. cloacae*
- No. of patients with *E. cloacae*
- No. of patients with bacteraemia due to carbapenemase-producing *E. cloacae*
- No. of patients with bacteraemia due to *E. Cloacae*

Carbapenemase-type (OXA-48; VIM; NDM; KPC; Others) for:

- *K. pneumonia*
- *E. coli*
- *E. cloacae*

Other

- No. of patients with bacteraemia due to *C. Difficile*
- No. of patients with bacteraemia due to MSSA (meticillin-sensitive S. aureus)
- No. of patients with bacteraemia due to VRE (vancomycin-resistant enterococci)
- No. of patients with bacteraemia due to CPE (carbapenemase-producing Enterobacteriaceae)

Other epidemiological indicators

- Reproductive ratio of the infections

- Mortality rate related to Healthcare-associated infections
- Mortality rate related to healthcare-associated infections due to MDROs

Table 10 – 'Superbugs'-related epidemiological indicators

Process/Activity Indicators

- Total no. of hospital admissions (all units)
- Total no. of ICU admissions
- Total no. of ER admissions
- No. of isolated patients due to MDROs
- Average length of stay (LOS) of the patients
- Average LOS of the patients affected by Nosocomial Infections
- Average LOS of the patients affected by Nosocomial Infections due to MDROs
- Time period for identification of MDROs infected/colonised patients
- Time period for making available an area/room after the detection of an MDRO infection/ colonization in that area/room
- No. of areas/room required to be cleaned per infection episode detected
- No. of microbiology tests performed
- Average time from suspicion of infection to results confirmation
- Antibiotic consumption/usage:
  - Total usage
  - Carbapenems
  - Piperacillin-tazobactam
- Consumption of disinfecting products usage for cleaning
- Consumption of disinfecting products usage for hand hygiene
- No. of side-effects' episodes suffered by hospital staff due to disinfecting products

Table 11 – Process/Activity indicators

Economic Indicators

- Overall cost of hospital stay per patient/day (all units)
- Overall cost of hospital stay per patient/day at ICU
- Overall cost of hospital stay per patient/day at ER
- Overall cost of hospital stay per MDRO-infected patient/day
- Cost of antibiotics consumption
- Cost of disinfecting products usage for cleaning

- Cost of disinfecting products usage for hand hygiene
- Cost of current cleaning practice per room/area
- Cost of current cleaning practice per room/area after MDRO infection
- Average cost of isolation materials per MDRO-infected patient
- Cost of specific material-disposal measures after MDRO infection
- Cost of microbiology test(s) related to current infection-surveillance practice
- Disability Adjusted Life Years (DALYs)
- Quality Adjusted Life Years (QALYs)

Table 12 – Economic indicators

Technical/performance Indicators
• Turn-around time of test (task time) • Sensitivity • Specificity • Usability • Task success rate / error rate

Table 13 – Technical/performance indicators

User Experience Indicators
• Level of satisfaction of inpatients • Level of patients' acceptability of ASB technology • Level of satisfaction of patient relatives • Level of satisfaction of clinicians • Level of satisfaction of nurses • Level of satisfaction of lab professionals • Level of satisfaction of maintenance professionals • Level of satisfaction of IT professionals

Table 14 – User experience indicators

4.2.3 STEP 3 – Validation

Responsible partners:

- Methodological definition: AQuAS (with the support of SBE, PAT and ICO).
- Contributors: enlarged ANTI-SUPERBUGS Buyers' Group
- Deadline: December 2017 – April 2018

Step description:

- Questionnaires developed in previous step, are used for validation of the requirements described by internal stakeholders among ANTI-SUPERBUG Procurers.
- Due to the complexity and particularities of the process and protocols related to HAIs and technology incorporation, partners are requested to involve in the validation relevant stakeholders that would be potentially affected by the deployment of ANTI-SUPERBUGS PCP solutions. Suggested profiles include: microbiologists, head and members of the infection control teams; infectious diseases specialist; and head and staff of ICT teams.
- Freedom was given to the procurers to better select the process for input collection; so they can suit better the schedules of all the actors to involve. Some procurers preferred to hold a focus meeting with all the relevant stakeholders identified and provide a consensual answer to the questionnaire. Others have performed one-to-one interviews with key actors to review the questionnaires; while in some cases each actor reviewed the questionnaire individually. All the partners had access to slides following the ones used during the OMC, which could be used to introduce the project to the stakeholders if needed.
- The following profiles have been involved in the validation of the requirements:
    - **ICO:** members of the **VINCat team** and staff from 6 different Catalan hospitals (microbiologist, nurses and technicians of the infection control team, infection disease specialist and directors of infection control team).
    - **PAT:** infectious disease specialists, microbiologist, hospital director, experts of the infection control team (physicians and nurses) and technologists with background in management of innovation and health technology assessment.
    - **STH:** medical device & innovation experts with biomedical and research backgrounds, consultant clinical microbiologist and lead researcher in laboratory medicine, infection control and microbiology teams, informatics team.
    - **UKA:** physician of the infection control team
    - **HELIOS:** Medical lead and MD responsible of the Medical Laboratory Diagnostics; MDs Responsibles for Prevention and Control Infection; MDs responsibles for Preventable Infections, and Heads of Dept. of innovation & Research and of Procurement;
    - **FMT:** Physician in charge of the ICU, Physician head of infection unit, nurse in charge of the infection surveillance, engineer and innovation coordinator, and a member of the Documentation Unit.
    - **MOH:** internist and infection disease specialist, infection control nurse, a lawyer (consultant of the MOH) and the coordinator of the centralized hospital appointment system.

OUTCOME G: *Main results of the compiled inputs received from the partners are summarized in* ***Section 6.2*** *and full details are presented as* ***Annex 7.4.*** *Baseline Questionnaire for Requirements validation is provided as* ***Annex 7.3.***

4.3 PHASE 3: Needs selection with ANTI-SUPERBUGS PCP main Buyers': Addressing recommendations from Project Review

Deliverable D2.1 was submitted to the EC on 27 March 2018, for the first review of the project. During the process of finalization of the document, the ANTI-SUPERBUGS PCP Buyers' Group experienced the withdrawal of the partner MOH. Thus, resulting on the following composition: ICO, UKA, STH, PAT, HELIOS and FMT.

At the project review, a set of recommendations and requirement were provided regarding the needs assessment that required the re-definition of the needs identified by the procurers.

"It is recommended ***focusing on the need*** *for key aspects that would have a positive* ***business case****. E.g., neglect the ICT platform and achieve instead the compatibility/interoperability of the developed device with the procurer's ICT system. Do not exclude solutions that might still involve swabs and manual handling, if they can reduce the time to bacteria detection and thus bring large benefits. Make use of the strong commitment of the 3 large contributors to the PCP budget (PAT, ICO and Helios) to identify the core-shared requirements on a short-term timeline (2-3 weeks)."*
"The panel of reviewers strongly recommends the consortium to consider the following: (...) clarify how the updated challenge brief was agreed upon with the current group of buyers (D2.1)."
"The revisions performed by the consortium (sent by email on the 23rd of May) are insufficient. Deliverables D2.1, D2.2 and D2.3 should be updated accordingly."

Table 15 – ANTISUPERBUGS PCP – Project review: Main recommendations for Deliverable 2.1

In order to address these recommendations, ICO (VINCat) led an additional review of the needs assessment in close collaboration with PAT, HELIOS, FMT and AQuAS. Focusing on the technologies and techniques assessed in the State of the Art (Update described in D3.1) (and the clinical and economical relevance of specific MDROs) ICO elaborated a proposal of re-defined needs assessment. A set of teleconferences and meetings were organized to allow discussion of the proposal among ANTI-SUPERBUGS Buyers' Group Members during April – May 2018. Emphasis of the discussions was placed on the MDROs to be detected, base

technology to be used for the detection and key ICT requirements for the ANTI-SUPERBUG solutions.

The selection of the needs during this phase considered the following items:

1. Selection of MDROs: according to Buyers' needs and technology readiness.
2. Essential MUST HAVE requirements identified as a strength by the buyers:
   - Non-invasive sampling
   - Environmental detection and sampling
3. Essential requirements to be used for the ranking of the bidders, based on their declared commitment:
   a. Autonomous and automatic detection
   b. Real-time detection
   c. High sensitivity
   d. High specificity

In a parallel process, the business case (presented in D2.2) was revisited. Resulting figures provided further decision elements for the review of the needs. The relevant importance of the Business case was considered for the final alignement of the needs of the Buyers' Group.

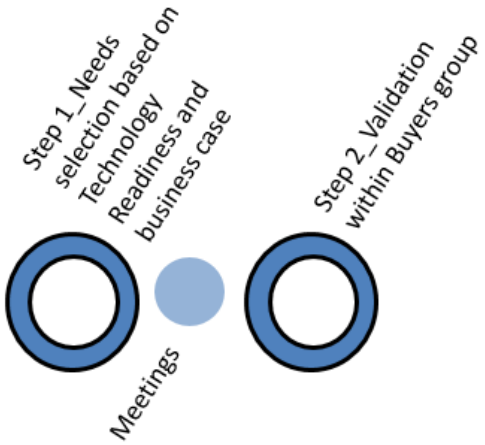

Figure 5 - Phase 3 ANTI-SUPERBUGS Need assessment

The updated presentation of the Challenge Brief (see Deliverable D2.3), including reviewed needs assessment in accordance with Phase 3 results was provided to the Project Officer on May 23th 2018 and is reflected in Section 6.3.

5. THE ANTI-SUPERBUGS SCOPE AND PROBLEM STATEMENT

5.1 Description of ANTI-SUPERBUGS Buyers' Group

The **initial buyers' group** included in ANTI-SUPERBUGS PCP proposal was composed by:

- Institut Català d'Oncologia, ICO (Catalan Institue of Oncology)
- Universitätsklinikum Aachen, UKA (Clinical university of Aachen)
- Sheffield Teaching Hospitals NHS Foundation Trust, STH
- Provincia Automona di Trento, PAT (Autonomous Province of Trento)

During the first year of the project, an active scouting of potential partners resulted in the expression of interest from 3 new procurers. Thus, by December 2017, the enlarged **ANTI-SUPERBUGS buyers' group** included:

- Initial buyers' group: ICO, UKA, STH and PAT.

And,

- HELIOS Universitätsklinikum Wuppertal, HELIOS (Wuppertal Clinical University from Helios hospital chain)
- Fundació Mútua de Terrassa per a la Docencia i Recerca Biomèdica i Social, Fundació privada catalana, FMT (Research foundation of Mútua Terrassa)
- Ministry of Health of Turkey, MOH.

Before the Project review, due to political reasons, MOH withdrew from the project, leaving the **ANTI-SUPERBUGS buyers' group** with the **final composition: ICO, UKA, STH, PAT, HELIOS and FMT** (description from MOH, included in the version of D2.1. submitted for project review, is now displayed as ***Annex 7.5***).

Two of the countries present in the Consortium, Spain (ECDC, ECDC country visit to Spain to discuss antimicrobial resistance issues, 2018)[2] and Italy (ECDC, 2017)[3], were visited by representative teams of the ECDC in February 2016 and in January 2017, respectivelly. Both visits confirmed that the AMR situation in those countries poses a major public health threat to their regions. **Italy** was identified as one of the Member States with the highest level of resistance in Europe, due to hyper-endemic levels of carbapenem-resistant Enterobacteriaceae (CRE) and Acinetobacter baumannii, together with meticillin-resistant Staphylococcus aureus (MRSA). In turn, **Spain** reported one of the highest antimicrobial consumption in primary care and hospitals in the European Union and European Economic

[2] European Centre for Disease Prevention and Control. ECDC country visit to Spain to discuss antimicrobial resistance issues. Stockholm: ECDC; 2018. Access March 25, 2018: https://ecdc.europa.eu/en/publications-data/ecdc-country-visit-spain-discuss-antimicrobial-resistance-issues

[3] European Centre for Disease Prevention and Control. ECDC country visit to Italy to discuss antimicrobial resistance issues. Stockholm: ECDC; 2017. Access March 25, 2018: https://ecdc.europa.eu/en/publications-data/ecdc-country-visit-italy-discuss-antimicrobial-resistance-issues#no-link

Area (EU/EEA). Levels of MRSA, extended-spectrum beta-lactamase (ESBL)-producing Enterobacteriaceae and Acinetobacter baumannii were also above the EU/EEA average at the time of the visit.

5.1.1 Institut Català d'Oncologia (ICO)

ICO, the Catalan Institute of Oncology, has been involved for a long time in prevention of nosocomial infections, devoting efforts both on designing procedural changes aimed at reducing risk exposure and on monitoring HAIs in Catalonia. In fact, since 2006 ICO manages the **VINCat program** for Nosocomial Infection (NI) surveillance in the Catalan Hospitals, launched by the Catalan Health Service. The program establishes a minimum and unified system of NI surveillance for acute care hospitals in the Network of Public Use Hospitals, and private hospitals that can participate voluntarily.

The network of hospitals in the public health system - under the direction of the Health Department of the Catalan Government – encompasses 64 hospitals that participate in the VINCat program (9 tertiary hospitals, 16 district hospitals and 39 small hospitals). This network covers the whole population of Catalonia (approximately 7,500,000 inhabitants).

VINCat encompasses the expertise gained in several previous national initiatives related to the control of HAIs. In recent decades, various initiatives have been developed by various medical and nursing societies, but none of these have provided a uniform and standardized surveillance system for all Catalan hospitals. During this time, other nationwide programs in Spain (including those using data from Catalonia) have been established (e.g. EPINE, which provides annual infection prevalence rates since 1990; HELICS ENVIN, which provides adjusted rates of incidence density of device-related infections in ICUs).

In 1999, an analysis was performed on the organization and HAI prevention and control activities of the eight public hospitals belonging to the Catalan Health Instiute (Institut Català de la Salut, ICS). This analysis showed that surveillance was poorly developed and heterogeneous, with widely varying targets, indicators, definitions and methodology among the hospitals. Their resources for infection control activities were limited, especially in terms of the number of infection control nurses. In response, ICS management promoted the creation of an expert workgroup to implement a standardized HAI surveillance program for its member institutions. This action was complemented by the incorporation of infection control nurses and the training of medical doctors. The resulting multidisciplinary, hospital-based program was called 'Surveillance of Nosocomial Infections in ICS hospitals' (Vigilància de les infeccions nosocomials en els hospitals de l'Institut Català de la Salut, VINICS). This program was well accepted by the various infection control committees, being able to provide aggregate data on the adjusted rates of especially relevant infections during the period 2000-2005. After its initial success, the possibility of refining the program and expanding it to the remaining acute care hospitals was considered feasible and suitable.

Thus, in 2006, all acute care hospitals included in the public health system network were invited to participate in a new HAI surveillance program, which was given the acronym VINCat (Vigilància de les Infeccions Nosocomials a Catalunya). Its main objectives and philosophy were essentially the same from VINICS: development and support of a standardized HAI surveillance system providing risk-adjusted, procedure-specific infection rates based on the specific work of multidisciplinary infection control teams from the participating hospitals.

The programm is deployed under the following structure: each hospital has a representative (preferably a member of the local infection committee team) who acts as a link between the hospital and the program management team. This team consists of the director and the coordination center (CC), supported by a technical advisory committee (TAC), with experts from different specialties. Based on the data from the hospital network and the aggregated data from other hospitals, each hospital must design their own intervention strategies for improving outcomes. The CC is in charge of i) collecting, analysing and reporting data periodically; ii) provding updates on procedures manual and real-time advice on conceptual and methodological problems, and iii) provide education and specific training for infection control teams. The TAC monitors the development of program objectives and key results, as well as technical and methodological aspects. In 2011, working groups were created, each led by a TAC member, in order to collaborate more actively with the CC in analyzing data on the indicators of the main surveillance objectives, to promote the implementation of specific preventive measures and to keep the program updated. Representatives of hospitals, CC and TAC meet once a year to review yearly results and issue an action plan for the coming year. Representatives of the pharmacy departments are convend to and specific meeting to present the results and activities regarding monitoring of antimicrobial use.

VINCat focusses on nine surveillance objectives regarding to monitoring of: 1) Overall prevalence of Hospital-Acquired Infections (HAI); 2) Nosocomial blood stream infections rates; 3) Surgical site infections rates; 4) Nosocomial infections rates in ICUs; 5) Surveillance of multi-resistant organisms; 6) In-hospital use of antimicrobials; 7) Infections in long-term care (LTC) facilities; 8) Catheter-related bacteraemia in neonatal units & paediatric intensive care; and, 9) Hand hygiene surveillance.

VINCat program conducts a yearly survey to collect information from the hospitals, with an average of over 10,500 patients involved each year and global NI prevalence ranging from 6,2% to 7,6% (data: 2008 – 2016). Figure 6 provides data on NI prevalence from the last 5 years available.

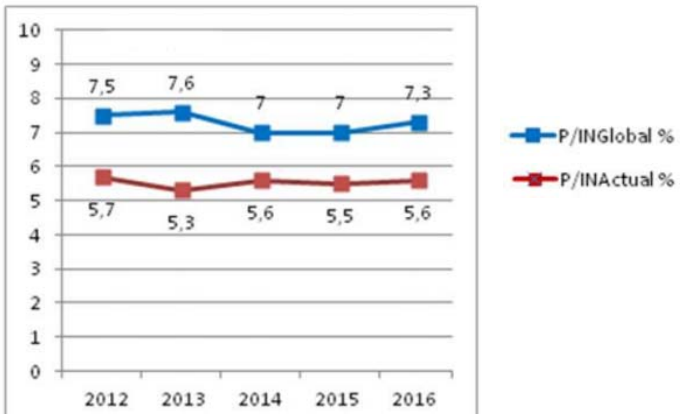

Figure 6 – Evolution of Nosocomial Infection Prevalence (VINCat, 2012-2016)
Global Nosocomial Infection (INGlobal) and Current Nosocomial Infection (INActual)

Considering the data reported for the surveys by the different Catalan hospitals, the top-5 most frequent microorganisms detected after culture growth and most relevant antibiotic resistances are provided in the table below (Table 16). These figures reflect the **evolution of key infection agents despite the surveillance mechanisms in place**. Additionally, there was an increase in the incidence of nosocomial infections due to *Clostridium difficile* (per 10,000 hospital stays) from 1.13 in 2012 to 1.54 in 2016. (VINCat, 2016) [4].

Percentage of detection	Gram	Enterobact.	2012	2013	2014	2015	2016	Average
E.coli	-	x	16.6	28.75	17.6	10.7	9.8	16.69
% CP			-	-	0.06	0.06	0.06	0.06
P. aeruginosa	-		8.75	15.6	11.5	3.9	5	8.95
K. pnemoniae	-	x	5.4	6.1	7.85	4.1	3.85	5.46
% CP			-	-	0.67	1.16	2.18	1.37
% ESBL			-	-	19.82	17.98	18.76	18.85
Proteus mirabilis	-	x	5.9	5.3	4.95	1.85	1.5	3.9
MRSA	+		6.65	6.95	5.7	2.8	2.7	4.96

CP: Carbapenemase-producing; ESBL: Extended-spectrum beta-lactamase-producing

Table 16 – Detection rates of key MDROs reported by VINCat Survey (VINCat, 2016)

It can be observed that, despite the implementation of the Surveillance programme since 2005, the prevalence of nosocomial infections in the main hospitals in Catalonia has decreased to a limited extend (VINCat, 2016).

