

AN INVESTIGATION INTO THE APPLICATION OF DESIGN
PROCESSES TO NOVEL SELF-USE MOLECULAR DIAGNOSTIC
DEVICES FOR SEXUALLY TRANSMITTED INFECTIONS

A thesis submitted for the degree of Doctor of Philosophy

by

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Abstract

The purpose of this research was to investigate the application of design processes to the development of novel self-use molecular diagnostic devices for sexually transmitted infections. The argument proposed in this thesis is that the application of design methods at the earliest research stages into miniaturised, low cost, molecular diagnostic technologies will accelerate and improve the process of translating proof of concept diagnostic technologies into usable devices. Concept development requirements and potential issues and barriers to development were identified through interviews with expert stakeholders. These requirements were further refined through a survey of a multidisciplinary diagnostic medical device research group. An action research method was applied to develop a proof of concept prototype to the preclinical trial stage. Through these research studies, a design process model was formulated for use in a research environment. The application of design methods to the proof of concept prototype described in the thesis have resulted in a preclinical trial prototype that exhibits the necessary features for development into a self-use molecular diagnostic device. Issues and barriers were identified and discussed, design guidelines for further development beyond preclinical trial were defined and a generalised design process model for self-use molecular diagnostic devices for sexually transmitted infections was proposed. This research highlights the need for design methods to be applied at the earliest possible stages of the development of novel molecular diagnostic devices.

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Chapter 1

Research Overview

1.1 Introduction

The miniaturisation and cost reduction of molecular diagnostic technology combined with the burden on health services caused by undiagnosed and untreated STIs make accurate, self-use molecular diagnostics an attractive prospect for healthcare providers, public health agencies and the public. This research conducts an investigation into concept development requirements for self-use molecular diagnostics for STIs, explores motivations for developing such devices and describes the issues and barriers that arise when doing so. An investigation into the potential benefits of applying design processes to an early research stage, proof of concept, molecular diagnostic technology suitable for self-testing is described.

Literature on design processes for medical devices in general is widespread (for examples see: Linehan *et al.*, 2007; Gilman, Brewer and Kroll, 2009; Pietzsch *et al.*, 2009; Medina, Kremer and Wysk, 2013). However, there is an absence of literature addressing the issue of how self-use molecular diagnostic devices might be progressed from the proof of concept stages and then designed for specific contexts of use. Only relatively recently have researchers developing miniaturised molecular diagnostic technologies begun to consider design requirements such as context of use (Nayak *et al.*, 2017). Research has not, so far, proposed how requirements (like the identification of a context of use) might be practically applied to the design of the self-use diagnostic devices of the future. Although researchers might not ordinarily be involved in this type of design task, the complexity of requirements and the number and variety of stakeholders involved in self-use molecular diagnostic development may necessitate their involvement. The studies described in this thesis contribute to addressing this gap in the literature.

In this chapter, a brief, introductory review of the research field is provided and a statement of motivation for the work is given. A description of the setting in which the research was carried out is also provided, in this case a multi-university research consortium and internal collaborations within Brunel University London. Included is a description of the eSTi² (Electronic Self-Testing Instruments for Sexually Transmitted Infections) research consortium to which the author belonged and which, through the UKCRC (United Kingdom Clinical Research Collaboration) provided funding and support for this research. Also described is the DoC Lab (Doctor on a Chip Laboratory) research group based at Brunel University London with whom the author collaborated while carrying out the research.

Aims and objectives of the project and the research questions are shown in this chapter. In order to provide a summary overview of the research, a description of and rationale for the layout and structure of the thesis is given.

1.1.1 The Pathway to Self-Use Molecular Diagnostics

Technologically enabled self-monitoring and self-management of one's health is an ongoing subject of research and development efforts in the healthcare sectors of developed countries (Kim *et al.*, 2016). This is epitomised by the development and subsequent use by consumers, of devices which allow them to carry out procedures previously confined to the GP's (General Practitioner's) surgery or hospital ward. A common example are the numerous brands of self-administered glucose monitors now available for use in the home and elsewhere (Dunne *et al.*, 2015).

For the healthy consumer, self-monitoring devices and software are available (often for use with smartphones), which are capable of keeping track of numerous indicators of one's health and wellbeing with a view to the prevention of health problems in future. This, for the most part, is a case of using smartphone applications to track footsteps, nutritional intake or sleeping patterns. Debate as to the validity, efficacy or clinical benefit of such applications continues (Harricharan *et al.*, 2015; Orr *et al.*, 2015; Van den Bulck, 2015). However, more cumbersome but well established devices such as blood pressure monitors might be used effectively by healthy individuals and provide a preventive clinical benefit (Verdezoto and Gronvall, 2016).

Fitting well between these two approaches, i.e. that of monitoring and managing one's health using portable computing technologies and that of using complex medical devices which have been developed so they can be used by someone without medical training, lies an area where the potential lies for the development of self-use molecular diagnostic testing devices for sexually transmitted infections.

Predominantly, diagnostic devices for sexually transmitted infections are large, laboratory based and centralised and although highly automated and capable of processing more than 90 biological samples at a time, require up to an hour of hands-on maintenance per processing run and may take more than 6 hours to produce results (Ratnam *et al.*, 2014). An example of the physical scale of widely used, laboratory based molecular diagnostics is shown in Figure 1-1 below.

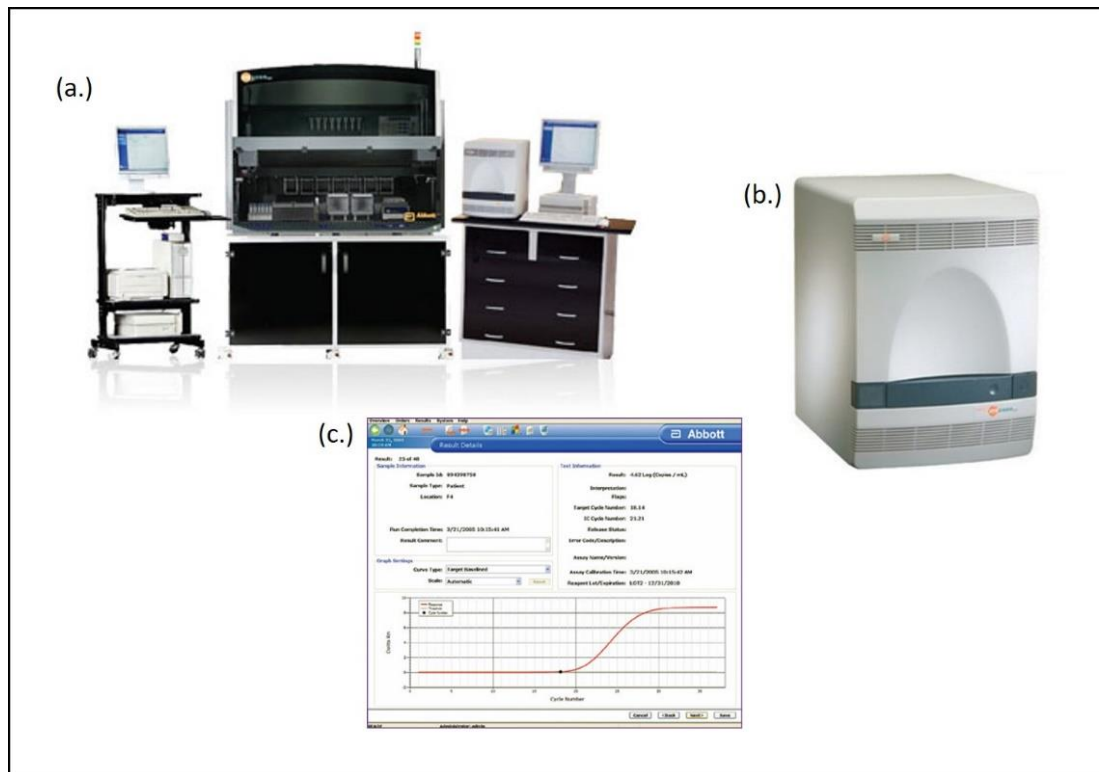


Figure 1-1. Laboratory based molecular diagnostics. A - The lab set up including sample preparation, amplification, detection and software user interface B - The m2000rp real time PCR system, a benchtop device for performing DNA amplification C - The software user interface for the system (HospiceCare, 2017).

To improve upon this situation, point of care diagnostic devices, most notably Cepheid Genexpert systems, the early versions of which were capable of processing between 1 and 96 samples in under 2 hours (Gaydos *et al.*, 2013), have been deployed in the UK with a view to decentralising the testing element of the STI diagnostics and treatment system. Their introduction has been shown to improve both clinical outcomes and the cost effectiveness of testing (Turner *et al.*, 2014). Continuing developments in point of care technologies like this will see sample processing times become shorter and testing devices become smaller and less reliant on laboratory conditions in order to function (Niemz, Ferguson and Boyle, 2011).

Where the collection of a biological sample from the patient is concerned, self-collection methods, be they urine or swab samples, have been used for STI screening purposes, may widen the uptake of testing and are highly acceptable to patients (Paudyal *et al.*, 2015). Self-collection of samples may also be more cost effective for health services (Taylor *et al.*, 2013). Research into novel methods of receiving and acting on test results are being improved by leveraging the capabilities of communications technologies. Mobile phones have been used to improve notification methods (Reed *et al.*, 2014). Improved and more secure communication architectures for transmitting sensitive patient data have been proposed (Tulasidas *et al.*, 2013)

and user centred design methods have been applied in producing acceptable and usable interfaces through which to receive and act upon test results (Gkatzidou *et al.*, 2015; Gibbs *et al.*, 2016).

With the common technological evolution from larger, more expensive devices to smaller, cheaper to produce devices, as well as a continued progression toward patient centred care, options for expanding the range of contexts of use within which diagnostics for sexually transmitted infections can be used are realised. For example, researchers have investigated the potential for the use of point of care testing devices for sexually transmitted infections in GP's surgery's (Hogan *et al.*, 2010), rural community settings (Guy *et al.*, 2013) or even vending machines in public places (Young *et al.*, 2014).

The studies in this thesis are largely concerned with the development of a case study, miniaturised and low cost molecular diagnostic technology for the detection of Chlamydia Trachomatis. Design requirements are defined for the device and the technology is progressed from the proof of concept to the preclinical trial stage of development. The application of the research methods described in the thesis may ensure that this technology will in future be suitable for point of care or self-use diagnostic applications.

1.1.2 Problem Statement and Motivation

As has been stated above, a direction that medical device technology research and development has been taking is toward home and self-use technologies which allow people to perform medical procedures without expert supervision. At the time of writing, this type of technology is restricted mostly to monitoring and management. Presently, however, diagnostic devices are becoming small and low-cost enough that the creation of accurate, self-use diagnostic devices is a distinct probability.

Research efforts are being applied to capitalise on the opportunities and mitigate the risks presented by the development of the technologies described. However, an academic understanding of how design methods and processes should be applied to the development of self-use molecular diagnostics for STIs is, to the author's knowledge, absent from the literature. This academic understanding will be beneficial, as many of the novel technologies in development which could be applied to self-testing are being developed in an academic setting.

The motivation for this work stems from the need for contributions to the literature regarding the best way in which novel, disruptive, self-use medical devices can be designed, developed, used and disposed of effectively and safely. The successful application of design methods and processes to novel diagnostic technologies at the very earliest stages of development may

improve the chances that self-use diagnostic devices are effective clinically, useful from a public health perspective and empower the patient.

1.2 Context and Scope

A description of the research groups and collaborations with whom this work was carried out provides context for the studies in the thesis. A description of the scope of the research defines the limits of the studies.

1.2.1 The eSTi² Translational Research Consortium

The research described here was funded by and conducted in collaboration with the eSTi² translational research consortium project (eSTi², 2014). The eSTi² consortium was funded by the UKCRC as a “translational infection research initiative consortium” (UKCRC, 2017). The stated aims of the project were as follows:

1. Collaborating with industrial partners and academia to develop rapid point of care diagnostics to accelerate effective clinical management.
2. Developing key enabling technologies to improve sample preparation, enhance diagnostic performance and reduce cost.
3. Implementing protocols to evaluate new diagnostics through preclinical testing to diagnostic evaluations, regulatory approval and service evaluations.
4. Researching and developing new clinical care pathways that allow patients to receive a diagnosis via their smartphone and interact with the care pathway to receive treatment and advice.
5. Developing new human computer interaction methodologies to ensure user experience and technology uptake. This is complemented by an investigation into the economic model for introducing such technology into a healthcare system.

(2017, www.esti2.org.uk)

These aims were carried out by four work streams spread across five universities, a UK government agency; Public Health England (PHE) and a number of industrial collaborators.

The research described in this thesis was carried out primarily in collaboration with work streams two and four. Work stream two was tasked with completing aim number 2 from the list above and work stream 4 was tasked with the completion of aim numbers 4 and 5. The research area of this work, based as it was, on design and design processes, lent itself particularly to input and collaboration from these two work streams and overlapped with the aims of both.

Below is a diagrammatical representation of where the research in this document was placed in the consortium:

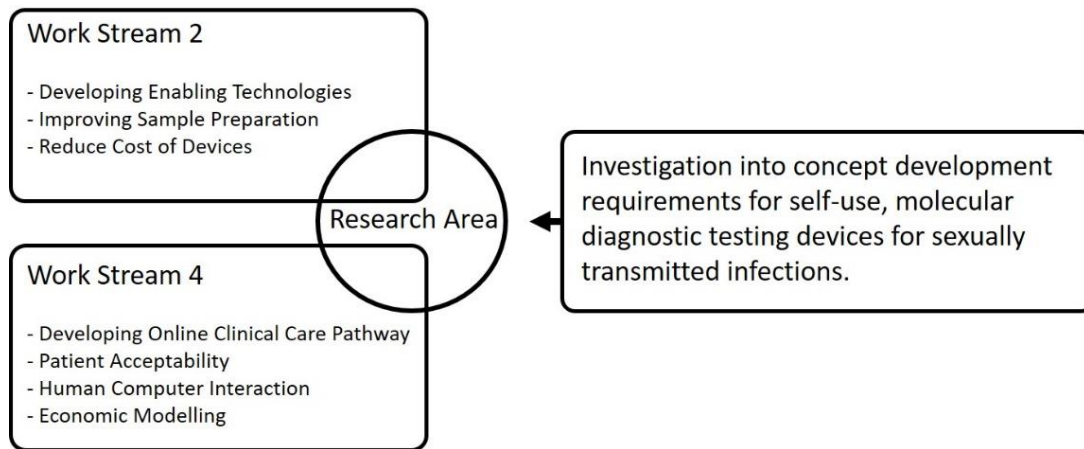


Figure 1-2. The research area encroaches on the research aims of both work streams two and four of the eSTi² research consortium.

Further elucidation of the work carried out by work streams two and four and their relationship to this research project is highlighted in subsequent chapters where relevant (i.e. Chapter 3 – Interviews of expert stakeholders from the eSTi² group, Chapter 4 – a survey of the eSTi² research group and Chapter 5 – Action research carried out in collaboration with Work Stream 2 of the eSTi² research group).

1.2.2 The DoC Lab Research Group

The Doctor-on-Chip Laboratory research group was situated at Brunel University London and made up a large proportion of work stream two of the eSTi² consortium research project described in the previous section. DoC Lab was comprised of undergraduate, masters and doctoral students as well as post-doctoral, research fellows, lecturers and industrial partners drawn from various disciplines relevant to technological research and development in the area of novel, miniaturised, low-cost and innovative medical devices and enabling technologies for medical devices (DoCLab, 2017).

The primary aim of the DoC Lab research group was to develop a miniaturised, modular sample in to answer out diagnostic testing system for infectious diseases (Branavan *et al.*, 2016).

Expertise in the group was tailored towards taking a broad approach to this problem, addressing the research and development issues of all aspects of the proposed diagnostic system. Thus, group members specialising in microfluidics, biology, biomedical engineering, wireless communications, micro-engineering and design all played various roles in the research collaboration.

For the purposes of this research, the author designed a working prototype, low cost, miniaturised molecular diagnostic platform for Chlamydia Trachomatis in collaboration with various members of the DoC Lab research group (See also Chapters List, Section 1.6). This task was undertaken as an action research activity wherein the author acted as a participant observer, conducting design, technical drawing and systems engineering tasks as a part of the process of design and development of the novel diagnostic testing platform.

1.2.3 Research Scope

This research contributes to the field of study of industrial design and/or design engineering and is primarily concerned with design and development processes as they are currently, or could in future be, applied to self-use molecular diagnostics for STIs. In summary, the scope of the research described in this thesis can be shown as follows:

Field: Industrial Design/Design Engineering

Research Area: Design process

Focus: Concept development requirements, issues and barriers with development, design process

Technology: Self-use molecular diagnostic tests for sexually transmitted infections

1.3 Research Aim

The aim of this research was to investigate a way in which design processes could be applied to self-use diagnostic technologies in the early research stages so that they might be more quickly and effectively progressed from proof of concept prototype stages into working systems which are useful from a clinical and public health perspective.

1.4 Research Objectives

The objectives of the research were as follows:

Objective 1: To provide, through a review of the literature, an overview of the field of study and background for the research described in the thesis.

Objective 2: To identify concept development requirements for self-use molecular diagnostic devices for STIs.

Objective 3: To propose design guidelines for future development efforts based on research data gleaned through the studies described.

Objective 4: To describe issues and barriers inherent in the development of self-use molecular diagnostics for STIs.

Objective 5: To formulate a design process model for use by medical device researchers, developers and designers for expediting the development of self-use molecular diagnostic devices for sexually transmitted infections.

Table 1-1 below, shows the tasks, methods and deliverables of the research project which contributed to the satisfaction of the research aim.

Table 1-1 - Research Structure

	Objectives	Task/Method	Deliverables	Chapter
	Objective 1 – Systematic Review of the Field	Literature Review	Deliverable 1 1.1 Review of areas of study relevant to developing this type of technology 1.2 Review of design process for medical devices 1.3 State of the art technology in the field	Chapter 2
	Objective 2 – Identification of concept development requirements,	Qualitative analysis of expert Interviews, Survey of designers, Validation survey	Deliverable 2 2.1 Concept Development Requirements 2.2 Issues and barriers associated with development	Chapters 3 and 4
Deliverable 2 informs:	Objective 3 – Proposition of design guidelines	Action Design Research	Deliverable 3 3.1 Pre-clinical trial working prototype platform designs 3.2 System requirements 3.3 Issues and barriers associated with development	Chapter 5
Deliverables 2+3 inform:	Objective 4 – Description of issues and barriers	Action Design Research, Interviews, Validation Survey	Deliverable 4 4.1 Final Issues and barriers associated with development	Chapter 5
Deliverables 1, 2, 3 + 4 inform:	Objective 5 – Formulation of design process model	Literature Review, Interviews, Validation Survey, Action Design Research	Deliverable 5 5.1 Generalised design process model for use in the early research stages of self-use diagnostic technology development	Chapter 5

1.5 Research Questions

The aim and objectives of the research can be expressed as research questions which are shown below:

1. What are the concept development requirements for self-use molecular diagnostic testing devices for Chlamydia Trachomatis from a clinical, public health and engineering perspective?
2. What are the issues and barriers associated with the development of self-use molecular diagnostic devices for sexually transmitted infections from a clinical, public health and engineering perspective?
3. How can the process of translating novel diagnostic technologies from the proof of concept stages to the clinical trial stages be accelerated?

1.6 Methods Overview

A mixture of research methods was used in the thesis, which are described in detail at the beginning of the chapters in which they are applied. Qualitative methods are used in the form of a series of semi-structured interviews. A quantitative survey of the participants in the eSTi² research group is included. Further qualitative research includes a survey of professional designers, and action research describing the process of development of a preclinical trial prototype self-use molecular diagnostic device for STI's.

A mixed methods approach is appropriate for this research. A broad understanding of the context in which self-use molecular diagnostic devices for STI's are developed is required to satisfy the research objectives. Qualitative methods, such as interviews and action research, provide an opportunity to investigate factors which are difficult to quantify, such as design requirements from various expert points of view, design methods and issues with the design and development process. Following on from this, a quantitative survey method provides more concrete evidence of findings which were made qualitatively, thus reinforcing the overall findings of the research.

1.6.1 Inclusion/Exclusion of Participants

1.6.1.1 Qualitative Interviews

Qualitative analysis of interview data is used to give an initial description of concept development requirements and issues and barriers to development. Participants in this study were chosen based on their high level of involvement with and understanding of the eSTi² research project. All the chosen participants were educated to doctoral level and active participants in their research field. This ensured that the expert opinions given were relevant

and reliable regarding the state of the art in diagnostics for STI's. Further detail is provided in sections 3.5 (Page 31) and 3.6 (Page 33) of Chapter 3.

1.6.1.2 Qualitative Survey of Design Professionals

A survey of professional designers was conducted to investigate design processes being used by professionals to design diagnostic devices and which issues are commonly encountered in their work on diagnostic medical devices. Participants were recruited online from established design consultancies or university departments actively developing new diagnostic technologies.

Participant were asked about their level of involvement in medical device development and whether they had any specific experience with diagnostics. These factors were considered when analysing the results. Further detail is provided in sections 3.5.2 (Page 32) and 3.8 (Page 62) of Chapter 3.

1.6.1.3 Quantitative Survey of the eSTI² Consortium

A quantitative survey was used to further refine the description of design requirements and issues with design and development. Participants for this study were recruited from the eSTI² research consortium. All members of the consortium were invited to participate in the survey as each had direct working knowledge of the development of self-use molecular diagnostics in the context of the eSTI² research project. No participants from outside of the consortium were invited to participate. Further detail is provided in sections 4.6 (Page 67) and 4.7 (Page 68) of Chapter 4.

1.6.1.4 Qualitative Action Research

Action research was then used to develop the preclinical trial prototype technology, propose design guidelines and formulate a design process model for application to proof of concept diagnostic technologies in a research environment. The action research was focussed around the design and development work of the author working in the context of the research consortium. As a result, the expert panels used to evaluate design work and develop the design process model consisted of experts directly involved in the eSTI² consortium. Experts were chosen from a range of relevant disciplines. Further detail is provided in sections 5.5 (Page 84) and 5.6 (Page 87) of Chapter 5.

1.6.2 Validity and Reliability

The measurement methods used in the research described are consistent with the nature of the research questions posed. Where research findings cannot be quantified, as in the case of design requirements or issues with development, which are subjective factors based on the participants involved and the context of the research, qualitative research instruments have

been used. Findings regarding design requirements and issues with development in the context of the eSTi² consortium project have been further validated using a quantitative survey method.

Triangulation of the data from each study described in the thesis reinforced the contributions that could be derived from the research. Further, the studies were arranged sequentially to reinforce their validity and reliability. For example, interviews provided the initial evidence for design requirements, this evidence was further reinforced through the quantitative survey of the eSTi² consortium and finally through the action research study. Likewise, evidence for issues and barriers to development were initially collected in the expert interviews and was further reinforced sequentially through the other studies detailed in the thesis. Further detail of this structure is provided in the discussion in Chapter 6 (Page 133).

Due to the subjective nature of many of the research outcomes described in the thesis, repeatability of the studies described may be affected by developments in technology or changes in working practices in diagnostic technology design.

1.7 Chapters List

The following is a list of the chapters in the thesis with a brief explanation of their contents.

Chapter 1 – Research Overview: This chapter contains an introduction to the thesis and an overview of its contents. Aims, objectives, research questions and a summary of the contribution of the research are shown.

Chapter 2 - Background: This chapter provides background to the research activities shown in later chapters of the thesis. Areas of literature relevant to the aims, objectives and research questions are covered. An overview is given of the clinical relevance of Chlamydia Trachomatis, the possible public health implications of novel self-use diagnostic devices and the role of translational research. Design methods and design process for medical devices are introduced and a gap is identified in the literature.

Chapter 3 – Expert Interviews and Survey of Professional Designers: Chapter 3 contains interviews of expert stakeholders. Qualitative analysis of the interviews provided a basis for defining concept development requirements for self-use molecular diagnostic devices for STIs. Issues and barriers associated with development were also identified. A small survey of professional designers is included giving an indication of medical device design process requirements in an industrial setting.

Chapter 4 – Validation Survey: A survey of the eSTi² research group is described in Chapter 4. The survey reinforces the findings of Chapter 3 showing general agreement or disagreement

with concept development requirements across disciplines. Issues and barriers are further illustrated through analysis of the survey results.

Chapter 5 – Action Research Design Activity: In Chapter 5, a working prototype proof of concept technology is progressed to the preclinical trial phase of development. Development is described through an action research method. A design process model for use on novel diagnostic technologies in a research setting is developed through the action research and presented at the end of the chapter.

Chapter 6 - Discussion: Chapter 6 contains a discussion of the research with comparisons to the literature and arguments for the unique contribution to knowledge of the thesis.

Chapter 7 – Conclusions and Further Work: In the final chapter, a description of how the research questions were answered and the research aim was satisfied is given. An explanation of the contribution of the thesis is provided. Summary conclusions are shown and further work beyond the scope of the thesis is suggested.

1.8 Contributions

The thesis provides the following contributions to knowledge in the field:

A generalised design process model for use in the research environment is described. The key contribution of the thesis is that action research design activity applied at the proof of concept stage of diagnostic technology development will accelerate and improve efforts to create novel, self-use and point of care diagnostics for infectious disease.

Concept development requirements for a self-use molecular diagnostic device for sexually transmitted infections have been proposed. There are no existing, functional examples of this type of device available for general use at the time of writing.

Technical design guidelines are proposed for development of a working prototype low cost, miniaturised diagnostic technology beyond the preclinical trial prototype stage. Technical design requirements constitute a research contribution because a part of the argument of the thesis is that where novel diagnostic technologies are concerned, technical requirements such as these are not being investigated, thus slowing the translation of diagnostic technology from the research environment to use in the field.

Issues and barriers associated with the development of self-use molecular diagnostic devices for STIs are described. Knowledge of issues and barriers for future development efforts may contribute to expediting the introduction of novel diagnostic technologies for general use providing a positive clinical and public health impact.

1.8.1 Challenges Highlighted by the Research

Challenges associated with the development of self-use molecular diagnostics have been highlighted through this research. In summary, the key challenges that have been identified are twofold. Firstly, the difficulties of working efficiently across the many disciplines required to successfully create self-use molecular diagnostic devices have been shown. Secondly, the bottleneck between carrying out the required research (biosciences, engineering and social sciences) in the subject area and the development of usable and commercially viable devices has been highlighted.

Proposals for the practical resolution of these challenges have been described in the thesis from the point of view of design engineering/industrial design.

1.8.2 Practical Implications of the Research

As described above in section 1.8, the research outcomes described in the thesis include a design process model and design guidelines and recommendations designed to be applied during the development of self-use molecular diagnostic devices. The intention of the author is that this information should be utilised by designers, scientists and engineers when developing this type of device in the future.

Issues and barriers involved in the development of self-use molecular diagnostics are described in the thesis. The practical intention of describing these issues is that through knowledge of them, they might be mitigated to some extent or avoided altogether by researchers or developers working on similar projects in the future.

1.10 Summary

An introduction and overview of the thesis was described in this chapter. The problem the research addresses was introduced and the scope and context of the research was defined. Chapter 2 will go on to describe the background for the research in greater detail.

Chapter 2

Background

2.1 Introduction

Chapter 1 provided an overall introduction to the thesis and the research studies described in it. The general aim of the thesis was established, which is to articulate an understanding of how the development of self-use molecular diagnostic devices can be accelerated from the proof of concept stages. Development of such devices is highly multidisciplinary. Accordingly, this chapter provides a review of the relevant literature, the intention being to highlight the multidisciplinary nature of the development activity and provide background for the key areas of investigation in the thesis. This chapter fulfils Objective 1 of the thesis.

The chapter is broadly split into three parts. In the first section, Chlamydia testing is described, why it is a priority and what the current testing methods are. The action research activity described in Chapter 5 concerns the development of a self-use Chlamydia testing device. Public health requirements for STI testing are then discussed, with consideration of how they might relate to self-use device design. The multidisciplinary nature of translational research into medical device design is then described. In the second section, diagnostic technology that could be well suited to self-testing for STIs are reviewed. Lastly, background on design processes generally and design processes for medical devices specifically is provided.

In the summary of the chapter, a gap in the literature, which is addressed by the research in the thesis is discussed.

2.2 Chlamydia Testing

The research in this thesis is mostly concentrated around the development of a self-use molecular diagnostic test for Chlamydia Trachomatis. Chlamydia is the most diagnosed STI in the UK (Public Health England, 2016). It has been shown to be the most prevalent amongst 15-24 year olds, with a recorded infection rate of 8%, which may in fact be much higher due to undiagnosed cases (European Centre for Disease Prevention and Control, 2012). Untreated Chlamydia infection has been shown to be a contributing factor in the development of pelvic inflammatory disease (PID) (Sweet, 2011). Compounding the problem of undiagnosed infection and the prevention of PID, Chlamydia is often asymptomatic (NHS, 2017). PID is predominantly detrimental to women's health as it can result in tubal factor infertility, ectopic pregnancy and chronic pelvic pain (Haggerty *et al.*, 2010).

The detection and treatment of Chlamydia Trachomatis infection is a public health priority in England (Jennison *et al.*, 2011). Annual screening for Chlamydia amongst sexually active individuals may reduce the incidence of PID brought about by it, although the quality of evidence in this area is in question (Low *et al.*, 2016). Regular screening, particularly in men and women under 20 years old, may also be more cost effective than waiting for symptomatic patients to seek testing and treatment (Adams, Turner and Edmunds, 2007). Due to the type of sample required, its high prevalence and the ease with which it can be treated, ordinarily with a single short course of antibiotics (Nwokolo *et al.*, 2016), there have been numerous initiatives providing access to Chlamydia screening online (Woodhall *et al.*, 2012). The most prominent of these is the National Chlamydia Screening Program, which allows individuals to take a sample themselves and post it to a laboratory for screening (NCSP, 2016). 7% of Chlamydia testing is accessed in this way with 11% of these tests returning a positive result (Harding-esch, Nardone and Lowndes, 2015).

Self-collection of samples for Chlamydia screening has been shown to be effective and acceptable to patients and may make patients more likely to get tested (Alexander *et al.*, 2008; Paudyal *et al.*, 2015), even in settings far removed from healthcare infrastructure (Bansil *et al.*, 2014). Recent studies have also demonstrated the potential benefits offered by access to a clinical care pathway online, giving the patient more autonomy when obtaining testing and treatment for Chlamydia (Gkatzidou *et al.*, 2015; Aicken *et al.*, 2016; Gibbs *et al.*, 2016). All of the above make Chlamydia Trachomatis an ideal case study for investigation into the technological feasibility of self-testing for sexually transmitted infections.

2.3 Public Health

When appraising design requirements for self-use molecular diagnostic devices for sexually transmitted infections, public health needs are a vital consideration. Public Health England (PHE) is responsible for sexually transmitted infection surveillance and disease control strategies in England (Public Health England, 2017). Currently, the surveillance of STI testing in England is achieved through the GUMCAD (Genitourinary Medicine Clinic Activity Dataset) system (Public Health England, 2015). This system collects data about patients and their test results from GUM (Genitourinary Medicine) clinics on a fortnightly basis. Analysis of the data collected contributes to disease control strategies and the understanding of epidemiology and instances of antimicrobial resistance (Lowndes and Hughes, 2010).

Use of point of care and self-use molecular diagnostics which may not be connected to current disease surveillance systems poses an issue for public health agencies (Harding-esch, Nardone and Lowndes, 2015). If self-testing devices do not deliver sufficient data to public health

agencies, addressing the problems of antimicrobial resistance, understanding the epidemiology of infections and lowering operating costs may become more difficult. Ongoing research is addressing the cost effectiveness and public health impacts of introducing point of care and self-testing devices for public use in the UK (Lowndes et al., 2014). It is clear that device design should take into account these surveillance needs from the earliest possible stage in any development process.

2.4 Multidisciplinary Translational Research

The research described in this thesis was conducted in collaboration with the eSTi² translational research consortium (See also Chapter 1, Section 1.2.1). The eSTi² consortium was funded by the UKCRC as a “translational infection research initiative consortium” (UKCRC, 2017).

Translational research is a branch of medical research, the purpose of which is to translate new innovations and discoveries from their research stages to a point where they are distributable to the public (Woolf, 2008).

Increasingly, biomedical research has included the terms translational research or translational medicine. Translational research projects require collaboration across a broad range of disciplines and may result in the creation of new drugs, devices, clinical practices or standards (van der Laan and Boenink, 2012). van der Laan and Boenink highlight that through translational research, stakeholders should be identified and future contexts of use of medical devices should be anticipated in order to maximise the utility of technological advances (2012). Sunderland and Nayak argue that engineering and design practices are by their nature translational, continuously developing novel technologies from the research environment into practical and useful contexts (2014). When investigating concept development and design process requirements of a novel medical device, ensuring that a broad range of stakeholders are considered from the outset and throughout the development process is vital (De Ana *et al.*, 2013).

2.5 The State of the Art

2.5.1 Diagnostic Technology and Self-testing

Molecular diagnostics for infectious disease offer the benefit of the direct identification of a biological pathogen through the detection of its DNA (Craw *et al.*, 2015). This is generally more accurate than other, indirect methods of detection which may rely on the detection of an immune response to an infection. Molecular diagnostics in general, at present require a sterile laboratory environment and bulky equipment.

Advances in technology bringing about cost reduction and miniaturisation indicate that accurate molecular diagnostic self-tests may be available for public use within a matter of years.

Users of such devices will be able to self-collect a biological sample and analyse it, remote from a health care facility, in under half an hour (Myers et al., 2013; Craw et al., 2015; Guo et al., 2015). Isothermal nucleic acid amplification of DNA used alongside an appropriate, low temperature assay, offers opportunities for testing devices to be lower powered and cost less (Craw and Balachandran, 2012; Craw et al., 2015). Microfluidic technology also offers many potential benefits, allowing sample preparation and amplification of DNA to be achieved on a single, miniaturised device (Balachandran et al., 2013).

2.5.1.1 The Point of Care

Microfluidic technologies have been shown to be particularly suitable for point of care testing applications (Jung et al., 2014). The point of care may refer to a GUM clinic, GP surgery, hospital ward or community setting (pharmacy, community centre) (Clerc and Greub, 2010). For sexually transmitted infections, this approach could be beneficial for timely diagnosis, preventing the adverse effects of long term infection (Natoli *et al.*, 2014). As can be seen in Figure 2-1 below, advances in point of care diagnostic technology bring testing devices to the table-top scale, allowing molecular diagnostics to be achieved in different contexts use.

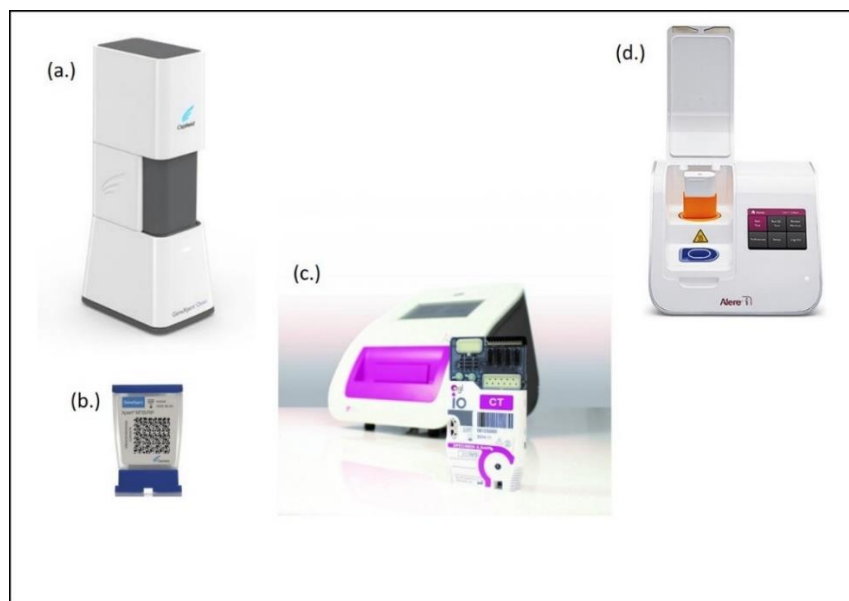


Figure 2-1: Point of care molecular diagnostics a = The GeneXpert Omni (Cepheid North America, 2015) uses PCR for TB and virology diagnostics at the point of care. b = GeneXpert standardised cartridge (Microbeonline, 2016) is used across the GeneXpert range of products for sample preparation. c = Atlas Genetics Io (Bath University, 2017) is capable of molecular Chlamydia diagnosis in 30 minutes d = Alere I Influenza A & B (Alere, 2017) for the molecular detection of influenza A and B at the point of care, facilitating a wider range of treatment options.

A noteworthy example of research into the expansion of contexts of use brought about by developments in point of care molecular diagnostics is the TTANGO (Test Treat ANd Go) project. In this project, GeneXpert diagnostic systems were used in difficult to access communities in the Australian outback (Guy *et al.*, 2013). In doing this, a rapid, sample in to answer out diagnostic mechanism for Chlamydia and Gonorrhoea was provided in the absence of an established laboratory.

2.5.1.2 Further Miniaturisation

Various research groups have approached the challenge of miniaturisation and cost reduction of genomic detection. A common theme in the design of these devices is the use of smartphones to provide a user interface and electronic control. This is fitting, as there are many examples of smartphones being used for various diagnostic applications at the point of care, for both in vivo (observation with no sample required) and in vitro (analysis of a biological sample) testing (Xu *et al.*, 2015). Myers and colleagues describe a handheld device controlled by a smartphone (Myers *et al.*, 2013). A battery powered, miniaturised, smartphone operated, molecular device for Chlamydia detection has been developed at Johns-Hopkins University (DeLong and Polen, 2015). Solar powered, smartphone driven molecular diagnostics have been proposed for use in remote locations (Jiang *et al.*, 2014). See Figure 2-2 below.

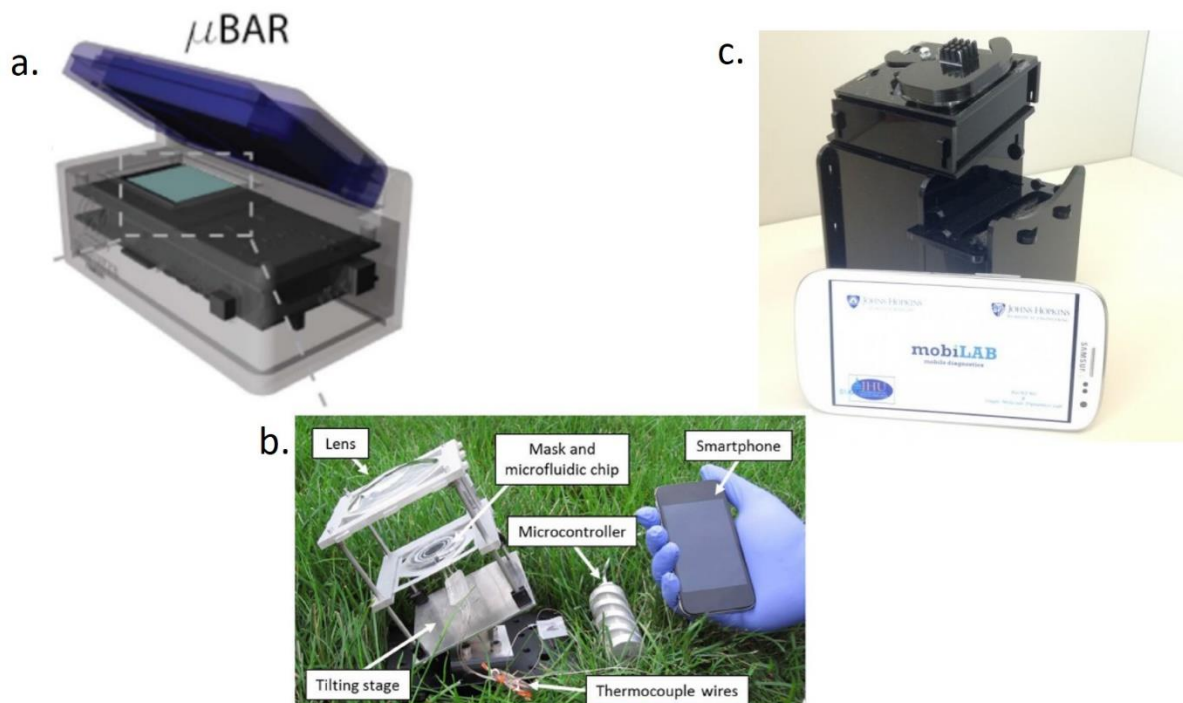


Figure 2-2: A. The MicroBar handheld, smartphone controlled genomic testing platform (Myers *et al.*, 2013). B. A solar powered PCR platform with smartphone (Jiang *et al.*, 2014). C The MobiLab Chlamydia diagnostic device (ScienceDaily, 2017).

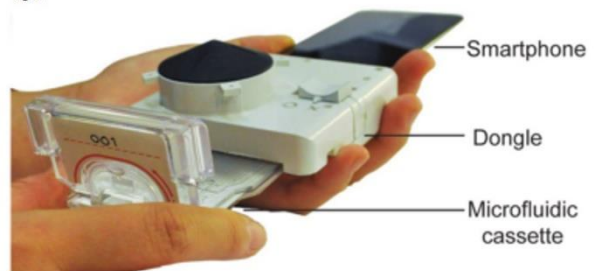
The above examples refer to molecular diagnostics. The use of smartphones in conjunction with lateral flow tests has also been proposed. These are ordinarily immunoassay tests, not as accurate as molecular diagnostics, but far faster from sample in to answer out. In one example, a rapid testing system attaches to the mobile phone camera using a clip on attachment that houses a lateral flow test, giving a 'better than the naked eye' reading of a test result (Mudanyali *et al.*, 2012). Other groups have proposed smartphone enabled reading of lateral flow and colorimetric tests without the use of a clip on attachment, utilising software that compensates for adverse light conditions and use error (Cooper *et al.*, 2011; Dell *et al.*, 2011; Yetisen *et al.*, 2014). Research has also demonstrated the use of the smartphone QR (Quick Response) code reader to identify the test being read (Lee *et al.*, 2011).

The many computational and sensing advantages of the smartphone are utilised in these examples, including GPS (Global Positioning Satellite) location tracking, memory storage, cameras, accelerometers (to sense the angle at which the phone is being held) a built in user interface and, in the case of Android phones, easily adaptable and reprogrammable software (Google Android, 2017).

a.



b.



*Figure 2-3: A. A smartphone based lateral flow test reader. The reader clips over the camera of the phone allowing it to read the line on the test, giving a 'better than the naked eye' result (Mudanyali *et al.*, 2012). B. A smartphone dongle based test, allowing the user to detect HIV antibodies, the fluidics in the test are activated by the user pushing the button on top of the dongle (Guo *et al.*, 2015).*

Smartphones are a useful research tool for demonstrating how portable diagnostic devices may function in the future. One example is designed as a plug in 'dongle' that directly attaches to the smartphone headphone socket and is capable of detecting HIV antibodies (Guo *et al.*, 2015). In this example, some user testing was carried out in a potential context of use. Currently, most smartphone based testing devices are being used to read colorimetric or lateral flow immunoassay tests, they are not molecular diagnostics. In future, accurate paper microfluidic molecular tests may function in the same way as a lateral flow immunoassay test (Xia, Si and Li, 2016) and be read using a smartphone.

The above provides a brief review of how research into molecular diagnostics is investigating how devices might be miniaturised, lowered in cost and controlled using portable computing technologies. The deployment of these devices for public use is an issue that fits into the broad definition of the translational research approach described above. Accurate, portable self-tests raise challenging questions for public health, clinical practice, patient acceptability and usability. An illustrative example of this is found in the HIV, lateral flow immunoassay self-test that has been approved for public use in recent years.

2.5.1.3 HIV Self-Testing

Most notable amongst publically available self-tests for sexually transmitted infections is the self-test for HIV (Human Immuno-Deficiency Virus) (Johnson *et al.*, 2014). The HIV self-test allows the user of the test to collect their own sample (a droplet of blood), apply it to the testing platform and obtain a result in minutes.



Figure 2-4: The BioSure HIV self-testing kit, which can be purchased for home use. The test requires a drop of blood from the user. One line appears on the lateral flow strip to indicate that the test has been successful, two lines indicate a positive result (BioSure, 2017).

The scholarly discourse surrounding HIV self-tests centres around how accurate they are (Ng *et al.*, 2012), how acceptable they are to patients (Krause *et al.*, 2013), how easy they are to use (Peck *et al.*, 2014) and how their use affects clinical practice and public health (Harding-esch, Nardone and Lowndes, 2015).

This shows that a similar approach is prudent where the development of self-use molecular diagnostics for Chlamydia is concerned. A broad appreciation of stakeholders, design requirements and potential contexts of use from the outset may bring benefits in clinical practice and public health later on in the lifecycle of the device. Design processes constitute a part of the research described in this thesis, consequently, the following is a review of typical design methods and design processes. The application of these methods and processes are explored further on in the thesis (Chapter 5).

2.6 Design Methods Overview

Design methods are the methods applied by the designer within a broader design process. The broader design process will likely involve numerous stakeholders, institutions and companies. Two design methods are repeatedly mentioned in the thesis; conceptualisation and development. A brief introduction to the two methods is provided below. Design processes and design process diagrams will be explained in further detail in later sections.

2.6.1 Conceptualisation

Conceptualisation is an information processing activity commonly found at the beginning of a design process (Lawson, 2006). Conceptualisation is the posing of potential solutions to a design problem using the available information.

The activity of conceptualisation refers to the period of time in which a diverse range of solutions to a problem are conceived. Research shows that decisions made in this phase of the design process heavily influence the future success of the product/device (Hsu and Liu, 2000). There is evidence that design intent even affects perceptions of a product when it is in use (Silva, Crilly and Hekkert, 2015).

Design concepts are often expressed by designers in the form of sketches but can be proposed by any stakeholder in a project using various means of communication (Pei, Campbell and Evans, 2011). These propositions are conceived with information about the design problem in mind and may be derived from a technical requirement, user need, material choice or the knowledge of a profitable market niche.

2.6.1.1 Concept Development Requirements

Concept development requirements are defined as the information that is required in order to formulate concepts. The origin and rigour of these development requirements strongly influences design decisions throughout the development lifecycle of the device (Pugh, 1991; Hsu and Liu, 2000). It is therefore essential that concept development requirements are meticulously formulated. This is well known in larger companies, where requirements engineers are employed for this task (Hagge and Lappe, 2005).

2.6.2 Concept Development

The development activity of a design process happens after initial concepts have been proposed. In the development phase of a design process, concepts are tested against the information available to stakeholders.

This process of conceptualisation, testing and adaptation of an idea is used by various stakeholders in the design process and is applied to every aspect of the artefact being designed. For example, prototypes may be built in order to test a function or the reaction of a user (Hartmann *et al.*, 2006). Similarly, different materials may be tested to see which is most appropriate for a particular application (Karana *et al.*, 2015).

A part of this research, shown in Chapter 5, is dedicated to how this process occurs when developing a working prototype diagnostic testing platform for sexually transmitted infections. Criticism of the process is provided and improvements are proposed as well as design guidelines and recommendations being made for future design activities for this type of device.

2.7 Design Process

The product development process is the mechanism by which technology or manufacturing companies create revenue and maintain a competitive advantage in the market place through the development of new products, new manufacturing methods or even new business models based around a new product or brand.

Design process diagrams depict how design activities occur in an organisation. It would be shown in a design process diagram that the information received regarding a design problem is contained in a detailed design brief or a specification (Pugh, 1991; Pahl, Beitz and Wallace, 1995). In fact, this information is likely to be gathered and applied gradually and iteratively by designers over the course of numerous meetings with various different stakeholders and from various differing information sources (Lawson, 2006). These seemingly opposing views describe the design process, an operationally useful concept companies use to manage their

design activities, and the methods of designing (explained in the previous section), which operate within the process but are not linear (Clarkson and Eckert, 2005).

Above, it has been argued that integrating the needs of many stakeholders' requirements and technical constraints is essential in the development of novel self-use molecular diagnostic devices. This requires a method for the management of large amounts of information. Fittingly, design engineering has been described as an information processing activity (Auricchio and Bracewell, 2013). Design process models are used to manage the large amount of information required to develop and distribute products, not least in the medical device industry (Linehan *et al.*, 2007; Medina, Kremer and Wysk, 2013).

An overview of the key components of the design process follows:

2.8 Stage Gated Design Processes

This formalised design structure can be expressed as a diagram with stages, a flow of direction and indications of the probable iterations within the process. When the design process structure is expressed in diagrammatical form, there are commonly numerous stages shown between the start and finish of the process, the titles of which are derived from the activities the designers, engineers and stakeholders in a project undertake at each stage (Cooper, 1990; Pugh, 1991; Pahl, Beitz and Wallace, 1995; Parraguez and Steven, 2015). Iteration is expected between each of the process stages.

2.8.1 Stage Gated Iterative Development Processes

Below is a description of Pugh's stage gated product development process (Pugh, 1991). This example is a good indication of the structure of stage gated design processes developed since, as will be shown below.

1. **Research/Specification Building:** The holistic gathering of information regarding the product which will be used in its design and development.
2. **Concept Development:** Using the information gathered in the research and specification phase, a number of concepts will be developed and assessed for their suitability by the team.
3. **Detail Design:** The information gathered through prototyping and from the research gathered initially will be used to determine which of the many concepts created in the previous stage will be developed further.
4. **Manufacturing:** Tooling, manufacturing lead times, the acquisition and processing of materials and components and other practicalities are considered at this stage of the process.

5. **Sell:** The initial sale of the device, depending on the industry into which it is introduced will be accompanied by post market surveillance and testing which will once again stimulate iteration in the process.

The stage gated, iterative form of the product design methodology is the predominant product design process used in the medical device industry (Linehan *et al.*, 2007; Medina, Kremer and Wysk, 2013).

A comprehensive literature review conducted by Stanford University involving 80 medical device development professionals concluded that a very similar structure was present in most medical device development processes (Linehan *et al.*, 2007; Pietzsch *et al.*, 2009). The five iterative, stage gated development steps proposed by Pietzsch and colleagues (2009) is shown below:

1. **Initiation, opportunity and risk management** – This is analogous to the research and specification stage described above.
2. **Formulation, concept and feasibility** – In the process described above, this is described as concept development. The iterative process described in the design methods section of this chapter of conceptualisation, assessment and iteration would occur here.
3. **Design and development, verification and validation** – Here the detail is designed into the concepts iteratively, where problems of integration between components and manufacturability are solved. In the Pugh process above, this is referred to as ‘Detail Design’.
4. **Final validation, product launch and preparation** – This is the point where the two processes differ slightly, as the Pugh process assumes manufacturing as a stage of its own. However, final validation of medical device design would have to involve manufacturing requirements.
5. **Product launch and post launch assessment** – This is analogous to the ‘sell’ stage of the Pugh process. A striking difference with medical device development may be that post launch surveillance is a safety critical activity.

2.9 Medical Device Design Processes

The emphasis on the use of product design process, which includes a well-defined design intent carried through a project and the use of a complete product design specification (PDS) has been shown to lead to successful product development (Cooper, 1990; Pugh, 1991; Pahl, Beitz and Wallace, 1995; Pietzsch *et al.*, 2009; Sommer *et al.*, 2015). Underestimation of the importance of a defined design process leads to manufacturing or product failures (Millward and Lewis, 2005).

The analysis of a number of SME's (Small to Medium Enterprises) specialising in medical device development has shown that those who rigorously adopt the use of a PDS and maintain clarity of design intent are notably more successful in the field than those that do not (Walters *et al.*, 2001).

2.9.1 Regulatory Requirements and Design Process

The consideration of regulatory requirements is a vital and integrated part of any medical device development process. Standards and regulatory agencies propose rigorous design methods for companies to follow. The International Electro-technical Commission (IEC) regulation 62366 shows an iterative development model designed to ensure a high level of usability is guaranteed in a new medical device. The FDA Centre for Devices and Radiological Health (CDRH) Medical Device Innovation Initiative proposes a similar, iterative design process model for the full lifecycle of a device. Both demonstrate that the medical device industry takes seriously the use of iterative design processes to ensure products are technically sound and safely usable (FDA, 2014).

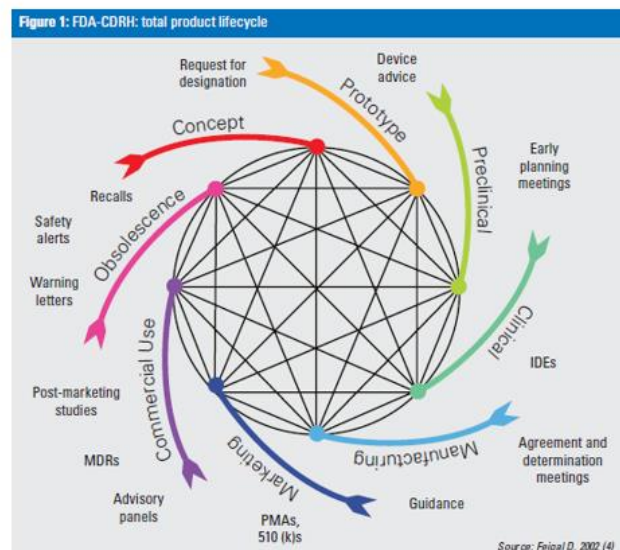
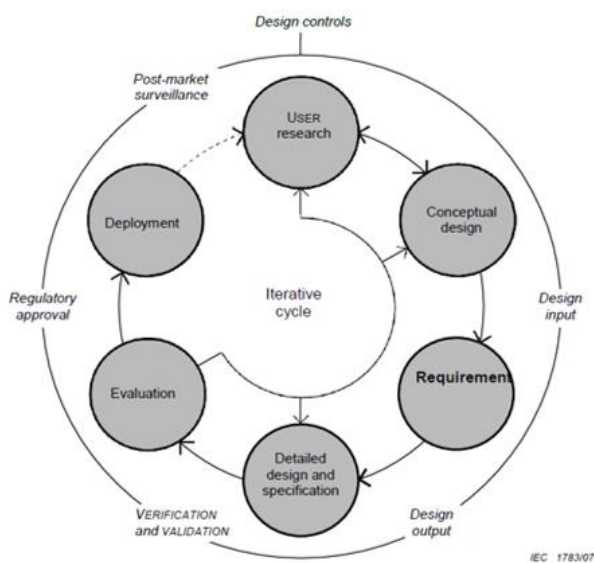


Figure 2-5: Left, The International Electro-technical Commission (IEC) regulation 62366 and right, the FDA Centre for Devices and Radiological Health (CDRH) Medical Device Innovation Initiative design process model (Linehan *et al.*, 2007)

These iterative processes are designed to be used in conjunction with stage gated development processes. Comparisons can once more be drawn between the Pugh design process shown

above and the FDA Innovation Pathway design process for medical device development, shown below in Figure 2-2.

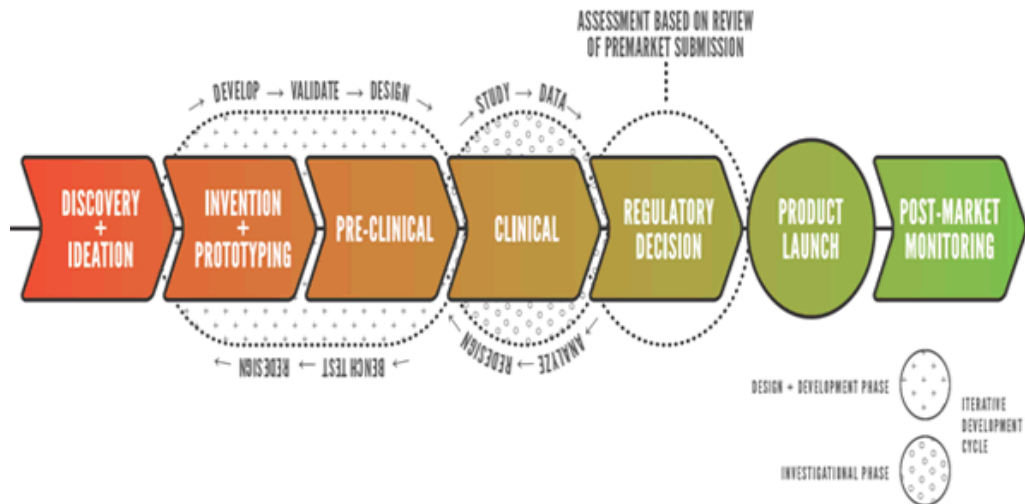


Figure 2-6: The FDA Innovation Pathway 2012 Full Development Cycle for Medical Devices, designed to speed up the process from research innovation to product roll out (FDA, 2014)

serious problem contributing to treatment errors (Kohn, Corrigan and Donaldson, 2000; Buckle *et al.*, 2006; Carayon, 2010) and devices are commonly designed in isolation from the systems for which they are intended. With the proposed new paradigm of diagnostic testing, where an entirely untrained user will be operating the testing device, margins for error must be managed even more carefully.

2.10 Systems, Human Factors and Ergonomics in Medical Device Design Process

The improvement of patient safety in medical device design requires that a broad approach is adopted, taking into account the context of use in which the device would be used at the same time as the initial design stages of the product. Research suggests that an approach that takes into account systems, human factors and ergonomics produces better device outcomes and reduces healthcare costs (Buckle, 2012; Hignett *et al.*, 2013). A similar approach is implied in the definition of translational research described above. Below, in Figure 2-3, requirements for the product are defined in context of the medical system.

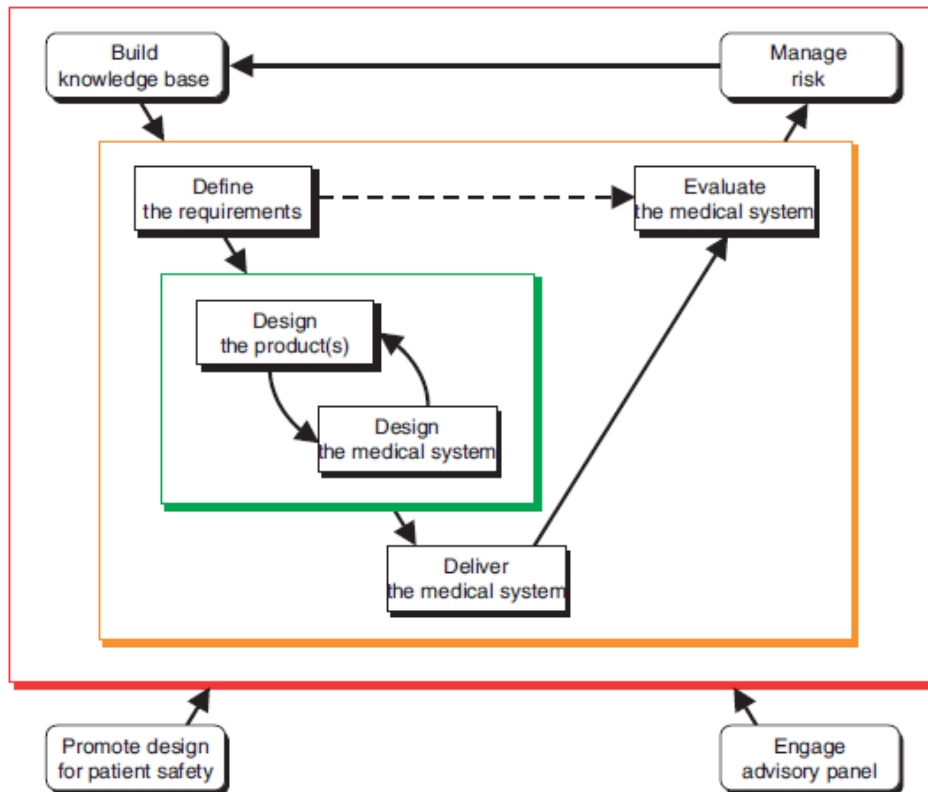


Figure 2-7: Medical devices should ideally be designed with rigorous consideration of the system within which they will be used (Buckle *et al.*, 2006)

The design of self-use molecular diagnostic device for sexually transmitted infections will likely be achieved using the stage gated design process shown. Iterative processes will be used to apply the design methods described to ensure that concept development requirements are satisfied. Regulatory requirements have a significant influence over the structure of the design processes that companies must use. Research suggests that the introduction of self-use or personalised diagnostics will require changes to the regulatory landscape (Milmo, 2015).

Consideration of systems, ergonomics and human factors in ensuring the development of safe, self-use diagnostic devices will be essential, as has been shown by various studies (Privitera and Murray, 2009; Waterson, 2009; Hignett *et al.*, 2013). There are considerable barriers to be overcome in involving users directly in the medical device design process, particularly where human factors and usability requirements are concerned (Privitera, Evans and Southee, 2017). These factors will have to be considered for the successful development of self-use molecular diagnostic testing devices in future.

2.11 Design Process for Self-Use Molecular Diagnostic Devices

There is a gap in the literature where design process for self-use molecular diagnostic devices is concerned. The closest equivalent research area is design for home use medical devices. In a similar vein to the translational research approach described above, Bitterman proposes that the design of home use medical devices requires increased collaboration between the varied stakeholders involved, including engineers, clinicians and patients (Bitterman, 2011).

As home use medical devices have been in use for some years, detailed assessments can be made of the human factors and usability requirements of devices in use, particularly where associated medical conditions are a factor (Fung *et al.*, 2015). Similarly, design methods such as inclusive design can be explored for designing devices that use established technologies in the home (Cifter, 2011).

Self-use molecular diagnostic testing will be enabled by technologies which are novel. The problems with commercialising novel diagnostic technologies have been recognised in the literature and a bottleneck beyond the proof of concept stage is known to exist (Chin, Linder and Sia, 2012; Volpatti and Yetisen, 2014). Research efforts in the field are only just beginning to consider the development process required beyond initial proof of concept stages. Kumar and colleagues integrate field testing into their process of developing novel, portable diagnostics, with the intention of accelerating the pathway from benchtop to use in the field (2015). Guo and colleagues have integrated simple usability testing into the assessment of their diagnostic design, giving an indication of how amendments can be made for future versions (2015). Nayak and colleagues link use-cases to point of care diagnostic technologies in detail, taking into consideration technological requirements, cost and infrastructure (2017).

As has been shown, while there are research efforts being applied to the many disruptive possibilities presented by self-use diagnostic technologies, much of this research is being carried out in the biomedical engineering, biosciences, public health and clinical science fields. There is, as yet, little in the way of an academic understanding of how, and when, industrial product design methods and processes should be applied to the design and development of such technologies.

2.12 Summary

The case study technology which is the subject of the action research described in Chapter 5 is for the detection of *Chlamydia trachomatis*, as a result, this chapter opened with an overview of the sexually transmitted infection with an explanation of why it is a clinical and public health priority. An overview was then given of the potential public health implications of self-use molecular diagnostics for STIs. This provides the background for a key design requirement

described in further detail in Chapter 3. A description of translational medical device research was included with an emphasis on its multidisciplinary nature, which is reflected in the formulation of a design process model in this thesis.

A review of the state of the art technology in the field was provided, showing that smartphone technology features frequently in the literature regarding miniaturised and low cost diagnostics. Design methods were then introduced, leading into an overview of design processes, showing that versions of the stage gate process proposed by Pugh in the 90's is still in common use in the medical device development field. Medical device design processes are then discussed, demonstrating that regulatory requirements govern design process in many respects.

Finally, a description of how systems, human factors and ergonomics improve medical device design is provided and compared with the theories of translational research introduced at the beginning of the chapter. A gap in the literature was identified, where design process could be applied to early research into diagnostic technologies. This has only relatively recently become a priority for point of care and self-use diagnostics research. In the next chapter, expert interviews and a survey of design professionals are described that begin to contribute toward this gap in the literature.

Chapter 3

Expert Stakeholder Interviews and Professional Designer Survey

3.1 Introduction

Chapter 2 provided background for the research studies described in Chapters 3, 4 and 5. It was shown that there is extensive research being carried out in the field of novel, portable diagnostic technologies but little in the way of research into how these technologies might be developed beyond the proof of concept stages. In order to begin to address this, one of the objectives of this thesis is to clarify what the concept development requirements for self-use molecular diagnostics for STIs should be.

The research described in this thesis was carried out in collaboration with the eSTi² research consortium which comprises experts from various disciplines related to diagnostic development. Interviews with a selection of these experts provided an initial indication of concept development requirements and the issues and barriers associated with device development. This chapter describes the interviews of six of the expert stakeholders who were involved in the eSTi² consortium project. Interviews were carried out by the author in the last year of the project, ensuring that a comprehensive impression of requirements, issues and barriers could be formulated.

Also included in this chapter is a short survey of professional designers that gives an indication of the design process requirements of medical device design and development companies.

Below, the research aim and objectives for the interviews are described and placed in context of the objectives of the thesis. Justification and description of the methods used when carrying out interviews and analysing the subsequent data is also described. A results section where the qualitative interview data is analysed by content and theme is included. A brief summary of the short survey of professional designers is included and finally, a statement of the limitations of the study is given with a summary of the chapter.

3.2 Aim

The aim of the interview research study and professional designer survey was to provide a broad, multidisciplinary selection of viewpoints on the concept development requirements for a self-use molecular diagnostic device for sexually transmitted infections, potential issues and barriers and possible design approaches.

3.3 Objectives

The objectives of the interview and survey research were as follows:

- To identify concept development requirements from a number of different points of view based on area of expertise.
- To identify and compare issues and barriers associated with device development from a number of different points of view based on area of expertise.
- To identify design process requirements from the point of view of design professionals.

3.4 Objectives in Context of the Thesis Objectives

The research studies described in this chapter partially fulfil objectives 2 and 6 of the thesis.

Firstly, the interviews partially satisfy Objective 2, described as follows:

Objective 2: To identify concept development requirements for self-use molecular diagnostic devices for STIs.

Conclusions drawn from the interview data also partially satisfy objective 4 of the thesis.

Objective 4 is as follows:

Objective 4: To describe issues and barriers inherent in the development of self-use molecular diagnostics for STIs.

3.5 Justification of Methods

3.5.1 Interviews

Interviews were conducted, transcribed verbatim and analysed qualitatively. The qualitative analysis of interview data was appropriate for an exploratory study such as is described in this chapter (Kvale, 2007). An attempt at acquiring the same information using a quantitative survey method would have required that the author knew which areas were most appropriate to enquire about in advance. As the interviewees were all highly experienced experts, this would not have been appropriate or yielded satisfactory results. A qualitative survey method would have removed the advantage of the author being present and able to follow up interesting and productive lines of enquiry.

Interviewing experts who had recently been involved in the eSTi² research consortium provided access to up-to-date information about their wider field of expertise. Further, with each of the experts interviewed being an active participant in their field, the information they provided may not be available in the published literature.

Interviewing experts from different fields independently as opposed to in a focus group environment avoided the eventuality of a minority of outspoken participants dominating the

conversation (Smithson, 2000). This avoided a biasing of the outcomes of the research toward one area of expertise.

3.5.1.1 Justification of Interview Analysis Method

Interview content was analysed using a deductive coding method. Deductive coding was appropriate where areas of interest were known by the author in advance, for example “Test Design Requirements”. This method of analysis of the interview data was appropriate as each of the interviewees came from a different area of expertise and were likely to have different answers to the same questions. Therefore, the deductive coding method, used in this instance, gave a broad overview of the differing points of view of each interviewee on the design requirements of the device. This data would contribute toward the creation of design requirements for the device as well as highlighting differences of opinion on device design between members of different disciplines.

