**Institution:** University of Bath

**Unit of Assessment:** 8 Chemistry

**Title of case study:** "Test and Treat" diagnostics for infectious diseases

**Period when the underpinning research was undertaken:** The relevant initial work was carried out in 2001-2005, with initial publication in 2004 and subsequently developed further forming the subject of patent applications and continued collaborative funding 2005-2018.

**Details of staff conducting the underpinning research from the submitting unit:**

| Name(s): | Role(s) (e.g. job title): | Period(s) employed by submitting HEI: |
|---|---|---|
| Christopher Frost | Professor of Organic Chemistry, previously Reader and Senior Lecturer | September 1996 – present |
| Toby Jenkins | Professor of Biophysical Chemistry, previously Reader, Senior Lecturer and Lecturer | September 2000 - present |
| Laurie Peter | Professor of Physical Chemistry | September 1993 – March 2020 |
| Frank Marken | Professor of Physical Chemistry, previously Reader and Senior Lecturer | September 2004 - present |
| Barrie Marsh | Lecturer, previously Research Officer | February 2008 – February 2010; October 2011 to September 2018; February 2019 – May 2019; September 2019 – present |

**Period when the claimed impact occurred:** 2014 – 2020

**Is this case study continued from a case study submitted in 2014?** N

## 1. Summary of the impact

Research at the University of Bath into the development of oligonucleotide sensors using electrochemical signals led, in the REF period, to:

- USD55,000,000 of new venture capital investment in a spin out company, Binx Health (formally Atlas Genetics), to make a total of USD115,000,000 raised by the company since its formation;
- The development of US Food and Drug Administration (FDA) and European CE Mark approved point of care test for sexually transmitted infections, chlamydia and gonorrhoea in 2019. By delivering accurate results within 30 minutes, this platform allows patients to receive treatment immediately, stemming the further spread of disease.

## 2. Underpinning research (indicative maximum 500 words)

The World Health Organization (WHO) estimates each year there are 127,000,000 new chlamydia and 87,000,000 new gonorrhoea infections globally. It is common for sexually transmitted infections (STIs) to be present without visible symptoms. With current central laboratory testing, patients can receive their results anywhere from 2 to 14 days later, which contributes to the onward transmission and rapid spread of STIs. Rapid diagnosis of sexually transmitted infections is required to ensure patients obtain diagnosis and comply with treatment prior to having further sexual contact. It is recognised that a significant proportion of patients

seeking treatment at sexual health clinics following initial consultation and genital swabbing do not wait for their results, and thus can become key transfection nodes in the epidemiology of STI infection though a population. However, a rapid test (less than 30 minutes) should ensure patients remain in-situ to receive a diagnosis and treatment plan. This is the rationale for Binx Healthcare's rapid STI test.

Professor Chris Frost leads research into the synthesis of electrochemically active ferrocene labels incorporating sites for conjugation to peptides and oligonucleotides. The detection of specific oligonucleotide sequences using electrochemistry has significant advantages over existing optical technology: no need for optical sample transparency; direct signal read-out; ease of miniaturisation and low-cost device manufacture with potential point-of-care (POC) applications. University of Bath research since 2001 developed an oligonucleotide sensor based on electrochemical detection, with an assay based on the appearance of a distinct electrochemical signal when a ferrocene label is cleaved from an oligonucleotide probe. The higher diffusion mobility and enhanced access of the enzymatically cleaved ferrocene label to the electrode surface results in an increase in ferrocene oxidation current. The labelled oligonucleotide probe is designed with a complementary sequence to a unique section of target DNA and by treating with an exonuclease enzyme that selectively digests hybridised DNA, the cleavage of the label from the probe and appearance of a signal occurs *only when the target is present.* This allows the sensing of any particular oligonucleotide sequence by a sensitive and rapid "switch on" electrochemical signal [1,2]. The ferrocene labels were designed and prepared in Bath and the initial research followed by collaborative knowledge transfer funding generated key intellectual property for a simple, widely applicable assay for detecting DNA targets [3-5].