[4] VINCat; Vigilància de la infecció nosocomial als hospitals de Catalunya. Informe 2016; 2017. http://catsalut.gencat.cat/web/.content/minisite/vincat/documents/informes/Informe-2016.pdf

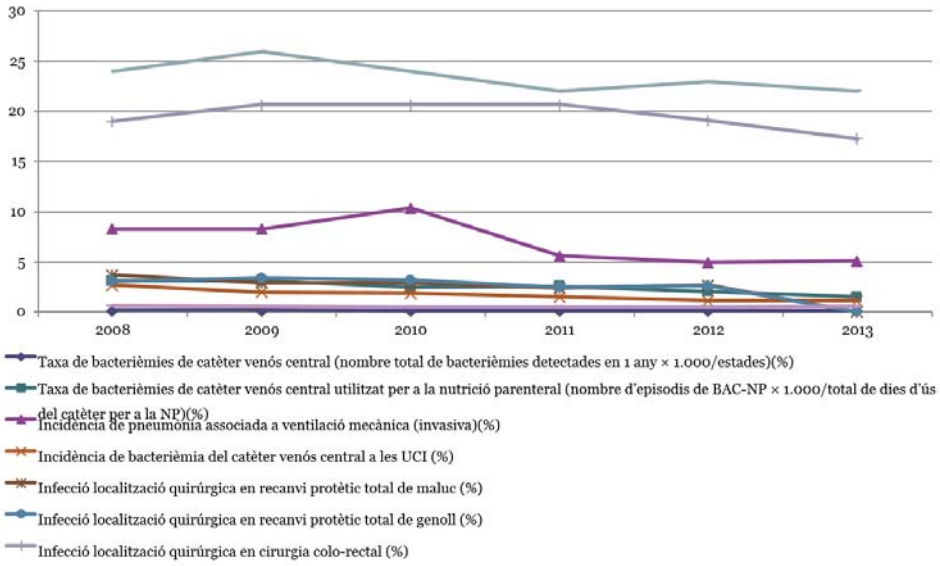

Figure 7 – Evolution of nosocomial infections in Catalonia, displayed by type of infection (VINCat, 2015)

An example of the costs that hospital-associated infections impose to the Catalan Health system can be extracted from a study published by VINCAt in 2015 (Shaw, 2015 (Suppl 1))[5]. Calculation of costs considered the data related to 2,276 elective colorectal surgery interventions. Organ/space (O/S) infection occurred in 193 (8.5%) out of the 2,276 patients. Patients with O/S were more frequently men (73% versus 60%; p =0.001); underwent a rectal procedure (43% versus 31%; p<0.001) and had a National Nosocomial Infection Surveillance (NNIS) index ≥1 (43% versus 34%; p =0.06). Median length of stay was greater by three-fold (22 days versus 7 days; p < 0.001) when O/S occurred which accounted for an extra cost of €3,052 per patient. Within the group of O/S infection, 45/193(23%) patients were readmitted with a median length of stay of 13 days [IQR8 - 17)]; 117/193 (60%) required re-operation and 56/193(29%) required intensive care unit stay with a median length of stay of 5 days [Interquartile Range (IQR): 3 - 12]. This added an additional cost of €2,235 per patient. Accordingly, 193 O/S infections accounted for an overall excess cost of €1,020,391.

Overall, the VINCat's interest in ANTI-SUPERBUGS PCP is based on the growing worldwide public health problem of MDROs, and – specifically – the identified microorganisms that negatively affect the hospitals based in Catalonia.

Continued success is one of VINCat goals along with improvement of the quality of the obtained data and the incorporation of new approaches and objectives. Accordingly, ANTI-SUPERBUGS PCP is also expected to contribute to the recommendations for building a successful public health surveillance system, as provided by the leaders of relevant

[5] Shaw et al.: 'Cost of organ/space infection in elective colorectal surgery. Is it just a problem of rates?' Antimicrobial Resistance and Infection Control 2015 4(Suppl 1):P77.

surveillance programs (e.g. VICNISS, in Australia, or the KISS, in Germany). These requirements include for example: i) adequate resourcing, including the development of specific software, and the establishment of a coordination center with multidisciplinary staff; ii) close contact between the participating hospitals and the coordination center; iii) ongoing efforts to improve the system, including new epidemiological knowledge and improved data validation and analysis methods; and iv) timely and regular data feedback to the institutions.

5.1.2 Clinical university of Aachen (UKA)

University Hospital Aachen (UKA) is a modern University hospital in Germany located in the "Euregio", next to Belgium and the Netherlands. It comprises 1.300 beds including more than 200 ICU beds caring for more than 45,000 in-hospital and 250,000 ambulatory patients annually. It offers superior expertise in intensive care, being the national centre of excellence. Since its foundation convergence of medicine and technology is the medical faculty's mission and core area being part of the RWTH (Rheinisch-Westfälisch Technische Hochschule), which is one of the Universities of Excellence in Germany. Development of innovative, telemedical solutions is part of the mid to long-term strategy of UKA, North-Rhine-Westphalia's and federal authorities. Therefore, UKA founded a centre for telemedicine at the university hospital.

5.1.3 Sheffield Teaching Hospitals NHS Foundation Trust (STH)

Sheffield Teaching Hospitals NHS Foundation Trust (STH) is one of the largest NHS Foundation Trusts in England and provides integrated secondary, tertiary and community services for more than 2 million adults from South Yorkshire and surrounding regions, as well as national referrals. STH employs around 16,500 staff, and has around 2,000 beds across multiple sites.

STH hosts **Devices for Dignity (D4D)**, a publicly-funded organisation that has the remit of developing and bringing new technologies into healthcare practice for the benefit of patients and healthcare organisations. D4D joined the ANTI-SUPERBUGS consortium because of the internationally recognised risks associated with healthcare associated infections and drug resistance. D4D has been involved in the development of 27 technologies that are either on or near market over the past 10 years, and bring their broad expertise in user-centric technology development to the ANTI-SUPERBUGS project.

It is estimated that healthcare associated infections affect approximately 300,000 patients each year in England, at a cost to the NHS nationally of £1billion per year. The number of antibiotics prescribed in England increased by 6% from 2010 to 2013; as also did the number of bloodstream infections caused by resistant organisms (e.g. one in five bloodstream infections with *Escherichia coli* were found to be resistent to at least one key drug). Thus, in 2014 Public Health England (PHE) set Antimicrobial resistance as one of the seven main

priorities to tackle for the next 5 years in order to improve and protect national health (PHE, From evidence into action: opportunities to protect and improve the nation's Health, 2014)[6]. With this aim in mind several actions are defined, including: the development of a new national strategy for infection prevention and control across the health and care System; the implementation of an improved surveillance and feedback systems for antibiotic prescribing and resistance and to deliver a new data capture system for reporting of healthcare-associated infections.

STH main infection control concerns relate to **carbapenemase-producing enterobacteria (CPE)**. The main hope is that the R&D procurement project will provide solutions to interrupt the transmission of dangerous infections to other patients and staff; and to support the implementation of PHE recommendations (Peter M Hawkey, 2018)[7].

The concern is shared at national scale. Samples of CPE bacteria sent to Public Health England by trusts for testing rose from three in 2003 to over 2,500 in 2016 (PHE, 2017) [8].

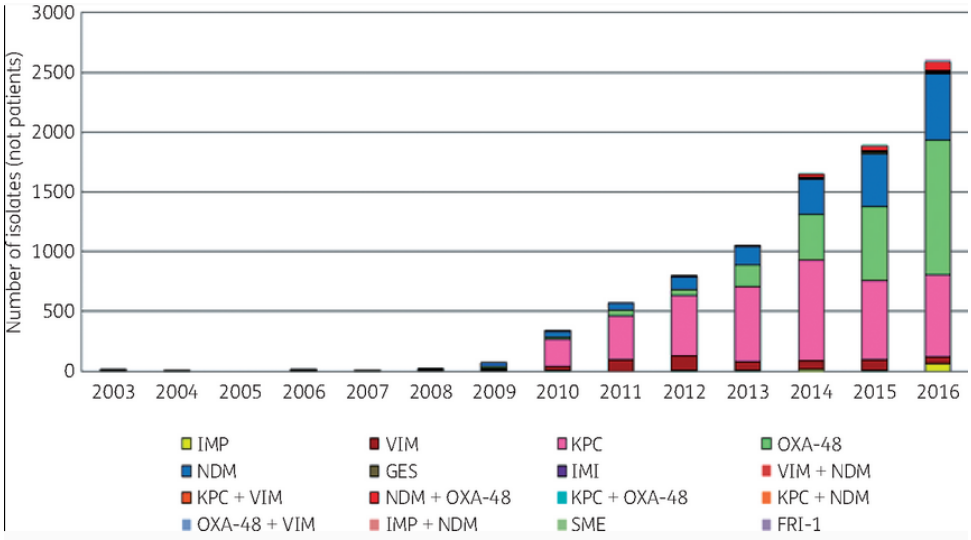

Figure 8 – Evolution of CP resistant isolates detection in laboratories in England (Source: PHE, 2017) [7]

[6] Public Health England; 'From evidence into action: opportunities to protect and improve the nation's Health', October 2014. *Access March 19, 2018:* *https://www.gov.uk/government/publications/from-evidence-into-action-opportunities-to-protect-and-improve-the-nations-health*

[7] Peter M Hawkey, et al.; Treatment of infections caused by multidrug-resistant Gram-negative bacteria: report of the British Society for Antimicrobial Chemotherapy/Healthcare Infection Society/British Infection Association Joint Working Party, Journal of Antimicrobial Chemotherapy, Volume 73, Issue suppl_3, 1 March 2018, Pages iii2–iii78

[8] Public Health England; English Surveillance Programme for Antimicrobial Utilisation and Resistance ESPAUR, Report 2017. *Access on March 20, 2018:* *https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/656611/ESPAUR_report_2017.pdf*

By April 2017, CPE outbreaks had been confirmed in Manchester and London - where dealing with CPE has cost NHS trusts almost **£10 million – Sheffield**, Liverpool, Leeds, Birmingham, Nottingham, Colchester, Edinburgh, Belfast, Dublin and Limerick, among others (Davies M. , 2017) [9].

5.1.4 Autonomous Province of Trento (PAT)

The Autonomous Province of Trento (Provincia autonoma di Trento, PAT) is an Italian alpine region of 540,000 inhabitants located in Northeast Italy.

Administratively, the Province enjoys a large degree of autonomy in the sectors of health, education, welfare and transport infrastructure. The instrumental entity of the provincial administration responsible for health is the **Healthcare Trust of the Autonomous Province of Trento (Azienda Provinciale per i Servizi Sanitari, APSS)**. The local health authority is part of the Italian National Health Services, a system founded on the principles of universal coverage, social financing through general taxation and non-discriminatory access to services. PAT enact health care policies and allocates resources to meet service demands of the health system and through the provincial agency for procurement and contracting manages public procurement.

The APSS employs approximately 7,900 staff and delivers public health, primary healthcare (primary medical care, outpatients care, home care), hospital care (including rehabilitation and long-term care), mental health and ambulance services. It runs 7 public hospitals (2 hubs and five spoke hospitals) and purchases services from 6 private clinics, 22 outpatient facilities and 60 nursing homes and other social care facilities.

Italy is among a group of EU countries with the highest percentage of bacteria resistance to antibiotics according to the European Centre for Disease Prevention and Control. Observations from a recent ECDC visit confirm that the AMR situation in Italian hospitals and regions poses a major public health threat to the country (ECDC, 2017) [10].

The levels of carbapenem-resistant Enterobacteriaceae (CRE) and *Acinetobacter baumannii* have now reached hyper-endemic levels and, together with meticillin-resistant *Staphylococcus aureus* (MRSA), this situation causes Italy to be one of the Member States

[9] Davies M.; 'Worse than MRSA: Doctors call for urgent action on deadly superbug threat'; The Bureau of Investigative Journalism; Press article; April 21, 2017. Access on March 06, 2017 https://www.thebureauinvestigates.com/stories/2017-04-21/worse-than-mrsa-experts-call-for-action-on-deadly-new-superbug

[10] European Centre for Disease Prevention and Control. ECDC country visit to Italy to discuss antimicrobial resistance issues. Stockholm: ECDC; 2017. Access March 25, 2018: https://ecdc.europa.eu/en/publications-data/ecdc-country-visit-italy-discuss-antimicrobial-resistance-issues#no-link

with the highest level of resistance in Europe. The proportion of MRSA blood isolates remains high, but it has decreased from 44.3% in 2000 to 34.1% in 2015.

The overall present AMR situation in Italy according to data from the European Antimicrobial Resistance Surveillance Network (EARS-Net), which Italy has been a member of since 2000, is worse than in many other Member States.

The EARS-Net 2015 report (ECDC, 2017)[11] confirms a high percentage of invasive bacterial isolates with disturbing AMR characteristics, significantly above the EU/EEA average. Actually, Italy reports the second highest percentage of *Klebsiella pneumoniae* blood isolates resistant to the last-line group of antibiotics, the carbapenems (33.5%, 2015 data from EARS-Net); whereas combined resistance (third-generation cephalosporin, fluoroquinolones and aminoglycosides) increased from 2.8% in 2005 to 29.7% in 2015.

For *Escherichia coli*, the proportion of blood isolates that are resistant to carbapenems remained low: 0.1% in 2007 to 0.2% in 2015 (0.6% in 2013), but combined resistance (third-generation cephalosporin, fluoroquinolones and aminoglycosides) increased from 0.8% in 2002 to 14.6% in 2015. The proportion of carbapenem-resistant *Acinetobacter spp.* blood isolates is very high - 83% (2012) and 78.3% (2015) -; similar to combined resistance (fluoroquinolones, aminoglycosides and carbapenems) - 77.4% (2012) and 72.6% (2015). The proportion of vancomycin-resistant *Enterococcus faecium* is rather high, but decreased from 15.0% in 2001 to 11.2% in 2015.

It has been reported an endemic situation in the country regarding carbapenemase-producing/carbapenem-resistant Enterobacteriacae (expert self-assessment for European Survey on Carbapenamase-Producing Enterobacteriaceae - EuSCAPE project).

Overall, in the following table, abstracted from the later mentioned national plan, are compared average resistance data for Italy and the European Union (ECDC, 2017) [10].

[11] European Centre for Disease Prevention and Control. Antimicrobial resistance surveillance in Europe 2015. Annual Report of the European Antimicrobial Resistance Surveillance Network (EARS-Net). Stockholm: ECDC; 2017.

	Italia 2015 (%) (categoria)[§]	Media europea 2015 (%) (categoria)[§]	**Trend 2012-15**[*]
Klebsiella pneumoniae			
resistente a cefalosporine 3° generazione	55,9 (6)	30,3 (5)	>
resistente agli aminoglicosidi	34,0 (5)	22,5 (4)	
resistente ai carbapenemi	33,5 (5)	8,1 (3)	
MDR (R a cefalosporine di 3° generazione + aminoglicosidi + fluorochinoloni)	29,7 (5)	18,6 (4)	
Escherichia coli			
resistente a cefalosporine 3° generazione	30,1 (5)	13,1 (4)	>
resistente a fluorochinoloni	44,4 (5)	22,8 (4)	>
resistente agli aminoglicosidi	20,2 (4)	10,4 (4)	
MDR (R a cefalosporine di 3° generazione + aminoglicosidi + fluorochinoloni)	14,6 (4)	5,3 (3)	
Pseudomonas aeruginosa			
resistente a piperacillina-tazobactam	29,5 (5)	18,1 (4)	
resistente a ceftazidime	21,7 (4)	13,3 (4)	
resistente agli aminoglicosidi	17,2 (4)	13,3 (4)	<
resistente a carbapenemi	23,0 (4)	17,8 (4)	
Acinetobacter spp.			
resistente a carbapenemi	78,3 (7)	Non riportata	
Staphylococcus aureus			
resistente alla meticillina	34,1 (5)	16,8 (4)	
Streptococcus pneumoniae			
NS alla penicillina	12,3 (4)	Non riportata	
NS ai macrolidi	24,5 (4)	Non riportata	<#
Enterococcus faecium			
resistente ai glicopeptidi (VRE)	11,2 (4)	8,3 (3)	>

Legenda

§ Categoria 1: <1%; Categoria 2: 1% - <5%; Categoria 3: 5% - <10%, Categoria 4: 10% - <25%; Categoria 5: 25% - <50%; Categoria 6: 50% - <75%; Categoria 7: >= 75%

* > trend in aumento statisticamente significativo (# non statisticamente significativo se si considerano solo gli ospedali presenti da più tempo nel database); < trend in riduzione statisticamente significativo

NS: non sensibile

Figure 9 – Frequency of isolation of Resistant bacteria from blood culture data (Italy and European Union)

If the current trends of carbapenem resistance and other major resistances in gram-negative bacteria (such as *K. pneumoniae* and *A. baumannii*) are not reversed, medical treatments will

be compromised in the near future. The above reported data show clearly the magnitude of the problem for Italy and its regions.

The APSS periodically publishes reports on the surveillance of AMR covering all the hospitals of the region. Prevalence of MRSA (at around 16%) and CRE (sporadically isolated) are lower than the Italian average and stable over time.

Regarding Healthcare-Associated infections (HAIs), according to international surveys, the percentage of patients with at least one HAI on a given day in Italian hospitals is similar to the EU/EEA average (6.3% vs. 5.7%, respectively); the rate for PAT is around 6%.

In the tabe below local data are reported concerning the number of alert microorganisms isolated from patients hospitalized and rate of hospital infections (normalised by 1,000 patient admissions and by 1,000 days of hospital stay) at the hospital of Trento. Current data (2016), as shown below, demonstrate the major impact of MDROs on hospital infections.

OSPEDALE DI TRENTO
SORVEGLIANZA MICRORGANISMI ALERT
PERIODO 1 GENNAIO – 31 DICEMBRE 2016

	TOTALE	Infezioni Ospedaliere
Totale pazienti coinvolti	418	
Totale segnalazioni	496	
Schede paziente non restituite	113 (27.03%)	
ESBL / AmpC / Carbapenemasi (Enterobatteriacee multiresistenti)	253	22 (8.7%)
MRSA	37	7 (18.9%)
Stafilococchi Linezolid R	3	1 (33.33%)
Legionella	17	4 (23.53%)
Pseudomonas MDR	33	5 (15.15%)
Acinetobacter MDR	1	0
Enterococchi Vancomicina Resistenti	17	3 (17.64%)
S. maltophilia	20	2 (10.0%)
Aspergillus	24	0
C.difficile	25	14 (56%)
RSV	10	0
Rotavirus	10	0
Salmonella	17	0
Streptococcus pyogenes da sangue	2	1 (50.0%)
Streptococcus agalactiae da liquor o sangue	1	0
Listeria da sangue o liquor	2	0
Mycobacterium tuberculosis	14	0
TOTALE Infezioni ospedaliere		58 (13.87%)
TOTALE Infezioni ospedaliere da MDRO		40 (68.96%)

Figure 10 – Number of microorganism isolated from patients and hospital-infection rates

(Source: Hospital of Trento)

DATI NORMALIZZATI PER 1000 PAZIENTI	
Totale pazienti nuove accettazioni	25165
Infezioni Ospedaliere	2.3
Infezioni Ospedaliere da MDRO	1.59
DATI NORMALIZZATI PER 1000 GIORNATE DI DEGENZA	
Totale giornate di degenza	194000
Infezioni Ospedaliere	0.3
Infezioni Ospedaliere da MDRO	0.2

Figure 11 – Impact of MDROs on hospital infections

(Source: Hospital of Trento)

The Province of Trento, with its hospitals, participates in the main surveillance networks existing in the country. It contributes to the national surveillances of surgical site infections and HAIs in intensive care units (ICUs). Italian ICUs tend to report a high incidence of intubation-associated pneumonia and central venous catheter-associated bloodstream infections. Gram-negative bacteria, including *Klebsiella* spp. and *Acinetobacter baumannii* are among the most common bacteria responsible for HAIs in Italian ICUs, and these are usually resistant to multiple antibiotics.

In Italy, antimicrobial consumption in humans is among the highest of all EU/EEA Member States (data from ESAC-Net 2015). With 28 defined daily doses (DDD) per 1,000 inhabitants and per day of antibiotics for systemic use in the community, Italy consumes many more antibiotics than the EU/EEA average of 21 DDD per 1,000 inhabitants and per day.

In the hospital sector, the consumption of antibiotics for systemic use (2.4 DDD per 1,000 inhabitants and per day) is among the highest of all EU/EEA Member States and more than double the EU/EEA average consumption in the hospital sector (1.0 DDD per 1,000 inhabitants and per day).

Since 2000, antimicrobial consumption has been reported on annual basis by the Medicine Utilisation Monitoring Centre (OsMed) at the Italian Medicines Authority mainly through the "National Report on Medicine Use in Italy". The report covers analyses of antimicrobial consumption in the outpatient and inpatient sectors.