Themes in the interviews were identified using an inductive coding method. Inductive coding allowed the author to identify potential themes as they appeared in an interview. Through the process of inductive coding, themes were identified where a subject was repeated by different interviewees without direct prompting from the interviewer. The inductive coding method contributed particularly to the identification of issues and barriers to device development which could not have been anticipated by the author in advance.

An example of deductive coding taken from the interview data is shown below in section 3.6.3.1. An example of inductive coding for the identification of themes in the interviews, showing the nodes that were identified through coding, is shown below in section 3.6.3.2.

3.5.2 Survey

An online qualitative survey method aimed at professional designers was carried out to enquire about design processes for medical devices. Due to the geographically distributed nature of design consultancies and companies, this online survey method allowed the author to reach as many participants as possible in a short amount of time.

The survey questions were designed to ensure that answers could be given regardless of the type of medical device the participant had worked on. If they had not worked on medical devices, they were given a short explanation of the self-use diagnostic device and asked to suggest which design methods they would apply to the problem. This ensured that some information could be gleaned from all participants.

Had focus groups or interviews been used to obtain the data, an untenable amount of organisation and time would have been required to attain results. When these methods were

suggested by the author to design companies, constraints of company time and concerns about the protection of intellectual property were cited as reasons why a different method would be more appropriate.

3.5.2.1 Justification of Survey Analysis Method

The data created through the survey of professional designers was analysed using a deductive coding method which was designed to show the overall opinions of professional design practitioners in two key areas. Firstly, design processes commonly used in medical device design and secondly barriers and difficulties that are commonly encountered in medical device development.

In a similar fashion to the deductive coding method used to analyse content in the interviews, deductive coding of the content of the survey responses provided a broad overview of the opinions expressed by different participants. Analysis of this data allowed the author to draw conclusions that could be generalised to the practice of medical device design.

The response rate of professional designers for this survey was low, the reasons for which are discussed in section 3.9 of this chapter. Therefore, the complete transcript of survey responses is shown in Appendix B. Minimal coding was required to draw conclusions from the data available. An analysis of the responses provided is shown in Section 3.8.1 below.

3.6 Interview Method

3.6.1 Interviewees

Six interviewees were chosen from different fields of expertise for this interview study. The interviewees were sent invitation letters by email explaining the purpose of the research and what would be required of them. In the emails, it was explained that ethical approval had been obtained to record their responses and that their responses would be anonymous. Consent forms were signed by each of the interviewees. Evidence of ethical approval is shown in Appendix A.

All the chosen interviewees have collaborated with the eSTi² research project and are from disparate fields of expertise. See figure 3-1 below for a description of the interviewees and their respective fields of expertise and background.

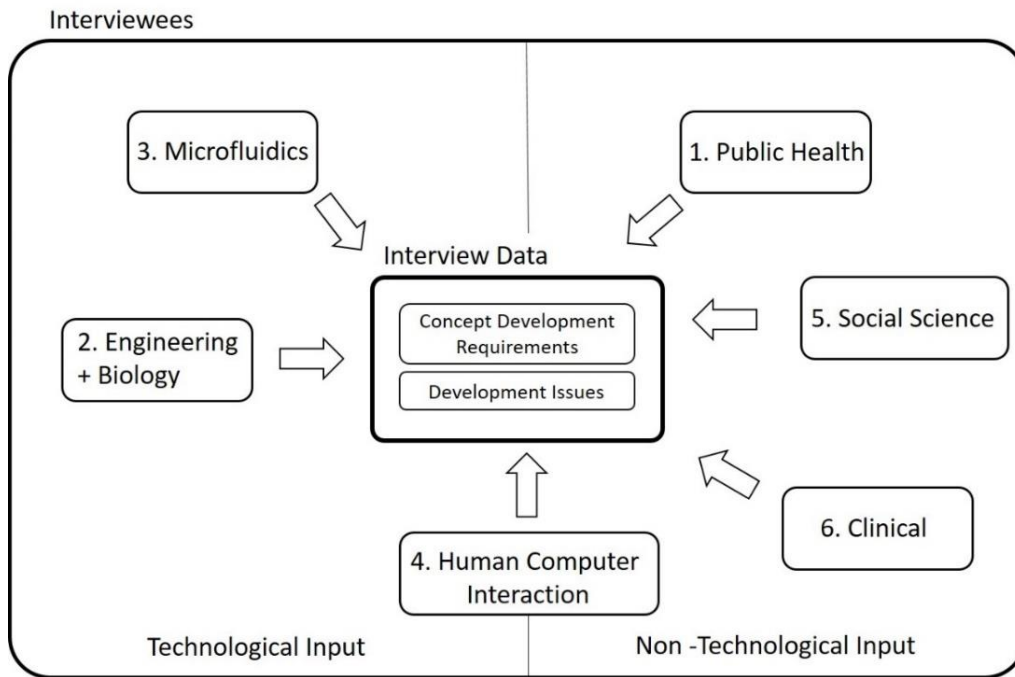


Figure 3-1: Interview data drawn from different inputs from either technological or non-technological backgrounds is consolidated in the interview data described in this chapter. The inputs are numbered in the chronological order in which the interviews took place, further information on the qualifications, fields of expertise and background of the interviewees is shown below in Table 3-1.

A description of the professional positions and research areas of each of the six interviewees is provided below. The interviewees are shown in the chronological order that they were interviewed. The interviewees have been given pseudonyms for the sake of anonymity and ease of description in the text. Each of the interviewees is qualified to doctoral level.

Table 3-1: Interviewee Information

Number in Figure #	Pseudonym	Professional Position	Research Area
1.	Laura	Principal Public Health Scientist	Epidemiology, public health and diagnostic evaluations
2.	Lee	Postdoctoral Research Fellow	Bioengineering and molecular biology
3.	Kara	Lecturer	BioMEMS (Microelectromechanical Systems), microfluidics and sample preparation for point-of-care molecular diagnostics

4.	Sharon	Reader	Human computer interaction (HCI) and human factors
5.	Samuel	Postdoctoral Research Fellow	Social science, impacts of new technology on health care delivery
6.	William	Reader and Consultant Physician	Sexual health and HIV (Human Immunodeficiency Virus) medicine, personalised medicine technologies, antimicrobial resistance testing and eHealth care

3.6.2 Interview Questions

The interviews were carried out using a semi-structured interview method over a time period of between 25 and 35 minutes. A guideline interview schedule was used for each of the interviews to ensure that the structure of each interview was approximately equivalent. The guideline interview structure was as follows:

3.6.2.1 Guideline Interview Schedule

1. What is your disciplinary area and your role within the eSTi² project?
2. From the point of view of [*your area of expertise...change as appropriate*], what attributes/features would be essential to see in a self-use molecular diagnostic device for STIs?
3. From the point of view of [*your area of expertise*], why are these attributes/features essential, are there any that absolutely could not be left out?
4. What are some of the barriers to achieving/developing a device with these features?
5. Broadly speaking, what do you think is the key technology which will (or has already begun to) enable self-use molecular diagnostic testing?
6. Is there anything that you see as a vital feature for a self-testing device for sexually transmitted infections that we haven't talked about?

The first half of the schedule (questions 1 – 3) addressed the question of what the preliminary concept development requirements of the proposed self-testing device might be. The interviewees were asked what features should be present in the device and what attributes the device should exhibit. Features and attributes of a device are defined as follows:

Features: Features of the device are physical features like size, appearance and weight. A feature can also contribute toward a technical requirement of the device. For example, a sample

collection device is a feature for collecting urine samples. Likewise, an isothermal amplification method is a feature associated with the low-cost detection of DNA.

Attributes: Attributes of the device are conditions that the device must meet. For example, attributes of the device are that it is easy to use, rapid, or portable or can be used in various different environments.

Questions 4 and 5 of the schedule were designed to provide an indication of issues and barriers associated with the design and development of the proposed device.

The final question was designed as a prompt to talk about any further features that it might be important that the device should exhibit i.e. things that may have been brought to mind as a result of talking about the issues and barriers associated with development.

The questions were adapted to be specific to the field of the person being interviewed. As the interviews were semi-structured, lines of interesting questioning were followed where relevant information could be gained by doing so. Interview questions tailored to the interviewees, invitation letters, ethical approval information and full transcripts of the interviews are shown in Appendix B.

3.6.3 Recording, Transcription and Analysis

The interviews were recorded on an iPad using the Voice Record Pro application. The interviews were then transcribed and coded using qualitative data analysis software (QSR International Pty Ltd, 2012). Following transcription, the interview transcripts were analysed. Statements in the interview transcripts were coded to identify relevant content and themes.

In the case of content analysis of the interviews, a deductive coding approach was adopted as the author was already aware of the desired data points, i.e. 'area of expertise', 'role within the eSTi² project' or 'essential features of the device based on your area of expertise'. When investigating issues and barriers or exploring further potential features the device may exhibit, an inductive, exploratory coding method was used, allowing themes to emerge from the transcript (See also 'Thematic Analysis' below) (Elo and Kyngäs, 2008).

Table 3-2 - Coding Scheme

	Role in eSTi²	Device Features	Device Attributes	Issues and Barriers
Content	✓	✓		
Theme			✓	✓

3.6.3.1 Content Coding

Content coding deductively captured statements describing the expertise of the interviewee, their role within the eSTi² project and their opinion on what the features of the proposed self-test should be. The data node titles for content coding were defined in advance of analysing the transcriptions of the interviews. Statements from each interview were categorised using the nodes shown in Figure 3-2 below.

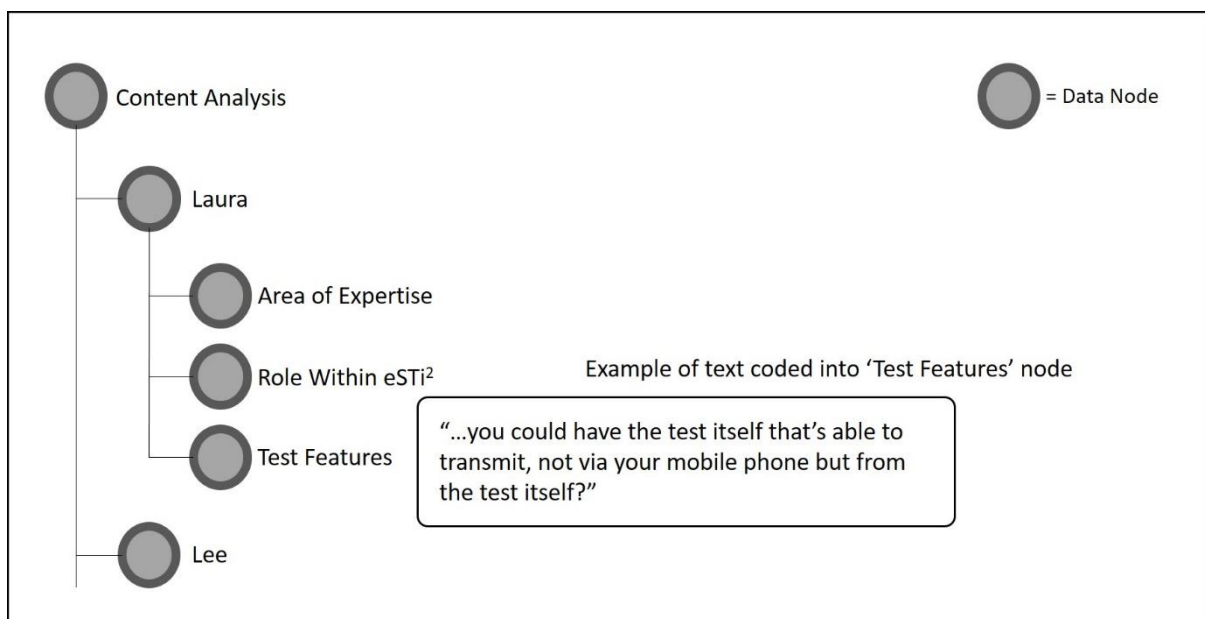


Figure 3-2: Relevant sections of text were coded into nodes that described their content. The nodes entitled 'Area of Expertise', 'Role Within eSTi²' and 'Concept Development Requirements' were used for each interviewee.

Shown below in Figure 3-3 is an example of the content coding used for this study in a screenshot taken from the NVivo qualitative data analysis program. The example shows nodes representing the content analysis questions posed to Kara and Laura during their respective interviews. The sources column shows that each node has one data source (the interview transcript of that interview). The references column to the right of this shows the number of

quotes which have been taken from the interview transcript which relate directly to the content type identified in that node.

The quotes referred to above are shown in the analysis of the results below in sections 3.7.1, 3.7.3 and 3.7.4.

Name	Sources	References
Content Analysis Interviews	0	0
Kara	0	0
Area of Expertise	1	2
Role within eSTI2	1	5
Test Design	1	3
Laura	0	0
Area of Expertise	1	4
Role within eSTI2	1	6
Test Design	1	2

Figure 3-3: An example of content coding taken from the NVivo qualitative analysis software.

3.6.3.2 Thematic Coding

Thematic analysis was used to inductively establish expert opinion on the attributes of the proposed device. Themes were established when statements about an attribute were made by more than one of the interviewees. Thematic data nodes were named as themes emerged during the analysis of the transcriptions. For example, if more than one interviewee made a statement regarding the ‘context of use’ of the device, a thematic node was established named ‘Context of Use’.

Thematic analysis was also used to identify issues and barriers associated with the design and development of the proposed device. A data node was named ‘Issues and Barriers’. Multiple themes were identified within the theme of issues and barriers and sub-nodes were created as these themes emerged. See also Figure 3-4 below.

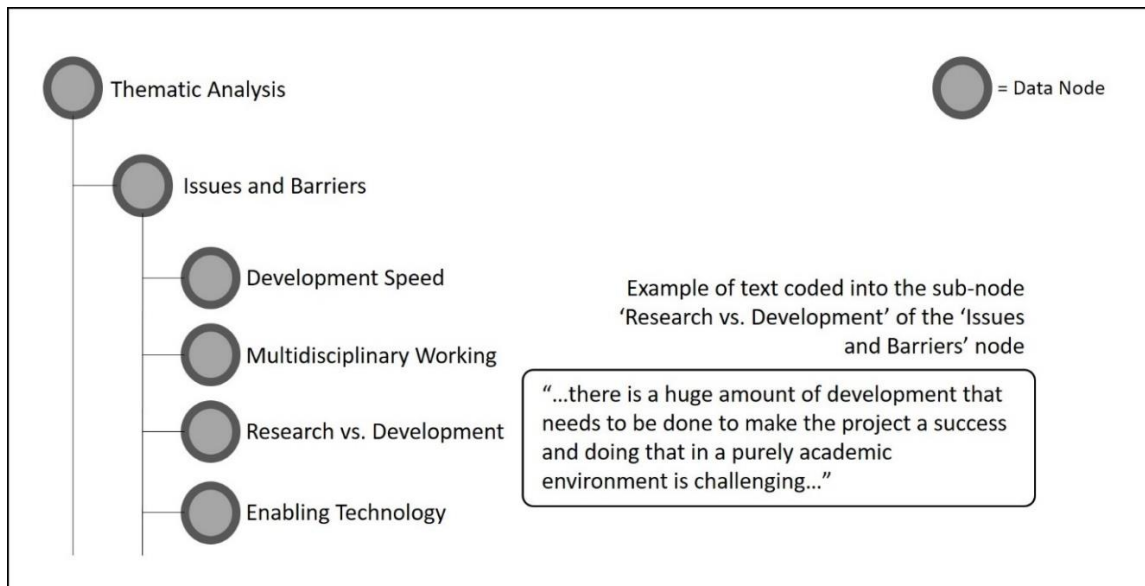


Figure 3-4: Relevant statements from the text were coded into nodes that described them thematically. These node titles were not predefined and emerged during the analysis of the text.

Shown below is an example of thematic coding. The example shows the thematic nodes which were identified as the analysis of the interviews progressed over time.

Nodes			
Name	Sources	References	
William		0	0
Thematic Analysis Interviews		0	0
Clinical Considerations		3	13
Context of Use		6	19
Cost		5	9
Development Issues		6	48
Guidelines and Regulations		1	2
Human Factors		6	31
Market		3	12
Patient Acceptability		2	13
Public Health		2	4
Sexually Transmitted Infections		3	4
Surveillance		3	19
Technology		4	13

Figure 3-5: An example of thematic coding taken from the NVivo qualitative analysis software.

Once again, the sources column identifies how many of the different interviewees spoke about each theme, for example, the theme of “Development Issues” was identified by all the interviewees, with 6 sources shown. Within this theme, 48 references, i.e. quotes taken from the interview transcripts, have been recorded. Below, figure 3-6 shows how the theme of “Development Issues” was further subdivided thematically to give a clearer picture of the issue being communicated by the interviewees.

Nodes			
Name	Sources	References	
Clinical Considerations		3	13
Context of Use		6	19
Cost		5	9
Development Issues	6	48	
Design		4	14
Development Speed		2	6
Multidisciplinary Working		2	7
Open Source		1	3
Guidelines and Regulations		1	2
Human Factors		6	31
Market		3	12
Patient Acceptability		2	13
Public Health		2	4
Sexually Transmitted Infections		3	4
Surveillance	3	19	
GUMCAD		1	1
NATSAL		1	2
Public Health England		1	2
Technology	4	13	

Figure 3-6: An example of thematic coding taken from the NVivo qualitative analysis software. The subdivisions of the “Development Issues” theme and the “Surveillance” theme are highlighted. The intention of this subdivision was to increase the depth of the analysis.

The quotes taken from the interview transcripts which were associated with these thematic nodes are shown below in sections 3.7.2 and 3.7.4.

3.7 Results

3.7.1 Content Analysis

The data was first analysed for content and then analysed for theme. Content comprised partly of information about the expertise of the interviewee and their role in the eSTi² project. A summary of the expertise of the interviewees can be seen in Table 3-2 above. Table 3-3, below summarises the roles that the interviewees played in the eSTi² project.

Table 3-3 - Interviewee Roles in eSTi²

Pseudonym	Role in eSTi ²
Laura	<p>Laura said that she has</p> <p>“...an understanding of the surveillance systems in place, how the data are collected...and therefore as we look at the STI technologies...what they look like now but what they may look like in the future [and] what the impact on surveillance would be.”</p> <p>and as a result was able to advise project partners on how to develop their diagnostic tests so that they might</p> <p>“...have the biggest public health impact and utility clinically and at the public health level.”</p>
Lee	<p>Lee worked on the development of assays and novel enabling technologies for the detection of sexually transmitted infections. In his own words</p> <p>“...they had a DNA extraction system somewhat complete and they needed an assay that would take that DNA that was extracted and detect...the most common sexually transmitted infections seen in the UK which [were] Chlamydia, Gonorrhoea [and] Mycoplasma Genitalium...so these were the targets I was developing assays for initially. And then that project...expanded to include the development of the hardware that would detect the amplification products.”</p> <p>Lee’s contribution to the project was the development of a miniaturised, low cost molecular detection platform for STIs.</p>

Kara	<p>Kara was involved in the development of microfluidic, lab-on-a-chip technologies, working toward sample preparation and amplification being accomplished on a miniaturised platform. She said</p> <p>“...I wasn’t just working on the microfluidics, I was also working on lysis and nucleic acid extraction, and so that was another part of my role...I developed a nucleic acid extraction membrane, just like a paper membrane which was coated in this biopolymer called Chitosan.”</p> <p>Kara’s work was directed toward the miniaturisation of sample preparation methods, preferably onto one integrated chip. This would allow nucleic acid extraction, amplification and DNA detection to happen on a single microfluidic chip.</p>
Sharon	<p>Sharon explained that her role within the eSTi^s project was</p> <p>“...to lead on the user interface design for the app that we ended up developing.”</p> <p>She went on to elaborate</p> <p>“In terms of [the app] we’re thinking about...how the end-user would use the product, how they’d understand the use of the product and how you then design to fit around user cognition.”</p> <p>She went on to explain how this was achieved:</p> <p>“We used a user centred design process and we started by running focus groups to understand the features that people would want from this kind of care pathway with...an example technology probe of what it might look like.”</p> <p>This research allowed Sharon to advise partners, researchers and app developers on human factors and human computer interaction requirements.</p>
Samuel	<p>Samuel interviewed young people aged 16-24 for the eSTi² project. From his point of view, the</p>

	<p>“...issues around self-testing are a lot about trust and it’s not just trust in the device, it’s trust in an individual’s ability to test themselves accurately, to sample themselves accurately and do the test correctly.”</p> <p>He used those interviews to ask the question</p> <p>“...what can we do to increase the chances of patients coming in...getting the right patients coming in, getting the test that they need, getting the diagnosis that they need, getting the right treatment and therefore stopping the chain of onward transmission of infection?”</p> <p>This enabled Samuel to advise the group on the acceptability and usability issues associated with a novel self-test.</p>
William	<p>William coordinated multidisciplinary teams of people across universities and industry, playing a leading role in</p> <p>“...the development of novel technologies for diagnosing sexually transmitted and other infections. Particularly molecular based, microfluidic and Nano-technology technologies that are both multiplexed and rapid.”</p> <p>He went on to explain that the wider role of the eSTi² group</p> <p>“...is to expand infectious disease research capacity as well as support the development, evaluation, implementation and deployment of cost effective and rapid, novel technologies for improving both STI care and reducing the burden of STIs in public health. As well as impact on antibiotic resistance.”</p> <p>From a management position, William was able to direct partners and researchers in the group on the clinical and technological requirements of the proposed device.</p>

3.7.2 Thematic Analysis on Design Features and Attributes

When talking about the possibilities for device design, interviewees were likely to suggest a device attribute, for example the attribute of being low-cost, rather than propose a well-defined design feature that would make the device low in cost. Each of the following attributes were

talked about by more than one of the interviewees.

The identified themes have been sorted into order of how many interviewees commented on each theme. Due to the small number of participants and the high level of expertise of the interviewees, it cannot be suggested that this proves the significance of one theme over another. It does, however, indicate that some themes are acknowledged across various disciplines.

3.7.2.1 Attribute Theme – Low Cost

The attribute of the device being low-cost was expressed by four of the six interviewees. From the engineering perspective, Lee expressed this as the key driver of engineering research projects with the goal of molecular self-testing in mind:

“Cost was the deal breaker...if we wanted to make this device for a million dollars, it would be easy...I mean, these devices already exist, at a high cost, they already exist in a large size...so size and cost I think were the two attributes that drove it, and cost being the primary one...it can easily be done at a high price, doing it cheap is the hard part.”

If the cost of the device to the consumer must be low, this has a direct impact on the engineering and design requirements of the device. There were other arguments expressed by the interviewees which pointed toward the need for a low-cost device. The very low cost of the device was important from the perspective of device access and user acceptability according to Samuel, who explained that

“...when you get into a situation where it’s on a shelf next to the pregnancy test in a grocery store and it’s cheap, you know, really cheap. Or you have the option of getting it for free in a pharmacy well that’s something...you’re looking at something that’s much, much more acceptable...and much more of an opportunity for young people to test.”

Sharon, drawing on her research on the human factors and human computer interaction requirements of a self-test, suggested that a driver of device cost might be where the designers of the device chose to place the required user interaction. Sharon posed the question, should the interaction with the testing device be through the device itself or through a second device, like a mobile phone? The argument was that using a mobile phone for user interaction could be beneficial from a cost perspective

“...because the complexity of the interaction that has to take place if you move beyond just getting a result means that you’d have to develop quite a complex

stand-alone device in order to do that which you probably don't want to do...for cost [reasons]"

The need for a low cost was argued on the basis of portability and user interaction by Sharon and Lee. William, from his point of view of interacting with multidisciplinary teams from both industry and academia, was able to provide a summary of the links between portability, affordability and the technology available. Initially, William stated that the ideal self-test would have to be

"...affordable...you can't buy a massive kit each time you want to have a test."

However, he went on to discuss that the technology required to achieve this goal remains unclear. From the technological perspective, the affordability and portability of a molecular self-test may, with the current state-of-the-art technology, present an issue. A molecular test would require

"...signal detection and usually require a reader of some kind and I think the readers will get smaller and smaller but you're not going to keep a reader in your house in any meaningful sense like the ones that we know about. They're going to be deployed in different places and different outlets like pharmacies."

This demonstrates that while affordability and portability (See below in Portability/Context of Use, Section 3.7.2.4) are perceived to be desirable attributes for the device, the technology required to make the proposed device affordable and portable is a notable barrier. William went on to elaborate on the direction this technological development is likely to take:

"There are ways in which you can have your own reader, which is your mobile phone...mobile phones will be your readers, so there are already programs of work in which the mobile phone is the reader of the test. Not just lateral flow tests but other kinds of tests and there's actually some types of very complex technology that is handheld. So I'm pretty certain that the potential for self-testing will be at the end of the phone or some type of similar hand held gadget that is personally owned."

It has been shown then that the expert interviewees thought it essential that the device be available at a low-cost. The last statement that William made above introduces the idea that the testing device may have to be associated with a computing and communication device like a mobile phone.

3.7.2.2 Attribute Theme – Smart Device or Smartphone Operated Device

The subject of whether the future of self-testing devices should be smartphone operated or the devices should be smart in themselves was identified as another theme discussed by multiple interviewees. William went on to elaborate on his previous comments, suggesting that the ideal device may not be smartphone operated, but smart in its own right:

“I think, for me what we should be aiming for is actually a device (mobile phone) free platform. That’s what I think...A device free molecular test...so the paper microfluidics are kind of lending itself to that but they still need some kind of signal detection. I don’t think it will be too long before we find something where actually you can get a highly accurate molecular type test, a bit like a lateral flow test but which is based on much higher accuracy, that either incorporates some kind of amplification of products or signal or something that allows you to really increase and ramp up sensitivity while maintaining specificity that is just easy, you don’t even have to have your phone with you.”

Here, the suggestion has been made that signal detection and therefore complex electronics, are included in the testing device. Statements made previously by Laura about data collection, would further suggest that a testing device like this would also need to collect and transmit data. When discussing the need for a self-testing device to collect data not just about the result of the test but about the person doing the test, Laura was ambiguous about how this might be done, saying that a smartphone or tablet might be used, or

“...you could have the test itself that’s able to transmit, not via your mobile phone but from the test itself?”

Laura asserted strongly, as has been shown above in the content analysis, that there was a definite need for the collection of the data, but how that data might be collected was not a priority from the point of view of disease surveillance. The mobile smartphone, however, remains the most portable and sophisticated technology available to explore the possibilities of remote self-testing. Looking at it from this perspective and the point of view of human computer interaction, Sharon reflected that the technological way the data were collected raised many questions:

“The initial kind of vision was that maybe it was something that you plugged directly into your phone and even used the power from your phone to run the test and if that was the case you could theoretically upload the result directly from the test itself, which removes a certain amount of difficulty from a user

perspective. But if they are envisaged as separate devices and there's some communication either between them or via the cloud...it's more likely that [the test] would communicate to the cloud to get [the] test result and then the cloud would communicate back to an individual users device which raises the question of how you either tell the device how to contact the user...or [how] the user identifies the test that they've used."

This statement suggests that, while the test may not include a complex user interface, the test itself should be smart in some way, at least to the point of being able to communicate whether or not it has recorded a positive or negative result. Also, it raises the issue of the user being able to identify the test that has been taken when looking at the result on their mobile device. Sharon suggests that there are potential problems with the test visually, rather than electronically, indicating a positive or negative result without a mobile phone or some other device involved:

"[The users] might expect, you know, [the] pregnancy test analogy, [which] would say that you get your line that shows whether you're pregnant or not, so you get your line that shows whether you've got Chlamydia or not. From a...big system design point of view you probably don't want that because you don't want people to just kind of look at it and say 'oh, I've got Chlamydia' and then do nothing about it. And nobody outside of that test knowing that that's the case."

This statement, taken alongside previous statements made by Laura about data collection requirements, shows that there are direct links between the interaction design issues discussed by Sharon and the public health needs discussed by Laura.

The statements made by William, Sharon and Laura above show that it is possible to envisage the technologies that will enable highly portable and smart self-testing devices and make arguments for why and how they should incorporate electronics, processing and communication elements. In doing so however, further questions are raised about usability and human factors.

3.7.2.3 Attribute Theme – Usability/Human Factors

From the point of view of operating the technology required to perform a molecular diagnostic test, the issue of usability was expressed by Samuel. Samuel had conducted interviews on the subject of patient acceptability and usability had been an important theme for discussion, he concluded that

"it would have to be something that was kind of, stupid proof, for lack of a better term, so making sure that it...it couldn't be a chemistry kit you know it

be one of these put the white in the blue and the blue in the red, like, that was not OK, very clearly not OK. It had to have a small number of steps..."

This need for a high level of usability in the testing device was echoed by Sharon in her work on the online clinical care pathway and mobile phone interface, where

"...the crucial thing...is having a clear...and it came out from our focus groups as well...the clear user journey and signposted user journey so that they know where they are and what they do and how the bits fit into that."

For the proposed self-test to be acceptable to the patient, Samuel thought that it should be as simple as possible, he went on to expand this point, while conceding that, if the technology required multiple steps, the device should be, as much as possible, restricted to only one way of operating it:

"If there were multiple steps it would have to be impossible to do [the test] incorrectly and there would have to be a helpline associated with [the device]."

The idea of a helpline being associated with the device was reinforced by the results of the research carried out by Work Stream 4 of the eSTi² project. Samuel also thought that the need for access to a helpline while using the device applied not only to the operation of the testing device itself, but to the need for the patient to collect a urine or swab sample themselves.

"When I did the interviews around the potential eSTi² device when we're looking at...giving people a sample to do themselves...I mean for men it's just weeing in a pot, it's kind of hard to do that wrong, but, you know...for women there's a little bit more variability because it's a self-swab, there's the question 'am I swabbing in the right place?', 'Am I swabbing to the right depth?', 'Is this correct?'"

Samuel argued that if the patients had access to a helpline to ask these questions, not only would the usability of the device be improved, but the clinical utility of the device would increase as well. He argued that

"...the issues around self-testing are a lot about trust and it's not just trust in the device, it's trust in an individual's ability to test themselves accurately, to sample themselves accurately and do the test correctly."

There is an indication then that the usability of the test is important from multiple perspectives. If it is more likely that the test has been performed correctly, the test will be deemed more

clinically useful by clinicians and the data collected from the tests will be more useful to public health agencies like PHE.

3.7.2.4 Attribute Theme – Portability/Context of Use

A key aspect of the usability arguments presented above was the context of use within which the device might be used. This was identified as a general theme in the analysis of the interviews, although no specific contexts of use were suggested, there was a general consensus that the device should be portable. William summarised his view on the portability of the device as follows:

“In some respect they’ve always got to be easy to handle, small, handheld, or some element of it has got to be handheld...”

On the same subject of portability Lee reflected that throughout the research project various ways of accessing the test were proposed, including getting the device in a pharmacy or hiring it from the health services, but that ideally, the design of the test should be driven by the self-testing element of the device:

“I think having it as something you hire or go into a pharmacy for reduces its power as a self-testing device because the device itself works a lot better if it’s something you take home and then you don’t need to go back and see anyone because part of the problem is the stigma that’s involved, so the fewer people you have to interact with when you’re going through that diagnostic process then the more effective it is in its purpose.”

This idea that the test must be portable because of the stigma associated with STI testing was also taken up by Samuel. In his work interviewing young people, Samuel found that the key to this might be in providing people with a lot of options for where the test could be accessed, these options were not necessarily health care facilities. When expressing this, he reinforced Lee’s point about the stigma involved in STI testing, stating that the young people he had interviewed were

“...really interested in something that you could get in a variety of different places... So young people have very specific concerns about privacy...and they have concerns about that because they have a lot of risk associated with being outed as sexually active. Especially young people that have a conservative family that might be coming from an immigrant background, were they come from very conservative countries or conservative cultures or have had conservative religious upbringings.”

The need to provide the patients with broad access options and portability as described has a direct impact on the design of the device from an engineering perspective. Returning to Lee's point of view, this need for privacy and portability indicates that the device

“...has to be low cost, preferably single use...preferably disposable, which would mean single use. It needs to be low power, so preferably something portable...It needs to be small, something discreet...”

Portability and the implied attributes that are associated with it (low power, low cost, small), are well defined by these arguments.

3.7.3 Content on Design Features and Attributes

Where only one interviewee mentioned a device design feature or attribute, it was defined as content as opposed to a theme. However, considering the expert level of the interviewees, this may not mean that the design features and attributes defined as content were less significant. After content analysis, it was found that there were two instances where a suggested design feature was expressed by just one interviewee. Firstly, Laura described the need for data collection and transmission from a self-test for public health reasons. Secondly, Samuel expressed the need for the self-test to be tailored to a clinical need. This content is described below.

3.7.3.1 Content – Data Collection and Transmission Capability

For Laura, an essential feature of the design of the device was that it was capable of collecting the same data about STIs that are currently available to Public Health England (PHE). She summed this up when talking about what the complexities might be of collecting data from a novel self-use molecular diagnostic test

“...there's the facility of capturing the data and transmitting it securely with all the data protection issues, an issue of linking that data into Public Health England and for [those data] to be of the appropriate format and going through the correct software...”

Here, when she refers to capturing data, she is referring to information about the person taking the test, whether the test was positive or negative and the resultant ability to compare that information with data gathered from other tests. There are established data collection practices used by PHE when collecting data from Genitourinary Medicine (GUM) clinics in the UK (Public Health England, 2015). She uses these as an example of how she might advise academic and industrial partners on the design of future tests.

“So we can say, for example, [use] my knowledge from the GUMCAD (Genitourinary Medicine Clinic Activity Dataset) which is one of the surveillance systems [that the clinics use to] feed their data to Public Health England, we’ve got the data set so we can look at trends over time...and we can see what the rates of Chlamydia, Gonorrhoea...and Mycoplasma Genitalium testing [are]. We can use those data from GUM and link it with other data like the NATSAL (National Survey of Sexual Attitudes and Lifestyles) which is population level data and we can put all that knowledge together and say, ‘for your test...for Gonorrhoea, it needs to be dual target because there are issues of specificity...because Neisseria has issues especially for pharyngeal infection of cross reactivity so it needs to be dual target and because the prevalence of Gonorrhoea nationally is very low, there are issues for the positive predictive value (PPV) which the BASHH (British Association for Sexual Health and HIV) guideline says, has to be at least 90%’. ‘So for your test to be implemented and supported by BASSH guidelines, then it needs to have a PPV above 90% and that’s what you need to work towards in terms of your specifications.’”

This shows one of the reasons that Laura thinks there is a need for a new test to have a means of recording and communicating data about its positive or negative outcome. As Laura has stated above, one of the uses of this information is to aid in the design of further tests.

Data captured refers not only to the outcome of the test but to information about the person doing the test. To further illustrate the need for capturing data regarding the person, Laura talked about the way in which data are currently gathered by the GUM clinics in the UK and how that information is used.

“GUMCAD...provide a report and...that’s where you kind of look at which are the STIs with highest prevalence or changed from previous years etc....and which target groups, is there more in MSM (Men who have sex with men) or is there more in certain ethnicities etc. so...it allows us to get a sense geographically and by population group, where we need to focus our control efforts.”

GUMCAD collects data from GUM clinics across the UK on a quarterly basis. These data are then transmitted securely to PHE. With the development of new self-tests, a part of Laura’s research efforts are directed toward investigating how data collection strategies may have to change. She uses the introduction of a HIV self-test in the UK (Johnson *et al.*, 2014) as an example of the potential ramifications, explaining that there is one company distributing the tests and they

have limited access to information about the people buying them.

“Basically they can try and work out their gender based on their name and...where their credit card is registered to or something like that...but you won’t get the information that we have on sexual orientation, ethnicity, age, etc., so we lose a lot of that depth.”

She then goes on to explain that, for HIV, this scarcity of information may be less of a problem than for other STIs. She explained that, as HIV is a chronic infection, if a person receives a positive result, they will be admitted into care and the health services will become aware of them. Many STIs however, could potentially be treated online. If a person could access a self-test and online treatment

“...we will never know anything about how many people are testing or what their result is because everything would be remote from us...from care services.”

Laura highlighted the importance of surveillance and capturing as much data as possible from a test regardless of it being a self-test performed away from health service facilities. Laura explained that PHE has rigorous ethical approval criteria for selecting which data are collected for disease surveillance and as result, if PHE were asked what information was most important to collect from a self-test, their response would likely be

“...we want it all, and actually, we want more rather than we want less.”

It is clear that in Laura’s view an ideal feature for the test to exhibit would be that it can collect the same data that are currently collected by the surveillance systems employed by PHE and the GUM clinics in the UK.

3.7.3.2 Content – Clinical Utility

Samuel expressed that an attribute of the device should be that it is tailored to a known clinical need. In doing so, he cites a number of examples where certain types of self-test could be particularly suitable for certain scenarios. For example, he describes how HIV self-tests can be particularly useful in specific situations, explaining that

“...how many clinics generally triage these kinds of test is that, well they’re quite expensive rapid HIV tests and they’re not quite as accurate as the laboratory test but they’re really good for people who are really high risk of being infected and they’re really good for people that are really anxious about whether or not they might be infected.”

Expanding on this theme, he cites another, clinically different situation where a rapid test (rather than a self-test) could be useful. Samuel describe the hypothetical case of a symptomatic patient, who comes in to the clinic with

“...genital discharge...you might do a Chlamydia/Gonorrhoea test as your first point of care test and then afterwards, if they find out that they’re not infected, but they still had the Chlamydia or Gonorrhoea [test], then, you’re kind of ruling out the top two potential infections. You can kind of go on to do...a test, for example, for lesser known pathogens like Trachomatis or...Mycoplasma Genitalium.”

This is an example of a useful application of a point of care, rapid test situated in a clinic but the concept of the test being useful because of a particular symptom can be applied to self-testing as well. If the patient had access to a self-test, they may have been able to rule out certain infections before coming in to the clinic, thus speeding up the clinical pathway.

Samuel admits that tailoring self-tests to a range of clinical situations is a challenge, but that he feels it is an important consideration for the design of a device. He explains that he thinks

“...that it’s extremely unpopular to say to somebody that’s building a bit of kit; ‘We need four of these that are different’...because it’s expensive and it’s complicated and that’s not really the way to maximise the profit on these types of things, but I do think...that type of scenario would provide the best patient benefit...”

This assertion by Samuel is an indicator that the test should either be available in a number of forms which can be deployed in different scenarios or should be tailored to one specific scenario for maximum clinical benefit.

3.7.4 Content and Thematic Analysis – Design Features and Attributes Summary

According to the interviewees, a well-designed molecular self-testing device should be usable and affordable for the patient, valuable from a public health data collection perspective and clinically beneficial. Defining how these features and attributes would be investigated and later achieved with only a hypothetical testing device envisaged by different stakeholders in different ways, was very difficult. Samuel summed this up early on in his interview, saying that

“...obviously, people want the all singing, all dancing, all pathogen STI test that happens in 5 minutes, but given that that’s not a possibility, you know, what is it that we can do to...within the constructs of real, possible science, given the constructs of the platform itself, what can we design and what are the

implications of that design on the clinic and then what are the implications the patients will have?"

The content and themes in the interview transcripts were analysed and features and attributes of the device were proposed by the interviewees. A summary of these features and attributes is shown in order of thematic significance in Table 3-4 below.

Table 3-4 - Features and Attributes Summary

Features/Attributes	Summary	Rationale	Endorsed by
1. Low-Cost	It should be possible to manufacture and distribute the device at a very low cost.	<ul style="list-style-type: none"> - The low cost of the device gives it a unique market niche. - The device must ultimately reduce the cost burden of STIs on health services. - A low cost to purchase increases accessibility to the test for the public. 	William, Samuel, Lee, Sharon
2. Smart Device or Smartphone Operated Device	The device should ideally be usable with some form of portable computing technology or should be able to transmit or receive data itself	<ul style="list-style-type: none"> - Molecular testing requires some form of signal detection requiring electronic components - Data from the test should ideally be communicable to health services (See also feature 1.) - The device should be clinically useful and part of a clinical care pathway (See also attribute 2.) the internet provides a means of doing this remote from health care facilities. 	William, Laura, Sharon
3. Portable	The device should be highly portable and accessible to the patient without having to visit a healthcare facility	<ul style="list-style-type: none"> - Portability increases the range of places the device can be accessed by the public. - Increases the likelihood that the device will be discreet, reducing concerns about stigma. 	William, Samuel, Lee

4. Easy to Use	The device should be easy to use without any prior knowledge by the user	<ul style="list-style-type: none"> - Successful use of the device improves its utility for the user and from a clinical and public health perspective. - Reduces the need for repeat testing. 	Samuel, Sharon
Content: Capable of Data Collection and Transmission	The device should be capable of collecting an equivalent data set to that currently collected by PHE.	<ul style="list-style-type: none"> - Data are used to guide further test development efforts in industry and academia. - Data are used to direct disease control efforts by PHE. 	Laura
Content: Clinically Useful	The device should be tailored to a clinical need and constitute a part of a clinical care pathway	<ul style="list-style-type: none"> - Improve clinical outcomes by speeding up care pathways and enabling more people to test. - Improve public health outcomes by ensuring useful data are captured from a trustworthy, clinically useful source. - Improve patient acceptability and satisfaction by providing a faster pathway from testing to treatment. 	Samuel

3.7.5 Thematic Analysis on Issues and Barriers Associated with Device Design and Development

In the second half of the interviews, the interviewees were asked about the issues and barriers associated with the design and development of self-use molecular diagnostic tests for sexually transmitted infections. After thematic analysis of the transcripts, it became clear that there were three themes associated with issues and barriers. The themes are described in detail below and are ordered based on their level of significance in the thematic analysis.

3.7.5.1 Issues and Barriers Theme – Multidisciplinary Working

William and Laura highlighted that the initial impetus for developing a new test is an issue that can have long lasting implications. A component of the issue of impetus was shown to be the competing interests of stakeholders from disparate backgrounds. This necessity for collaboration across disciplines continues throughout the process of developing novel

diagnostics. Samuel provides an example, summarising the differences between clinical and public health collaborators working on the same project. He explains that

“...in public health we look at what is the greater good for the whole population, well the greater good for the whole population is not what clinicians are interested in. The clinicians are interested in what is...the greatest good for the person that’s sat in front of them...and that is not the same thing.”

In Samuel’s view, a lack of compromise in areas like this is the key barrier to the development of novel diagnostics. He believes that an acknowledgement of the complexity of the situation is an important step toward improving it. He went on to say:

“...when you’re looking at personalised medicine, which is really kind of the field that we’re looking at, at this point [it’s] personalising rapid self-tests for infection. Then it’s a real push/pull between public health and individual patient care and you’ve got the medical establishment, you’ve got the department of health and you’ve got patients and how to make all of those things work in concert... so that the people...who are the most at risk, know they’re the most at risk and get themselves into a situation where they can get a diagnosis and treatment as soon as possible.”

Samuel suggests here that coordinated input from multiple disciplines is required for successful design and implementation of novel, self-use diagnostics. The challenges of working across disciplines were also highlighted by Sharon, who commented that inadequate collaboration between engineers, human factors experts and medical experts was a notable barrier in her research experience in the eSTi² project:

“I think...what we’ve experienced in the project is the interaction between the different disciplines involved and the difficulty surrounding that...because engineering will always kind of try and home in on a kind of solution that works in a narrow way of looking at the problem without appreciating the wider issues which include the human factors issues but also include the medical system issues into which everything fits.”

This point of view was confirmed by one of the interviewees who had been working on the engineering for the eSTi² project. Kara, an expert in engineering and microfluidics, admits that

“...engineers sometimes get really carried away with detail and I think that’s something...you need to look at it as the bigger frame and take things like

Work Stream 4 (human factors) and what Work Stream 4 are looking at [into consideration]”

These examples show that, in the opinion of the interviewees, multidisciplinary collaboration when developing new diagnostic devices is necessary. However, they also demonstrate the interviewee’s view that inadequacies in collaboration are a barrier to ensuring that the best diagnostic testing options are ultimately delivered to patients.

3.7.5.2 Issues and Barriers Theme – Development Speed

A second issue that became apparent through the thematic analysis of the interview transcripts was the speed of development of diagnostic technology, from conception (as discussed in the impetus section above) to deployment and use. Kara, in her work on microfluidics, found that progress on the technology she was working on was slow as a result of essential information being unavailable in the published literature. She explained that for microfluidics

“...there’s no handbook. No, it wasn’t until I’d met [another academic in the field] and I’d met him a few times and then he said to me...‘you had to set all that up at [your university] and I know what it’s like because I had to do that at [my university] and now I’ve taken that to [another university].’ ...it wasn’t until I met him and he said ‘oh that must be really painful for you because I know each lab has their own protocol and you’ve obviously had to set that up on your own’ [that I realised].”

Kara felt that this lack of transparency between academic laboratories had slowed the progress of her work significantly. She went on to conclude that

“MEMS and microfluidics are a bit of a black art so, we now have all our own protocols in place but I’ve had to...develop them...that’s part of the reason that it’s taken us a bit longer...we didn’t have any equipment.”

When discussing speed of development, comparisons were often made between academic research labs and industrial companies developing molecular diagnostics. Kara brought up the examples of the Cepheid GeneXpert, stating that in the cases where devices had been brought to market, both more time and more money were available for industrial ventures and it was not a realistic expectation for academic groups to produce marketable devices:

“the only group that are really point of care, that’ve kind of nailed it, is Cepheid with their GeneXpert...but they’ve been going for years ... you know, we were put on this five year project, six year project it’s been now and it’s not

something that you can turn around in 5/6 years, it's something that takes years."

This shows that in Kara's opinion, an academic research group is not where molecular diagnostics can be developed to maturity. Lee pointed out however, that research groups developing diagnostic technology in academia do have the advantage of access to a broad range of disciplines and as has been pointed out, multidisciplinary collaboration is essential for developing diagnostics. However, developing technologies in academia which yield no research output will be slow. Lee describes his position on the issue; that in academia there are pitfalls in

"...trying to do it as a design project or...R and D work as part of academia [it] might not have been the best place for it. We were good for developing the independent technologies...but then the integration and the tinkering that's required to bring them all together probably doesn't produce a lot of academic output...but it's valuable stuff to do and that's what would bring the project forward but you're not going to publish a lot of papers talking about how you made the sample prep join up with that (extraction and amplification)...I mean the effort would require, you know, a thousand man hours and you'd get one paper out of it. I don't think academia is necessarily the best place for doing it."

This shows that the opinion of Kara and Lee was that technology development was slow in an academic environment. This was as a result of a lack of availability of necessary information, time constraints and a lack of incentives to produce deliverables which did not contribute toward publishing original research. William summed this up in his interview with the following:

"I think...academia is driven by its own needs which...are not necessarily public health needs. Academics have their own needs that are driven by those who employ them. Just like anybody, so I don't think we should think that academics are in a sense pure and really thinking about the right questions. They might be thinking more about things like REF (Research Excellence Framework) and how many grants they can get and publications they can get...and how many tick boxes they can tick in the environment they have. They're not necessarily thinking about what can be deployed and what might make a real translational difference and that's no criticism, that's just an expression of reality."

A review of the combined opinions of the interviewees shows that the design and development of self-use molecular diagnostic devices is complex in multiple ways. The issues of development

speed, multidisciplinary working and design and development impetus are closely intertwined and should be considered together.

3.7.5.3 Issues and Barriers Theme – Impetus for Design and Development

Finally, a concern of some of the interviewees was the initial impetus for bringing a new test into existence and the long-term effect that the nature of this impetus could have on the utility of the test. William explained that a root cause for conflicts in deciding what kind of a test needed developing was the need for collaboration between academia and industrial partners. He explained the situation as follows:

“It’s not usual for academic groups to be able to have the economic clout to be able to develop tests on their own. Partnering with companies and at some point larger companies to be able to scale up and deploy tests and to be able to...have the financial power to conduct diagnostic trials that would allow assessments of efficacy or accuracy to be made...you can only do that if you partner up with large companies.”

This describes the necessity of collaboration between academia and industry when a new diagnostic test is going to be developed. He then went on to explain further that the priorities of academic groups and industrial partners may differ and that this could be a source of tension:

“For example it may be that...you might be interested in a particular pathogen or a few pathogens that are relevant to a public health problem that might be neglected or perhaps not as prevalent, or only prevalent in certain settings whereas some companies might be wanting to try to get something that’s a little more deliverable [to a] much larger market...attracting a much larger profit, and that might be a source of tension.”

Companies often use academics and clinicians as consultants to inform them where there might be a niche for a new type of test. There may also be many other stakeholders, including share-holders, commissioners, biochemists, doctors and technologists. William went on to summarise that there are potential consequences if an agreement is not reached between each of the stakeholders early on in the process.

“So the commissioners, the people who are going to pay for it, the doctors who will be receiving the results of it, public health physicians who would need to understand how they can monitor the results of those tests and so forth. Pharmacies where those tests might be taken to get treatment...It’s really very, very important to be able to kind of get all of that in place as part of the

technology design. So if you get the technology design and you frame the chemistry wrong at the beginning and it's incompatible with the kind of design frame that you want taking it forward, you kind of get stuck in a black hole and then what tends to happen is the companies continue because they've invested so much and they get a suboptimal...or they possibly might get a suboptimal product..."

This example shows that a suboptimal product may result if the impetus for the development of the test was misguided or poorly communicated between stakeholders. In the example above, William gives the impression that the problem may lie with companies prioritising profit over public health or clinical needs. However, in the example he gives below, he shows that clinicians are also capable of providing a faulty impetus for the development of a test.

"I think companies also get frustrated with clinicians because they're a mixed lot and they have very biased opinions and it's actually quite difficult for companies to pull out the right clinicians. If there is such a thing. Of course clinicians are shaped by the experiences they have and those are...even though they might be quite intense and broad anecdotal experiences they're not necessarily what's needed at the public health level. And the experiences can be quite transitory in terms of how important they really are."

These are examples of tensions between clinical and industrial input when the need for a test is being identified and defined. Laura also expressed concerns about the initial impetus for designing a test from a public health perspective. She explained that what should be involved in the early decision-making process for the development of new tests and their subsequent implementation in health services remains an unknown. She explained the challenges of implementing new tests in clinics:

"...generally for tests...a major issue for everybody is how does a test get...adopted and implemented because even if you do things like NICE (National Institute for Health and Care Excellence) adoption where you get your stamp saying you've got our mark of approval, doesn't mean anything, it doesn't mean that a clinic is about to start using your test and that's a major issue that all the companies come up against. They can tick the boxes, but still no one's going to use their test because it needs to be cost effective, it needs to fill a niche."

If the cost effectiveness of the test and the niche it should fill are defined in advance as was suggested by William, these problems of implementation might be avoided. Laura went on to

state that communication requirements between stakeholders are poorly understood and this is an important area for further research. She described a research project she is working on to address this issue:

“...our focus is on point of care tests for STIs; what are the considerations that are really important for you to decide...so that companies can know what they need to focus on and know how to approach different people. So understanding the structures of commissioning in the UK and how...the decisions about budgets [are made] and what things influence the commissioning decisions and the providers’ decisions and the clinicians’ decisions because you kind of need buy in from all of them to make a test successful.”

It is clear from these examples that the issue of where the impetus for the development of a new test comes from is closely related to another issue that was highlighted by the interviewees; that of the necessity of working effectively across disciplines to successfully develop new diagnostic tests. Again, it is shown that the issues and barriers expressed by the interviewees are linked.

3.7.6 Thematic Analysis – Issues and Barriers Summary

According to the interviewees, there are three major issues and barriers associated with the design and development of self-use molecular diagnostic devices for sexually transmitted infections. These issues and barriers are summarised in order of thematic significance in the table below:

Table 3-5 - Barriers and Issues Summary

Barrier/Issue	Summary	Raised by
1. Multidisciplinary Working	- Communication between different disciplines can be poor.	Kara, Sharon, Samuel
2. Speed of Development	- Poor information sharing, lack of funds and incentives which do not drive development hinder the development speed of new devices.	Kara, Lee, William
3. Impetus for Design and Development	- Academic, clinical and industrial drivers for developing new devices differ. - Differences between drivers expressed by different fields are sometimes difficult to reconcile.	William, Laura

3.8 Survey of Design Professionals

The interview data described in this chapter gives an indication of the concept development requirements for self-use molecular diagnostic devices for STIs and issues and barriers associated with those development activities. In order to give an appreciation of the design process requirements for self-use molecular diagnostic devices, a survey was distributed to professional designers. While the concept development requirements identified in this chapter apply to the design of the device itself, the survey gave an indication of the process required to design diagnostic devices.

The survey was distributed via a link in an email to 70 companies. The companies were a mixture of product design consultancies, medical device design consultancies and spin off companies originating from university research labs. The structure of the survey appears in Figure 3-4 below, a full version of the survey questions, consent form and responses is shown in Appendix B.

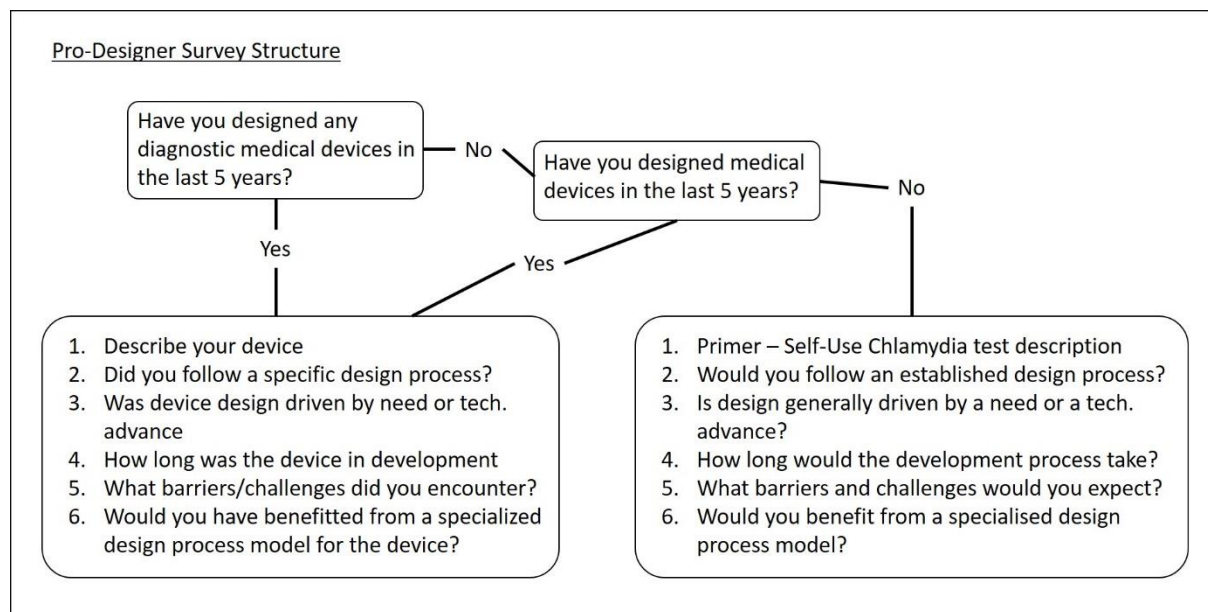


Figure 3-7: Diagram of the questionnaire delivered to professional designers regarding medical device design processes.

3.8.1 Survey Responses

The response to the survey was poor, with 16 out of the 70 contacted companies participating (22%). Of the responses that were received however, some useful information could be gleaned. The survey participants' responses provided information regarding general design process and regulatory requirements. A brief summary of the survey responses follows.

3.8.2 Survey: Key Findings

Described below are the key findings from the survey of professional designers. These conclusions were drawn from the data through content analysis using a deductive coding method based around the information required as dictated by the research objectives for this chapter (as described in Sections 3.3 – Objectives and 3.5.2.1 – Justification of Survey Analysis Method, above).

3.8.2.1 Design Process

The participants indicated that ordinarily a user centred design process was used when developing medical devices. Some of the approaches mentioned for user centred design included surveys and focus groups. The process was often said to be iterative, involving repeating cycles of design, prototype and testing. The participants frequently mentioned that the customer need would drive the design of the test, with investigation into the available technologies coming later.

Most of the participants strongly endorsed the use of structured design processes, although some admitted that the design process was often tailored to the needs of a project. A few of the participants mentioned that predefined stage gate or agile design processes were more than adequate for any device design needs they may have. One participant felt that the definition of design guidelines for a specific type of device was more important than design process as medical device design processes are well established and robust.

3.8.2.2 Regulatory Requirements

On a number of occasions, the participants mentioned ISO (International Standards Organisation) 13485:2016, Medical Devices – Quality Management Systems – Requirements for Regulatory Purposes (ISO, 2017) stating that design processes for medical devices had to be structured around it. This standard ensures that companies compile all the necessary documentation for regulatory approval of a device as they are progressing through the design process. ISO 14971:2007 was also mentioned by one of the participants. This standard is associated with risk management and control and once again was said to have a controlling effect on the design process used by the company (ISO, 2007).

Participants mentioned use of the IEC 62366 – Application of usability engineering to medical devices standard (ISO, 2015). The standard was mentioned in the context of there being insufficient knowledge of it in the medical device design sector. This may suggest that usability and human factors are under prioritised.

3.8.2.3 Other Issues or Barriers

The amount of time a product takes to develop was mentioned a number of times. Also, one of the participants mentioned that they felt the motives for initiating product development were often profit driven and not necessarily based on the needs of the patient/user. Another stated that the internal politics and bureaucracy involved with working with the NHS was overly time consuming.

3.8.3 Survey Summary

The survey offered a limited view of the design process needs of design professionals. Further work could be applied to this area beyond the scope of this thesis. The survey gave an indication that there are well established and robust design processes in use in the industrial medical device design sector. The designers seemed more interested in design guidelines than the development of entirely new design processes. Further work would more usefully employ in depth interview methods to learn more about design processes for novel medical technologies.

3.9 Limitations

As can be seen in Figure 3-1 in the methods section above, the intention in the design of the interview study was to achieve a balance of input between technological fields of expertise on the left-hand side of the diagram and non-technological fields on the right-hand side. Human Computer Interaction (HCI), falls between these definitions as a field of research where human factors associated with technology use are investigated. There is therefore a bias in the participants toward non-technological fields of research.

The sample size of the research is small and restricted to the eSTi² research project, meaning that the responses to the interview questions were heavily influenced by the goals and direction of that project. Aside from this potential bias, the high level of expertise and experience shared by the interviewees compensated to some extent for the small sample size.

The survey of professional designers provided a very small response of 22% of those contacted. Therefore, while some interesting indications of design process needs for medical devices were shown, a more rigorous investigation into this research area is required.

3.10 Summary

The responses of the interviewees gave an indication of desirable features and attributes of the proposed device from various expert perspectives. A summary of the features and attributes is shown in Table 3-4. Issues and barriers associated with the development of self-use devices for STIs from the point of view of various areas of expertise were also explored. A summary of the issues and barriers is shown in Table 3-5.

The survey of professional designers showed that strict and robust design processes, often dictated by regulatory standards are used in design companies. This assertion is supported by the background literature shown in Chapter 2.

Further definition and validation of concept development requirements and issues and barriers is shown in Chapter 4 using a validation survey of the entire eSTi² research consortium to show general agreement or disagreement with the results shown in this chapter.

Chapter 4

Validation Survey

4.1 Introduction

Chapter 3 described expert opinions on what the concept development requirements for a self-use molecular diagnostic device should be. The requirements identified in the chapter were therefore limited by the sample size of the study and potential biases of the participants. To alleviate this limitation, this chapter is dedicated to a survey of the members of the eSTi² research consortium, the purpose of which was to validate the design requirements used to create concept and component designs in Chapter 5.

The survey also highlights differences in opinion between the different Work Streams regarding certain design requirements, development time scales and the way in which a device may work in use. The examination of these differences contributes toward the definition of issues and barriers associated with the development of self-use molecular diagnostics for STIs.

The chapter describes an overarching aim and objectives which are then framed in context of the objectives of the thesis. Justification for the use of a quantitative survey method is provided, the method is described and the results of the survey are presented and analysed. The survey data, along with data from Chapter 3 and 5 were later applied to the formulation of a descriptive design process model which is then assessed and adapted for general use by researchers developing proof of concept diagnostic technologies.

4.2 Aim

The aim of the survey described in this chapter was to provide validation for the design requirements formulated through the study described in Chapter 3 of the thesis.

4.3 Objectives

The research objectives of the study described in this chapter were as follows:

- To identify agreement or disagreement from the entire eSTi² research consortium regarding the concept development requirements previously defined in Chapter 3 of the thesis.
- To identify disagreements between project Work Streams or areas of expertise, thus highlighting possible issues and barriers with development.

4.4 Objectives in Context of the Thesis Objectives

The objectives of this chapter were carried out in partial fulfilment of thesis objectives 2 and 4. Concept development requirements were further refined using the survey. Objective 2 of the thesis is as follows:

Objective 2: To identify concept development requirements for self-use molecular diagnostic devices for STIs.

The survey described in this chapter demonstrates some of the issues inherent in the development of self-use molecular diagnostics for STIs. Objective 4 of the thesis is as follows:

Objective 4: To describe issues and barriers inherent in the development of self-use molecular diagnostics for STIs.

4.5 Design Requirements Validation Survey

A survey was designed to validate the suitability of the design requirements that will be applied to the full system concept designs and working prototype designs described in Chapter 5. All four Work Streams of the eSTi² research consortium were surveyed at once, meaning that members from a range of disciplines answered the survey questions. The disciplines of those surveyed included molecular microbiology, genomics, biomedical engineering, epidemiology, public health and clinical sexual health. Thus it was possible to see whether there was general agreement or disagreement from a majority of the members of the consortium regarding the design requirements that had been applied in the action research.

4.6 Justification of Survey Method

An online survey method, as opposed to a focus group or further interviews, was chosen to validate design requirements for a number of reasons. The target population of the survey were highly qualified experts from varied disciplines who worked at different, geographically distant institutions. A small number of the survey participants even filled the survey in from locations in a different country. An acknowledged advantage of the use of online surveys in the literature is the ease with which participants can be reached online and the speed at which data can then be accessed and analysed (Sills and Song, 2002). Participants were able to access and fill in the survey online at their convenience, which was appropriate for the busy and mobile lifestyles of the target population of participants.

The eSTi² consortium comprises 32 members spread across 6 institutions. Although this is a small population for the typical use of a survey method, an interview method was ruled out by the population size and disparate locations of the participants as a result of time constraints. Another advantage of the survey method against interviews, especially as the validation of

design requirements partly devised by the author was in question, was that the potential for interviewer bias was counteracted (Van Selm and Jankowski, 2006).

A focus group could have been conducted, with participants from each of the Work Streams and a cross section of the disciplines involved in the project present. Logistically this would have been very time consuming and inconvenient for the participants. It would also be difficult to ensure a balance of input from the wide range of different disciplines involved in the project. Broadly different disciplines are sometimes present within one Work Stream, for example, Work Stream 4 comprised psychologists, clinicians and social scientists. The survey research method also avoids the possibility of dominant personalities dictating the direction of the discussion as may be the case with a focus group.

4.7 Survey Method

The survey was distributed to the 32 members of the eSTi² consortium. Emails were sent to prospective participants with a link to the survey website. Once the participants had accessed the survey, they were initially asked which Work Stream they had been a part of and if they had been a part of more than one Work Stream, which one they spent the most time with. They were then asked what their area of expertise was. In the event that they were not officially part of the eSTi² consortium but had been closely involved with it, a 'not applicable' option was offered allowing the participant to fill in their area of expertise and the institution or company they were affiliated with.

The participants were instructed to imagine they were assessing the design of the first sample in to answer out Chlamydia self-test to become available in the UK. They were then asked to assess the importance of design criteria. The questions predominantly used a Likert scale with 5 options ranging from 'Not at all important' to 'Extremely important'. The last two questions asked for an estimation of acceptable testing time in minutes and an estimation of appropriate development time in years, using a scale from 0-120 and 0-15 respectively. The questions covered the following topics which had been used as design criteria for the development of the concept systems and working prototype described in Chapter 4.

1. NHS/Public Health England access to test data.
2. Usability
3. Cost
4. Context of use
5. Size
6. Smartphone enabled
7. Speed of test

8. Development time to use by the public

An example of a Likert scale question in the survey was as follows:

Q. How important is it that test data and demographic data from the test are available to health services such as the NHS and Public Health England?

The participants were given the options of answering with one of the following statements: 'Not at all important', 'slightly important', 'moderately important', 'very important' or 'extremely important'.

As an example of the utility of this question, the action research detailed in Chapter 4 and the development work carried out generally by DoC Lab and Work Stream 2 had been operating with the requirement that test data must be collected from the test. This question was designed to assess the level of agreement with this criteria from the group as a whole.

A question regarding how long it was appropriate for the test to take was asked toward the end of the survey in the following way:

Q. Taking into account both the technology being used and the person using it, what is the maximum amount of time in minutes that is acceptable for the test to go from the sample collection stage to the output of a result?

The participants were then given a scale that could be moved between 0 and 120 minutes to indicate their answer. The technology being developed by the DoC Lab group and Work Stream 2 was potentially capable of processing a sample and obtaining a result in <20 minutes. This question would give an indication of agreement across the eSTi² group of whether this amount of time was too long or too short.

All of the questions in the survey are shown in Appendix D. At the end of the survey, the participants were asked to make comments on the content of the survey or any thoughts on the subject of test design that may have been inspired by taking it.

4.7.1 Participants

22 participants responded to the survey. Of the 32 members of the eSTi² research group, 19 responded. Three of the participants were from outside the group but had been closely involved with one of the Work Streams.

The number of participants from each Work Stream was as follows:

Work Stream 1 – 3 participants (1 from external organisation)

Work Stream 2 – 9 participants (2 from external organisations)

Work Stream 3 – 2 participants

Work Stream 4 – 8 participants

The imbalance in the numbers of participants between Work Streams is explained by the much larger size of Work Streams 2 and 4 compared to Work Streams 1 and 3. The analysis section below goes into further depth regarding this issue.

The participants came from a broad range of disciplinary areas, which are shown in Table 4 -1 below:

Table 4-1 – Validation Survey Participant Expertise

Expertise	Number of Participants
Microbiology	4
Biomedical Engineering	3
Electronic Engineering	1
Computer and Numerical Modelling	1
Public Health	2
Health Technology Assessment	1
Epidemiology	1
Systems Architecture	1
Clinical Sexual Health	3
Microfluidics	2
General Practice	1
Patient Impact of Novel Diagnostics	1
Systems Engineering	1

4.7.2 Analysis

The results of the survey were compiled into a spreadsheet and analysed using R statistical analysis software (R Core Team, 2016). Responses were a level of importance were given were assigned numerical values from 1 to 5, i.e. 'Not important at all' = 1 and 'Extremely important' =

5. As has been stated above, the evaluation and assessment of the design work described in Chapter 4 was carried out by Work Stream 2 and the DoC Lab research group. A key aim of the validation survey was to address the potential limitation in design rigour that this caused by showing whether or not the other Work Streams agreed with the design requirements that had been applied to the design activity.

Each of the Work Streams had a different number of members, with Work Streams 2 and 4 outnumbering Work Streams 1 and 3 significantly (By 6 participants in both cases). In order to address this imbalance, the answers to the survey questions were divided by Work Stream and for each question, a mean response was calculated. This meant that the answers of the 3 participants from Work Stream 1 would have the same weight as the 9 participants from Work Stream 2. A grand mean was then calculated for each question to give a mean response across all four Work Streams, showing the extent to which the group as a whole considered a design requirement to be important or not.

This analysis method could not be applied meaningfully to questions that asked for an estimated length of time that the test should take or the estimated development time in years for the finished system. A consequence of the design of the survey was that disagreements between Work Streams were highlighted and could then be visualised in bar charts. In the cases of test time and estimated development time, this method was used to display results. This contributed to the description of issues and barriers associated with development of the type of device to which the survey refers.