This research led to the launch of a University spin out Atlas Genetics in 2005 (renamed Binx Health in 2018), to develop ultra-rapid point-of-care tests for infectious diseases based on the described ferrocene reagents and electrochemical assay [1-6]. The platform consists of a small, benchtop instrument and single-use, assay-specific cartridge that can process an unprocessed patient sample with no user interaction once the sample is added to the cartridge. The cartridge has the ability to test for up to 24 targets. To achieve this requires multiple ferrocene labels that produce unique electrochemical signals. Using specific chemical methodology, University of Bath researchers were able to modify ferrocene to afford access to novel compounds with distinct oxidation potentials [3,4]. The successful development of the requisite multiplex ferrocene labels for attachment to oligonucleotide probes for the detection of chlamydia (CT) and gonorrhoea (NG) has been led by Frost at University of Bath during the REF period with the establishment of a new post for a senior chemist, 3 days per week at Bath and 2 days per week at Binx Health.

## 3. References to the research

[1] Hillier, SC, Flower, SE, Frost, CG, Jenkins, ATA, Keay, R, Braven, H & Clarkson, J 2004, 'An electrochemical gene detection assay utilising T7 exonuclease activity on complementary probe-target oligonucleotide sequences', *Electrochemistry Communications*, vol. 6, no. 12, pp. 1227-1232. https://doi.org/10.1016/j.elecom.2004.09.019

[2] Hillier, SC, Frost, CG, Jenkins, ATA, Braven, HT, Keay, RW, Flower, SE & Clarkson, JM 2004, 'An electrochemical study of enzymatic oligonucleotide digestion', *Bioelectrochemistry*, vol. 63, no. 1-2, pp. 307-310. https://doi.org/10.1016/j.bioelechem.2003.10.028

[3] Marsh, B, Frost, C & Pearce, D Dec. 27 2013, *1,1 '-[[(SUBSTITUTED ALKYL)IMINO]BIS(ALKYLENE)]BIS-FERROCENES AND THEIR USE IN I ELECTROCHEMICAL ASSAYS BY LABELLING SUBSTRATES OF INTEREST*, Patent No. WO2013190328(A1). https://worldwide.espacenet.com/publicationDetails/biblio?II=0&ND=3&adjacent=true&locale=en_EP&FT=D&dat

[4] Marsh, B, Sharp, J, Flower, S & Frost, C Jun. 28 2012, *Novel Ferrocene Labels For Electrochemical Assay and Their Use in Analytical Methods*, Patent No. WO 2012/085591 A1. http://worldwide.espacenet.com/publicationDetails/biblio?CC=WO&NR=2012085591A1&KC=A1&FT=D&ND=3

[5] Marsh, B, Frost, C & Sharp, J Apr. 16 2015, *Labelling compounds and their use in assays*, Patent No. WO2015052516A1. https://worldwide.espacenet.com/publicationDetails/biblio?II=0&ND=3&adjacent=true&locale=en_EP&FT=D&da

[6] Marsh, BJ, Hampton, L, Goggins, S & Frost, CG 2014, 'Fine-tuning of ferrocene redox potentials towards multiplex DNA detection', *New Journal of Chemistry*, vol. 38, no. 11, pp. 5260-5263. https://doi.org/10.1039/c4nj01050g

**Funding**

G1: TCS Programme grant (Company partner-Molecular Sensing plc, 2001-2003). Value GBP94,320. Title-*To develop the synthesis of redox active chemical probes and investigate their application in the sequence specific detection of DNA*. Prof C. G. Frost (PI) Other investigators-Dr John Clarkson (MS), Dr Toby Jenkins (Bath); KTP Programme grant (Company partner-Molecular Sensing plc, 2005-2008). Value GBP150,930. Title-*To develop the synthesis of redox active chemical probes and investigate their application in the sequence specific detection of DNA*. Prof C. G. Frost (Co-I) Other investigators-Dr John Clarkson (MS), Dr Toby Jenkins (Bath).