Data from the Italian Observatory on Medicine Consumption show a meaningful regional variability in antimicrobial use not explainable by epidemiologic factors. In 2016, the overall consumption of antimicrobials by systemic use in the Autonomous Province of Trento confirmed to be lower than the Italian average (16.1 in Trento vs 20.1 in Italy) (APSS, 2016) [12]. In all group of antimicrobials, the consumption of PAT is significantly below the Italian average. This is particularly evident for third generation cephalosporins (-41%), sulphonamides and trimethoprim (-31%), fluoroquinolones (-22%) and association of penicillins (-19%).

International data from the latest Eurobarometer survey on AMR show that the proportion of the general population that had taken antibiotics during the past year increased from 36% in 2013 to 43% in 2016, the fourth highest of all EU Member States. This is much higher than the EU average of 34% for 2016 (decrease from 35% in 2013).

Therefore, all objective and subjective current data and surveys indicate that the situation in Italy is much worse than in most EU Member States. Excessive and inappropriate use of antimicrobial treatments, especially antibiotics and poor infection control practices have

[12] Healthcare Trust of the Autonomous Province of Trento (www.apss.tn.it), 2016.

transformed AMR in a serious threat to public health in the country, and despite reporting better results than the Italian average the Autonomous Province of Trento is not exempted.

National and regional governments, and all clinical stakeholder of the Italian National Healthcare Service, are aware of this and have acted. The issue of AMR in the last months reached a high level of political focus and led to the approval of the National Plan against Antimicrobial Resistance (2017-2019). Its overarching goal is to preserve the possibility of effective treatment of human and animal infections, reducing the emergence and spread of AMR, and improving the current outcomes related to AMR and HAI. This must be achieved through: surveillance, prevention and control of infections; appropriate use of antibiotics - including antimicrobial stewardship; education, communication and information; and research and innovation.

The plan is mandatory for all regions and it includes evidence based actions to be deployed at different levels of the health care systems: 67 national actions and 59 regional and local (hospital) actions. The plan includes indicators and targets with measurable outcomes and deadlines for its operational, such as: reduction of 10% of consumption of antibiotics, reduction of the consumption of specific categories (fluoroquinolones), reduction of prevalence of MRSA and CPE isolated in blood samples. Actions in the area of research and development are focused on fostering transfer of research and innovation in clinical services. In the plan, a specific mention is made to the important role of EU projects financed under Horizon 2020.

In such context, the contrast of antimicrobial resistant microorganisms became a top priority for public health and health care service in the Autonomous Province of Trento. Current regional priorities include: the integration of regional and central surveillance and development of tools for alerting and reporting within hospital and other healthcare settings, and investment in research and development, regarding also the uptake of new technologies through innovation procurement.

As regulator body in charge of public health and health care policies, the Department of Health and Social Solidarity of the PAT joined the ANTI-SUPERBUGS PCP challenge with the aim of reducing the burden of AMR. In the current context, tackling actively AMR is mandatory and PAT must to be compliant with national standards and improvement goals. This can be enabled by novel ICT solutions for early detection of resistance and increase timely of feedbacks for practitioners. Tools for timely and effective feedback on easily understandable AMR data, must be acknowledged as a critical component of any AMR strategy.

5.1.5 HELIOS Clinical University of Wuppertal (HELIOS)

HELIOS Universitätsklinikum Wuppertal (HELIOS) is a house of the maximum supply belonging to a hospital chain in Germany with more than 114 hospitals nationwide. The University Clinic itself is the largest hospital, providing medical services for approximately 50000 in-patients and 100000 outpatients. About 2500 employees work in medicine, care and provisioning relevant department to ensure high quality in medical services.

With the support of the **Department of Innovation of Research Support (D.I.R.)**, HELIOS encompasses several multidisciplinary teams developing research and innovation pilot projects (basic -, clinical - and health care research) based on needs of end-users. Most are especially considering the challenges of a digital world and demographic change, and the opportunities of patients to be empowered to participate in their own health-status. One of the **multidisciplinary research team** is working in the context of **Faster diagnostics and Faster Detection of (Specific) Germs and AntisuperBugs**.

Additionally, HELIOS includes the **Institute for Medical Laboratory Diagnostics (IML)** that performs approx. 3 million analysis/year, covering the Microbiology service for 7 hospitals (>3000 beds). IML is a reference Laboratory for Infectious Diseases of the Reference Institute for Bioanalytics (RfB) of the German Society of Clinical Chemistry and Laboratory Medicine (DGKL e.V.).

The following table illustrates the MDROs of interest for HELIOS, and related prevalence according to data provided by HELIOS MD responsible of the Medical Laboratory Diagnostics, 2017.

MDRO	Prevalence
MRSA	9 %
MDR-gram negative Enterobacteriaceae / carbapenem resistance	< 1%
VRE	13-14 €
Mycobacterium tuberculosis	(2 cases)

Table 17 – HELIOS MDRO data

The biggest impact of the HAIS is observed in the excess of hospitalization days (LOS) for infected patients, when compared with the average of the patients' LOS. This results on an overcosts for Helios' centers as the reimbursement received is based on the average figures (Figure 12).

Haus	Fälle	Fälle %	Σ VWD	Ø VWD	Avg (MittlereVwd_Kat)			
ATT	89	1,37%	1.021	11,5	11,1			
BO	151	2,33%	3.176	21,0	17,9			
DUN	1.225	18,90%	17.419	14,2	11,7			
GM	121	1,87%	1.417	11,7	11,2			
KR	970	14,97%	22.871	23,6	17,4			
KRH	133	2,05%	2.415	18,2	14,7			
LEN	204	3,15%	1.938	9,5	10,5			
NDB	446	6,88%	6.200	13,9	11,5			
OB	180	2,78%	2.849	15,8	15,7			
SU	525	8,10%	6.968	13,3	11,6			
SWE	481	7,42%	6.736	14,0	12,7			
WAR	143	2,21%	1.913	13,4	11,6			
WUP	1.813	27,97%	30.140	16,6	13,3			
NRW	6.481	7,69%	8081,77	15,13	13,16			
				F=durchschnittliche Verweildauer				
				E= Mittlere gemittete verweildauer der DRG´s dieser Patienten		z.B.89		
				> wir haben E und wollen unter F				

Figure 12 – Cases of HAIs reported by HELIOS clinics at the North-Rhine Westphalia region (13 centers) and LOS days of infected patients and LOS days reimbursed by the payer (Source: HELIOS D.I.R.)
Fälle: Cases; Ø VWD: LOS of infected patients (days); Avg: LOS reimbursed (days)

5.1.6 Research Foundation of Mútua Terrassa (FMT)

FMT (Research foundation of Mútua Terrassa) is the research and innovation arm of Mútua Terrassa. The Foundation, a private non-profit organisation founded in 2000, promotes and develops biomedical research and innovation within Mútua Terrassa. Mútua Terrassa, founded in 1900, integrates various health and social care service units. Mútua Terrassa has an extensive network of primary care centres and the **Hospital Universitari Mutua Terrassa (HUMT)**; which is associated with the University of Barcelona for education in pre- and postgraduate courses.

The centre belongs to the Public Hospital Network (Xarxa Hospitalària d'Utilització Pública, XHUP) of Catalonia, and is part of a network of 8 hospitals with greater complexity in Catalonia. It is a state-of-the-art hospital equipped with all the means of diagnosis and all the specialties, with a permanent emergency service and comprehensive external consultations. HUMT has more than 460 beds, 34 medical departments and received in 2016 more than 2,000,000 visits. It offers healthcare coverage to a significant proportion of the regions of Vallès Occidental Oest and Baix Llobregat (Barcelona, Catalonia). Its reference population is over one million inhabitants for some specialties.

FMT shares the concern on MDROs and AMR as key threat for hospitals across Europe, with increasing risk. New ICT surveillance and management technologies can be useful to detect rapidly and accurately, and improve treatment suitability for infected patients. The HUMT

participates in the Catalan infection surveillance **VINCat program**. The ICU and Internal Medicines Units take care of the supervision and prevention of infectious diseases.

Nosocomial infection prevalence rates at HUMT vary from 3,3% to 9,8% over the last ten years (
Figure 13 and Figure 14), with a special relevance of infections due to ESBL (extended-spectrum beta-lactamase)-producing *Klebsilella pneumoniae* and to Clostridium difficile. In 2017 it has been reported 1 case of infection related to Carbapenem-Resistant Gram-Negative Bacilli and specific interest is focused in avoiding the spread of this kind of MDROs.

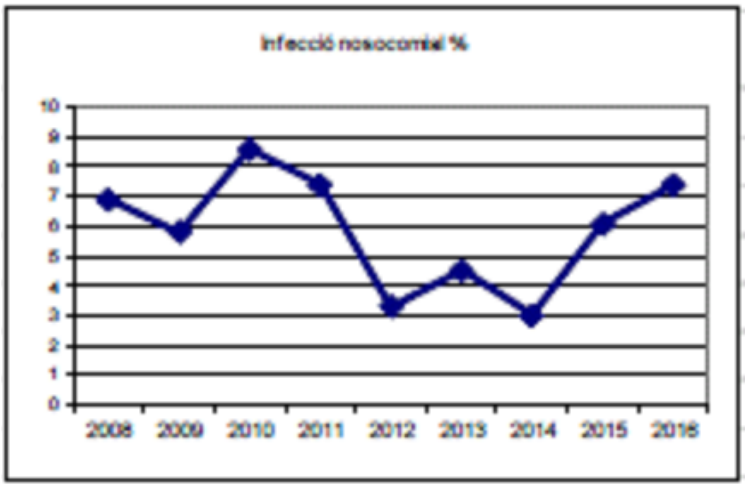

Figure 13 – Nosocomial infections rates (%) in HUMT (2008 – 2016)

Hospital Universitari Mútua Terrassa

Infeccions relacionades amb l'atenció sanitària (IRAS) 2008-2016

Indicadors de resultat	2008	2009	2010	2011	2012	2013	2014	2015	2016
Infecció nosocomial i consum antimicrobians									
Pacients infecció nosocomial ingrés actual / total pacients x 100	6,9	5,8	8,6	7,4	3,3	4,5	3,0	6,1	7,4
Bacterièmia									
Bacterièmies nosocomials / total estades x 1000	0,78	0,84	0,65	0,88	0,86	0,94	0,68	0,94	0,96
Bacterièmies per SARM nosocomials / total estades x 1000	0,04	0,01	0,02	0,02	0,00	0,03	0,01	0,00	0,01
Bacterièmies urinàries nosocomials / total estades x 1000	0,20	0,24	0,16	0,24	0,18	0,23	0,15	0,24	0,34
Bacterièmies catèter nosocomial / total estades x 1000	0,16	0,24	0,16	0,21	0,19	0,18	0,10	0,21	0,24
Bacterièmies catèter nosocomial *S.aureus* / total estades x 1000	0,05	0,05	0,02	0,04	0,05	0,04	0,05	0,05	0,03
Microorganismes especial rellevància									
SARM casos nous nosocomials HUMT (mostres clíniques) / total estades x 10000	1,47	0,85	1,33	1,60	0,74	1,05	0,62	1,42	2,00
EDR *Pseudomonas aeruginosa* nosocomial (mostres clíniques) / total estades x 10000	0,00	0,70	0,25	0,71	0,92	0,38	0,62	1,02	1,90
Pacients *C. difficile* nosocomial (infecció) / total estades x 10000 (adults)	1,80	6,59	3,07	2,73	1,65	1,61	2,59	3,06	1,87
Pacients *Kleb. pneumòniae* BLEE nosocomial (mostres clíniques) / total estades x 10000	2,79	1,24	1,00	0,62	1,94	2,11	1,54	3,45	3,50
Pacients Acinetobacter baumannii nosocomial (mostres clíniques) /total estades x 10000	0,16	0	0	0	0	0	0	0,00	0,00
Legionel·losi nosocomial nre. Casos	0	1	0	1	2	2	0	0	0
Vigilancia infecció localització quirúrgica									
Pacients ILQ colon recte / total pacients IQ colon recte x 100	23,0	25,3	21,6	23,6	18,2	20	19,5	16,1	10,2
Pacients ILQ pròtesi genoll maluc / Total pacients pròtesi genoll maluc x 100	5,3	1,5	1,9	4,1	2,1	0,8	1,2	0,9	2,2
Pacients ILQ hemiartroplàstia / Total pacients hemiartroplàstia (fractura femur) x 100							8,2	7,4	2,7

Hospital Universitari Mútua Terrassa

Infeccions relacionades amb l'atenció sanitària (IRAS) 2017 HUMT

	GEN	FEB	MAR	ABR	MAI	JUN	JUL	AGO	SET	OCT	NOV	DES	Acum. 2017	Acum. 2016	Total 2016	Dife. 2017-6	Dif %
Multiresistents																	
SARM casos nous nosocomials mostres clíniques	2	6	1	0	2	1	0	1	2	0	1	2	18	20	20	-2	-10%
EDR *Pseudomonas aeruginosa* nosocomial mostres clíniques	1	2	0	1	0	2	0	0	1	0	0	0	7	19	19	-12	-63%
Pacients *C. difficile* nosocomial (infecció)	6	1	4	5	4	3	0	0	2	3	3	2	33	18	18	15	83%
Pacients *K. pneumoniae* BLEE nosocomial mostres clíniques	3	0	3	3	3	2	1	3	8	3	5	1	36	35	35	0	0%
Pacients BGN productor carbapenemases	0	0	1	0	0	0	0	0	0	0	0	0	1	0	0	1	

Figure 14 – Nosocomial infections data reported by HUMT (2008-2017)

5.2 Overall problem statement

5.2.1 'Superbugs' prevalence/incidence and related costs

Health care-associated infections (HAIs), or "nosocomial" and "hospital" infections, are defined as infections acquired in hospital by a patient who was admitted for a reason other than that infection. This means, an infection occurring in a patient in a hospital or other health care facility in whom the infection was not present or incubating at the time of admission. This includes infections acquired in the hospital but appearing after discharge, and also occupational infections among staff of the facility (WHO, Prevention of hospital-acquired infections. A practical guide (2nd edition), 2002)[13].

According to the technical report from the European Centre for Disease Prevention and Control published in 2017 (ECDC, 2017) [14], the most frequent types of HAI are: surgical site infections, urinary tract infections, pneumonia, bloodstream infections and gastrointestinal infections. ECDC studies have estimated that 2,609,911 new cases of HAI occur every year in the European Union and European Economic Area (EU/EEA) (Cassini A, 2016)[15].

The uncontrolled transmission of multi-drug resistant organisms (MDROs, aka 'Superbugs') via patient to patient, patient to staff to patient, or patient to surface to patient, is a major problem in health care systems. This cause significant morbidity, mortality and increased hospitalization and costs, as well as adversely affecting patient experience. ECDC reports that the **cumulative burden** of the main HAIs is estimated at 501 DALYs (disability-adjusted life years) per 100,000 general population each year in EU/EEA. Pneumonia and primary bloodstream infection impose the highest burden, representing over the 60% of the total estimation. Additionally, studies (Henderson & al., 2013)[16] following the indications by the Centers for Disease Control and Prevention (CDC) Network at the US, suggest that the **total annual costs** for the 5 major infections were $9.8 billion (95%CI, $8.3-$11.5 billion). Surgical site infections contributing the most to overall costs (33.7%of the total), followed by ventilator-associated pneumonia (31.6%), central line–associated bloodstream infections (18.9%), *C difficile* infections (15.4%), and catheter-associated urinary tract infections (<1%).

[13] World Health Organization; Prevention of hospital-acquired infections. A practical guide (2nd edition); 2002; WHO/CDS/CSR/EPH/2002.12

[14] European Centre for Disease Prevention and Control. Economic evaluations of interventions to prevent healthcare-associated infections. Stockholm: ECDC;2017.

[15] Cassini A, et al. Burden of Six Healthcare-Associated Infections on European Population Health: Estimating Incidence-Based Disability-Adjusted Life Years through a Population Prevalence-Based Modelling Study. (2016) PLoS Med 13(10): e1002150. https://doi.org/10.1371/journal.pmed.1002150

[16] Henderson D; Tamir O ; Franz C; et al. Health care–associated infections: a meta-analysis of costs and financial impact on the US health care system. JAMA Intern Med. 2013; 173: 2039-2046

HAIs are also related to a more pressing problem worldwide: **antimicrobial resistance** (AMR). AMR is responsible for 25,000 deaths and a loss of €1.5 billion in extra costs (treatment and societal costs) every year in the EU alone. Worldwide, 10 million deaths per year are projected between 2015 and 2050 and expected cumulative losses in OECD countries due to AMR will be USD 2.9 trillion by 2050, if current infection and resistance trends are not reversed. AMR accounts for USD 10,000 to 40,000 additional hospital costs per patient in OECD countries and these figures are likely to double if considering other indirect costs. (EU, 2017) [17]

Thus, infections caused MDROs is a common severe problem in the majority of the healthcare services of worldwide communities (including the ones of ANTI-SUPERBUGS PCP contracting authorities). The most relevant MDROs highlighted by ANTI-SUPERBUGS procurers are:

- **Gram-negative *Enterobacteriaceae* resistant to carbapenems** poses one of the most serious problems in the field of AMR. These bacteria can spread quickly in health care facilities, thanks to the presence of carriers that can disseminate the pathogen in absence of disease. Such MDROs usually present combined resistance to other antibiotics, and are quickly spreading across some geographic areas such as the Mediterranean basin.

  Klebsiella spp. and *E. coli* are between the ten most frequently isolated microorganisms in HAIs. According to data by the ECDC surveillance reports, the proportion of reported *E. coli* isolates resistant to third-generation cephalosporins (most **ESBL-producers**) ranged from 3% to 36% and had increased significantly in more than half of EARS-Net reporting countries. In 2011, 22.3% of all *K. pneumoniae* invasive isolates were resistant to at least three antimicrobial classes. A significant increase in resistance to carbapenems in *K. pneumoniae* from 8% to 15% was reported over the period 2005–2010. Remarkably, the 'Global priority list of antibiotic-resistant bacteria' published by the WHO (February 2017) considers the *Enterobacteriaceae* (including *Klebsiella* and *E. coli*) within the 'Critical' category, according to the urgency of need for new antibiotics (WHO, 2017) [18].
- *S. aureus*, a Gram-positive bacillus, is also between the ten most frequently isolated microorganisms in infections, and is included in the 'High-priority' category for new antibiotics needed due to its methicillin resistance (MRSA).
- *C. difficile* (also a Gram-positive bacillus) was the 8th most frequently detected microorganism among HAIs in the ECDC point prevalence survey of (HAIs) and

[17] EU factsheet 'AMR: A major European and Global challenge', 2017. Access: February 15, 2018. https://ec.europa.eu/health/amr/antimicrobial-resistance_en

[18] WHO Media Center; WHO publishes list of bacteria for which new antibiotics are urgently needed; February 27, 2017. Access: February 14, 2018. http://www.who.int/mediacentre/news/releases/2017/bacteria-antibiotics-needed/en/

antimicrobial use in European acute care hospitals 2011-2012 (ECDC, 2013) [19], and is leading cause of diarrhoea among hospitalized patients (Cioni & al., 2016)[20].