Participant comments which were added at the end of the survey provide some further indication of potential issues and barriers to development and have been added to the results section of this chapter. A complete list of responses to the survey and the R statistical analysis code used to analyse results is shown in Appendix D.

4.8 Design Requirements Validation Survey Results and Discussion

4.8.1 Importance Ratings

Questions about ease of use, cost, size, context of use, NHS and PHE access to test data and the way in which the test would interact with a smartphone were given importance ratings in the survey. Where an importance rating exceeds .5 above the numerical value of the importance rating, it has been rounded up to the next importance rating, below .5 it has been rounded down.

4.8.2 Significance of the Mean Responses

The mean responses shown below are significant in the larger context of the research in the following way. The mean responses provide clarification for the design guidelines described in the thesis (Chapter 7, section 7.4.2). For example, where a mean response indicates a higher level of overall approval across the members of the consortium for a design feature, this suggests that the feature should be prioritised over features with lower levels of mean approval.

Where an approval rating is low, this could indicate disagreement between members of the group from different disciplinary backgrounds. Examples of this are further discussed in sections 4.8.3 and 4.8.4.

While the overall mean results provide an indication of the validity of the design requirements proposed in the thesis, disagreements between members of the consortium may constitute a barrier to the development of self-use molecular diagnostic devices as has been discussed in Chapter 3.

Below are shown the mean responses to the survey questions regarding design features of the potential self-use, molecular diagnostic device for sexually transmitted infections.

Ease of Use – Mean Response – 4.78

This shows that across the consortium the participants considered ease of use to be extremely important.

NHS and PHE Access to Test Data – Mean response – 4.13

Across the consortium, it was considered very important that data gathered from the test was available to the National Health Service and Public Health England.

Cost – Mean Response – 3.69

The participants were asked how important it was that the device should be given to the public for free through the NHS. The group considered that it was very important that the device was free at the point of delivery. The lower mean response to this question may indicate that the participants considered that the device being affordable rather than completely free may be acceptable.

Pocket Sized – Mean Response – 2.94

It was considered moderately important by the group that the device was small enough to carry in your pocket. This may suggest that a certain level of portability was considered desirable but a very high level of portability was not considered necessary.

4.8.2.1 The Role of the Smartphone

Participants were asked what role a smartphone should play in interacting with the test. They were asked to rate the importance of the smartphone being able to interact with the test in the following three ways:

Data Transmission – Mean Response – 3.75

The participants considered that the use of a smartphone to facilitate the transmission of test data from a self-use diagnostic device was very important. This may be linked to the result showing that recovering test data for NHS and PHE use was very important.

Data Processing – Mean Response – 3.03

The importance of the test data being processed on a smartphone was rated as moderately important.

Powered by Smartphone Battery – Mean Response – 2.44

The importance of the smartphone providing power to the test was rated as moderately important, slightly less so than the mean response to the importance of data processing on the smartphone. These three responses show that the group rated it most important that the test data is captured from the test. It may be the case that how this occurs, either using a smartphone or other means, is considered less important by the participants in this survey.

4.8.2.2 Context of Use

When asked about the importance of the design of the device being tailored to a specific context of use, participants were asked to respond using the Likert scale in a different way. The answers offered ranged from 'Not at all tailored (Device can be used anywhere)' to 'extremely tailored (device will not work in another location)'. The results were as follows:

Clearly Defined Context of Use – Mean Response – 2.16

This indicates that it was the mean opinion of the group that the test should be slightly tailored to a context of use. This strongly indicates that a self-test that relies on the infrastructure of healthcare facilities or any specific equipment to be operated was not a desirable requirement according to the participants in the survey.

4.8.3 Test Speed and Development Time Scales

4.8.2.1 Test Speed in Minutes

The participants were asked to estimate what they thought was an appropriate amount of time for the test to take from the introduction of a sample to the acquisition of a result. There was

some disagreement between the Work Streams on this point, as can be seen in the bar chart below.

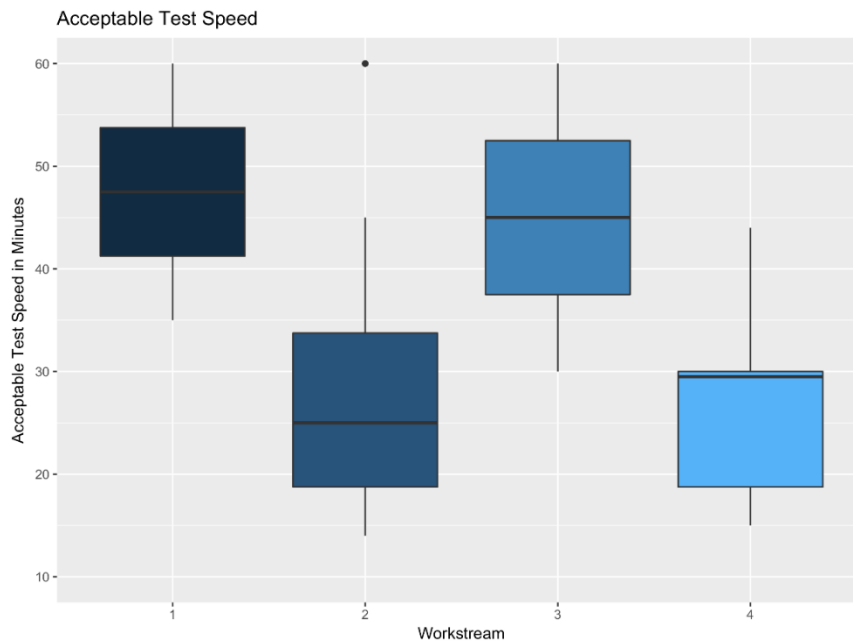


Figure 4-1 – Bar chart showing estimated appropriate test speed from sample in to answer out. An outlier in Work Stream 2 has suggested a full 60 minutes acceptable testing time.

The bar chart shows the Work Streams 1 and 3 consider an appropriate testing time in minutes for a self-test to be almost 50 minutes. Work Streams 2 and 4 however estimate that a testing time under 30 minutes would be appropriate. This may be because of the differences in the work being carried out by 2 and 4 and 1 and 3. Where 1 and 3 were more focussed on microbiology and the development or evaluation of current tests, 2 and 4 were concerned with the development of entirely novel tests and clinical care pathways which would ideally be faster. It is likely that the assertion that a testing time of almost 50 minutes would be acceptable was based on what is possible using current technologies. Work Stream 2, however, have been working on an isothermal amplification method that could allow a sample to be analysed in under 20 minutes (Craw *et al.*, 2015). Work Stream 4 may have given a lower mean testing time as a result of their research into young people's perceptions of potential self-testing methods (Aicken *et al.*, 2016).

It may be the case that the differences in results between 1 and 3 and 2 and 4 are a result of the differences in sample size between the groups. However, the difference in expertise area between the groups suggests that this may be unlikely, with Work Stream 1 entirely comprised of microbiologists and Work Stream 3 comprising of microbiologists and an expert in public health and diagnostic evaluations. With the exception of public health, these areas of expertise

are not found in the other Work Streams, which may provide an explanation for the differences in opinion.

4.8.2.2 Development Time in Years

The participants were asked to estimate how many years they thought it would be before a self-use, sample in to answer out Chlamydia test would be available to the public. Once again, a disagreement could be seen between the Work Streams of the consortium as can be seen in the bar chart below.

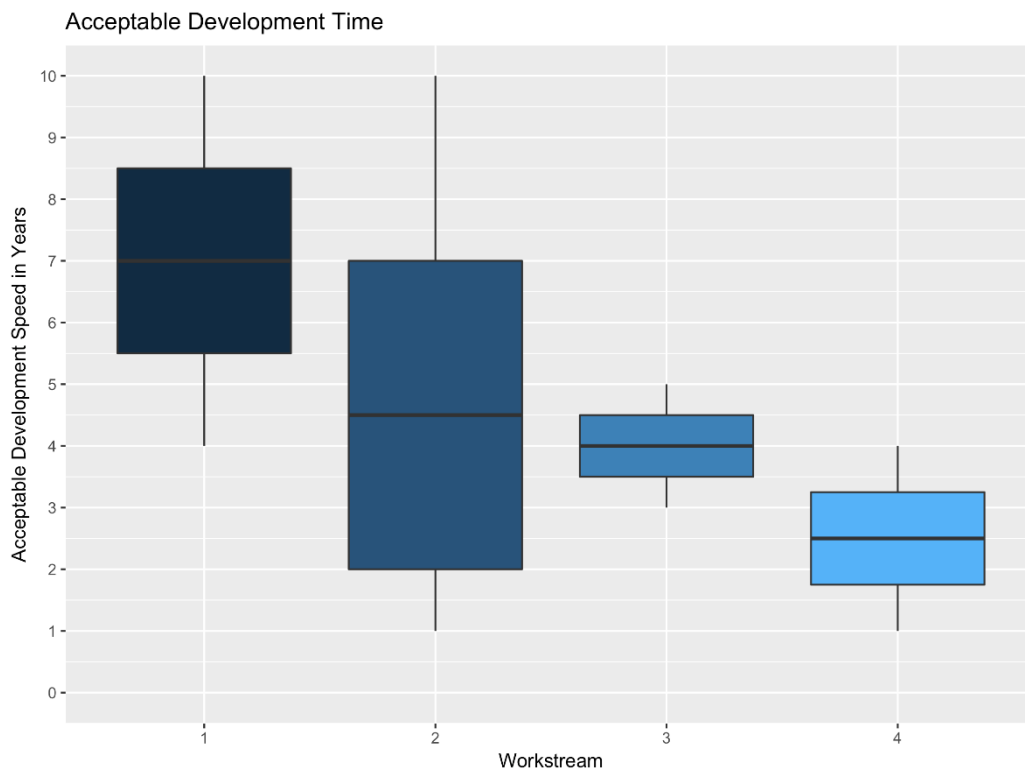


Figure 4-2 – Bar chart showing estimated development time in years until an accurate self-use diagnostic device for Chlamydia is available to the public.

A marked difference can be seen between Work Stream 1 - around 7 years, and Work Stream 4 - around 2.5 years of expected development time before an accurate sample in to answer out test for Chlamydia is available to the public. The difference between Work Stream 2 and Work Stream 4 is also significant, with Work Stream 2 estimating double the development time of Work Stream 4. There may be many similar reasons to those given above regarding test speed in minutes as to why there is such a discrepancy between estimated development times. A likely explanation may be that communication between Work Streams regarding technology readiness is not efficient and this constitutes an issue and barrier to test development which will be discussed further in Chapter 6.

4.8.4 Further Disagreement between the Work Streams

There were two other instances of significant disagreement between Work Streams which can be seen when the responses to the survey questions are shown as mean results in a bar chart. Firstly, there is moderate disagreement between the Work Streams regarding how important it is that the test is pocket sized, as can be seen below:

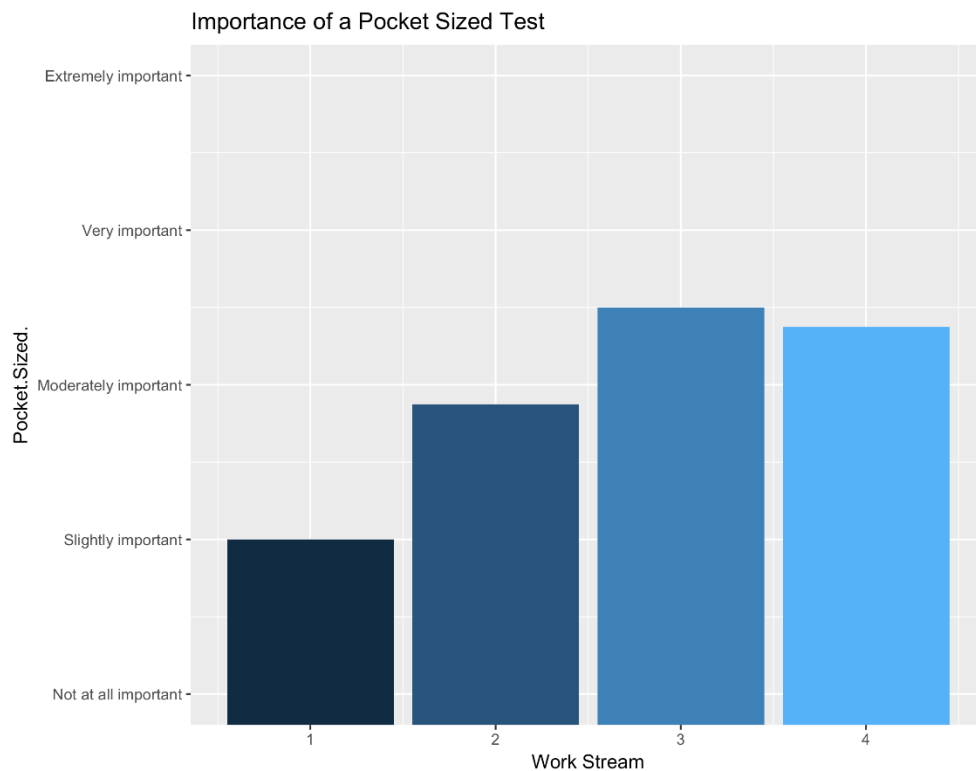


Figure 4-3 – Bar chart showing how important the participants thought it was that the test could be carried around in a pocket.

The biggest difference in opinion regarding how important it is that the test is small enough to fit into a pocket is between the members of Work Stream 1 and the members of Work Stream 4. This difference may be attributable to the point of view of the technology afforded to the different groups by their areas of expertise.

The second instance where there was significant disagreement between the groups was in their opinion regarding the importance of a smartphone being used to provide power. This was considered by the consortium as a whole to be moderately important. However, there was a significant discrepancy between the mean opinion of Work Stream 1 and the other Work Streams as is shown in the bar chart below:

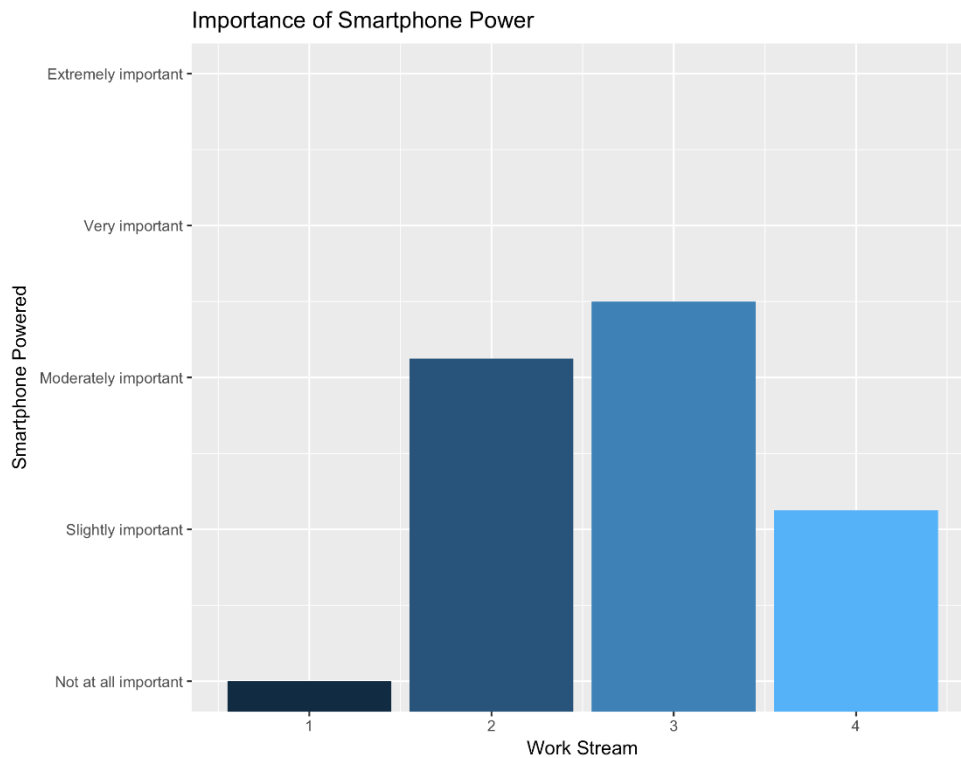


Figure 4-4 – Bar chart showing how important the participants thought it was that the test was powered using a smartphone.

It is possible that the microbiologists taking the survey, who were predominantly represented in Work Stream 1, were influenced by the possibility of highly portable lateral flow tests being the most likely candidates for self-testing devices, which would require no power at all (Gwyn *et al.*, 2016). They would, however, not be as accurate as known methods for nucleic acid detection, which are at present generally benchtop systems that use more power to operate than would be acceptable to draw from a smartphone battery (Craw and Balachandran, 2012).

It is notable that Work Stream 4 also only rate the importance of drawing power from the smartphone as slightly important. This may be for the non-technological reason that study of patient acceptability has shown that it would not be desirable to directly connect a smartphone to a diagnostic testing device.

All of the bar charts showing the mean results of the answers from each of the Work Streams are shown in Appendix D.

4.9 Survey Participant Comments

At the end of the survey the participants were asked to add further comments or thoughts regarding test design. Comments that were added that directly related to the design of the test were on the subject of the interaction with a smartphone and the context of use within which

the test would be used. One participant commented on smartphone interaction with the following:

“I said it was moderately important for a Smartphone to process and send the result, but I also believe that the device should be able to be used standalone, without the need for a Smartphone. This allows privacy in use to ensure that some are not put off using it by thinking that big brother is watching them - especially in these days of hacking.”

Although the comments were added independently, another participant expanded on this point, stating that

“...the trade-off between being able to make a test available which can't transmit surveillance data with the fact a self-test may reach a population who have not previously tested is an interesting one.”

The strong suggestion offered by these comments is that flexibility in the design of the device meaning that it can be used with or without a smartphone was considered important by at least some of the participants. This flexibility may offer benefits not just in patient acceptability, where the patient feels their privacy is being protected as is suggested in the first comment, but in the successful diagnosis of infections in groups which would otherwise have been difficult to access by health services. One of the participants offered a more direct opinion on smartphone integration with the following:

“I think that smartphone integration is a gimmick and little is gained in terms of cost, size or performance from having any device attach to a smartphone.”

This comment may be inspired by the increased ubiquity of miniaturised computing devices which would render connection to a smartphone as opposed to any other type of computing or communication device unnecessary, particularly if data storage and communication components could be incorporated into the device itself. This would also potentially increase the contexts of use within which the device could be used, a subject which was considered to be the key to device design by some participants, as the following comment illustrates.

“I've answered from a "realistic, but ideal test" perspective. However, if proper market research were performed nationally to get a sense of who would buy this test and where it would be used, we would get a better sense of the needs for size, smartphone enabled components, cost etc. I think the Context of Use question is the key.”

This suggests that it is, at present, impossible to make direct assertions about things like the cost and size of the test without the collection of more data. A balance would then presumably have to be struck between what people were willing to purchase and use and the capabilities of the technology that enabled the device to perform an accurate test. As was shown in the expert interviews in Chapter 3, the suggestion is that the design of the test is highly dependent on the context within which it should be used. Another participant commented that

“...it really depends on the type of test one is thinking of. It is more important for the test to have faster results if it is in a clinic or a pharmacy, e.g. where the patient is waiting, than it is if the patient is performing the test themselves, e.g. at home.”

This assertion by some of the participants is in contradiction with the overall result of the question regarding how tailored a test should be to the context of use it will be used in. The mean answer to that question showed that the group thought that the test should only be slightly tailored to a specific context of use. Here, the point is made that tailoring to a context of use is also important.

All participant comments are shown in full in Appendix B.

4.10 Validation Survey Results Summary

The key design requirements applied to the action research design activity described in Chapter 4 were that the device should be clinically useful, easy to use, portable, low cost and capable of transmitting or storing test data. The results of the validation survey showed that three of the key design requirements which had been used to develop system design concepts and working prototype component designs in Chapter 4 were considered by the group to be either extremely important or very important. These requirements being ease of use, transmission of test data and low cost.

The group were not asked about the clinical utility of the proposed device as this was assumed in the introduction to the survey where they were asked to imagine the first accurate Chlamydia self-test available to the public in the UK (it's availability to the public suggesting clinical utility had been confirmed already).

The group assessed the portability of the test to be moderately important. This may have been because of the way the question was asked in the survey, wherein participants were asked how important it was that the test was pocket sized. The responses suggest that portability is important but a very high level of portability is not necessary.

A key interpretation of the survey results is that the device should not necessarily be designed specifically for interaction with a smartphone. Data processing and power provision by a smartphone were rated as moderately important, however, comments supplied by some of the participants state that while interaction with a smartphone may be useful, it may also be restrictive and add little value to the test. The need for data transmission through a smartphone was rated as very important, this, however may not mean that direct interaction with a smartphone is a desirable attribute in itself, rather that data transmission is essential to the utility of the test from a clinical and public health perspective.

The survey highlighted that there are differences in opinion regarding test design between different Work Streams of the eSTi² project. These differences in opinion were seen primarily where test speed, portability and the importance of drawing power from a smartphone were concerned. There were also differences of opinion across the consortium regarding how many years it would take to develop the proposed self-use Chlamydia diagnostic test. While there may be many reasons for these differences, ranging from the area of expertise of the participants to the subject of the research they had carried out for the consortium, it may be the case that these differences represent significant issues and barriers to the development of self-use molecular diagnostic devices for STIs in a general sense, beyond the margins of the eSTi² project.

4.11 Survey Limitations

The main limitation of the design of the validation survey was that it gave an impression of the opined importance of design requirements while giving no direct indication of why the participants had rated the level of importance as they had. An indication of this would have provided a more in depth understanding of the differences in opinion between the Work Streams.

The survey was conducted within the eSTi² research consortium to the exclusion of any participants from other research projects or from any larger demographic of the public. The answers provided in the survey may therefore have been biased by the research findings and prevailing opinions within that project. An extension of the survey to a non-expert audience would have provided information on how expert opinions regarding test design differ from the opinions of non-experts who have not considered the design of a self-test before.

4.12 Summary

This chapter includes a survey of the members of the eSTi² research consortium that was designed to validate the concept development requirements that have been used to design research prototypes in this thesis. The survey showed that the members of the consortium generally agreed with development requirements defined. There were disagreements between

certain Work Streams and disciplines which contributed to the issues and barriers associated with the development of self-use molecular diagnostic devices for STIs. It was shown that direct interaction between the test and a smartphone may not be a desirable design characteristic.

Chapter 5

Action Research Design Activity

5.1 Part 1: Action Research Design Activity - Introduction

In Chapter 3, exploratory research described the features and attributes that a self-use molecular diagnostic device for sexually transmitted infections might ideally exhibit. Issues and barriers that may arise when conducting research, design and development activities associated with such a device were also identified. These findings were further refined in Chapter 4, through a survey of the eSTi² research group.

The study presented in this chapter reinforces the findings of Chapters 3 and 4 through further investigation of the design requirements of hypothetical, self-use molecular diagnostic devices. This chapter describes the author's participation in the development of a technology from proof of concept to preclinical trial stage.

An action research method is applied in this chapter giving the author hands-on access to a proof of concept technology for molecular STI diagnostics. Collaboration as a participant observer with the DoC Lab research group meant that the author could understand technical details of the technology, formulate design requirements, propose concepts and test design methods as the prototype was developed. A record of the design work carried out to this end is shown in the chapter along with descriptions of how and why the design of the prototype changed over time.

As the design of the prototype progressed iteratively and was assessed by an expert panel and formal design assessment methods, it became clear that, in order to be a practical, clinical and public health success, the proof of concept technology would have to be incorporated into a wider system of supporting technologies. Design methods were identified and applied to the action research to reflect this finding. As a result, the incremental development of a design model for self-use molecular diagnostic devices is described in this chapter. This descriptive design process model is presented in full in the second part of the chapter.

This chapter includes a description of the aims and objectives of the action research and how they contribute toward the wider aim of the thesis. A justification for the use of the action research method is given with a description of how it was applied. Evidence of the design activity is shown and an analysis of the research is discussed along with the limitations of the method and a summary of the findings of the chapter. The second part of this chapter shows a

descriptive design process model which was formulated using the information generated in the studies described in Chapters 3, 4 and the first part of Chapter 5 of the thesis. Design concepts, which have been developed using the design process model are presented and assessed. The potential is then explored for the design process model to be generalised for use in improving and expediting the design and development of self-use molecular diagnostic devices for STIs in future development efforts in research environments.

5.2 Aim

The aim of the study described in this chapter is to provide a technical evidence basis for design issues, guidelines and recommendations associated with the development of self-use molecular diagnostic devices for STIs. This technical basis has also been applied to the accompanying design process model.

5.3 Objectives

The following objectives have been carried out in completion of the research described in this chapter:

- Identification of a case-study, proof of concept stage technology to develop toward a viable self-testing system.
- The identification of a clinical care pathway with which the technology might be used and an explanation of the way the technology would be used within it.
- The execution of design experiments and the production of concept designs which, having been assessed through periodic meetings with experts and the use of established design methods, would determine how the technology should be improved.
- The identification of appropriate design methods for use in developing a proof of concept diagnostic technology from the preclinical trial prototype stage.
- Description of the contexts of use that the proof of concept technology could feasibly be deployed into.
- Completed designs for a pre-clinical prototype portable diagnostic platform for the detection of STIs.

5.4 Objectives in Context of the Thesis Objectives

The research in this chapter was carried out in partial fulfilment of objectives 2, 3 and 5 of the thesis. Objective 2 of the thesis is as follows:

Objective 2: To identify concept development requirements for self-use molecular diagnostic devices for STIs.

The action research described in this chapter is the sole section of the thesis which was carried out in fulfilment of Objective 3 of the thesis. Objective 3 of the thesis is as follows:

Objective 3: To complete designs for a working prototype, miniaturised and low-cost diagnostic platform for sexually transmitted infections, created in collaboration with the Brunel DoC Lab research group and the eSTi2 research consortium.

A combination of literature (Chapter 2), interviews, questionnaires (Chapter 3) and the hands-on research shown in this chapter contribute toward the fulfilment of Objective 5 of the thesis, which is as follows:

Objective 5: To formulate a design process model for use by medical device researchers, developers and designers for expediting the development of self-use molecular diagnostic devices for sexually transmitted infections.

5.5 Justification of Action Research Design Activity Method

An overall aim of the thesis is to investigate a way in which self-use diagnostic technologies might be more quickly and effectively progressed from proof of concept prototype stages into working systems which are useful from a clinical and public health perspective. As a result of the research described in this chapter, the author has been able to hypothesise that the use of industrial design methods, applied from the proof of concept research stages and in a research environment, will speed up this progression.

In this chapter, action research and design research methods have been used to develop a diagnostic technology from the proof of concept stage to the preclinical trial research prototype stage. In formulating the aforementioned hypothesis and creating a design process model for self-use diagnostic devices, iterative methods, similar to those used in industrial design practice, were used to simultaneously develop the preclinical trial prototype and design process model.

5.5.1 Action Research

Where action research methods are used, the researcher actively involves themselves in the group, organisation or activity that is the subject of their research interests (Ottosson, 2003). This is done in order to gain an understanding of the group or activity they are investigating and to simultaneously provide a positive and adaptive contribution to it (Baburoglu and Ravn, 1992). Action research has been applied in the fields of information systems (Baskerville and Wood-Harper, 1996) and management research (Whitehead, 2005) wherein researchers have participated in the operation of said systems or management structures in order to understand and improve upon current practice.

Action research is highly flexible and examples of the diversity of applications of the method can be found in the literature. For example, action research has been used to investigate the operation of complex supply chains (Näslund, Kale and Paulraj, 2010), virtual community health networks (Lau and Hayward, 2000) and the gamification of service design (Klapztein and Cipolla, 2016).

In this last example of gamification, the researchers introduced an element of design practice. The research method described was action design research, a combination of action research and design research. Action design research has been applied to information technology and software research, where the researcher participates in proposing design solutions and evaluates the effect of their contribution (Maung K. Sein, Ola Henfridsson, Sandeep Puroo, Matti Rossi, 2006).

The action research and action design research methods described have heretofore been used for the improvement of information technology systems, large-scale software applications and management structures. They have not ordinarily been applied to industrial or product design issues such as are described in this thesis. However, the successful development and subsequent deployment of a useful diagnostic device requires the involvement of a large variety of disciplines, stakeholders and technologies, spanning across software, hardware, biological, clinical and public health needs. Therefore, it is appropriate when seeking to describe design issues, guidelines and recommendations and a design process model for such devices, to apply a research method that has been proven to be successful where complex systems are involved.

5.5.2 Design Research

The author has an academic and professional background in industrial design. Consequently, the majority of the action taken by the author in conducting action research was designing (i.e. creating 3D models and 2D manufacturing drawings, designing mechanisms and altering the configuration of components and assemblies). This constitutes the active use of design as part of a research method.

Aside from the action design research described above, arguments have been made for the use of design as part of a research method, particularly in the field of human computer interaction (HCI), where the advantages of the application of action research methods alongside the use of design techniques like user centred design and participatory design have been discussed (Hayes, 2011).

The case for the use of design in HCI research has been made where so called 'wicked problems' are in question (Wolf *et al.*, 2006). A wicked problem occurs where the description of the problem and the conditions of its resolution are in constant flux over time (McCall and Burge,

2016). The design problem described in this thesis, with its many stakeholders, technologies and shifting requirements, suits this description.

In this chapter, artefacts are designed and assessed and the knowledge gained from the activity of designing and the assessment of the result contributes to the research output. This method has also been proposed in the field of HCI, where the production and assessment of designed 'research artefacts' are used to inform HCI practitioners (Zimmerman, Forlizzi and Evenson, 2007). Staying with HCI, Fallman proposes a method for design research where the researcher alternates between focussing on design practice, design exploration and design studies (2003). In that approach, design practice refers to the act of designing an artefact, design exploration refers to conceptualisation of how the artefact may develop in future and design studies assess previous design work and design process. This approach provides a rich picture of the design problem, potential solutions to it and methods for how those solutions might be achieved by others in future.

The Design Council provides examples of where design methods have been used to simultaneously investigate and answer a research question while providing solutions to improve upon a situation. The Design Bugs Out project of 2008 was aimed at identifying and remedying the causes of healthcare associated infections, where they were associated with the design of equipment used on wards ('Design Bugs Out-Rethinking Hospital Furniture', 2009). A number of items of ward furniture were redesigned or introduced as a result of the project. Similarly, the Design Council project for reducing violence in accident and emergency departments in the UK advocated the method of designing, prototyping and testing solutions to problems in departments and measuring the resultant changes (*Reducing Violence and Agression in A and E Through a Better Experience*, 2011). Both of these projects could be said to be actively applying design thinking, a systemic, creative and iterative approach to problem solving (Brown and Wyatt, 2010). Parallels can be drawn between the approach the Design Council applied to these projects and the action research approaches described in previous paragraphs.

5.5.3 Synthesis of Action Research and Design Research Methods

The research method applied in this chapter is a combination of action research and design research as it has been applied in the field of HCI. A mixture of these two approaches afforded the author the opportunity to collaborate with the broad range of stakeholders in the DoC Lab

research group and eSTi², whilst simultaneously gathering information about how novel diagnostic technologies might be successfully developed in future.

5.6 Method

The author collaborated with the DoC Lab research group in progressing a diagnostic technology from the proof of concept stage to the preclinical research prototype stage. Throughout this development activity, the author conducted design experiments proposing how the technology might be adapted so that it could be incorporated into a wider system, rendering it useful from a clinical and public health perspective for a particular application. In this case, the application was the detection of the sexually transmitted infection, Chlamydia Trachomatis.

A proof of concept technology was developed by the DoC Lab research group. This proof of concept technology was used as a starting point for the action research design activity. The goals of the activity were as follows:

1. **Design for Pre-Clinical Trial** – The system must be capable of testing 100 urine samples. 50 positive for Chlamydia Trachomatis and 50 negative and incorporate a negative control for each test.
2. **Design for Clinical Care Pathway** – The design of the system must be tailored toward eventual use in a clinical care pathway for Chlamydia Trachomatis testing with descriptions of how it will be further developed from the pre-clinical trial phase.
3. **Design Process Formulation** – Information gathered from the cyclical design, assessment and redesign of the system will be used to formulate a descriptive design process model of how the author approached the design of a self-use molecular diagnostic device for STIs.

5.6.1 Design Experiments

Design work was carried out by the author in consultation with experts in the research group. Design criteria were formulated using the expertise of the group and supporting literature. These design criteria were then used to propose design solutions which were assessed informally by the author before being discussed with the experts as a panel for further assessment. The information collected from the assessment of the design proposals was then used to enhance future proposals and formulate a design process model.

Records were kept of the presentations and meeting details where design proposals were presented. A record was also kept of other technological development occurring in the research group where it related to the design experiments. Three design experiments are documented in this chapter, each building on the information gathered during the previous experiment. The

first experiment was exploratory and based on the technical requirements of the proof of concept technology and the clinical care pathway in which the technology would function in future.

The findings of the three design experiments were applied to the final design of a portable, low-cost, isothermal nucleic acid amplification test for Chlamydia Trachomatis. The design of the preclinical trial prototype is detailed in the chapter.

A selection of the design work conducted as a part of the work described in the thesis is shown in this chapter. Further design work and supporting documentation that do not directly fulfil the objectives of this chapter are shown in Appendix C.

5.7 New Technology as part of a Clinical Care Pathway

A novel diagnostic technology that is to be useful from both a clinical and public health perspective must be designed to be part of a clinical care pathway. A clinical care pathway is the pathway that must be taken from the introduction of the patient to health services through to the successful treatment of the infection they have presented with (Nwokolo *et al.*, 2016). From a public health perspective, the clinical care pathway will include a mechanism for collecting patient data which will be used to understand the epidemiology and prevalence of infections (Public Health England, 2016).

It is important that any new testing device is designed with such a pathway in mind and that data collection from the pathway would still be possible with the use of the new device (Price and St. John, 2014). Recent research has investigated the feasibility and patient acceptability (Aicken *et al.*, 2016) of moving a Chlamydia care pathway online and a framework for doing so has been proposed (Gibbs *et al.*, 2016).

An online clinical care pathway affords the opportunity for testing to be carried out at locations remote from healthcare facilities. There may be significant advantages to giving consideration to the online clinical care pathway from the very earliest proof of concept stages of development of a new technology. The NCSP (National Chlamydia Screening Programme) provides a logical model pathway for the development of the new technology to be based around. The NCSP is a screening programme that encourages patients to seek testing services online, collect samples themselves and send them via the postal service to a laboratory for screening (*National Chlamydia Screening Program*, 2003). Figure 5-1 shows the care pathway used by the NCSP.

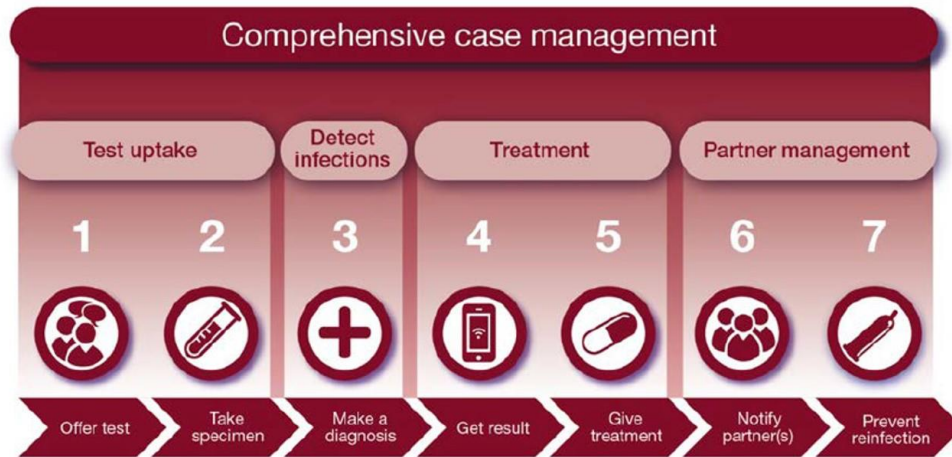


Figure 5-1 – The NCSP Chlamydia pathway (NCSP, 2016) showing the pathway from test uptake to partner notification and reinfection prevention.

5.7.1 Use-Steps

The use-steps shown below in Figure 5-2 and described in detail thereafter are based on the online clinical care pathway used by the NCSP in the UK and were developed through consultation with experts from the eSTi² and DoC Lab research groups. These steps were used to inform the action research design activity.

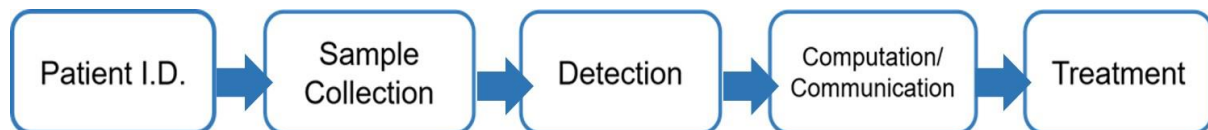


Figure 5-2 - The consecutive steps of the clinical care pathway for Chlamydia Trachomatis detection and treatment used to define design requirements for a self-use molecular diagnostic for Chlamydia

5.7.1.1 Patient Identification.

Patient identification is necessary to the extent of linking the patient definitively to the test they have carried out and confirming that the biological sample given is their own and not somebody else's. This link between the identity of the patient and the test ensures the safety of treatment and that the right person receives treatment for the right infection.

5.7.1.2 Sample Collection.

A sample must be collected by the patient. The self-test pathway proposed here is for the detection of genital, pharyngeal or rectal Chlamydia Trachomatis infection to the exclusion of conjunctival Chlamydia infection. For a genital Chlamydia test for men, the preferred method of sample collection is a urine sample, for a genital Chlamydia test for women a vulvovaginal swab

(Nwokolo *et al.*, 2016). Research has also shown that samples collected using self-sample collection methods for pharyngeal and rectal Chlamydia infections are comparable to samples collected by clinicians (Alexander *et al.*, 2008).

After successful sample collection, the sample must undergo sample preparation. Sample preparation, in the case of the technologies described in this chapter, requires cell lysis, DNA extraction and purification and finally DNA amplification, which will allow the DNA of the pathogenic bacteria to be detected (Balachandran *et al.*, 2013).

5.7.1.3 Detection.

Detection of the pathogenic DNA can be achieved by the proof of concept technology described below. The technology uses an isothermal amplification method and fluorescence detection to detect target pathogenic DNA (Craw *et al.*, 2015).

5.7.1.4 Computation/Communication.

Data are produced through the process of DNA detection. To be a true self-test, these data must be transmitted to the patient in the form of a positive or negative result. It is worth considering that the sample collection and detection mechanisms in this system may be used in the absence of a computer, tablet or smartphone. In that situation, it may be considered whether or not the device is capable of storing information for later retrieval or indicating a result to the patient in real time.

5.7.1.5 Treatment.

The treatment of uncomplicated urogenital and pharyngeal Chlamydia infection requires either a one off dose of Azithromycin or a 7 day course of Doxycycline antibiotics, the latter being the preferred treatment for rectal infection (Nwokolo *et al.*, 2016). These antibiotics would have to be prescribed in a way that allows the patient as much privacy and autonomy as possible. How the patient receives the treatment falls outside the scope of this research, however, consideration of the fact that the patient will receive a result and instructions on how to procure treatment remotely may have an impact on the design requirements of the testing device.

5.8 From Proof of Concept to Pre-Clinical Trial Prototype

5.8.1 Proof of Concept Technology

The following is a description of the proof of concept technology that was used as the starting point of the action research design activity. Technical details have been described where knowledge of them was relevant to the author in enabling the execution of useful design changes to the technology. This proof of concept technology would be developed to work within the clinical care pathway described above.

One of the proof of concept technologies developed in the DoC Lab research group was a low-cost, simple and miniaturised platform for real-time isothermal nucleic acid amplification (Craw *et al.*, 2015). The technology was developed as part of the overall effort in the DoC Lab research group to produce a modular, sample in to answer out, point-of-care diagnostic system for sexually transmitted infections (Branavan *et al.*, 2016). Figure 5-3 below shows the research areas pursued by DoC Lab to this end. The research areas related to the proof of concept technology subject of the design experiments described in this chapter are highlighted.

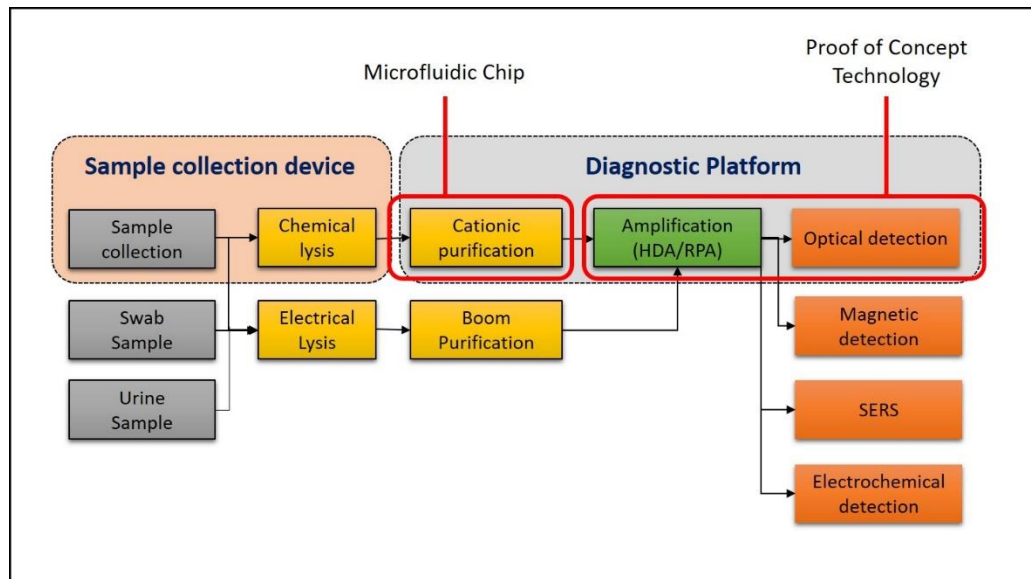


Figure 5-3 - The various research areas in the DoC Lab research group dedicated to the modular development of a sample in to answer out portable testing system for STIs. Highlighted are the technologies used in the proof of concept prototype and the microfluidic chip that was designed for use with it.

Figure 5-3 shows that the proof of concept technology would, in a full sample in to answer out system, be used in conjunction with a microfluidic chip for sample preparation. In the microfluidic chip prototype, the sample is introduced to the chip using a pipette and the chip is placed onto the heat sink in the top of the platform. The reaction chambers, where fluorescence occurs as a result of the presence of amplified target DNA, were required to line up with the LED's (for excitation) and fibre optic channels (for optical fluorescence detection). The key functional components of the proof of concept platform are as follows:

1. 2 x Arduino Uno (Arduino, Turin, Italy) reprogrammable microprocessors for heating and optical detection control.
2. Photodiode Array PCB – 6 x photodiodes for optical fluorescence detection of amplification signal.

3. 6 x Optical fibres and band pass filters – mounted above the photodiodes for signal transmission from reaction chamber to photodiode.
4. Heater and LED Array PCB – Heater provides the correct temperature for amplification and LED's excite the sample in the reaction chamber to produce fluorescence
5. Opaque Casing – An opaque casing prevents interference with the amplification signal from external light sources.

The list above are examples of design constraints, crucial to the operation of the technology, which therefore remained constant throughout the design experiments. See also Figure 5-4 below.

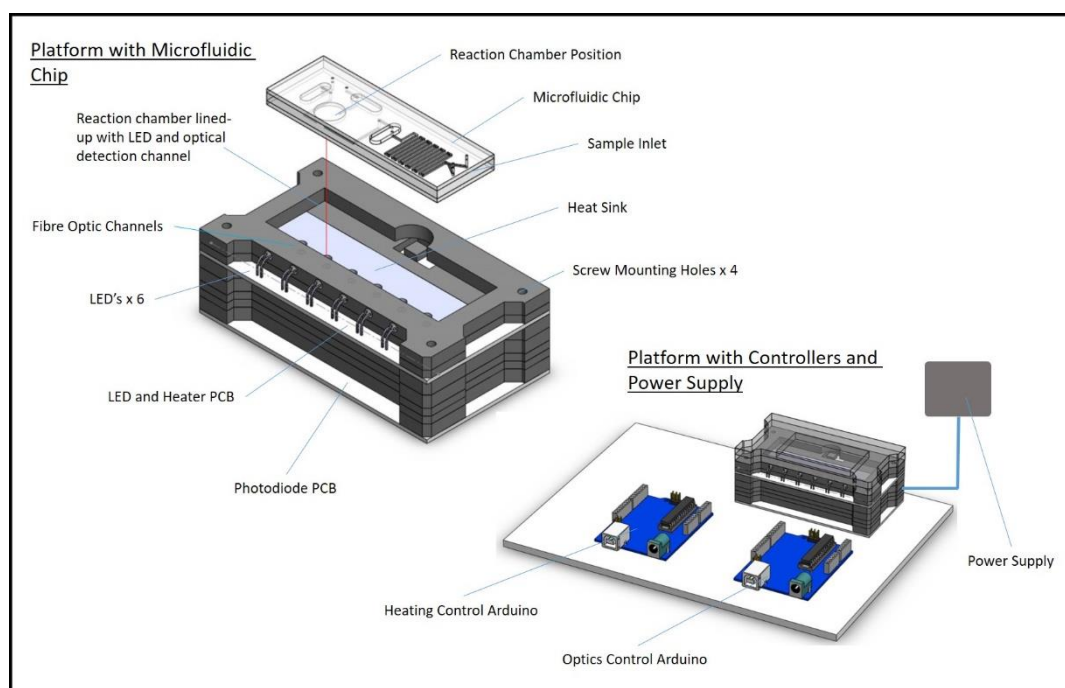


Figure 5-4 - The proof of concept amplification and detection platform, shown with prototype microfluidic chip and Arduino control boards (Bottom right corner).

The platform uses an isothermal nucleic acid amplification method, capable of achieving DNA amplification at a steady, relatively low temperature (60-65 °C) (Where HDA – Helicase Dependant Amplification, assay and reagents were used this is the case. Later, the device used RPA – Recombinase Polymerase Amplification assay, which functions optimally at 37 °C) (Branavan *et al.*, 2016). The isothermal amplification method avoids the need for thermal cycling between high (92-96 °C), low (45-65 °C) and medium (68-74 °C) temperatures which is characteristic of polymerase chain reaction (PCR) nucleic acid amplification methods (Jiang *et al.*, 2012). This allows the platform to be constructed at a lower cost and use less power than a PCR diagnostic device (Craw and Balachandran, 2012). The platform constitutes robust, off the shelf components to keep costs down and make repeat construction of the prototype easier.

5.8.2 Size and Construction

The proof of concept platform was constructed using layers of laser cut plastic. The layers of plastic provided support for the PCB's (Printed Circuit Boards) which carried the key functional components of the device (principally the photo diode arrays, LED array and heating system). The layers also provided housing for the fibre optics which carry the amplification signal from the microfluidic chip to the photodiode array. The construction method was chosen because it made the platform low-cost and ensured that the repeat construction of the device would require minimal tooling (Craw *et al.*, 2015). See Figure 4-5 below for further description of the function and configuration of the layers of the device.

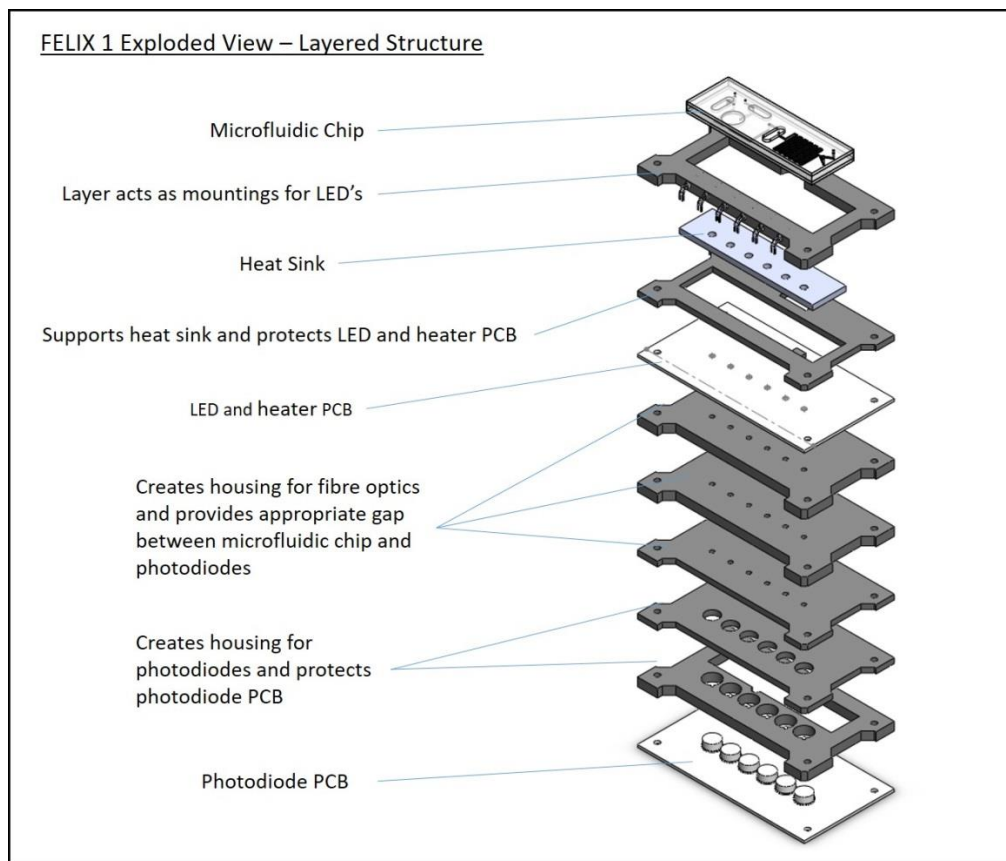


Figure 5-5 – The layered structure of the proof of concept technology.

At the proof of concept stage, the platform was controlled by two Arduino Uno reprogrammable microprocessors (See also Figure 4-4 above) and it was a requirement that testing was carried out inside an opaque container to avoid ambient light causing interference with the fluorescent amplification signal.

5.8.3 Automation

As is described above, the proof of concept technology was controlled by two reprogrammable microprocessors. These microprocessors ensured that when the heaters were activated, the

LED's would excite the sample in the sample chamber in conjunction with data being collected from the photodiodes. In the proof of concept prototype, this process had to be performed manually and monitored by the user of the device. This represented a key design challenge, as an untrained user would have to be capable of operating the device in the simplest way possible. Automation of the sample preparation and activation of the detection mechanisms would therefore have to be designed into the preclinical trial prototype version in order to increase its potential for use as a self-testing device.

In summary, the proof of concept device was designed to prove that a miniature, low cost, simplified nucleic acid amplification test (NAAT) was feasible. The construction of the device was intended to be low-cost and easily repeatable. Open source, reprogrammable microprocessors were used to control the device in order to provide flexibility to the researchers carrying out experiments with it.

The following design experiments were devised to investigate whether and how the proof of concept technology described could be developed toward incorporation into a clinical care pathway for Chlamydia self-testing and what design methods should be applied to the task.

5.9 Design Experiments

Three design experiments were carried out. The first of the experiments was exploratory, focussing on investigating how the criteria defined by the DoC Lab and eSTi² research groups might be satisfied through development of the proof of concept platform. Design criteria for each experiment are described in their respective sections below. The subsequent experiments built on the findings and investigated which design methods would be appropriate to the design problem. A summary of the experiments is shown below:

Experiment 1 - Casing Design – An exploratory investigation to determine to what extent the platform in its current form was suitable for the clinical care pathway for Chlamydia self-testing.

Experiment 2 - Miniaturisation – An iterative design activity to alter the construction method of the platform in order to improve functionality.

Experiment 3 - Contexts of Use – An investigation into the differing contexts of use implied by the constraints of the technology.

5.10 Design Experiment 1 - Casing Design

The first design experiment explored the feasibility of using the proof of concept technology in its current state as a self-use molecular diagnostic for the detection of sexually transmitted infections. Firstly, design criteria were established which are shown in Table 5-1 below. The

design criteria are based on the studies shown in Chapters 3 and 4 and are tailored to the clinical care pathway described above.

Table 5-1 - Design Criteria Table – Design Experiment 1

Design Criteria	Source and Constraints
Handheld/highly portable	<p>The proof of concept prototype was described as a point of care device when published (Craw <i>et al.</i>, 2015). Point of care devices are ordinarily desktop based and are therefore typically larger than handheld devices and are ordinarily powered using the mains (240v power supply).</p> <p>The technology in the handheld prototype was, however, lightweight, simple, and low-cost and had a low power requirement, allowing for flexibility of design.</p> <p>Interviews described in Chapter 3 confirm that a high level of portability was a key requirement expressed across experts of various disciplines involved in the project.</p>
Molecular diagnostic	<p>The isothermal nucleic acid amplification testing (INAAT) method and the HDA (Helicase Dependant Amplification) assay and reagents used were not negotiable in any design changes made. Later, the HDA assay was replaced with an RPA (Recombinase Polymerase Amplification) assay which allowed the test to run at a lower temperature (optimal 37°C) (Branavan <i>et al.</i>, 2016). The use of the RPA assay allowed for a faster, more reliable and lower power test that could be run in approximately 20 mins.</p> <p>Regardless of this change from the original published description of the proof of concept technology, the use of microfluidics and optical fluorescence detection cannot be altered through these design experiments.</p>
Mobile phone controlled or a smart device	<p>The work of Work Stream 4 of the eSTi² project was based around a clinical care pathway for Chlamydia being developed that was usable online, probably on a mobile phone. This constraint was carried over into the technical work of Work</p>

	<p>Stream 2 and DoC Lab and, as a result, into the design experiments described.</p> <p>The importance of the communication of test data is highlighted in the description of the clinical care pathway given above.</p>
Low cost	<p>The functional components of the proof of concept device are low-cost and free of complex instrumentation. As a result, it is a priority that the outcomes of the design experiment do not unduly increase the cost of the device.</p>
Easy to use	<p>The proof of concept prototype is not usable by ordinary users/patients as its use requires specialised laboratory and that complex protocols are followed.</p> <p>Expert interviews recorded in Chapter 3 confirm that ease of use is a key requirement of the self-use system.</p> <p>If the system is to be a self-use system, this issue must be addressed throughout the execution and assessment of the design experiments.</p>

5.10.1 Design Method

The design methods described for use in the experiments would later be compiled into the design process model shown in the second part of this chapter. This process was repeated iteratively so that the design process developed alongside the working prototype designs. For this experiment, key functional components were measured or relevant technical specifications were acquired so that the components could be modelled using SolidWorks 3D modelling software (Dassault Systemes, Velizy, France). Casing concepts were sketched by hand and then converted into 3D models. Where appropriate, 3D models were converted into STL (Stereo-Lithography) files and 3D printed (Objet30 Pro, Stratasys, Eden Prairie, MN, USA) to allow for an appreciation of scale by the expert panel.

5.10.2 Experiment 1 - Design Outcomes - 1

The outcome of the first design experiment is shown below in Figure 5-6. The first design outcome was an attempt to incorporate the form of the proof of concept technology into a casing that would be usable in contexts of use coherent with the requirements of the clinical care pathway.

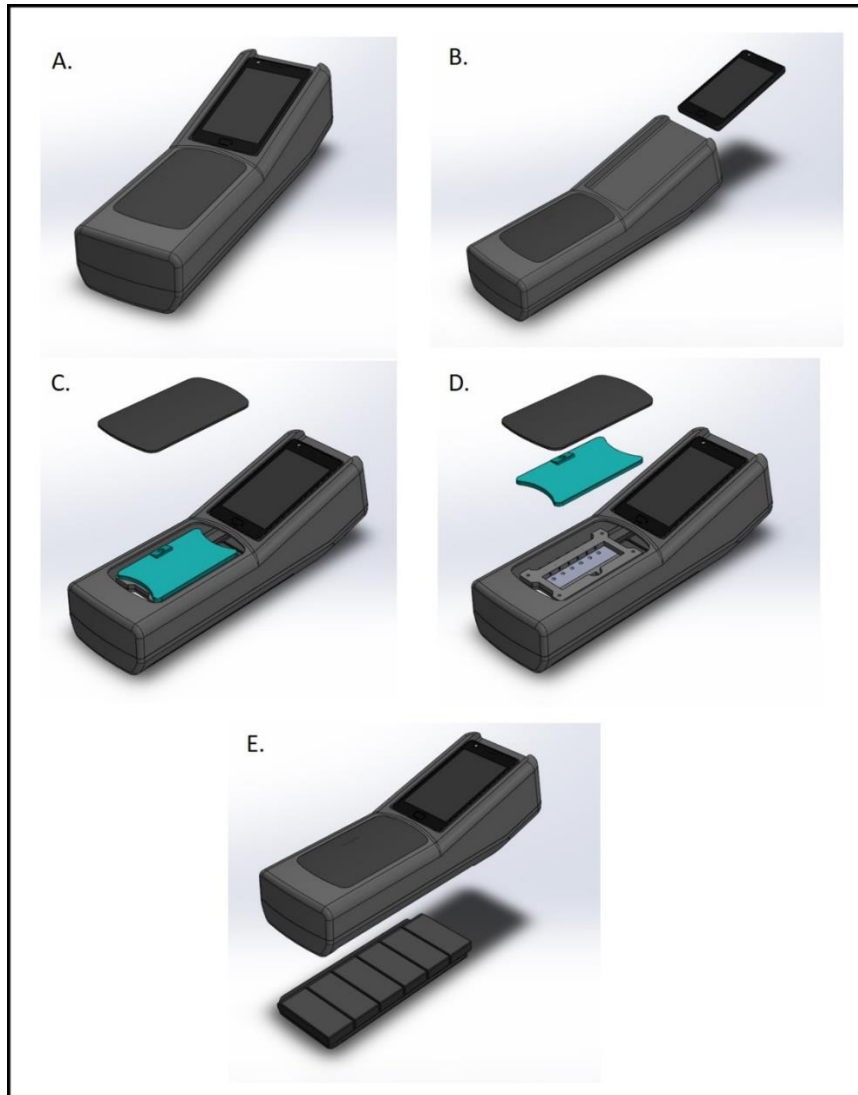


Figure 5-6 - The first design experiment explored the possibility of a handheld/portable casing designed around the current configuration of the proof of concept platform technology.

Figure 5-6 shows images of the concept designs that were developed in the first design experiments. The images displayed in the figure are described below:

- A. The casing design shown is an attempt to make the platform handheld and incorporate a smartphone to provide a user interface. The tilted angle of the smartphone screen was designed to improve visibility for the user at the same time as increasing space inside the casing for the required internal components.
- B. It would be possible for the smartphone to communicate with the testing device either through a wired or wireless connection. In this design, the concept was that the smartphone could be either placed in the cradle on the top side of the device during use or used independently.

- C. In this configuration, access to the testing platform would have to be gained through an opening in the top of the device. Through this opening, the user would be able to insert the microfluidic chip with a sample loaded into it.
- D. A cover or panel would be incorporated into the design of the casing or the microfluidic chip to ensure that external light could not interfere with the testing process.
- E. The rechargeable battery pack would allow the platform to run a number of tests between each charge. The battery pack in this configuration was designed to be removable.

The images in Figure 5-6 above show the exterior elements of the concept, below, in Figure 4-7, the internal components are shown in greater detail.

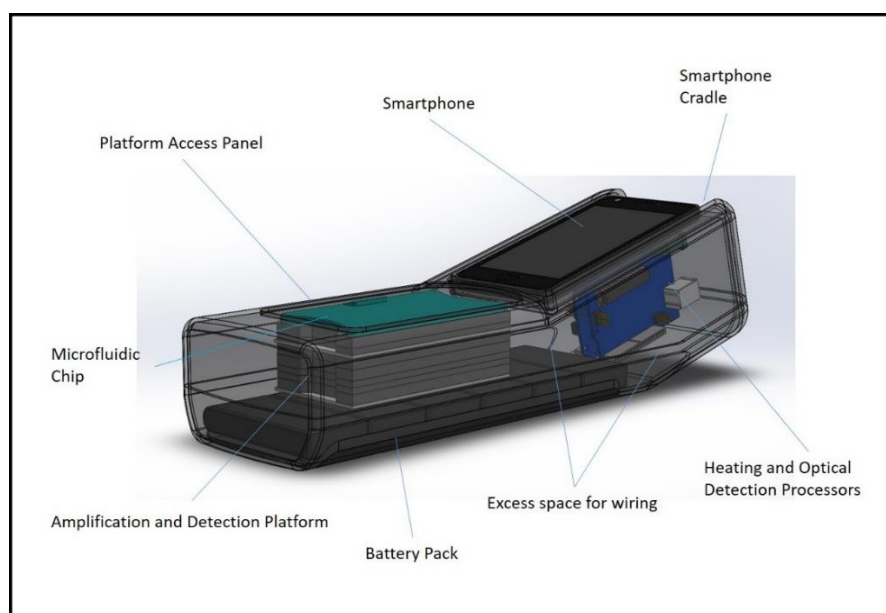


Figure 5-7 - A concept was developed to fit the system components into a handheld/portable casing design.

It was clear that the dimensions of design outcome 1 were excessive for a highly portable, handheld device and raised numerous questions about an appropriate context of use for the device if it appeared in this form. At approx. 300mm in length, the device would be unsuitable for use in the context of the clinical care pathway described due to its lack of portability. Furthermore, it does not fulfil the concept design requirements defined in Chapters 3 and 4. Further explanation of the dimensions of the device are shown in Appendix C - 1.

5.10.3 Experiment 1 - Design Outcomes – 2

A second design was produced as part of design experiment 1. The same design method was used to show what the design outcome would be if the casing was designed to match as closely as possible the dimensions of the proof of concept platform and associated components.

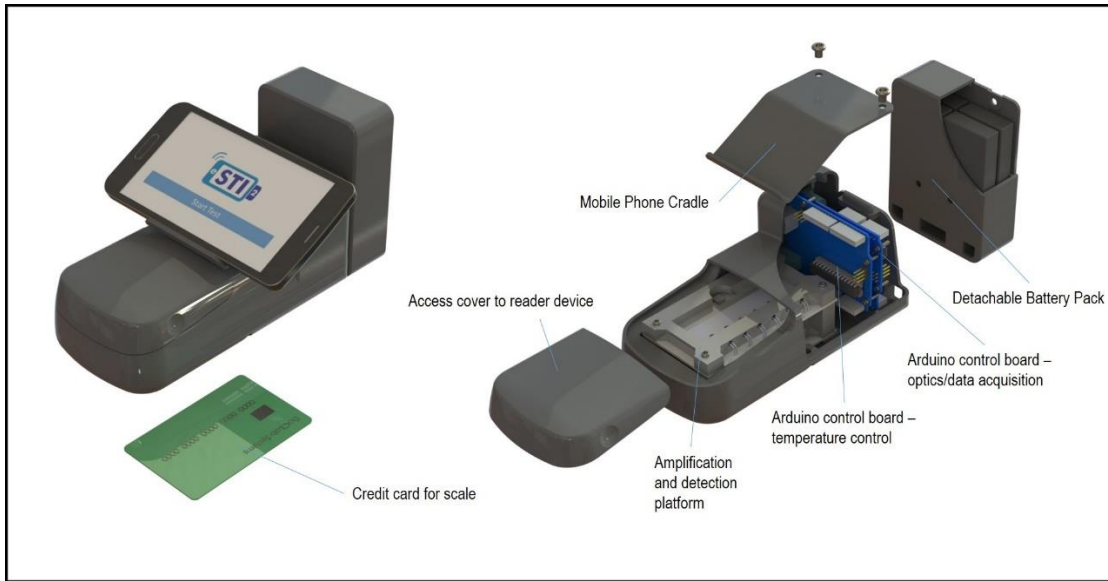


Figure 5-8 - Design experiment 1, design outcome 2. The design has been miniaturised to exactly fit the components of the proof of concept technology.

The second outcome of design experiment 1 is shown in Figure 5-8 above. It was clear that this was the smallest that the device could be while maintaining the structure and construction methods of the proof of concept prototype and the components associated with it.

Dimensions of the second design outcome and the 3D printed model which was created for a demonstration of scale is shown in Figure 5-9 below:

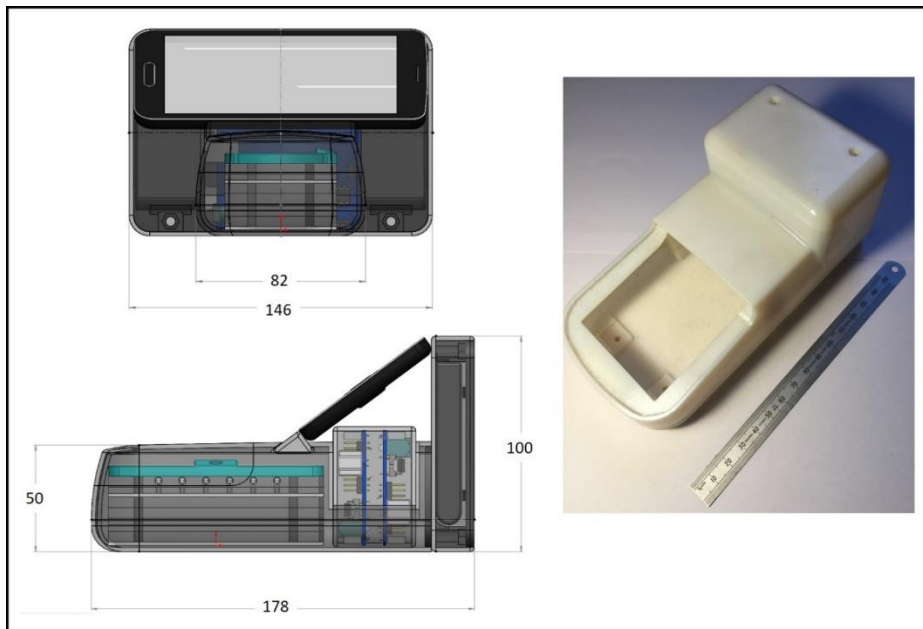


Figure 5-9 - Design experiment 1, design outcome 2. Dimensions and 3D printed prototype used for assessment by the expert panel

5.10.4 Assessment of Design Experiment 1

The two design outcomes were presented to a panel of experts for assessment. After assessment by the expert panel, the designs were assessed by the author through the creation of storyboards of use scenarios. The expert panel consisted of the following:

Table 5-2 - Design Experiment 1 Assessment Panel

Expertise	Position
Systems and Electronics Engineering, Micro-engineering and Molecular Diagnostic Technologies	Professor
Electronic Engineering and Artificial Intelligence	Professor
Human Centred Design and Computer Science	Postdoctoral Research Fellow
Biology and Paper Microfluidics	PhD Student
Requirements Modelling	PhD Student
Microfluidics	Postdoctoral Research Fellow

The minutes and details of this meeting are shown in Appendix C-2.

5.10.4.1 Design Outcome 1 Assessment

The group found that the overall appearance of the design was appropriate for a handheld device. However, the size of the device, at some 300mm in length, was clearly a problem. Assessment of the design then centred on the transfer of a urine and/or swab sample from a sample collection device to the microfluidic chip and thereafter from the chip to the amplification and detection platform. A separate cover or panel which had to be opened to allow the microfluidic chip to be inserted into the amplification and detection platform was deemed to be inconvenient.

The problem of the result of the test being stored or transferred to the mobile phone and how this might be achieved was discussed. While this is an important point, it may not relate directly to the physical appearance of the device.