G2: Direct industrial funding from Binx Health to University of Bath (2011-2018). Value GBP420,480 for the project *The Synthesis of Multiplex Labels For Point-of-Care Diagnostics*. Prof C. G. Frost (PI).

## 4. Details of the impact

Binx *io* is a small, desktop instrument that processes a single-use, assay-specific cartridge for the detection of sexually transmitted infections (STIs) with no sample preparation necessary. The point of care (POC) instrument developed by Binx Health combines ultra-rapid, polymerase chain reaction (PCR) amplification with sensitive electrochemical detection technology developed by Bath Chemistry. Binx *io* is fully automated and easy to use. Simply load the cartridge into the device and in about 30 minutes, the *io* provides easy-to-understand results allowing “test and treat” to become a reality.


Key impacts from this work are investment, people and a new technology

- SME has generated investment raising a total of USD55,000,000 venture capital investment (Series C in 2015 and Series D in 2017) [C];
- Creation of highly skilled jobs (growing to 43 FTE), recruitment of industry leaders, including from an environment for career development (KTP Associate with University of Bath progressed to Chief Technical Officer) [B];
- A new diagnostic technology has been tested and approved for sale (successful clinical trials of the binx *io* platform in 2019 led to European CE Mark approval and FDA 510(k) clearance in the US to test and treat women for chlamydia and gonorrhoea) [I].

**The Chief Technical Officer at Binx Health** said: “*In August 2019, we received 510(k) regulatory clearance from the U.S. Food and Drug Administration for our chlamydia and gonorrhoea test (CT/NG). This marks a huge milestone for the company, and one drawn from*

*many years of development from the original research at Bath. The key contribution from the Chemistry collaboration has been the design and synthesis of novel ferrocene labels that can be tagged onto different target oligonucleotide sequences and used in a multiplex assay as in the CT/NG test*" [A].

**Economic, Wealth and Opportunity Creation**

Atlas Genetics was launched in 2005 with GBP500,000 initial funding, 50% of which came from the Sulis Seedcorn Fund, established by the University of Bath to provide support for new businesses. Since 2014, the diagnostic platform incorporating the Bath electrochemical technology has been manufactured, tested and approved for sale. In 2018, the company rebranded to Binx Health in preparation for the global launch of the POC platform, the binx io. Concurrently, the company opened an office in Boston, US to focus on delivering successful clinical trials, sales and marketing in the US. The company also added healthcare leaders in new roles on the management team [B]. The number of full-time staff across both sites increased to 43, the majority of whom have higher education qualifications in science (MSc/PhD), engineering (BEng/MEng) or business (MBA).

Binx Health is currently venture capital funded and to date has raised approximately USD115,000,000. During the REF period this has included completion of Series C (in 2015) and Series D (in 2017) financing, raising USD55,000,000 to specifically fund the clinical trials, device manufacture and commercial launch of a dual test for the electrochemical detection of chlamydia and gonorrhoea [C].

The *io* cartridge was developed in collaboration with Bespak, a global market leader in the development and manufacture of medical devices. The manufacturing line for the *io* cartridge has been established within dedicated purpose-build ISO Class 8 cleanroom at the Bespak site in Kings Lynn, UK. This strategic investment in UK manufacturing will facilitate the future scale-up in capacity for Binx products [D].