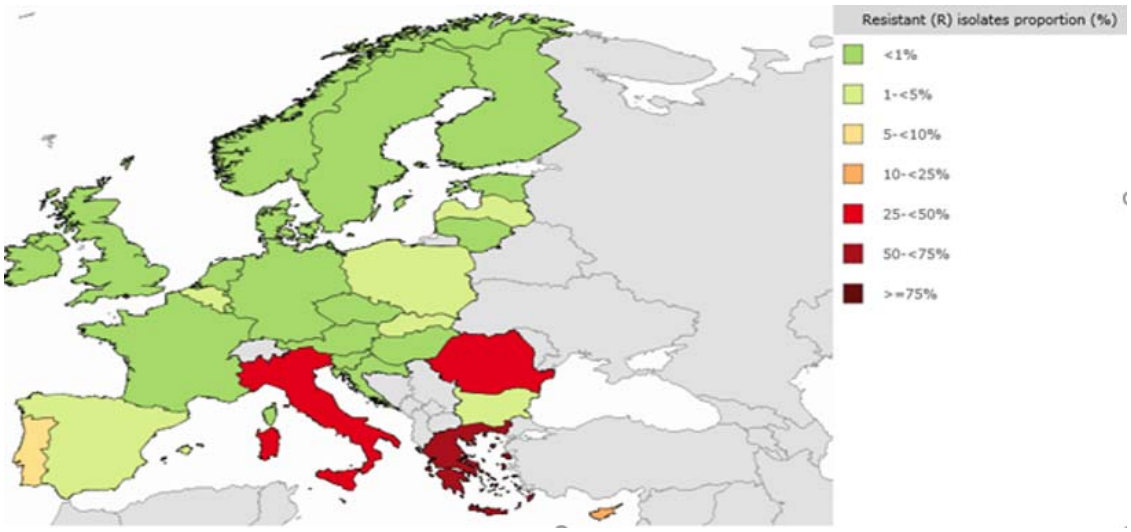

Figure 15 – Proportion of *Klebsiella spp*. with carbapenem resistance (2016)
(Source: EARS-net. ECDC Surveillance Atlas - Antimicrobial resistance) [21]

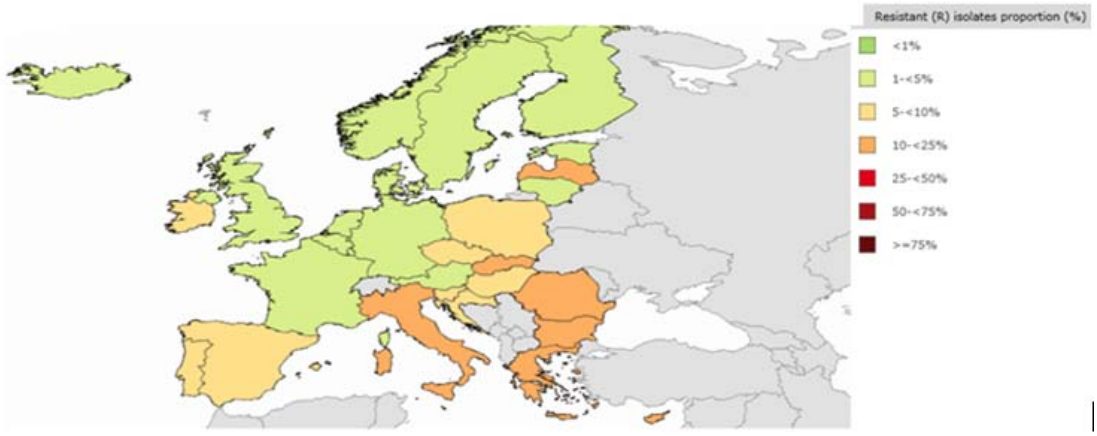

Figure 16 – Proportion of *E. coli* with combined resistance to 3rd generation cephalosporins, fluoroquinolones and aminoglycosides (2016)
(Source: EARS-net. ECDC Surveillance Atlas - Antimicrobial resistance)

[19] European Centre for Disease Prevention and Control. Point prevalence survey of healthcare-associated infections and antimicrobial use in European acute care hospitals. Stockholm: ECDC; 2013.
[20] Cioni, G., Viale, P., Frasson, S., Cipollini, F., Menichetti, et al.. (2016). Epidemiology and outcome of Clostridium difficile infections in patients hospitalized in Internal Medicine: findings from the nationwide FADOI-PRACTICE study. BMC Infectious Diseases, 16, 656. http://doi.org/10.1186/s12879-016-1961-9
[21] ECDC Surveillance Atlas of Infectious Diseases. Access December 14, 2017. https://ecdc.europa.eu/en/antimicrobial-resistance/surveillance-and-disease-data/data-ecdc

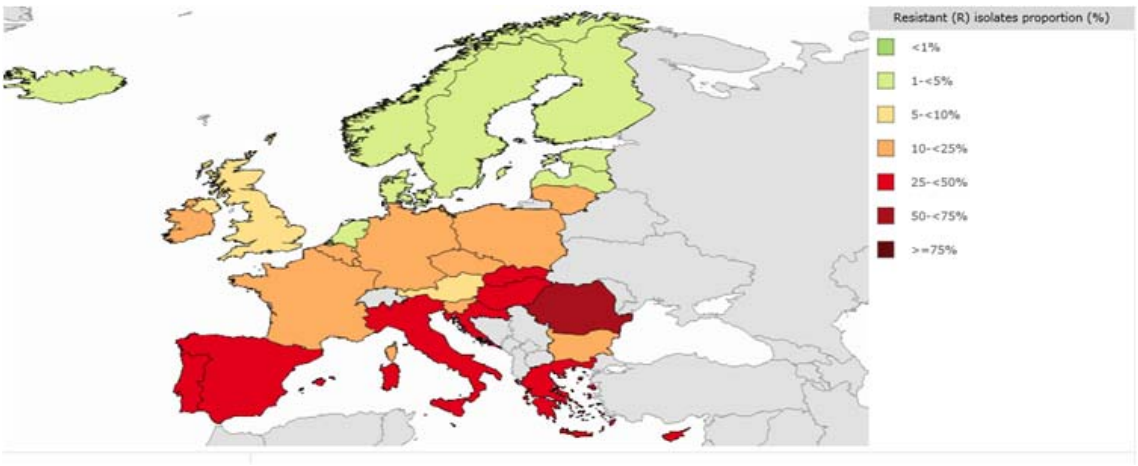

Figure 17 – Proportion of *S. aureus* with methicillin resistance (MRSA) (2016)
(Source: EARS-net. ECDC Surveillance Atlas - Antimicrobial resistance)

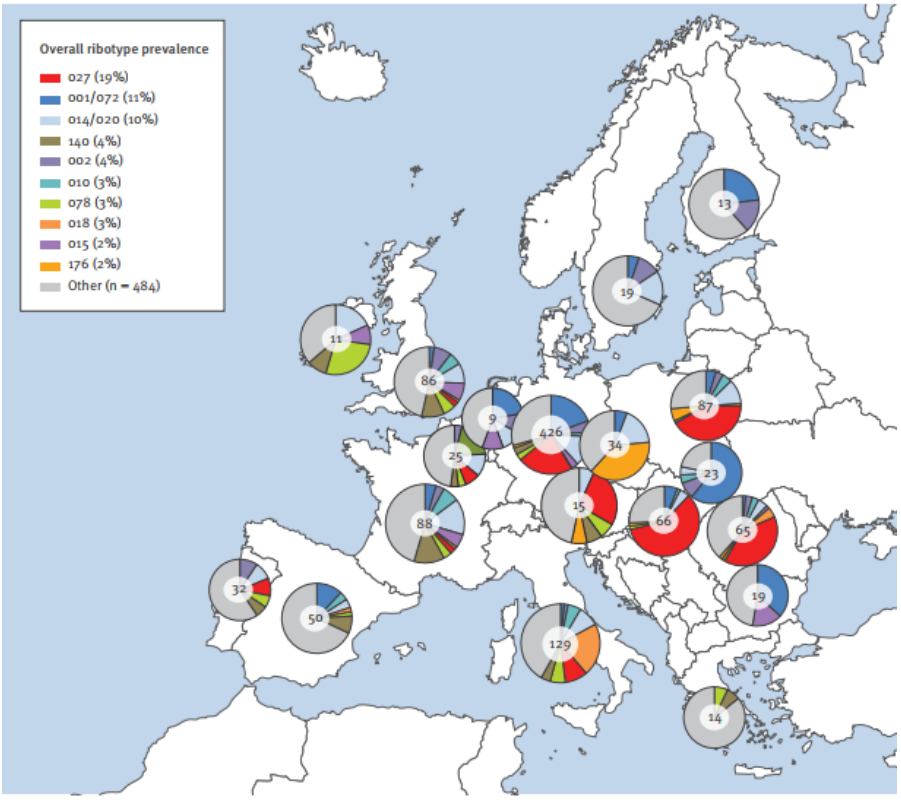

Figure 18 – Geographical distribution of *C. difficile* PCR ribotypes, by participating European country in the EUCLID study (Davies, Longshaw, Davis, & al., 2014) [22]

[22] Kerrie A Davies; Christopher M Longshaw; Georgina L Davis; et al. Underdiagnosis of Clostridium difficile across Europe: the European, multicentre, prospective, biannual, point-prevalence study of Clostridium difficile

In addition to development of drug-resistance mechanisms, these 'superbugs' also share a great capacity to resist in surfaces, which has a important impact in their infection potential and in the cleaning practices in healthcare facilities. Most gram-positive bacteria, such as *Enterococcus spp.* (including VRE), *Staphylococcus aureus* (including MRSA), survive for months on dry surfaces. Many gram-negative species, such as *Acinetobacter spp.*, *Escherichia coli* or *Klebsiella spp.*, can also survive for months. ***C. difficile* spores** can be shed to the environment by both asymptomatic and symptomatic patients and may survive for up to 5 months on inanimate surfaces. (Caselli, 2017) (Kramer, 2006) (T., S., & H., 2014) [23, 24, 25]

5.2.2 The operational context and today's process of care for prevention and infection control

HAI are potentially preventable in around 30% of cases and deadly in around 1% of cases. Data by ESCMID (Tacconelli & al., 2014) [26] shows that infection prevention and control (IPC) measures that have been applied in hospitals vary widely, both within and between different countries. According to ESCMID guidelines for the management of the infection control measures to reduce transmission of multidrug-resistant Gram-negative bacteria in hospitalized patients, the current measures for HAIs prevention are defined in the areas listed in the Table below (Table 18), which illustrates a summary of the Basic Recommendations provided by the ESCMID (Tacconelli & al., 2014).

infection in hospitalised patients with diarrhoea (EUCLID); The Lancet Infectious Diseases Vol 14, Issue 12, December 2014, pp. 1208-1219; https://doi.org/10.1016/S1473-3099(14)70991-0

[23] Caselli, E. (2017). Hygiene: microbial strategies to reduce pathogens and drug resistance in clinical settings. *Microbial Biotechnology*, *10*(5), 1079–1083. http://doi.org/10.1111/1751-7915.12755

[24] Kramer A.; Schwebke I; Kampf G.: How long do nosocomial pathogens persist on inanimate surfaces? A systematic review; BMC Infectious Diseases 2006 6:130; https://doi.org/10.1186/1471-2334-6-13

[25] T., Claroa; S., Daniels; H., Humphreysa Detecting *Clostridium difficile* Spores from Inanimate Surfaces of the Hospital Environment: Which Method Is Best? J. Clin. Microbiol. September 2014 vol. 52 no. 9 3426-3428 doi:10.1128/JCM.01011-14

[26] E. Tacconelli; et al.; ESCMID guidelines for the management of the infection control measures to reduce transmission of multidrug-resistant Gram-negative bacteria in hospitalized patients; Clinical Microbiology and Infection; 2014, Vol 20, s1; p1-55.

Area	EPIDEMIC SETTING	ENDEMIC SETTING
Hand Hygiene	***Strong recommendation:*** Implement HH education programmes to reduce the transmission of ESBL-producing Enterobacteriaceae. MDR-A. baumannii, Stenotrophomonas maltophilia (moderate level of evidence); MDR-K. pneumoniae, MDR-P. aeruginosa and Burkholderia cepacia (very low level of evidence)	***Strong recommendation:*** Implement hand hygiene (HH) education programmes to reduce the transmission of extended-spectrum β-lactamase (ESBL)-producing enterobacteriaceae, multidrug-resistant (MDR)-Klebsiella pneumoniae, MDR-Pseudomonas aeruginosa, MDR-Acinetobacter baumannii (moderate level of evidence); Stenotrophomonas maltophilia and Burkholderia cepacia (very low level of evidence)
Contact Precautions	***Strong recommendation:*** Implement contact precautions (CP) for all patients colonized and/or infected with extended-spectrum β-lactamase (ESBL)-producing Enterobacteriaceae, multidrug-resistant (MDR)-Klebsiella pneumoniae, MDR-Acinetobacter baumannii (moderate level of evidence); and Pseudomonas aeruginosa (very low level of evidence)	***Strong recommendation:*** Implement contact precautions (CP) for all patients colonized with extended-spectrum β-lactamase (ESBL)-Enterobacteriaceae (with the exception of Escherichia coli), multidrug-resistant (MDR)–Klebsiella pneumoniae, MDR-Acinetobacter baumannii, and MDR-Pseudomonas aeruginosa (moderate level of evidence)
Alert code	***Strong recommendation:*** Use alert code to identify promptly patients already known as colonized with ESBL-producing Enterobacteriaceae and MDR-K. pneumoniae at hospital/ward admission and perform screening and pre-emptive CP (moderate level of evidence)	***Strong recommendation:*** Use alert code to identify promptly patients already known as colonized with MDR-A. baumannii at hospital/ward admission and perform screening and pre-emptive CP (moderate level of evidence)
Isolation room	***Strong recommendation:*** Isolate colonized and infected patients in a single room to reduce the risk of acquisition of ESBL-producing Enterobacteriaceae, MDR-K. pneumoniae (moderate level of evidence); MDR-A. baumannii and MDR-P. aeruginosa(low level of evidence)	
Cohort staff	***Strong recommendation:*** Cohort staff to reduce the risk of acquisition of MDR-K. pneumoniae (moderate level of evidence)	
Active Screening Cultures	***Strong recommendation:*** Implement a programme of active screening culture at hospital admission followed by contact precautions to reduce the spread of extended-spectrum β-lactamase-producing Enterobacteriaceae, multidrug-resistant (MDR)-Klebsiella pneumoniae, MDR-Acinetobacter baumannii (moderate level of evidence); and MDR-Pseudomonas aeruginosa(very low level of evidence)	

Environmental Cleaning	***Strong recommendation:*** Monitor cleaning performance to ensure consistent environmental cleaning (EC). Vacate units for intensive cleaning. Implement regular EC procedures and, when available, dedicate non-critical medical items for use on individual patients colonized or infected with extended-spectrum β-lactamase Enterobacteriaceae and multidrug-resistant-Acinetobacter baumannii (moderate level of evidence)	***Strong recommendation:*** Implement regular environmental cleaning (EC) procedures and, when available, dedicate non-critical medical items for use on individual patients colonized or infected with multidrug-resistant-Acinetobacter baumannii (moderate level of evidence)
Antimicrobial Stewardship	***Strong recommendation:*** Implement an antimicrobial stewardship programme to reduce the spread of extended-spectrum β-lactamase-producing Enterobacteriaceae (moderate level of evidence)	***Strong recommendation:*** Implement an antimicrobial stewardship programme. Plan interventions of restriction of antibiotic usage to reduce the spread of extended-spectrum β-lactamase-producing Enterobacteriaceae (moderate level of evidence)
Infrastructure and Education	***Strong recommendation:*** Conduct educational programmes to ensure that healthcare workers understand why extended-spectrum β-lactamase-Enterobacteriaceae are important epidemiologically, why prevention of spread is critical for control, and which measures for preventing spread have proven to be effective (moderate level of evidence)	***Strong recommendation:*** Conduct educational programmes to ensure that healthcare workers understand why multidrug-resistant-Acinetobacter baumannii is important epidemiologically, why prevention of spread is critical for control, and which measures for preventing spread have proven to be effective (moderate level of evidence)

Table 18 – Summary of ESCMID guidelines for the management of the infection control measures to reduce transmission of multidrug-resistant Gram-negative bacteria in hospitalized patients. (Tacconelli & al., 2014)

These initiatives and measures differ in application depending on the incidence of the infections (i.e. endemic vs epidemic settings) and in evidence-based level. A harmonized approach based on the application of evidence-based core strategies considering local characteristics and context could be beneficial.

A result of **poor infection control practices** and **excessive and inappropriate use of antimicrobial medicines** is **antimicrobial resistance (AMR).** The consumption of specific antibiotics used for treatment of multidrug-resistant bacterial infections has almost doubled in Europe from 2010 to 2014; with a high variability of antibiotic consumption across OECD countries and leading. Three of the countries where the ANTI-SUPERBUGS procurers are located – i.e.: UK, Spain and Italy -, have an average consumption of antibiotics over the average from all OECD countries (Figure 19).

Figure 19 - Antibiotic consumption in 2014 (defined dose per 1000 inhabitants per day)

(Source: EU factsheet 'AMR: A major European and Global challenge'. 2017)[27]

Continuous surveillance has been demonstrated effective to prevent the propagation of specific MDROs infections and to reduce the length of stay (Souverein D, 2016)[28] . However, continuous surveillance is currently very expensive and not feasible for all organisms. Moreover, the ability of different facilities and different countries to implement it varies widely. Although great effort has been concentrated on admission epidemiology, surveillance and Infection Control, patients continue to acquire MDROs in hospital and their clinical outcomes are adversely affected compared to their initial prognosis. Currently, the main intervention which healthcare organisations can undertake to prevent the spread of AMR organisms is follow aseptic methods where appropriate, and practicing good hand hygiene.

ANTI-SUPERBUGS PCP novel solutions shall support the implementation of best practices for Infection control and preventiom.

5.2.3 The ANTI-SUPERBUGS problem statement

HAIs are of considerable concern to patients, healthcare professionals and policymakers and have become important targets for quality improvement and patient safety initiatives. In some European countries, the measures mentioned in the previous section seem to have led to a subsequent reduction in the incidence of these infections in recent years. However, the published literature (ECDC, 2017)[29] highlights the difficulties in reducing the incidence of these infections and the huge potential clinical and economic benefits if a reduction could be achieved.

HAIs, and in greater extend MDROs, impact quality of care process affect patient outcomes resulting in increased morbidity and mortality and hence in excess of hospital stay. In turn, this has direct repercussions in hospital costs and operational capacity due to infections and complexity of their treatment. At a greater extend, hospital acquired infections are interrelated to community and social care as infected and colonized patiens may be referred between different centers, increasing the risk of infection.

Feedback received from ANTI-SUPERBUGS Buyers' Group and stakeholders, illustrates that even if proven cost-effective in the literature (ECDC, 2017) [28], current fast diagnostic tools

[27] *EU factsheet 'AMR: A major European and Global challenge' (2017)* https://ec.europa.eu/health/amr/antimicrobial-resistance_en

[28] Souverein D, Houtman P, Euser SM, Herpers BL, Kluytmans J, Den Boer JW (2016) Costs and Benefits Associated with the MRSA Search and Destroy Policy in a Hospital in the Region Kennemerland, The Netherlands. PLoS ONE 11(2): e0148175. doi:10.1371/journal.pone.0148175

[29] European Centre for Disease Prevention and Control. Economic evaluations of interventions to prevent healthcare-associated infections. Stockholm: ECDC;2017.

are not fully incorporated within the daily clinical practice nor is the active continuous screening of patients. Integration of data for rapid cooperation between infection control teams is hindered by the time to diagnosis and infection confirmation, limitation of resources within the microbiology labs and different stages of development of information systems. Real time information is paramount for the assessment of infection risk, effective implementation of control measures and appropriate theraphy prescription.

A comprehensive technology is missing to align the key priorities of microbiologists, infection disease experts and technicians, infection nurses, surveillance teams and national/regional programmes and patients, in order to provide an integrated solution to MDROs global problem.

6. THE NEED ELICITATION AND DESCRIPTION

6.1 The ANTI-SUPERBUGS challenge elicitation

The emerged challenge is to:

- ✓ Improve the quality of care processes in hospitals;
- ✓ reduce both the costs and the operational impact resulting from infections caused by MDROs;
- ✓ improve the appropriateness of antimicrobial medicine usage;
- ✓ reduce the community and social care impact of MDROs acquired in hospitals.

Figure 20 – ANTI-SUPERBUGS PCP Challenge

6.2 Main requirements for the ANTI-SUPERBUGS solutions

Following the completion of the validation and prioritization questionnaires mentioned in ***Section 4.2.4***), the following requirements presented in Sections 6.2.1 and 6.2.2 have been considered as a "MUST HAVE" by the majority of the procurers (i.e. selected as "relevant" by 4 partners or more, over 7 procurers).