5.10.4.2 Design Outcome 2 Assessment

A key difference between design outcome 2 and design outcome 1 was that the mobile phone would be mounted on a cradle on top of the test and would communicate wirelessly with the testing device. This was considered by the group to be a more desirable design as it avoided the need for a user to plug their phone directly into the device. This meant that in the event of the user not having a mobile phone, the test would not be rendered unusable.

The smaller dimensions of the test were considered an improvement but it was still pointed out that the test, at that size, did not constitute a highly portable self-test. The issue of the removable battery pack on the back of the device was raised as the power provided by the batteries was not adequate to allow multiple tests to be carried out.

In light of this discussion, the author constructed storyboards to assess how the test might be used, an example is shown below in Figure 5-10.

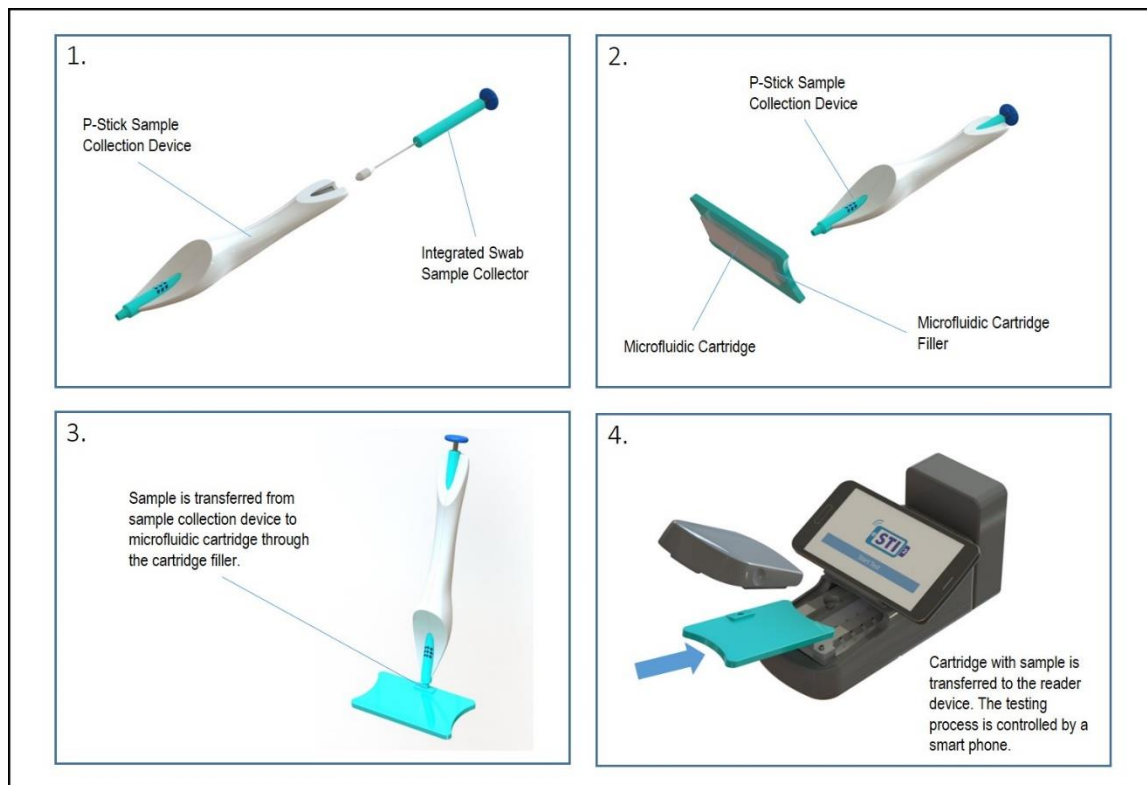


Figure 5-10 - Design experiment 1, design outcome 2. Story boards explaining use steps were used to assess the design and how it would fit into a full, self-use sample in to answer out system

The storyboarding exercise showed how a separate sample collection device, which had been developed within the DoC Lab research group, would be used to collect the sample. The sample would then be transferred to the microfluidic chip and the chip would be transferred to the detection device. Carrying out the design work and storyboards for this highlighted the areas where improvement of the design was required if it were to be clinically useful in a particular context of use. It also made clear that the device could not be designed in isolation but that the design of each of the components of the testing system were interdependent.

5.10.5 Design Experiment 1 - Conclusions

Design experiment 1 allowed the author to conclude that the proof of concept system was too large to be incorporated into the design of a usable self-testing device and required structural

modification. This was due to the requirement that a self-test be as portable as possible. Design experiment 1 also made it clear that the technologies that corresponded with each section of the clinical care pathway could not be designed in isolation and were highly interdependent.

The expert panel and the author concluded that while the mobile phone was essential to the operation of the device, it should not have to interact physically with it. This is in keeping with views expressed by interviewees in Chapter 3 and focus group participants from the work of Work Stream 4 (Gkatzidou *et al.*, 2015). The conclusion was also drawn that the Arduino processors were too large and caused an unreasonable impact on the design of the device, as a manufactured version of the system would have very small processors incorporated into the heating, LED array or photodiode PCB's.

Even with the removal of the Arduino processors and the assumed reduction of the battery volume by a considerable margin, the device would be somewhat bulkier than a smartphone. Figure 5-11 shows the concept design produced as a result of these conclusions. This concept was used to direct further design experiments. The concept represents an estimate of the possible scale of the device using the proof of concept technology approximately in its original form and shows the supporting equipment required and how they would map onto the clinical care pathway.

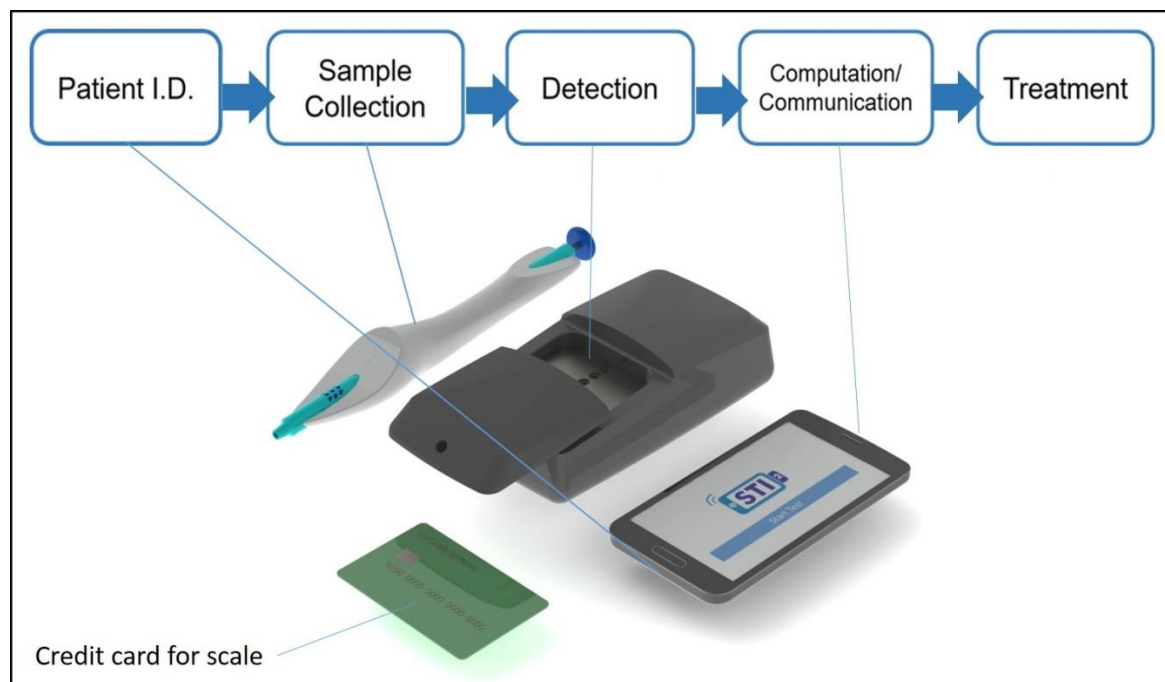


Figure 5-11 - Design experiment 1, final conceptual outcome showing one way in which the proof of concept technology might be used in a sample in to answer out system for a Chlamydia clinical care pathway.

5.11 Design Experiment 2 – Miniaturisation and Component Configuration

The focus of design experiment 2 was the miniaturisation of the proof of concept technology with consideration of how the technology would better interact with the microfluidic chip. Building on the conclusions of design experiment 1, further design criteria were established.

Table 5-3 - Design Criteria Table – Design Experiment 2

Design Criteria	Source and Constraints
Improved Microfluidic Chip Loading	The previous experiment showed that the microfluidic chip would need to be loaded with a sample prior to being inserted into the detection device. A user friendly way of achieving this had not yet been considered. The size and arrangement of the microfluidic chip was dependant on the manufacturing method used in the group, which allowed for rapid prototyping and experimentation with microfluidics.
Less Bulky Structure	The layered structure of the proof of concept platform was prohibitively bulky. The original rationale for the layered structure, that of making it easy to manufacture at a low cost with minimal tooling, was not referred to as essential in the expert panel assessment or expert stakeholder interviews. The importance of a miniaturised device however, was expressed from various points of view.

5.11.1 Design Method

It had become clear at this point that the design experiments were following a pattern found commonly in design practice; that of design, iteration, assessment and redesign (Fallman, 2003; Keefe *et al.*, 2010; West *et al.*, 2014). Design processes that follow this iterative cycle have been suggested as a way of managing the complex and diverse needs of the varied stakeholders involved in medical device design (De Ana *et al.*, 2013) and are a key component of the usability engineering requirements laid out in the IEC (International Electro-technical Commission) Standard 62366 - Application of Usability Engineering to Medical Devices (Hegde, 2013). The design cycle shown below, which is a representation of the activity undertaken by the author in

the action research design activity, is an adaptation of the basic design cycle described in the Delft Design Guide (Boeijen *et al.*, 2013).

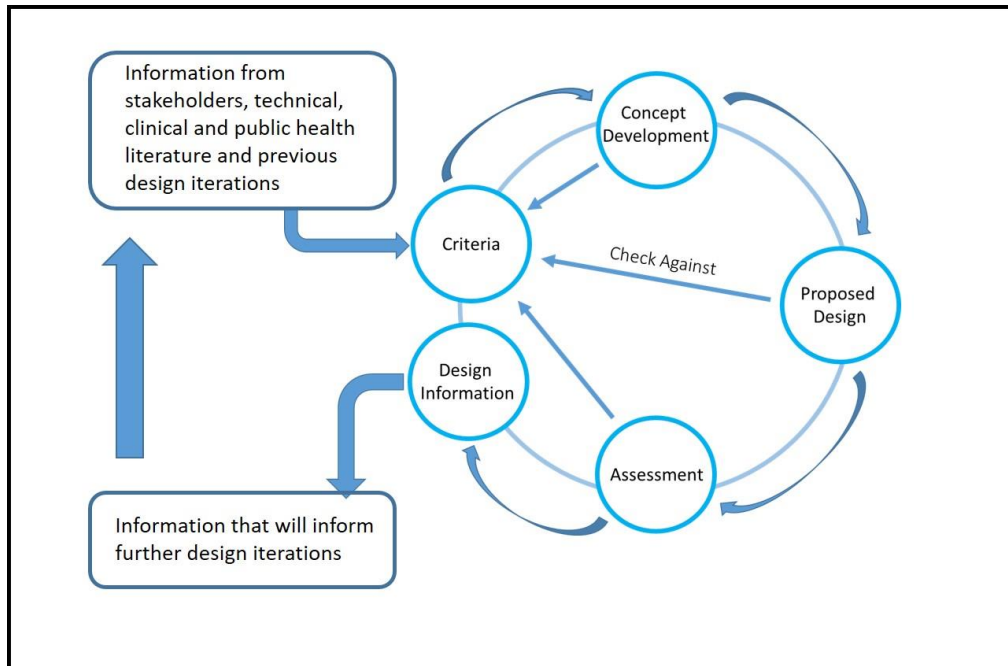


Figure 5-12 – A design cycle based on observation of the impact of the action research design activity in the research group.

The method shown in Figure 4-12 above was applied from design experiment 2 onwards in the action research design activity. The design methods described in this chapter are cumulative, i.e. the conceptual design process used in design experiment 1 was also used in this design experiment and is represented in the diagram above in the circle entitled 'Concept Development'. This cycle would later be incorporated into the design process model described in the second part of this chapter.

Design experiment 1 showed that the proof of concept technology could not be developed in isolation; the various components of the technology, such as the sample collection device, had to be considered together. The iterative cycle shown was therefore used simultaneously for various component designs as well as to iteratively develop the system design as a whole.

5.11.2 Experiment 2 - Design Outcomes - 1

Miniaturisation of the proof of concept platform was first attempted through removal of the laser cut plastic layers which provided the structure of the device. Doing this allowed the author to propose a significantly miniaturised version of the technology, as is shown below in Figure 5-13.

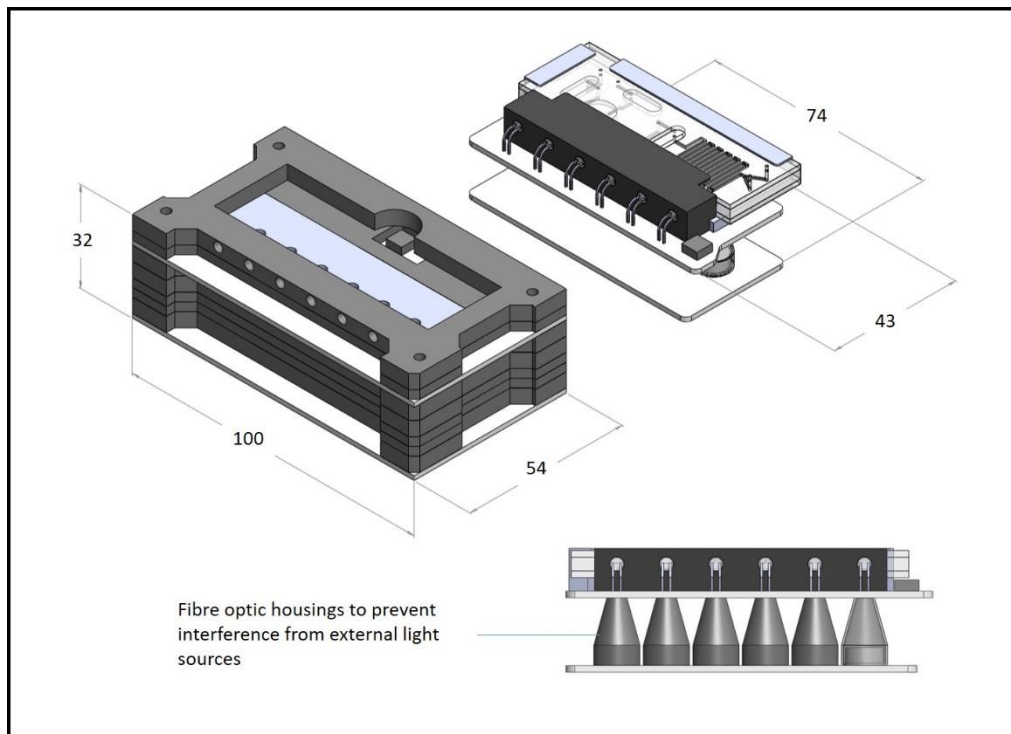


Figure 5-13 - Design experiment 2, design outcome 1. Size reduction of the proof of concept prototype components.

The laser cut plastic layers were removed leaving areas of empty space which could be utilised for wiring or other components, thus potentially reducing the size of the complete device significantly. The diagram shown in Figure 5-13 shows a concept design of the size that the PCBs could be, dependent on the dimensions of the microfluidic chip. Removing the plastic layers also provided more options for the way in which the microfluidic chip could be loaded onto the device. With no plastic layers in the way, the chip could be loaded from the sides of the device as well as from the top.

As well as being structural, the plastic layers were designed to prevent external light interference from effecting the signal carried by the fibre-optics and band-pass filters to the photodiodes. New, smaller components could be added to fulfil these requirements and a concept for these are shown at the bottom of Figure 5-13.

A smaller device, with more options for how the sample-carrying microfluidic chip might be inserted provided a higher level of design flexibility to make concept proposals that would fit in with the clinical care pathway described above.

5.11.3 Experiment 2 - Design Outcomes - 2

The adaptation of the structure of the device provided the opportunity to consider changes in functionality. For example, if the microfluidic chip could now be loaded from the side as

opposed to the top, it would be possible to design a device capable of detecting the DNA of more than one pathogen, as, theoretically, more than one optical fibre could be lined up with each reaction chamber in the microfluidic chip.

A number of concepts were developed around this possibility. The question was raised of whether the proof of concept technology could be applied in various different types of device and in various contexts of use where the detection of multiple pathogens was required.

Figure 5-14 below shows design concepts that were devised by the author and shared with the research group. It is an example of how criteria were applied to the development of concepts and then assessed for their utility through collaboration with the research group. Collaborating with the group through sharing these design concepts brought about changes in the design of the components of the proof of concept system. Further examples of this cycle are shown in Appendix C-3.

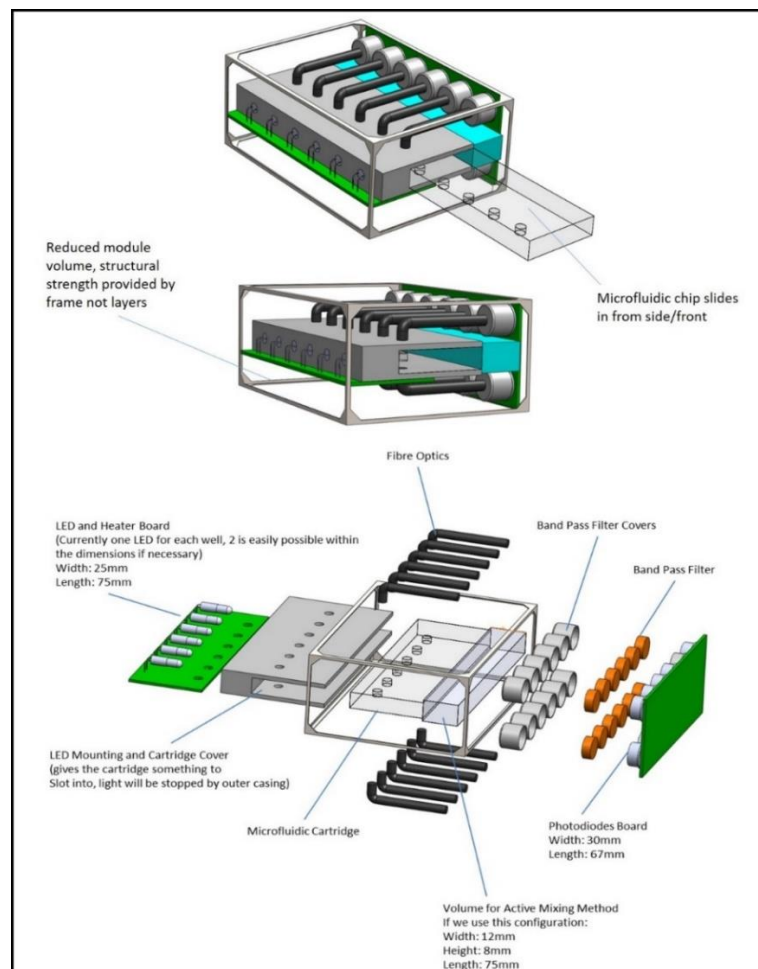


Figure 5-14 - Design experiment 2, design outcomes 2. Experiments with concept multiplexed systems which were assessed in collaboration with the research group and redesigned iteratively.

5.11.4 Experiment 2 - Design Outcomes – 3

The iterative cycle of concept development, proposal, assessment and further development brought about a redesign of the components of the proof of concept technology. The structural element of the amplification and detection module was provided by the housings for the optical fibres and rods placed at each corner of the PCB instead of layered plastic or the frameworks proposed as part of Design Outcomes 2. To further reduce the size of the components, the LEDs were replaced with OLEDs (Organic Light-Emitting Diodes), which were mounted onto a separate PCB.

PCB diagrams were drawn by a member of the research group and translated by the author into 3D models that could be incorporated into a system assembly model, see Figure 5-15 below. At this point, the size of the microfluidic chip had increased to accommodate the requirements of the preclinical trial prototype, making the device larger. Previous design experimentation had shown however that the technology could function in different ways in a number of sizes.

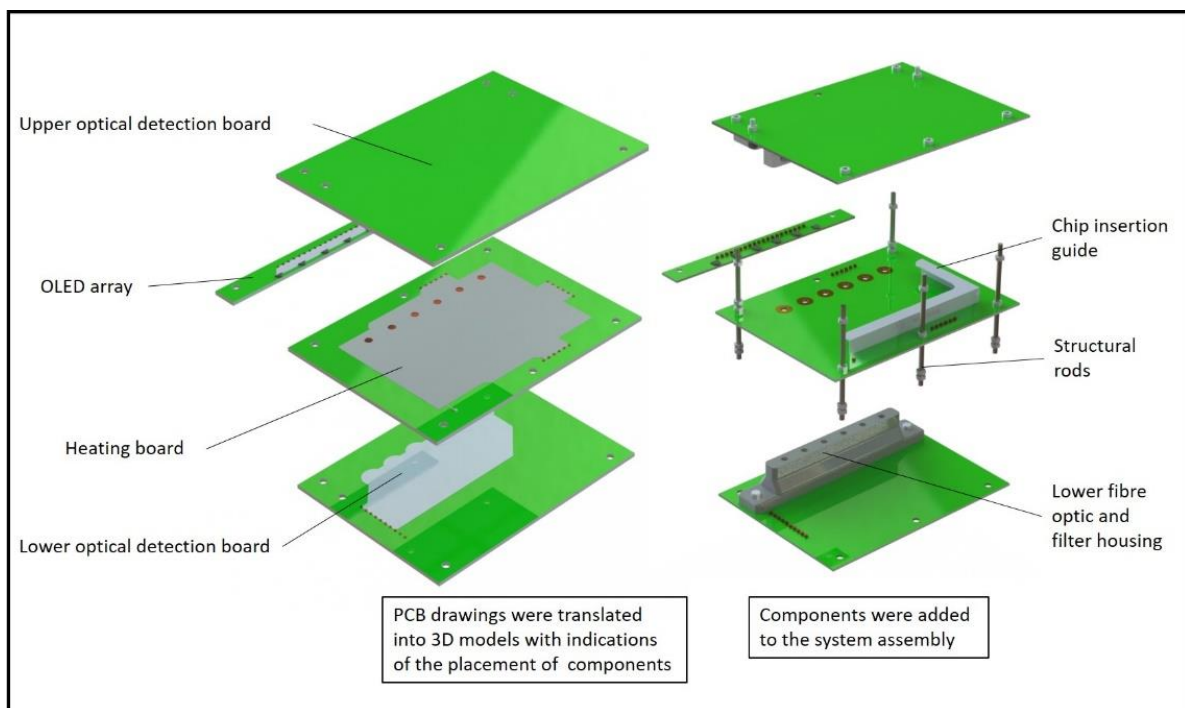


Figure 5-15 - Design experiment 2, design outcome 3. Final PCB designs translated into 3D drawings for system design purposes.

The different iterations and configurations of the device design were stored as 3D assembly models. The use of assembly models allowed the author to keep track of the components of the system, as making changes to one component has an impact on the components with which it interacts. The design cycle of concept development, assessment and redesign could be applied

on both an individual component level and the systemic level of an assembly of components. Further detail appears in Appendix C – 2.

5.11.5 Assessment of Design Experiment 2

The design work carried out as a part of design experiment 2 was highly iterative and was conducted in close collaboration with the DoC Lab research group. Therefore, assessment of the design work was continuous and conducted by the core members of the group, the details of whom are shown in the table below.

Table 5-4 - Design Experiment 2 Continuous Assessment Panel

Expertise	Position
Systems and Electronics Engineering, Micro-engineering and Molecular Diagnostic Technologies	Professor
Electronic Engineering and Artificial Intelligence	Professor
Molecular Biology and Engineering	Postdoctoral Research Fellow
Biology and Paper Microfluidics	PhD Student
Biomedical Engineering	Research Assistant
Microfluidics	Postdoctoral Research Fellow

5.11.6 Design Experiment 2 - Conclusions

Throughout design experiment 2, the key functional attributes of the proof of concept technology were preserved. That is to say that the arrangement of the functional components required to carry out amplification and detection in as many as 6 reaction chambers remained unchanged.

Through iterative conceptualisation, assessment and redesign, it was shown that the redesign of elements not directly associated with amplification and detection brought to light that the technology may be usable in different ways and in various contexts of use. For example, the amount of detection channels could be increased by including more detection components (as shown in Design Outcome 2) just as they could be decreased to reduce the size and cost of the device considerably. Making these changes may also alter the way in which the microfluidic chip can be loaded into the platform and thus effect the way in which a test is performed by the individual using the device.

The significant conclusion that can be drawn from design experiment 2 is that the proof of concept technology was modifiable to the point of being useful in a number of contexts.

5.12 Design Experiment 3 – Contexts of Use

The aim of design experiment 3 was to explore the possibilities and limits of the contexts that the proof of concept technology could be deployed in. Design criteria were based on these possible contexts of use. In design experiment 3, a design outcome was produced from each of the design criteria rather than a linear development of concept iterations.

Table 5-5 - Design Criteria Table – Design Experiment 3

Design Criteria	Source and Constraints
Context 1 – Repeat Use Detection Module	Design experiment 2 showed that the proof of concept technology could be modified to include up to 12 detection channels, allowing for multiplex detection of numerous infections in a single sample. While this makes the platform larger, it is still rapid (<20 mins) and low-cost and could be used as a point of care screening device for STIs. As this could, in theory, take the testing element of the screening process out of the lab, samples could still be self-collected in some way. Potential users have indicated that they would like to be able to access a test in numerous ways and locations. Providing a low cost, low power device may facilitate this even if a full self-testing experience is not possible.
Context 2 – Single Use Detection Module	A self-testing device should ideally be low-cost, easily accessible to the public, single use and disposable. The single use detection module criterion is designed to explore how this might be achieved with the proof of concept, optical detection technology.

5.12.1 Design Method

At this stage a further iterative step was taken in the understanding of how the design model originally shown in Figure 5-12 should be used. In this section, an assessment method to assist with management of the complexity of the diagnostic device is proposed. Figure 5-16 below highlights this. The assessment method used in this experiment is a complex systems diagram tool which is described below.

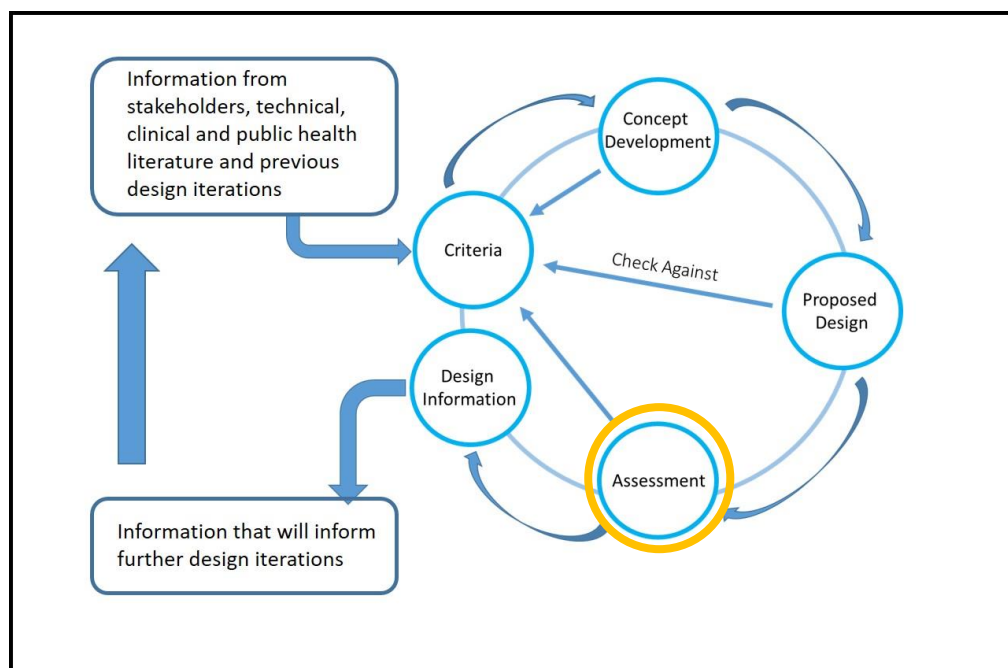


Figure 5-16 – Further iterative development of the design process model. Design experiment 3 test assessment methods in the design cycle. A system diagram building tool is used in this experiment to assess and improve design outcomes and the information available from them.

Design proposals for the different contexts of use were developed using the conceptual and iterative design processes described for design experiments 1 and 2. As a result of the complexity of the full sample in to answer out system proposed by DoC Lab, the number of components, requirements and stakeholder needs that could be applied to potential design outcomes had become difficult to manage.

To remedy this, a system diagram creation tool was used to manage design requirements and system component details. Bracewell and colleagues have proposed that adequately capturing design rationale requires the use of complex diagram creation tools capable of capturing various different types of information (2009). The subsequently devised DRed (Design Rationale Editor) was designed to be used throughout the design and in-service use of a

complex device, recording design changes, problem identification and communicating design rationale to a large and diverse team of stakeholders.

Similarly, Function Analysis Diagrams (FADs) have been proposed in research carried out in collaboration with aerospace and automotive companies showing that complex diagrams including information about function as well as structure and design rationale can be beneficial in managing complex design tasks (Auricchio and Bracewell, 2013). For this work, an open source diagram creation tool, designVUE (Visual Understanding Environment) (Auricchio, Bracewell and Armstrong, 2013) has been used to manage design complexity and has been used for design experiment 3 and the design of the preclinical prototype described below.

The designVUE editor allows the designer to create complex system diagrams which also act as a file storage system capable of storing concept drawings, technical drawings, spreadsheets and text documents. Figure 5-17 below shows an example of how the designVUE editor was used to track design information relevant to design experiment 3.

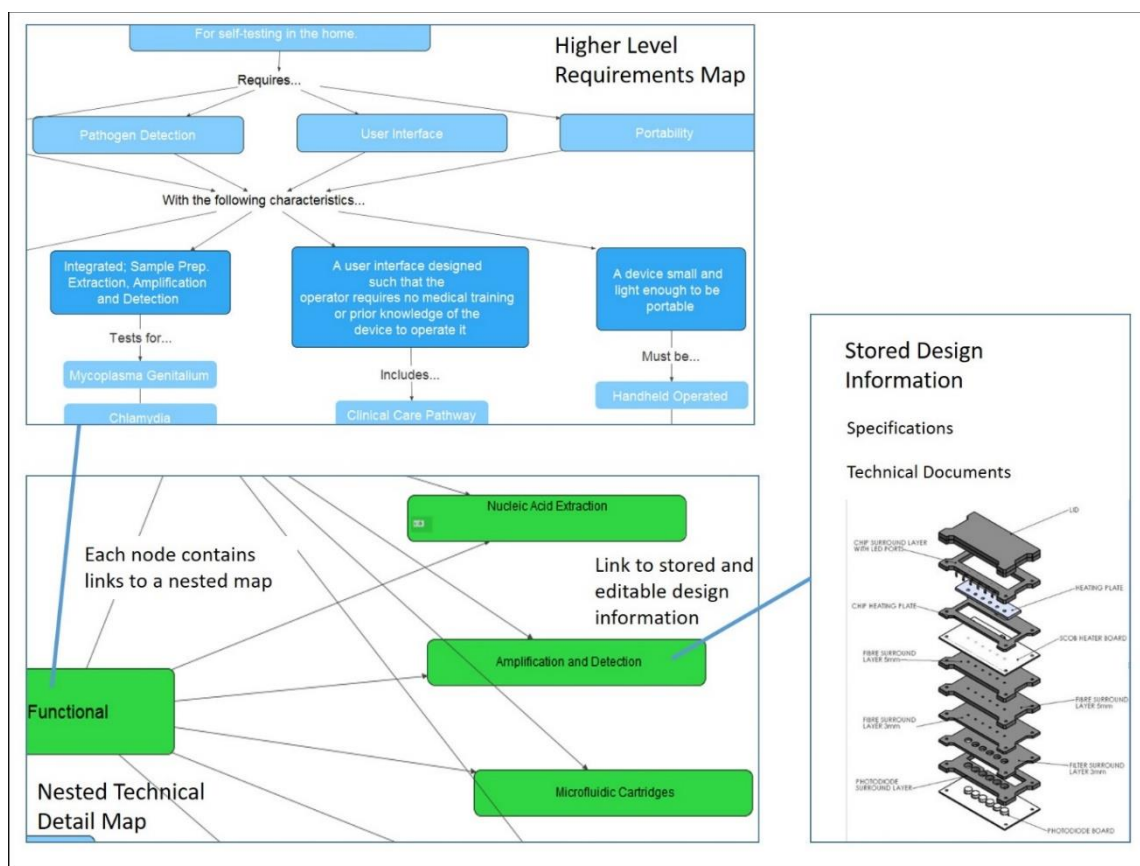


Figure 5-17 - Design experiment 3, system diagram for management of design information, see also Appendix C for full diagrams.

5.12.2 Design Outcomes

5.12.2.1 Context of Use 1 - Repeat Use Detection Module

If the proof of concept prototype were developed to include a large number of detection channels, it could feasibly be deployed as a desktop, point of care testing system for sexually transmitted infections, capable of the detection of a number of pathogens. The design outcome for context of use 1 in design experiment 3 was an exploration of how this might be achieved and is shown in Figures 5-18 and 5-19 below.

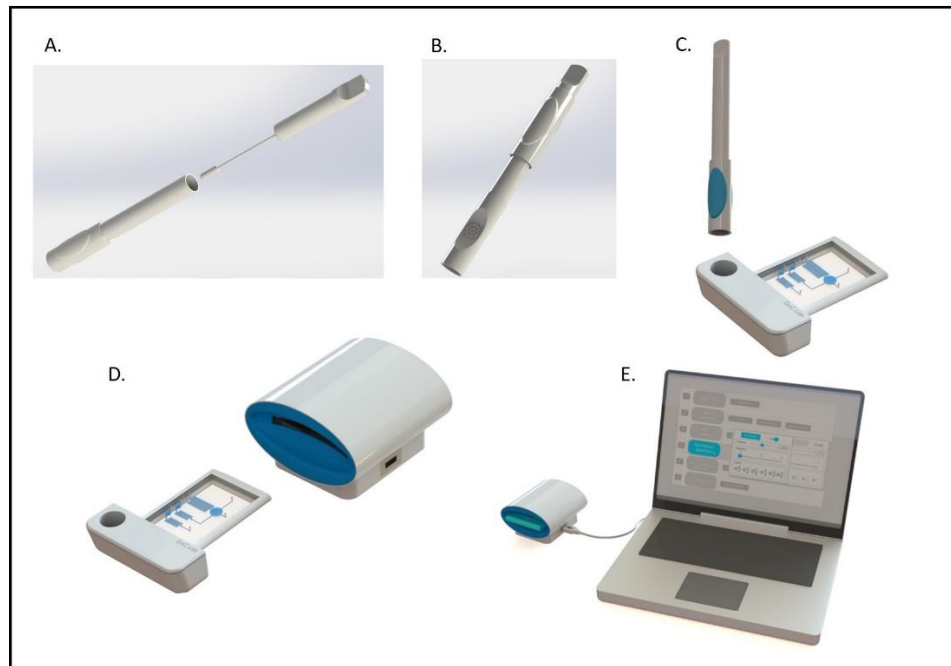


Figure 5-18 - Design experiment 3, context of use 1. System designs for a point of care reusable detection system using the proof of concept technology

The diagrams that are shown in Figure 5-18 are described in sequence below:

- A. For a Chlamydia test where the user is to self-collect a sample, the sample collection device would have to be capable of collecting a swab sample and/or a urine sample of a certain volume and be usable by both sexes.
- B. If the sample collection device was to be self-operated in a private environment, it would have to be designed so that it could be delivered to the operator of the detection module safely and hygienically.
- C. The sample would have to be transferred from sample collection device to microfluidic chip module.
- D. Once the sample had been loaded into the microfluidic chip and all resultant sample preparation processes had happened, the microfluidic chip would be inserted into the detection module.

- E. Data from the detection module would be collected by a laptop or similar form of portable computing equipment. Power for the detection module would be supplied by mains power or the laptop USB dependant on requirements.

Below, in Figure 5-19, is an exploded view of the concept, showing the components that could be present in it.

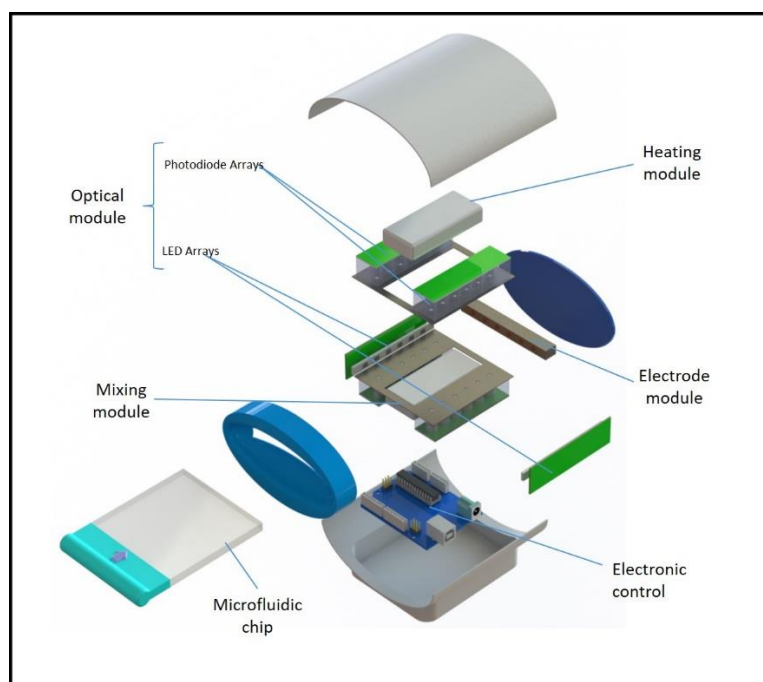


Figure 5-19. Design experiment 3, context of use 1. Concept of internal component configuration.

There are few examples of technology shown in the exploded view of the proposed concept that are not commercially available in some form at present. A key technology shown in the diagram that would require research in order to be viable is the mixing module placed below the optical module. This would assist with fluid movement and mixing in the microfluidic chip. There are, however, other ways this could be accomplished which are detailed in the description of the preclinical trial prototype in this chapter.

5.12.2.2 Context of Use 2 – Single Use Detection Module

If the number of detection channels in the prototype were reduced to the required number for a single use self-test (likely a test channel and negative control channel). The size, cost and power requirements of the device could be reduced significantly. The microfluidic chip could be incorporated into the device itself and sealed. The sample would then be introduced, using a sample collection device, to the combined microfluidic chip and detection module. Once this had been accomplished and the appropriate data collected, the entire system would be discarded.

The key question arising from this proposal is how much the cost of the device could be brought down in order to make a single use self-test, utilising the proof of concept technology, cost effective and how much it would be acceptable for a user to pay for it.

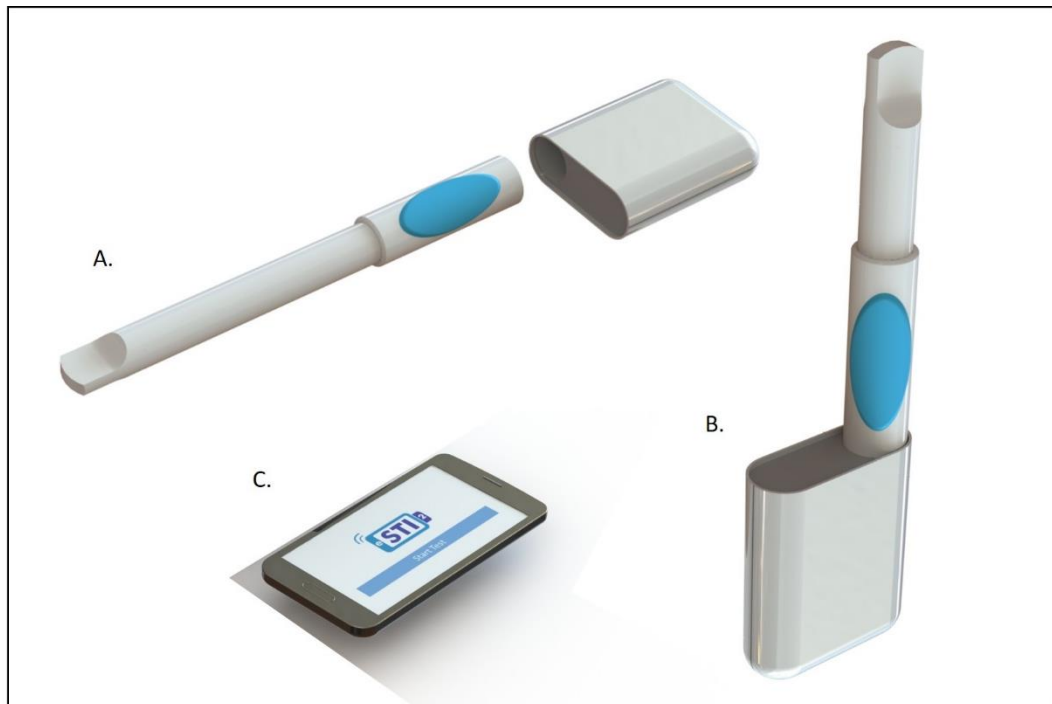


Figure 5-20. Design experiment 3, context of use 2. Full system design for a self-use, single use device using the proof of concept technology

Figure 5-20 above;

- A. Shows the sample collection device proposed as a part of the design outcome for concept 1. The user would self-collect a sample and load the sample directly into the combined microfluidic/amplification and detection device.
- B. After the device had processed the result, the device would be discarded.
- C. Results would be transmitted wirelessly to a portable computing device.

The design outcome for context of use 2 is entirely conceptual. However, the previous design experiments have shown that the proof of concept technology is highly flexible. Therefore, there is evidence to suggest that the concepts shown could be feasible proposals.

5.12.3 Assessment of Design Experiment 3

The outcomes of design experiment 3 were continuously assessed through collaboration with the core of the DoC Lab research group (See also Table # for details). The group found that with the development of entirely conceptual systems based on the proof of concept technologies

being researched in DoC Lab, questions about regulatory approval, patient acceptability and cost were being raised. The group recommended that further investigation into what would be required to convert the concepts into viable, clinically useful proposals was required. The experts were of the opinion that the proposed concepts were technically feasible within a time span of 2 to 3 years with appropriate funding.

5.12.4 Design Experiment 3 - Conclusions

Design experiment 3 showed that the proof of concept technology could feasibly be developed for use in two distinct contexts of use where varying degrees of self-operation by the patient would be possible. A purely self-test, where the patient would collect and test the sample themselves and act upon the result was shown to be technically possible within 2 to 3 years.

The design method of iterative conceptualisation, assessment and redesign used alongside a diagram building tool to manage system complexity was shown to be useful where producing technically feasible concepts.

A record of all the design iterations created during the design experiments is shown in Appendix C-4.

5.13 Pre-Clinical Trial Prototype

The preclinical trial prototype was required to be capable of testing 100 Chlamydia positive and negative samples, proving the viability of the molecular diagnostic technology and progressing it toward clinical trial and regulatory approval. Simultaneously, the development of the preclinical trial prototype provided the opportunity to test elements of the design proposals which have been described in this chapter. The outcomes of the design experiments described in this chapter are evident in the design of the preclinical trial prototype system as follows:

1. Battery powered. Proving that Chlamydia testing can be carried out using a battery powered system is a step toward ensuring the portability of future device designs.
2. PCB Configuration. The preclinical trial prototype uses the adaptable PCB configuration detailed in design experiment 2. Preclinical trial validation of this configuration will contribute toward future development of new configurations for deployment in varied contexts of use.
3. Sample in to answer out. The preclinical prototype, like the proposed self-testing concept detailed in design experiment 3, is a full sample in to answer out system.
4. Automated. The preclinical trial prototype incorporates methods for the automation of fluidic actuation which would be essential for sample preparation in a self-testing device.

5.13.1 System Iterations

The preclinical trial prototype was designed using the same iterative methods tested in the design experiments detailed in this chapter. Also in common with the design experiments, iteration occurred at both the component and system level. Figure 5-21 below shows the iterative development of the amplification and detection element of the preclinical trial prototype. The iterations show how the design of the system changed as the configuration of the microfluidic chip and fluidics module iteratively progressed.

5.13.2 System Version 1

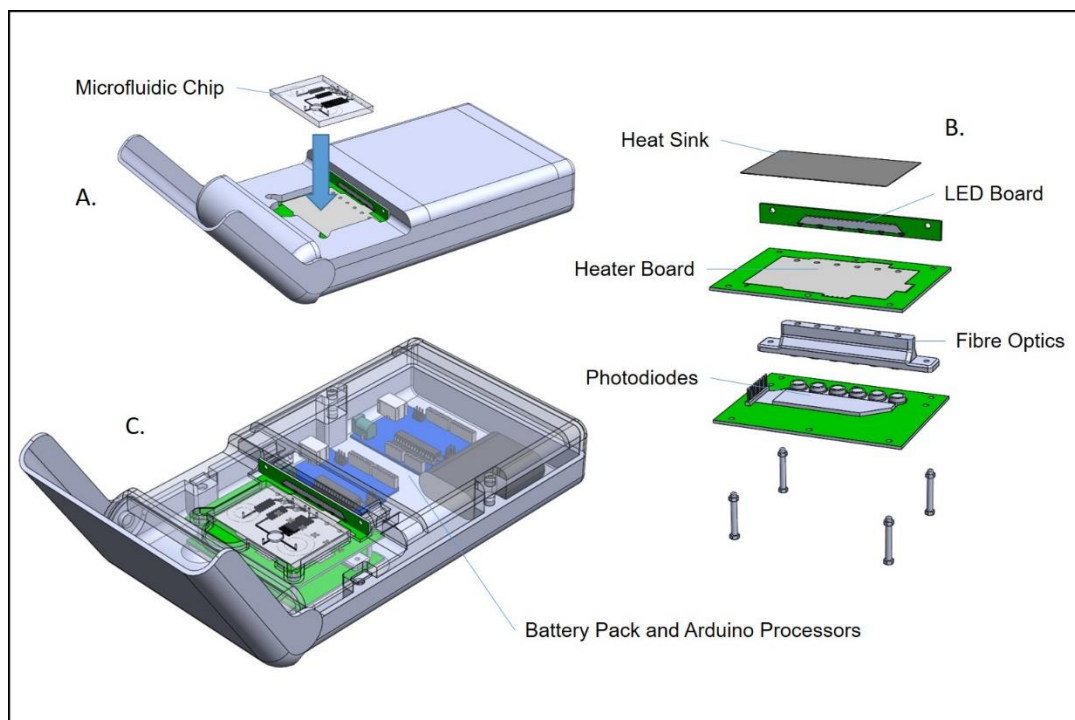


Figure 5-21 - Preclinical Trial Prototype – System Version 1

Figure 5-21 shows the first version of the preclinical trial prototype. An explanation of each of the images in sequence follows:

- A. In this initial version, the microfluidic chip was going to be loaded with a sample off-platform and then loaded onto the platform for testing.
- B. The PCB configuration devised in design experiment 2 was used throughout the iterative development of the preclinical trial prototype. The top layer of photodiodes was removed as only two detection channels were required for the preclinical trial.
- C. The platform was designed to be an enclosed unit encompassing the battery, electronic control, amplification and detection module, and once the lid was closed, the loaded microfluidic chip.

The system in this configuration did not, however, reflect the full system sample in to answer out design requirements defined by the research group. Changes to the design of the microfluidics would allow the sample to be loaded into the microfluidic chip while it was in position on the platform. The iterative development of the microfluidic chip is shown in Figure 5-22 below:

5.13.2 1 Microfluidic Chip Development

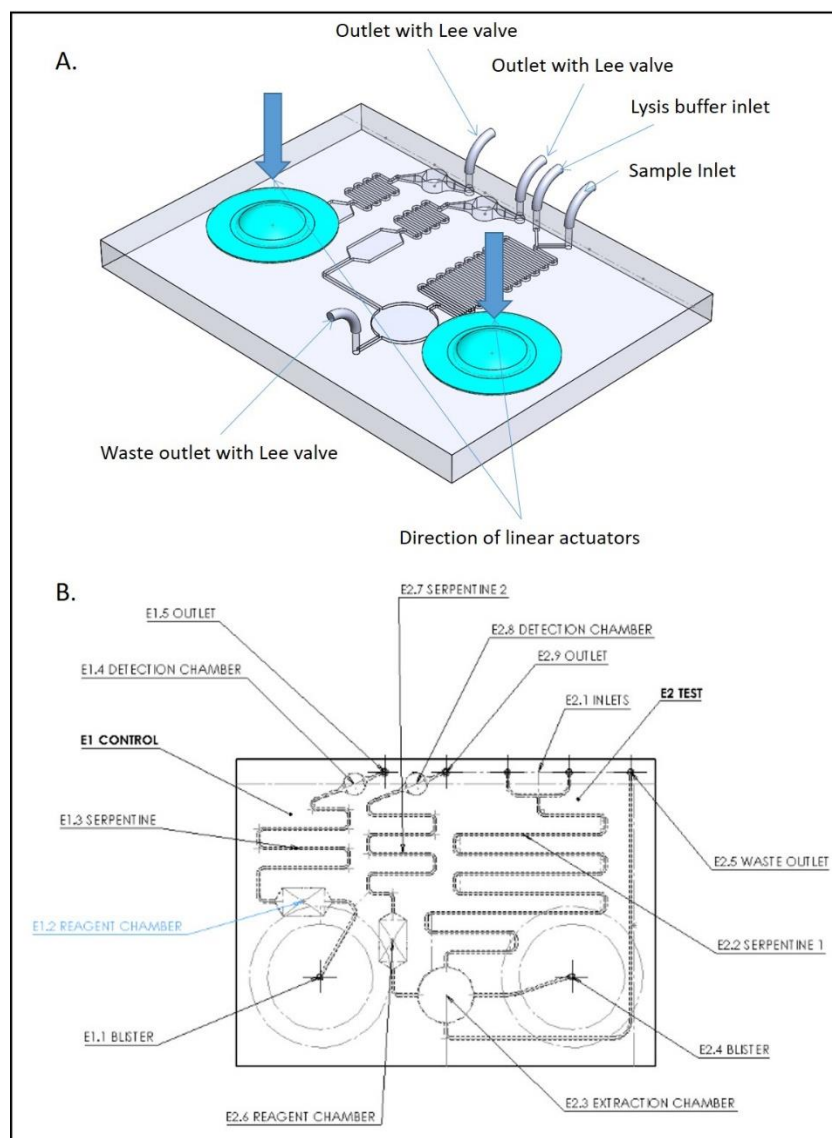


Figure 5-22 - Preclinical Trial Prototype – System Version 1, microfluidic chip transition from prototype to batch production model.

The microfluidic chip was further developed by the DoC Lab research group so that the fluids could be moved automatically by actuators integrated into the platform. Sample, lysis and waste flow would be controlled by valves mounted into the fluidics module that would be added to the

system. The author collaborated in redesigning the chip so that a batch of 100 could be manufactured for the preclinical trial.

In Figure 5-22 the images show the following:

- A. The initial prototype, blister actuated microfluidic chip. Sample and lysis buffer would be pumped into the chip using a Fusion 100 Infusion syringe pump (Chemyx Inc, Stafford, UK). Blister would be actuated in sequence to activate the test control and the extraction solution. The actuation method had yet to be determined at this point in the development process. Lee FMT 2 Port valves (The Lee Company, Essex, UK), would control the inlet and outlet flow of lysis buffer, sample and waste from the chip.
- B. The author liaised with the chip manufacturer (MiniFAB, Melbourne, Australia) to make appropriate changes to develop the chip from prototype to batch production ready. Inlets and outlets were realigned to one side of the chip for more efficient valve placement in the proposed fluidics module. The gaps between the fluidic channels was increased to allow for more reliable adhesion between layers of the chip material. The position of the reagent chambers was adapted to take into account the structural requirements of placing two blisters into the chip design.

The redesign of the microfluidic chip had a broad impact on the overall system design, prompting another iteration of development.

5.13.3 System Version 2

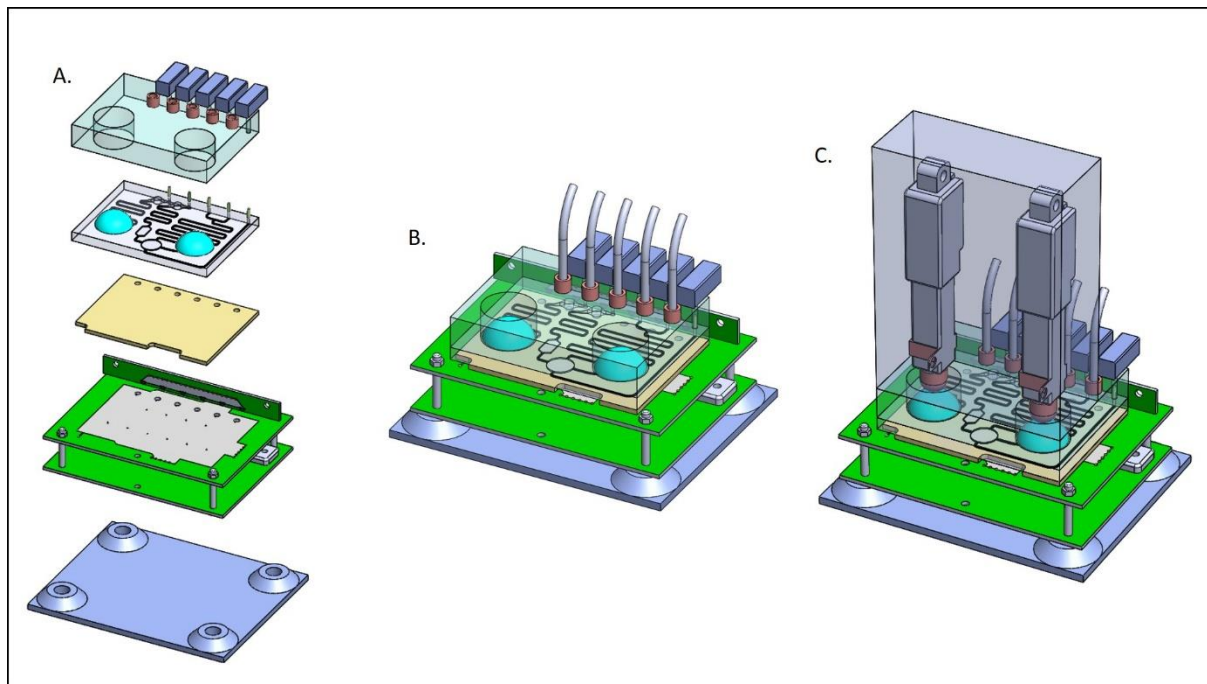


Figure 5-23 - Preclinical Trial Prototype – System Version 2.

The images of system version 2 in Figure 5-23 above, show the following:

- A. The exploded view shows the first concept of the fluidics module necessitated by the change in microfluidic chip design. The Lee valves are aligned at the far side of the concept drawing, in line with the inlets/outlets on the microfluidic chip.
- B. The initial concept drawings of the new components (fluidics module and valves) are simple volumes drawn to scale to assess their effect on the system design. The microfluidic chip in this drawing is an accurate representation of the preclinical trial version chip.
- C. Firgelli L12 actuators (Firgelli Automations, Ferndale, WA, USA) were chosen to actuate the fluidics blisters in the microfluidic chip. As with the fluidic module, initial concept housings were drawn to understand the systemic impact of these components.

5.13.3.1 Fluidics Module Development

A fluidics module, including actuators, valves and fluidic connections was designed. A jig was included to ensure that the fluidic connections from the syringe pump and the waste outlet lined up every time a new chip was inserted. A description of the fluidic module is shown below in Figure 5-24.

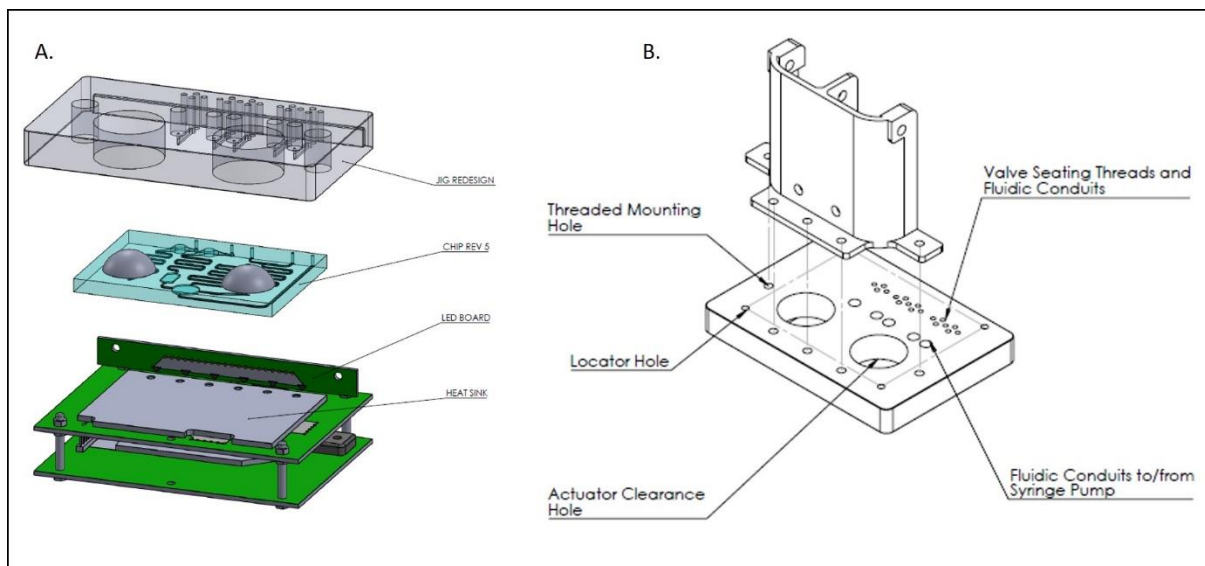


Figure 5-24 - Preclinical Trial Prototype – System Version 2. Transition from initial prototype of fluidics module to final preclinical trial version.

Designs for the fluidics module were created in collaboration with the microfluidic chip manufacturer. This guaranteed compatibility between the microfluidic chip and the fluidic connections and valves. The author created 3D models to ensure that the design of the fluidics

module was also compatible with the mounting bracket for the actuators and with the amplification and detection platform. The images in Figure 5-24 show the following:

- A. Assembly drawings ensured that the fluidics jig, microfluidic chip and amplification and detection platform would interact.
- B. The final fluidic jig and actuator bracket. The module was designed to be taken off the platform after each test run and replaced in exactly the same position each time.

5.13.4 Preclinical Trial System

The final system design for the preclinical trial prototype incorporated the developments described. A frame was designed which would support the components and allow easy access to the device. A diagram of the final system is shown in Figure 5-25.

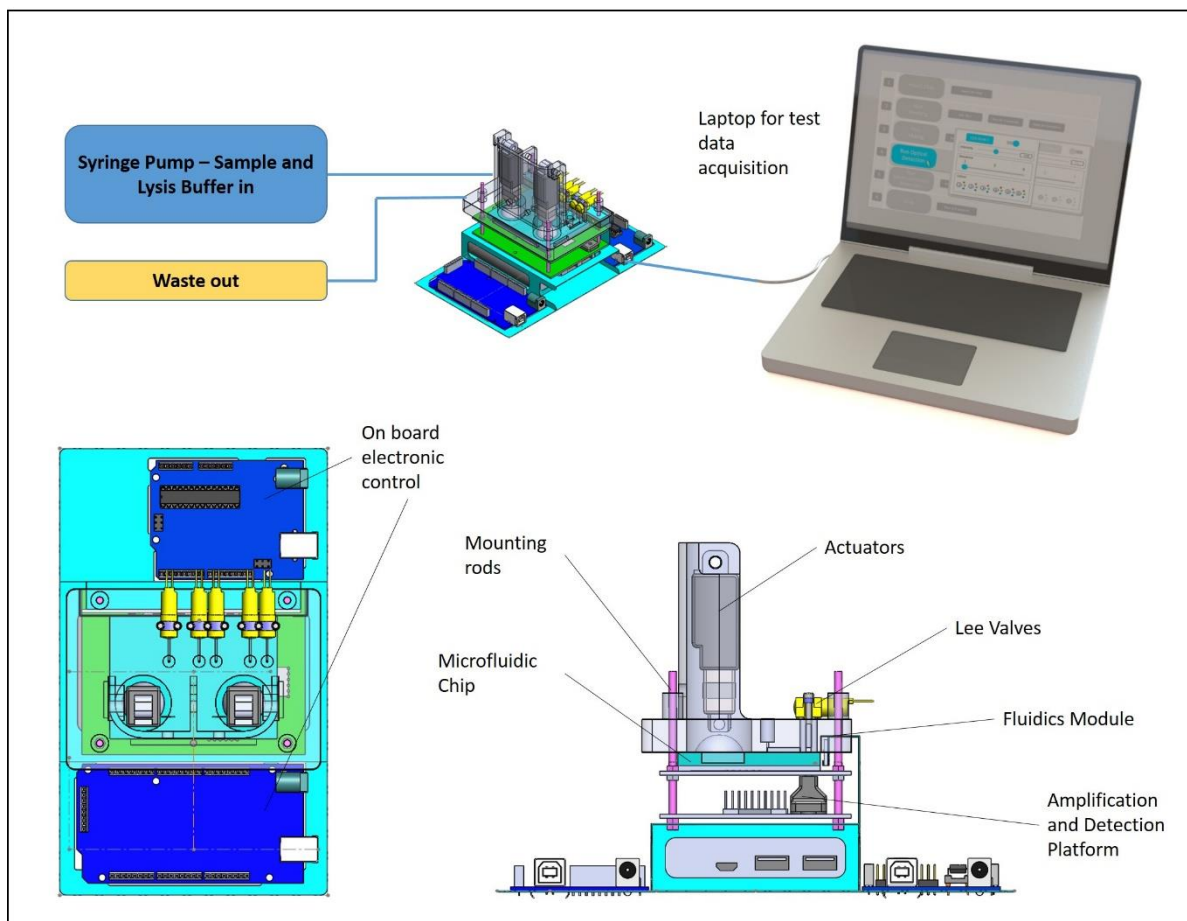


Figure 5-25 – Final iteration of the preclinical trial prototype system.

The preclinical trial prototype will be operated in a PCR hood to prevent cross contamination between test runs. The prototype will also be housed in an opaque casing to prevent light interference from external light sources. From a design perspective, one of the concerns of the group was the extra size added to the platform by the actuators. In future prototypes, smaller

actuators would be specified, sourced and tested. The final design iteration carried out as part of the action research project explored options for reconfiguring the actuators so that they would occupy as little space as possible, this design is shown in Appendix C-5. Technical drawings and data sheets for the components and assemblies described are also documented in Appendix C-6. Figure 5-26 below shows the preclinical trial prototype in the initial testing phase inside a PCR hood.

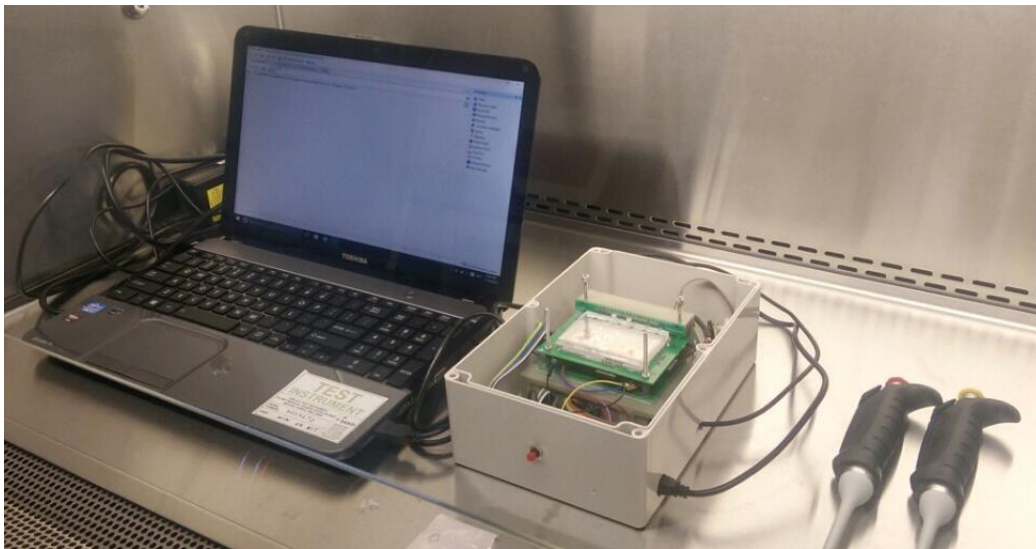


Figure 5-26 - Preclinical Trial System, initial testing in PCR hood

5.13.5 Preclinical Trial Prototype Design Assessment

The following design requirements were proposed for design experiment 1. These requirements were built upon in design experiments 2 and 3. Below is an assessment of how far the preclinical prototype fulfils the initial design requirements and where it could be improved to further progress the prototype toward a viable self-testing diagnostic device.

Handheld/highly portable – The prototype is battery powered and the components that have been used can be reduced in size significantly in further iterations. This applies particularly to the Arduino control boards. The detection apparatus in the prototype can be scaled up or scaled down (with an increase or reduction in the number of detection channels) dependent on the context of use, clinical or public health requirements for which a future iteration of the device is designed.

Molecular diagnostic – The prototype is an isothermal nucleic acid amplification test. In a future self-test using this technology, appropriate safety standards would be adhered to in the use and disposal of the test.

Mobile phone controlled or a smart device – Test data is acquired from the prototype using a laptop. User interface development has not been considered in this prototype and is an area for further research. A USB cable is required for communication between the prototype and the laptop. Bluetooth and other wireless communication technologies can be incorporated into the design of the prototype in future system iterations.

Low cost – The cost price of the components of the proof of concept prototype was approximately £80. This cost has increased during the development of the prototype to the preclinical trial stage. The cost of further iterations of the system could be reduced through an analysis of the required production scale for the prototype.

Easy to use – The sample preparation, amplification and detection functions of the prototype are automatic as a result of the use of a blister actuated microfluidic chip. For future system iterations, a mechanism for easy introduction of the sample to the detection module can be designed. In a self-testing system, the internal operations of sample preparation, amplification and detection will be entirely automatic.

5.13.6 Suitability for Chlamydia Clinical Care Pathway

The design of the preclinical trial prototype has been tailored so that the devices derived from it in future will be suitable for certain contexts of use. These contexts of use, both entirely portable and self-use or point of care and partially self-use, will be suitable for integration with the Chlamydia care pathway. Sample collection, detection and the communication/computation required to interact with health services are conceivable further developments of the preclinical prototype as a result of the combination of component and system design activities shown in this chapter.

5.14 System Risk Assessment – Identifying Areas for Further Research and Development

One of the objectives of the thesis was to provide general design guidelines for the further development of diagnostic technologies that may be suitable for self-use applications (Objective 3). In order to achieve this, the preclinical trial prototype was further assessed using a design structure matrix (DSM) modelling technique (Eppinger and Browning, 2012). The DSM modelling technique involves the creation of spreadsheets that show the interactions between the components of a system. The technique has been proposed as a way of improving methods for the design of complex products (Eppinger *et al.*, 1994). DSM's can also be used to analyse multiple domains of a complex product architecture, including interactions between components, interactions between components and functions and the interactions between components and design teams (Eppinger *et al.*, 2013).