**Clinical Implementation**

The electrochemical technology at the core of the binx *io* tests offer a time-to-result turnaround of less than 30 minutes, which enables the opportunity to test and treat in near-patient settings reducing the spread of infections for millions who require screening under medical guidelines. The pathway to regulatory clearance and European CE Mark approval has involved clinical trials with Public Health England (PHE) and the National Institutes of Health (NIH) in the US [E]. In 2018, a team at Johns Hopkins University tested binx's rapid POC test for chlamydia at clinics in Maryland and Ohio. The study, consisting of 296 recruited patients, determined the binx test provided an accurate positive result 93% of the time and an accurate negative result 99% of the time for vaginal self-obtained swabs [F]. In 2019, the company completed a 1,523-person, multi-centre clinical study on the binx *io* in a POC setting. The outstanding results showed a 96.1% sensitivity and 99.1% specificity for chlamydia and 100% sensitivity and 99.9% specificity for gonorrhoea in women tested. Binx received its CE Mark for CT/NG (Chlamydia trachomatis/Neisseria gonorrhoeae) in May 2019 [G] and FDA 510(k) clearance in August 2019 [H, I].

In the first "real world" use, a collaboration with 3 NHS Trusts and St. Georges University of London, the binx *io* platform is being used by clinicians to diagnose patients who otherwise would have faced up to several days of delay between infection, identification and treatment. **Clinical consultant Lewisham and Greenwich NHS Trust** said: "*So far, we have tested about 90 patients, have had 17 CT and two NG positives and were able to provide the right antibiotic in a single visit. British Association of Sexual Health and HIV quality standards suggest treatment within three weeks of testing. We can now provide the right antibiotic in one visit. This is game-changing for us*" [J].

## 5. Sources to corroborate the impact

[A] Letter of evidence of impact, CTO Binx Health. 18 September 2020

[B] Company rebranding to Binx Health and key talent added to workforce. https://mybinxhealth.com/news/atlas-genetics-announces-company-rebranding-changes-name-to-binx-health/

[C] Series C (in 2015) and Series D (in 2017) financing *raises $55 million* to finance the clinical trials and commercial launch of a test for the detection of both chlamydia and gonorrhoea. https://mybinxhealth.com/news/atlas-genetics-raises-35m-in-series-d-fundraising/

[D] Development of io cartridge and establishment of manufacturing capability at Bespak UK. https://www.consortmedical.com/news/atlas-completes-development-io-cartridge/

[E] February 2016 – Proprietary chlamydia test receives European CE Mark approval. https://www.prnewswire.com/news-releases/atlas-genetics-gains-ce-approval-for-first-product-567999661.html

[F] November 2018 – Completion of a successful pilot study for binx' rapid POC test for chlamydia funded by the United States' NIH's National Institute of Biomedical Imaging and Bioengineering (NIBIB). Widdice, LE, Hsieh Y, Silver B, Barnes M, Barnes P, Gaydos CA. (2018), 45, 723. Sex Transm Dis. *Performance of the Atlas Genetics Rapid Test for Chlamydia trachomatis and Women's Attitudes Toward Point-Of-Care Testing*. DOI: 10.1097/OLQ.0000000000000865 https://www.nibib.nih.gov/news-events/newsroom/new-chlamydia-test-delivers-results-about-30-minutes/

[G] May 2019 – Proprietary CT/NG test receives European CE Mark approval. https://mybinxhealth.com/news/binx-health-receives-ce-mark-for-rapid-chlamydia-and-gonorrhea-test-for-mass-markets/

[H] August 2019 – Following completion of *successful multi-centre clinical trial* for the dual CT/NG test, Binx Health received 510(k) clearance from the U.S. FDA to market the binx *io* platform to test and treat women for a dual CT/NG test. https://mybinxhealth.com/news/binx-health-receives-fda-510k-clearance-for-rapid-point-of-care-platform-for-womens-health/

[I] August 2019 - FDA 510k clearance for the binx *io* platform: https://www.fda.gov/medical-devices/510k-clearances/august-2019-510k-clearances

[J] Sep 2019 – First real-world use of the binx *io platform*, delivering *same-visit diagnosis and treatment* for chlamydia and gonorrhoea. https://mybinxhealth.com/news/binx-health-announces-first-patients-benefiting-from-single-visit-test-and-treatment-for-chlamydia-and-gonorrhea/