The full detail of the information provided by the ANTI-SUPERBUGS procurers to the questionnaire is presented in the ***Annex 7.4***.

Recommendations provided during the Project Review required an additional iteration to further focus the extensive list of needs identified in Phases 1 and 2 of the initial needs elicitation process. The re-defined requirements are presented in **Section 6.2.3** below.

The requirements indentified call for a later **requirement engeneering process** in order to be defined as functionalities with the proper granularity. The results of this engeneering process are reported as the base for the Challenge Brief (Deliverable D2.3).

6.2.1 Clinical functional and performance requirements (Phases 1 and 2 of the needs assessment)

ASB' ICT solutions shall be able to detect:

- Klebsiella spp. with carbapenem resistance
- Escherichia coli with combined resistance to 3rd generation cephalosporins, fluoroquinolones and aminoglycosides
- S. aureus with methicillin resistance (MRSA)
- Carbapenem-resistant producing gram-negative bacilli +/- extended-spectrum beta-lactamases (ESBLs) production
- ESBL producing Gram - bacteria (such as Klebsiella pneumonia and Escherichia coli)
- MultiDrug-Resistant Gram - rods (MDR GNR), such as Enterobacter spp., Pseudomonas aeruginosa
- Carbapenemase-producing Enterobacteriaceae (CPE)

The 'ASB' ICT solutions shall be designed as:

- Stand-alone medical device (HW & SW)
- Environmental/surface sensor (remote detection of colonization/infection) triggering alerts to be confirmed by a point-of-care test/microbiology lab (HW & SW)
- In situ alert system that rapidly detects Carbapenem-resistant producing gram-negative bacilli +/- extended-spectrum beta-lactamases (ESBLs) production. Any positive detection by the 'ASB' ICT solutions shall be confirmed later by the microbiology service

The 'ASB' ICT solutions shall be:

- Acceptable to patients
- Minimally intrusive technology

The '***ASB' ICT solutions shall provide***:

- Flexibility to integrate detection capabilities for additional MDROs or future proofing
- Flexibility to integrate detection capabilities for additional clinically relevant HAIs microorganism and vectors
- Sensitivity at least of PCR test (low false negatives)
- Deployment/installation into existing healthcare environments
- The possibility to be used in crowded areas
- Availability of remote alert system
- Availability of alert system to be triggered where the contamination is detected
- Inform in real time the hospital information system of the risks of infection
- Integration with electronic patient health record and the hospital information system (linking the infection with the place of detection) using interoperability standards (HL7, etc.)

Sensing components of the ASB ICT solution shall include: sensors with proven accuracy levels comparable to medical grade devices with similar functions

SW components of the ASB solution shall ensure:

- secure authentication of users in accordance with the existing methods of the procurers
- clear differentiation in reporting data related to environment or to patients
- an on-line how-to manual with both a quick guide to appropriate sampling and instruction for use
- registration of the geographical location and time of bug detection for epidemiological purpose

6.2.2 Other life-cycle functional and performance requirements

INSTALLATION AND REPLACEMENT: 'ASB' ICT solutions shall:

- Allow to be integrated in the regular health care and support staff routines
- Be easy to integrate into different hospital facilities and architectures

INSTALLATION AND REPLACEMENT: 'ASB' ICT solutions shall be installed/available in:

- In patient room(s)
- In Intensive care units (ICU)
- In Emergency rooms (ER)
- Operating theatres

USE AND MANAGEMENT: The 'ASB' ICT solutions shall be:

- Comfortable for users (inpatients and health & support staff) (HW & SW)
- Easy and risk-free to use, minimally demanding human interaction for early detection
- Continuously working system (24 hours) with high frequency sensing and providing highly interoperable data

USE AND MANAGEMENT: The 'ASB' ICT solutions shall have:

- A self-diagnostic function
- Highly usable user interfaces

MAINTENANCE, SCALABILITY AND RENEWAL: The 'ASB' ICT solutions shall be:

- Easy to maintain; self-manageable by the responsible maintenance staff
- Easy to upgrade and renew
- Easy to deploy throughout the system

MAINTENANCE, SCALABILITY AND RENEWAL: The 'ASB' ICT solutions shall have:

- Minimal or no recalibration required
- Cheap consumables (if any)
- A cleanable covering material (if any) of the sensing components

DISPOSAL: The 'ASB' ICT solutions shall:

- Not include nor generate any toxic material to be handled by the personnel
- Use existing disposal routes
- Be environmentally friendly, limited amount of single-use material

Considering the added functionalities to be provided by the 'ASB' ICT solutions, procurers' agreed that the **cost-effectiveness** should be comparable to procurers' common practice for patient screening.

6.2.3 Focussed needs assessment after Project Review (Phase 3)

In order to address the **recommendations provided during the first Project Review (April 2017)**, the ANTI-SUPERBUGS Buyers' Group agreed to re-focus the needs assessment to be covered by the ANTI-SUPERBUGS solutions developed during the PCP:

ASB Technology is a medical device whose intended use is:

- *Volatile organic compounds (VOC) detection to determine contaminations/colonisations of fomites and inanimate hospital environment on the following:*
  - *Clostridium difficile spores and/or microorganism (higher priority will be given to spores detection),*
  - *and either Klebsiella pneumonia (including, if possible, the detection of its carbapenem & ESBL production resistances) or Acinetobacter baumannii (including, if possible, the detection of its carbapenem & ESBL production resistances) or both*
  - *including, if possible, the detection of MRSA, additional Gram-negative pathogens and additional resistances*
- *The provision of an alert system to aid in the correct management of contaminated/colonized patients and inanimate hospital environments*
- *The provision of a local Surveillance & Infection Control System of the target microorganism(s).*

ASB Technology comprises the following ICT elements:

- A **volatile organic compounds screening device** able to detect the contaminations/ colonisations from target microorganism(s) & **software** (client & server) for the proper application of the device

- A **local Surveillance & Infection Control System of the target microorganism(s):** able to:
    - Store all the data collected by the screening device and all the results from the laboratory regarding contaminations/colonization found on patients that were screened as carriers of the specific microorganisms the ASB technology is able to detect
    - Export data sets able to be imported and analyzed by other central Surveillance & Infection Control Systems (i.e. ECDC)
- An **interoperability engine**:
    - Able to send screening outcomes and alerts on identified fomites to HIS/LIS/HER, electronic hygiene control systems and indication-relation control systems
    - Able to receive (1) confirmations from microbiology service and (2) compliancy if indication-relevant actions have been undertaken by relevant clinical actors
- An **alert system engine** able (1) to identify patients at risk of infection after having analysed their health conditions, their patient history, the geolocalised area history and the staff indication relation compliancy and (2) to generate alerts to be sent to the HIS/HER and recommend a patient screening

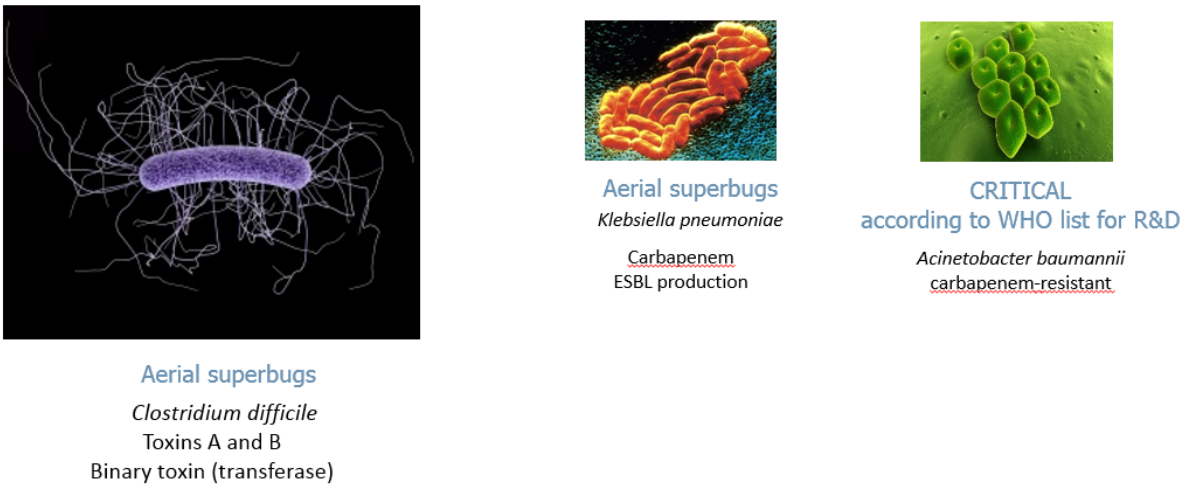

Figure 21 – ANTI-SUPERBUGS PCP Reviewed MDROs to be detected

Complete details of the ANTI-SUPERBUGS requirements and functionalities to address are further described in the **Deliverable D2.3 – Challenge Brief**.

7. ANNEXES

The following Annexes cover some of the materials created for the ANTI-SUPERBUGS Needs Assessment and validation:

- ***Annex 7.1:*** A **Glossary** with relevant medical terms has been produced by ICO (VINCat team) to ensure common understanding among partners and facilitate group discussions.
  This Glossary is considered a live document and is available for update by all partners in the shared repository of the project. The version included here represents the status of the Glossary at the time of Deliverable D2.1 submission.

- ***Annex 7.2 – 7.3:*** **Semi-structured and structured questionnaire** templates provided beforehand by Sara Bedin and AQuAS, used by ANTI-SUPERBUGS Buyers' group to report to the consortium on the common uncovered needs in terms of MDROs detection devices.

- ***Annex 7.4:*** **Questionnaire compiling** all the responses and comments received from ANTI-SUPERBUGS Procurers to the structured questionnaire on Requirements/ Functionalities of the ANTI-SUPERBUGS solutions.

- ***Annex 7.5:*** **description of the institution Ministry of health of Turkey (MOH):** This Annex reflects the description of the Ministry of Healt of Turkey (MOH) included in version 1.0 of this deliverable. MOH confirmed its interest to join the ANTI-SUPERBUGS PCP Buyers' Group by December 2017 and participated in the Phase 2 of needs definition. Later, before the Project review, MOH withdrew without finalizing their ormal accession to the project, due to political reasons.

7.1 ANTI-SUPERBUGS GLOSSARY

ANTI-SUPERBUGS PCP

GLOSSARY OF MEDICAL and TECHNICAL TERMS

Authors: Enric Limón and Gonçalo Rodrigues (ICO-VINCat)
Contributors:

Term	Description	Reference(s)
Antibiotic	An agent or substance that is produced from microorganisms that can act against another living microorganism. Antimicrobial substances that are synthetic, semisynthetic, or those derived from plants or animals, are therefore, by strict definition, not considered antibiotics.	World Health Organization, WHO (2016). Critically Important Antimicrobials for Human Medicine.
Antibiotic resistance	The genetically-acquired capacity for bacteria to withstand antibiotic treatment.	Holmes, A.H., et al (2016). Understanding the mechanisms and drivers of antimicrobial resistance. Lancet, 387(10014).
Antibody	A protein found in the blood that is produced in response to foreign substances (e.g., antigens) invading the body. Antibodies protect the body from disease by binding to these organisms and destroying them.	
Antigen	A foreign substance, usually protein or carbohydrate substance (as a toxin or enzyme) capable of stimulating an immune response, usually the production of antibodies.	

Antimicrobial agent	A general term for drugs, chemicals, or other substances that either kill or slow the growth of microbes. Different classes exist that are specific to the class of microbe, including: antibacterial drugs (antibiotics) that treat bacterial infections; antiviral agents that treat viral infections; antifungal agents that treat fungi; and antiparasitic agents that treat parasites.	Holmes, A.H., et al (2016). Understanding the mechanisms and drivers of antimicrobial resistance. Lancet, 387(10014).
Antimicrobial stewardship	Coordinated interventions designed to promote, improve, monitor, and evaluate the judicious use of antimicrobials so as to preserve their future effectiveness and to promote and protect human and animal health. Antimicrobial stewardship encompasses the 5Rs of AMU: responsibility, reduction, refinement, replacement, and review.	National Farmed Animal Health and Welfare Council, (NFAHWC) 2016. Antimicrobial Stewardship in Food Animals in Canada.
Antimicrobial resistance	The result of microbes changing in ways that reduce or eliminate the effectiveness of drugs, chemicals, or other agents to cure or prevent infections.	
Acquired resistance	When a particular microorganism obtains the ability to resist a particular antimicrobial agent to which it was previously susceptible.	Page, S.W., and Gautier, P. (2012). Use of antimicrobial agents in livestock. Rev. Sci. Tech. Off. Int. Epiz.31(1).
Antiseptic	A germicide that is used on skin or living tissue for the purpose of inhibiting or destroying microorganisms.	
Asepsis	Prevention from contamination with microorganisms. Includes sterile conditions on tissues, on materials, and in rooms, as obtained by excluding, removing, or killing organisms.	
Bloodborne pathogens	Disease-producing microorganisms spread by contact with blood or other body fluids from an infected person.	
Bloodstream infection	A condition in which bacteria enter the blood. This may occur through a wound or infection, or through a surgical procedure or injection.	
Broad-spectrum antibiòtic	Antibiotics that work against a wide range of Gram-positive and Gram-negative bacteria.	Page, S.W., and Gautier, P. (2012). Use of antimicrobial agents in livestock. Rev. Sci. Tech. Off. Int. Epiz.31(1)..

CA-MRSA	Community-associated (CA) methicillin-resistant Staphylococcus aureus (MRSA). Colonization or infection with this organism develops in people who have not recently been evaluated or treated at a healthcare facility therefore, it is defined as originating from the community.	
Caregivers	All persons who are not employees of an organization, are not paid, and provide or assist in providing healthcare to a patient (e.g., family member, friend) and acquire technical training as needed based on the tasks that must be performed.	
Carrier	An individual who is found to be colonized at one or more body sites with an organism, but has no signs or symptoms of active infection.	
Clostridium difficile	An anaerobic, gram-positive, spore-forming bacillus that can cause diarrhea and other intestinal diseases when competing bacteria in the gut are diminished by antibiotics.	
Colonization	The presence of microorganisms on or within body sites without symptoms, detectable host immune response, cellular damage, or clinical expression. Colonized individuals may become a source of transmission.	
Community-associated infections (CA)	Infections that are contracted outside of a healthcare facility and are present or incubating at the time of admission or develop within a designated period of time after admission, unlike healthcare-associated infections (HAIs). Formerly known as community-acquired infections.	World Health Organization (2014). Antimicrobial Resistance: Global Report on Surveillance.
Contamination	The presence of an infectious agent on a body surface or on clothes, gowns, gloves, bedding, furniture, computer keyboards, or other inanimate objects that may be capable of producing disease or infection.	

Critically important antimicrobials	A classification system described by the World Health Organization (WHO) and the World Organization for Animal Health (OIE) for medical and veterinary antimicrobials, respectively, that defines the two criteria used to classify antimicrobials by their level of importance. For veterinary antimicrobials, Criteria 1 is that the importance of the antimicrobial class is widely recognized, and; Criteria 2 is that the antimicrobial agents in this class are widely identified as essential for the treatment of serious animal disease and few alternatives are available. For human medical antimicrobials, Criteria 1 is that the antimicrobial agent is used as the sole therapy or one of few alternatives to treat serious human disease, and; Criteria 2 is that the antimicrobial agent is used to treat diseases caused by either a) organisms that may be transmitted via non-human sources or b) diseases caused by organisms that may acquire resistance genes from non-human sources. Both veterinary and human medical antimicrobial agents are thus classified based on whether they meet their respective criteria, i.e. they are classified as: 'critically important' if they meet criteria 1 and 2, 'highly important' if they meet criteria 1 or 2, and 'important' if they meet neither criteria 1 nor 2.	World Health Organization (2011). Critically Important Antimicrobials for Human Medicine, 3rd revision. Page, S.W., and Gautier, P. (2012). Use of antimicrobial agents in livestock. Rev. Sci. Tech. Off. Int. Epiz.31(1).
Decolonization therapy	Topical and/or systemic antibiotic treatment used with the intention of eliminating carriage (colonization) of a microorganism.	
Decontamination	A process or treatment that renders a medical device, instrument, or environmental surface safe to handle because it is no longer capable of transmitting particles of infectious material.	
Defined Daily Dose (DDD)	Assumed average maintenance dose per day for a drug used for its main indication in its target species.	World Health Organization (2003). Introduction to Drug Utilization Research.
Disinfection	The destruction of pathogenic and other kinds of microorganisms by physical or chemical means. Disinfection is less lethal than sterilization, because it destroys most recognized pathogenic microorganisms, but not necessarily all microbial forms, such as bacterial spores.	

Drivers of antimicrobial resistance (AMR)	Increased and continued transmission of antimicrobial resistance mechanisms to other microbes by standards of infection control, sanitation, access to clean water, access to assured quality antimicrobials and diagnostics, travel, and migration. Although emergence of antimicrobial resistance in microorganisms is a natural phenomenon, antimicrobial resistance selection can be expedited by antimicrobial exposure in healthcare, agriculture, and the environment.	Holmes, A.H., et al (2016). Understanding the mechanisms and drivers of antimicrobial resistance. Lancet, 387(10014).
Efflux pump	A resistance mechanism that allows bacteria to pump out any antibiotics that penetrate them.	Holmes, A.H., et al (2016). Understanding the mechanisms and drivers of antimicrobial resistance. Lancet, 387(10014).
Endotoxin	A toxin produced by certain bacteria. For example, Clostridium difficile toxin can cause diarrhea.	
Epidemiologically important pathogens	Infectious agents that have one or more of the following characteristics: 1) are readily transmissible; 2) have a proclivity toward causing outbreaks; 3) may be associated with a severe outcome; or 4) are difficult to treat. Examples include Acinetobacter, MRSA, and C. difficile.	
Epidemiology	The study of the distribution and determinants of disease in human populations. Epidemiologists are often sent to investigate outbreaks.	
Extended-spectrum β-lactamase (ESBL)	β-lactamases are bacterial enzymes that inactivate some antibiotics, such as penicillin. ESBLs are bacteria that have acquired these enzymes and become resistant to those drugs.	Holmes, A.H., et al (2016). Understanding the mechanisms and drivers of antimicrobial resistance. Lancet, 387(10014).
Gram stain	A laboratory staining technique used to distinguish between two groups of bacteria, Gram-positive and Gram-negative that differ in their cell wall structure	Holmes, A.H., et al (2016). Understanding the mechanisms and drivers of antimicrobial resistance. Lancet, 387(10014).

Healthcare-associated/Hospital-acquired infection (HAI)	Healthcare-associated infection (HAI): An infection that develops in a patient who is cared for in any setting where healthcare is delivered and is related to receiving health care. Formerly known as nosocomial infection.	
Healthcare-associated methicillin-resistant Staphylococcus aureus (HA-MRSA)	MRSA colonization or infection that develops in people who have had recent contact with a healthcare facility or have been in a healthcare facility for greater than 48 hours.	
Husbandry	The art, science, and tradition that encompass responsible livestock production, which includes providing appropriate facilities that provide for animal comfort, adequate space, proper flooring, ventilation, heating, and access to clean water.	National Farmed Animal Health and Welfare Council, (NFAHWC)2016. Antimicrobial Stewardship in Food Animals in Canada. Page, S.W., and Gautier, P. (2012). Use of antimicrobial agents in livestock. Rev. Sci. Tech. Off. Int. Epiz.31(1).
Immunity	Protection against a disease. Immunity is indicated by the presence of antibodies in the blood and can usually be determined with a laboratory test	
Immunization	The process or procedure by which a subject is rendered immune, or resistant to a specific disease. This term is often used interchangeably with vaccination or inoculation, although the act of inoculation/vaccination does not always result in immunity.	
Inappropriate antimicrobial use	When antimicrobials are used unnecessarily or for non-therapeutic reasons, such as over prescribing or as feed additives in agriculture.	Holmes, A.H., et al (2016). Understanding the mechanisms and drivers of antimicrobial resistance. Lancet, 387(10014). Page, S.W., and Gautier, P. (2012). Use of antimicrobial agents in livestock. Rev. Sci. Tech. Off. Int. Epiz.31(1)..