In this instance, a DSM has been used to identify areas of high technology risk in the preclinical trial prototype. The aim of the technology risk assessment was to identify areas where further research and development were required to achieve the goal of a sample in to answer out self-testing device for sexually transmitted infections.

Firstly, an exercise of system decomposition was undertaken, where the prototype was split into key modules and each of the modules was divided into component parts, thus showing in component dependencies in diagrammatical form. The designVUE environment introduced in design experiment 2 was used to achieve this. See Figure 4-27 below.

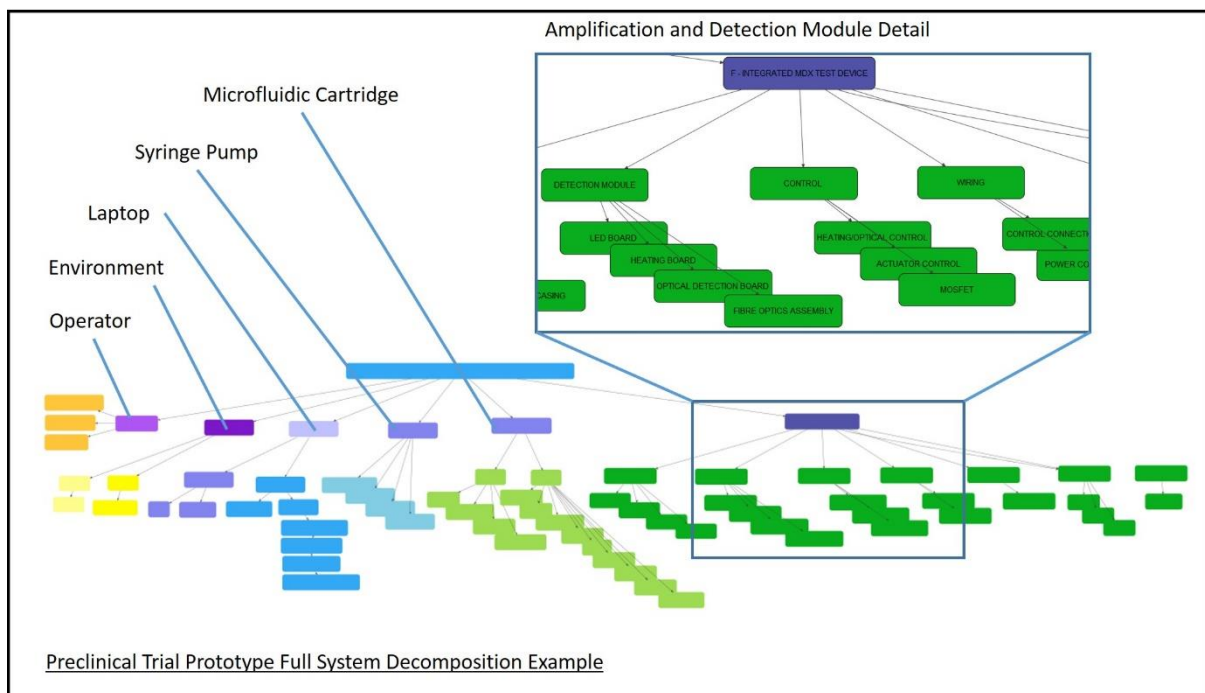


Figure 5-27 – System decomposition of the preclinical trial prototype showing key modules, and dependent components.

Once decomposition of the system was complete, interactions between each of the elements of the prototype was described. Interactions between the elements were assigned interface dependency values based on whether interactions were physical, energetic or information based. Assembly drawings of system designs and spreadsheets were used to achieve this.

Interface dependency values were defined using a scoring system modified from a NASA (National Aeronautics and Space Administration) and MIT (Massachusetts Institute of Technology) technology risk assessment of the Mars Pathfinder Rover (R.Browning, 2012). A physical interaction between elements was assigned a score of 2. An interaction where energy is transferred, such as the heating element of the amplification process or the force applied by an actuator, was also given a score of 2. Direct informational interactions, such as the transmission of test data from the detection element to the laptop were assigned a score of 2, whereas

situations where information is indirectly transferred between elements, such as feedback regarding the status of an actuator, were given a score of 1.

A technology risk factor (TRF) was then assigned to each of the elements of the system using a modified version of a scale used by NASA for describing technology risk factors as a function of technology readiness level (TRL) (NASA, 2008). This was particularly pertinent in the case of this prototype, as the system comprised a mixture of established technologies and research stage technologies. A modified version of the NASA scale is shown in Table 4-6.

Table 5-6 - Technology Risk Factor (TRF) and Technology Readiness Level (TRL) Scale

TRF	Modified NASA TRL Descriptions	TRL
1	Off the shelf, proven technology with successful track record	9
2	Thoroughly tested and proven technology (in-house developed)	8
2	Technology already in use in a clinical environment	7
3	Prototype technology tested in a relevant environment	6
4	Technology undergoing clinical trial	5
4	Technology undergoing preclinical trial	4
5	Proof of concept technology	3
5	Technology concept defined	2
5	Basic principles of technology understood	1

A simple calculation was performed using the interface dependency values, technology risk level and technology risk factor values. This provided a risk value associated with each interaction between elements of the system. The calculation used was as follows:

$$\text{TRF of component A} \times \text{TRF of component B} \times \text{Interface dependency value A-B} = \text{A-B risk value in DSM.}$$

5.14.1 Results of System Risk Assessment

The technology risk assessment DSM is shown below in Table 4-7. The highlighted areas for improvement are very likely to be applicable to most miniaturised, low cost diagnostic technologies. As a result of the design methods used and how they relate back to the clinical

care pathway, the areas for improvement relate to how an untrained user would operate the technology.

Table 5-7 - Preclinical Trial Prototype Technology Risk Assessment

	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P	Q	R	S	T	U
1	Element Name	TRF	8	9	9	7	4	8	6	3	3	4	7	4	7	9	3	4	8	2	19
2	User	8	1	4	8	8	8			10	10	8	4	8			20	16	8	20	
3	Room	9	4	2													20				
4	Benchtop	9	4	2	3																
5	Laptop	7	8		4	4										4		16			
6	Laptop Software	4	8			32	5			24	20	20	16	16	4						
7	Syringe Pump	8	12		4			6								4			16		
8	Fluid Handling	6						24	7	60	60			12	12	12		30			
9	MF Chip Control	3							60	8		80									
10	MF Chip Test	3							60		9	80									
11	Det and Amp Module	4		8						80	80	10	16	16	16			40			
12	Onboard Control HW	7								20	20	16	11		8			20			
13	Onboard Software	4								24	20	20	16	16	12	16					
14	Onboard Power	7														13		20			
15	Benchtop Power	9	8	2	4												14				
16	Casing	3		20	10				30			40	20					15			
17	UI Laptop	4	32			16			12	20	20	16	16	32					16		
18	UI Syringe Pump	8	12				8													17	
19	UI FELIX	2	60						15	25	25	20	20	40	20			50			18
20		19																			19

The table shows clusters of high risk interactions between elements of the preclinical trial prototype system. The table shows that the highest technology risk area is the microfluidic chip interaction between the actuators and the fluidic connections. This technology has not been tested elsewhere in this configuration and it is expected that it would constitute a risk. At the bottom of the table, a cluster of high risk interactions is shown where user interaction is required with the testing platform, syringe pump and laptop. A third cluster appears above the centre of the table where informational feedback interactions about the status of the testing device pose a risk. Apart from this, a number of high risk interactions are scattered along one side of the table where the casing of the system interacts with other components.

The high risk areas highlighted in the DSM describe areas for further development as follows:

1. Reliability and repeatability testing of the fluidic module, microfluidic chip and actuator components of the prototype.
2. Development of dedicated system software, ranging from user interface down to component status feedback (such as actuator positions, successful test indication etc.). This will be essential in guaranteeing the reliability of a self-use molecular diagnostic device being used in a location remote from healthcare facilities by a non-expert user.
3. Physical user interface design including casing design to guarantee a high level of usability, reliability and robustness.

5.15 Part 2: Design Process Model

5.15.1 Design Process in Context of the Thesis

When the research studies and design activities which have been applied to device design in this thesis are considered in overview, a descriptive diagram can be devised showing the process that has occurred, from the identification of a need, (i.e. a self-use molecular diagnostic test for Chlamydia) to the development of a preclinical trial prototype and system concept prototypes.

A design process model can be created showing how the design activities described in the thesis relate to the concept development requirements derived through expert stakeholder interviews, collaboration with the eSTi² research consortium and collaboration with the DoC Lab research group. This design process model is shown below in Figure 5-28.

5.15.2 Research Design Process Model

Figure 5-28 shows, in diagrammatical form, the iterative process that was used to create system concepts and a preclinical trial prototype. A description of each section of the diagram follows below.

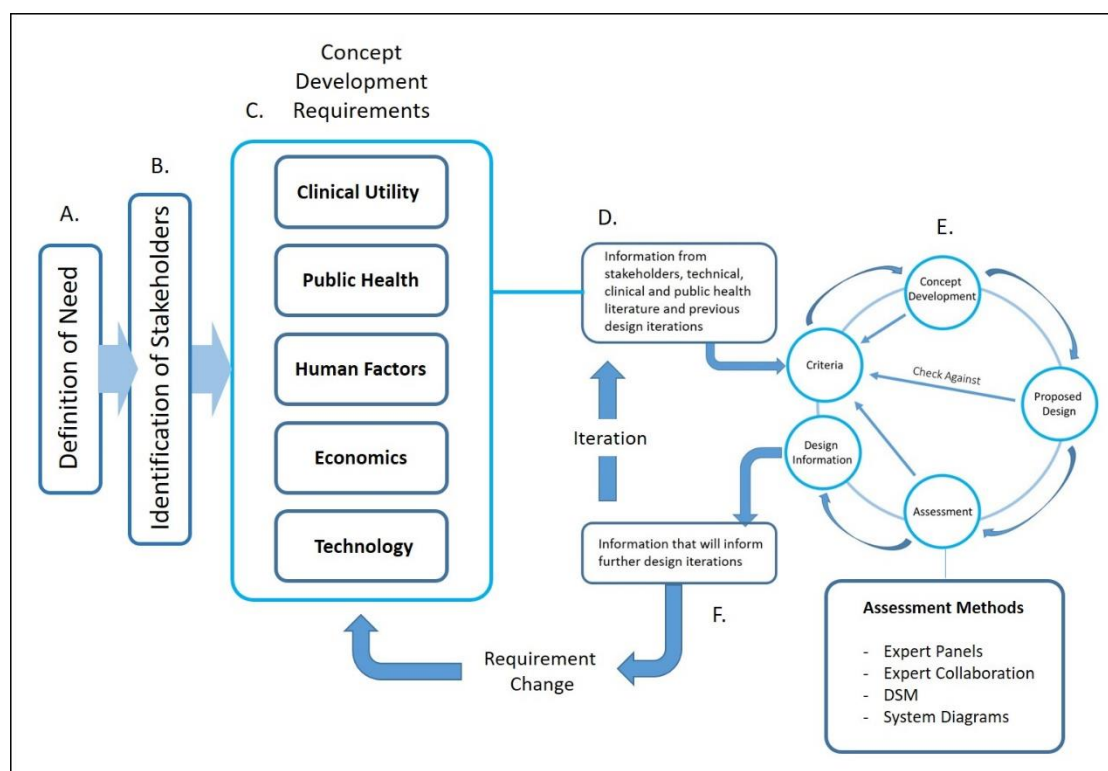


Figure 5-28 – A descriptive process diagram showing how the concept development requirements were applied to the design of the preclinical trial prototype and system concepts.

- A. *Definition of Need* – The need for a self-test for Chlamydia was defined through collaboration with the eSTi² research consortium. Chlamydia is the most prevalent

sexually transmitted infection amongst 15-24 year olds in the UK (Public Health England, 2016) with an incidence rate likely to be in excess of the reported 8% due to the infection often being asymptomatic (European Centre for Disease Prevention and Control, 2012). Chlamydia is ordinarily treated with a single short course of antibiotics with a high success rate (Nwokolo *et al.*, 2016) making it an ideal infection for piloting novel methods of detection and treatment, as has been demonstrated through the National Chlamydia Screening Programme (NCSP, 2016) and is being further investigated through pilot studies of online Chlamydia care pathways (Gibbs *et al.*, 2016).

- B. *Identification of Stakeholders* – Stakeholders were identified through collaboration with the DoC Lab research group and the eSTi² consortium. A sample of key stakeholders whose input was essential to the design of a self-use device were interviewed in the expert stakeholder interviews detailed in Chapter 3 of the thesis.
- C. *Concept Development Requirements* – Concept development requirements were defined through collaboration with the research groups, interviews with key stakeholders and the iterative process of concept development, assessment and redesign.
 - i. *Clinical Utility* – Clinical utility refers to the likelihood of the self-use device increasing the quality of the clinical outcome for the patient (See also Chapter 3, section 3.7.3.2).
 - ii. *Public Health* – The device should be capable of collecting, storing or transmitting test data in order to ensure that the use of a self-test as opposed to the usual GUM clinic method of testing does not result in a loss of information for public health agencies (See also Chapter 3, section 3.7.3.1).
 - iii. *Human Factors* – Research suggests that the device should be easy to use with a strictly defined method of operation (See also Chapter 3, section 3.7.2.3). The device should ideally be portable and designed so that it can be used in various contexts of use (See also Chapter 3, section 3.7.2.4 and Chapter 5, section #)
 - iv. *Economics* – The device should be built at a low-cost rendering it affordable to the patient. Ideally, introduction of the test will provide an economic benefit to health services (See Chapter 3, section 3.7.2.1, Chapter 4, section 4.8.1 and Chapter 5, section #).
 - v. *Technology* – The enabling technology was an isothermal nucleic acid amplification and fluorescence detection method developed in collaboration with the DoC Lab research group. Should the requirements

of the ideal test clearly outweigh the capabilities of this technology, the iterative nature of the design model would allow for the selection of a new enabling technology.

- D. *Design Criteria* – concept development requirements were converted into appropriate design criteria for the component or system that was being designed.
- E. *Iterative Design Cycle* – Component or system designs were conceptualised and assessed against the criteria defined by the concept development requirements. Assessment methods described in Chapter 4 included evaluation by an expert panel, ongoing collaborative assessment with the DoC Lab research group, the use of detailed system diagrams and the use of design structure matrices.
- F. *Iteration* – Information gleaned through the activity of design and assessment was used to create the criteria for further redesigns where necessary. The assessment of a design may show that a key concept development requirement needed to change. For example, a change in enabling technology may be brought about in order to ensure that the test can be smaller and operated with a lower power requirement.

5.16 Application of the Research Design Process Model

The iterative design process model described in the section above was formulated using the action design research activity described in the first half of this chapter and finalised using data from the other studies described in the thesis. Examples of the design iterations produced for part of the diagnostic testing system using the model are shown below in Figure 5-29.

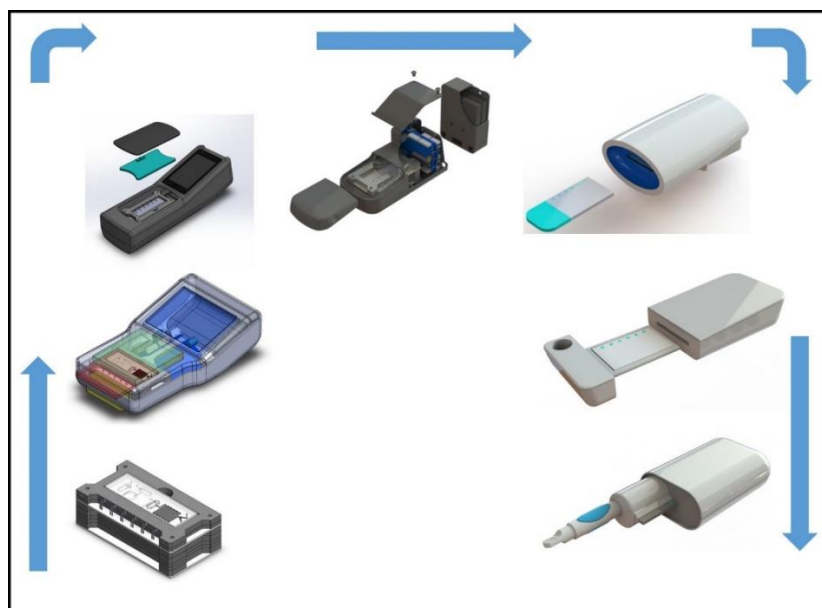


Figure 5-29 – The development of the detection platform over time. Other parts of the system are integrated as they are designed on the right hand side of the diagram.

The iterations shown in Figure 5-29 show the incremental development of the detection and amplification element of the testing system, where the enabling technology used was the low cost, isothermal nucleic acid amplification platform described in the first part of this chapter.

As the iterations develop over time, the design of the detection platform begins to incorporate other elements of the system, such as the microfluidic chip for sample preparation and the sample collection device. The incorporation of these elements may alter the design of the detection platform just as the design of the sample collection device is reliant on the configuration of the microfluidic chip. As a result, the iterative design process was applied to different elements of the system simultaneously. This process was expedited by the use of detailed system diagrams as described in Section 5.12.1. Below, in Figure 5-8, design iterations are shown for the sample collection device which was developed alongside the detection platform.



Figure 5-30 – Iterative changes to the design of the sample collection device followed the iterative changes to the design of the microfluidic chip and detection platform.

It is necessary then, to apply the design model to various parts of the system simultaneously. Iterations in the design of each element contribute toward the creation of a comprehensive specification for a system suitable for a specific context of use.

Experimenting with adding different contexts of use to the concept development requirements section of the process model allowed the author to propose concepts showing how the device might appear in the future. In Figure 5-31 below are examples of the final outcomes of iterative design cycles, created using the design process model.

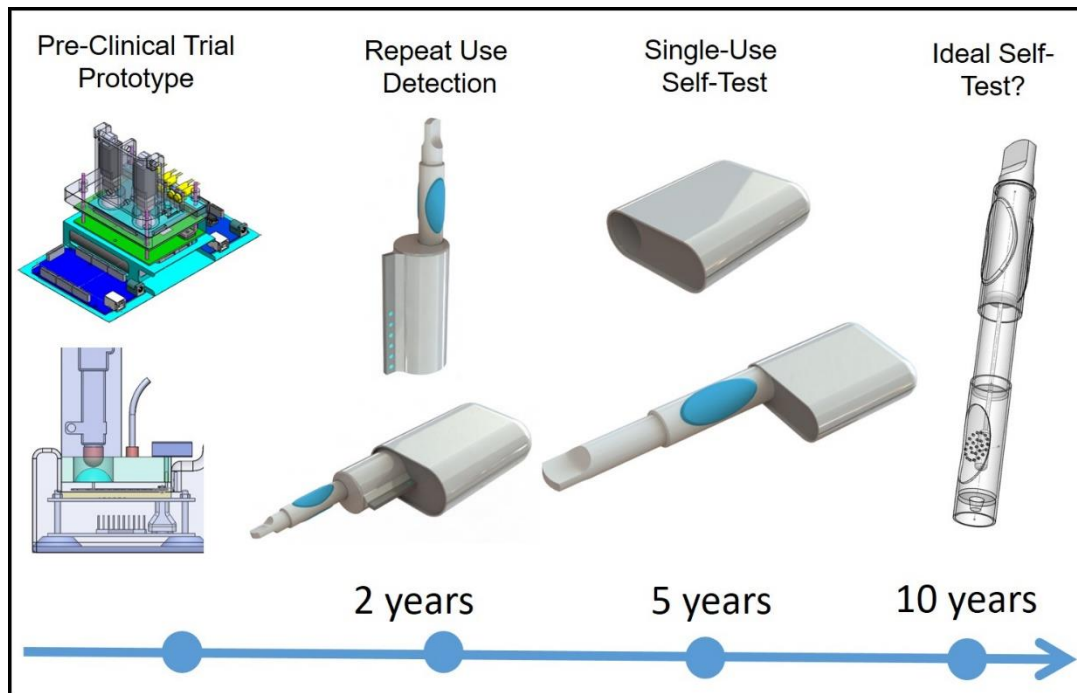


Figure 5-31 – Concept systems were designed alongside the preclinical trial prototype to provide design intent for the components of the real prototype system.

On the left of Figure 5-31 is the preclinical prototype developed during the action research design activity in the first part of this chapter. This was iteratively developed at the same time as the other concepts shown, which allowed design decisions to be made for the components of the preclinical trial prototype which would increase the chances of it being developed into one of the other concepts in future.

The final ‘ideal self-test’ concept shown is an example of a case where the assessment phase in a design cycle finds that the test size requires that the enabling technology is changed. This change in technology would then become a new concept development requirement and suitable criteria for the new technology, appropriate to the context of use, would be devised.

The above is an example of how the design process model was applied to the research project described in this thesis. The model was further developed so that it could be used more generally for the development of self-use or point of care diagnostic tests for infectious diseases.

5.17 Generalised Design Process Model

Figure 5-32 below shows the generalised version of the design process model which has been developed. The generalised design process model proposes that the required system elements for a diagnostic device are simultaneously and iteratively developed.

5.17.1 Generalised Design Process Model

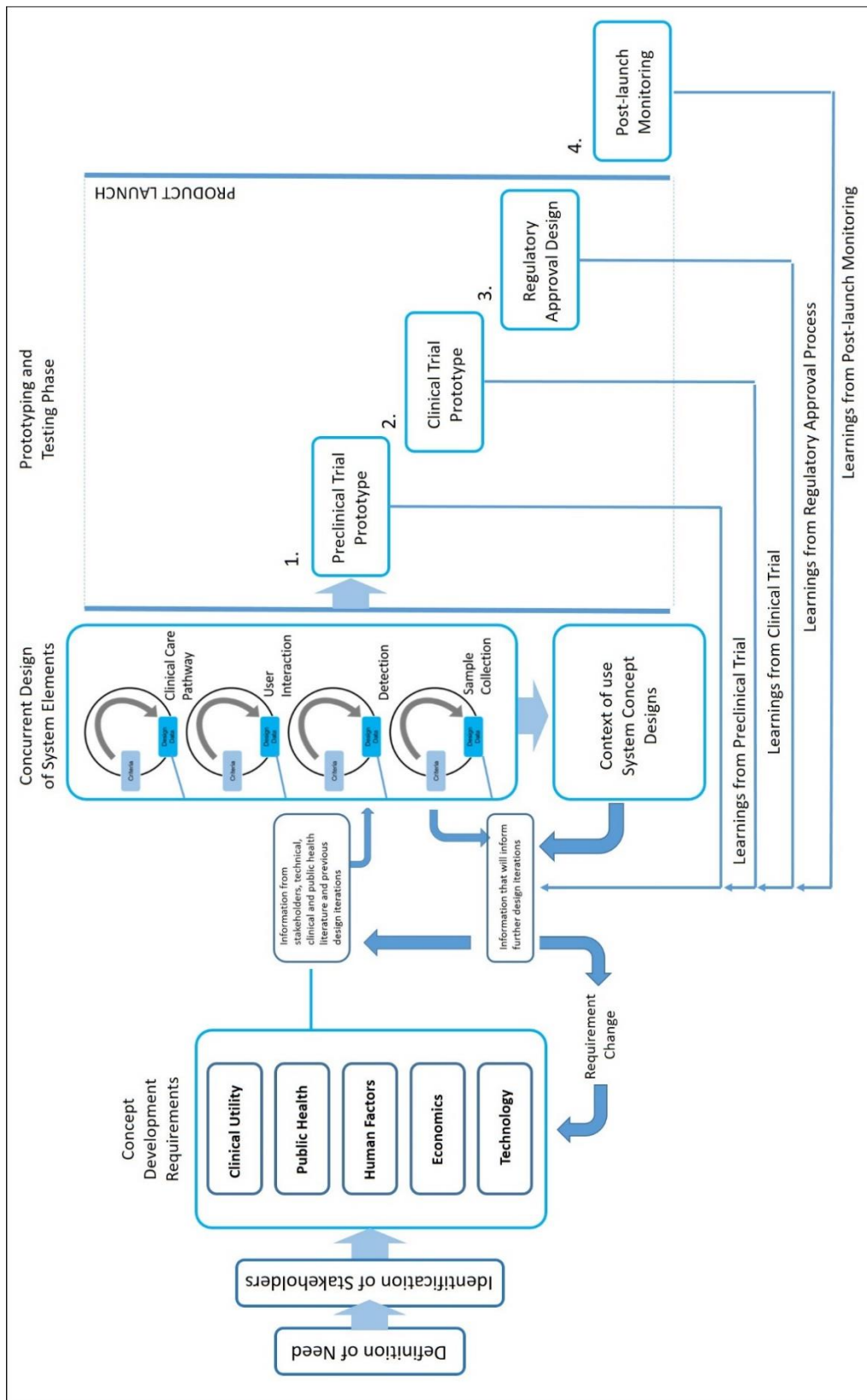


Figure 5-32 – A generalised design process model for the development of self-use diagnostic medical devices for infectious disease in an academic research environment.

The model also proposes that concept designs for contexts of use are created alongside the iterative development of actual system components. As was shown in the previous section, this will directly affect the design of the system components and provide design intent. This may reduce the amount of iterations necessary and therefore accelerate development from proof of concept to product launch.

5.18 Limitations

Due to time constraints imposed on the research in this chapter, it was not possible to assess the performance of the preclinical trial prototype in the trial itself. This would have afforded the opportunity to gather data on usability issues, software requirements for future iterations of the system and design requirements for a casing and physical user interface.

The action research design activity described in this chapter provides an indication of the impact of applying design methods to a proof of concept, research stage prototype. However, it is difficult to draw comparisons between this research and other research like it as development activities similar to those described here are most often done by companies and are not published. Furthermore, academic research in this area tends to focus on enabling technologies rather than full systems and contexts of use; this line of enquiry has only recently been emerging in the point of care and self-use diagnostic technology literature.

5.19 Summary

An action research method was devised and applied to the development of a proof of concept technology. Design requirements for the proof of concept technology were defined through identification of a clinical care pathway for Chlamydia self-testing. Three design experiments showed that the technology could be applied to two distinct contexts of use. A preclinical trial prototype was subsequently designed and assessed to identify priority areas for further research and development.

A design process model describing how the research studies in the thesis relate to the action research described in Chapter 4 was presented. A description was then given of how the design model was applied to the design problems of creating a self-use diagnostic for STIs. The design process model was then generalised for use with self-use diagnostic medical devices for infectious disease. Arguments were presented for how the process model could be used beneficially in an academic research environment and represents a contribution to the field.

Chapter 6

Discussion

6.1 Introduction

The research studies described previously in the thesis were designed to articulate an understanding of how to design self-use molecular diagnostic devices for sexually transmitted infections in a research environment. In this chapter, a discussion of the research is presented. Each of the research studies is discussed in the sequence in which they appeared in previous chapters. A discussion of the thesis contribution in overview is followed by a summary of the chapter.

6.2 Discussion

6.2.1 Expert Interviews

Interviews of expert stakeholders were used to identify concept development requirements for the self-use diagnostic device as well as identify potential issues and barriers to development. Through the interviews, a range of requirements were qualitatively identified. Agreement between stakeholders was documented and taken as an indication of the importance of a requirement, particularly considering the variation in areas of expertise of the interviewees. The value of recognising the input of a broad range of stakeholders has been recognised in the literature as a challenge for medical device development in general, with iterative processes recommended to ensure that all stakeholders are exposed to design proposals (De Ana *et al.*, 2013).

A large proportion of the literature regarding design, particularly for commercial/consumer products, emphasises the involvement of end-users, rather than expert stakeholders, in the design process (Goodman-Deane, Langdon and Clarkson, 2010). This may be achieved through user centred, or even participatory design methods (Wilkinson and De Angeli, 2014). However, where radical innovation through the use of a novel technology is involved (a category that self-use molecular diagnostics, the author believes, falls into), the application of user centred design methods is restricted, or even restrictive. Norman and Verganti argue that radical innovations are associated with a design research approach, where the potential of new technologies are explored alongside new design methods, whereas human centred design approaches are better suited to incremental change in the application of established technologies (2014).

Interviewing potential users, or asking them to participate in a design process where the constraints of the enabling technology are not known, or are changing as the technology develops, may be highly inefficient. Where the technology has been well established, for example in the case of the online care pathway using mobile technology as developed by Work Stream 4 of the eSTi² project, interviewing potential users (Aicken *et al.*, 2016) and employing user centred design practices are highly effective (Gkatzidou *et al.*, 2015).

The expert interviews provided the initial concept development requirements for the self-use testing device. The anonymity of the interviewees may have contributed to the variety and honesty of the opinions expressed, even where opinions were contrary to those of the research group as a whole. This advantage when anonymously interviewing expert stakeholders may improve the design outcomes brought about through application of the design requirements expressed by the interviewees.

At the early stages of technology development, combining the opinions of engineers with those of clinicians, public health experts and social scientists, gave a reliable, predictive indication of what the needs of the users of the device may be once the technological constraints have been well defined. Once technological constraints have been well-defined, the list of stakeholders will be extended to include potential users of the device. User centred and participatory design research methods can then be applied to the design of the self-use molecular diagnostic device more usefully.

6.2.2 Professional Designer Survey

The professional designer survey shown in Chapter 3 alongside the expert stakeholder interviews gave a limited insight into the design process needs of medical device design companies. The most prominent point that could be taken from it was that design processes used in an industrial environment are governed by the regulatory requirements of standards organisations. This may contribute to the notoriously slow development speed of medical devices, where innovation may be stifled and products left unrealised by the rigorous needs of regulation, as has been argued is the case in the United States (Citron, 2011).

The documentation produced by initiating design processes in the early research stages of technology development, as is suggested in this thesis, may speed the process of regulatory approval later on. It is important that the needs of regulatory agencies do not stifle innovation in the diagnostic medical devices field. For this reason, the design process proposed in the thesis is not based on the compilation of strict specifications but reflects the cycle of design, prototype and test which is already seen in technological research groups, as was shown in the action research activity described in Chapter 5.

6.2.3 Validation Survey

The validation survey described in Chapter 4 served the purpose of further refining the concept development requirements described in the previous chapter. The survey was limited by the small number of participants and it being restricted to the eSTi² research group only. Having said this, a substantial proportion of the eSTi² research group (68%) were included in the survey.

The results of the survey cannot be said to be generalizable to all potential self-use molecular diagnostics. They were, however, valuable in showing some level of consensus amongst the varied areas of expertise represented in the research group. Disagreements between areas of expertise could be an indicator of a barrier to development. It may be valuable in future to poll the members of a number of translational research groups about their opinions on development requirements and issues associated with the technology they are working on. Doing this may provide an extra, perhaps anonymous, dimension to the usual collaborative methods of regular meetings and email communication. The anonymity of the participants in the survey may have contributed to their willingness to express opinions sometimes contrary to the prevailing opinions of the group.

6.2.4 Action Design Research

The action design research described in Chapter 5 was used to argue that the application of design methods at the earliest stages of technology research may speed up the translation of novel diagnostic technologies from the proof of concept stages.

The action research design activity described in the chapter applied design requirements based on a clinical care pathway, expert interviews (Chapter 3) and literature to the progression of a proof of concept diagnostic technology to the preclinical trial stage. Design methods were identified, the application of which assisted in this progression. To the author's knowledge, there are no other examples of literature that have described this progression with continued reference to a clinical care pathway and public health need (See also chapter 2, Section 2.3 re: Chlamydia public health burden).

There are a wealth of examples in the literature of proof of concept diagnostic technologies which could in future be deployed in diverse locations for point of care use or self-testing (Myers *et al.*, 2013; Jiang *et al.*, 2014; Damhorst *et al.*, 2015). However, description of the development stage that comes after a technological concept is proven are rare and is addressed by the research presented in this chapter.

Having carried out the action research design activity, the author speculates that more common use of design methods such as those applied in this chapter would help in speeding up the

progression of proof of concept technologies from the benchtop to the field more generally. Kumar and colleagues make the point that a reason that this does not occur more may be because of

“...an argument, sometimes heard in universities, that academic scientists should be concerned only with discovering new methods and enabling new technologies and that actual reduction to practice...should be left to companies.” (2015, p. 5837)

This is one factor that goes some way toward explaining known bottlenecks in the commercialisation of microfluidic technologies for diagnostics (Chin, Linder and Sia, 2012; Volpatti and Yetisen, 2014). Design experiment 1 in Chapter 5 was an example of an activity, ordinarily left to companies, wherein design requirements were applied to a technology and the designed outcomes were tested against those requirements. Doing this at the research stages and in a research institution, where clinical, public health and user needs can be discovered and investigated in a relatively neutral environment, may significantly increase the chances of that technology being commercially successful in the future.

Design experiment 2 in Chapter 5 was entirely concerned with the activity of development, where nothing new was discovered but the configuration of the known components of the technology were adapted to find ideal configurations. The outcome of this experiment was that routes of development could be defined for the technology at a very early stage, methods like this have only very recently been considered in the literature of the field (Nayak *et al.*, 2017). Showing in detail that a technology can feasibly become a self-test or a point of care partial self-test before preclinical trial, and informed by knowledge of clinical and public health needs, provides vital information about how clinical trials should be conducted.

Nayak and colleagues propose how diagnostic technologies could be matched to contexts of use because of their functional attributes and scalability (2017). The research in Chapter 5, particularly in design experiment 3, goes into detail about how a proof of concept technology could be applied to a context of use utilising a specific clinical care pathway. Further, concept designs are shown and assessed for their potential feasibility.

The preclinical trial prototype described was tailored toward further development that may be more likely to result in a commercially successful device because iterative design processes, not often associated with the medical device research work of universities, have been applied to it. Iterative design processes that encompass the needs of the many and varied stakeholders involved in medical device development have been proposed elsewhere as a step toward faster deployment of new medical technologies (De Ana *et al.*, 2013). A further advantage of the

research presented in the chapter may be to reduce the iterations required in future research and development efforts for self-use molecular diagnostic technologies.

A technological risk assessment of the preclinical trial prototype was undertaken and described in Chapter 5. If commercial companies could be informed of the highest risk areas of technology in advance of embarking on the creation of a new diagnostic, their task may be quicker and possible at a lower cost. Cost savings like this could be passed on to the consumer, particularly where a device is being designed for the NHS. This may also apply to university research groups, where design experiments like the ones described in this chapter contribute to the identification and prioritisation of research areas.

6.2.5 Process Model

The generalised design process model described in the second part of Chapter 5 shows that beyond the finalisation of a preclinical trial prototype, a clinical trial prototype is required, followed by design for regulatory approval before a product is launched. The launched product is then monitored while in use to assess the need for further design changes. This follows the recommendations of the FDA (Food and Drug Administration) innovation pathway for medical devices (FDA, 2014).

The model shows that the information gained from each of the developmental stages (preclinical trial, clinical trial, regulatory design) feeds back into the process where necessary. Design cycles undertaken for clinical trial and design for regulatory approval may utilise different methods of design assessment. For example, usability studies could be carried out from the preclinical trial phase onwards. In the clinical trial phase, patient acceptability studies may be appropriate. The iterative use of usability and acceptability studies during these design phases is recommended in the IEC 62366 application of usability engineering to medical devices standard (Hegde, 2013).

Medical device development processes are often linear and stage gated (Pietzsch *et al.*, 2009). This means that after each important stage of development, a 'gate' is signed off to allow the product to continue through the process, a method that has been common in new product development for almost 30 years (Cooper, 1990). Recent research has suggested that although iteration between stages in the process occurs, the linear nature of the design process is restrictive (Sommer *et al.*, 2015). For this reason, the generalised design process model is intended to be highly iterative on every level beyond the identification of a need. This means that where necessary, concept development requirements or identified stakeholders can be modified to suit the requirements of the identified need. This is in keeping with the

recommendations of the CDRH (Centre for Devices and Radiological Health) innovation initiative wherein iteration is advised on a total product lifecycle level (CDRH, 2011).

In the academic field of diagnostic technology, a bias exists toward the realisation of enabling technologies and novel testing methods and away from the need to develop these discoveries into viable products (Kumar *et al.*, 2015). The application of the generalised model shown within a research environment alongside, as opposed to after, the proof of concept stage of technology development, may speed up the progression of diagnostic technologies from the laboratory benchtop to use by the public.

Rapid prototyping, enabled by rapid cycling through design iterations in the generalised model may provide significant benefits to research outcomes in diagnostic technology. Taking on the highly iterative nature of Agile software development methods (Cohen, Lindvall and Costa, 2003) for diagnostic hardware may provide significant benefits when controlled using a generalised design model as shown. Research has shown that a combination of the traditional stage gate product development process and highly iterative Agile software development methods offers significant improvements in the efficiency of the design process (Sommer *et al.*, 2015).

Rapid prototyping in software is a low cost venture due to the nature of the medium. Iterative development processes have been shown to be instrumental in producing robust software for point of care and self-use diagnostic applications (Tulasidas *et al.*, 2013). Iteratively cycling through hardware (rather than software) prototypes may be restrictively expensive. However, utilising methods of rapid prototyping including 3D printing and 3D CAD (Computer Aided Design) have shown significant benefits in speeding up the medical device design process for some products (Yee and Shyan, 2008).

The academic research environment, where less of an emphasis is placed on the production of profitable design outcomes or patents, lends itself to this type of rapid prototyping and iterative design. The CDRH and FDA innovation pathway initiatives recommend total lifecycle product iteration, where design efforts are concentrated throughout the lifecycle of the product until it is disposed of and/or recycled. There are, however, no initiatives that suggest that creative, iterative design methods are used in the very earliest stages of the creation of diagnostic medical devices. This provides a strong argument for experimenting with the utilisation of the design process model shown in an academic research environment, as a part of the research and development of novel technologies for point of care or self-use diagnostics.

6.3 Discussion Overview

The central argument offered in this thesis is that there are significant benefits that could be gained by using action research methods to apply design processes at the proof of concept stage of novel diagnostic technology development. A version of this activity may already be being applied by diagnostic companies, however, a limitation of this activity is that details of it are unlikely to be disseminated to the wider diagnostic technology development community as a result of intellectual property and competitive concerns.

In the early proof of concept stages, technologies are flexible in terms of how they are configured, physically arranged, powered and controlled. As a result of this, more diverse applications for technologies may be discovered through the application of action research design activities. Research environments may be less susceptible to profit driven design intent and more open to using information from a broad range of stakeholders to identify numerous contexts of use for a technology, thus maximising the potential of novel miniaturised, low-cost diagnostic technologies.

Systems engineering methods (DSM and system diagrams) were employed to assess the design outcomes described in Chapter 5. While it was recommended that various tools could be used in the assessment phase of the cyclic design process, viewing diagnostic devices systemically may have significant advantages in expediting development. The WHO (World Health Organisation) recommends the ASSURED criteria for new point of care diagnostics (Affordable, Sensitive, Specific, User-friendly, Rapid and Robust, Equipment free and Delivered to those who need it) (iSense, 2017). The application of rigorous, multi-stakeholder, iterative design methods that use systems engineering methods to assess and improve design outcomes may help to advance more proof of technologies toward this goal.

6.4 Summary

The chapter has provided a discussion of the research studies shown in Chapters 3, 4 and 5 of the thesis. An overview of the thesis argument was also discussed. In Chapter 7, an overview is given of how the aim and objectives of the thesis have been achieved through these studies and the literature review. Contributions are presented, recommendations for further work are made and a conclusion to the thesis is given.

Chapter 7

Conclusions and Further Work

7.1 Introduction

The research studies described in this thesis were designed to articulate an understanding of how to design self-use molecular diagnostic devices for sexually transmitted infections. In so doing, concept development requirements were defined, a preclinical trial prototype diagnostic platform was developed and a design process model was devised which may aid in accelerating the design and development of future self-use molecular diagnostic devices. Through these research activities, issues and barriers associated with the development of self-use molecular diagnostic devices were also identified. The intent in compiling a list of concept development requirements, guidelines, recommendations, issues and barriers is that future design, research and development efforts in the field might be enriched and accelerated through their knowledge.

This chapter comprises the contributions, conclusions and recommendations for further work of the thesis. A review of the research questions posed in Chapter 1 is shown, with an explanation of how each research question has been addressed. The research objectives described in Chapter 1 are then examined, showing how the completion of each objective contributed to the satisfaction of the overall research aim. A description of the contribution to the field offered by the thesis is then included, followed by a statement on the limitations of the research, opportunities for further work and summary conclusions.

7.2 Answering the Research Questions

Listed below are the research questions identified in Chapter 1. These research questions were addressed through the objectives of the thesis which are described in the next section.

7.2.1 Research Questions:

4. What are the concept development requirements for self-use molecular diagnostic testing devices for Chlamydia Trachomatis from a clinical, public health and engineering perspective?
5. What are the issues and barriers associated with the development of self-use molecular diagnostic devices for sexually transmitted infections from a clinical, public health and engineering perspective?
6. How can the process of translating novel diagnostic technologies from the proof of

concept stages to the clinical trial stages be accelerated?

7.3 Fulfilling the Research Aim and Objectives

7.3.1 Research Objectives

The research objectives were devised to fulfil the overall aim of the thesis. The overall aim of the thesis was as follows:

The aim of this research was to investigate a way in which self-use diagnostic technologies might be more quickly and effectively progressed from proof of concept prototype stages into working systems which are useful from a clinical and public health perspective.

The following is a description of where evidence is found in the thesis for the satisfaction of each of the objectives. Also described is how completion of each objective related to answering the research questions shown in the previous section.

Objective 1: To provide, through a review of the literature, an overview of the field of study and background for the research described in the thesis.

7.3.1.1 Objective 1 – Evidence Sources

A review of the relevant literature is presented in Chapter 2. The review highlights the multidisciplinary nature of the development of novel diagnostic devices. Fields relevant to the successful design of a self-use molecular diagnostic device for sexually transmitted infections are covered. The state of the art in technologies suitable for self-testing for sexually transmitted infections are reviewed. Clinical, public health and engineering perspectives are also addressed in overview. Finally, a review of design processes and regulatory requirements suitable for the development of self-use diagnostic devices is included.

A gap in the literature was identified. There is an abundance of literature describing novel, miniaturised and low cost molecular diagnostics. It is often stated briefly that these technologies are suitable for self-use, use at the point of care or for use in developing countries. Stating this is often as far as the researchers will go in describing how or where the technologies might be used. How the design of the technology might be effected by the context of use or the person using it is rarely addressed and field testing to confirm the suitability of the technology is rare. The gap in the literature is that there is little investigation identifying contexts of use in detail based on the capabilities of the technology, with suggestions of how proof of concept technologies should be developed to suit them.

Chapters 3, 4 and 5 go on to address this gap in the literature, suggesting that where self-use diagnostic devices are concerned, the iterative design activity normally conducted outside an

academic research setting (in industrial product development companies) can be usefully integrated with technological, clinical and public health research.

Objective 2: To identify concept development requirements for self-use molecular diagnostic devices for STIs.

7.3.1.2 Objective 2 – Evidence Sources

Concept development requirements are defined as the information required for the formation of concept designs for self-use molecular diagnostic devices for STIs. The initial concept development requirements were defined through expert interviews. In Chapter 3 of the thesis, interviews with expert stakeholders are described. The expert stakeholders were identified through collaboration with the eSTi² translational research project. The eSTi² project was investigating the potential for and feasibility of electronic self-testing instruments for sexually transmitted infections.

Analysis of the interview transcripts allowed the author to define concept development requirements from a diverse range of disciplinary areas relevant to the development and subsequent use of self-testing devices for STIs. The concept development requirements defined in Chapter 3 were further validated through a survey of the entire research consortium which is described in Chapter 4. This validation survey ensured that the members of the consortium project, who represented various areas of expertise, agreed with the defined requirements.

Concept development requirements were further refined through the action research activity detailed in Chapter 5. By participating in the development of a technology from proof of concept prototype to the preclinical trial stages, the author was able to identify technical concept development requirements. The completion of this objective answered the first question of the thesis research questions which are shown above. A full list of the concept development requirements defined through the research is shown in the contributions section below.

Objective 3: To propose design guidelines for future development efforts based on research data gleaned through the studies described.

7.3.1.3 Objective 3 – Evidence Sources

The action research described in Chapter 5 allowed the author to define design guidelines. Assessment of the designs shown in Chapter 5 using a design structure matrix method highlighted the aspects of the system where design efforts could be applied in future. Further assessment, through collaboration with experts and assessment by an expert panel also contributed to the definition of design guidelines.

The design guidelines derived from the activities described above constitute one of the

contributions to knowledge of the thesis and are shown in full in the contributions section.

Objective 4: To describe issues and barriers inherent in the development of self-use molecular diagnostics for STIs.

7.3.1.4 Objective 4 – Evidence Sources

The outcome of the interviews described in Chapter 3 highlighted issues and barriers associated with the development of self-use devices for STIs. A section in Chapter 3 describing a small survey of professional designers and their experiences with medical devices also contributes. Issues and barriers were further highlighted by the validation survey shown in Chapter 4, where disagreement regarding concept development requirements between different groups in the consortium were described.

Chapter 2 highlights that the academic literature in the field concentrates far more on the discovery of novel technology than on the development of viable products. This may be acting as a significant bottleneck in the development of self-use devices for STIs.

The description of issues and barriers enabled by the evidence described above answers research question two of the thesis. The complete list of issues and barriers described in the thesis is shown below in the contributions section.

Objective 5: To formulate a design process model for use by medical device researchers, developers and designers for expediting the development of self-use molecular diagnostic devices for sexually transmitted infections.

7.3.1.5 Objective 5 – Evidence Sources

A design process model was formulated during the action research activity described in Chapter 5. The model was formulated using the experience of the author in developing a proof of concept diagnostic technology. The methods of design and development recommended in the design process model were appropriate to the context in which the technology was being developed and the nature of the technology. Literature in the area of medical device design process and a review of the applicable regulatory requirements also governed the structure of the model.

The final process model is shown in Chapter 5, section #. Below, in the contributions section, a rationale for how the model constitutes a contribution to knowledge is given.

7.3.2 Satisfaction of the Aim

The overall aim of the research was satisfied by the completion of the objectives above. A review of the literature and identification of a gap established that there is an issue with the speed of development of novel diagnostic technologies. This slow speed of development is partially attributable to contexts of use for the technology not being considered in detail until

after proof of concept prototypes have been developed. Applying action research methods to facilitate design activity at the proof of concept stage alleviates this issue.

The identification of concept development requirements for a specific diagnostic application facilitated action research on a case study technology. Through the execution of the action research on the case study technology, design guidelines could be identified which can be applied to the acceleration of future development efforts. The action research also contributed to an understanding of the necessary pathway from proof of concept technology to a product that can be used by the public that is useful from both a clinical and public health perspective.

A description of issues and barriers associated with the development of the case study technology contributed to the satisfaction of the aim of the research. The knowledge of these issues and barriers will allow future researchers and medical device developers to organise their development efforts accordingly and thus accelerate development efforts. The formulation of a design process model brings the learnings of the thesis together in diagrammatical form. Application and adaptation of the design model to future research and development efforts for novel, miniaturised, low cost diagnostic technologies may improve research outcomes in the field of translational research for diagnostic medical devices.

7.4 Contributions

7.4.1 Primary Contribution

The primary contribution of this thesis demonstrates the advantages of combining action research and design methods in the early research stages of diagnostic technology development. The application of design methods to the proof of concept prototype described in Chapter 5 of the thesis have resulted in a preclinical trial prototype that exhibits the necessary features for development into a self-use molecular diagnostic device. Using this method, the process of translating the technology from proof of concept to use is accelerated and improved.

7.4.2 Contributions Overview

The research described in the thesis provides the following contributions to the field of industrial design.

1. When designing self-use molecular diagnostic devices for sexually transmitted infections, the following concept development criteria should be considered in detail from the outset of proof of concept technology research and development:
 - a. *Clinical Utility*
 - i. Definition of a target infection
 - ii. Identification of a clinical care pathway

- b. *Public Health Requirements*
 - i. The ability collect, store and transmit data about the result, location and person taking the test
- c. *Human Factors*
 - i. Restricted use-steps so that the test cannot be performed incorrectly
 - ii. Portability
 - iii. Definition of the contexts of use within which the test may be used
- d. *Economic Impact*
 - i. Available at a low cost to the patient
 - ii. Positive economic impact on health services
- e. *Technological Requirements*
 - i. Consideration of the capability of the chosen technology to fulfil the previous criteria

Simultaneous consideration and application of these criteria, using design methods, at the earliest research stages of technology (i.e. proof of concept stage) is highly unusual. There are no publically available molecular diagnostic self-tests at the time of writing. The concept development requirements represent a contribution to knowledge which is the most beneficial if the criteria are applied in a research environment to proof of concept technologies which have the potential to be developed into self-use molecular diagnostic devices.

2. Guidelines for the future research, design and development of self-use molecular diagnostic devices for sexually transmitted infections have been defined. These guidelines are designed to be applied after the preclinical trial phase of development of a diagnostic technology.
 - a. *User Interface Software Development*
 - i. Beyond the preclinical trial phase of development, the design of user interface software linking the actions of the user of the test to the requirements of the diagnostic technology should be commenced.
 - b. *Physical User Interface Development*
 - i. In conjunction with software design, the design of the physical user interface of the device should be initiated. Physical user interface design, casing and housing designs and user interface software development should be developed iteratively and in parallel with one another.
 - c. *Automated System Feedback*
 - i. Refinement of automatic systems in the device should be a priority

beyond the preclinical trial phase of development. Reliability of the systems and feedback of the status of components indicating the success (or otherwise) of a test to the user or other stakeholders should be a design priority.

Trust in how successfully a test can be operated is important for the user and the clinical and public health stakeholders involved in its operation. These design guidelines constitute a contribution to knowledge as they were derived from action research activities applied to the development of a preclinical trial prototype, novel, low-cost, isothermal nucleic acid amplification diagnostic technology. Development of the technology for specific, self-operated contexts of use with such a broad disciplinary input from the very early research stages is novel in the diagnostic technology literature to the author's knowledge.

3. A description of the issues and challenges pertaining to development processes for self-use molecular diagnostic devices has been given. The issues and barriers identified in the research are as follows:

- a. *Impetus for Design and Development*

- i. Academic, clinical and industrial drivers for investigating or developing new technologies and devices differ. For example:

1. Academic – Attractive publishing area, REF (Research Excellence Framework) scores
 2. Clinical – Prioritisation of perceived clinical issues based on personal or anecdotal information not necessarily constituting a public health priority
 3. Industrial – Profitable areas not necessarily in line with clinical or public health needs. Continued production of devices after effectiveness has been disproven in order to justify investment.

- ii. The differences between the drivers of different fields are difficult to reconcile.

- b. *Multidisciplinary Working*

- i. Communication and understanding between disciplines can be poor.

- c. *Speed of Development*

- i. Technologies which exist in the academic sphere are developed slowly as development may not be seen as an academic pursuit.
 - ii. Information sharing between research groups is inefficient, with duplication of technological know-how without dissemination of the

knowledge.

The tension between commercial, academic and clinical interests is highlighted through this research and provides an explanation for the slow development of point of care, portable and self-use molecular diagnostic devices for STIs. Improved collaboration between diverse disciplines is essential for the successful development and distribution of complex self-use medical technologies. A cross section of the varied and diverse experts working on projects such as these being situated at the same institution or even in the same office may improve collaboration and communication between disciplines. This is a key area where further research is required as is described below in the further work section.

4. A highly iterative design process model has been proposed for use when developing self-use molecular diagnostic devices. The design process model is designed for use in an academic research environment, as opposed to in an industrial environment. The process model combines the requirements of regulatory bodies for medical device design and development with rapid techniques for design, assessment and redesign of concepts using a wide range of informational inputs. The process model is based on rapid, iterative software development methods. This approach allows development to happen in a research environment without the potential restrictions on innovation that might be caused by attempting to use a stricter, more linear design process model.

7.5 Limitations

A generalised design process model, for use in the early research stages of self-use molecular diagnostic device development, has been proposed as a part of this research. Proving beyond doubt that the application of this design process model at the proof of concept research stages accelerates development overall is difficult within the confines of the thesis. Comparisons would have to be made between similar devices which have been developed from the proof of concept stages using different methods. As there are no self-use molecular diagnostic devices, to the author's knowledge, that have been developed to this point, this is not possible at present. Also, information regarding development processes and prototype design may represent intellectual property. As a result, they are often held by companies and are therefore confidential.

Other than the review of the background literature shown in Chapter 2, the data gathered throughout the research studies in the thesis were collected exclusively within the eSTi² research consortium. As a result, the data may be biased toward the prevailing opinions and working methods of that consortium.

An attempt was made to obtain information on design processes for medical devices from professional design consultancies, many of them specialising exclusively in medical devices. Spin off companies from well-known academic research groups specialising in diagnostic devices were also contacted. In all, 70 companies were contacted with only a relatively small response of 16 (a 22% response rate). While this has been used (in Chapter 3) as an indication of how design processes are applied to medical device development by professional designers, it did not provide a representative sample. An employee of one of the companies openly admitted that they were not allowed to partake in academic research surveys. The protection of intellectual property and ensuring surveys are not conducted on company time may explain this.

7.6 Further Work

The preclinical trial prototype technology has reached a stage where the functional needs of the various components of the diagnostic system can be described in a detailed specification document. This specification document could be used for further engineering research and development of the prototype.

Further work would include the fulfilment of the design guidelines described above, including the design of user interface software, physical user interaction solutions and automated internal systems. A key technical bottleneck is the problem of transferring a biological sample from the sample collection device to the microfluidic chip in a manner that mitigates user error; this line of research should be pursued.

Concept prototypes for usability and patient acceptability studies can now be based on the functional requirements of the technology and the clinical and public health needs described in the thesis. These concept prototypes could be shown to potential users of the technology for assessment. Usability studies showing how an individual operates the technology would be informative. Focus groups including potential users as well as clinicians and public health experts would provide insights into how further iterations of the technology might be realised.

A wider appreciation of the potential of using design processes at the early diagnostic technology research stages could be garnered through the application of interview and survey techniques (such as those described in Chapters 3 and 4) to other translational research groups. The iSense (EPSRC in IRC early warning sensing systems for infectious diseases) translational research group (iSense, 2017) aim to use mobile technologies to enhance the way influenza, MRSA (methicillin-resistant *Staphylococcus aureus*) and HIV are detected and treated. Their research goals and interest in novel, highly portable and connected diagnostic devices are similar to that of the eSTi² project. Surveys and interviews on the subject of device design and

potential issues and barriers to development aimed at this project would provide an informative comparison to the work presented in this thesis, which was solely focussed on the eSTi² project.

Similarly, the Precise research group are investigating the potential impacts of rapid, point of care diagnostics on current STI detection and treatment practices in the UK (Precise, 2017). Investigation into how this group is gathering stakeholder information and applying it to technology development would be valuable for future development efforts for novel, rapid diagnostics. Likewise, the ADREU (Applied Diagnostic Research and Evaluation Unit) based at St George's University, London, experiment with novel approaches to STI detection and treatment based on emerging technologies (Harding-Esch *et al.*, 2017). Qualitative investigation of the approaches taken by the stakeholders involved in ADREU could provide a valuable contribution in understanding how design processes can best be applied to the development of novel, rapid diagnostic devices.

Alleviation of the issues and barriers identified in the thesis offer an opportunity for further research. Investigating a way in which research projects into self-use diagnostic technologies could be more collaborative would be valuable. Research investigating how to identify the drivers of diagnostic technology development and to ensure that the 'right' diagnostics are being developed for maximum clinical and public health benefit is an emerging area in which design process research could play a valuable part. Understanding design intent at the very earliest stages, when the drivers of diagnostic research and development are being identified, could provide valuable clinical and public health benefits.

A method for proving that the design process model described in this thesis provides a tangible, rather than only a theoretical benefit, would provide an important contribution to the design process and diagnostic technology research fields. Proving this would be very difficult, as it may require comparing a translational group that has used design methods with one that has not. There may be ethical problems with this if it is shown that the research outcomes are significantly better or worse in either case. However, data on the application of design methods could be collected throughout a number of research projects and the outcomes could be compared to the outcomes of similar projects conducted in the past. This may prove that applying design processes in the early research stages provides a tangible benefit.

7.7 Summary Conclusions

Increasing success in creating miniaturised and low cost molecular diagnostic technologies means that there will be further demand for investigation into ways in which these technologies can be developed and then deployed for public use. User centred design methods are excellent

for showing the best way in which an established technology should be presented to and used by people. However, in the case of an emerging diagnostic technology for self-use, this thesis has shown that a holistic approach, taking into account technical requirements of the technology alongside human factors, clinical, public health and economic requirements is appropriate.

The thesis proposes that this holistic, highly iterative design approach should be applied to the development of emerging diagnostic technologies at the earliest possible opportunity. Doing so may contribute to accelerating the development of diagnostic technologies from the early research stages to deployment that is beneficial from a clinical and public health perspective.

The application of iterative design methods at the earliest stages of research is unusual; research groups investigating diagnostic technologies consider that research entails the discovery of novel technologies and diagnostic methods, whereas development activities ordinarily happen outside the academic sphere. Aspects of the design and development process, as have been shown in this thesis, becoming accepted elements of the research process for discovering diagnostic technologies could allow significant gains to be realised in the speed and efficiency of translating diagnostic technologies from the laboratory benchtop to use in the field.

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Appendix A: Expert Stakeholder Interviews

Ethical Approval for Interview Study



College of Engineering, Design and Physical Sciences Research Ethics Committee
Brunel University London
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22 November 2016

LETTER OF APPROVAL

Applicant: Mr Thomas Stead
Project Title: eST12 Design Requirements Interviews
Reference: 4604-LR-Nov/2016- 4540-1

Dear Mr Thomas Stead

The Research Ethics Committee has considered the above application recently submitted by you.

The Chair, acting under delegated authority has agreed that there is no objection on ethical grounds to the proposed study. Approval is given on the understanding that the conditions of approval set out below are followed:

- The agreed protocol must be followed. Any changes to the protocol will require prior approval from the Committee by way of an application for an amendment.
- The Committee recommends that you complete the Ethics Training module via Blackboard Learn prior to commencing your research project. Please click on the link below and complete the course online.
https://blackboard.brunel.ac.uk/webapps/blackboard/content/listContent.jsp?course_id=_8579_1&content_id=_322757_1

Please note that:

- Research Participant Information Sheets and (where relevant) flyers, posters, and consent forms should include a clear statement that research ethics approval has been obtained from the relevant Research Ethics Committee.
- The Research Participant Information Sheets should include a clear statement that queries should be directed, in the first instance, to the Supervisor (where relevant), or the researcher. Complaints, on the other hand, should be directed, in the first instance, to the Chair of the relevant Research Ethics Committee.
- Approval to proceed with the study is granted subject to receipt by the Committee of satisfactory responses to any conditions that may appear above, in addition to any subsequent changes to the protocol.
- The Research Ethics Committee reserves the right to sample and review documentation, including raw data, relevant to the study.
- You may not undertake any research activity if you are not a registered student of Brunel University or if you cease to become registered, including abeyance or temporary withdrawal. As a deregistered student you would not be insured to undertake research activity. Research activity includes the recruitment of participants, undertaking consent procedures and collection of data. Breach of this requirement constitutes research misconduct and is a disciplinary offence.

Professor Hua Zhao

Chair

College of Engineering, Design and Physical Sciences Research Ethics Committee
Brunel University London

Interview Transcripts

Public Health and Diagnostic Evaluations Expert: Pseudonym – Laura,
Interview conducted: 1st December 2016. 13:45, Duration: 00:35:22

Interviewee = LR

Interviewer Tom Stead = TS

TS: Now we're recording, are you OK with us recording?

LR: I am OK with us recording.

TS: Excellent. Right. So, your disciplinary area and your role within the eSTi2 project?

LR: OK, so my...focus is diagnostic evaluations...and the impact on public health and surveillance. So my role within the eSTi2 project, was to be based at public health England as a principle scientist but the...Work Stream 3, so the diagnostic evaluation trial coordinator...So it was to do the bridge between the public health and St. George's diagnostic, led...diagnostic evaluations. Um...so I bring in my expertise in how to conduct diagnostic evaluations...and also...public health and by being sat in the HIV/STI department, I've got awareness of the issues currently at hand...that people talk about. Access to people who work there...an understanding of the surveillance systems in place, how the data are collected...and therefore as we look at the STI technologies...what they look like now but what they may look like in the future what the impact on surveillance would be.

And so that knowledge...is useful in the diagnostic evaluations and the work that we do with developers, either academic or companies and what we might suggest would be good ideas for them to do...in order for them to... have the biggest public health impact and utility clinically and at the public health level. But also for the companies...to...have a bigger market and, because they obviously want to sell their tests...so they want a test that people are gonna buy so they need to know what's...whether there's a market for their test and for example what...targets to put on their platforms.

TS: That leads nicely into the next questions [laughs]

LR: OK...[looking for question on sheet]

TS: So the people developing these tests, do you...you can inform them a little bit on what sort of features they need to include and how they need to work, not just from the sort of technology that does the diagnosis but the, the context that fits in, the system that fits into?

LR: Yes, so...we, so we're very open, from the eSTi2 perspective that we work with multiple partners...anything that's proprietary knowledge from a company we obviously don't divulge to anyone else but anything that's common knowledge or just our, like a consultancy, our kind of general expertise...so mine, public health...[Boss's Name], clinical...um...other people...um...then we talk about that because it's nothing that's, if you weren't an expert you wouldn't not know. ...so we can say, for example...so for example my knowledge from...the GUMCAD which is one of the surveillance systems from, so the GUM clinics feed their data to Public Health England, we've got the data set so we can look at trends over time so it's reported quarterly and we can see...what the rates of Chlamydia, Gonorrhoea...um...and now there's just started Mycoplasma Genitalium testing...um...we can use those data from GUM and link it with other data like the NATSAL which is population level data...and we can know...what the BASHH guidelines are and we can put all that knowledge together and say, 'for your test' for example, 'for Gonorrhoea, it needs to be dual target because there are issues of specificity because it's, because Neisseria has issues especially for pharyngeal infection of cross reactivity so it needs to be dual target...um...and because the prevalence of Gonorrhoea nationally is very low, there are issues for the positive predictive value which the BASHH guideline says, has to be at least 90%'. 'So for

your test to be implemented and supported by BASSH guidelines, then it needs to have a PPV above 90% and that's the, that's what you need to work towards in terms of your specifications.

TS: Brilliant. Cool, so just going back a little bit to those, the data collection thing...how does the GUMCAD work and what's the national...the...

LR: The NATSAL?

TS: Yeah, how do they, how do they both work, sort of on a practical, down to, how is it directly collected?

LR: So they're very different. The NATSAL is a UCL led...er...like, project...um...that's run every ten years, so NATSAL 3 has just happened...um...so it's a research project where it's random selections of the population and individuals get invited to participate and...er...if they consent and they provide some samples and fill in a relatively in depth questionnaire about their attitudes towards...lifestyle and sexual behaviour and so you get, so it's the best estimate that we have of the general population prevalence.

TS: So, that's kind of separate from the GUM clinic...

LR: It's completely separate. Yes.

TS: Completely separate. So they haven't been to a GUM clinic that's...

LR: So no, so the NATSAL they don't target GUM clinics, so you might have individuals in NATSAL who attended a GUM clinic but that's not the reason why they've been selected, it's a random selection of the population, within a sampling frame.

TS: uh huh.

LR: Whereas GUMCAD is specifically data from GUM clinics.

TS: And that is recorded using...how is that recorded?

LR: So the clinics feed their data back...to PHE via a kind of secure portal so they upload it on a quarterly basis, there's a whole load of codes, they're called 'SHAPT' codes so for what you've been tested for, what you've been diagnosed with...and...er...and then GUMCAD writes a, provide a report...um...and you can, that's where you kind of look at which are the STIs with highest prevalence or changed from previous years etc....and which target groups, is there more in MSM or is there more in certain ethnicities etc. so you, it allows us to get a sense geographically and by population group...where we need to focus our control efforts.

TS: So I guess one of the big issues with moving from a centralised sort of GUM clinic thing to testing out in the population is this data collection methods...

LR: Exactly...

TS: ...have to change.

LR: Yes. So if, so basically my, one of my roles, and we wrote a paper on it, last year...was, if we end up with a pregnancy test style test for STIs, so there's one for HIV now but the HIV data collection system is different from the STI one anyway, er because...

TS: Do you know much about it, or...?

LR: So, I, they don't look at it so much on a, kind of like on an individual level to my understanding, so they kind of have algorithms to kind of work things out...whereas for GUMCAD for STIs, although they have HIV from the GUM clinics, it's different from the HIV department, it's called HARS is their data set, so they have their own dataset which looks at access to care and...um...when people get tested for HIV, how recently were they infected, so, to

try and work out what proportion of the population is an unknown, is infected but don't know that they're infected. So for the HIV self-test, so at the moment it's just one company that's licensed to distribute it in the UK...and there have been conversations with them about whether we can get some of the data on how many people have bought it and very, very basic information on them, basically they can try and work out their gender based on their name and...er... kind of where, where their credit card is registered to or something like that, so it's really, but you won't get the information that we have on sexual orientation, ethnicity, age, etc., so we lose a lot of that depth. But, the advantage for HIV is, because it's a chronic infection, if they're HIV positive, they will come into care... [Phone in background, slight distraction] they will come into care for their HIV care whereas for STIs, say Chlamydia you can get your online, your test...

TS: Yep.

LR: ...and then you can get online treatment and we will never know anything about how many people are testing or what their result is because everything would be remote from us, from us, from care services.

TS: So, that's a major issue...how to connect those things up, is a major issue for people developing these types of tests, sort of collaborating with Public Health England and the NHS I suppose?

LR: Yep. Yep exactly.

TS: ...to connect things up.

LR: Yep.

TS: ...cos what I'm sort of getting at is that, we have this pregnancy test idea, this sort of, black box idea of what the test is and what I'm trying to get at with these interviews is like, an idea of what essential features there are. So obviously if there was this device we're developing that isn't being developed but could exist...an essential feature would be the connection, the data collection that is connected with the NHS with methods like GUMCAD?

LR: Yes exactly, and that's something that...um...we're, kind of within eSTI2 we're trying to advocate for the companies to do that because it's beneficial to us to get those data 'cos we can then have our public health interventions but like I said, it's beneficial for the companies, because without the knowledge of how much Chlamydia there is they don't know whether it's worthwhile doing a Chlamydia test, so it's hard for them to make the business case to their companies to invest in the development of this test.

TS: eSTI2's doing this obviously with a few companies.

LR: Yes. But we don't work with every company and even with the companies that we work with, their primary focus is [to] get a test that's got sufficient diagnostic accuracy that's gonna get implemented in the NHS or sold in the UK and anything on top of that is extra...um... and it's all about share-holders and making a profit ultimately for a profit led company.

TS: Yeah, I've got this question half way down here, 'from the point of view of public health, what features of this [a] test would be absolutely essential, can't be left out?' in the ideal test, if you had control over what these companies were doing, so that might be a leading question there...[laughs]...totally leading...

LR: But I think I've led you to ask that question in that I, from my perspective it is essential, cos...otherwise we risk losing those, those data.

TS: You've sort of started answering the next one as well, so what are the barriers to achieving this, so, if this is what we really need from a public health perspective, we really need this data collection thing, the barriers to achieving that?

