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D1.2 User Requirement Specification Document for diagnostics of CAARTI

VALUE-Dx

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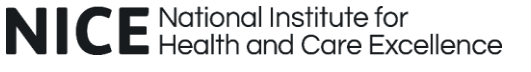
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1. Introduction

The VALUE-Dx project aims to transform clinical practice, improve patient outcomes, and combat antimicrobial resistance (AMR), through the widespread use of clinical and cost-effective innovative diagnostics strategies to achieve more personalized, evidence-based antibiotic prescription and use in community care settings.

To achieve this, we aimed to develop evidence-based target product profiles (TPPs) derived from user requirement specifications (URS)[1] to support future development and implementation of rapid diagnostics for Community Acquired- Acute Respiratory Tract Infections (CA-ARTI), and to refine the methods and processes to make them applicable to point of care diagnostic developments for other infectious disease indications.

The TPPs were developed in the following stages:

1. Preparation of draft TPPs diagnosis of CA-ARTI by an expert group
2. Public consultation via an online survey of users
3. TPP refinement by the Focus Group based on online survey responses
4. Consultation with VALUE-Dx Management Board and General assembly
5. TPP finalisation by Focus Group in response to comments received by VALUE-Dx Management Board and General assembly

2. Approach

2.1. URS/TPP Focus Group

To develop the TPPs for VALUE-Dx a focus group as part of WP1.2 was convened which met fortnightly to monthly, depending on upcoming tasks. The membership was chosen to have a balanced representation of the VALUE-Dx project partners and expertise.

Table 1: Members and former members of the URS/TPP Focus Group

Members	**Former Members**
Till Bachmann, University of Edinburgh (Lead)	Alex Van Belkum, BioMérieux
Benjamin Hommel, BioMérieux	Anders Ros, Abbott
Herman Goossens, University of Antwerp	Marie-Francoise Gros, BioMérieux
Suzanne Seme, Abbott	
Céline Blangy, BioMérieux	
Celine Roger-Dalbert, Becton-Dickinson	
Janneke van de Wijgert, UMC Utrecht	
Jennifer Osborn, FIND	
John Verrant, Janssen	
Mical Paul, RAMBAM	

[1] In the context of this task, we consider 'User Requirement Specifications' (URS) synonymous to 'Target Product Profiles' (TPP), both of which are essential, intertwined tools in the development and implementation of rapid diagnostics.

2.2. Draft TPP preparation

The Target Product Profiles (TPPs) developed here are intended to represent the User Requirement Specification (URS) as outlined in the VALUE-Dx project plan. The preparation was started with a single draft TPP taking input from existing examples from the literature.[2,3,4] From discussions and feedback from the VALUE-Dx Management Board on this single draft TPP, the VALUE-Dx URS/TPP Focus Group concluded that two TPPs were better representing the specifications needed for instrument and instrument free diagnostic tests for CA-ARTI. Subsequently, two draft TPPs were iteratively developed through the Focus Group. The first TPP describes an instrument-free test for CA-ARTI to inform treatment decisions. This TPP included 42 characteristics. The second TPP describes an instrument and cartridge-based diagnostic platform to inform CA-ARTI and consists of 49 characteristics. Based on the draft TPPs, an online survey was sent for a public consultation. Outputs from the survey were used to inform discussions with the URS/TPP Focus Group to decide on revisions to specific TPP characteristics. Those specifications that were modified based on the survey input are denoted with an asterisk.

2.3. User Requirement Assessment

2.3.1. Online survey outline

To develop an evidence-based to inform the draft TPP specifications, an online survey was conducted to gather input from clinicians to inform the TPP draft specifications. A total of 311 clinician responses were collected and outputs from the survey were discussed with the URS/TPP Focus Group to inform specification revisions for both draft TPPs.

The online survey was created using Alchemer software. A link to the online survey was circulated via the European Society of Clinical Microbiology and Infectious Diseases (ESCMID) and European Respiratory Society (ERS) newsletter and members of the TPP focus group also distributed the link amongst their respective networks. The survey was open for 8 weeks. Survey respondents were asked to provide basic demographic information and were then queried to inform a subset of critical characteristics of the TPPs including the following critical characteristics:

- intended use
- target use setting
- target patient population for the test
- target users
- target diseases
- preference for diagnostic test format
- test and instrument costs
- ranking of test properties of importance
- diagnostic assay targets

[2] Target product profiles for antibacterial resistance diagnostics. Geneva: World Health Organization; 2020. Licence: CC BY-NC-SA 3.0 IGO.
[3] Gal M, Francis NA, Hood K, Villacian J, Goossens H, Watkins A, Butler CC; RAPP-ID consortium. Matching diagnostics development to clinical need: Target product profile development for a point of care test for community-acquired lower respiratory tract infection. PLoS One. 2018 Aug 1;13(8):e0200531.
[4] Dittrich S, Tadesse BT, Moussy F, Chua A, Zorzet A, Tängdén T, Dolinger DL, Page AL, Crump JA, D'Acremont V, Bassat Q, Lubell Y, Newton PN, Heinrich N, Rodwell TJ, González IJ. Target Product Profile for a Diagnostic Assay to Differentiate between Bacterial and Non-Bacterial Infections and Reduce Antimicrobial Overuse in Resource-Limited Settings: An Expert Consensus. PLoS One. 2016 Aug 25;11(8):e0161721.

- specimen types
- time to result
- ease of use
- connectivity
- data export

Survey validation was included so that respondents were presented with questions based on their answer to their preferred intended use. All respondents were requested to answer questions specific to an instrument vs. non-instrumented test format. Survey results were analysed for all respondents collectively and included partial responses. The Alchemer survey report was generated for all countries as well as for European countries only. Furthermore, a sub analysis was conducted to determine if region or role influenced survey responses for a subset of critical characteristics (intended use, use of the test and test information).

2.3.2. Survey respondent demographics

Of the 311 people who access the online survey, 124 completed the full survey, and 187 completed partial responses. For the European sub analysis, 54 total responses, with 35 completed surveys and 19 partial responses. Survey respondent characteristics are summarized in the below.

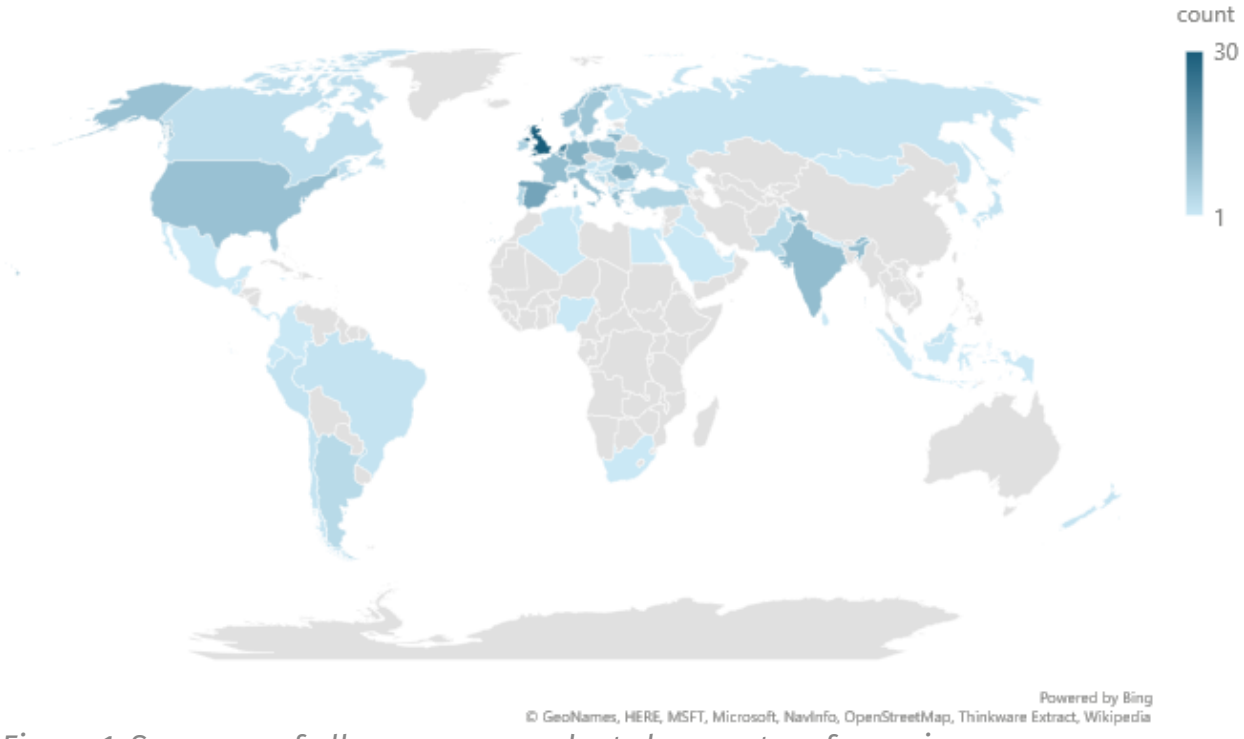


Figure 1: Summary of all survey respondents by country of experience

Survey responders were geographically diverse and had technical experience across 68 countries, including 20 European countries. Survey respondents also were predominately general practitioners, though many held multiple roles. The figure below is an overview of each role selected by the total 311 respondents (multiple selections were acceptable).

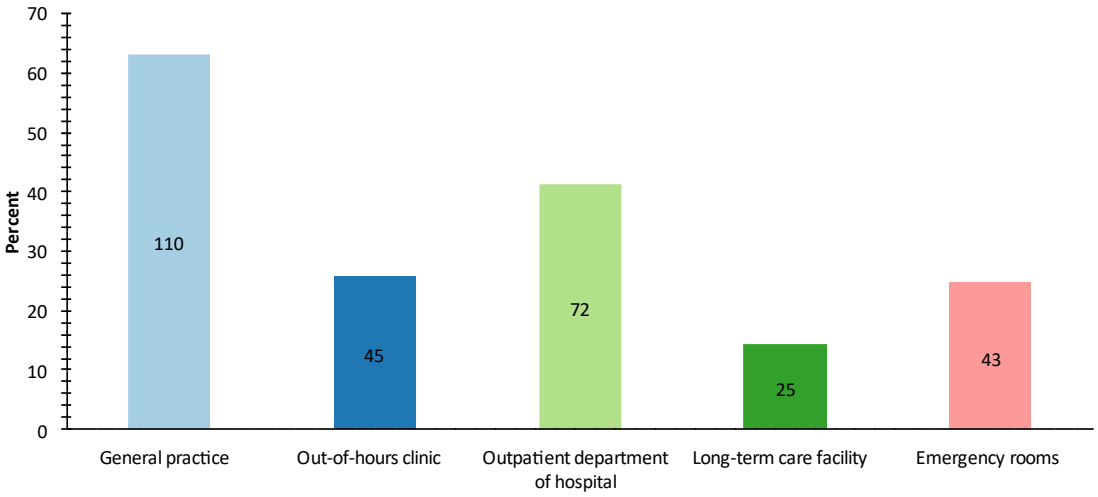


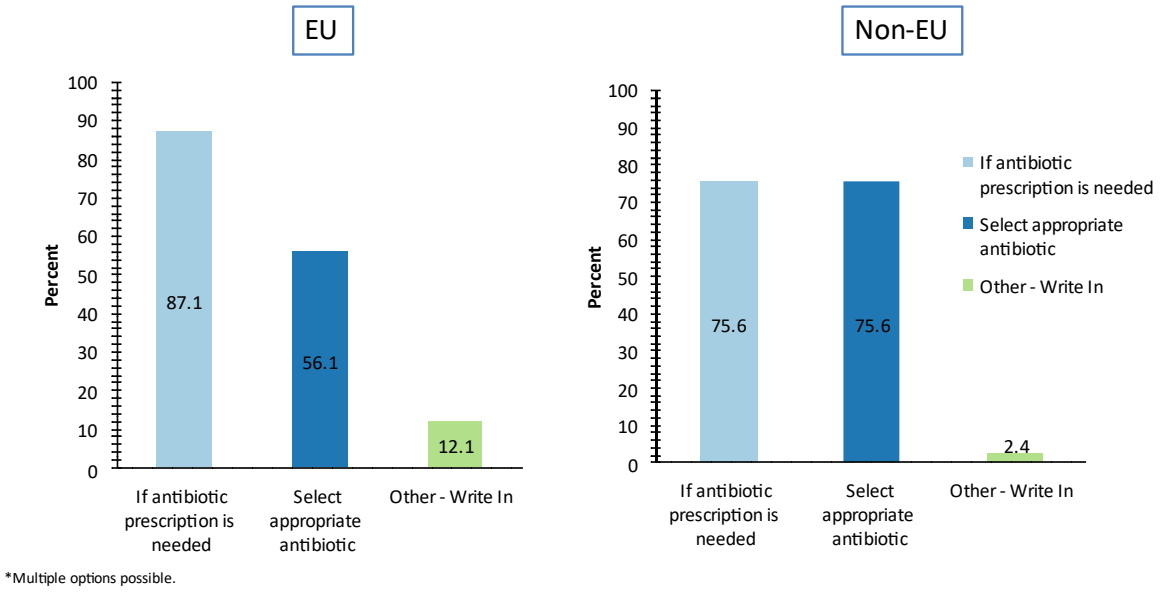
Figure 2: Summary of survey respondent's primary roles

The sub analysis to determine if the role influenced survey responses for a subset of critical characteristics (intended use, use of the test and test information) indicated no significant differences in responses (data not shown).

2.3.3. European vs. Non-European survey results

In general, similar trends in responses were observed between global responses and the European responses. There was a preference for a simple test over an instrumented system that could provide more sophisticated diagnostic testing, regardless of whether the intended use of the test as for LRTI, URTI or both LRTI+URTI. Sample type preferences did vary between EU and Non-EU response for URTI, but the primary preferred sample types were in agreement for LRTI and LRTI+URTI were sputum and nasopharyngeal swabs were the preferred specimen types respectively. Across the use cases there was a preference by Non-EU respondents for tests with a fewer number of manual steps compared to EU respondents where more steps were tolerable. For instrumented systems there was a preference for data connectivity and automatic data export regardless of intended use. A few selected survey responses are listed below including preferred intended use, target population, target user, target diseases, as well as analytical targets.

Intended Use: For which question would you like to use the test?*



*Multiple options possible.

Figure 3: Intended use question

Analytical target preferences varied by region as well as intended use (URTI, LRTI or URTI+LRTI), though in general there is a preference for bacterial vs. viral or infection vs. not infected status from the test results.

2.3.4. Sub analysis by region and role

Furthermore, an additional analysis was conducted to explore if a difference in roles influenced survey outcomes between EU and non-EU responses. For this analysis, we evaluated the results for the preferred intended use, the preferred result of the test (If antibiotic prescription is needed vs. informing antibiotic selection based) and what information respondents wanted the test to provide (infected vs. not infection, severity of infection, bacterial vs. viral, viral pathogen identification, bacterial pathogen identification, and antibiotic susceptibility/resistance information). Roles were evaluated by those respondents that selected general practitioners only compared to those that selected general practitioners and out of hours clinics, general practitioners and outpatient clinics, general practitioners and long-term care facilities, general practitioners and emergency room doctors and all general practitioners with any combination of other roles. The majority of survey respondents were general practitioners only. No significant differences were seen between role, suggesting aggregating the responses by role does not introduce a bias to the survey results.

2.4. TPP finalization

The survey outputs were reported to the working group and suggested revisions were made to the draft TPP documents based on survey feedback. These revised drafts were then circulated with the VALUE-Dx Management Board and General Assembly for final

review and feedback prior an in-person meeting in September 2023 alongside the VALUE-Dx Annual Meeting. Responses to the highest priority characteristics were discussed and the final TPPs complied subsequently. A decision was made not to include numerical values for the end price to customers for the assay, cartridge or instrument as these are depending on various technical, geographical as well as business factors not fully addressed in TPPs.

3. Dissemination

A manuscript based on the presented work and results has been compiled and will be submitted imminently to a journal relevant to the target audience of VALUE-Dx.

4. Conclusion

In conclusion, the surveyed users expressed a strong desire for an easy-to-use, rapid and cost-effective test which ideally addresses both upper and lower respiratory tract infections and provides information to aid in deciding whether an antibiotic prescription is needed. As expected, there was a good range of user requirements and technical feasibility and ambition. We reflected this in the TPPs through the assignment of minimal and optimal requirements with the latter being the target for the Technological Roadmap which is covered in WP 1.3.

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