Incidence	The number of new cases of infection or disease or colonization identified in a specific population in a given time period.	
Incidence rate	The number of new cases of disease during a specific time period divided by the population at risk.	
Infection	The invasion of the body by pathogenic microorganisms and their multiplication which can lead to tissue damage and disease.	
Infection rate	Number of infections reported in a specified period of time divided by the population at risk for the infection during the same specified period of time.	
Innovation	Creating new solutions to counteract loss in antimicrobial effectiveness through research and development. For example, developing new and/or improved rapid diagnostic tests or alternatives to antimicrobials, such as probiotics or vaccinations.	Dar, O.A, et al (2016). Exploring the evidence base for national and regional policy interventions to combat resistance. Lancet, 387
Intensive care unit (ICU)	Hospital unit that provides intensive observation and treatment of patients either dealing with or at risk of developing life-threatening problems. Also known as a critical care unit.	
Invasive procedure	A medical procedure that involves entering the body, usually by cutting or puncturing the skin or by inserting instruments into the body.	

Maximum Kill Rate (MKR)	Maximum rate at which organisms are killed. The MKR is usually obtained from in vitrotime–kill experiments and the estimated value is thereforedependent on a number of experimental (technical)factors. These include: (i) The time over which themaximum kill rate is measured. The time pointsincluded in the regression analysis to determine theMKR should include at least two points above thedetection limit. (ii) For some antimicrobials, there is alag-time before the kill rate is maximal; in those cases,a maximum kill rate should not be determined fromtime = 0 h or at least be interpreted with caution. (iii) For drugs with a concentration-dependent effect over awide concentration range, special care should be takenfor carry-over drug effects at high concentrations (e.g.killing by quinolones may be so fast when carrying outtime–kill experiments for some microorganisms thatsignificant kill is observed during sampling and plating).(iv) The maximum kill rate may be very high fora very short period of time and much slower whenmeasured over a longer period (two-phase kill). If theMKR is reported, this should be taken into consideration.(v) Although some bacteria may be killed duringa certain period of time, growth may still occur.	Mouton et al., 2005 - Standardization of pharmacokinetic_pharmacodynamic terminology for anti-infective drugs: an update.
mcr genes	There are colistin resistance genes that are on plasmids and, thus, mobile meaning they can be readily transferred between bacteria. They confer resistance to colistin, which is a polymyxin. To date, two genes have been identified; mcr-1 and mcr-2.	(WHO). World Health Organization (2016). Critically Important Antimicrobials for Human Medicine.
Mechanisms of antimicrobial resistance	The way that a microbe becomes resistant to an antimicrobial drug, e.g. acquisition of resistance genes. Three fundamental mechanisms of antimicrobial resistance are (1) enzymatic degradation of antibacterial drugs, (2) alteration of bacterial proteins that are antimicrobial targets, and (3) changes in membrane permeability to antibiotics. However, there are many mechanisms and the science is continually updated.	Holmes, A.H., et al (2016). Understanding the mechanisms and drivers of antimicrobial resistance. Lancet, 387(10014). Page, S.W., and Gautier, P. (2012). Use of antimicrobial agents in livestock. Rev. Sci. Tech. Off. Int. Epiz.31(1). Dever, L.A., Dermody, T.S. (1991). Mechanisms of bacterial resistance to antibiotics. Arch Intern Med. 151(5).

Metaphylaxis	Mass treatment of populations currently experiencing any level of disease before the onset of clinical illness. Pattern characteristics: short duration of use, group administration through injection, feed, or water. Veterinary example: control of bovine respiratory disease (BRD) in feedlot cattle through injection of animals with antimicrobials on arrival at the feedlot. Human medical example: risk management for those potentially exposed to a specific pathogen, e.g. Streptococcus pneumonia or highly pathogenic H5N1 avian influenza virus	Page, S.W., and Gautier, P. (2012). Use of antimicrobial agents in livestock. Rev. Sci. Tech. Off. Int. Epiz.31(1).
Methicillin- resistant Staphylococcus aureus (MRSA)	A type of Staphylococcus aureus bacterium resistant to methicillin and other beta-lactam antibiotics. No longer confined to hospitals, MRSA has caused infectious outbreaks in community groups. Not all Staphylococcus aureus strains are resistant to these drugs. Sensitive strains are called MSSA.	Gleband et al. (2015). State of the World's Antibiotics. Center for Disease Dynamics, Economics and Policy. CDDEP: Washington, D.C.
Minimum inhibitory concentration (MIC)	Lowest concentration of an antimicrobial that will inhibit the visible growth of a microorganism following overnight incubation, usually reported as mg/L.	Mouton et al., 2005 - Standardization of pharmacokinetic_pharmacodynamic terminology for anti-infective drugs: an update
Multi-drug resistant organism (MDRO)	A microbe that is resistant to the effect of more than one antimicrobial drug, i.e. multiple distinct drugs do not kill the microbe.	Holmes, A.H., et al (2016). Understanding the mechanisms and drivers of antimicrobial resistance. Lancet, 387(10014).
Multiple-drug resistance	A phenomenon when one or more micro-organism is resistant to the effects of more than one antimicrobial drug (i.e. the drug no longer works to kill the microbe).	Holmes, A.H., et al (2016). Understanding the mechanisms and drivers of antimicrobial resistance. Lancet, 387(10014).
Natural resistance	Innate ability of a bacterial species to resist activity of a particular antimicrobial agent through its inherent structural or functional characteristics, which allow tolerance of a particular antimicrobial drug or class.	Holmes, A.H., et al (2016). Understanding the mechanisms and drivers of antimicrobial resistance. Lancet, 387(10014).
Nosocomial infection	An infection acquired in the hospital, excluding infections incubating at time of admission.	(WHO). World Health Organization (2011). Burden of endemic health care-associated infections worldwide.

Optimal duration treatment	The ideal length of time for treatment with antimicrobials to prevent disease relapse and antimicrobial resistance, and also to ensure patient safety and cost-effectiveness.	Holmes, A.H., et al (2016). Understanding the mechanisms and drivers of antimicrobial resistance. Lancet, 387(10014).
Outbreak	An increase in the incidence of disease in a facility above the baseline level or a cluster of new cases that are epidemiologically linked.	
Point-of-care (POC)	Point-of-care testing (POCT) refers to any diagnostic test administered outside the central laboratory at or near the location of the patient. POCT in family practice is a test to support clinical decision making, which is performed by a qualified member of the practice staff nearby the patient and on any part of the patient's body or its derivatives, during or very close to the time of consultation, to help the patient and physician to decide upon the best suited approach, and of which the results should be known at the time of the clinical decision making	Larsson et al., 2015 - The state of point-of-care testing; Schols et al., 2018 - International definition of a point-of-care test in family practice
Prevalence	The total number of disease cases (new and existing) within a population at a given time.	
Priority microbes	Micro-organisms considered most important in the spread of antimicrobial resistance, including those important for clinical disease impact, spectrum of resistance, appearing in novel environments or geographical regions, and/or economic consequences. See also 'clinically important pathogens'.	Page, S.W., and Gautier, P. (2012). Use of antimicrobial agents in livestock. Rev. Sci. Tech. Off. Int. Epiz.31(1).
Prophylaxis	Preventive medicine by administration of an antimicrobial to exposed healthy humans/animals considered to be at risk for developing a disease, but prior to the onset of the disease symptoms and for which no etiologic agent has yet been confirmed by culture or other detection methods. Pattern characteristics: intermediate duration of use, group administration of the antimicrobial through injection, feed, or water. Veterinary example: medicated milk replacer fed to calves to prevent diarrhea; human medical example: antimicrobials given through injection or by oral administration before surgical procedures (pre-operative prophylaxis).	Page, S.W., and Gautier, P. (2012). Use of antimicrobial agents in livestock. Rev. Sci. Tech. Off. Int. Epiz.31(1).

Rapid diagnostic tools	A quick and easy-to-perform test for a specific microbe that formerly only laboratory tests could measure; they are intended to provide point of care and same day results to reduce unnecessary antimicrobial use.	Holmes, A.H., et al (2016). Understanding the mechanisms and drivers of antimicrobial resistance. Lancet, 387(10014).
Rate	An expression of the risk of an event, such as infection or death, in relation to a unit of population during a specified time period.	
Resistance prevalence	The number of cases of a disease caused by antimicrobial resistance that are present in a particular population at a given time.	Holmes, A.H., et al (2016). Understanding the mechanisms and drivers of antimicrobial resistance. Lancet, 387(10014).
Resistant (microbe)	A microbe that is unaffected by an antimicrobial, i.e. that is able to withstand treatment with antimicrobials.	Holmes, A.H., et al (2016). Understanding the mechanisms and drivers of antimicrobial resistance. Lancet, 387(10014).
Ribosomal protection	A resistance mechanism that allows bacteria to interfere with an antibiotic's ability to prevent the bacteria to make proteins necessary for their survival.	Holmes, A.H., et al (2016). Understanding the mechanisms and drivers of antimicrobial resistance. Lancet, 387(10014).
Societal drugs	Drugs whose use and misuse have societal consequences well beyond the individual who is taking them. (E.g. Antimicrobials are considered societal drugs because once they become ineffective, they are ineffective for everyone, not just the person taking them.	Levy, S.B. (1998). The challenge of antibiotic resistance. Scientific American, March. Levy, S.B. (2002). Factors impacting on the problem of antibiotic resistance. Journal of Antimicrobial Chemotherapy,49.
Spectrum of activity	The range of an antimicrobial's effectiveness, i.e. able to kill multiple types of microbes or specialized to target one type of organism. See 'broad-spectrum antibiotic'	Holmes, A.H., et al (2016). Understanding the mechanisms and drivers of antimicrobial resistance. Lancet, 387(10014).

Spore	The dormant stage some bacteria will enter when environmental conditions cause stress to the organism or no longer support its continued growth. C. difficile spores are highly resistant to cleaning and disinfection measures, and the spores also make it possible for the organism to survive passage through the stomach, resisting the killing effect of gastric acid.	
Static activity	An antibiotic's ability to disarm bacteria without killing the bacteria.	Holmes, A.H., et al (2016). Understanding the mechanisms and drivers of antimicrobial resistance. Lancet, 387(10014).
Stationary concentration	The concentration of antimicrobial at which growth equals kill, i.e. no net growth or kill. Measure in concentration (e.g. mg/L)	Mouton et al., 2005 - Standardization of pharmacokinetic_pharmacodynamic terminology for anti-infective drugs: an update
Sterilization	The use of a physical or chemical procedure to destroy all microorganisms.	
Stewardship	Conserving the effectiveness of existing treatments through infection prevention and control guidelines, education and awareness, regulations, and oversight. The multi-faceted and dynamic approaches required to sustain the clinical efficacy of antimicrobials by optimizing drug use, choice, dosing, duration, and route of administration while minimizing the emergence of resistance and other adverse effects.	National Farmed Animal Health and Welfare Council, (NFAHWC) 2016. Antimicrobial Stewardship in Food Animals in Canada.
Sub-MIC effect	Any effect of an antimicrobial on a microorganism at concentrations below the MIC. The effect can be described both morphologically as well as time to growth, growth rate or another parameter.	Mouton et al., 2005 - Standardization of pharmacokinetic_pharmacodynamic terminology for anti-infective drugs: an update

Sub-therapeutic	Involving or relating to drug dosages administered at too low a level to produce a therapeutic effect, i.e. below the level necessary to treat disease, but the presence of the antimicrobial even at low levels can promote resistance in the microbe population being treated; antimicrobials administered at a level not powerful enough to have a therapeutic effect.	Holmes, A.H., et al (2016). Understanding the mechanisms and drivers of antimicrobial resistance. Lancet, 387(10014). Page, S.W., and Gautier, P. (2012). Use of antimicrobial agents in livestock. Rev. Sci. Tech. Off. Int. Epiz.31(1).
Superbugs	Bacteria with resistance to several commonly used antibiotics.	World Health Organization (2014). What is antimicrobial resistance Q & A.
Surveillance	The ongoing, systematic collection, analysis, interpretation, and dissemination of data regarding a health-related event for use in public health action to reduce morbidity and mortality and to improve health. Detecting and monitoring trends and threats in order to inform strategies to reduce the risks and impacts of antimicrobial resistance (AMR).	National Farmed Animal Health and Welfare Council, (NFAHWC) 2016. Antimicrobial Stewardship in Food Animals in Canada.
Susceptible (microbes)	Microbes that are vulnerable to the therapeutic effect of antimicrobials, i.e. they are destroyed by antimicrobials.	Holmes, A.H., et al (2016). Understanding the mechanisms and drivers of antimicrobial resistance. Lancet, 387(10014).
Unmetabolized antibiòtics	Antibiotics that are excreted in an active form from animals/humans that enter the environment, including water and sewage systems.	Marshall, B.M. and Levy, S.B. (2011). Food animals and antimicrobials: impacts on human health. Clinical Microbiology Reviews, 24. O'Neill, J. (2016). Tackling Drug-Resistant Infections Globally: Final Report and Recommendations. Review on antimicrobial resistance to the Government of the United Kingdom. HM Government, London.

7.2 ANTI-SUPERBUGS NEEDs ASSESSMENT QUESTIONNAIRE

TASKs 2.1. and 2.2. NEEDs ASSESSMENT tool

Author: S. BEDIN

Dissemination level: Restricted to the partners for the AntiSuperbugs purpose **(internal document)**

This tool has been designed and developed by Sara Bedin, then transposed in .xls format and adapted to conduct the WP2 of AntiSuperBugs project.
It may not be used for other purposes, nor reproduced, transmitted in any form or by any means, in whole or in part, without the express written consent of the author.

This tool, incorporating the methodologies WIBGI (wouldn't it be great if...?, LT-TLC (long-term and total life-cycle performance description) and FAST (Functional to be used along the needs assessment, selection & description, provide a systemic approach to the need assessment phase, finalized to elicit innovation challenges.

Instructions:

Who have to fill in the questionnaire?
Who are best-placed to see the problems of, or the inefficiencies with, the particular area of service addressed by AntiSuperBugs and work within the system delivering it on daily basis.

How has to be described the need?
You are asked to define your real and genuine need for innovation in terms of functional and performance requirements, without identifying a specific solution. You have to define the problem and the need. The market will propose divergent and alternative solutions, though equivalent from the point of view of performance. The opportunity to do not pre-define the technical solution and to open to alternative technical ways to address the needs expressed in functional and performance based requirements, doesn't mean to define the need in general and short terms. This is a crucial point, as the only way in which solutions will meet their performance targets and expected behaviours is for them to be specified upfront, clearly and unambiguously.

Name of respondent/s:.....		Name of institution:.....	Date: .. Version:	
1	**What are the specific processes and areas of service affected by a cost-quality problem?**		Areas of services / processes	ption (of the problem)
			1.	
			1.1	
			2	
			2.1	
2	**How exactly work the relevant services today / the services are delivered?**		*Please provide a very schematic and not discorsive description and focus attention on your "business" (service delivered, operative process)*	
			1	
			2	
			3	
			4	

3	AS-IS: How could be represented the actual service delivery and what roles are involved? Please define a flow-chart as attachment, pointing out relationships between major (internal and external user) interface elements		*Please focus attention on SERVICES and OPERATIONAL KEY PROCESSES and not on the enabling technical solution and Please elaborate an attachment*			
4	What are the (specific) bottlenecks or inefficiency to be solved or areas of improvement?		1 2 3 4			
5	TO-BE. How could be represented the desired service delivery and what new potential roles and interfaces could be implemented?		*Please focus attention on SERVICES and OPERATIONAL KEY PROCESSES and not on the enabling technical solution and Please elaborate an attachment*			
6	Could you describe the desired solution in functional and performance terms?		**functionalities** *The basic element of a system is the Function executed. The function describes the original intent or purpose that a solution expected to be performed. The description of a Function is restricted to a two words format: Active Verb + Measurable Name. The Verb is used to answer to the question: What does it do? While the Name is used to answer to the question: What does the Verb apply to?*		**performances** *The performance is the measurable KPI or target to be achieved implementing a specific function*	
		installation and replacement	1 2 3 4 5 6	installation and replacement	1 2 3 4 5 6	
		use and management	1 2 3 4 5	use and management	1 2 3 4 5	
		maintenance	1 2 3 4	maintenance	1 2 3 4	
		disposal	1 2 3	disposal	1 2 3	
7	(With particular reference to functionalities and performances) What are the main apparent technical contradictions to face?		**contradictions and trade off**			

7.3 ANTI-SUPERBUGS REQUIREMENTS/FUNCTIONALITIES QUESTIONNAIRE

ANTISUPERBUGS PCP
Grant Agreement: 688878
Questionnaire related to 'D2.1 - Needs elicitation' and 'D2.2 - Business case'

ANTI-SUPERBUGS PCP: REQUIREMENTS VALIDATION QUESTIONNAIRE

Dear partners,

This questionnaire is intended to collect your input regarding the prioritization of the **needs** identified during the exercises performed for the completion of D2.1 and the discussions for the Open Market Consultation Events.
Requirements listed or mentioned are based in the input provided by the ANTI-SUPERBUGS partners for D2.1 and/or D2.2 through meetings, questionnaires and emails. If any, references to literature are included as comments in the relevant cell(s).
We would appreacite whether you can circulate this questionaire to the relevant actors within your institution that could provide further input to the needs assessment.
Thank you in advance for your collaboration!

INSTRUCTIONS TO COMPLETE THE FORM:

- *Complete only the cells highlighted in blue color:* *(ex.)*
- *For those sections that require the prioritization of items listed, please complete the cells by choosing between '1' (i.e. 'Yes') or '0' (i.e. 'No') according to the priority you consider to be assigned to each item within the scope of ANTI-SUPERBUGS Project.*
  Please keep in mind that, every time you select the category 'MUST HAVE' you should be able to assess that the delivered solutions(s) complies with the described functionalities in case a pilot is carried out in your facility.
  In case you are not able to test in your facility a desired functionality, but you consider this functionality as a 'MUST HAVE' please select the category 'NICE TO HAVE' adding a comment 'impossible to validate through a pilot'.
- *For open questions, please include all the information you consider relevant for each section.*
- *Specific indications are also included in each of the sections.*
- *For any doubts or comments, please contact esther.arevalo@gencat.cat*
- ***Once the questionnaire is completed, please send it to** antisuperbugs.aquas@gencat.cat*

ANTISUPERBUGS PCP
Grant Agreement: 688878
Questionnaire related to 'D2.1 - Needs elicitation' and 'D2.2 - Business case'

H2020 call: ICT-36-2015 - H2020-EU.2.1.1.-Industrial Leadership —Leadership in enabling and industrial technologies —Information and Communication Technologies (ICT)

ANTI-SUPERBUGS PCP: REQUIREMENTS VALIDATION QUESTIONNAIRE

Name (optional):	*PLEASE COMPLETE (OPTIONAL)*
Institution:	*PLEASE COMPLETE*
Position:	*PLEASE COMPLETE*
Date:	*PLEASE COMPLETE*

TARGETED 'SUPERBUGS'

Please complete the cells by choosing between '1' (i.e. 'Yes') or '0' (i.e. 'No') according to the priority you consider to be assigned to each item.

Please notice that some of the listed items might be duplicated, depending on the description approach provided (e.g. group of bacteria vs. Individual microorganims); we represent here all the inputs received so far by the procurers. We might need to re-define and clarify the descriptions later for the deliverable creation.