LR: So there's a technological barrier, so, is that actually something that can be done...which I think, more or less on most platforms there's, y' know, through computer style things, like smart phones etc. there you can enter data so there's barriers like we've seen in work stream 4 of...at what point do you ask people for the data and is it gonna put them off doing the test...and so there's a lot of, of that kind of questions, how many questions can you ask? Cos I think there's a difference between you buying a test at a supermarket and doing it at home and then being asked to do all these questions for the benefit of public health versus going into a GUM clinic where they ask you all these questions and especially if you're selling this test in a supermarket and you're asking these questions and someone else is selling a test at a supermarket and not asking these questions you might actually then decide it's not worth it if people are not gonna buy my test anymore because they don't want to answer all these questions.

So there's a, I think there's a barrier in terms of patient acceptability of answering the questions, there's the facility of capturing the data and transmitting it securely with all the data protection issues, an issue of linking that data into Public Health England and for it to be of the appropriate format and going through the correct software and all of those things.

TS: 'Cos there's the, the secure network isn't there...

LR: Yeah, and so they've got a new thing called SGSS which is second generation...SS...can't remember what it stands for...

TS: I'll look it up...

LR: So, we have looked into... with one of the companies, for, not for an STI but using it as a proof of concept because we don't have an STI test...seeing whether we could do that and it was already...but that was when SGSS was only just starting and we didn't move ahead with it...but, to see whether there's feasibility of doing that, but there's clearly capabilities of feeding data in from outside because they do it from the GUM clinics and from...labs and things like that for the Chlamydia testing activity dataset which is a Chlamydia specific dataset that we also have at Public Health England...so they do have these forms of data coming in from elsewhere so it's just a matter of doing that.

Then, and then you've got the problems of analysing the data because you don't know whether those people have also then gone to a GUM clinic and so can you [de-?] duplicate, probably not. Then you have to probably have to have some kind of algorithms of how much overlap you think there is in the populations etc. but that's not necessarily a barrier for the test, it's more a barrier of how we can maximise the utility for Public Health England.

TS: It might be worth just going over what Work Stream 4 have done in overview with the clinical care pathway just to explain for the guy who's gonna transcribe this...because that's, a lot of that is, it's that isn't it, it's addressing the barriers.

LR: So yes, with the online Chlamydia care pathway...er...so one of, part of my role, in my public health bit, was to provide public health input into the online Chlamydia care pathway to look at what data variables to include...and because of the way that we ended up running the pilot, by having patients who were already in a GUM clinic and already in the NCSP whereas previously we had planned on it being a community setting. So we, in a way, overcame that barrier because we'd spend quite a lot of time looking at what are the basic data variables to include, so rather than the full set that we collect from GUM clinics or from the NCSP there's kind of the minimum data set that's acceptable, and then we didn't have to do that anymore when we shifted the population that we ended up testing from a community setting like a further education college into NCSP and GUM clinic patients.

TS: Why not? So there's the amount of data that's normally being collected and then you manage to whittle it down to essentials based on, because of the population you...

LR: Yeah because when we did the pilot in the end, we used patients who were already enrolled in the NCSP and GUM clinic, so their data, all the data variables that you routinely collect in NCSP and GUM were already being collected so we could just have those...

TS: Right...

LR: ...then the question was about, at what point do we ask for those data, but previous to the pilot being actually rolled out the original plan had been to run the study in further education colleges where you don't collect routine data so we were having to think about what's the minimum dataset. So we don't put people off wanting to do it because we're asking them this massive, massive questionnaire with all the stuff that you ask about normally in a GUM clinic. We were just gonna ask a minimum dataset so that we had what we needed as a minimum for Public Health England and didn't put them off participating in the pilot.

TS: Then that's the challenge isn't it...

LR: Yep.

TS: ...that's the, because it's got to be acceptable...

LR: Exactly, yep, otherwise you kind of lose the point of the test if no one's gonna buy it and use it because they find it too intrusive or it takes too long.

TS: So how far did we get with answering that question of what the minimum is that you can get away with and it be...[inaudible]

LR: ...we did have a set of questions, but there was still debate kind of going on because obviously in Public Health England they were like, well there's a...you have to justify any...in Public Health England when you do your data...when you set up your database it has to be ethically approved, it has to go through this board and you have to justify every single data variable that you've asked for. So, there's a reason for every question already being collected, so to be able to say actually we don't need this question is kind of saying 'well, why did you have it in the first place?'. So it was quite difficult because Public Health England were kind of saying well, we want it all, and actually we want more rather than, we want less. So we, I don't think we fully resolved it, and then because of the issues of,,, potential...because this was a pilot of a completely new process, it was decided to not do it in a further education college just in case there were problems with it and people got upset etc. in a further education college. 'Cos it was remote and it's people not actively seeking testing, you're kind of asking them to get tested and then doing it all remotely and then if there were issues there might have been, kind of, I don't know, kind of governance problems around it.

So, by going for patients already in the NCSP and GUM clinics, they're people who are already actively seeking to be tested for Chlamydia...and obviously then we had the health advisor anyway that people could phone up and they could choose to drop off the online Chlamydia care pathway at any point and it wasn't going to affect their care. But they were already kind of a patient that were seeking testing, so there weren't the same potential ethical issues around...

TS: So how do you envisage tackling that, cos like, in my mind it seems like you'd have to...it's all done on...well, the idea is it'll be done on mobile phone or tablet, is it just having better ways of getting the information off people...if it's a matter of...well it's two things isn't it, it's acceptability and getting all of the information required so how do we tackle that?

LR: Well no it's a really good question and I don't think that's been answered.

TS: Yeah.

LR:...and I imagine it will probably have to be a partnership between the company and Public Health England and the other thing that we've seen from... the Work Stream 4 work with the user interviews that [Colleague's Name] and [Colleague's Name] did is the trust people place in

the NHS, so by having the NHS stamp...and therefore you would assume that perhaps the test might actually be free and people aren't paying for it...then...through...you're still biasing your sample to people who are accessing the test for free and willing to answer all these questions, as opposed to the HIV self-test is £30. And there are people buying it, so why are people buying a test you have to pay £30 for rather than going to a clinic that's free? So there...people still choose that pathway, so we would still lose those people but if there was a test that was adopted in the NHS so that we could collect the data then...er...we could still perhaps access those people.

TS: So it's almost like the test, physically and the software that goes with it and everything would be an NHS...

LR: ...possibly...

TS: ...thing... possibly

LR: Yep, ideal world...not sure how you would get there but er...

TS: Yeah, that's well...ideal world is what I'm...because I'm collecting sort of ideal world design requirements, so like, in the best possible situation...so...[pause] onto the next one, what is the key technology which will or has already begun to enable self-use molecular diagnostic testing? It's probably...it's... mobile phones, and it's...telecommunications isn't it? Not to answer your question...sorry...

LR: ...key technology that will enable self-use...well I think it's two things, so depends on which perspective you're taking, so from the data transfer side, I'd say mobile phones...but you could have a technology, you could have the test itself that's able to transmit, not via your mobile phone but from the test itself?

TS: Yeah...

LR: ...Somehow, that's not my area of expertise...but it might not be mobile phone dependent. It's like data transfer mobile, kind of or wireless network transfer. But also I think that, in terms of the key technologies, I think it's the micro-engineering type technologies, the things that work stream 2 has been working on with like the paper-based microfluidics and the different types of amplification, different reagents for sample preparation, all those kinds of things, I think it's the, there's the way that the testing platform technologies are progressing as well because say 20 years ago, you know, PCR machines were still kind of, you would do them on your stove like with saucepans of different temperature...well not quite...but different temperatures and you'd move your thing between each thing as opposed to now our lovely, you know the kind of tests that we're doing like shoebox sized platforms and the isothermal, where it's all like the same temperature and you don't even need to do ramping up or ramping down of temperatures, so I think there's advances in the test technology, not only in the data transfer technology and it's the combination that makes the future for the public health purposes. Obviously, if you forget about the data capture bit and you're just looking at 'can we have a pregnancy test style STI test' then actually it's only about the technology, it's not about the data transfer.

TS: Yeah, I'm trying to look at it as a whole thing because like you said earlier, it's vital that that's the case. ... [Pause]...so where are we? So, we've done vital features, is there anything we haven't talked about?

LR: So, things we haven't talked about, so I guess, so I think key, is going to be the partnership and the buy in and the political will and the public health, the push, so, how do you get there? Um...and I don't know what the answer for that is but that would have to happen. For it to be seen, for example, by Public Health England as a priority that we work on this, and at the

moment, it's not a Public Health England priority to enable self-tests to be linked up to our surveillance systems, it's my public health priority, but not at an organisation level a priority.

TS: Why is it not a priority?

LR: I think because it's not a problem yet...and....so I'm trying to kind of, look ahead that in ten years' time... because the tests don't exist and no one really knows when the tests will exist, it's not actually a problem. And who knows also what's going to happen to our NHS structures in the meantime anyway. So for example you've got the London transformation project which is trying to basically do the self-sampling at home, send your samples off, get your results at home, do things more remotely like an SH24 model for asymptomatic patients so then the GUM clinics are more for complex and symptomatic patients, so to kind of split it that way to reduce the burden on the GUM clinics. So there might be massive, organisational changes like that, that impact the way that we do testing and that impact the way that a self-test might be implemented and distributed and the desire for it. So it might actually make it more desirable to have a self-test, if those structures are in place...um...I don't know, because it's still kind of being developed.

And then also I'd say, things are constantly evolving in terms of the infections and the things that are of interest to us so say Gonorrhoea at the moment, that we've had a high level Azithromycin outbreak, so that's a massive public health interest at the moment because potentially we're very limited in the treatments in the sense that we only have one effective treatment left for Gonorrhoea. So we may be wanting to actually have more information on resistance data. So there would need to be feedback between, from, Public Health England to the companies to constantly update and evolve and for it to be done in partnership with the test because otherwise the test would no longer be fulfilling the Public Health England requirements needed so it would need a lot of collaboration, communication and a mechanism for updating.

TS: Yes...well...

LR: It's quite complex...

TS: Yeah, it's very complex, it's interesting... I don't know where to go from there...er... Our time is up actually.

LR: Oh is it...

TS: It says in the ethics form 30 minutes so we are now...

LR:it said approximately 30 minutes.

TS: Approximately yes.

LR: We could do 35.

TS: ...because you've answered the last question because I've said 'considerations beyond just the technology' so the context of it, within which the technology has to fit and how they'll develop which is exactly what you were just talking about so...

LR: And, generally for tests, which is a major issue for everybody is how does a test get actually adopted and implemented because even if you do things like NICE adoption where you get your stamp saying you've got our mark of approval, doesn't mean anything, it doesn't mean that a clinic is about to start using your test and that's a major issue that all the companies come up against. They can tick the boxes, but still no one's going to use their test because it needs to be cost effective, it needs to fill a niche.

TS: Can we quickly go into how might it be adopted, how might you get in to this, to the market, how, what has to happen?

LR: Well, so that's actually the subject of a grant application that we're going to submitting next year to try and really work out, from different key stakeholders what are the considerations and what would be helpful in order to be able to decide whether you want to implement...our focus is on point of care tests for STIs but what are the considerations that are really important for you to decide that, so that companies can know what they need to focus on and know how to approach different people. So understanding the structures of commissioning in the UK and how...how the decisions about budgets...how do they get made and what things influence the commissioning decisions and the providers' decisions and the clinicians' decisions because you kind of need buy in from all of them to make a test successful.

TS: So the stakeholders are the clinicians and then the...

LR: So speaking to the people that...so like, speaking to the sexual health facilitators who kind of support commissioners, specifically on sexual health...they said that the key people to talk to are going to be the commissioners, the providers...so like...who can be either, like, clinic managers or things like, you know Virgin Healthcare type people and then the clinics as well. And then it depends on your local area...how much of a voice your clinicians have or how much of a voice your commissioners have.

TS: How does it depend?

LR: For example on what type of funding structure if you're block funded or tariff funded...and also just how things work; relationships between people, other public health...areas that require more or less funding.

TS: So the first step is going in and talking to these people about the adoption of technology and talking about how it...how it's going to change things, is that what we're... [Talking about?]

LR: ...so, to understand how...what's involved in the decision making process.

TS: Right and that's a question being asked?

LR: ...that we will hopefully ask if we get funded. Because it's unknown. So you've got for example say the Cepheid GeneXpert which is the closest that we have of a...it's a rapid test that's for Chlamydia/Gonorrhoea that is being implemented and you can kind of see how they've done it in that they've had a relatively aggressive sales method of going into clinics, mapping clinic pathways, trying to see if your clinic is going to take this on board. They've got high performance which is really important and because it's a nucleic acid amplification test with high performance, it ticks the box that you need to use a nucleic acid amplification test with high performance...and because they've got varying size of machine from kind of a single cartridge to whatever it is, 128...and it's...independent compartments so you can run samples as they come in and it's 90 minutes, it's actually suitable for different environments, so it's, they've kind of adapted to the needs as well. Obviously when they first started out they had fewer platforms and less flexibility but now as they've progressed I think...and...basically as one clinic adopts and...If you find the right clinic that publishes the papers and is influential then the other clinicians go 'oh that's really good, oh I might try that'. And then it starts...so it's a...so it's getting it into the key...so for them what seems to have worked, aside from that their test works well...is that certain key clinics have taken them on board and because they can put other things on it like TB, it's not just CTNG it becomes like, it can be like your Hologic or your BD Max or those kinds of big platforms that you can run different tests high throughput if you want to.

TS: It's interesting because it kind of touches on the question I'm asking some of the companies to do with what drives the innovation, is it the technology driving it, becoming available or is it the need being assessed and then you develop the technology to fulfil the need. It sounds like that's the technology driving it, kind of, because they're going in and saying we have this...

LR: Well they...you need to know the need to know there's a market...

TS: Yes...yeah

LR: Otherwise you wouldn't invest in...you would imagine...that you wouldn't invest in developing a technology if there's no market to sell it in...

TS: OK

INTERVIEW ENDS

Engineering and Molecular Biology Expert: Pseudonym – Lee, Interview conducted: 5th December 2016. 21:21, Duration: 00:27:40

Lee = LE

Interviewer Tom Stead = TS

TS: We haven't been recording, but we are now, are you OK with us recording?

LE: I am OK with us recording as I put on the form. I sent you the form didn't I?

TS: Yes, I've got it yep. I'm going to have to turn you up a bit.

Alright, so, what's your disciplinary area and what was your role within the eSTi2 project, as you see it?

LE: I was a PhD student...in Work Stream 2...working initially to develop the isothermal amplification assay...for the desired targets...which were sexually transmitted infections so...do you want me to go into what isothermal amplification is or just leave it at that?

TS: Yeah go into it yeah, and go into why it's appropriate yeah.

LE: Yes OK, so, I joined Work Stream 2 when there was...or the DoCLab, which is the same as Work Stream 2 almost...which, when they had a DNA extraction system somewhat complete and they needed an assay that would take that DNA that was extracted and detect whatever the target was...the target would be the most common sexually transmitted infections seen in the UK which was Chlamydia...Gonorrhoea...Mycoplasma Genitalium...so these were the targets I was developing assays for initially. And then that project changed, expanded to include the development of the hardware that would detect the amplification products.

So then I would develop the assays which was the biological part of the PhD project and then also the electronic and optical hardware that detected these assay being performed because the assays themselves produced a fluorescence and they had to be held at a certain temperature so I developed the electronics that did that.

TS: Do you think it's essential to develop the electronics alongside the assays or...I imagine that's quite unusual...?

LE: Yes...yeah I do think it's...it is important. You can develop one and then the other...but it helped because we were able to optimise both of those modules...so both the way that the assay worked in terms of biochemistry and also the optics, so that they were closely synced whereas if you developed one and then the other you might not have them matching up. So that certainly made life a bit easier and because of the small amounts of reagents and the small quantities being used because it's a handheld device you don't want to have bucket loads of these things because that would require a lot of energy to run it. By developing the two in parallel we were able to optimise each of those to fit with the lowest, sort of, energy footprint...and make sure that the detection was as cheap as possible.

Having one person do it, I suppose, was challenging...but yeah, certainly the principle of having them both developed at the same time did actually work quite well.

TS: So, moving in, that moves us nicely into the next question about combining engineering and biology and because I'm doing these interviews to try and come up with say a list of design requirements from many different points of view...what sort of attributes and features...and I mean be as broad or as specific as you like...does a self-use device need...so I mean, it needs sample collection...

LE: So what are my views on what the attributes of a system would be?

TS: Yeah, so from...the needs of a biologist and engineer so...the needs from the point of view of the device from an engineering perspective and a biology perspective as well.

LE: Firstly, from the engineering standpoint it needs to be...if it's a self-use test it has to be cheap because a person has to buy it and take it home...I think having it as something you hire or go into a pharmacy for reduces its power as a self-testing device because the device itself works a lot better if it's something you take home and then you don't need to go back and see anyone because part of the problem is the stigma that's involved so the fewer people you have to interact with when you're going through that diagnostic process then the more effective it is in its purpose.

Otherwise if you're going to have to interact with a lot of people when you return the device or hire it or whatever then you might as well just go to the doctor. So I think cost is one of the key driving factors, it has to be low cost, preferably single use...preferably disposable, which would mean single use...generally. It needs to be low power, so preferably something portable, people don't always necessarily want to plug something in but also plugged in things tend to be more expensive. It needs to be small, something discreet...

TS: So I think a lot of your work was in the small...small, low power area wasn't it, that's sort of what you ended up...

LE: Yeah, and making it...I mean, devices that can do the equivalent thing already exist so...if we wanted to do a benchtop device we'd just go buy one, so the novelty of what I did was making it low power, small and cheap. And that was the basis of my PhD...doing it in a way that would facilitate its use in a portable device that would fit the eSTi2 requirements as I saw them which was portable, low cost, cheap.

TS: So... [Pause]...I'm not sure how well this question applies in this context...What...I'm trying to get an idea of...priorities of features...in my mind, as a designer the priorities come out as 'you have to have a sampling system that's very usable' and I understand it might be different from your point of view. So I've got this question in here about...what could absolutely not be left out...maybe that's a bit of an odd question...from an engineering perspective...

LE: ...just a moment. This is question 4?

TS: 3.

LE: 3... [Pause] ...well, yeah, yeah, I think all of those attributes, I think cost, power...certainly cost, cost was the deal breaker...if we wanted to make this device for a million dollars, it would be easy...

TS: That's...so cost is a deal breaker...that's good to know...

LE: Yeah, cost is the deal breaker because, I mean, these devices already exist, at a high cost, they already exist in a large size...so size and cost I think were the two attributes that drove it and cost being the primary one...it can easily be done at a high price, doing it cheap is the hard part.

TS: Did you ever look into anything to do with disposability of these materials with the stuff you were doing? Because I...what I'm thinking you're using this in the world...cost absolutely, and size, and the problem of 'what then?'...you know, once the test is done, what happens to it?

LE: So the...what do they call that in your world...product lifecycle...end of life...

TS: Yeah, product lifecycle...

LE: It was brought up...it was, it's not that we completely...well we did completely ignore it would be the simple answer because at that point in the development...cost was the key driving force and certainly from an environmental perspective...yeah, we were just looking to see how cheap we could do it...and there were informal discussions about printing it on and disposable electronics and things like that but there was never a formal path or even a formal consideration.

One thing that was a consideration was...actually in saying that, some of the chemicals we used we did think about how toxic they would be when disposed of and some of the people doing the microfluidics, not myself directly but I know that whenever you're building microfluidics we did talk about the plastics and would they be incinerated and would they contain the contamination...so yeah actually there was some thought in that. But certainly for my project, developing the electronics it was way, way, way down the list.

TS: I know there was a bit of a focus on the developing world for your project. Was it...because it was a prototype platform, in its earliest stages, was it just the idea that it...this technology could one day go any of those ways. It could end up in the developing world but it could also end up as a self-use device maybe using that technology...or is microfluidics not the technology for self-use devices?

LE: The device itself...we always...the primary goal with eSTi2 to develop for use in the UK as part of the NHS. But then we always realised that whilst that was always a huge financial incentive to develop for that market, we could develop it for the developing world...where the...humanitarian or the...public good was probably even greater.

Chlamydia is a huge health burden on the NHS but the other diseases you could easily...once the device was existing, you could use it for other things such as HIV diagnostics, Malaria diagnostics and all these other things which arguably had a much bigger human impact. So there was always kept in the back of our mind that development...one, the cost was kept down for the NHS but also the cost would be kept down to facilitate its use in the developing world. Does that make sense?

TS: Yeah, yeah so....moving on...so you got to particular point with the technologies with DoCLab and Work Stream 2...what were the barriers that came up against the technology...between where it is now and getting to, you know, some sort of commercially viable device/system?

LE: Well, apart from the money you mean? I think there's a lot of development that needs to be done...we're still a long way from integrating it...

TS: I guess I'm talking about technological barriers as opposed to like, you know...do you mean money as in, like, funding...I mean barriers as in where are the technological bottlenecks. For me it always felt like it was the interaction between the different components of the system, you know, getting a sample into a device...things like that.

LE: Yep...yes, I think...but that also was because the technology for each of those wasn't clearly defined...it wasn't a set...we didn't have a technology ready to go to do the sample extraction, we didn't have a detection [inaudible] ready to go or...well, that's what I developed...and then the electronics to control it. So if we had all of those, then the interaction between those...integration between them might be easier. But yeah, I think that's a fair comment, I probably agree with that, your assessment of the situation was that the interaction of each of those modules...

TS: It wasn't an entirely leading statement...I hope... [Laughs]

LE: No, no, it's good, it led me to where I wanted to be so we'll go with that.

TS: What do you think is the technology that's going to do it? That's going to...maybe that's a terribly broad statement because it's such a complex field and...there's going to be different technologies are going to be applied in different contexts but because I'm specifically looking at a potential self-use device for the NHS...I mean I've got the question there, you can probably see that I'm straying from it a little bit...I've already said what do you think the key technology is that's going to enable self-use diagnostic testing...?

LE: That's a good question... [Pause]...I don't know if there's any...I don't think there's any huge bottlenecks left, I think...but I do think that it's a very complicated question of integration like you said before that requires just a huge investment in terms of the microfluidics and the electronic control and so there's no...[pause - interruption]...so where was I. It's going to be...it just needs a bigger team, more people working on it. I don't think there's any major...I mean, what we have at eSTi2 I think could easily do it but it just needs more investment in terms of time. I think people underestimate the complexity of that systems integration...and to do it on PhD students...I mean it can be done with PhD students but as, I think, we've all seen...it's...what am I trying to say...it's a massive design, R and D process and it can't be done with PhD students. If you paid a team of twenty people, each with their own specialties to work together to do it, I think it could be done, with the right amount of financial investment.

Where eSTi2 probably fell apart is that they're trying to do it as a design project or a design R and D work as part of academia might not have been the best place for it. We were good for developing the independent technologies and [Colleague's Name]'s Chitosan work and my work on the detection were all great things but then the integration and the tinkering that's required to bring them all together probably doesn't produce a lot of academic output...but it's valuable stuff to do and that's what would bring the project forward but you're not going to publish a lot of papers talking about how you made the sample prep join up with that. I mean, you could argue that you could but it wouldn't...I mean the effort would require, you know, a thousand man hours and you'd get one paper out of it. I don't think academia is necessarily the best place for doing it.

TS: So, in future, you know when people do the next eSTi2, whatever that is...is it an idea that...do you think people should be trying harder to make it like an industrial R and D...because it seems like that's what happened...you know trying to make it like an industrial R and D department a bit. Should they try harder to do that, get more designers, systems engineers in...

GAP FOR LOST SKYPE SIGNAL...

TS: We were talking about...research projects like eSTi2 in the future...in your opinion do you think maybe there needs to be more of a look at things like the...systems integration or maybe they need to focus more on the fundamental research thing and leave that to industry.

LE: Well I mean it's...hmmm

TS: That's not a loaded question, I'm genuinely interested, and I'm not looking for any sort of, specific thing...for my research

LE: Well I don't know, I'm obviously not the best person to speak to about that but I think the project itself, is hugely multi-disciplinary...which they recognised and that's a compliment to eSTi2 is that they realised that it would require designers, engineers, biologists, clinicians...but what I don't think was appreciated was just the scale of the task and the finances required to drive it...and, it does require a lot more resources which I suppose means money, and more people working on specific parts of the task.

So, I don't know if academia's the place for it to be happening because there's just so much R and D and probably more of the D in the R and D than the R maybe it just doesn't lend itself to academia.

TS: I always figured the advantage of being involved with academia might be that...you can be connected more easily to things like the NHS and Public Health England, you know, you can get, like a real good exchange of information with people like that.

LE: Yeah, absolutely, and that's definitely one of the powers of eSTi2 was that it can access all of these people without the commercial interests getting in the way but then there are some...there are a lot of parts of the process which I think just require people to knuckle down and do some development work and that's academically unproductive, just sitting down and working on...as you mentioned, you've had to push (I don't know if I can say that on the record there but take it off if required) but you've had to push to get the academic, the research side of things out...

TS: Yes

LE: ...and there's, then there's been a push from the project perspective just to do development work I think those two are...there are times when they're mutually exclusive. If you're doing academic research, you're not doing the development that needs to be done to move the project forward...so I think that that is a complicated area and I think that there's a lot of benefits that come from doing it as part of academia.

TS: I think that can go on the record, I think that's something that...what is academia is if it can't be critiqued in itself...if you can't...

LE: No, I'm happy, Tom, for it to be critiqued I just don't want me to be doing the critiquing.

TS: Oh you'll be completely anonymous...

LE: Oh no I know...Yes...I think you're absolutely right and I think it is a difficult question and I actually don't think anyone would disagree with me that there is a huge amount of development that needs to be done to make the project a success and doing that in a purely academic environment is challenging if you want to have academic research outputs. If you can get a huge grant from someone to develop the end product, fantastic. But then there's going to be commercial interests I'm sure...involved...and I think eSTi2 did it quite well because they got that investment but I just think, that maybe needs to be an order of magnitude more investment to actually make it a success...I mean then if someone's willing...because what was eSTi2 all up? ...how many million? 5 million or something?

TS: Somewhere around there...

LE: It may well need to be an order of magnitude more...maybe not an order of magnitude, but maybe two or three times more, and then whether that investment is worthwhile from the taxpayers perspective...needs to be argued and I don't know the answer to that....anyway, I've rambled...

TS: No, that's great, it's good to talk about...we've moved away from....considerations beyond features and attributes...actually no, that's exactly, the last question we've kind of answered it there...beyond features and attributes of the device, what needs to be taken into account when developing self-tests for sexually transmitted infections and I think we've talked about that just then, actually...

LE: Yeah, that was all sort of, much higher level stuff wasn't it I suppose...and in fact, I've sort of focussed on the engineering side but just to bring it back around to the design side there probably is actually quite a lot of research, genuine good academic research that can be done in terms of the user interaction and the design of the product itself because that's not

already...that's sort of unknown...so that would be my amateur designer perspective is that there is actually room for design to do academic research and find out how the user interacts with it whereas a lot of the engineering is just electronics and electronic control which has all been done for many, many years and just needs to be done but you won't actually get any academic contribution to knowledge out of doing it.

TS: I guess...the only thing left to talk about that we haven't talked about is...we didn't really talk about the open source thing and how the open source thing...helps. Because I find it interesting that we talk about...we're talking about, you know, designing devices for the NHS, well, I've been thinking about that and actually a lot of the big leaps forward seem to be done with open source technologies...rapidly prototyped using open source methods and things, like...I'm trying to remember the name of that device... [Handheld genomic platform]... there's one that's...

LE: Arduino...

TS: No, not Arduino...there's an isothermal, fluorescence detection system that's open source, well yours is that as well so...

LE: Well...I'm not sure if ours is that, that was always sort of a contentious issue. I would've like to have gone down that route...And open source doesn't necessarily mean that it's free, you can still have rights over it, all it means is that the end user gets to see how it works. So open source and open hardware would just mean that we'd provide the source code, we'd provide the hardware, we can still own the rights to it and prevent anyone else from doing it they just get to see how we do it which then allows them to modify and fix it if they wish.

TS: Makes you wonder if using these open source platforms is one way of sort of circumventing the possible...it's a different route than having to worry about the commercial interests and the big businesses getting involved if you're doing it all openly and collaborating across institutions internationally, you know.

LE: But the problem is then, if people see as being no commercial return then they won't invest in the first instance which then makes you almost wholly dependent on philanthropy or government grants which may not have the resources to fund the whole project. And you might end up being short on resources which then predisposes the whole project to failure. So it's a challenging one, I would've liked to see the whole thing open source...although I think ours probably would've been because I think we did publish a lot of the source code and things, it's all out there...

TS: A lot of it is yeah...

LE: So...but also having...not even us producing it...but having open source things like the Arduino platform for us to use did drop our development costs, it made it a lot easier for us. I mean we made extensive use of Arduino software and Arduino hardware...and because all of that information is publically available we can make use of it and adapt it and it's also very cheap because it brings the price down being open source because if lots of people can make them there's a lot more competition in the market. So we've benefitted, in eSTI2, we benefitted from the availability of these open products.

TS: Direct evidence of a benefit?

LE: Yeah

TS: Is there anything else you can think of we haven't talked about?

LE: No, no I think we've got quite a thorough discussion there.

INTERVIEW ENDS

Microfluidics and Engineering Expert: Pseudonym – Kara, Interview conducted: 7th December 2016. 11:21, Duration: 00:35:12

Kara = KR

Interviewer Tom Stead = TS

TS: We are recording, are you OK with us recording? I have to ask you on tape.

KR: Yes.

TS: Brilliant. So, let's talk about your disciplinary area and what your role was within the eSTi2 project...and why does your disciplinary area relate to the eSTi2 project.

KR: So...my disciplinary area was, or is, MEMS, so Micro Electro Mechanical Systems and then...came into eSTi2 as a postdoc having just done my PhD in MEMS and I came in really to do microfluidics, so I was kind of changing disciplines when I came in to eSTi2, to learn about microfluidics. I'd never actually done any microfluidics before.

TS: Oh, cool!

KR: You probably didn't even know that.

TS: I didn't know that no.

KR: So there you go. Yeah, I wanted to change fields, I wanted to go into microfluidics because I'd been to lots of conferences and...about MEMS and...as a PhD student and it was very much like the up and coming thing was microfluidics so I wanted to change disciplines and I was quite into, I'd read lots about George Whitesides' group over in Harvard and paper microfluidics and actually I wanted to get into paper microfluidics but, when I came into the group, [Colleague's Name] had already started paper microfluidics so I was very much brought in to work on the plastic microfluidics work and soft lithography because I had expertise in SU8...which is an epoxy that's used in soft lithography. So they brought me in to kind of start up the work in SU8 to make microfluidic moulds but...when I actually got here, there were no clean room facilities so it turned out that I had to kind of come up with novel ways to make the microfluidics and...I was supposed to have access...sorry...to the London Centre for Nanotechnology but there wasn't any access so I had to come up with really kind of novel ways to make the microfluidics.

So one of my first jobs was to set up...I had to set up the clean room facilities...and then...I basically had to come up with ways of making the microfluidics. So one of the first people I met was [Colleague's Name] who was like 'thank God you've arrived' because I can't make any microfluidic devices here and how can we make them?

TS: Do you think there was an advantage to finding novel ways to make the microfluidics, for the project, for the research?

KR: Yeah

TS: Because it like...

KR: Yeah, and it's really interesting because along the way I've met different people...and I've met people like [Colleague's Name] from ETH Zurich and...it's a kind of closely guarded secret on, how to make microfluidic devices so people will give you a kind of overview in their papers but you speak to different labs and they won't give you the intricate details, so things like connections and things like that, you have to come up with your own protocols.

TS: Huh, that's really interesting...

KR: It is really interesting...

TS: So it's like a 'Black Art'...

KR: Yeah MEMS and microfluidics are a bit of a black art so, we now have all our own protocols in place but I've had to, I've had to develop them at Brunel, that's part of the reason that it's taken...that's one of the reasons actually it took us a bit longer at the beginning to get everything set up was because when I came in we had Jeremy down in Wales who hand made everything and they were very intricate microfluidic devices made out of PMMA but they took a long time to make...and he literally milled all the parts and then heat bonded them but we needed to come up with a way that we could fabricate new devices really quickly. So I came up with a method using 3D printing. It took quite a long time to come up with, you know, how to make the ports and how to connect everything up really quickly and we didn't have any equipment, we didn't have like...

TS: ...so there isn't like a handbook out there that you can like...

KR: ...there's no handbook. No, it wasn't until I'd met [Colleague's Name] and I'd met him a few times and then he said to me...'you had to set all that up at Brunel and I know what it's like because I had to do that at Imperial and now I've taken that to ETH Zurich. And it wasn't until I met him and he said 'oh that must be really painful for you because I know each lab has their own protocol and you've obviously had to set that up at Brunel on your own.'

TS: Could that have something to do with the slow pace of research with microfluidics? Everyone's keeping it to themselves...

KR: yeah, sorry that's got nothing to do with...

TS: I think it does...

KR: I think it also has something to do with, slightly, the slow pace of eSTi2 because...and there was no one else at Brunel doing microfluidics.

TS: No, really?

KR: There was [Colleague's Name] group but they didn't have anything that was really set up, they talked about microfluidics but nobody was actually really doing the research. There's no one else doing really microfluidics at Brunel.

TS: Interesting. So within the eSTi2 project how did that work...I suppose the microfluidics specifically, fit in with what eSTi2 was doing on the whole, do you think?

KR: So, what eSTi2 was doing on the whole? So, the engineering work was very much about...eSTi2 as a whole...to me it's kind of like the crux...but to other people it's probably not so Work Stream 4 probably wouldn't see it as the crux but to me it's kind of central.

TS: Because it's the key technology?

KR: Because it's the key technology, it's the thing...

TS: It's where the reaction happens that gives you a diagnosis.

KR: Yeah.

TS: Well, not a diagnosis, a test result.

KR: It is, and...so Work Stream 4 were obviously working on their mobile device...Work Stream 1 was supposed to be developing the assays, which, they weren't doing. Work Stream 2, so our work stream, were actually developing...

TS: ...yeah well I was talking to [Colleague's Name] and he was talking about developing the assays.

KR: ...and that might where...yeah, so...basically to me, the key to eSTi2 was, is the platform so that's the central thing that was being developed, that's the key technology you're...the key tangible output.

TS: Yeah.

KR: Well, there were two key tangible outputs, there's the...the app that's developed by Work Stream 4 and then there's the technology, but, I don't really want to be...I don't want to put down the app and the clinical pathway.

TS: No well, it's an interesting thing because it's...the connection between the two...

KR: ...has never, ever come about, you've never got that bridge that's been built which is the connection between the two and I think that's really sad and that's something that we discussed many, many times and we lost that connection and I did try in some Scientific Steering Committees to bring that about...but that connection was never made and I know Chris Hudson as well tried to make that point, that that connection was never made...I think that's really, really sad that that connection was never made. Because I think we could have had something that was really, really interesting.

TS: Very novel!

KR: Yeah, really novel...but, it is academics and academic ego's...

TS: Yeah, I think there's sometimes...people I've been talking to...people tend to think...it's like, it might've been a, not a better job for industry but it's something that would've been better suited to industry, to connect all the pieces up. Whereas the academics...what's the word, in silo's?

KR: Yeah, I think it would've been better in one industry because you had disparity...you know, because the...or even if it was done at one institution.

TS: Yeah, I guess yeah...

KR: If you'd have had that connection at one institution. I think they tried to have it by having part of Work Stream 4 at Brunel, but because you didn't have that connection within Brunel, part of that app wasn't developed. I think they tried to have it with having [Colleague's Name] and [Boss's Name] at Brunel but we never got that connection.

TS: So...anyway, back to...

KR: Yes, anyway...so I think the thing with Work Stream 2 and the technology...it was huge, the actual technology development at Brunel was huge...and the microfluidics was huge. So first of all we had the problem that we had to develop...we didn't have any protocols in place, so, first of all, there was nothing in place, so we didn't have any facilities in Brunel to develop. So first of all we didn't have the lab, so I had to wait for the lab to be developed so I was working first of all in a non-clean room...so I had to wait for the clean room to be developed, so I did my best in that room that I had upstairs.

TS: Oh yeah!

KR: Yep...the other thing was I wasn't just working on the microfluidics, I was also working on lysis and nucleic acid extraction, so that was another part of my role so...I developed a nucleic acid extraction membrane, just like a paper membrane which was coated in this biopolymer called Chitosan, so that was another part of my role. So, I'd never done that side of things either before, so that was really interesting for me, it was picking up all the biological processes. So things like cell culturing and then quantifying nucleic acid extraction, so learning those techniques, the biological techniques, so how much DNA you've actually extracted and things like that and learning about things like the BOOM method. And then the normal nucleic acid extraction techniques that you'd use...and then trying to develop this new method. So, at first it wasn't on a

paper membrane, at first I tried lots of different techniques so like electrospinning, Chitosan, which took me months and never really worked. So I tried really extravagant methods, and then, I just got really, really...and I tried to do things like I tried to make Chitosan foam sponges, so lyophilising the Chitosan...and, you know, I'd go to meeting after meeting on a Monday and everyone would come up with these really extravagant ways of how I could make Chitosan filters and, you know, could we do it on silica beads, which is the normal method of how you extract DNA. And in the end, I got really fed up and I thought, you know what I'm going to go for a really simplistic method.

I literally just dipped paper filters into Chitosan and then came up with a method of bonding the Chitosan onto paper.

TS: This is how the hybrid chip came about?

KR: Yeah, yeah and that's how the hybrid chip came about and it was just, honestly it's like the simplest method. I just thought, I just want to go for something that's really, really, really simple. And then I embedded those...at first into plastic chambers so working with [Colleague's Name] down in Wales...so he was another research assistant...and then, yeah and then I just embedded those into plastic chambers and then I worked with [Colleague's Name] who was a research assistant from IIT, the Indian Institute of Technology and then [Colleague's Name], an MSc student came over as well and she worked on that for some time looking at the extraction efficiencies and then mixing it with, in microfluidic devices. By this time we finally had the clean room set up...and looking at the extraction efficiency and what kind of flow rates you needed.

TS: So, technically speaking, from a considerations and features and attributes point of view if you've got a device that uses the hybrid microfluidic chip, what considerations do you need to take into account? If we think really simplistically like it's got to be kept upright, it's got to...

KR: It doesn't...no, no not necessarily, it doesn't necessarily have to be kept upright.

TS: Does it not?

KR: No, no, it could be any orientation now, now it could be any orientation...

TS: Oh, that changes things, that's interesting I didn't realise that.

KR: Now the chamber is much shallower and now we've got a new, I've got a new undergraduate student in who's looking at the sample collection device and he's come up with a really nice method of how we could actually put the Chitosan into a sample collection device and how we could actually then transfer that into the microfluidic chip, finally. He's come up with a really nice method of how we could actually transfer that across and then just like, literally break it away and transfer it onto that microfluidic chip.

TS: Nice.

KR: Yep. Finally.

TS: Yeah, cool, brilliant, that'd be interesting to see that.

KR: But, no, no, so orientation wise I think with the latest version it wouldn't necessarily have to be orientation dependent but for the current device it will be, because...because of the current device and the way that it's set up, it is literally a box, that sits on the table and it will just...

TS: It just goes on top of it yeah.

KR: Yep.

TS: What are the sample sizes, how...?

KR: At the moment it's 2 millilitres.

TS: And that's gone from 4.

KR: But that's not us, that's St George's.

TS: Right, because it was initially based on the First Burst...

KR: It was initially based on the First Burst...it was to do with...the sample size was a big...a huge debate...it was to do with how long your... the male urethra was, and how much epithelial cell you'd have flushed off...

TS: yeah I remember the First Burst thing. Did they find in the end that it doesn't...?

KR: It didn't really matter...yeah, Marcus, I remember Marcus Pond was saying to me it wouldn't really matter because you could have a volume of say 20ml and you could just take out a ml of urine, it was what you would normally do in a normal PCR lab, if you just took off a ml and put it in it wouldn't really matter.

TS: So it we think of where we want to get to, with a...

KR: Mobile phone and a...

TS: ...and a device, yeah. There's a couple of questions in there isn't there, so, is plastic microfluidics the way, or is paper microfluidics the way and what are the barriers to getting to that usable device? Or working prototype I suppose, that somebody could use.

KR: So, I think we're quite close, well, we're very close now, we're pretty much at the working prototype, but not to an eSTi2...

TS: Yeah, we're not a self-test...

KR: We're not a self-test. We're at a small working prototype that could be used in a lab or a pharmacy, or a doctor's surgery, we're not at an eSTi2...we're not an electronic self-testing instrument.

TS: Why not?

KR: The problem with molecular diagnostics is all the processes that have to be done and I think this was the point that was missed or has been missed throughout the project and I think it's a big...it's a big sticking point...I think the only way that you'll get there is to go...[pause].

You're going to have to...I think you'll have to move away from plastic microfluidics, I think plastic microfluidics has too many problems with...it's got too many problems with the fluidics. The fluidics are a pain you have issues with...

TS: Sealing...maybe?

KR: You have issues with sealing, you have issues with...our whole system is no valves, there are no valves but sometimes you get like, airlocks in the system and if you get an airlock in the system that's it, you can't overcome that pressure difference and that's it, the fluidics just stops. And you might get, you'll get like this backpressure and you can't overcome that backpressure and in fluidics, that's it nothing will move.

TS: It springs to my mind that you'd end up with a reliability issue...a repeatability issue.

KR: You have a huge reliability issue, you have a huge repeatability issue and microfluidics has never delivered and the whole funding...all the funding bodies can see this now...yes, all the funding bodies can see this now. I think the only way that you could get there with...the funding bodies are now saying that molecular diagnostics should be done at the reference laboratories.

TS: Reference laboratories?

KR: Yes, so it should be done in laboratories, and so...nucleic acid testing, so PCR in the reference laboratories and it should be things like serology and antibody tests that should be done at the point of care.

TS: Right.

KR: So we should look for like, viral...whether it's a virus or a bacteria. So there are things that you can do like...

TS: ...I suppose that's a start isn't it, for the...using fewer antibiotics.

KR: Yeah. So you can do, there's a new test...or there are tests they're looking for like...so it's looking for new markers basically so there's one, the foundation for [inaudible word] diagnostics said that you could do...so there's one that's like, you do a CRP load and an MXA which would be an antibody/antigen...or a serology test, at the point of care and that will tell you whether or not you've got a virus or a bacteria. OK, so it would be like a lateral flow test...and then if you got a bacteria, you then send it off to the hospital where they then do PCR and then say what it is and then say which antibiotic you need.

TS: It's like the first step on the road to bedside testing.

KR: Yeah, because your lateral flow will be like, 2 or 3 minutes. Yep and then the next step is, what it is...So that's one alternative, so that's something that we're now starting to look into on another...that's another funding application I'm looking at, at the moment. So there's like about, I think there's like, 9 markers that you can do.

The other alternative is that you go, instead of doing the plastic microfluidics you do the paper microfluidics...so that is a kind of...so where we started with the paper membrane for the extraction of DNA, you take that forward and you try and do everything on that one paper, so you do your extraction on that paper, you do your amplification on that paper and then you do your detection on that paper. And you can do the detection on that paper but it's like a lateral flow and that's what we'd...what [Colleague's Name]'s gone on to develop. But it's not 100% reliable yet, but it's moving that way, so that's what...he could tell you more about that I think, in his interview.

But, I think, plastic microfluidics I think the funding will start to dry up because nobody is...well the companies that have developed it...I think eSTi2, I think Work Stream 2 got about 1 million and that's split between Work Stream 4 and Work Stream 2 and if you look at Atlas Genetics I think they have something like 35 million to develop their platform and they're leaps and bounds ahead of where we are with our platform...but it's not that...

TS: I was looking at the OJ...is it OJ Bio...

KR: Yeah OJ Bio, they're antibody/antigen...

TS: ...yeah, and they had 25 engineers, full time, 25, on one device.

KR: ...and we had [Colleague's Name] and me...developed what we developed and then [Colleague's Name] at the end and that's it. And Chris Hudson did it for a bit.

TS: So that's answering the next question, because the next question is about what's the key technology...paper microfluidics, or that, changing the strategy of how you do the testing.

KR: I think it'll be the two, the only way I think if we can do molecular diagnostics at the point of care I think it'll have to go to paper because I don't think...I think the group that...the only group that are really point of care, that've kind of nailed it, is Cepheid with their geneXpert, but that's not really point of care and if you read the paper that I just sent you earlier, it's not really point of care. You need a power supply. You don't with their newer one with the INAT...I think it's called the INAT, the little one...

TS: I feel like yeah, I was just going to say, I feel like a big part of their success is scalability they've got...isn't it, you can go from here to...

KR: You can go from one slot now up to, kind of, you know, that massive one.

OMITTED SECTION

KR: ...but they're the ones who've really nailed it, but they've been going for years and they started off in a suitcase and they've been going for absolutely years and you know, it's taken them years. The thing with diagnostics it, you know, we were put on this five year project, six year project it's been now and it's not something that you can turn around in 5/6 years, it's something that takes *years*.

TS: What do you think of the role...I think I can ask you this...what do you think of the role of design in this?

KR: I think design is absolutely critical...I think usability is absolutely critical. I think that you have to have the...I think it's something that we've completely and utterly neglected within the project.

TS: Obviously I'm biased...I think...but I sometimes worry that we're not at a stage where design can be involved, or should it be involved? That's the question.

KR: I think you have to have the engineering...you have to have the engineering specifications in place before you can also involve design and I don't think that we were at a stage where we had the engineering specifications in place. I think we are now just in a place where we have the engineering specifications in place.

TS: So we're just getting there now?

KR: I think we've just reached the point where we've got the engineering specs in place, for the first time, ever.

TS: It's an interesting question all this stuff with the design, because people...

KR: But, I think you need the designers as well because I think you need...I think we've now got, like a system. I think we've finally now got a system, a desktop system that you can now kind of rip apart and go 'right, this is what you need to do with it'. But at the same time, [Colleague's Name]'s device now, that could also do with some really good design work. The SLIC device.

TS: Is that what it's called?

KR: Yeah, it's called an integrated cartridge, something, S L I C.

TS: Because it's interesting this design thing because...what happens with this design thing...because it's...I think people's perception of design is that it's...you come up with concepts like 'it'll be like a pregnancy test'...

KR: I don't think you can do that though.

TS: You can't do that, until you have the engineering specifications?

KR: Yeah, I think personally, that's my feeling and I think we've finally arrived at the engineering specifications now. But I think it's taken us a very long time to get there. And I think part of the reason it's taken us a very long time to get there is because of the reasons I gave you right at the very beginning...is...when I came in. I remember when I came for the interview right, at the very beginning...I don't think you should put this in...

TS: Shall we do the last question, it is...I think the point that you're making generally is very valid in that there's no...if there isn't collaboration between the labs then everybody's having to

learn again, what might already be known by a competitor, it slows the research down as a whole.

KR: The research was very slow at the beginning, [Colleague's Name]'s part was really fast because...but, he would tell you and I'm sure he probably told you in his interview when he started...before I came I think [Colleague's Name] had been there for about a year and a half, Sara had been there for about a year and a half, maybe a bit longer than [Colleague's Name], like 18 months, no, she'd been there for like 24 months or something like that. But [Colleague's Name] had sat there for about a year and a bit just reading papers and learning how to work in the lab and then he taught me how to work in the lab, which was fine but there was no microfluidics and they'd just been sitting there waiting for me to come down and do the microfluidics and then when I got there, there was no microfluidics so then I had to, you know, slowly establish myself in...and I'd come there to learn microfluidics, I had to then teach myself the microfluidics.

TS: ...I think we've covered the last questions because I...the last one says are there any considerations, beyond technical things, and I think we've covered that.

KR: Yeah, I think it was the discussion...the labs. And also the lack of integration between Work Stream 2 and Work Stream 1. Certainly for [Colleague's Name], that was a slow...

TS: It's interesting...and we've also talked about the lack of integration between Work Streams 2 and 4. So it's like...communication is an issue for development.

KR: We tried...

TS: It's funny because, with these interviews I'm trying to talk about...I'm trying to talk about design features and design and so often it comes up that, you know, it's all about sharing information.

KR: It is sharing information. But I think at the same time as you saying that we need the design specs I think there's still scope for the designers but...we had the design students in really early on as well and they were all like 'can you give us the specs, what volume do you need?' and it was so embarrassing because I could never tell them what volume we needed.

TS: Do you think there's been an advantage though that's the question because you've had design students in early on and there's been the odd designer sort of employed and there's been me doing the PhD in design. I wonder, has it sped things up a little, or has it helped or has it not?

KR: It's helped having you on board definitely, it's really helped having you on board...it has. The design students, no I don't think so. [Colleague's Name] helped with the design of the P-Stick.

TS: Maybe it's got to be a designer of a particular sort of level coming in, not learning but somebody who already knows the trade.

KR: I think, I think the design students did help with the design of the sample collection stuff yeah, I think it did help.

TS: I just wonder if it...it's all hypothetical, but if, you know, would we be at the same position now had there been no design involved, as we are, because it's a part of what I'm arguing in my thesis.

KR: ...I think you were absolutely, I think you're imperative in the design of the current platform.

TS: Yeah, because part of what I'm arguing in the thesis is that this stuff...design, designers and the design skills need to be involved earlier in research than it...because then it doesn't end up being so...you can involve more things like understanding what the public health needs are and

human factors needs are rather than it going to a company and their primary concern being profit.

KR: I believe that they do...I think you need to have them because otherwise you'll end up...listen, you should see the current device, I don't think you've seen the current device.

TS: Erm, I've seen...I've seen the frame...the frame was kind of the last thing I worked on.

KR: No, you haven't seen the current device, I honestly think that you need designers in there, and I think you need to look at the whole system rather than just the device as it is and you do need to...you need a designer to...it's not just about specs...you need the designer at the end to come in and look at the specs and then to finish off the device but you also need a designer to look at the whole system, from the start and to, kind of, guide the engineers through.

TS: Do you think there's a role there?

KR: I do think there's a role there and I think you gave us some really good guidance...at one point, like a few months ago you came in and said no you need to stop and you need to order in the parts...

TS: Yeah, yeah I remember.

KR: ...and you need to then put them down and you need to design around them, and we did that, and if it wasn't for you I don't think...the design would've just carried on changing, changing, changing. But you came in as the designer and you kind of put your foot down and you said 'no', this is what you need to do.

TS: Interesting. So, it's really interesting to think about how the skills that you learn in design school...because what I'm learning is it's not necessarily academic and research skills, but they're very applicable, hopefully to research.

KR: But sometimes...so you need the designer to do that and you need the designer to look at it in a bigger, as a bigger picture, whereas the engineers sometimes get really carried away with detail and I think that's something that...you need to look at it as the bigger frame and take in things like Work Stream 4 and what Work Stream 4 are looking at and that's where the design can aid. So I think you maybe don't need a whole design team throughout the whole process but it's good to have a designer to guide and to look at the different points. You know and things like...it is always interesting to know...and guide the specifications and you know what, what sample volume you've got coming in and whether or not the platform has to be flat or upright and whether or not, if somebody pours Tango into it, what the hell's going to be the output.

Because that's the kind of question that designers ask that engineers don't always ask.

TS: Context sort of questions?

KR: Yeah it's context of use, whereas I, I'm starting to ask these questions now whereas before I would never have asked these questions.

END OF INTERVIEW

Human Computer Interaction Expert: Pseudonym – Sharon, Interview conducted: 7th December 2016. 15:18, Duration: 00:23:37

Sharon = SN

Interviewer Tom Stead = TS

TS: Is this recording, are you OK with us recording?

SN: Yup, that's fine.

TS: Perfect. OK, so, what's your disciplinary area and how did that fit into the eSTI2 project?

SN: OK so my disciplinary area is human computer interaction, HCI, which sits within the computer science department here, in some areas it sits within a psychology department. So it draws on several background disciplines, quite a lot from psychology but also computer science and a range of other behavioural disciplines as well...and my role within the eSTI2 project was to lead on the user interface design for the app that we ended up developing.

Initially it was envisaged that that would be the user interface design of the device or at least that it would link directly to the testing device, however it was clear quite early on that the testing device wouldn't be something that was kind of actually usable and developed in the timeline of the project to allow us to then test a user interface design that linked to it, so quite a lot of our early discussions were about how we would pair the test with the mobile phone application. But in the end that wasn't part of the scope of the work because we had to develop something that sat outside of the self-testing process as envisaged for the future. Although people did self-test in our trial because they were using home testing kits that they used and then sent back to the National Chlamydia Screening Service.

TS: So I suppose what we end up having to do then for these interviews is imagine, if we were going to be designing the perfect test, if we were further on and we were at that point where we could develop a test, from the perspective of HCI and human factors, how would it need to work between the test and the phone?

SN: Well, we had a lot of discussion about this and what it might look like and there's no kind of simple answers because...I mean the initial kind of vision was that maybe it was something that you plugged directly into your phone and even used the power from your phone to run the test and if that was the case you could, theoretically upload the result directly from the test itself, which removes a certain amount of difficulty from a user perspective but if they are envisaged as separate devices and there's some communication either between them or via the cloud...it's more likely that you would communicate to the cloud to get test result and then the cloud would communicate back to an individual users device which raises the question of how you either tell the device how to contact the user or you...or the user identifies the test that they've used.

TS: How does that fit in with...those are human factors...

SN: Yeah

TS: ...what do we mean exactly by human factors when we...? Can we try and define it a little bit?

SN: Well, so we're thinking about...

TS: I mean in terms of this define it a little bit...

SN: Yes, in terms of this we're thinking about what...how the end-user would use the product, how...particularly we're interested in how they'd understand the use of the product and how you then design to fit around user cognition...in the broadest sense human factors is about fitting around every element of a human, so anthropometric measurements of a human...physical movements up to cognition...but HCI the focus tends to be on the cognition end of things, so what they have to understand in order to operate the devices.

TS: How was that applied in the development of the app and I guess of...obviously the device couldn't be too much involved but when you were doing the app how did you apply that there?

SN: So, we used a user centred design process and we started by running focus groups to understand the features that people would want from this kind of care pathway with a...an example technology probe of what it might look like...

TS: An example technology probe?

SN: Yeah, we used...so you can use, in focus groups you can use an artefact as a probe to initiate discussion.

TS: So, like a pregnancy test is that...

SN: No, no, no not that kind of a probe. A probe like...

TS: No I don't mean literally a probe, I mean like the example technology...

SN: ...I see what you mean....so, it wasn't presented as an example technology, it was presented as a...a kind of user interaction flow chart. I don't know if you've seen it?

TS: I have seen it yes, it's a long time since I've seen it.

SN: There's animation...

TS: I don't think there's any indication in it of what the test looks like?

SN: No there isn't no but there's, I think there's kind of ideas of a screenshot of a mobile what it looks like.

TS: Yeah, it somehow interacts with the mobile.

SN: It's just getting the idea...because...it's such a novel thing, people can't necessarily understand what it is we're asking them about and therefore that probe, which was the animation was designed in order to get them to start thinking about the kind of, the steps you have to go through in order to do a test, get the results on your phone and then do something with it and that was then used to...around a kind of set of questions around what it should look like, what the actual interaction should look like and wider issues as well but...

TS: What the interaction should look like with the phone or with the app?

SN: With the app, or even whether it is an app. So, you know, technology...forgotten what the word is, kind of agnostic at the start...would this be something you would use on your phone or would it be something you'd use on a fixed computer or would it be...you know and if you had it on your phone would it be a...so would it be a downloadable app or would it be a, just a mobile.

TS: I was always interested if any idea of what the test would look like was in everybody's mind at that point, you know, when you were designing this test, this...the experiment, the study, whether...you end up with this idea of a pregnancy test or something like that I suppose you sort of do don't you...

SN: Yeah, it wasn't, I don't think it was presented to people like that, I mean you'd have to talk to [Colleague's Name] a...kind of a reminder of what it was that they actually...she might have had a picture of pregnancy test type thing in the slides but I can't remember now, I can visualise the start of the slide animation set I can't...

TS: I think I can get hold of the slides quite easily...

SN: Yeah, you will be able to.

TS: Quite easily Googleable actually. So...I guess...on a practical level when it comes to the device the human factors of the device are an unknown, still because the device is not...because my next question is 'what are the barriers to achieving a device with the right features that...that gives you appropriately considered human factors but...if we don't have a device that's...it seems like we're not quite in a position.

SN: No, I mean I think there's kind of a question about how much of the user interaction sits on a device versus how much sits on something else...

TS: Yeah, like a mobile phone...

SN: ...like a mobile phone or other computer...because, there are problems, which aren't necessarily human factors problems they're more kind of, overall, big picture, service design problems or having everything sitting on the device.

TS: When you say everything you mean you mean the physical interaction with the device or everything as in the amount of data that ends up on...

SN: As in having the user interaction with the device itself because the complexity of the interaction that has to take place if you move beyond just getting a result means that you'd have to develop quite a complex stand-alone device in order to do that which you probably don't want to do...for cost...

TS: Or can you do, even, at the moment...because I had an interesting conversation with [Colleague's Name] about that...the design has to come after you have engineering specifications about how it works and I wonder if it's the same for the interaction...is it better that you have a device that you can then investigate or do you investigate as part of the development of the device?

SN: Well, you have to have hypotheses' about what the device might look like and then either do you know kind of design hypothetically for those scenarios and compare those ideas or you have something that then gives you constraints and you design around those constraints it's probably better if you've got more choices rather than fewer choices...but I think that...it needs...the key challenge is making it clear what, from a user perspective, what functions sit on the device and which sit outside of the testing device, do they even get their result on the device, because they might expect you know, pregnancy test analogy would say that you get your line that shows whether you're pregnant or not so you get your line that shows whether you've got Chlamydia or not. From a system design point of...big system design point of view you probably don't want that because you don't want people to just kind of look at it and say 'oh, I've got Chlamydia' and then do nothing about it. And nobody outside of that test knowing that that's the case.

TS: I imagine lots of ethical considerations then come up don't they?

SN: Yeah, so if someone can use a test without having said who they are and it comes up positive, you've got this positive test which you might, you know the device might transmit that it's done a positive test and it might know where it is but if there's no means for the user to have identified themselves...and it's quite difficult to get a user to identify themselves on the device if the device is very small.

TS: Yeah, this is the ongoing thing of connecting the user with their test, this was an ongoing debate wasn't it in the research.

SN: Absolutely. So I think, you know, the crucial thing is that...is having a clear...and it came out from our focus groups as well...the clear user journey and signposted user journey so that they now where they are and what they do and how the bits fit into that.

TS: Did we do much work in the context, you know when that original work was done I assume it was self-test that could've been performed anywhere?

SN: Yeah...

TS: Not so much like, the pharmacy...because I know the technology constraints led Work Stream 2 toward...

SN: To focus on pharmacies.

TS: ...maybe a pharmacy or a GP surgery.

SN: So the initial ideas that I remember being discussed were, were kind of vending machines in clubs or pubs and that kind of thing so the idea is somebody might, you know go to a club and

then pick up a test from a vending machine and then go home and do it, or even do it in the toilets at the club. So that was what was being talked about early on and then it became, no actually you might need to do this in a pharmacy because we're thinking of this, you know, shoebox sized thing as opposed to a, you know small disposable thing. And the other kind of concept was always that there was some small chip type thing that somehow was...the test was done and then that you would plug into your phone but then that caused all sorts of kind of 'do you want to be plugging that kind of thing into your phone directly?'

TS: Did anyone ask any questions about that to people?

SN: I can't remember...

OMMITTED SECTION

TS: I've got this question here which I guess was really with the engineering...'what's the key technology that's going to enable this'...and obviously the engineers all said it's going to paper microfluidics [did they??] and it will end up like a pregnancy test but I imagine from a human computer interaction...what would you say the key technology is that's going to make this possible, commercially possible?

SN: Well it depends what this is.

TS: Yeah...yeah, I guess yeah...whether it becomes like a pregnancy test or not.

SN: Yeah, and I think there are...there are issues about it being quote: like a pregnancy test. Like I've said I don't know about...I don't know how the paper microfluidics would kind of conceptually they imagine it would give you your result but if it is like a pregnancy test in that it's a line that appears and you can read that by eye then that's potentially problematic for the reasons that I went through before.

TS: Yeah, I think that's why they were looking into the idea of having something read it for you so you don't actually get to see it and then it transmits that information to whatever supporting device there is.

SN: But I think, you know, from my perspective, there isn't any HCI development that has to...there isn't any kind of, you know big leap in the understanding of human computer interaction that's needed to get to the next step it's knowing what it is that you're dealing with and then producing something usable and appropriate from that.

TS: So you think the HCI is all...is all...

SN: ...I think it doesn't...I don't think it raises any challenging HCI issues other than ones that researchers are already aware of.

TS: It's sort of a high technology readiness of HCI...apparently that's what NASA call it...

OMMITTED SECTION

TS: ...the last thing that's probably relevant is the...I was...I've been asking people about the features and attributes of the device itself and what they might be like...but I've also been trying to ask about the context it fits into and how it might be developed because there's...the possibility that maybe a research environment isn't ideal for the development of the device itself maybe it'll end up having...like you said there's no challenging questions about HCI that are coming up with the user interface and stuff so what's the question...are there any considerations for how these things might be developed in future that we haven't discussed?

SN: Well I mean I think the other issue is just that, is what we've experienced in the project is the interaction between the different disciplines involved and the difficulty surrounding that, you have to...because engineering will always kind of try and home in on a kind of solution that works

in a narrow way of looking at the problem without appreciating the wider issues which include the human factors issues but also include the medical system issues into which everything fits. So actually just having a design process that brings together those parties is important.

TS: That's good to hear...yeah I've been asking...you might have an opinion on it as well...the role of...what's the role of design because it's been a constant problem, well, not problem...for me it has been but...should design be applied at this stage of research or is there a role for it in these sort of projects. I'd be interested if people in future will be, you know, looking to get design involved in these technology projects or not I don't know.

SN: Well, I mean, I think the whole thing is design but people don't necessarily recognise or label it as that and therefore it might be useful to have a kind of clear role for design in processes like that.

TS: Yeah, because the design is happening, it's happening anyway.

SN: Yeah, it's happening anyway, yeah, you can't just kind of do all the work then say you're going to slap on a design later. I mean it's like, kind of classic human factors used to be described as flower arranging...so, in BT this was...they used to call the human factors department the flower arrangers because the engineers would design everything and then they'd take it to the human factors people to pretty it up...but that...you can't produce a usable system if you do that because you're only tinkering with the edges of it you're not addressing the fundamental interaction models which have already been pre-specified. You could say the same about design, you can't think of it as a pretty add on, let's make it pretty at the end, it's kind of fundamental to the whole thing I would have thought.

TS: Well I agree but I'm quite biased...

SN: But maybe designers need to communicate what value they can add more clearly.

TS: Yes, I...I think there's definitely something to that because I find designers come across as if they think design is like the answer to everything, the be all and end all and people don't really know what they mean...what it is...what they're offering.

SN: Yeah, so if their offer was clear I think that would be positive.

TS: Yeah, it's got this sort of, slightly exclusive atmosphere to it.

SN: yeah and there is this kind of tendency for designers to kind of come from a slightly more arty side of the world kind of use fluffy arty language which might not always be well understood by the engineering side of the world.

INTERVIEW ENDS

Social Science, Usability and Acceptability Expert: Pseudonym – Samuel,
Interview conducted: 8th December 2016. 16:03, Duration: 00:26:35

Samuel = SL

Interviewer Tom Stead = TS

TS: ...brilliant, we're now recording. So yeah, your work has been, as you were saying...

SL: ...so yeah, recently I've been doing...well, you know, through eSTi2 I worked with young people, I'm sure you remember the young people's qualitative study when I stepped in and did those interviews and helped out while [Colleague's Name] was on maternity leave. So I don't know if you've spoken to her already have you?

TS: Not yet no, I'm trying to keep it down to not too many interviews as well because of the transcription time involved.

SECTION OMITTED (Talking about transcription services)

SL: ...as I was saying, so I did...so that was kind of my initial work...was looking at the young people that we interviewed in FE colleges in South London. So that was based on the hypothetical eSTi2 pathway so it was more along the lines of...not just the device, so it wasn't...obviously [Colleague's Name] was doing the HTI (Human Technology Interaction) kind of stuff, so it was separate from that and again I'm working kind of separate from the actual physical brick and mortar kind of thing, but there's a lot of overlaps. So I'm working on a grant called PRECISE right now and the PRECISE study is a multidisciplinary collaborations. So, [Colleague's Name] is working on the public health side, [Boss's Name] is obviously overseeing the whole thing but particularly the clinical aspects...we have...and we're working with a company called Atlas Genetics. They are building the bit of kit and then a whole bunch of microbiologists that are helping to develop the actual assays for the test. So, what my bit was, was to look at patient and clinician perspectives of the implications of different designs on the clinical pathway.

So it's all kind of hypothetical work, which, you must be quite familiar with, but given a kind of set of constraints...so obviously, people want the all singing, all dancing, all pathogen STI test that happens in 5 minutes, but given that that's not a possibility, you know, what is it that we can do to...within, kind of, the constructs of real, possible science, given the constructs of the platform itself, what can we design and what are the implications of that design on the clinic and then what are the implications the patients will have. So...obviously in the end, what we want in terms of a public health perspective is to make sure that as many patients as possible who are at high risk, preferably are coming in to get tested, getting their positive diagnosis and then immediately receiving the correct treatment. So...

TS: All within a very short time period?

SL: Right, well what can we do to increase the chances of patients coming in...getting the right patients coming in, getting the test that they need, getting the diagnosis that they need, getting the right treatment and therefore stopping the chain of onward transmission of infection. So, that's kind of the main goal is to have this perfect world where everybody that's infected goes to the clinic straight away and has this fantastic test that gives us all the right answers and including the right medication to take and everybody gets [it directly observed therapy] and that's the end of the infection and no more transmission happens to the rest of their sexual partners.

Given that that's impossible, we work backwards from there, so that's what the work has been about.

TS: Have you been...it sounds like you've been coming at it from two points of view, you've been coming at the engineering constraints, you know what...pushing what's possible as well as talking to what people are going to be OK with doing. Am I allowed to ask what your conclusions are? I imagine you're going to be publishing this soon.

SL: Yes, we are going to be publishing it soon, I'm working on some abstracts right now so it's a little bit secret but it's not that secret, essentially the answer is it depends. So, why people got to...why people go to the clinic is very much related to what they want out of their clinic experience and what they will tolerate in terms of change that they don't necessarily see as for the better. For example, tests that may make them stay in clinic for longer. So you might know...for example the GeneXpert, so that's a 90 minute test. The problem with that is that it's far longer than the actual clinical pathway is and you don't want people sitting around in the clinic for 90 minutes, that's kind of not good for the clinic as well but if you put that into 25 minutes, it's still longer than the actual consultation, it's still longer than that part of the pathway that patients might not normally stay for that long, depending on the clinic. But, so it might actually make their time longer in clinic but they would come out with more information. So they'd come out with

their test results and if they were positive they'd come out with treatment for that specific diagnosis.

So, given all of those things on balance, what do patients want to do and the answer is really 'well it depends on why they're there.'

TS: Right.

SL: OK, so I suppose a lot of my responses to your questions are going to be 'I think that, based on my work, what we need to do is...given that the all singing all dancing test is not possible...that we design multiple tests...'

TS: Yes.

SL: ...that are usable in multiple different scenarios that will be able to target specific patients based on the criteria that we do have clinically that we know is useful and then...and those patients for example who extremely anxious or extremely worried and would be, for example, getting a rapid HIV test. OK, it's what, how they...how many clinics generally triage these kinds of test is that, well they're quite expensive rapid HIV tests and they're not quite as accurate as the laboratory test but they're really good for people who are really high risk of being infected and they're really good for people that are really anxious about whether or not they might be infected.