	'MUST HAVE'	'NICE TO HAVE'	NOT RELEVANT	
ASB' ICT solution shall be able to detect:				
Klebsiella spp. with carbapenem resistance				
Escherichia coli with combined resistance to 3rd generation cephalosporins, fluoroquinolones and aminoglycosides				
S. aureus with methicillin resistance (MRSA)				
Clostridium difficile				
Carbapenem-resistant producing gram-negative bacilli +/- extended-spectrum beta-lactamases (ESBLs) production				
ESBL producing G- bacteria, such as *Klebsiella pneumonia* and *Escherichia coli*				
ESBL producing G+ bacteria, such as *Clostridium difficile* or MRSA				
MultiDrug-Resistant gram negative rods (MDR GNR), such as *Enterobacter spp. , Pseudomonas aeruginosa*				
Vancomycin-Resistant Enterococci (VRE)				
Acinetobacter baumanii				
Neisseria gonorrhoaea				
MRSA bacteraemia				
MSSA bacteraemia				MSSA: meticillin-sensitive *S. aureus*
E.coli bacteraemia (extending to wider selection of Gram - in near future)				
VRE bacteraemia (local not national)				
CPE				CPE: carbapenemase-producing Enterobacteriaceae
If not included in the list, please add any other "superbug" that you migth consider relevant for your institution/region.				
TOTAL	0	0	0	

CLINICAL USE REQUIREMENTS OF ANTI-SUPERBUGS ICT SOLUTIONS

Please complete the cells by choosing between '1' (i.e. 'Yes') or '0' (i.e. 'No') according to the priority you consider to be assigned to each item.

	'MUST HAVE'	'NICE TO HAVE'	NOT RELEVANT	
The 'ASB' ICT solutions shall be designed as:				
- Stand-alone medical device (HW & SW)				
- Environmental/surface sensor (remote detection of colonization/infection) triggering alerts to be confirmed by a point-of-care test/microbiology lab (HW & SW)				
***In situ* alert system that rapidly detects:**				
- Carbapenem-resistant producing gram-negative bacilli +/- extended-spectrum beta-lactamases (ESBLs) production				
- Either *E. coli* or *Clostridium difficile* or both				
Any positive detection by the 'ASB' ICT solutions shall be confirmed later by the microbiology service				
The 'ASB' ICT solutions shall be:				
- Acceptable to patients				
- Non-invasive				
- Minimally intrusive technology				
The 'ASB' ICT solutions shall provide:				
- Flexibility to integrate detection capabilities for additional MRDOs or future proofing				
- Flexibility to integrate detection capabilities for additional clinically relevant HAIs microorganism and vectors				
- Continuous or high frequency detection				
- 99,9% of sensitivity (also in adverse environments) and specificity of micro-organism identification *(read text in rows 65 and 76 and comments)*.				sensitivity must be higher enough to avoid workload increase due to false negatives and still demonstrate cost-effectiveness of the ASB ICT solution
- Sensitivity at least of PCR test (low false negatives)				Any new better definition of sensitivity and specificity that we could apply to ASB ICT solutions?
- Continuous or high frequency surveillance system for contamination by MRDOs (including colonized individuals) and potentially other healthcare associated pathogens on high contact surfaces				

- Ability to sense all the places at more risk of either to be colonized or to be HAIs vectors (e.g.: flush handles, commodes, sinks, bed rails, remote controls, bed linen, curtains, door handles, keyboards, tablets)			
- Deployment/installation into existing healthcare environments			
- The possibility to be used in crowded areas			
- Availability of remote alert system			
- Availability of alert system to be triggered where the contamination is detected			
- Inform in real time the hospital information system of the risks of infection			
- Integration with electronic patient health record and the hospital information system (linking the infection with the place of detection) using interoperability standards (HL7, etc.)			
- Destruction of specific superbugs			
Sensing components of the ASB ICT solution shall include:			
- sensors with proven accuracy levels comparable to medical grade devices with similar functions *(see comments below)*			
- the possibility to operate without line power supply (e.g. battery operated)			
- compact dimensions to be fitted on desktops with portable design.			
SW components of the ASB solution:			
- secure authentication of users in accordance with the existing methods of the procurers			
- reading information about patient's infective events (current, historic) from the existing system infrastructure of the procureres			
- monitoring prioritized according to the patients infescyion histories and environemnt infection history			
- multiple user interface according to their professional profile (microbiologist, infectivologist, nurse, etc). Different users should have access to specific content.			
- notifications and alerting according to a prioritization scheme that could be updated according to local epidemiological data			
- report using collected data and visual (graph, tables). Reports should be available in different format (eg. Pdf, HTML) and print friendly			
- the possibility to share epidemiological data with national survelliance centers of the procurers			
- the possibility to perform meaningful queries with the data (e.g. infected patients for a specific superbug in a certain area)			
- real time indication on the remaining time to superbug identification			

- clear differentiation in reporting data related to environment or to patients			
- an on-line how-to manual with both a quick guide to appropriate sampling and instruction for use			
- the possibility for integrating existing tools to enable communication between users when their status indicates availability (e.g. chat, voice message, video conferencing)			
- regisration of the geographical location and time of bug detection for epidemiological purpose			
- wireless connectivity			
- the possibility for integrating data about genetic bug profile for epidemiologic cluster analysis and disease mapping			
If not included in the list, please add any other requirement that you migth consider relevant for your institution/region.			
TOTAL	0	0	0

Comments on Clinical Use Requirements

Please use this section to include any other information that you might consider relevant regarding CLINICAL USE REQUIEREMENTS for the ASB solution

Comments on sensitivity, specificity and accuracy:

Accuracy is related to sensitivity and specificity mentioned above. Should we define ASB ICT accuracy instead of sensitivity and specificity? Please comment

Comments on the sensitivity, specificity and accuracy 'ASB' solutions should comply with and the relevant definition:

OTHER LIFE CYCLE REQUIREMENTS OF ANTI-SUPERBUGS ICT SOLUTIONS

Please complete the cells by choosing between '1' (i.e. 'Yes') or '0' (i.e. 'No') according to the priority you consider to be assigned to each item.

	'MUST HAVE'	'NICE TO HAVE'	NOT RELEVANT
INSTALLATION AND REPLACEMENT: 'ASB' ICT solutions shall:			
- Allow to be integrated in the regular health care and support staff routines			
- Be easy to integrate into different hospital facilities and architectures			
- Allow to be integrated into existing supply management channels			
INSTALLATION AND REPLACEMENT: 'ASB' ICT solutions shall be installed/available in:			
- In patient room(s)			
- In Intensive care units (ICU)			
- In Emergency rooms (ER)			
- In common/public areas or the healthcare facility			
- Operating theaters			
- Microbiology labs			
- Attached to other medical devices (e.g. mechanical ventilators)			
- *Other (please specify)*			
USE AND MANAGEMENT: The 'ASB' ICT solutions shall be:			
- Comfortable for users (inpatients and health & support staff) (HW & SW)			
- Easy and risk-free to use, minimally demanding human interaction for early detection			
- Continuously working system (24 hours) with high frequency sensing and providing highly interoperable data			
USE AND MANAGEMENT: The 'ASB' ICT solutions shall have:			
- A self-diagnostic function			
- Highly usable user interfaces			
MAINTENANCE, SCALABILITY AND RENEWAL: The 'ASB' ICT solutions shall be:			
- Easy to maintain; self-manageable by the responsible maintenance staff			

ANTI-SUPERBUGS PCP Project is co-funded by the EC.

- Easy to upgrade and renew			
- Easy to deploy throughout the system			
MAINTENANCE, SCALABILITY AND RENEWAL: The 'ASB' ICT solutions shall have:			
- Minimal or no recalibration required			
- Minimum or no consumables			
- Cheap consumables (if any)			
- A cleanable covering material (if any) of the sensing components			
DISPOSAL: The 'ASB' ICT solutions shall:			
- Not include nor generate any toxic material to be handled by the personnel			
- Use existing disposal routes			
- Be environmentally friendly, limited amount of single-use material			
If not included in the list, please add any other requirement that you migth consider relevant for your institution/region.			
TOTAL	0	0	0

Comments on Other Life-cycle Requirements

Please use this section to include any other information that you might consider relevant regarding OTHER LIFE CYCLE REQUIEREMENTS for the ASB solution

ECONOMIC REQUIREMENTS OF ANTI-SUPERBUGS ICT SOLUTIONS

Please complete the cells by choosing between '1' (i.e. 'Yes') or '0' (i.e. 'No') according to the priority you consider to be assigned to each item.

	YES	NO
Considering the added functionalities to be provided by the 'ASB' ICT solutions:		
- Would you consider acurate to compare its cost-effectiveness to your common practice for patient screening?		
- Would you consider acurate to compare its cost-effectiveness to a weekly patient screening by PCR or culture?		
- Would you consider acurate to compare its cost-effectiveness to your common practice for surface screening?		
- Would you consider acurate to compare its cost-effectiveness to existing surface screening practices (e.g.: ATPase testing)?		
TOTAL	0	0

Comments on Economic Requirements

Please use this section to include any other information that you might consider relevant regarding ECONOMIC REQUIEREMENTS for the ASB solution

7.4 COMPILED INPUTS RECEIVED FROM ANTI-SUPERBUGS PROCURERS TO QUESTIONNAIRE ON FUNCTIONALITIES AND REQUIREMENTS

ANTISUPERBUGS PCP
Grant Agreement: 688878
Questionnaire related to 'D2.1 - Needs elicitation' and 'D2.2 - Business case'

H2020 call: ICT-36-2015 - H2020-EU.2.1.1.-Industrial Leadership —Leadership in enabling and industrial technologies —Information and Communication Technologies (ICT)

ANTI-SUPERBUGS PCP: REQUIREMENTS VALIDATION QUESTIONNAIRE

Name (optional):	
Institution:	*INFORMATION COMPILED FROM ANTI-SUPERBUGS PROCURERS*
Position:	
Date:	*Last update 15/03/2018*

TARGETED 'SUPERBUGS'

Please complete the cells by choosing between '1' (i.e. 'Yes') or '0' (i.e. 'No') according to the priority you consider to be assigned to each item.
Please notice that some of the listed items might be duplicated, depending on the description approach provided (e.g. group of bacteria vs. Individual microorganims); we represent here all the inputs received so far by the procurers. We might need to re-define and clarify the descriptions later for the deliverable creation.

	ICO (VINCat)				PAT	STH	UKA	Helios	MoH	FMT	'MUST HAVE'	'NICE TO HAVE'	NOT RELEVANT
ASB' ICT solution shall be able to detect:	Infect.	Microb.	'ICT' Tech.	**'AVERAGE'**									
Klebsiella spp. with carbapenem resistance	MUST	MUST	MUST	MUST	MUST		MUST	MUST	MUST	MUST	6	0	0
Escherichia coli with combined resistance to 3rd generation cephalosporins, fluoroquinolones and aminoglycosides	MUST	MUST	MUST	MUST	MUST		MUST	MUST	MUST	MUST	6	0	0
S. aureus with methicillin resistance (MRSA)	MUST	MUST	MUST	MUST	MUST		MUST	MUST	MUST	NICE	5	1	0
Clostridium difficile	MUST	MUST	MUST	MUST	MUST		NICE	NICE	MUST	NICE	3	3	0
Carbapenem-resistant producing gram-negative bacilli +/- extended-spectrum beta-lactamases (ESBLs) production *(see comments from VINCat below)*	MUST	MUST	MUST	MUST	MUST		MUST	MUST	MUST	MUST	6	0	0
ESBL producing Gram - bacteria (such as *Klebsiella pneumonia* and *Escherichia coli)*	MUST	MUST	MUST	MUST	MUST		NICE	MUST	MUST	MUST	5	1	0
ESBL producing Gram + bacteria (such as *Clostridium difficile* or MRSA)	MUST	MUST	MUST	MUST	NOT		NOT	NICE	NOT	NICE	1	2	3
MultiDrug-Resistant Gram - rods (MDR GNR), such as *Enterobacter spp. , Pseudomonas aeruginosa*	MUST	MUST	MUST	MUST	MUST		MUST	MUST	MUST	NICE	5	1	0
Vancomycin-Resistant Enterococci (VRE)		MUST		MUST	NICE		NICE	NICE	MUST	NICE	2	4	0
Acinetobacter baumanii		MUST		MUST	MUST		NICE	NICE	MUST	NOT	3	2	1
Acinetobacter baumanii - resistant *(grey cells indicates partner providing the item)*		MUST		MUST				MUST			2	0	0
Neisseria gonorrhoaea		MUST		MUST	NICE		NOT	NOT	NICE	NOT	1	2	3
MRSA bacteraemia (meticillin-resistant *S. aureus*)	MUST	MUST	MUST	MUST	NICE		NICE	NICE	MUST	NICE	2	4	0
MSSA bacteraemia (meticillin-sensitive *S. aureus)*	MUST	MUST	MUST	MUST	NICE		MUST	NICE	MUST	NOT	3	2	1
E.coli bacteraemia (extending to wider selection of Gram - in near future)	MUST	MUST		MUST	NOT		NICE	NICE	MUST	NICE	2	3	1
VRE bacteraemia (local not national)		MUST		MUST	NOT		NICE	NICE	MUST	NOT	2	2	2
Carbapenemase-producing Enterobacteriaceae (CPE)		MUST		MUST	MUST		NICE	NICE	MUST	MUST	4	2	0
Added items (grey cells indicates partner providing the item)													
Single global resistance mechanism/indicator		MUST		MUST						MUST	2	0	0
Stenotrophomonas maltophilia									MUST		1	0	0
TOTAL									**61**	**29**	**11**		

*Comments from **VINCAt (Head of microbiology lab)** : Carbapenem-resistant producing gram-negative bacilli +/- extended-spectrum beta-lactamases (ESBLs) production is maximum priority*

CLINICAL USE REQUIREMENTS OF ANTI-SUPERBUGS ICT SOLUTIONS

Please complete the cells by choosing between '1' (i.e. 'Yes') or '0' (i.e. 'No') according to the priority you consider to be assigned to each item.

	ICO (VINCat)				PAT	STH	UKA	Helios	MoH	FMT	'MUST HAVE'	'NICE TO HAVE'	NOT RELEVANT
The 'ASB' ICT solutions shall be designed as:	Infect.	Microb.	'ICT' Tech.	'AVERAGE'		KJW							
- Stand-alone medical device (HW & SW)	MUST	MUST	MUST	MUST	MUST	NICE	NICE	MUST	MUST	MUST	5	2	0
- Environmental/surface sensor (remote detection of colonization/infection) triggering alerts to be confirmed by a point-of-care test/microbiology lab (HW & SW)	MUST	MUST	MUST	MUST	MUST	MUST	NOT	NICE	NICE	MUST	4	2	1
***In situ* alert system that rapidly detects:**													
- Carbapenem-resistant producing gram-negative bacilli +/- extended-spectrum beta-lactamases (ESBLs) production	MUST	MUST	MUST	MUST	MUST		NICE	MUST	MUST	MUST	5	1	0
- Either *E. coli* or *Clostridium difficile* or both	MUST	NICE	MUST	MUST	NICE		NOT	MUST	MUST	NICE	3	2	1
Any positive detection by the 'ASB' ICT solutions shall be confirmed later by the microbiology service	NOT	MUST		MUST	MUST/ NICE?	MUST	MUST	NICE	NOT	MUST	4	1	1
The 'ASB' ICT solutions shall be:													
- Acceptable to patients	MUST	MUST	MUST	MUST	NICE	MUST	NICE	MUST	MUST	MUST	5	2	0
- Non-invasive	MUST	MUST	MUST	MUST	NICE	NICE	NICE	NICE	NICE	MUST	2	5	0
- Minimally intrusive technology	MUST	MUST	MUST	MUST	MUST	MUST	NICE	NICE	NICE	MUST	4	3	0
The 'ASB' ICT solutions shall provide:													
- Flexibility to integrate detection capabilities for additional MRDOs or future proofing	MUST	MUST	MUST	MUST	NICE	MUST	NICE	MUST	MUST	MUST	5	2	0
- Flexibility to integrate detection capabilities for additional clinically relevant HAIs microorganism and vectors	MUST	MUST	MUST	MUST	NICE	MUST	NICE	MUST	MUST	NICE	4	3	0
- Continuous or high frequency detection		MUST	MUST	MUST	NICE	NICE	NICE	NICE	MUST	MUST	3	4	0
- 99,9% of sensitivity (also in adverse environments) and specificity of micro-organism identification *(read text in rows 65 and 76 and comments)* .	MUST	MUST	MUST	MUST	NICE	NICE	MUST	NICE	NICE	MUST	3	4	0
- Sensitivity at least of PCR test (low false negatives)	MUST	MUST	MUST	MUST	NICE	MUST	MUST	NICE	MUST	MUST	5	2	0
- Continuous or high frequency surveillance system for contamination by MRDOs (including colonized individuals) and potentially other healthcare associated pathogens on high contact surfaces	MUST	MUST	MUST	MUST	NICE	MUST	NICE	NICE	MUST	NICE	3	4	0
- Ability to sense all the places at more risk of either to be colonized or to be HAIs vectors (e.g.: flush handles, commodes, sinks, bed rails, remote controls, bed linen, curtains, door handles, keyboards, tablets)	MUST	MUST	MUST	MUST	MUST	MUST	NICE	NICE	NICE	NICE	3	4	0
- Deployment/installation into existing healthcare environments	MUST	MUST	MUST	MUST	MUST	MUST	MUST	MUST	MUST	MUST	7	0	0
- The possibility to be used in crowded areas	MUST	MUST	MUST	MUST	NOT	MUST	NOT	MUST	MUST	MUST	5	0	2
- Availability of remote alert system	MUST	MUST	MUST	MUST	MUST	NICE	NICE	MUST	MUST	MUST	5	2	0
- Availability of alert system to be triggered where the contamination is detected	MUST	MUST	MUST	MUST	MUST	MUST	NOT	MUST	MUST	MUST	6	0	1
- Inform in real time the hospital information system of the risks of infection	MUST	MUST	MUST	MUST	MUST	NICE	NICE	MUST	MUST	MUST	5	2	0
- Integration with electronic patient health record and the hospital information system (linking the infection with the place of detection) using interoperability standards (HL7, etc.)	MUST	MUST	MUST	MUST	MUST	NICE	NOT	MUST	MUST	MUST	5	1	1
- Destruction of specific superbugs	NOT	NOT	NOT	NOT	NOT	NICE	NICE	NICE	NOT	NICE	0	4	3
Sensing components of the ASB ICT solution shall include:													
- sensors with proven accuracy levels comparable to medical grade devices with similar functions					MUST	MUST	MUST	NICE	MUST	MUST	5	1	0
- the possibility to operate without line power supply (e.g. battery operated)					NOT	NICE	NICE	NICE	MUST	NICE	1	4	1
- compact dimensions to be fitted on desktops with portable design.					NOT	MUST	NICE	NICE	MUST	NICE	2	3	1

SW components of the ASB solution:														
- secure authentication of users in accordance with the existing methods of the procurers					MUST	NICE	NICE	MUST	MUST	MUST	4	2	0	
- reading information about patient's infective events (current, historic) from the existing system infrastructure of the procureres					MUST	NICE	NICE	NICE	ASB_FunctionalitiesVali NOT	NOT	1	3	2	
- monitoring prioritized according to the patients infescyion histories and environemnt infection history					MUST	NICE	NICE	NICE	NOT	NOT	1	3	2	
- multiple user interface according to their professional profile (microbiologist, infectivologist, nurse, etc). Different users should have access to specific content.					MUST	NICE	MUST	NICE	MUST	NOT	3	2	1	
- notifications and alerting according to a prioritization scheme that could be updated according to local epidemiological data					MUST	MUST	NICE	NICE	NICE	NICE	2	4	0	
- report using collected data and visual (graph, tables). Reports should be available in different format (eg. Pdf, HTML) and print friendly					NICE	NICE	NICE	NICE	NICE	NICE	0	6	0	
- the possibility to share epidemiological data with national surveliance centers of the procurers					NICE	NICE	NICE	NICE	NICE	NICE	0	6	0	
- the possibility to perform meaningful queries with the data (e.g. infected patients for a specific superbug in a certain area)	MUST				MUST	NICE	MUST	NICE	NICE	NICE	2	4	0	
- real time indication on the remaining time to superbug identification					NICE	NICE	NOT	NICE		NOT	0	3	2	
- clear differentiation in reporting data related to environment or to patients					MUST	NICE	MUST	MUST	MUST	NICE	4	2	0	
- an on-line how-to manual with both a quick guide to appropriate sampling and instruction for use					MUST	MUST	MUST	NICE	MUST	MUST	5	1	0	
- the possibility for integrating existing tools to enable communication between users when their status indicates availability (e.g. chat, voice message, video conferencing)					NICE	NICE	NOT	NICE	NICE	NOT	0	4	2	
- regisration of the geographical location and time of bug detection for epidemiological purpose					MUST	MUST	NICE	MUST	MUST	NICE	4	2	0	
- wireless connectivity					NICE	NICE	NICE	MUST	MUST	NICE	2	4	0	
- the possibility for integrating data about genetic bug profile for epidemiologic cluster analysis and disease mapping					MUST	NICE	NICE	NICE	MUST	NOT	2	3	1	
Added items (grey cells indicates partner providing the item)														
Following of all the guaranteened patients		MUST		MUST?						NICE	0	1	0	
No risk for patients associated with its use that can generate more costs than dealing with MR		MUST		MUST?						MUST	1	0	0	
Statistics regarding detection: number of detections/day/week/month/year, species detected, etc.	MUST			MUST?							0	0	0	
Detection and identification of molecular biology (epidemic strains)			MUST	MUST?							0	0	0	
TOTAL									**130**	**108**	**22**			

Comments on Clinical Use Requirements

Please use this section to include any other information that you might consider relevant regarding CLINICAL USE REQUIEREMENTS for the ASB solution

*Comments from **VINCat (Head of Microbiology Lab)**: Protoype should detect resistance and virulence factors (e.g. toxins in Cl. Difficile). Our maximum interest is in the carbepenems because determines the therapeutic action. WE must previously detect the genes related to resistance and define its importance and cross-check with gram-positive and gram-negative -- this can only be done away from the laboratory by a monotest detection. Rate of repetition of tests - how many tests can be done and in what time.*

*Comments from **PAT - HTA Node**: We should considers the opportunity to have not a one shot solution, but a bundle of technologies offering different approaches and outputs at different level of infection management (surveillance, enviromental safety, first patient screening, patient early diagnosys,...), Data should feed a computer based register enabling decision support systems*

*Comments from **Dr. Nejad (Helios)**:*
- stand alone device connectable with clinical software or other labratory/preventive information-systems
- E.coli must have, rest nice to have
- measurements must be controlable with means of internal quality controll like other POCT devices
- continuous detection is not necessarely needed
- interfaces to HIS systems especially: SAP, ISH/ISHMED, MEDICO etc.
- compatible with existing software used for epidemiological survailance
- possibility to perform meaningful queries with the data is not necessary if the data is exportable
- Relevant "Must have" use-cases have been already sent by th eteam to the Consortium leader and are integrated in actual publications of ASB
- also to be considered: is there any option to use the new system to faster detect by next-next-generation -sequencing-technologies!

Comments on Sensitivity, Specificity, Accuracy

Accuracy is related to sensitivity and specificity mentioned above. Sensitivity must higher enough to avoid workload increase due to false negatives and still demonstrate cost-effectiveness of the ASB ICT solution. Should we define ASB ICT accuracy instead of sensitivity and specificity? Any new better definition of sensitivity and specificity that we could apply to ASB ICT solutions?

Please use this section to include any comments on the sensitivity, specificity and accuracy 'ASB' solutions should comply with and the relevant definition:

Comments ***from PAT - HTA node:*** *Sensitivity and specificity should be trimmed according to the intention of use of the bundle technology, i.e.: screening need high sensitivity, early diagnosis should enhance specificity. A decision support system should improve diagnosys and surveillance capability.*

OTHER LIFE CYCLE REQUIREMENTS OF ANTI-SUPERBUGS ICT SOLUTIONS

Please complete the cells by choosing between '1' (i.e. 'Yes') or '0' (i.e. 'No') according to the priority you consider to be assigned to each item.

	ICO (VINCat)				PAT	STH	UKA	Helios	MoH	FMT	'MUST HAVE'	'NICE TO HAVE'	NOT RELEVANT
INSTALLATION AND REPLACEMENT: 'ASB' ICT solutions shall:	Infect.	Microb.	'ICT' Tech.	'AVERAGE'		KJW							
- Allow to be integrated in the regular health care and support staff routines	MUST	MUST	MUST	MUST	NICE	MUST	NICE	MUST	MUST	MUST	5	2	0
- Be easy to integrate into different hospital facilities and architectures	MUST	MUST	MUST	MUST	NICE	MUST	MUST	MUST	MUST	MUST	6	1	0
- Allow to be integrated into existing supply management channels	MUST	MUST	MUST	MUST	NICE	MUST	NICE	MUST	NICE	NICE	3	4	0
INSTALLATION AND REPLACEMENT: 'ASB' ICT solutions shall be installed/available in:													
- In patient room(s)	MUST	NICE	MUST	MUST	NICE	MUST	NICE	MUST	NICE	MUST	4	3	0
- In Intensive care units (ICU)	MUST	NICE	MUST	MUST	NICE	MUST	NICE	MUST	MUST	MUST	5	2	0
- In Emergency rooms (ER)	MUST	NICE	MUST	MUST	NICE	MUST	NICE	MUST	MUST	MUST	5	2	0
- In common/public areas or the healthcare facility	MUST	NICE	MUST	MUST	NICE	MUST	NOT	MUST	NOT	NICE	3	2	2
- Operating theaters	MUST	NICE	MUST	MUST	NOT	MUST	NOT	MUST	MUST	NICE	4	1	2
- Microbiology labs	NOT	MUST	NOT	NICE	NOT	MUST	NOT	MUST	NOT	NOT	2	1	4
- Attached to other medical devices (e.g. mechanical ventilators)	NOT	NICE	NOT	NOT	NOT	MUST	NOT	NICE	NICE	NICE	1	3	3
- Other *Added items (grey cells indicates partner providing the item)*													
No aplication in psychiatric wards											0	0	0
Diagnostic equipment and surfaces (e.g. MRI)										NICE	0	1	0
Hematology/Oncology clinics									MUST		1	0	0
USE AND MANAGEMENT: The 'ASB' ICT solutions shall be:													
- Comfortable for users (inpatients and health & support staff) (HW & SW)	MUST		MUST	MUST	MUST	MUST	MUST	MUST	MUST	MUST	7	0	0
- Easy and risk-free to use, minimally demanding human interaction for early detection	MUST		MUST	MUST	MUST	MUST	MUST	MUST	MUST	MUST	7	0	0
- Continuously working system (24 hours) with high frequency sensing and providing highly interoperable data	MUST		MUST	MUST	MUST	MUST	NICE	MUST	MUST	MUST	6	1	0
USE AND MANAGEMENT: The 'ASB' ICT solutions shall have:													
- A self-diagnostic function	MUST		MUST	MUST	NICE	MUST	NOT	MUST	MUST	MUST	5	1	1
- Highly usable user interfaces	MUST		MUST	MUST	MUST	MUST	NICE	MUST	MUST	MUST	6	1	0
MAINTENANCE, SCALABILITY AND RENEWAL: The 'ASB' ICT solutions shall be:													
- Easy to maintain; self-manageable by the responsible maintenance staff	MUST		MUST	MUST	NICE	MUST	NICE	MUST	MUST	MUST	5	2	0
- Easy to upgrade and renew	MUST		MUST	MUST	NICE	MUST	NICE	MUST	MUST	MUST	5	2	0
- Easy to deploy throughout the system	MUST		MUST	MUST	NICE	MUST	NICE	MUST	MUST	MUST	5	2	0
MAINTENANCE, SCALABILITY AND RENEWAL: The 'ASB' ICT solutions shall have:													
- Minimal or no recalibration required	MUST		MUST	MUST	NICE	MUST	NICE	NICE	MUST	MUST	4	3	0
- Minimum or no consumables	MUST		MUST	MUST	NICE	MUST	NICE	NICE	NICE	NICE	2	5	0
- Cheap consumables (if any)	MUST		MUST	MUST	NICE	MUST	NICE	MUST	NICE	MUST	4	3	0
- A cleanable covering material (if any) of the sensing components	MUST		MUST	MUST	NICE	MUST	NICE	MUST	NICE	MUST	4	3	0
DISPOSAL: The 'ASB' ICT solutions shall:													
- Not include nor generate any toxic material to be handled by the personnel	MUST		NOT	NICE	NICE	MUST	NICE	MUST	MUST	MUST	4	3	0
- Use existing disposal routes	MUST		NICE	MUST	NOT	MUST	NICE	MUST	MUST	MUST	5	1	1
- Be environmentally friendly, limited amount of single-use material	MUST		MUST	MUST	NICE	MUST	NICE	MUST	MUST	MUST	5	2	0

	Added items (gray cells indicates partner providing the item)													
ANTI-SUPERBUGS PCP	data gererated data must be protected from external misuse (datasavety and datasecurity, IT security)								MUST	ASB_FunctionalitiesVali	1	0	0	nex D2.1
	data gererated will be storred on clinical servers								MUST		1	0	0	
										115	51	13		

TOTAL

Comments on Other Life-cycle Requirements

Please use this section to include any other information that you might consider relevant regarding OTHER LIFE CYCLE REQUIEREMENTS for the ASB solution

*Comments from **VINCat (Head of Microbiology Lab)**: There are 3 phases in management of the analysis: pre-testing (simple analysis); processing that requires great complexity; validation (it must be the microbiology services the ones who receive the central information). Analysis - environmental conditions must not alter the results of the technology (e.g. acinetobacter - when it is detected, it is already a resistant form because it doesn't naturally exist in human body environment; other types already exist in the human body but are not damaging, so it must be able to distinguish in between healthy amounts and unhealthy amounts). PCR - tradition; Point of Care - isothermical amplifications (type of technology used currently in microbiology - most famous one is the detection flu strain virus species which is what launched the detection technological advancement) - e.g. Cepheid GENEXPERT - detection of resistant microorganisms.*

*Comments from **Dr. Nejad (Helios)**:*
- Easy to upgrade and renew: also IT security and datasafety, with firewall to prevent external usage
- Cleanable covering material inside and outside

ECONOMIC REQUIREMENTS OF ANTI-SUPERBUGS ICT SOLUTIONS

Please complete the cells by choosing between '1' (i.e. 'Yes') or '0' (i.e. 'No') according to the priority you consider to be assigned to each item.

	ICO (VINCat)				PAT	STH	UKA	Helios	MoH	FMT	YES	NO
Considering the added functionalities to be provided by the 'ASB' ICT solutions:	Infect.	Microb.	'ICT' Tech.	**'AVERAGE'**			***KJW***					
- Would you consider acurate to compare its cost-effectiveness to your common practice for patient screening?	YES	YES	YES	YES	YES	YES	YES	YES	YES	YES	7	0
- Would you consider acurate to compare its cost-effectiveness to a weekly patient screening by PCR or culture?	YES	YES	YES	YES	NO	NO	YES	NO	NO	YES	3	4
- Would you consider acurate to compare its cost-effectiveness to your common practice for surface screening?	YES	YES	YES	YES	YES	NO	NO	YES/NO	NO	NO	2	4
- Would you consider acurate to compare its cost-effectiveness to existing surface screening practices (e.g.: ATPase testing)?	YES	YES	YES	YES	YES	NO	NO	NO	NO	NO	2	5
TOTAL									14	13		

Comments on Economic Requirements

Please use this section to include any other information that you might consider relevant regarding ECONOMIC REQUIEREMENTS for the ASB solution

*Comments from **VINCat (Head of Microbiology Lab)**: Cost per patient for the technology must be determined, but it is more important to know the structural cost of the circuit of result validation.*

*Comments from **Dr. Nejad (Helios)**: must have to measure how the new ICT system achieves (EA: Comments more related to INDICATORS; also included in that questionnaire.) :*
- average hospital stay shortend
- less transmission to other patients, peoples,
- less noscominale infections
- less effort and costs to be generated in the labratory diagnostic depatments
- faster time to diagnostic
- faster time to positivity for MDRo carriers

7.5 MOH description

Ministry of Health of Turkey (MOH)

The Ministry of Health Turkey (MOH), established in 1920, is the main government body responsible for health sector policy-making, implementation of national health strategies through programs and direct provision of health services in Turkey. MOH is the major national provider of primary, secondary and tertiary health care services. It is essentially the only provider of preventive health services through an extensive network of health facilities (Public Health Centres): as of December 2015, MOH has more than 900 hospitals and more than 7,000 health centres – about twice as many as a decade ago.

MOH currently comprises nine general directorates: 1) Health for Border and Coastal Areas; 2) Health Services; 3) Emergency Health Services; 4) Administrative Services; 5) Health Promotion; 6) Health Information Systems; 7) Health Research; 8) Health Investments; and, 9) EU and Foreign Affairs. The organization is essentially structured along vertical lines of responsibility reflected in the topic-based, functional divisions within each directorate, also at provincial level and, - to a certain extent -, in hospitals and health centres. At the provincial level, provincial health directorates (for 81 provinces) are responsible for administering health services provided by MOH.

General Directorate of Health Information Systems (GDHIS), which will lead the works and studies regarding the ANTI-SUPERBUGS project, is responsible for country-wide policies, strategies and standards for information systems and communication technologies in healthcare services, information systems and projects for personal health records. It is the host to the NHIS (national health information system) of Turkey.

MOH has already taken actions in order to improve the surveillance efficiency aligned with WHO's Global Action Plan on Antimicrobial Resistance. Beyond that, the Ministry is committed to taking further steps to reduce the number of MRDOs infection and focus on conducting R&D on the issue. As indicated by The Economic Policy Research Foundation of Turkey following G20 Leaders' Summit, "*among countries with the necessary data, Turkey is the second country with the highest rate of antimicrobial resistance in the world. Turkey is also the country with the highest rate of consumption of antibiotics. Due to this correlation, it stands out as one of the countries with the highest potential for increased resistance rates in the coming period.* "

According to 2015 National Antimicrobial Resistance Surveillance System (NAMRSS) Report in Turkey, third-generation cephalosporin resistance in invasive (blood and CSF cultures) *E. coli* isolates was found to be 51%, whereas according to EARSS-Net data this ratio was 13.1% in EU countries. In Turkey and EU countries, fluoroquinolone resistance in invasive *E. coli*

isolates were found to be 48% and 29.7%, respectively. In invasive *K. pneumoniae* isolates third-generation cephalosporin resistance were found to be 68%, fluoroquinolone resistance were found to be 48% and carbapenem resistance were found to be 30% in Turkey. These numbers were 30.3%, 29.7% and 8.1% in EU countries, respectively. Piperacillin-tazobactam resistance in invasive *P. aeruginosa* isolates were found to be 30% in Turkey and 18.1% in EU countries and carbapenem resistance in invasive *P. aeruginosa* isolates were found to be 32% in Turkey and 17.8% in EU countries. Methicillin resistance in invasive *S. aureus* isolates were also found to be 25% in Turkey and 16.8% in EU countries. At last, vancomycin resistance in invasive *E. faecium* isolates were found to be 16% in Turkey while 8.3% in EU countries. Based on these data, it can easily be said that, antimicrobial resistance is a major health problem in Turkey.

The Economic Policy Research Foundation of Turkey (TEPEV) published "*Antimicrobial resistance in Turkey: Economic evaluation and recommendations*" report in 2017. In this report, due to high numbers of antimicrobial resistance, it is estimated that Turkey carries the risk of experiencing an economic loss between 220 billion and 1.4 trillion dollars until 2050. If Turkey maintains its current level of antibiotic resistance in years, the total loss to affect the economy is calculated as 220 billion dollars. But in the worst case scenario, if resistance rates increase, it is estimated that the economic loss will reach to 1.4 trillion dollars.

8. LIST OF TABLES

9. LIST OF IMAGES

10. REFERENCES

APSS. (2016). *Healthcare Trust of the Autonomous Province of Trento*. Retrieved from www.apss.tn.it

Bedin, S. (2012). TLC-PE method developed and implemented in Lombardy Region for PCP and PPI projects. (S. Bedin, 2012).

Caselli, E. (2017). Hygiene: microbial strategies to reduce pathogens and drug resistance in clinical settings. *Microbial biotechnology*.

Cassini A, e. a. (2016). Burden of Six Healthcare-Associated Infections on European Population Health: Estimating Incidence-Based Disability-Adjusted Life Years through a Population Prevalence-Based Modelling Study. *PLoS Med*.

Cioni, G., & al., e. (2016). Epidemiology and outcome of Clostridium difficile infections in patients hospitalized in Internal Medicine: findings from the nationwide FADOI-PRACTICE study. *BMC Infectious Diseases*.

Davies, K. A., Longshaw, C. M., Davis, G. L., & al., e. (2014). Underdiagnosis of Clostridium difficile across Europe: the European, multicentre, prospective, biannual, point-prevalence study of Clostridium difficile infection in hospitalised patients with diarrhoea (EUCLID). *The Lancet Infectious Diseases*, 1208-1219.

Davies, M. (2017, 04 21). *The Bureau of Investigative Journalism*. Retrieved from https://www.thebureauinvestigates.com/stories/2017-04-21/worse-than-mrsa-experts-call-for-action-on-deadly-new-superbug

ECDC. (2013). *Point prevalence survey of healthcare-associated infections and antimicrobial use in European acute care hospitals.* Stockholm.

ECDC. (2017). *Antimicrobial resistance surveillance in Europe 2015. Annual Report of the European Antimicrobial Resistance Surveillance Network (EARS-Net).* Stockholm.

ECDC. (2017, 12 12). *ECDC country visit to Italy to discuss antimicrobial resistance issues.*

ECDC. (2017). *ECDC country visit to Italy to discuss antimicrobial resistance issues.* Retrieved from European Centre for Disease Prevention and Control: https://ecdc.europa.eu/en/publications-data/ecdc-country-visit-italy-discuss-antimicrobial-resistance-issues

ECDC. (2017). *European Centre for Disease Prevention and Control. Economic evaluations of interventions to prevent healthcare-associated infections.* Stockholm.

ECDC. (2018, 01 10). ECDC country visit to Spain to discuss antimicrobial resistance issues.

EU. (2017). *Factsheet - AMR: A major European and Global challenge.* Retrieved from EU Action on Antimicrobial Resistance : https://ec.europa.eu/health/amr/antimicrobial-resistance_en

Henderson, D., & al., e. (2013). Health care–associated infections: a meta-analysis of costs and financial impact on the US health care system. *JAMA Intern Med.*

Kramer, A. (2006). How long do nosocomial pathogens persist on inanimate surfaces? A systematic review. *BMC Infectious Diseases*.

Peter M Hawkey, e. a. (2018). Treatment of infections caused by multidrug-resistant Gram-negative bacteria: report of the British Society for Antimicrobial Chemotherapy/Healthcare Infection Society/British Infection Association Joint Working Party. *Journal of Antimicrobial Chemotherapy, Volume 73, Issue suppl_3*, Pp. iii2–iii78.

PHE. (2014). *From evidence into action: opportunities to protect and improve the nation's Health.* London.

PHE. (2017). *English Surveillance Programme for Antimicrobial Utilisation and Resistance (ESPAUR); Report 2017.*

Shaw, e. a. (2015 (Suppl 1)). Cost of organ/space infection in elective colorectal surgery. Is it just a problem of rates? *Antimicrobial Resistance and Infection Control*, p. 77.

Souverein D, e. a. (2016). Costs and Benefits Associated with the MRSA Search and Destroy Policy in a Hospital in the Region Kennemerland, The Netherlands. *PLoS ONE 11(2)*.

T., C., S., D., & H., H. (2014). Detecting Clostridium difficile Spores from Inanimate Surfaces of the Hospital Environment: Which Method Is Best? *J. Clin. Microbiol.* , 3426-3428.

Tacconelli, E., & al., e. (2014). ESCMID guidelines for the management of the infection control measures to reduce transmission of multidrug-resistant Gram-negative bacteria in hospitalized patients;. *Clinical Microbiology and Infection*, p1-55.

VINCat. (2016). *Vigilància de la infecció nosocomial als hospitals de Catalunya. Informe 2016.*

WHO. (2002). *Prevention of hospital-acquired infections. A practical guide (2nd edition).*

WHO. (2017). *WHO publishes list of bacteria for which new antibiotics are urgently needed*. Retrieved from http://www.who.int/mediacentre/news/releases/2017/bacteria-antibiotics-needed/en/