So, using that same kind of rationale, then we would say OK, well somebody that comes in with genital discharge...say it's a man that comes in with genital discharge...you might do a Chlamydia/Gonorrhoea test as your first point of care test and then afterwards, if they find out that they're not infected, but they still had the Chlamydia or Gonorrhoea [test], then, you're kind of ruling out the top two potential infections. You can kind of go on to protect...a reflex test for example for lesser known pathogens like Trachomatis or...

TS: Mycoplasma Genitalium.

SL: Mycoplasma, yeah exactly. So essentially that's...and if that patient is experiencing symptoms and wants to receive correct treatment then they might...then they're more likely to wait for another point of care test. So this is all based on hypothetical situations, so it comes with the massive caveat that we don't know what actually happens when it comes down to it, you know, does that feeling translate into patients actually sitting down and waiting and would that be a potentially acceptable thing in terms of a clinical pathway.

TS: Has much of your work looked at the possibility of sample collection and maybe testing outside of the clinic and how...and when you involve the clinic if you do that outside of the clinic and how you involve it?

SL: Well, that was mostly the work that I did with eSTI2. So that is largely...so the issues around self-testing are a lot about trust and it's not just trust in the device, it's trust in an individual's ability to test themselves accurately, to sample themselves accurately and do the test correctly. So there's a lot, I mean, there's been some of that on self-sampling but less so because it goes to a professional person afterwards, like it gets put in the post and goes to a lab or it gets given to a clinician.

TS: That's the NCSP isn't I think?

SL: What's that?

TS: The NCSP is that what that is?

SL: Yeah, so like postal kit testing and things like that. You see that a little bit but when I did the interviews around the potential eSTi2 device when we're looking at not only giving people a sample to do themselves, so they're...I mean for men it's just weeing in a pot, it's kind of hard to do that wrong, but, you know, and for women there's a little bit more variability because it's a

self-swab there's the question 'am I swabbing in the right place?', 'Am I swabbing to the right depth?', 'Is this correct?'. You know 'Am I swabbing it for long enough?' or...you know all sorts of things like that but...although I have to say the majority of people still don't have a problem with that. Men who have with men who are getting Pharyngeal and rectal swabs can self-complete those too and again, the majority of people don't have an issue but you mirror those same kinds of 'is it in the right place?' ...is it...you know that kind of...that dialogue is mirrored in men as well, it's not a gendered thing, it's just a swab thing.

TS: So you're saying, the people doing it, they're OK with doing it, but then the trust issue comes...so there's two things, there's the...you're not able to ask the question easily 'Am I doing this right?', and the, once the sample comes to the lab they don't know whether you did that right. That's what I'm trying to clarify.

SL: There's that, so there's a small percentage of people like I said that have an issue with self-sampling regardless OK. The majority of people do accept it and it's why it is the kind of standard of care. But, because it also kind of, ironically, maybe not ironically...it provides better results than a lot of clinician collected swabs which is quite interesting but...some studies have shown that...but what we found in the eSTi2 interviews with young people was that, it wasn't just about the sampling, it was about the doing of the test. So, it would have to be something that was kind of, stupid proof, for lack of a better term so making sure that it wasn't...it couldn't be a chemistry kit you know it be one of these put the white in the blue and the blue in the red, like, that was not OK, very clearly not OK. It had to have a small number of steps, it had to be...you know something where it wouldn't need to be temperature dependent. If it were something that, you know they could put it in a chip and put that chip...somehow transmit that chip to the lab electronically or something. Something that was really easy and quite bound, so...

TS: When you say 'bound' you mean, there is only one way of doing it?

SL: Right. Right, you know like, you stick the thing in and it lights up or something and they're like 'OK, did it right.' You know, like that kind of a thing, so, if there were multiple steps it would have to be impossible to do it incorrectly and there would have to be a helpline associated with it. And that was something that I'm sure you probably heard the results from Work Stream 4 really bang on about we need a helpline for the potential online pathway and that's regarding results delivery but I do think that there was also an aspect of that in terms of, am I doing this right about the kit.

So, yeah...and I've spoken to other people, again this is a few years ago off the back of that work with eSTi2 through...I did a consultation with the WHO on point of care testing for STIs and they were very, very interested in looking at this idea of a self-test. So, not a home sample, not a point of care test, but a self-test.

TS: The sampling and the testing all happens in the one device, yeah?

SL: Exactly, you know, and the that...when you start to talk to those people, you start to talk about issues in terms of the developing world where it would have the most impact, something like this would have the most impact. And then we're talking about it needs to have no cold chain [look up] required, it needs to be battery operated, it...you know, that kind of a thing.

TS: So, it's a very complex situation it's kind of gradations, from, between self-test and sampling and point of care. Like you said at the beginning, there's probably lots of answers, lots of ways forward.

SL: Yes. Yeah, absolutely, there's...I do think that it's extremely unpopular to say to somebody that's building a bit of kit; 'We need four of these that are different' ...because it's expensive and it's complicated and that's not really the way to maximise the profit on these types of things, but I do think that is the most...that type of scenario would provide the best patient benefit and that's where my interests lie...is translating what the patients want to the people that are developing it.

TS: That's...its good because you've kind of answered the first four questions in my...schedule there, which is very cool yeah that's nice. Because the fourth one is about...from your work, how are people expecting a self-test to look, work and be accessed, I think the only thing we've not really talked about it access to the test. Do you have any indication on that, because I know we talked about vending machines and things but then this is all very hypothetical isn't it?

SL: I talked to young people about that for the eSTi2 work as well and they were really interested in something that you could get in a variety of different places so...and this is specific I think to young people. So young people have very specific concerns about privacy...and they have concerns about that because they have a lot of risk associated with being outed as sexually active. Especially young people that have a conservative family that might be coming from an immigrant background, were they come from very conservative countries or conservative cultures or a conservative religious upbringings. So, there was a lot of discussion about how this kind of a thing would be better than a postal test, so better than the self-sampling, because actually getting something in the mail is not really ideal. And again that's because you know, parents open children's mail and things like that, so, not ideal.

So there is a lot of discussion around the current situation which is...we're between, will I be seen walking into a physical clinic and if I'm not seen and everything's private and actually I'm very in control of getting my results as long as nobody looks at my phone...and getting a postal kit and making sure that you're home before your parents to get the mail. So this would be something that they would want to access at Sainsbury's as well as...

TS: So, maybe not even the pharmacy, or would a pharmacy be acceptable?

SL: Yes and no, I mean I think that it would be better than it is now but it's not as ideal as something like the grocery store.

TS: Yes, exactly.

SL: So, when you get into a situation where it's on a shelf next to the pregnancy test in a grocery store and it's cheap, you know, really cheap. Or you have the option of getting it for free in a pharmacy well that's something...you're looking at something that's much, much more acceptable...and much more of an opportunity for young people to test. But because of the...especially when a technology is new, so in the initial first, I would say probably few years, you probably know more about that than me, in terms of technology adoption, people felt that they would need to test multiple times to make sure it was right.

TS: Yep.

SL: So, that the technology was right, that their sampling technique was right that...and that led to a correct diagnosis.

TS: Yeah, which again might not always be the ideal situation, yeah...

SL: So that, it presents its own problems. I mean, I think we need to be really aware that, even if we were to be able to invent and implement and provide universal free access to the all singing, all dancing STI test - that pee on a stick and you get the answer straight away - that it is going to open up a whole host of other questions. You know, and issues about, you know, false positives and false negatives and repeat testing and resources and who is paying for all of this and all that kind of stuff.

TS: Which leads us nicely into...what the barriers...my second to last question...and we've talked about some of them already but what are the barriers to achieving this all singing, all dancing self-test. And I think we've talked about a lot of them already but, it'd be interesting to talk a bit more...

SL: Yeah, sure, I mean I think...well the first thing would be the technology. So...yeah, I mean, I, as a social scientist, knew nothing about the actual scientific and technological barriers to

implementation, to discovery, to building these kinds of tests. Now I know quite a bit more about it and it almost amazes me that anything happens in the first place.

So, I have quite a lot of respect for the microbiologists and the technology experts and the people trying to make microfluidics and Nano-technology things in little tiny tubes and all sorts of things like that, but obviously that's not my area of expertise. I think socially, what the barriers are...are quite a few. I think that, if you're talking about...so if you're talking about a point of care test I would say that there's a large barrier in terms of adoption into medical services and I think even if you're talking about a self-test, what I think would need to be ideal about that is that it would need to be lined to surveillance and care and so that we're aware of who we should be promoting to use these types of test. So, thus the surveillance aspect of it...knowing who's infected, which groups etc. ...and linking to care so that there's prompt, correct, safe treatment. And any sort of change in clinical care is like, you know, trying to turn around a two ton train on a hairpin curve. I mean it's really hard. And it's something that I've become increasingly interested in and I'm bidding to get some funding to look at more deeply, what kind of barriers to implementation of rapid tests are because we know there's a heck of a lot more rapid tests out there than are actually in the clinics in use.

TS: Yes exactly, this is something I'm very interested in as well actually. Getting them from where they are, you can look them up on...you can see them, published papers about these rapid tests, getting them from there to people actually using them...

SL: Yeah, absolutely, I mean, I think some of them probably have some, how do I say, slightly optimistic results...it's clinicians...See there's a couple of things that are happening, so, in public health we look at what is the greater good for the whole population, well the greater good for the whole population is not what clinicians are interested in. The clinicians are interested in what is the better...the greatest good for the person that's sat in front of them, OK, and that is not the same thing.

TS: Interesting.

SL: So, when you're looking at personalised medicine, which is really kind of the field that we're looking at, at this point is personalising rapid self-tests for infection. Then it's a real push/pull between public health and individual patient care and you've got the medical establishment, you've got the department of health and you've got patients and how to make all of those things work in concert so that the people, like I said going back to the very beginning, who are the most at risk, know they're the most at risk and get themselves into a situation where they can get a diagnosis and treatment as soon as possible is really difficult because you have to interface with all of those different things.

So, it's complicated, you know, and I would say that the first thing is to be aware of how completely complicated the situation really is and not to fool ourselves into thinking that there really is an all singing all dancing test for everybody. You know, because the more that I talk to people, the more clinicians that I talk to and the more patients that I talk to, their all singing all dancing tests are not the same and so that's why it's not possible.

TS: That's really interesting, that's really good, and I think I might have to stop you there because we're right on time.

INTERVIEW ENDS

Clinical Sexual Health Senior Doctor: Pseudonym – William, Interview conducted: 14th December 2016. 14:34, Duration: 00:31:40

William = WM

Tom Stead = TS

WM: You can record now and I can ask you questions if that's OK? Is that alright?

TS: Oh yeah absolutely, it's not super structured. So it's...

WM: OK, fine, so the question I had was, when you talk about a self-testing device, just define what you actually mean.

TS: A self-test where the sample is given and the answer is given at the same...so the self-testing device where the actual testing happens on site, so point of care, as opposed to maybe sample collection that is sent off. It's if you take the sample and the processing happens on site, where you are; where the person tested.

WM: OK, so I'm going to summarise what I think you mean, so just tell me if I've got it wrong so we're on the same page. So a self-test in this particular definition, for this particular interview is a test which is in the control of the individual who is being tested, who is sampling themselves and putting their own sample on the testing platform and reading their own and interpreting their own result with or without help through the internet, for example.

TS: Exactly, yes, exactly.

WM: So, they could just read off a result, or they could be in a position where they interpret a result that's sent to them through external help.

TS: Yep, which is one of the questions involved in it, you know should they be able to?

WM: OK, and that's the limits of the self-test definition. What you then do with that result is beyond that, so you might go to clinic or you might go to a pharmacy or you might engage online...an online care pathway...

TS: Yes, but the context that the testing happens in might effect that, so if it's your opinion maybe that the pharmacy testing...self-testing in a pharmacy is helpful, where a person gives a sample and interprets a result and they're already there...

WM: You're not constraining the definition by self-testing within a particular site, it could be equally at home, in a pharmacy, in a clinic, in the park, at the cinema, kind of thing.

TS: Exactly, I'm not constraining it at all for the purpose of the interview.

WM: OK, good, OK.

TS: So, the first question, I wanted to get an idea of your background and expertise how that fits into and informs what the goals of [Translational Research Project] were/are.

WM: OK, alright, so I'm a physician and I qualified in medicine in 1989 at [University in England] and I trained in various fields but generally let's just say general medicine and started working...worked abroad for a short while, while working at the [London University] in tropical medicine. When I came back from sub-Saharan Africa, which was a short stint with the Medical Research Council, I completed my medical training and entered the field of STIs and HIV medicine 20 years ago as a registrar and I trained in that field and also acquired, completed an MD, a doctorate thesis in medicine.

I became a consultant in 2003 at [A London University] at the same time as being a senior lecturer in [arm of] infection and immunity. I have...my main area of clinical expertise is in both HIV and sexual health medicine, particularly treating men and women with a variety of sexually transmitted disease syndromes. And I also have been specialising in male sexual health problems in the last few years.

I've also been working in genomic medicine both on the HIV side, in host genomics and particularly on diagnostic technologies for the last 8 or 9 years. And I've been, fair enough to say I've been involved and sort of, pioneering the development of novel technologies for diagnosing

sexually transmitted and other infections. Particularly molecular based, microfluidic and Nano-technology technologies that are both multiplexed and rapid.

I work with individual academic groups like those at [A London University] and I also work with companies and we also develop our own tests, my group. I was funded by the Medical Research Council, sorry by the UK Clinical Research Collaboration. I'm the principle investigator of the [Translational Research Consortium], which is a multidisciplinary consortium, involves multiple institutions and multiples specialty groups, the remit of which is to expand infectious disease research capacity as well as support the development, evaluation, implementation and deployment of cost effective and rapid, novel technologies for improving both STI care and reducing the burden of STIs in public health. As well as impact on antibiotic resistance.

I'm also principle investigator of the [Research Project] program which is developing antibiotic resistance point of care tests for STIs in collaboration with Atlas Genetics. I'm also director of the applied diagnostic research and evaluation unit, which is a translational science group that was borne out of [Translational Research Consortium] funding and is now self-sustaining through grants and collaborative research and commercial evaluations, which was its initial remit and it's important for me to disclose and declare that, as director of [Research Project], my group receives funding from a wide variety of mainly diagnostic companies for doing both commercial and non-commercial assay development...evaluations and assay development. It's been doing this over the last two or three years and those companies include Atlas Genetics, Alere, Twist Dx (which is linked to Alere) Hologic, Health Care Diagnostics and...I think...there's a couple of others and they've just gone from my head but I can give that to you if you need to have my disclosure statement.

...I also sit on the [International Technical Committee] for point of care STIs and probably do other things as well but I can't remember ...

TS: Excellent, that's a nice broad view of it, so I can tell from that obviously that it's a very complex, broad thing that you do, you're managing quite a lot of different inputs. From my point of view as a designer I focus on the device, so what I'm trying to do is figure out what features we might have in this self-test device we've sort of loosely defined just now and I guess from your point of view what features might be needed? Or maybe how even you manage that, so, you say you talk to companies, so how you manage what the device might turn out like, how it might end up looking, what input you have there? I don't mean looking as in an aesthetics way, I mean working and functioning.

WM: Yeah, so there's a...I mean, in a way answering that question is in essence the essence of how groups like mine and other groups that work with companies function. Because there is a tension of intent if you like, between groups who want to make both an academic, public health or clinical difference, groups that are involved in supporting the development in whatever way, of novel technologies and sort of wanting to create a difference, and companies who want to do the same thing but their motivations are also, completely legitimately, profit motivated because they're companies with shareholders and investors.

And the priorities of these competing groups, including the public health arms, can be quite different. And even with the non-company groups the arms can be different, so there are groups that primarily do this for kind of academic exercises and see what proof of concept kind of technologies could work. There are others that are a bit more like ours, are kind of more interested in what might come to market and be affordable and cost effective. There are others that are focusing on the developed world i.e. high income countries. There are others that focus on either low income or low/middle income countries and the developed world as well. And these have all different competing elements to them and that can be a source of difficulty, it's not usual for academic groups to be able to have the economic clout to be able to develop tests on their own. Partnering with companies and at some point larger companies to be able to scale up and deploy tests and to be able to conduct and have the financial power to conduct diagnostic trials

that would allow assessments of efficacy or accuracy to be made, can...you can only do that if you partner up with large companies. The tension is that the larger companies then have a greater scope for dictating or directing the way in which those particular tests are going to be formatted, for whom and for what and so there is an issue there.

So a good examples are, for example it may be that, we maybe, you might be interested in a particular pathogen or a few pathogens that are relevant to a public health problem that might be neglected or perhaps not as prevalent, or only prevalent in certain settings whereas some companies might be wanting to try to get something that's a little more deliverable [to a] much larger market...attracting a much larger profit, and that might be a source of tension. That's just an example, for example.

It may be that you're trying to push something that is going to be much more rapid and usable within the context of a particular clinical care pathway and it's not necessarily achievable in the way that you want from the company that you work with. Equally I think companies don't...I think companies can get frustrated with clinicians as well, I think it's very easy just to blame companies. I think companies also get frustrated with clinicians because they're a mixed lot and they have very biased opinions and it's actually quite difficult for companies to pull out the right clinicians. If there is such a thing. Of course clinicians are shaped by the experiences they have and those are largely...even though they might be quite intense and broad anecdotal experiences they're not necessarily what's needed at the public health level. And the experiences can be quite transitory in terms of how important they really are in sort of a temporal representative way.

So for example there may be a particular pattern of prevalence or transmission of particular infections at a particular time that spans a reasonable period with a particular clinician or a group of clinicians' time in a particular clinic and that can in a sense misrepresent what might be the actual problem and that can then be passed on to, crucially to developers. The point is, it gets past on in a sort of early phase of development that can result in the direction of particular kinds of technology being set and that then can throw...you know you spend all that time developing that and the companies are sort of taking the source from doctors and...I'm not slating doctors, I just think that this is an important issue to understand that it works both ways. And both companies and...both want slightly different things but they also want the same thing and doctors also get...go to companies thinking that the companies are telling them that they've got a particular kind of technology, it may not be that the technology can really deliver what the doctor wants.

So you kind of have to really try to have a broader scope of interaction with different types of both...on the doctor's side or for the academic side, different kinds of companies who have different kinds of ways of working. And companies need to be much broader in the way they think about developing their test. And I think for them to be successful with their test they need to engage with all the people that are actually very important when it comes to delivering...in terms of deploying and enabling that test to have maximum impact and that doesn't just mean patients, that also means...and not just the doctors who'd be using these tests...not just the patients in terms of, for example, a self-test, not just the patients who'd be testing the sample, but also the people involved in the whole care pathway that springs up as a result of that self-test. So all the way from commissioning those tests, whether it's going to be bought entirely privately by the person who's self-testing or whether it's going to be substantially subsidised wherever it's put on the market, or whether it's going to be paid for completely by the provision of sexual health care.

And so the commissioners, the people who are going to pay for it, the doctors who will be receiving the results of it, public health physicians who would need to understand how they can monitor the results of those tests and so forth. Pharmacies where those tests might be taken to get treatment and so forth. It's really very, very important to be able to kind of get all of that in place as part of the technology design. So if you get the technology design and you frame the chemistry wrong at the beginning and it's incompatible with the kind of design frame that you want taking it forward, you kind of get stuck in a black hole and then what tends to happen is the

companies continue because they've invested so much and they get a suboptimal...or they possibly might get a suboptimal product and there are examples of that out there.

So for example, I think for example GeneXpert, when it comes to Chlamydia and Gonorrhoea, was really taken as a model following from the work with TB, I mean, with TB it's been a great success. The GeneXpert I think for Chlamydia and Gonorrhoea is an incredibly good diagnostic platform. I think, thinking about it though, was around about it being a point of care test and actually the turnaround time...I'm not talking about the recent iteration of the Omni and perhaps more recent iterations in which the time will be much shorter but the original rapid GeneXpert test for CT and Gonorrhoea which is being deployed in a number of clinics around the UK does have a very long turnaround time for it to be used as a point of care test. So it might not be usable in that way. And I think in terms of CT and NG, its utility as a point of care test in a clinical care pathway would require it to have a shorter time from sample to result. I think that's important, it's only an example, it's not actually a criticism of the company at all. It's more a reflection of how engaging with the right kind of stakeholder makes a difference when it comes to thinking about design.

In some ways you can say the design was already made and they were then taking it to different people who might be able to use it and I suppose that's an extreme example of that process where actually it's already been made. What I'm saying is that actually if you're developing the test, you need to engage quite widely before making a decision about where to...about how to develop the test. It actually impacts on the design space and that space is also obviously deeply and highly constrained by the science. So if the science can't deliver certain kinds of things that you're using, that's going to be one of the major constraints of the test design. But equally, you need to be able to undertake a kind of a...not just a market analysis but a kind of a design, almost a sort of multidimensional design frame analysis, from different stakeholders, about what's important. And then try to package something together, in a way that is maximally usable and most effectively usable in the systems that exist.

TS: yeah, I've always wanted to ask because I look at the [Translational Research Project] project and I feel like that was your intention from the off, to...what I was thinking was, you've talked about some of the issues and you've actually talked about what some of the solutions are as well to the issues and I always thought the [Translational Research Project] project looked like that was what it was, it was bringing all the stakeholders in.

Obviously I'm coming from the bias of a designers mind because I saw all these different stakeholders...

WM: Yeah, so I think that is the reality of [Translational Research Project], but I think what we've learnt in [Translational Research Project] is reality. So that's the ideal situation, in which you do all of that, but if you then reflect back on what I was saying earlier on which is actually the world doesn't work that way, people are motivated by other things. They don't necessarily want to invest in stakeholder involvement and actually many of the companies want to create something quickly so that they can make a rather quick profit for their investors and their aim is not to develop the final CE marked test and deploy it and be praised for the development. Their aim, is ultimately to be...many of them, to be bought out at a strategically appropriate time by a larger company.

TS: Yeah, by one of the big companies.

WM: Yeah exactly, and I think that that is the private world of diagnostics so you do have to...you can't approach these problems without having, in my opinion and I'm sure that my colleagues would probably disagree with me, some of them...I don't think the whole diagnostic world is immune from the whole global health, medical health challenge that we have in terms of deploying health effectively. You can't pretend it is because the strains of a market orientated global health system, which is what it largely is, I mean we have an NHS, we have systems but

actually medicines and diagnostics and technologies and a lot of delivery is actually privately provided...

TS: Generally market driven?

WM: ...market driven economies. I think there are problems with it. There are problems with delivering the right kind of, in this case diagnostic technologies for the right kinds of purposes because actually the motivation behind developing them are not in sync with actually what clinical and public health needs are. So you kind of have to...you have to think out of the box that way and technology developers, all the way from fantastic groups like what you've got at Brunel in a very prestigious University in terms of development all the way up to real kind of private enterprise, full private enterprise...don't routinely buy in, to that kind of almost public owned or publically owned driven development.

Now I don't, personally I don't believe that you need to have publically owned development...some of my colleagues do but I don't. I think you have to have a balance, but you have to have, when thinking about developing and investing in diagnostics, you have to have a global and public health and political hat on to be able to know how to deliver it. And so that's where the challenge is. And I know that the funders and the NIHR are thinking this way and they're putting the constraints and the terms of reference in a lot of their grant funding for example in translational science to kind of meet that need but it kind of needs to happen a little bit more I think if we're going to really get effective diagnostics coming through the pipeline.

I think for self-testing technologies this is a real threat. Is actually...the self-testing technologies could make a big difference, there's still more science to be done about whether they will make or could make a difference. But I think the problem is, even if they could make a difference and companies started developing them, I'm not sure that they would necessarily be developed appropriately because actually the tensions in terms of the market economy will move them to something that might not be necessarily what we really need to have.

TS: That's very interesting. We're coming up on 3 o'clock...but can I just ask quickly a sort of double barreled question? So back to the test, it's probably, after talking about how complex everything is it's probably a little whimsical really but, in your opinion, what is the key driving criteria that's going to make a self-test happen? For example, some people say it's cost, some people say it's got to be cheap, or some people say size or...you know...and the other thing, which technology do you reckon it's going to be...I say technology as in, you know we've done a lot of work on plastic microfluidics and starting to work on paper microfluidics...where are we at with it from your point of view?

WM: Oh OK, well in the strict sense of a, let's just think about a self-test in the way that we defined it earlier I think is probably going to be of two types.

TS: Right.

WM: I think that the one type...I they've got to be, in some respect they've always got to be easy to handle, small, handheld, or some element of it has got to be handheld...and affordable. OK, we're not talking about, you can't buy a massive kit each time you want to have a test. So, where that pathway then sort of separates out is how that affordable test is then able to be read.

Now, there are different ways in which that can be done and I think each equally possible. I think the issue of a reader for a molecular test is...in a sense the issue, because the molecular tests require signal detection and usually require a reader of some kind and I think the readers will get smaller and smaller but you're not going to keep a reader in your house in any meaningful sense like the ones that we know about. They're going to be deployed in different places and different outlets like pharmacies.

But there are now, and the work that Brunel's doing for example, there are ways in which you can have your own reader, which is your mobile phone and mobile phones will be your readers so there are already programs of work in which the mobile phone is the reader of the test. Not just lateral flow tests but other kinds of tests and there's actually some types of very complex technology that is handheld. So I'm pretty certain that the potential for self-testing will be at the end of the phone or some type of similar hand held gadget that is personally owned. I don't think that's really...I mean that was the aim of [Translational Research Project]...

TS: Of course yeah...

WM: ...but I think we are probably ahead of our time and actually the development happening within private enterprise is just far outstripping any capability of academic groups to be able to really deliver that in any way. It's already happening and I think I kind of realised that about a year in, that that was going to be the case. And I think we're pretty close to it, I don't think we're that far from actually having mobile phones doing the testing, it's just not exploded on the scene, it might do in the next year or so.

TS: It's interesting, I've had that conversation a few times with people around [Translational Research Project], the development thing, not having the clout to do the development in academia.

WM: And I think, just as a side thing, academia is driven by its own needs which again are not necessarily the needs...are not necessarily public health needs. Academics have their own needs that are driven by those who employ them. Just like anybody, so I don't think we should think that academics are in a sense pure and really thinking about the right questions. They might be thinking more about things like REF and how many grants they can get and publications they can get marks they get and how many tick boxes they can tick in the environment they have. They're not necessarily thinking about what can be deployed and what might make a real translational difference and that's no criticism, that's just an expression of reality.

And just sort of going back to the different types of platform, I think, for me what we should be aiming for is actually a device free platform. That's what I think...

TS: A device free platform?

WM: A device free molecular test yeah, so the paper microfluidics are kind of lending itself to that but they still need some kind of signal detection. I don't think it will be too long before we find something where actually you can get a highly accurate molecular type test, a bit like a lateral flow test but which is based on much higher accuracy, that either incorporates some kind of amplification of products or signal or something that allows you to really increase and ramp up sensitivity while maintaining specificity that is just easy, you don't even have to have your phone with you.

TS: So when you say device free you mean...

WM: Even having a phone with you has its limits. But actually peeing on a, sorry, passing urine...peeing on a stick for your result and getting that as a really highly accurate result, I think that's definitely doable. I don't think we're far away from that either. I mean that's the kind of thing that'll win the longitudinal prize when it comes to antibiotic resistance and I think that's why they put that out because that's the kind of test actually that will make the biggest difference and sort of relying on sort of complex tests for...basic point of care tests, I'm not necessarily saying at this stage we're talking about complex metagenomics diagnosis, I'm just talking about simple tests, I think you...that's what the aim should be. And I think that's also achievable.

It may well be that you can get different tiers of excellence or quality of the different types of test afforded by the different kinds of technology, so it might well be that actually you do need that high end reader in the pharmacy to be absolutely confident and your mobile phone would give

you something pretty similar but, is useful at a public health level. And then on a global health level we might find that that kind of other...that final test is something that could be both useful, affordable and effective so that's something that I would say.

Sorry I'm just getting texted by my next thing so.

TS: Yep, brilliant, that's brilliant...you've covered everything I've got on my sheet here so that's really, really great.

END OF INTERVIEW

Survey of Professional Designers Ethical Approval



College of Engineering, Design and Physical Sciences Research Ethics Committee
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13 December 2016

LETTER OF APPROVAL

Applicant: Mr Thomas Stead
Project Title: Ecological Validation Email Study
Reference: 4772-A-Dec/2016- 4892-1

Dear Mr Thomas Stead

The Research Ethics Committee has considered the above application recently submitted by you.

The Chair, acting under delegated authority has agreed that there is no objection on ethical grounds to the proposed study. Approval is given on the understanding that the conditions of approval set out below are followed:

- The agreed protocol must be followed. Any changes to the protocol will require prior approval from the Committee by way of an application for an amendment.
- Approval granted for amendments, following letter of approval on 9 December 2016.

Please note that:

- Research Participant Information Sheets and (where relevant) flyers, posters, and consent forms should include a clear statement that research ethics approval has been obtained from the relevant Research Ethics Committee.
- The Research Participant Information Sheets should include a clear statement that queries should be directed, in the first instance, to the Supervisor (where relevant), or the researcher. Complaints, on the other hand, should be directed, in the first instance, to the Chair of the relevant Research Ethics Committee.
- Approval to proceed with the study is granted subject to receipt by the Committee of satisfactory responses to any conditions that may appear above, in addition to any subsequent changes to the protocol.
- The Research Ethics Committee reserves the right to sample and review documentation, including raw data, relevant to the study.
- You may not undertake any research activity if you are not a registered student of Brunel University or if you cease to become registered, including abeyance or temporary withdrawal. As a deregistered student you would not be insured to undertake research activity. Research activity includes the recruitment of participants, undertaking consent procedures and collection of data. Breach of this requirement constitutes research misconduct and is a disciplinary offence.

A handwritten signature in cursive script, appearing to read 'Hua Zhao'.

Professor Hua Zhao

Chair

College of Engineering, Design and Physical Sciences Research Ethics Committee
Brunel University London

Survey of Professional Designers Complete Responses

Professional Designer Survey – Responses – Diagnostic Medical Devices

Response 1

Consent. Yes/No - *Yes*

Which company/institution do you work for? - *Lucid Group Ltd*

What is your job title? - *Director*

In the last 5 years, have you been involved in the design of a medical diagnostic testing device for infectious disease? **Yes/No** – *Yes*

If Yes...

Please briefly describe the function of the device you designed. - *Wearable interstitial fluid sampling*

Did you follow any particular design process as guidance during the development of your device? (E.g. concept development, prototyping, manufacturing and detail design stages...) - *From user and interested party needs definition, thru concept design, design verification iterations with prototyping and manufacturing verification, all to ISO 14971 and 13485*

Was the design and development of the device driven by the identification of a need or by the development of a new technology which offers new capabilities? - *User needs defined prior to investigation of alternative technologies.*

How long was/has the device been in development? - *13 months.*

What barriers/challenges did you encounter when developing the device? - *Difficulties in designing for compliance with wireless communications.*

Do you feel you would've benefitted from the use of a specialised design process model for this type of device? Why or why not? - *We have developed design a process to follow the ISO 13485 framework to achieve compliance.*

Response 2

Consent. Yes/No – *Yes*

Which company/institution do you work for? - *PDR*

What is your job title? - *Senior Design Consultant*

In the last 5 years, have you been involved in the design of a medical diagnostic testing device for infectious disease? **Yes/No** - *Yes*

If Yes...

Please briefly describe the function of the device you designed. - *Under NDA, sorry*

Did you follow any particular design process as guidance during the development of your device? (E.g. concept development, prototyping, manufacturing and detail design stages...) - *Structured around ISO13485. Concept design, development, detailing*

Was the design and development of the device driven by the identification of a need or by the development of a new technology which offers new capabilities? - *Identification of a need*

How long was/has the device been in development? - *12 months*

What barriers/challenges did you encounter when developing the device? - *None*

Do you feel you would've benefitted from the use of a specialised design process model for this type of device? Why or why not? - *No*

Response 3

Consent. Yes/No - *Yes*

Which company/institution do you work for? - *Maddison Product Design*

What is your job title? - *Managing Director*

In the last 5 years, have you been involved in the design of a medical diagnostic testing device for infectious disease? **Yes/No** - *Yes*

If Yes...

Please briefly describe the function of the device you designed. - *To capture the first 5ml of male urine for chlamydia detection*

Did you follow any particular design process as guidance during the development of your device? (E.g. concept development, prototyping, manufacturing and detail design stages...) - *Yes, user centred product development, starting with concept generation, development and then prototyping, user trials, refinement and introduction into manufacture*

Was the design and development of the device driven by the identification of a need or by the development of a new technology which offers new capabilities? - *User needs led*

How long was/has the device been in development? - *2 years*

What barriers/challenges did you encounter when developing the device? - *User testing in the third world*

Do you feel you would've benefitted from the use of a specialised design process model for this type of device? Why or why not? - *No, we have an experienced team and follow strong user-centred design processes.*

Response 4

Consent. Yes/No - *Yes*

Which company/institution do you work for? - *Renfrew group*

What is your job title? - *Engineering manager*

In the last 5 years, have you been involved in the design of a medical diagnostic testing device for infectious disease? **Yes/No** - *Yes*

If Yes...

Please briefly describe the function of the device you designed. – *Assay*

Did you follow any particular design process as guidance during the development of your device? (E.g. concept development, prototyping, manufacturing and detail design stages...) - *Brainstorming/concept generation, risk assessment, schematic engineering cad design, detailed eng schematic, various prototyping, testing and evaluations.*

Was the design and development of the device driven by the identification of a need or by the development of a new technology which offers new capabilities? - *Can be both depend on the project / clients requirements*

How long was/has the device been in development? - *6-8 months*

What barriers/challenges did you encounter when developing the device? - *Materials technology*

Do you feel you would've benefitted from the use of a specialised design process model for this type of device? Why or why not? - *Maybe, depends on what benefits it would give us.*

Response 5

Consent. Yes/No – *Yes*

Which company/institution do you work for? - *Renfrew Group*

What is your job title? - *Senior Designer*

In the last 5 years, have you been involved in the design of a medical diagnostic testing device for infectious disease? **Yes/No** - *Yes*

If Yes...

Please briefly describe the function of the device you designed. - *Isolation tent to contain infection around a hospital bed space in an open ward*

Did you follow any particular design process as guidance during the development of your device? (E.g. concept development, prototyping, manufacturing and detail design stages...) - *The usual design process, concept sketches, rigs and detailed drawings. Prototypes made and tested. Modifications made based on feedback from tests.*

Was the design and development of the device driven by the identification of a need or by the development of a new technology which offers new capabilities? - *Identification of need*

How long was/has the device been in development? - *2 years*

What barriers/challenges did you encounter when developing the device? - *The tent was very complex and time consuming to erect and expensive.*

Do you feel you would've benefitted from the use of a specialised design process model for this type of device? Why or why not? - *Not sure*

Response 6

Consent. Yes/No - *Yes*

Which company/institution do you work for? - *Johns Hopkins*

What is your job title? - *Postdoctoral Fellow*

In the last 5 years, have you been involved in the design of a medical diagnostic testing device for infectious disease? **Yes/No** - *Yes*

If Yes...

Please briefly describe the function of the device you designed. - *Nucleic acid amplification test*

Did you follow any particular design process as guidance during the development of your device? (E.g. concept development, prototyping, manufacturing and detail design stages...) - *Iterative process between concept development, prototyping and testing*

Was the design and development of the device driven by the identification of a need or by the development of a new technology which offers new capabilities? - *Driven by the identification of a need*

How long was/has the device been in development? - *3 years*

What barriers/challenges did you encounter when developing the device? - *Access to affordable and adequate prototyping resources*

Do you feel you would've benefitted from the use of a specialised design process model for this type of device? Why or why not? - *Yes, although the outcome would have been constrained by resources*

Professional Design Survey – Responses – Other Medical Devices

Response 1

Consent. Yes/No - *Yes*

Which company/institution do you work for? *The medical device company ltd*

What is your job title? - *Director*

In the last 5 years, have you been involved in the design of a medical diagnostic testing device for infectious disease? **Yes/No** - *No*

If Yes...Standard Medical Device

Please briefly describe the function of the device you designed. - *Equipment to produce large pieces of artificial skin*

Did you follow any particular design process as guidance during the development of your device? (E.g. concept development, prototyping, manufacturing and detail design stages...) - *Yes*

Was the design and development of the device driven by the identification of a need or by the development of a new technology which offers new capabilities? - *Need and technological advances*

How long was/has the device been in development? - *5 years*

What barriers/challenges did you encounter when developing the device? - *Costs of parts, sterilisation challenges, mould tool issues, material selection, manufacturing process, user requirements...*

Do you feel you would've benefitted from the use of a specialised design process model for this type of device? Why or why not? - *Not aware of such a model, in my experience our standard design process needs adapting for each new project to suit its specific requirements*

Response 2

Consent. Yes/No - *Yes*

Which company/institution do you work for? - *Oval Medical Technologies*

What is your job title? - *Director of Device Development*

In the last 5 years, have you been involved in the design of a medical diagnostic testing device for infectious disease? **Yes/No** - *No*

If Yes...Standard Medical Device

Please briefly describe the function of the device you designed. - *Drug delivery devices*

Did you follow any particular design process as guidance during the development of your device? (E.g. concept development, prototyping, manufacturing and detail design stages...) - *Yes - a stage-gate driven process whereby a series of major milestones are defined with a list of criteria that must be fulfilled at each one (determined by a team review) before the project can progress to the next stage.*

Was the design and development of the device driven by the identification of a need or by the development of a new technology which offers new capabilities? - *Identification of a need.*

How long was/has the device been in development? - *3 to 4 years.*

What barriers/challenges did you encounter when developing the device? - *Achieving functional performance consistently and reliably (given various external challenges such as environmental, misuse, drop etc.)*

Do you feel you would've benefitted from the use of a specialised design process model for this type of device? Why or why not? - *Yes - we did use a model and without it, the development would have not proceeded in a well organised, well documented and thorough fashion all of which are essential to the development of safe and effective medical devices.*

Response 3

Consent. Yes/No - Yes

Which company/institution do you work for? – PDR

What is your job title? - Senior User Centred Designer

In the last 5 years, have you been involved in the design of a medical diagnostic testing device for infectious disease? **Yes/No - No**

If Yes...Standard Medical Device

Please briefly describe the function of the device you designed. - *I've done a few - fetal monitoring (various devices) - oesophageal doppler - transcranial magnetic stimulator - diabetes pumps.*

Did you follow any particular design process as guidance during the development of your device? (E.g. concept development, prototyping, manufacturing and detail design stages...) - *I work mainly in the Human Factors and Usability Engineering (HF/UE) side of it.*

We recommend an initial stage of generative research in which they uncover user needs - then an iterative prototype-test cycle in which the product is developed and refined - culminating in a summative test just prior to manufacture.

However only some clients will buy into our teams services for the whole process. Some will engage us just for a single test element

Was the design and development of the device driven by the identification of a need or by the development of a new technology which offers new capabilities? - *Usually a new technology - however we recommend a stage of research to ensure that this new technology actually fits a user need. Most companies do this in some form or another as it is an expensive process they don't want to develop something that is not in line with user need.*

How long was/has the device been in development? - *Again it all varies. A long time mostly. I've never seen a product that has taken less than 2 years from when they get involved with us. And usually there's at least a year worth of work before that I've been involved with products that are 7 years+*

What barriers/challenges did you encounter when developing the device? - *From my point of view: a lack of understanding in the HF/UE standards (ISO 62366 / HE:75) and the benefits that they can bring beyond ensuring testing against a risk assessment and it being a tick box activity (e.g. that you can use user testing to inform development and aid decision making). In general I think understanding of all the various regulations and design control systems. Very few people have a complete understanding - and it usually takes a team of people to have a full knowledge on the process. Also these stringent regulations mean that cost is high - raising capital to finance this is a problem even if you product could save many lives!*

Do you feel you would've benefitted from the use of a specialised design process model for this type of device? Why or why not? - *Yes - I think having a easy to understand flow which takes you through all the design controls and regulations would help. However, I do find that many companies are not interested in doing the job to make the best product and more to make the most profit and therefore would want to see a minimal viable option version of this process model rather than 'make the best medical product' process model.*

Response 4

Consent. Yes/No - *Yes*

Which company/institution do you work for? - *Renfrew*

What is your job title? - *Industrial Designer*

In the last 5 years, have you been involved in the design of a medical diagnostic testing device for infectious disease? **Yes/No** - *No*

If Yes...Standard Medical Devices

Please briefly describe the function of the device you designed. - *Splint, carry chair, ear lobe blood sampler*

Did you follow any particular design process as guidance during the development of your device? (E.g. concept development, prototyping, manufacturing and detail design stages...) - *Yes, as above - my experience was with a previous company (Canard Design) we operated more of a lean approach. In both so in the case of the splint the 2 key criteria were: was it transparent to x-rays and could we make it stiff enough. Concepts were produced to think about creative solutions, then test rigs were made. Once we had an understanding of the mechanics we developed the concept and produced prototypes*

Was the design and development of the device driven by the identification of a need or by the development of a new technology which offers new capabilities? - *Identification of a need*

How long was/has the device been in development? - *It was developed over a 6 months A pilot study took a further year there were numerous delays due to funding development for full scale clinical trial including tooling and manufacture took a further year*

What barriers/challenges did you encounter when developing the device? - *The bureaucracy and internal politics of the NHS was extremely difficult to navigate. Creating a stiff enough form from x-ray transparent material was very challenging.*

Do you feel you would've benefitted from the use of a specialised design process model for this type of device? Why or why not? - *No. There is no doubt that this project required a particular approach. I have a good knowledge of prince 2 and a working knowledge of agile product development. I believe that the methodology laid out in both give enough flexibility to define the correct process for an individual project. It's also worth considering that the medical device directive offers templates for technical files that require certain information and due diligence, although not a template used in combination with the above it gives quite a thorough methodology. It is my experience that every project is different and a single pathway might constrain the process too much or be so vague as to offer no real benefit from the general prince/agile/combination of approaches. Where it would have been useful is informing who to use as clinical experts and where to go to talk about ethical approval.*

Response 5

Consent. Yes/No - *Yes*

Which company/institution do you work for? - *John Pacey-Lowrie Ltd*

What is your job title? - *Consultant Ocularist*

In the last 5 years, have you been involved in the design of a medical diagnostic testing device for infectious disease? **Yes/No** - *No*

If Yes...Other Medical Device

Please briefly describe the function of the device you designed. - *Light reactive pupil prosthetic eye*

Did you follow any particular design process as guidance during the development of your device? (E.g. concept development, prototyping, manufacturing and detail design stages...) - *All of the above*

Was the design and development of the device driven by the identification of a need or by the development of a new technology which offers new capabilities? - *Patient needs for enhanced quality of life*

How long was/has the device been in development? - *Five years*

What barriers/challenges did you encounter when developing the device? - *Miniaturisation of the components*

Do you feel you would've benefitted from the use of a specialised design process model for this type of device? Why or why not? - *No as this is a completely uncharted area of medical device design*

Response 6

Consent. Yes/No - *Yes*

Which company/institution do you work for? - *Haughton Design*

What is your job title? - *Managing Director*

In the last 5 years, have you been involved in the design of a medical diagnostic testing device for infectious disease? **Yes/No** - *No*

If Yes...Other Medical Device

Please briefly describe the function of the device you designed. - *Various devices, diabetes diagnostics, auto-injectors etc.*

Did you follow any particular design process as guidance during the development of your device? (E.g. concept development, prototyping, manufacturing and detail design stages...) - *Yes, we have 10 step stage gate process*

Was the design and development of the device driven by the identification of a need or by the development of a new technology which offers new capabilities? - *Both*

How long was/has the device been in development? - *2-4 years*

What barriers/challenges did you encounter when developing the device? - *Technical challenges around space constraints, manufacturability and existing patents*

Do you feel you would've benefitted from the use of a specialised design process model for this type of device? Why or why not? - *No, we already have our own methodology*

Professional Designer Survey – Responses – Non-Medical Device Design

Response 1

Consent. Yes/No - *Yes*

Which company/institution do you work for? - *Animal*

What is your job title? - *Garment technologist*

In the last 5 years, have you been involved in the design of a medical diagnostic testing device for infectious disease? **Yes/No** - *No*

If No...

Imagine you have been asked to design a self-use diagnostic test for Chlamydia. This test must be able to be used by ordinary consumers (non-medical professionals) and be able to receive a biological sample, process the sample and provide a positive or negative result. Please answer the questions below about how you would go about designing this hypothetical product. Would you follow an established design process as guidance during the development of your device? (E.g. concept development, prototyping, manufacturing and detail design stages...) - *Yes as above and also get feedback from consumers through a focus group if needed on the design.*

In your experience, would the design and development of a device like this be driven by the identification of a need or by the development of a new technology which offers new capabilities? - *Initially a need would drive the design, then look at what technology has to offer, however you could be inspired by a technology and immediately see its uses towards the design so both technology or need can drive the design.*

How long would you predict the development process would take, from concept to market? - *Designing a product for the companies I've worked in from process to concept can take minimum 1 year up to 2 or 3 years depending on the product, but then sales are working to sell lots of products at once. For a medical device maybe it would be 2-3 years depending on the need that's out there.*

What major barriers/challenges would you expect to encounter when developing the device? - *Initial concepts could be rejected, so you would have to be flexible to adapt and rethink aspects of the design. Winning over people who don't understand what you are doing. Technicalities of moving from design to manufacturing, can it be mass produced easily. Even when it gets to manufacturing the quality control would need to have specific controls in place because of the nature of the product. Packaging would also be important that the product is sealed properly.*

Do you feel you would benefit from the use of a specialised design process model for this type of device? Why or why not? - *I think that during the concept development for this device you will be able to see whether it needs a special design process.*

Response 2

Consent. Yes/No - *Yes*

Which company/institution do you work for? - *Nottingham Trent University*

What is your job title? - *Reader*

In the last 5 years, have you been involved in the design of a medical diagnostic testing device for infectious disease? **Yes/No** - *No*

If No...

Imagine you have been asked to design a self-use diagnostic test for Chlamydia. This test must be able to be used by ordinary consumers (non-medical professionals) and be able to receive a biological sample, process the sample and provide a positive or negative result.

Please answer the questions below about how you would go about designing this hypothetical product. Would you follow an established design process as guidance during the development of your device? (E.g. concept development, prototyping, manufacturing and detail design stages...)

- *Yes*

In your experience, would the design and development of a device like this be driven by the identification of a need or by the development of a new technology which offers new capabilities? - *By user centred and even participatory design methods*

How long would you predict the development process would take, from concept to market? - *2 years*

What major barriers/challenges would you expect to encounter when developing the device? - *Clinical guidelines and standards*

Do you feel you would benefit from the use of a specialised design process model for this type of device? Why or why not? - *Yes, but depends on claims of the device*

Response 3

Consent. Yes/No - *Yes*

Which company/institution do you work for? - *Maddison ltd*

What is your job title? - *Designer*

In the last 5 years, have you been involved in the design of a medical diagnostic testing device for infectious disease? **Yes/No** - *No*

If No...

Imagine you have been asked to design a self-use diagnostic test for Chlamydia. This test must be able to be used by ordinary consumers (non-medical professionals) and be able to receive a biological sample, process the sample and provide a positive or negative result. Please answer the questions below about how you would go about designing this hypothetical product. Would you follow an established design process as guidance during the development of your device? (E.g. concept development, prototyping, manufacturing and detail design stages...) - *I would start by a strong user research phase to understand the processes currently available and how the users and physicists interact with these processes, their feedback would also help in understanding what works and doesn't work with the current processes. Then I would follow a more traditional design process including market research, brainstorming, concept research, concept development, prototyping, user trials, development for manufacture and finalisation.*

In your experience, would the design and development of a device like this be driven by the identification of a need or by the development of a new technology which offers new capabilities? - *It could be either*

How long would you predict the development process would take, from concept to market? - 12 to 24 months

What major barriers/challenges would you expect to encounter when developing the device? - *Organising the user groups for user research and user trials*

Do you feel you would benefit from the use of a specialised design process model for this type of device? Why or why not? - *I'm not sure. I don't really believe in set design processes, each project is different and the development process varies from project to project. I think guidelines would be more helpful than a process.*

Response 4

Consent. Yes/No – Yes

Which company/institution do you work for? - *Renfrew Group International*

What is your job title? - *Design Engineer*

In the last 5 years, have you been involved in the design of a medical diagnostic testing device for infectious disease? **Yes/No** - *No*

If No...

Imagine you have been asked to design a self-use diagnostic test for Chlamydia. This test must be able to be used by ordinary consumers (non-medical professionals) and be able to receive a biological sample, process the sample and provide a positive or negative result. Please answer the questions below about how you would go about designing this hypothetical product. Would you follow an established design process as guidance during the development of your device? (E.g. concept development, prototyping, manufacturing and detail design stages...)- *Yes*

In your experience, would the design and development of a device like this be driven by the identification of a need or by the development of a new technology which offers new capabilities? - *Identification of a need comes first, then the available technology that can facilitate the solution assessed.*

How long would you predict the development process would take, from concept to market? - *Difficult to estimate depending on the complexity of the device, but the process of approving it for medical use is lengthy.*

What major barriers/challenges would you expect to encounter when developing the device? - *Medical approval for materials.*

Do you feel you would benefit from the use of a specialised design process model for this type of device? Why or why not? - *Not particularly, general design processes already exist for medical applications that are robust.*

Validation Survey – Participant Comments

Participant ID: R_3ikDVgeG9Dh8pFE **Work Stream:** 2 **Expertise:** Electronic Engineering

Comment: In addition to being easy to use, the device needs to be idiot proof to ensure that it cannot be used wrongly, or if it is, the device rejects the result. Providing a guide to the user as to how to use the device is important, i.e. taking the user through step-by-step bit also allowing the user to back track or cancel the test. I said it was moderately important for a Smartphone to process and send the result, but I also believe that the device should be able to be used

standalone, without the need for a Smartphone. This allows privacy in use to ensure that some are not put off using it by thinking that big brother is watching them - especially in these days of hacking.

Participant ID: R_3dRMEnxaEVqWzGh **Work Stream:** 3 **Expertise:** Public health and diagnostic evaluations

Comment: Test design is clearly complex, and I think the key question is where is the test going to be deployed, and this will determine many of the answers to the questions. I've answered from a "realistic, but ideal test" perspective. However, if proper market research were performed nationally to get a sense of who would buy this test and where it would be used, we would get a better sense of the needs for size, smartphone enabled components, cost etc. I think the Context of Use question is the key.

Participant ID: R_sulkw1Rnx6HnznX **Work Stream:** 4 **Expertise:** Health Technology Assessment

Comment: My DCE results found that test accuracy is the most important factor to young people followed by time to result for chlamydia testing. One of the dilemmas I had was running the DCE on chlamydia only when the focus groups with young people identified that the range of tests (they wanted to get tested for as many STIs as possible) was very important to them. This is an issue which may influence uptake of a new self-testing device.

I am very focused on the NHS i.e. accessible to all, free at the point of delivery. However, a test does not have to follow that path, pregnancy testing is a good example of that. The issue regarding surveillance data is interesting in that context because there are a number of pharmacy websites offering private i.e. fee-paying STI testing services where the results are not shared with PHE. The trade off between being able to make a test available which can't transmit surveillance data with the fact a self-test may reach a population who have not previously tested is an interesting one.

My thoughts on the development period are the pace of technology development for eHealth/ mHealth is very different to drugs. I think there is a real risk that the technology could be obsolete before it is available for mainstream use. This view is mainly driven by the pace of the base technology development e.g. smartphones. Potentially this would be different for a self-test compared to e.g. an app for treatment but I think it needs to be considered (I am less familiar with the test technology).

Participant ID: R_3p6nvwq74jB5RbT **Work Stream:** 2 **Expertise:** Diagnostics Engineering

Comment: I think that smartphone integration is a gimmick and little is gained in terms of cost, size or performance from having any device attach to a smartphone

Participant ID: R_xlxhF9jbl3YH7ih **Work Stream:** 2 **Expertise:** Microfluidics

Comment: Regarding processing a result on the mobile phone, the mobile phone can process the result but it absolutely must not do the diagnosis. This is extremely important. Otherwise each and every phone has to be FDA approved. Also time to result, ideally 10 minutes but with molecular diagnostics this is simply not possible.

Participant ID: R_pGfyTqq7AqrBnOh **Work Stream:** 4 **Expertise:** patient impact of novel diagnostics

Comment: Slightly difficult to answer these as it really depends on the type of test one is thinking of. It is more important for the test to have faster results if it is in a clinic or a pharmacy, e.g. where the patient is waiting, than it is if the patient is performing the test themselves, e.g. at home. while it would be ideal that the device is self-powered or powered via the mobile phone, if it were battery operated either using changable batteries or a chargable

battery, it becomes less important, though again, it depends on the market (i.e. developing world versus UK market).

Participant ID: R_RsMwgFhKpA3r509 **Work Stream:** 4 **Expertise:** public health

Comment: For some of these (e.g. time to results) you really need to ask the users of a self-test! And it will vary by context - waiting at home is very different from hanging about feeling awkward in a public place like a pharmacy. Please see WS4's publications.

I also think that in order to interpret the answers to this questionnaire you aren't going to capture *why* we think things are important. So if it comes to making trade-offs between characteristics you might need to seek further advice...

Appendix C: Action Research Design Activity

C-1 Design Experiment 1 – Design Outcome 1 – Dimensions

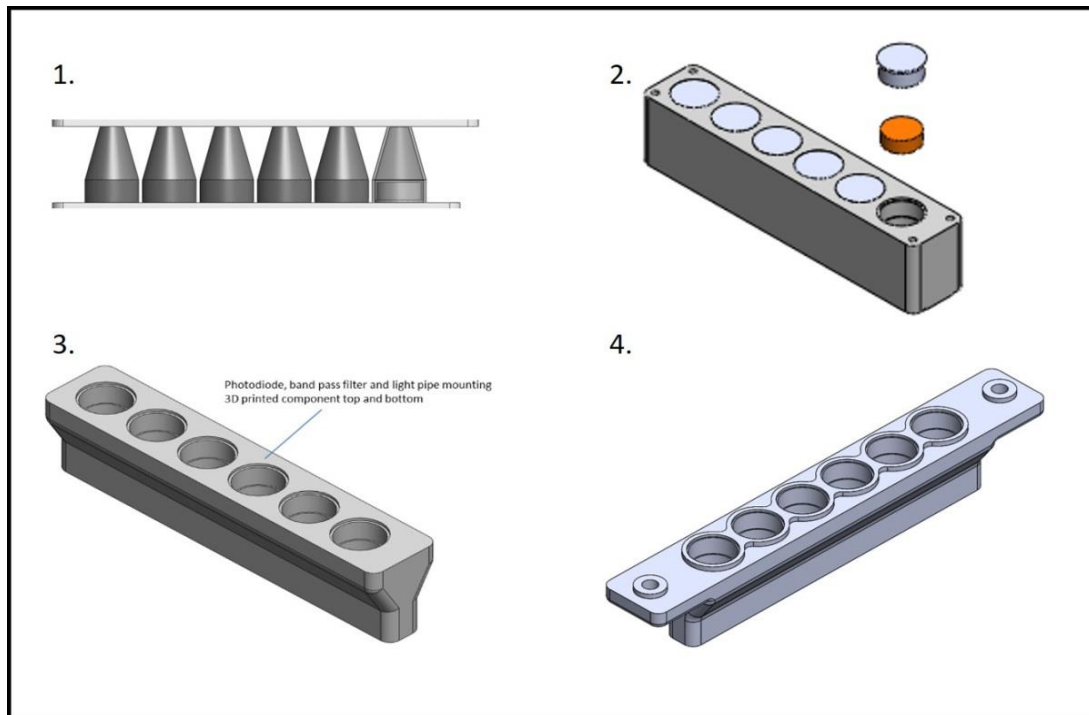
The dimensions of the proof of concept platform were constrained by the method of construction that had been used. The rechargeable battery pack shown was specified in collaboration with engineers in the DoC Lab research group and was a key driver of the size of the casing, measuring in millimetres, Width – 60, Height – 15 and Length – 140. The proof of concept platform component measured W – 54, H – 32 and L – 100. Control of the optical detection and heating elements of the platform were controlled by two Arduino Uno reprogrammable microprocessors which measured W – 53 and L – 68 with a height taking into account wiring connections of roughly 20mm. The dimensions of all of these components contributed to the overall dimensions of design outcome 1, which were approximately W – 70, H – 80 and L - 300.

C-2 Meeting Notes – Expert Panel – Design Experiment 1

27/05/2014	WB, CH, NM, VG, TS, US, JdF, BN, TS, Tu (sk), RM	TS presentation, POC functionalities and prototype.	<p>User interaction: clinician and patient: POC and mobile. Data communications discussion. Different scenarios, 1 device, 1 device and mobile, where does the data go, how does it link with the clinical care pathway. Use constraint modelling. What do the clinicians want, what does the user want? Within the POC device, how should the data appear? Focus on molecular diagnostics, not LFIA. Where will we be in 5 years' time, the future POC device?</p> <p>NOTES: Size an issue, further consideration of interaction between components required. Could conduct a thorough risk analysis of all the technology. What are the regulatory requirements, software must be CE marked. Look at the IVD directive. MHRA regulation. Context of use, who are the user(s). False positives/negatives, depend on test and reader. What is the clinical utility? Is the decision on the phone or server? Mind map, what needs to be addressed, initial prototypes, fully functional spec. How will the use of the smartphone change the healthcare system?</p>
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C-3 Design Experiment 2 – Design Outcome 3 – Photodiode Mounting Evolution

Below is an example of this component evolution, where the optical fibre and band-pass filter mounting component was adapted iteratively.

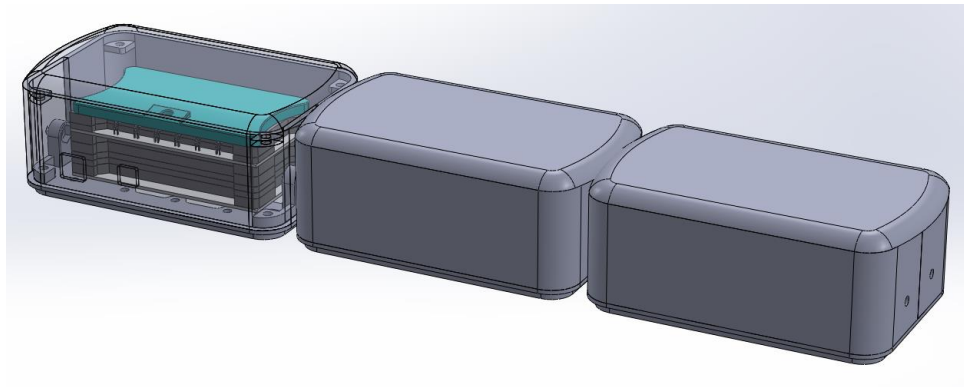
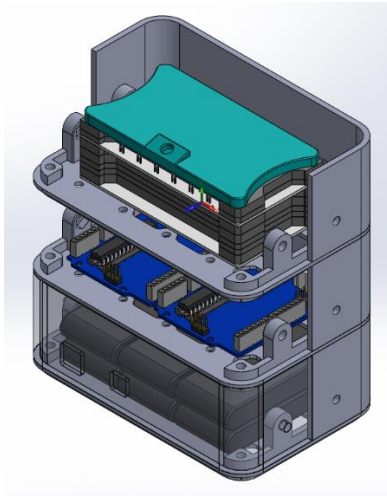


A description of the design changes shown in the figure follows:

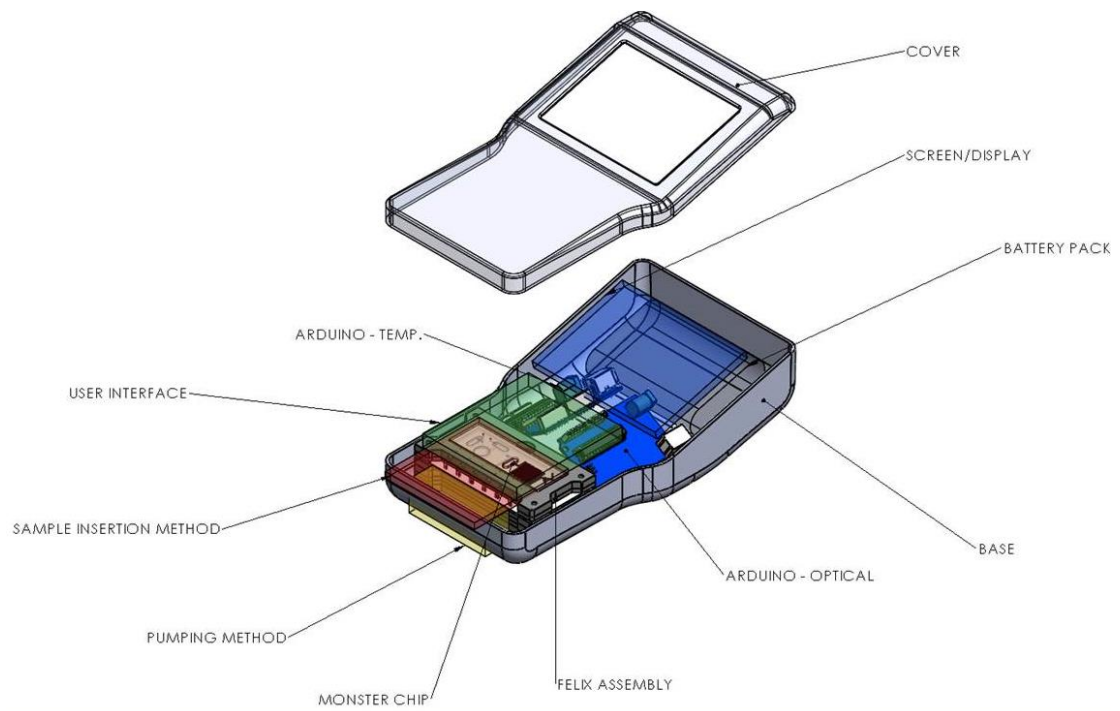
1. The photodiode, band-pass filter and optical fibres are each encased individually. This is because the criteria being followed here was the need to prevent interference from external light sources. The need for the mounting to be structural as well as opaque was understood but had not been considered in detail at this point.
2. A solid block of material would provide some structural strength to the module while encasing the necessary components. At this point, a manufacturing technique had not been chosen for the prototype component.
3. A prototyping company was identified who could provide opaque 3D printed parts. The shape of the component was changed to reduce the amount of material required to achieve the requirements and free up more space in the platform for wiring and other components.
4. Further reduction of material reduced the footprint of the device that was in contact with the PCB and reduced concerns relating to how much of the material was in contact with circuitry or components on the surface of the PCB.

C-4 Action Research Design Activity – Iterations Timeline

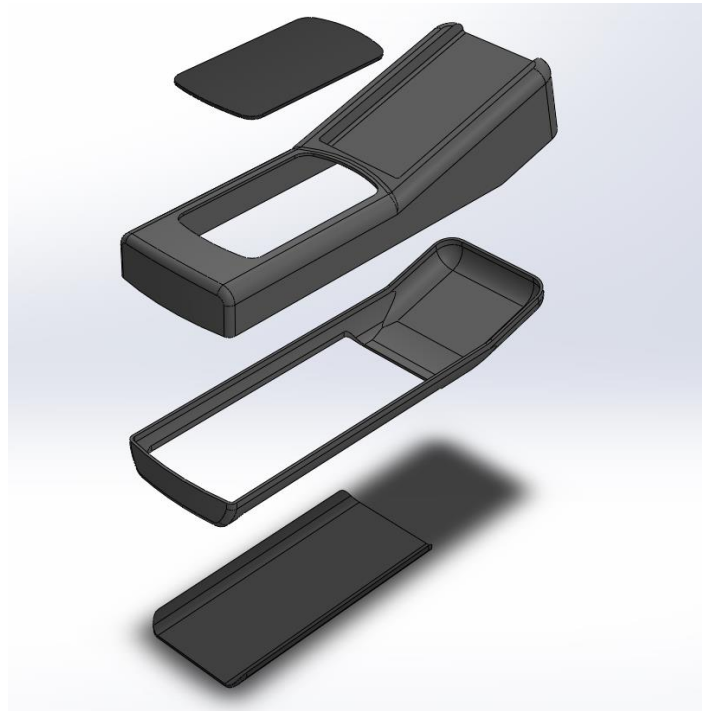
Modular casing design separating functional components into modules:



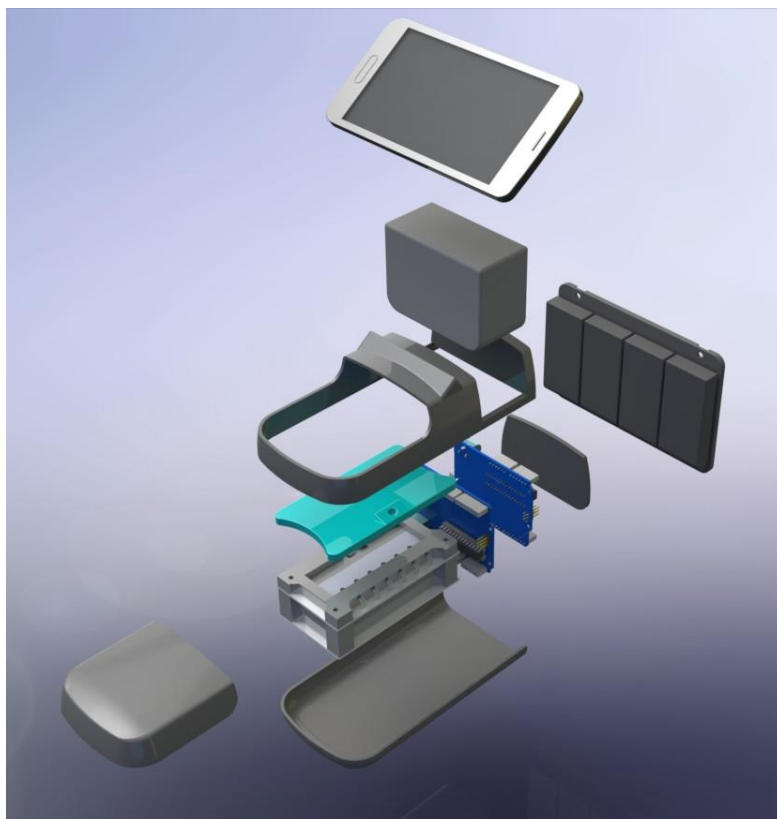
Initial casing and user interface design using proof of concept technology dimensions:



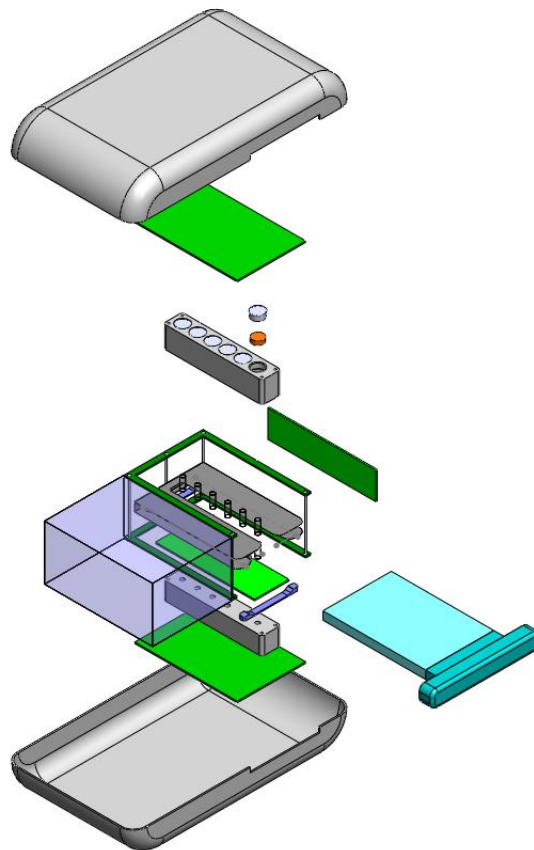
Further casing development for design outcome 1 of design experiment 1:



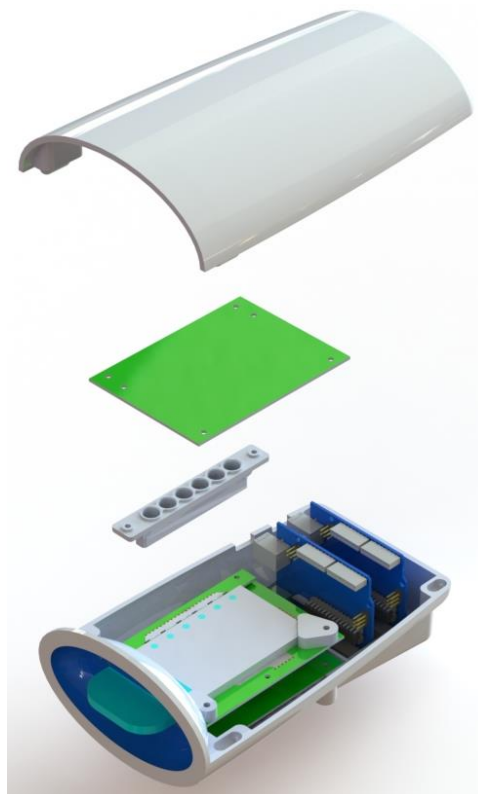
Volume study for design experiment 1 – design outcome 2:



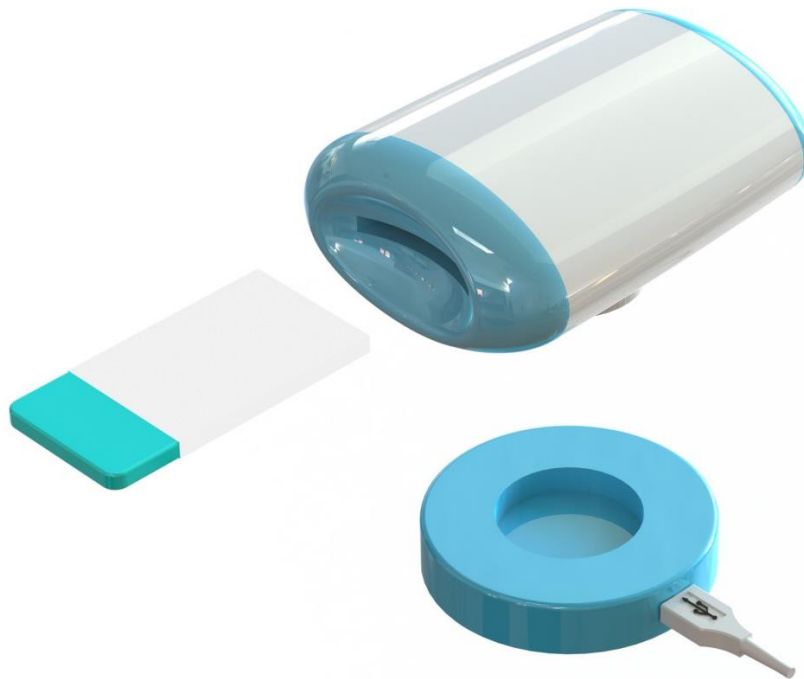
Casing design for miniaturised internal components:



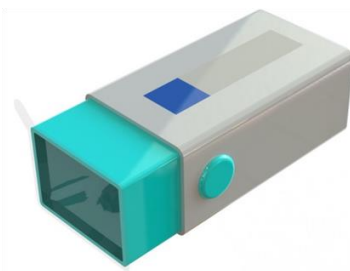
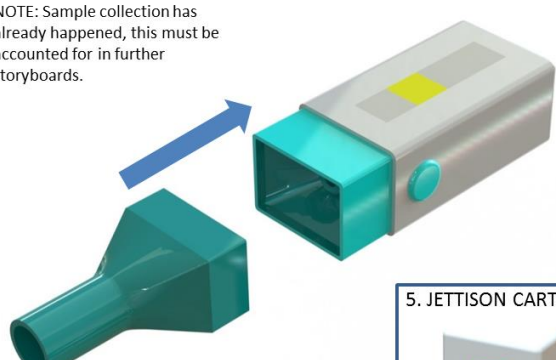
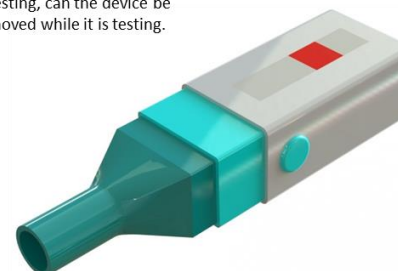
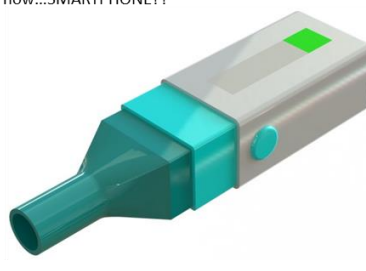

Casing design for point of care concept using the same diagnostic platform technology:



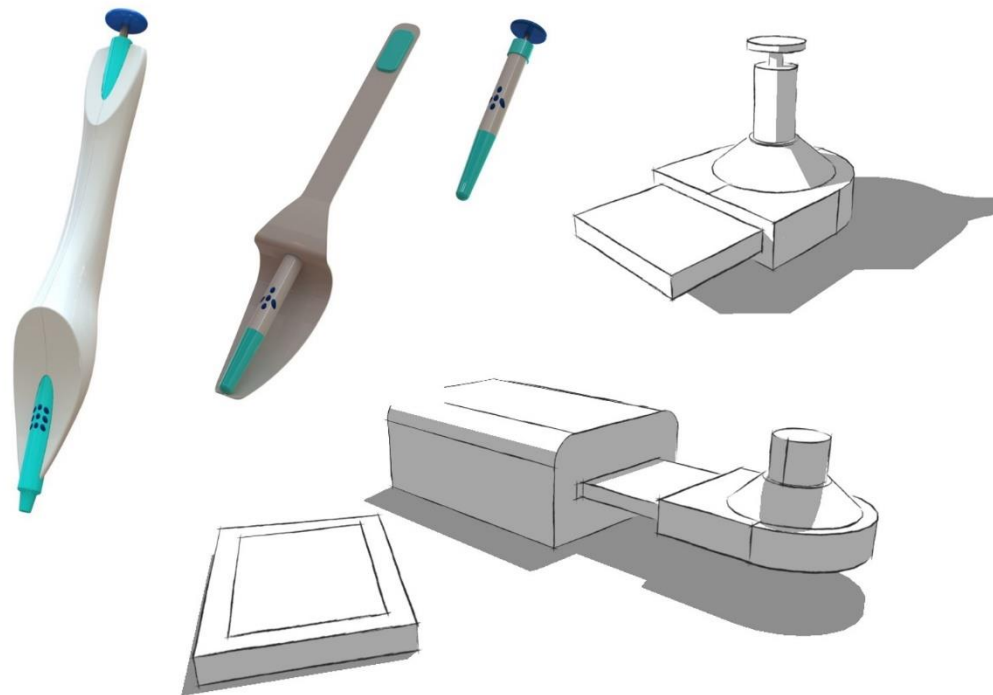
Portable point of care device concept for use in GP surgeries:



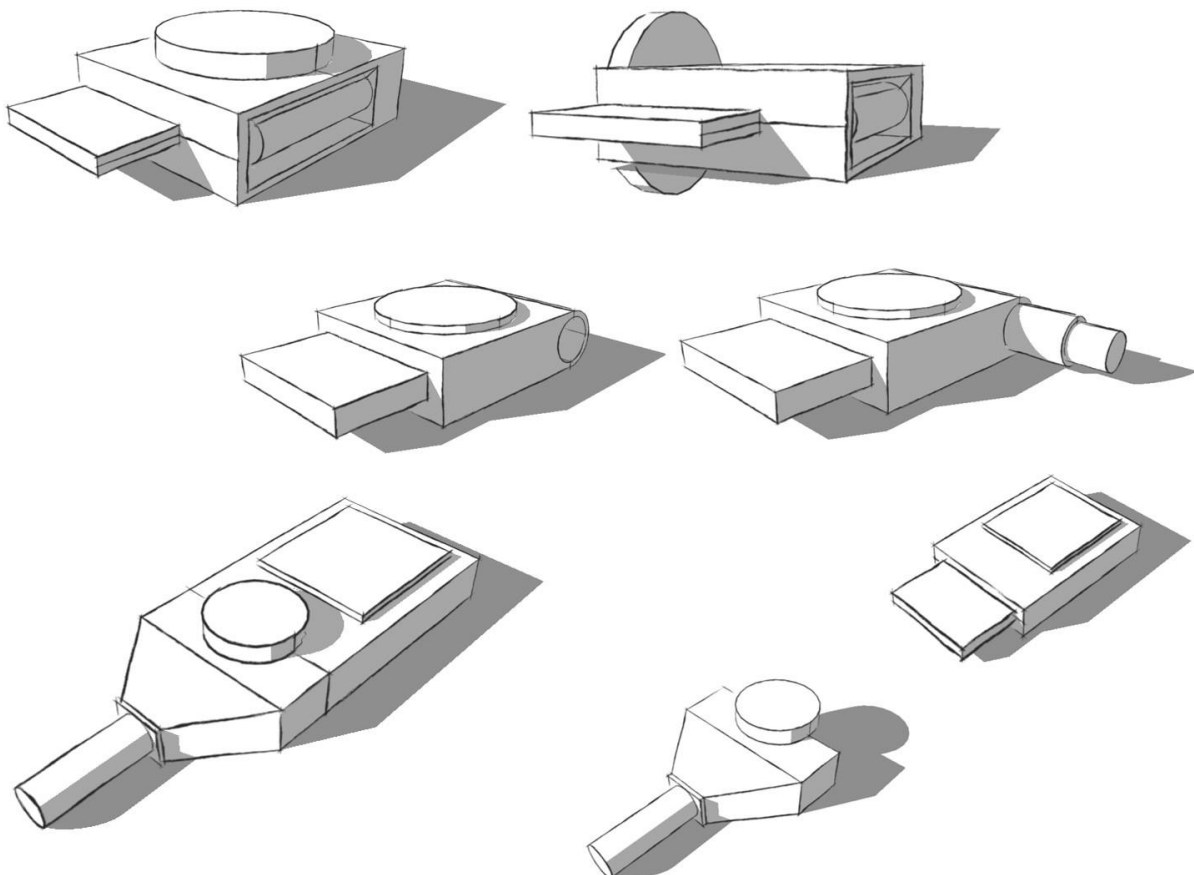
Storyboard investigating further miniaturisation for self-use:

<p>1. READY</p> <p>NOTE: Seal must be removed to make this possible, the chip is in situ here, would it be purchased like this?</p> 	<p>2. INTRODUCE SAMPLE</p> <p>NOTE: Sample collection has already happened, this must be accounted for in further storyboards.</p> 	
<p>3. TESTING...</p> <p>NOTE: The red indicator light denotes that the device is testing, can the device be moved while it is testing.</p> 	<p>4. DONE</p> <p>NOTE: The device is finished testing, what now...SMARTPHONE??</p> 	<p>5. JETTISON CARTRIDGE...</p> <p>NOTE: Push button to release.</p> 

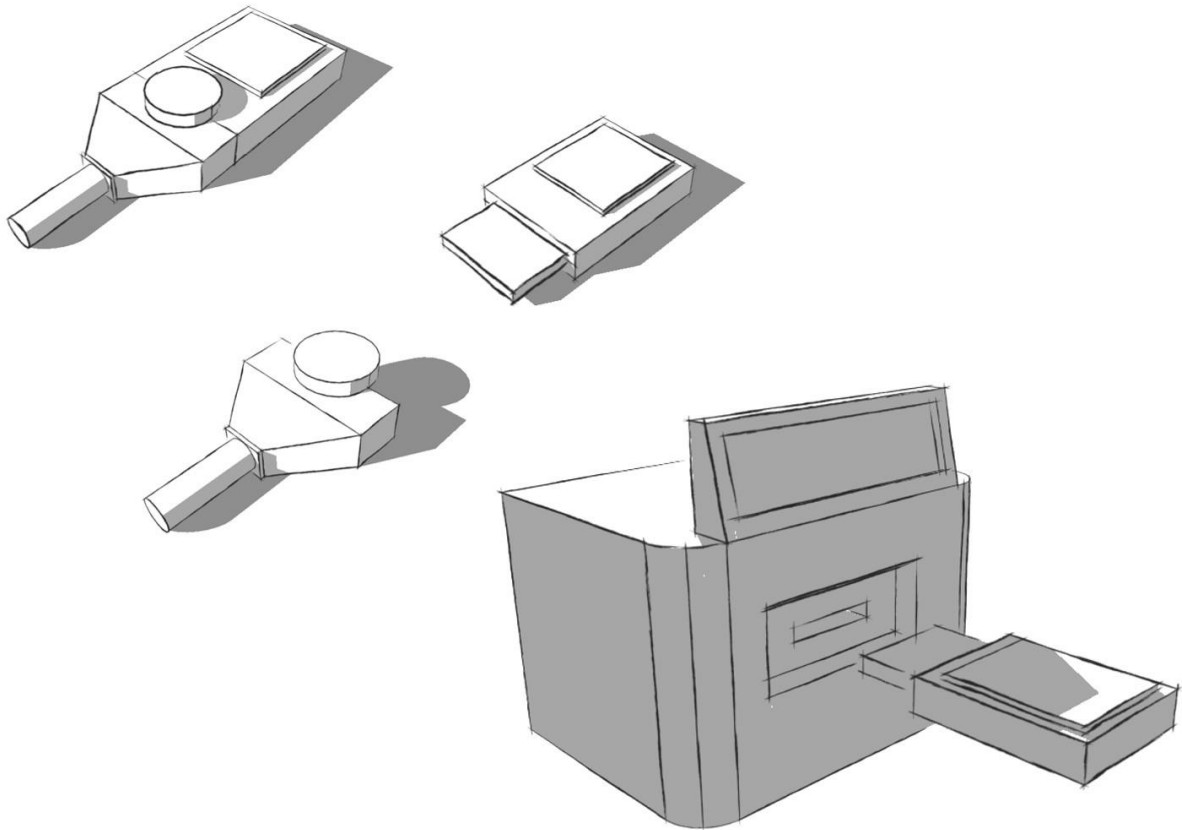
Sketch concepts for sample collected interaction with microfluidic chip sample preparation device:



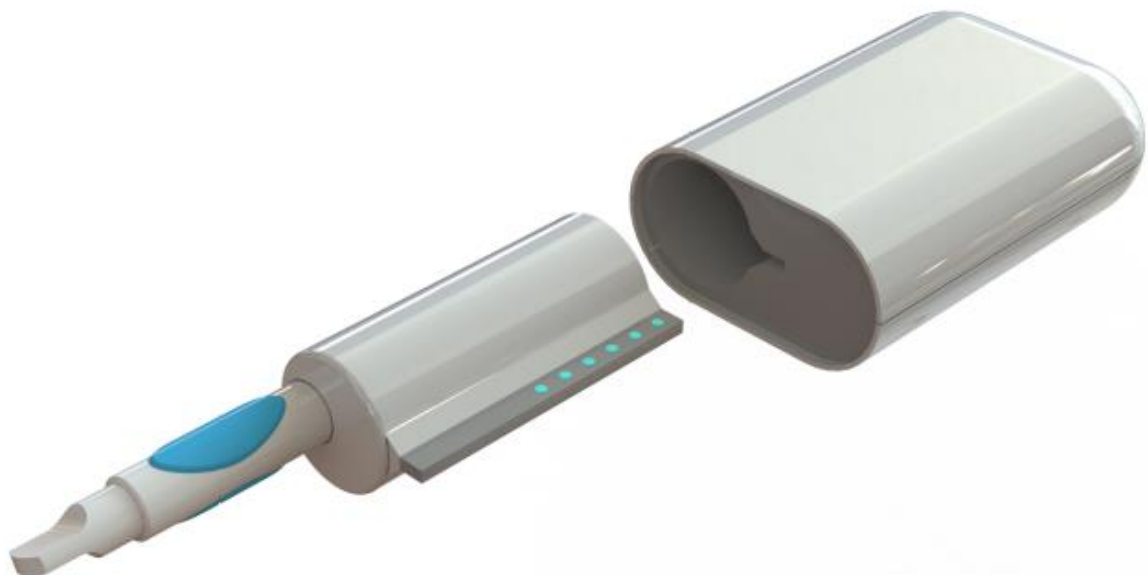
Further sketch concept generation of sample collector/microfluidic chip interaction:



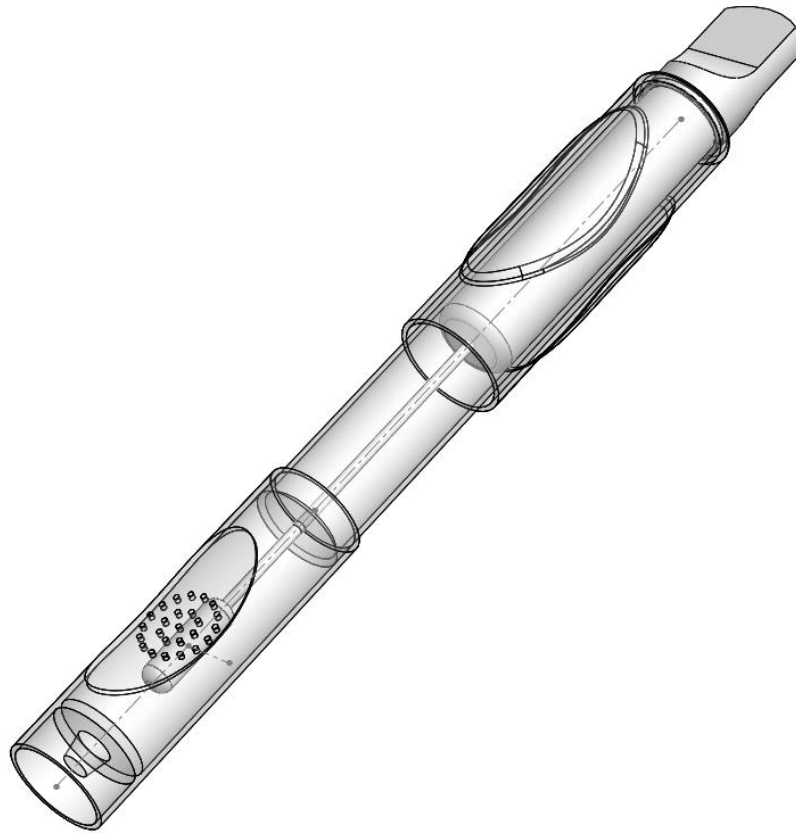
Sketch concepts of sample collector/microfluidic chip interaction with pharmacy based benchtop device:



Final concept of point of care, repeat use detection diagnostic device:

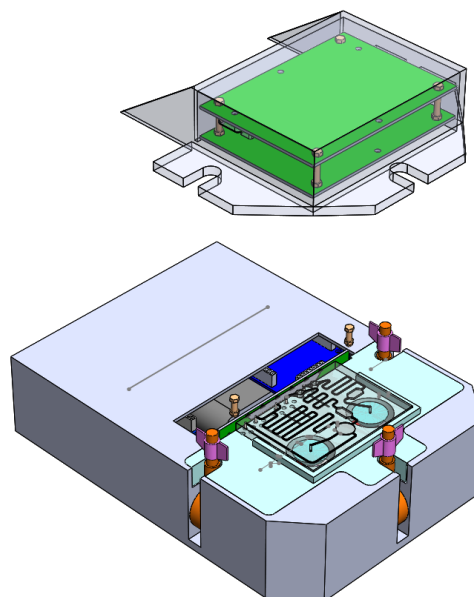


Sample collector (swab and urine) designed for use with concept prototypes and eventual independent use:

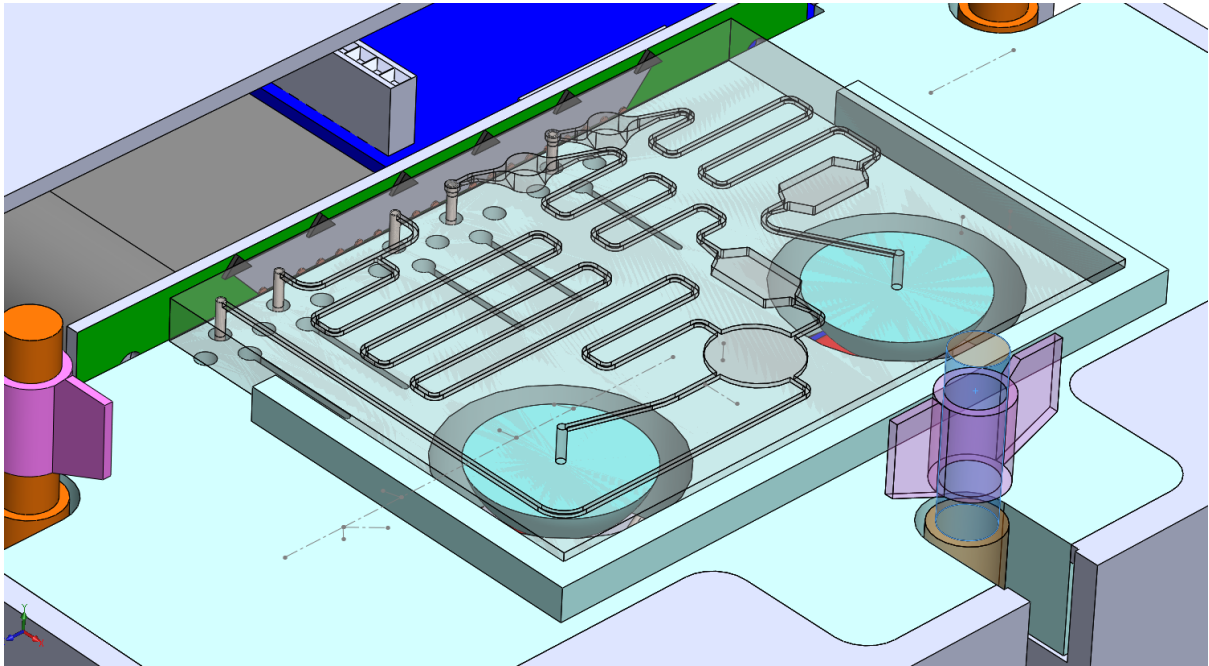


C-5 Preclinical Trial Actuator Configuration

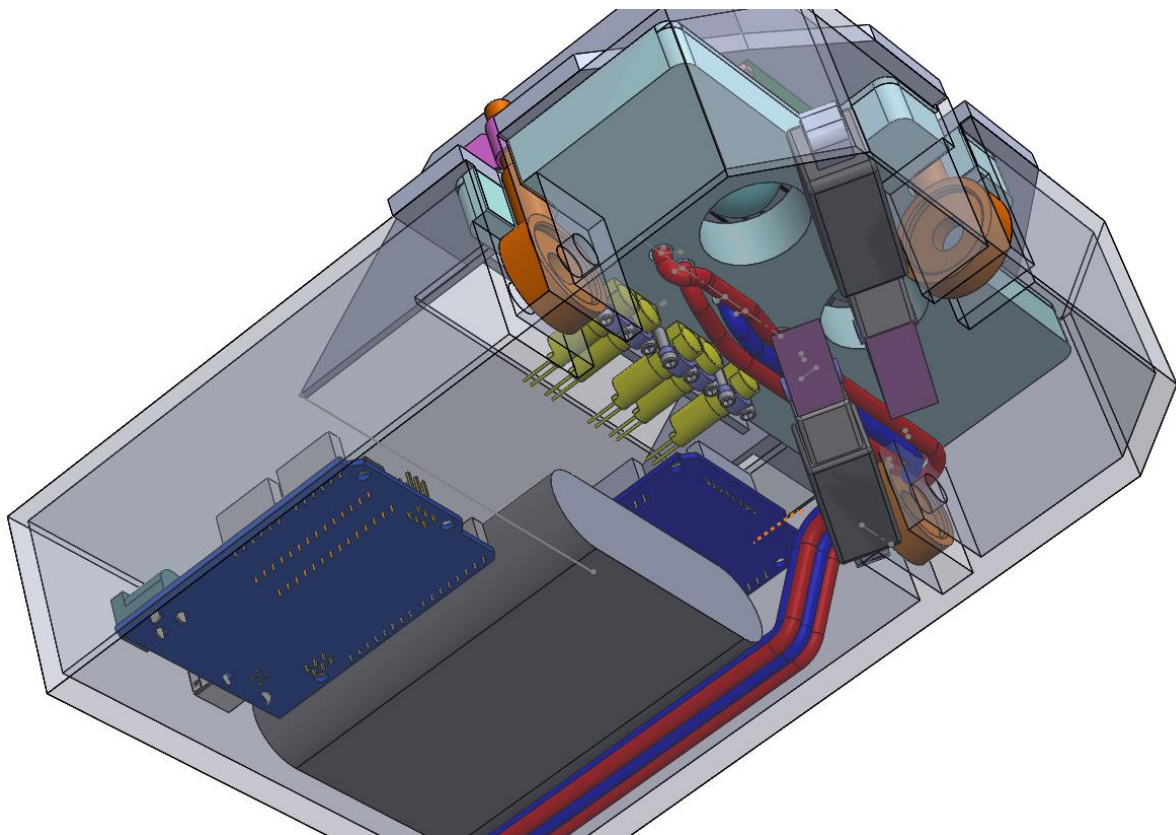
Inverted detection concept for size reduction purposes and ease of chip insertion. Detection on top:



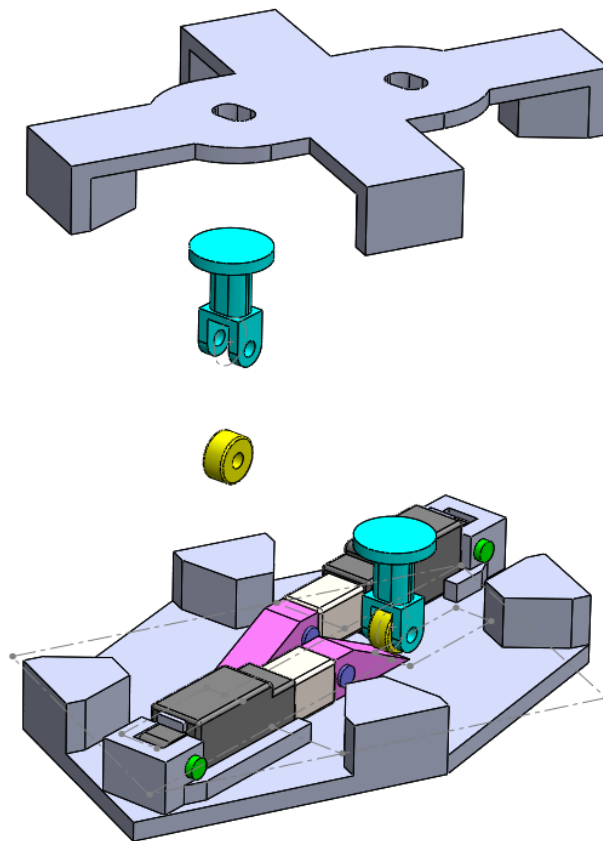
Microfluidic chip to fluidics module interface in inverted version:



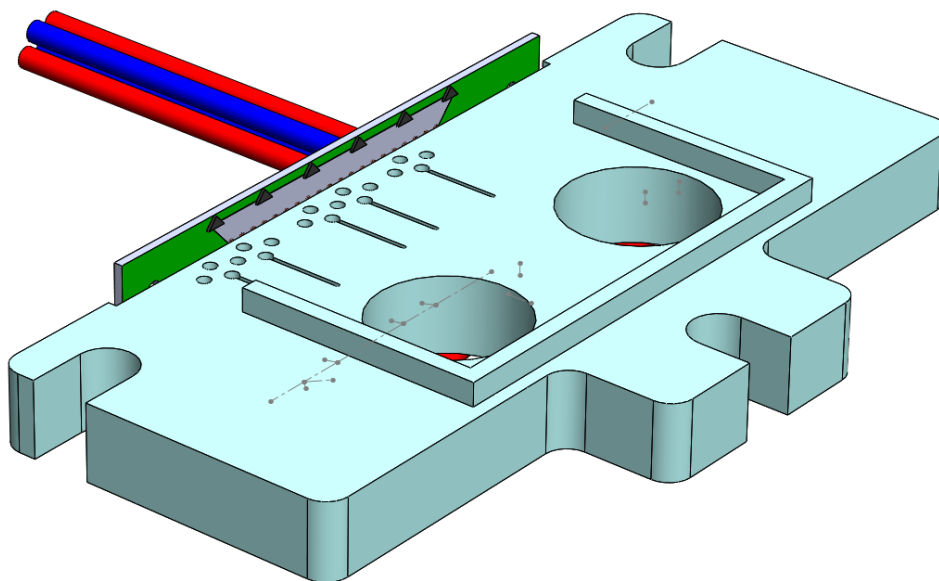
Fluidics and actuator configuration under microfluidic chip:



Miniaturised actuator assembly for size reduction of preclinical trial prototype:

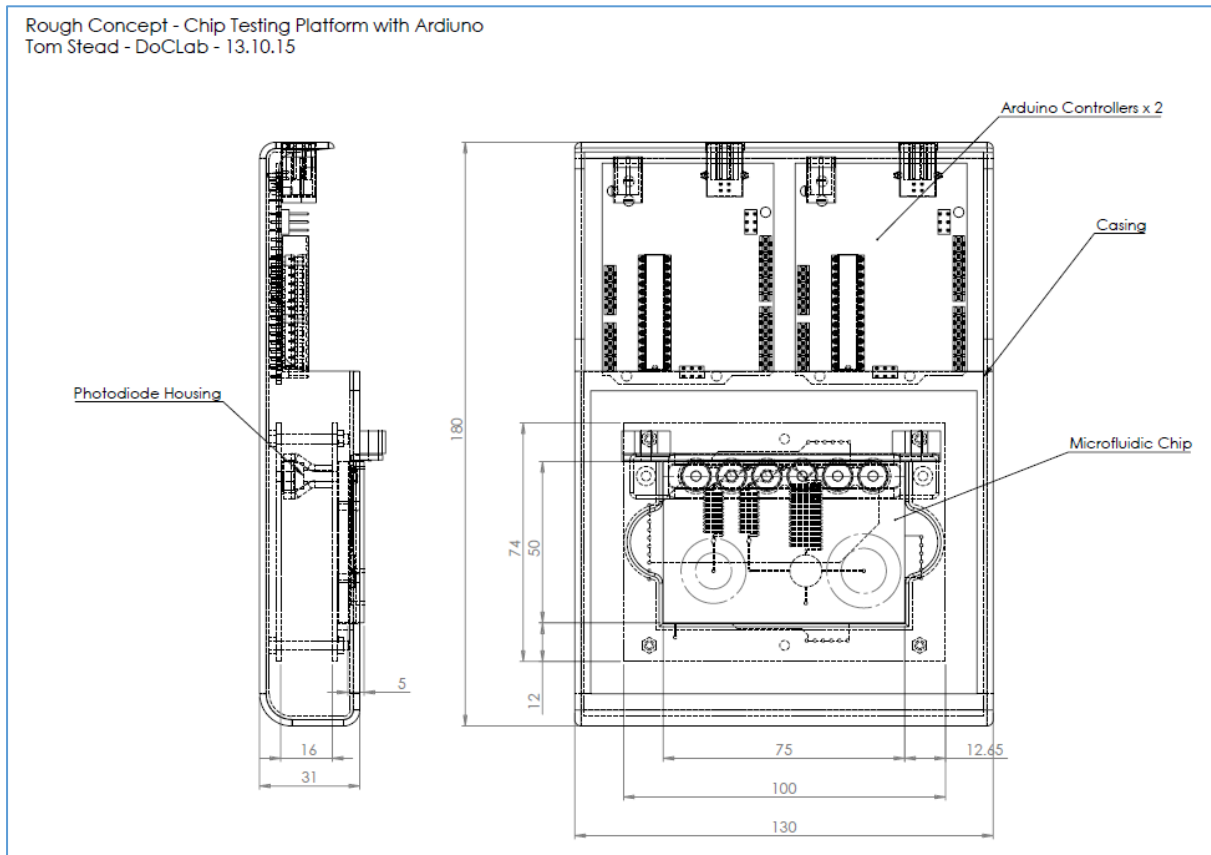


Inverted fluidics module assembly with locating lugs:

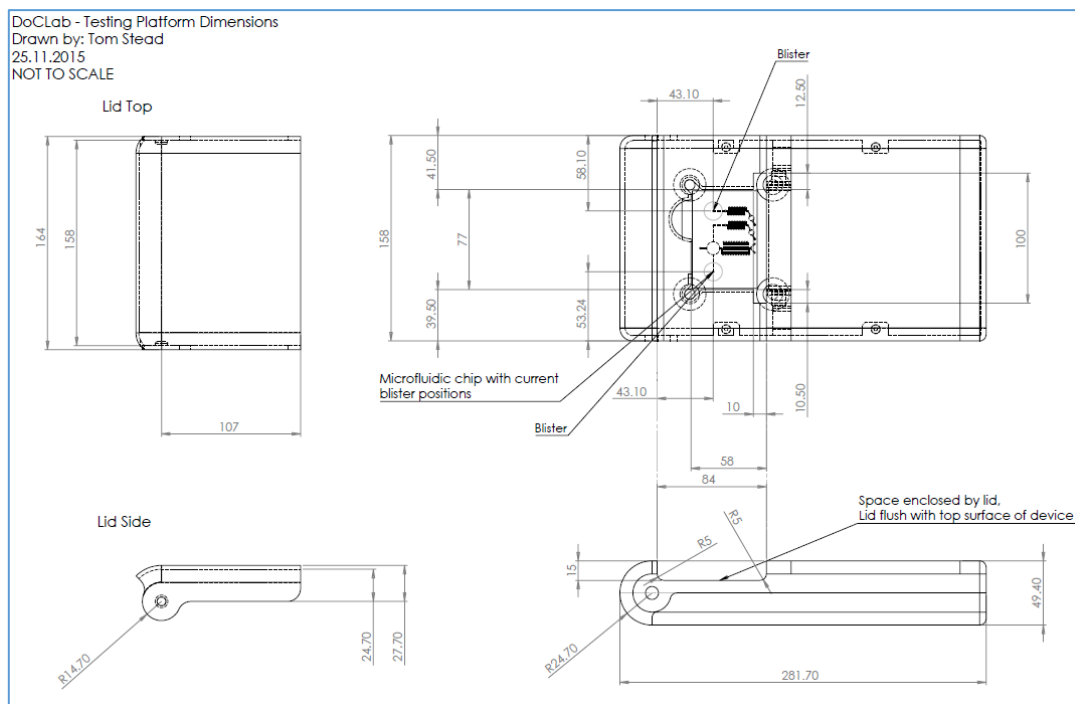


C-6 Preclinical Trial Prototype - Technical Drawings

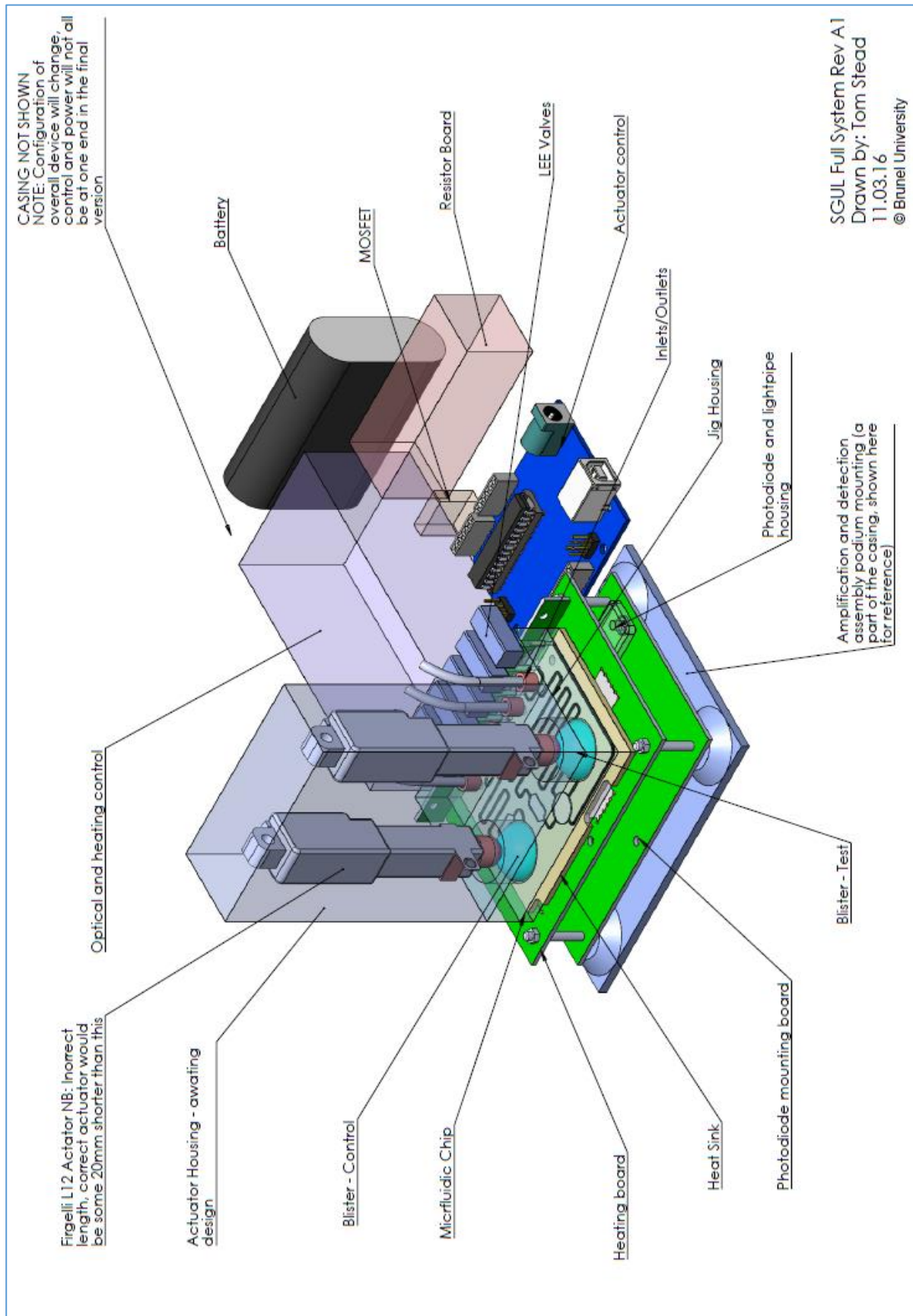
Early concept preclinical trial prototype general assembly drawing:



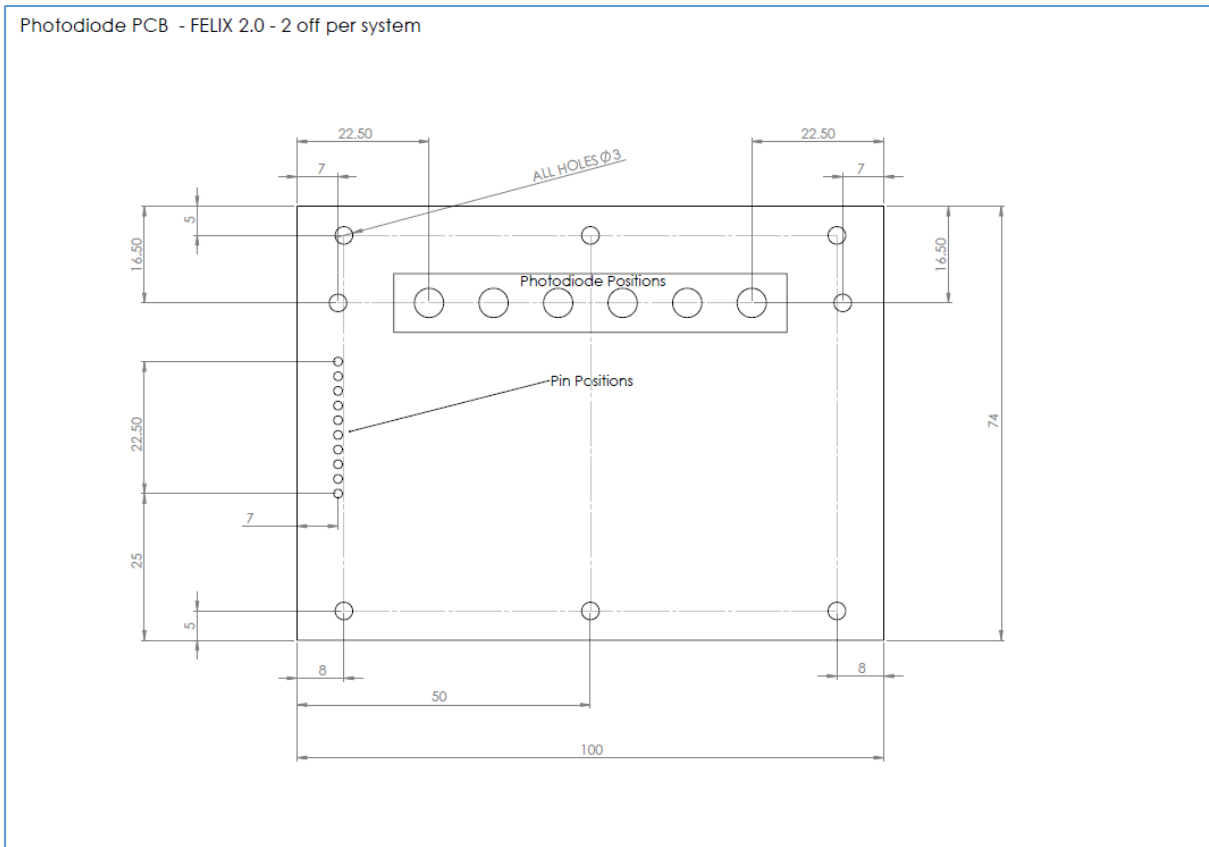
Further iteration of above concept with improved casing design:



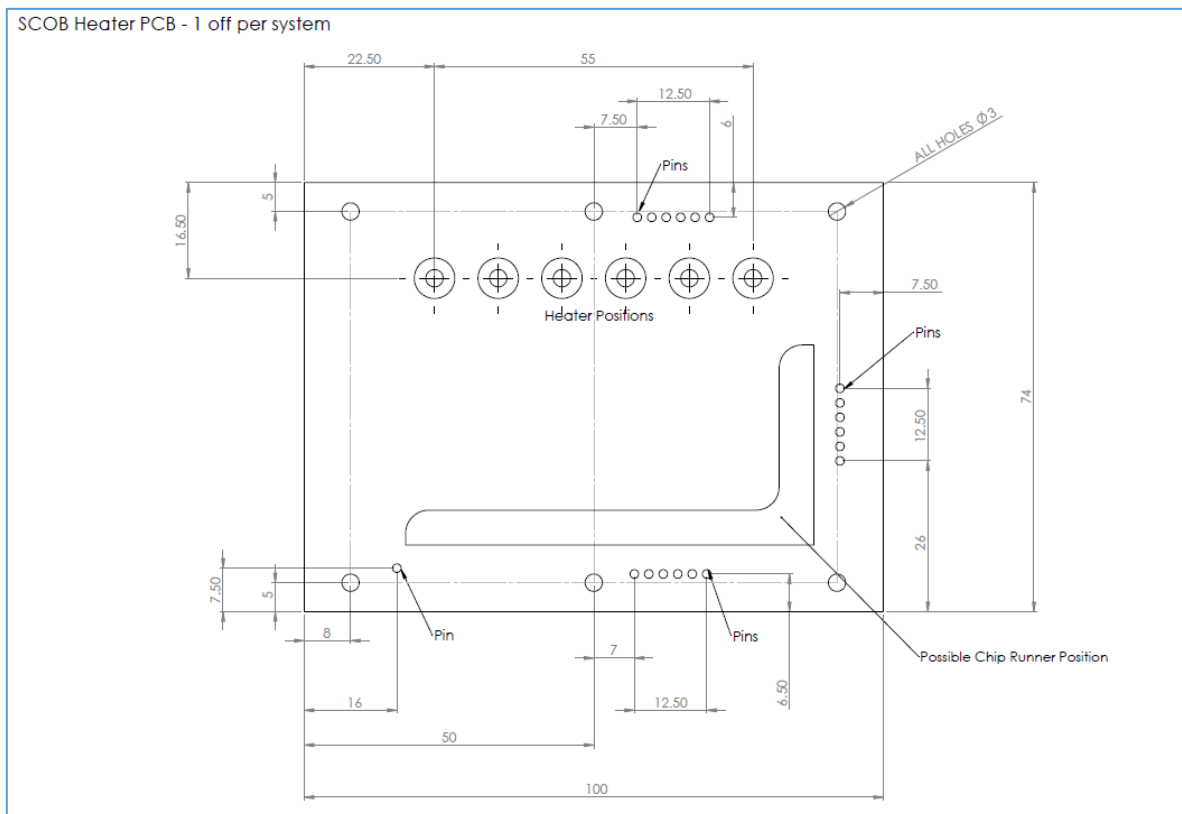
Full system overview drawing for preclinical prototype development:



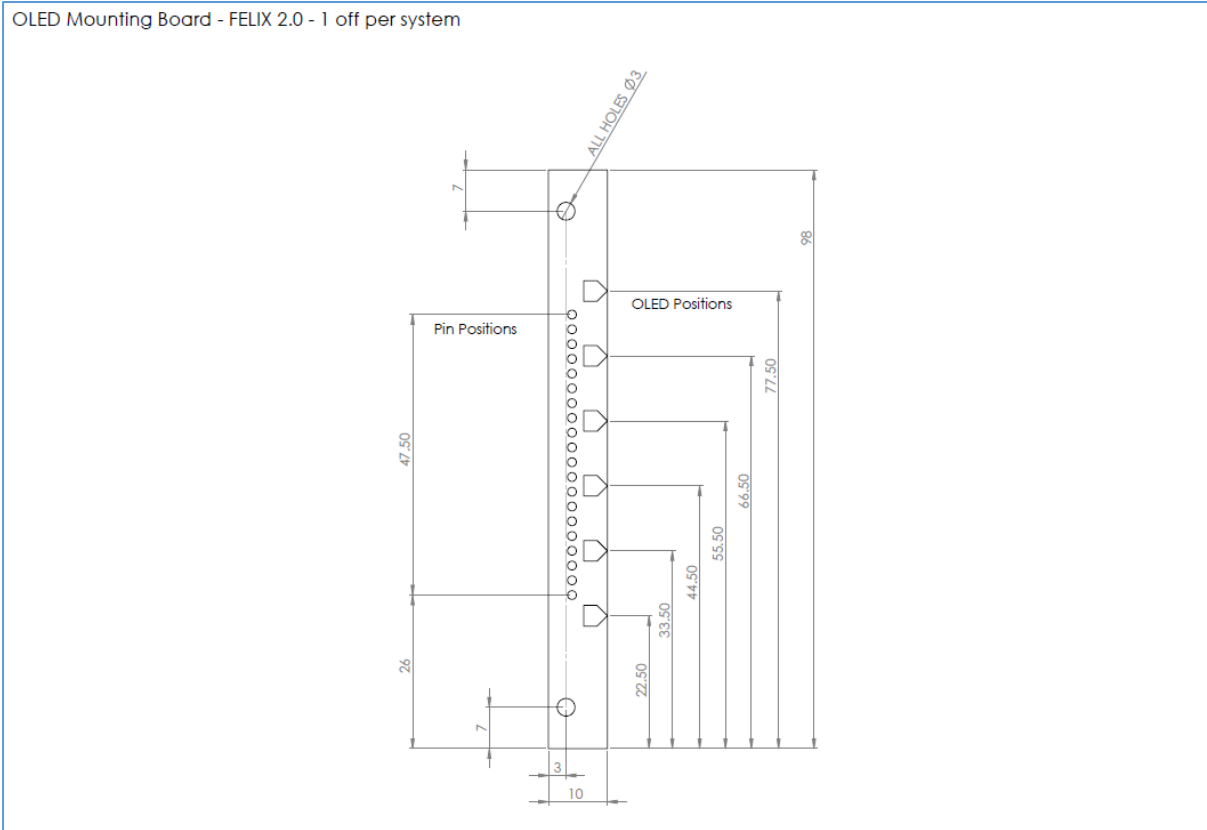
Photodiode PCB layout schematic:



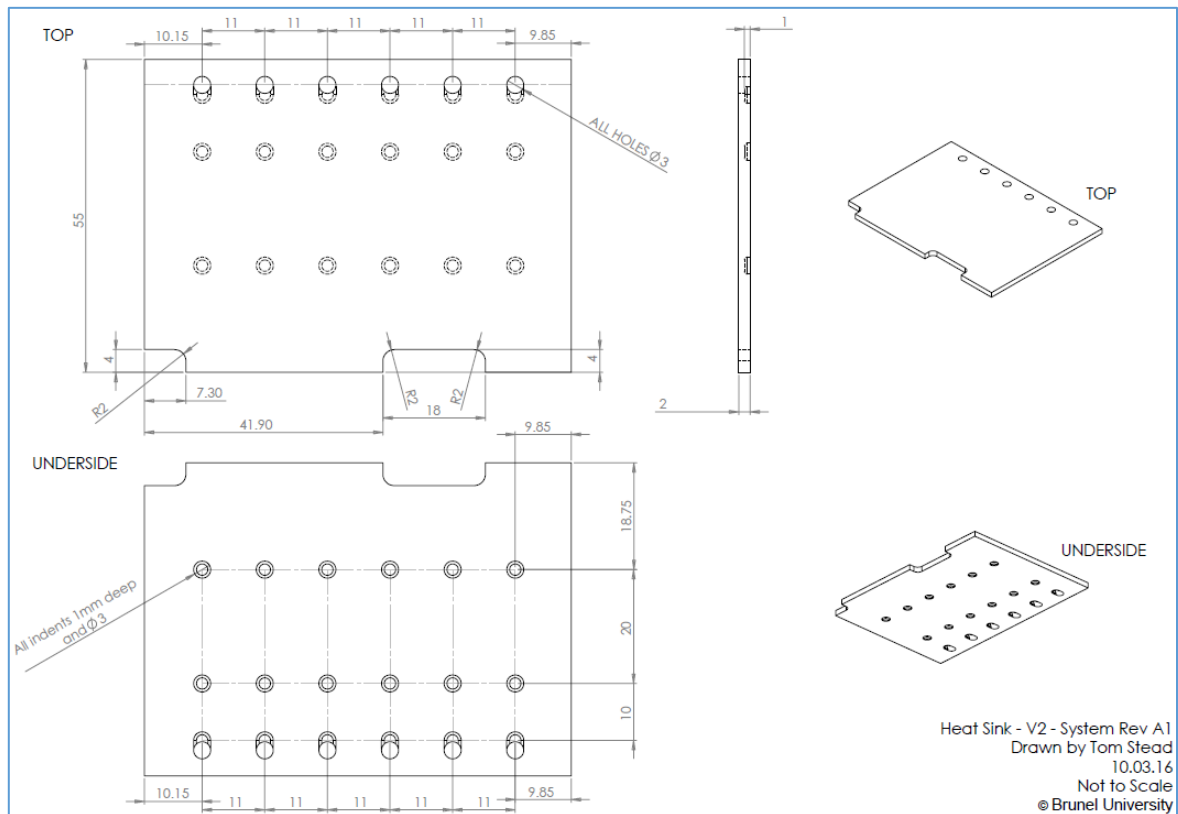
Heater PCB layout schematic:



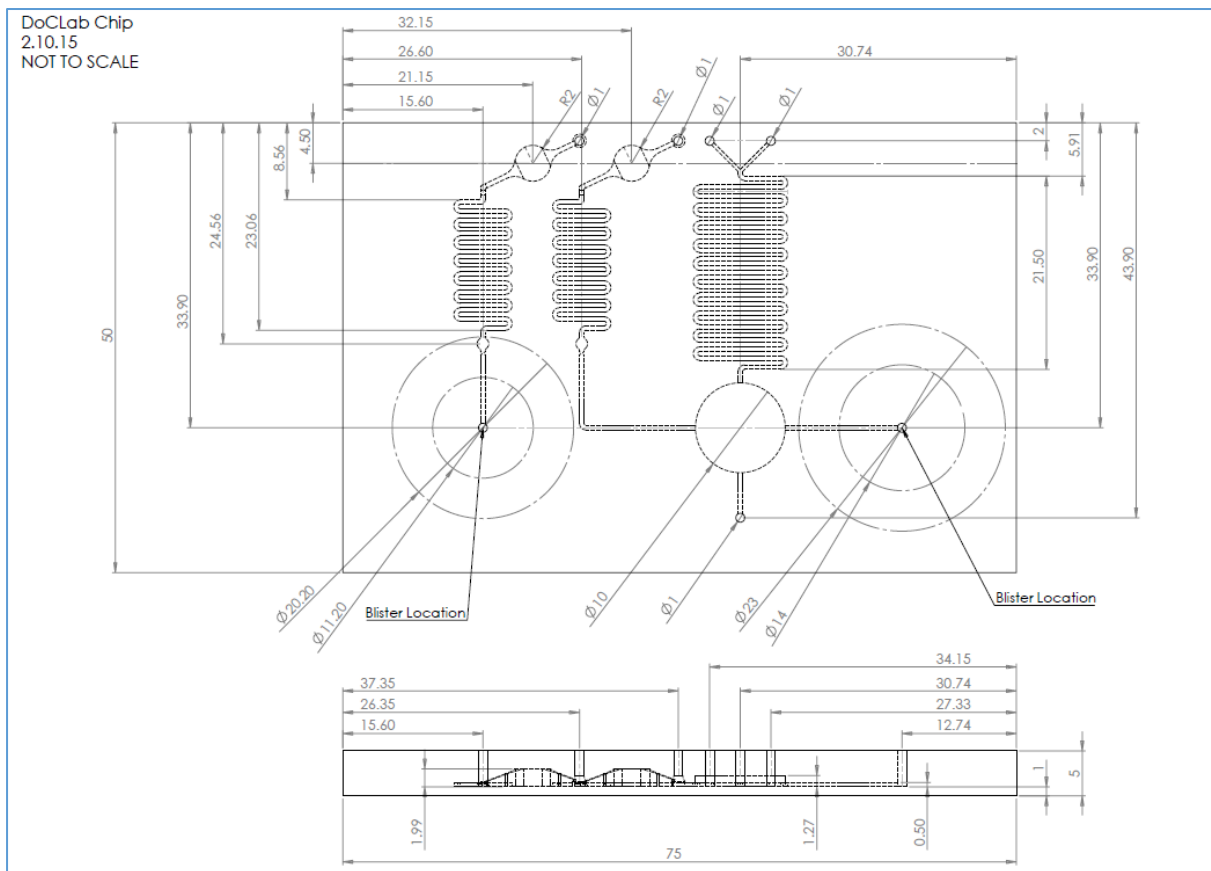
OLED mounting board layout:



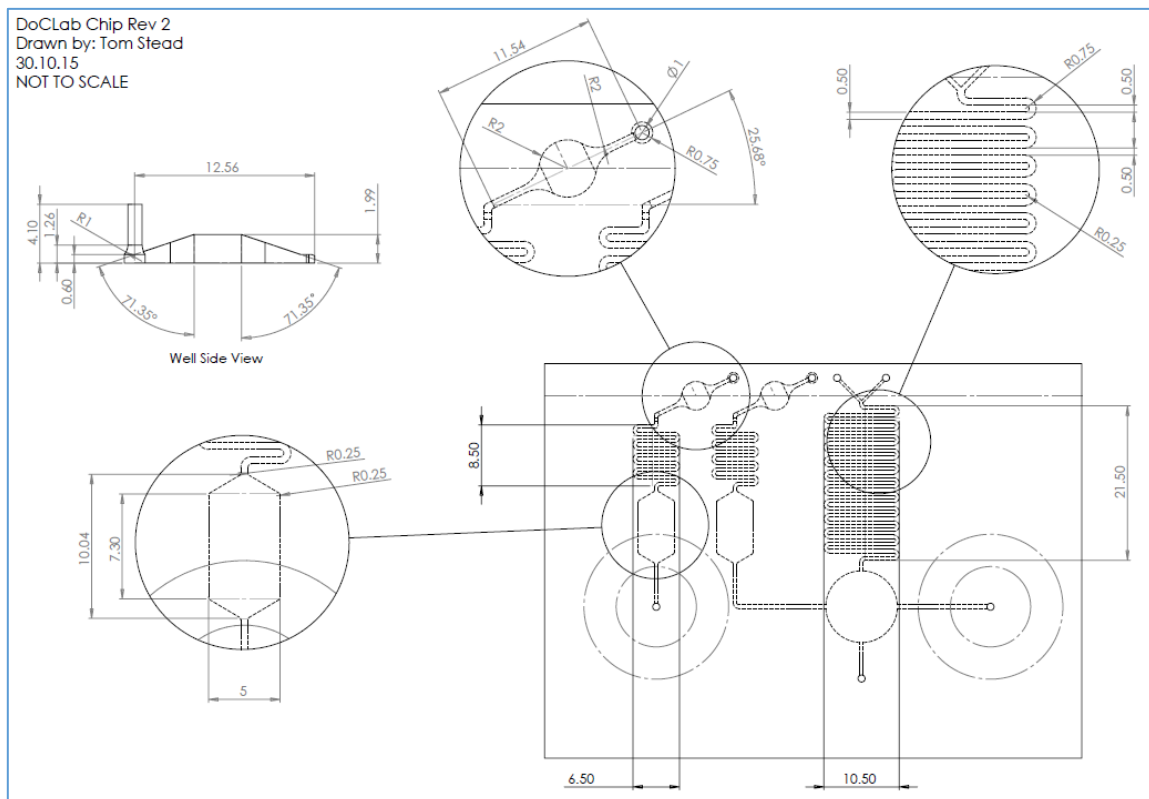
Milled heat sink drawing:



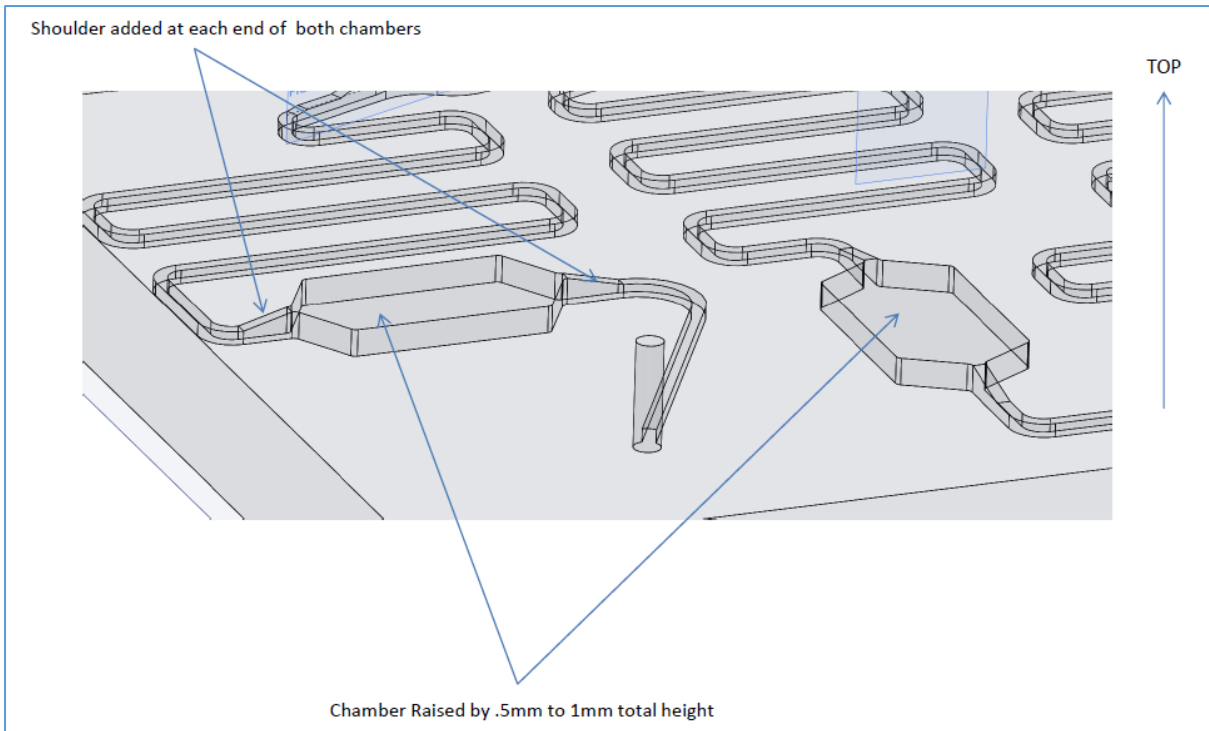
Prototype microfluidic chip layout:



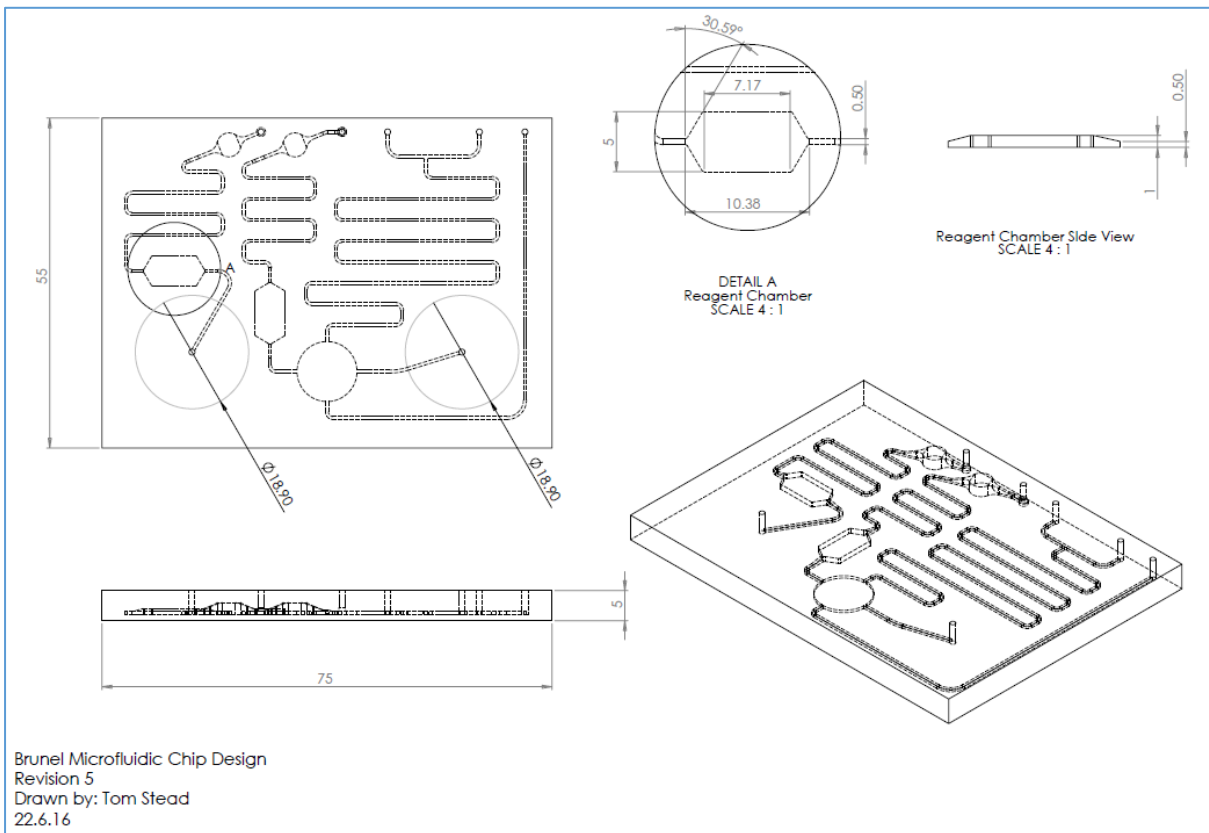
Prototype microfluidic chip detail schematic:



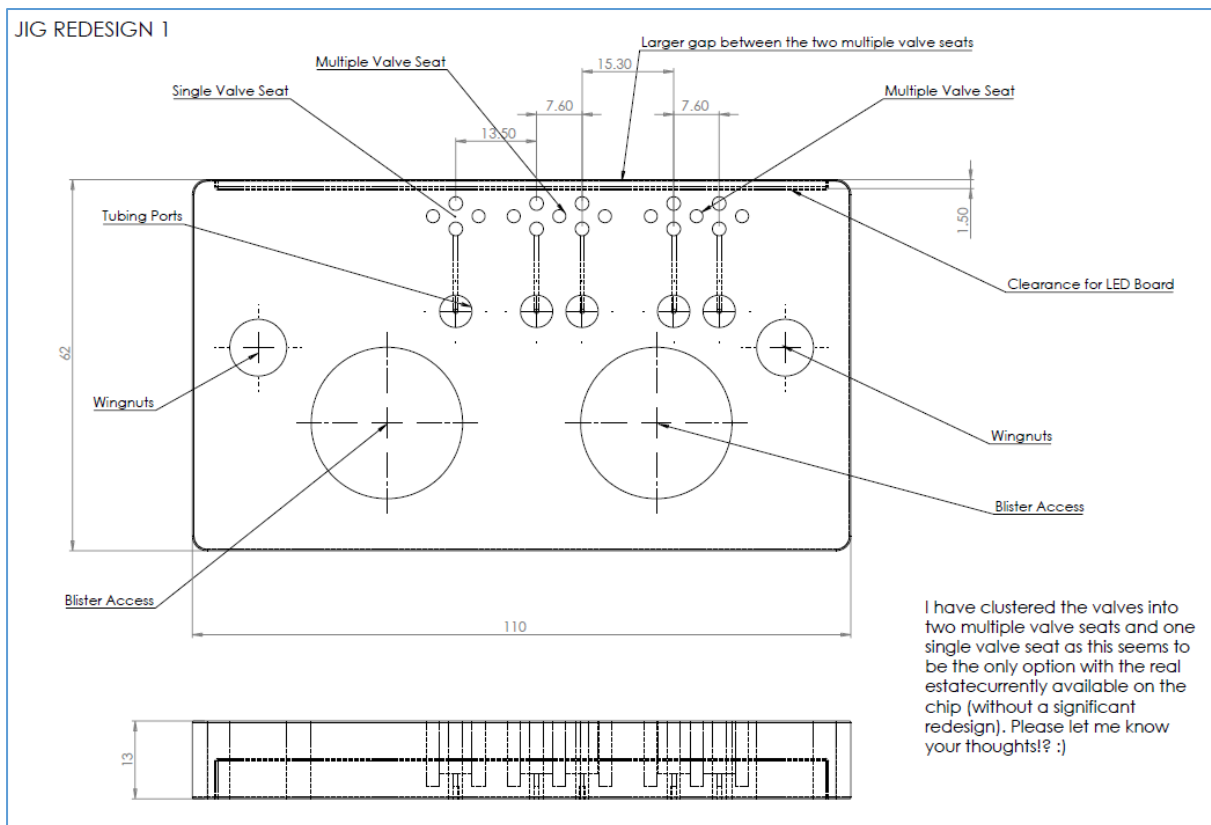
Reagent chamber adjustment for manufacturing prototype:



Manufacturing prototype microfluidic chip:



Fluidics module jig layout:



Fluidics module jig final version with actuator mountings:

