

The Pathogen Genomics Delivery Plan for Wales 2026-2029

<FOREWARD – To be added>

1. Setting the scene: why are we doing this and where are we now?

Pathogen Genomics was established as a capability in the NHS in Wales in 2016, with the aim of delivering services for HIV and TB/NTM diagnostics in Wales. Since the 2017 Welsh Government Genomics for Precision Medicine strategy, Wales has seen a transformation in its ability to generate and utilise pathogen genomic data at a range of scales – from patient to population.

Working as part of Genomics Partnership Wales (GPW), the Public Health Wales Pathogen Genomics Unit (PenGU) has built a set of ISO accredited pathogen genomics services, which have collectively sequenced pathogens from more than 300,000 Welsh patients since its inception. This work has been co-created, involving staff from across the NHS in Wales, as well as our patients and the Welsh public, in addition to collaborators in academia from Wales and the wider UK.

The COVID-19 pandemic demonstrated the importance of pathogen genomics for public health and demonstrated the world leading capability that existed in Wales to use pathogen genomic data in response to a global pandemic. As we emerge from the pandemic, the pathogen genomics capability within Wales is stronger than ever before, and there is an opportunity to push on and deliver a range of benefits from the investment in pathogen genomics in Wales to date. While traumatic, the pandemic has been a foundational event in developing staff knowledge, skills, and experience, leaving Wales with a critical mass of pathogen genomics expertise that can now be harnessed to deliver benefits to the people and patients of Wales over the longer term.

This document lays out a delivery plan for Pathogen Genomics in Wales, placing the pathogen genomics capability in Wales in context, and identifying a set of key areas of activity, as we further mainstream pathogen genomics for diagnostic and public health purposes in Wales.

The COVID-19 pandemic demonstrated in stark terms the importance and value of pathogen genomics as a component of the public health and health protection response. Although the threat of COVID-19 is now receding, there remain many pathogens and associated challenges – such as antimicrobial resistance – where genomics can realise a similar impact in the coming years. Key genomic technologies, such as metagenomics, also offer the potential to develop and implement wholly new services, changing how care is delivered and improving patient outcomes. Knowing the potential, here we outline a bold plan for the development of our pathogen genomics capability in Wales, and to support wider activities in the UK, to deliver excellent services for pathogens that we face now – while also being better prepared for the threats that we will face in the future.

1.1 Wider strategic context – where does this fit?

Building on the intentions of *A Healthier Wales: long term plan for health and social care*, in September 2020, Wales signed as a partner the UK Government's strategy *Genome UK: The Future of Healthcare*. This ten-year strategy sets out the ambition for the UK to have a world-leading genomic healthcare system for the benefit of patients. In March 2022, we

committed to working collectively with our UK partners to progress our objectives over the next three years; to deliver better health outcomes, work towards the UK being the best location globally to conduct genomics research and to grow new genomics healthcare companies.

Genome UK identifies a set of aims that are specific to pathogens, with Genome UK envisaging that we will aim to:

- Sequence pathogens quickly and easily using point of care sequencing technology, helping us control outbreaks and fight antimicrobial resistance.
- Understand the role of the genome in differing patient outcomes from infectious disease.
- Rapidly utilise advances in sequencing technology to develop and deploy new diagnostics and support better, more integrated, surveillance of infectious diseases.
- Provide international leadership in supporting the development of best practice in infectious disease genomics and public health, through international projects such as the Global Alliance for Genomic Health, the Public Health Alliance for Genomic Epidemiology.

Further, aims within Genome UK relating to evaluation of technologies/approaches, co-production and co-creation with clinical stakeholders and pharmacogenomics are also all relevant to pathogen genomics activity.

Genomic advancements involve both devolved and reserved functions of government; for example, health is devolved whilst other areas such as ethics and Medicines & Healthcare products Regulatory Agency are not. *Genome UK: Shared Commitments for UK-wide implementation 2022 to 2025* details how the four nations will work together for the next three years, and this delivery plan expands on how we will deliver genomics for Wales during this period.

In 2022, Welsh Government published its Genomics Delivery Plan for Wales, articulating a plan of action that will realise a vision of partnership across government, healthcare, academia, and industry focused on “Working together to harness the potential of genomics to improve the health, wellbeing and prosperity of the people of Wales”.

The combination of decreasing sequencing costs combined with increasing computational power create a range of opportunities to realise the potential of pathogen genomics in Wales. Wales already hosts a set of world-leading pathogen genomics services and sits at the heart of a wider ecosystem in Wales and the UK which offers significant potential for growth and development.

As part of the Genomics Delivery Plan for Wales for 2022-2025, Welsh Government included an objective to develop a Pathogen Genomics Delivery Plan, recognising the distinctive opportunities for the use of genomics with respect to infectious disease, while also providing a basis for Wales to meet its obligations under the shared commitments, and realise the objectives articulated within Genome UK. This document is the realisation of work undertaken under the Genomics Delivery Plan for Wales to provide a unified and coordinated plan for the delivery of pathogen genomics clinical and public health services in Wales. It forms part of a group of delivery plans relating to different aspects of genomics in Wales, all of which have the ultimate aim of developing our genomic capabilities and mainstreaming the use of genomics across the healthcare system.

1.2 The potential of pathogen genomics

Pathogen genomics provides the best lens through which pathogens can be characterised and analysed. Pathogen genomics can be used at many scales – from patient to population – simultaneously, by different parts of the healthcare and public health system. In essence, genomic data is one of the key locks we must unpick to enable true precision public health – to enable the right intervention, in the right population at the right time.

Over the course of the SARS-CoV-2 pandemic, the value of pathogen genomics was demonstrated globally. Wales played a leading role internationally in early work to use genomics to understand what was a human pathogen that was new to science. Wales sequenced a higher proportion of its positive cases (~25%) than any other UK nation and was in the top 5 nations in the world for sequencing coverage of positive cases. This information was used at every level – from patient management in immunocompromised individuals through to national- and global-level analysis to detect trends in the viral population that pointed to the emergence of new variants.

The SARS-CoV-2 pandemic is a timely reminder of the potential of pathogen genomics to inform healthcare and public health at multiple scales, and points towards the larger potential of pathogen genomics to improve our population-wide understanding of infectious disease. This improved understanding creates opportunities to improve existing services and develop new approaches to old problems. Insight from pathogen genomics also creates opportunities for prevention – which is particularly important in the case of vaccine development and vaccine preventable diseases, as well as in system-wide challenges such as antimicrobial resistance and hospital acquired infection.

It is also important to note that there are many infectious diseases – such as TB – where both the probability of being infected and the severity of outcomes are directly linked to social determinants of health and health inequalities. Societal issues such as those that relate to housing, economic deprivation, educational attainment, and diet all have direct impacts on infectious disease, and therefore pathogen genomics provides an opportunity to reduce inequalities in healthcare both through understanding transmission and preventing disease, and through providing better diagnostics and treatment pathways, leading to better outcomes when individuals are infected.

Alongside the applications of pathogen genomics in healthcare, genomics is also emerging as a cornerstone of efforts to improve the UK's biological security, with genomics playing a prominent role as part of the delivery of outcomes 9, 10 and 11 of the UK Biological Security Strategy. This work exists to enhance the ability of the UK as a whole to detect and respond to biological threats, and requires a whole-system, whole-UK collaborative effort, in which pathogen genomics has a key part to play.

There are literally thousands of potential pathogen species, and the potential applications of pathogen genomics are therefore similarly enormous in scale. Understanding this, it is vital to have the right structures in place to identify where to apply effort, combined with core capabilities that enable a rapid response to any urgent threat. Wales was able to stand up its SARS-CoV-2 sequencing within 24 hours of being asked because it possessed an interdisciplinary team that had built a modular sequencing and analysis system to enable an agile response to new threats. Wales was able to contribute to the research response to the pandemic through partnerships that had been built over the course of years with key academic groups across the UK. Wales possesses a mature pathogen genomics capability – and what is needed now is a plan to enable that to be built upon in a sustainable way, to ensure that the people and patients of Wales can reap the benefits of this technology.

1.3 Our Journey so far and our Pathogen Genomics Ecosystem

Within Wales, pathogen genomics services are delivered on an All-Wales basis by Public Health Wales (PHW). Whole genome sequencing capacity was first established within PHW in 2016, following the purchase of a set of MiSeq instruments, with a view to providing genomics services for HIV and TB. This early-stage work then formed part of the basis of the Welsh Government 2017 Genomics for Precision Medicine Strategy, which saw the formation, in 2018, of Genomics Partnership Wales to deliver that strategy. 2018 also saw the formation of a Pathogen Genomics Unit within PHW, to undertake the pathogen genomics work that was envisaged.

From the small team that existed in 2018, Wales has developed a set of clinical pathogen genomics services accredited to ISO 15189 standard including HIV and TB. In addition to these originally planned services, Wales has built a world-first ISO accredited service for typing *C. difficile* using genomics, and the first ISO 15189 accredited end-to-end SARS-CoV-2 genomics service in the UK – both of which were developed and launched during the pandemic, as well as providing genomics services to support surveillance (e.g., Influenza) and outbreak response. Some of the key services that we provide relate to pathogens that are particularly significant for communities (LGBTQ+) or those with risk factors (age, poverty) which could lead to inequalities in access, treatment, and outcomes.

Within Wales, the pathogen genomics ecosystem includes research activity at universities including Aberystwyth, Bangor, Swansea, Cardiff University and Cardiff Metropolitan University. More broadly, Welsh pathogen genomics data is globally shared, and research and public health collaborations exist between Welsh pathogen genomics professionals and those in the three other nations of the UK and globally. There is extensive collaboration with the other UK public health agencies, and Wales currently provides routine TB genomic services for the South West of England. Wales has also provided expertise to support the development of services in Northern Ireland, and frequently collaborates with Scotland and England in the genomics space.

Underpinning this is the modular sequencing and analysis platform that has been built by the Pathogen genomics team in Wales. This platform lowers the barrier to implementing and operating new services, which combined with an integrated microbiological laboratory network creates an environment that enable agile action, and the delivery of precision public health.

1.4 Our vision and guiding principles

Our first guiding principle is that we will work in an open and transparent manner with patients and the public, using their collective experiences to shape and add value to the work of the Genomics Partnership and future genomics services in Wales. The foundation of our work is our patients and the wider public, and we recognise that they are also the cornerstone of our success to date.

Placing our patients and the public at the heart of what we do, we will adopt and make use of the same three-layered approach as outlined in the Genomics Delivery Plan for Wales. In common with other public health agencies in the UK and internationally, we recognise the challenges of ethics, data sharing and public communication and engagement, and acknowledge the significant benefits that can come from an engaged public in terms of realising better health outcomes and in reducing inequalities.

Our second guiding principle is to work in a prudent way. Doing no harm and working only where necessary. Genomics has huge potential in where it can be applied - but we must be guided by the evidence in choosing where to focus our efforts. Where evidence does not exist, we may seek to develop it - but we will always aim to follow the evidence and use this as a basis to develop our services.

While we will be guided by the evidence, our third guiding principle is to be bold in what we do, and the impacts that we aim for. Our vision for pathogen genomics is that we should be a world leader in the development and use of pathogen genomics, to protect and improve health and well-being and reduce health inequalities for the people of Wales.

As part of this, we want to realise a world class public health system where pathogen genomics data is routinely used in real-time across the gamut of public health activity.

To achieve this, our ambition is to build and embed the capability for public health genomics in the Welsh NHS to better enable the right intervention, in the right population at the right time.

Our fourth guiding principle is to work collaboratively, within the GPW partnership, and with stakeholders across Wales and the wider UK. The GPW partnership provides a structure – bringing together the Wales Gene Park and the All-Wales Medical Genomics Service along with PHW – which allows for the development of a translational pipeline, from research into practice. The unique setup in Wales provides us with significant potential to work collectively to provide innovative solutions to urgent and important problems. We recognise the public health system as multifaceted and that there are many component parts that must come together to deliver services. Only by working together can we achieve the ambitious programme of work that we have planned.

1.5 Alignment with strategic priorities

PHW, as the Welsh National Public Health Institute has a key role to play in developing Wales' pathogen genomics services and capabilities. Achieving our ambition in Pathogen Genomics aligns directly with the PHW long term strategic priority to deliver excellent public health services to protect the public and maximise population health outcomes.

We also recognise that pathogen genomics has a role to play in realising the delivery of other PHW priorities including influencing the wider determinants of health, supporting the development of a sustainable health and care system focused on prevention and early intervention, and tackling the public health effects of climate change.

In turn, pathogen genomics has a role to play in the delivery of Welsh Government strategic priorities including the HIV action plan for Wales, the Public Health Respiratory Framework, and the TB elimination plan, as well as UK government priorities such as the AMR Action Plan. We also recognise that pathogen genomics activities have the potential to contribute to other UK activities, such as PATH-SAFE and the UK Microbial Forensics Consortium – activities that require multi-sector engagement and collaborative working. Genomics is also a key technology to support the implementation of new vaccination programmes and has a critical role to play in reducing hospital acquired infections and antimicrobial resistance, which is critical to underpin efforts to prevent disease.

2. Pathogen Genomics Delivery Plan

As the need for SARS-CoV-2 sequencing reduces following the pandemic, the modular approach developed in Wales provides the opportunity for the introduction of future pathogen services.

Our ambition is to build on the established, accredited clinical pathogen genomics services already developed in Wales.

As part of the commitment outlined in the Genomics Delivery Plan for Wales 2022-2025, we outlined an objective to identify areas where the GPW partners can continue to work with stakeholders across Wales to improve patient and well-being objectives for population health by focusing on delivering a set of objectives aligned to three key areas:

- a. Infectious disease surveillance;
- b. The application of pathogen genomics to improve healthcare through transforming existing services and developing new capabilities
- c. Providing a capability to sit at the heart of future public health crisis response.

This document presents a set of specific objectives identified as part of Pathogen Genomics activity that sit across three of the themes outlined in the Genomics Delivery Plan for Wales, covering clinical services, Research and Innovation and underpinning Enablers. These objectives provide a target to aim for and set of specific measures to undertake to realise the continuing potential of pathogen genomics in Wales. This detailed plan sits alongside other specific plans – such as the Pharmacogenomics Delivery Plan – and forms part of the wider plan for developing genomics in Wales, as articulated in the Genomics Delivery Plan for Wales.

2.1 Activity under Genomics Delivery Plan for Wales, Theme 2: Clinical Services

The Genomics Delivery Plan for Wales 2022-2025 identified two deliverables that are specific to Pathogen Genomics, namely;

- To embed genomics as part of the core vision for PHW, with the creation of a cross-organisational programme for Public Health Genomics within PHW.
- Development of a Pathogen Genomics delivery plan for Wales, co-produced with stakeholders; it will provide a roadmap for the Public Health Genomics programme and provide an agreed framework for the evolution of pathogen genomics services in Wales.

From these, and the detail included in Annex 1 of the delivery plan we have identified 11 objectives within the Clinical Pathogen Genomics area, which will enable us to provide an agreed framework for the evolution of pathogen genomics services in Wales. All 11 objectives will be led by PHW, reflecting the fact that PHW hosts the majority of Wales' microbiological diagnostic laboratories, Wales' health protection and infectious disease surveillance capability, and hosts Wales' clinical pathogen genomics capability. However, many areas of activity will involve and require collaboration with other organisations and partners both within GPW and externally. While PHW is well placed to deliver in many areas, we recognise that a system-wide approach is required, and this is reflected in the activities identified under each planned objective.

2.1.1 Objective 1: Development of key structures in Pathogen Genomics to oversee work in Wales

Reflecting the growth in pathogen genomics in Wales, the Genomics Delivery Plan for Wales envisaged the mainstreaming of pathogen genomics, and deeper integration with microbiological and health protection services. As part of this, a key objective is the development of genomics as a part of the core vision for PHW. As a key enabling structure to do this, PHW has created a cross-organisational programme – that sits alongside other All-Wales programmes within PHW including the Vaccine Preventable Disease Programme (VPDP) and the Healthcare Associated Infection Programme (HARP).

The Public Health Genomics Programme brings together key subject matter experts within PHW to coordinate, develop and manage the growth of clinical and public health pathogen genomics in Wales. The programme also provides a point of strategic integration for PHW with other areas of genomics activity developed and undertaken as part of Genomics Partnership Wales.

The core Public Health Genomics Programme structure is in place, and we have established that the Public Health Genomics Programme will contribute to, and oversee, a set of objectives as part of the PHW IMTP – reflecting the mainstreaming of genomics into the business-as-usual activities within PHW. The Public Health Genomics Programme will also oversee and be responsible for the delivery of this plan, working as part of GPW, with partners across Wales.

Objective 1 focuses on the further development of the Public Health Genomics programme. To achieve Objective 1, PHW will:

ACTION: Develop additional internal structures within PHW for monitoring, management, governance, and accountability of genomics activity. These structures will form part of the Public Health Genomics Programme, with reporting both to the PHW board and to the GPW programme and governance boards.

ACTION: The development of a working model for the PHW Public Health Genomics Programme to provide a new point of integration with GPW and Welsh Government.

2.1.2 Objective 2: Improvement of existing pathogen genomics services

Wales already hosts a set of pathogen genomics services. These services are amongst the most advanced of their type in the world, but as part of the Duty of Quality, we must ensure that Wales continually develops and improve these services. Specifically, to achieve this objective, PHW will;

ACTION: Improve Mycobacterial services through Wales- and UK-wide collaboration and development.

ACTION: Improve *C. difficile* service through the development of tools for local management of IP&C and to improve surveillance.

ACTION: Develop and implement standardised software platforms for cluster tracking.

ACTION: Achieve improvements to existing service through developing underpinning service elements.

2.1.3 Objective 3: Pandemic Preparedness and Response to Threats

Developing pathogen services that could be applied to outbreaks, epidemics and pandemics has always been an implicit part of business-as-usual activity for Pathogen Genomics in

Wales. The appropriateness of the systems that were put in place within PHW with respect to genomics for pandemic preparedness was evidenced by the commencing of sequencing within 24 hours of the request being made by PHW GOLD, and then the scaling up rapidly to the point where Wales was consistently in the top 3 countries globally for the coverage and number of SARS-CoV-2 genomes sequenced over the course of the pandemic.

The COVID-19 pandemic demonstrated the importance of genomics in every level of the pandemic response, and while pandemic planning with respect to genomics to date has been more implicit, as a lesson learnt from the pandemic, we will make explicit how we are developing our capabilities to support future pandemic and epidemic response. In particular, PHW specifically and GPW as a whole will seek to act upon relevant recommendations from the COVID-19 enquiry, in addition to acting on our own 'lessons learnt' to ensure that Wales is even better placed to respond to future threats. This work will particularly encompass ensuring that pathogen genomics services are pandemic ready and developing the collaborative links so that Wales is ready when we need to engage partners in a crisis.

Specifically, to deliver this objective, PHW has identified a set of activities that will include;

ACTION: Identify and implement measures for improved pandemic preparedness following the COVID-19 pandemic, including implementing recommendations from the COVID-19 Inquiry.

ACTION: Implementation of metagenomics and rapidly-deployable sequencing services in Wales to support our pandemic and threat preparedness. This covers;

ACTION: Develop our collaborative links with academia and industry to enhance our preparedness and ability to respond to urgent threats. This includes;

ACTION: Develop the ability of genomic data to be generated and used across PHW and ensure that knowledge gained from the development and operation of genomics services is retained. Key activities to embed genomics as part of our overall preparedness include;

ACTION: Contribute our expertise and engage with UK Government initiatives relating to Biological Security, in particular the UK Microbial Forensics consortium (UKMFC), to support the development of UK capabilities that will detect and respond to future threats.

2.1.4 Objective 4: Planning for new pathogen genomics services, building on existing Welsh expertise

Wales currently hosts a set of specialist microbiological laboratories that have international standing and expertise. Building on existing UK-wide reference laboratory services delivered in Wales is critical both to deliver UK-wide benefits for key areas of activity, and to provide an environment that secures this Welsh expertise into the future. From this, we have identified three key areas where PHW will work to bring genomics services to key reference laboratory services:

ACTION: Develop and aim to introduce genomics into routine Cryptosporidium and Toxoplasma outbreak characterisation work, based at the UK Reference Laboratory in Swansea.

ACTION: Scope potential fungal genomics services, and develop an implementation plan where appropriate to be taken forward for new Mycology Genomics Services in Wales.

ACTION: Extend anaerobic genomics in Wales as part of the UK Anaerobe Reference Unit beyond *C. difficile*, to develop accredited genomic services for other anaerobic pathogens, and to support the development of a Faecal Microbiota Transplant (FMT) bank for Wales.

ACTION: Audit current genomic services in Wales, and examine the cost and performance of the services provided, to identify if there is a case for repatriation into Wales. Where better value would be provided through repatriation, we will begin the process of developing the services to make this happen.

2.1.5 Objective 5: Developing transformational new pathogen genomics-based services

Engagement with stakeholders across Wales to identify and plan out opportunities for transformational services that genomics enables, for example in sexual health, which could be developed and delivered in Wales;

Specifically, to achieve this objective PHW will:

ACTION: Engage with stakeholders across the NHS, academia, industry and charities to identify key microbiological services that need transformation, and where genomics could play a key role.

ACTION: Undertake preliminary work to identify how genomics could be used for STI diagnostics and health protection. The preliminary analysis will be followed by the development of an implementation plan for putting STI genomics into service in Wales.

ACTION: Identify current evidence gaps and needs with respect to the use of metataxonomics and metagenomics in clinical service. Alongside this work, PHW will develop its capacity to perform close to patient sequencing with a view to enabling metagenomics in hospitals in Wales.

2.1.6 Objective 6: Improvement in genomic pathogen surveillance

While the focus of the first years of development of pathogen genomics activity in Wales has been on diagnostic pathogen genomics, the COVID-19 pandemic demonstrated how critical genomics is as a tool for monitoring pathogens in our hospitals and communities. A key element of the work following on from the pandemic is to develop systems for identifying where genomics is required to support pathogen genomic monitoring of pathogens as part of our public health surveillance system. To do this, PHW will;

ACTION: Develop and further embed the use of genomic data as part of surveillance systems in Wales, including building on PHW's established Genomic Epidemiology Unit.

ACTION: Work with partners and stakeholders to develop new sources of genomic surveillance data, and support the generation of evidence to enable their use in Public Health practice.

2.1.7 Objective 7: Developing ONE health genomics services, including working with external stakeholders across the UK to understand pathogens in the environment and how this impacts human health

In the past twenty years, there have been spillover events from animals into human including SARS-CoV-1, MERS, Ebola, Zika as well as two pandemics that involved a jump from an animal into humans - Swine flu and SARS-CoV-2. Beyond these zoonotic pathogens, it is increasingly clear that understanding the interaction of pathogens and the environment, humans, and animals is critical to help manage and prevent future threats. With issues such

as antimicrobial resistance, food security and climate change representing global challenges, we must recognise that ONE health is critical. Further, genomics has a major role to play in understanding the interplay of pathogens/humans/animals, as it provides a mechanism to characterise pathogens in different context. We recognise that some elements of ONE health are reserved areas, but at the same time also reflect on the importance of working with all the agencies that act within Wales, and on a UK-wide basis to support the public health utilisation of ONE health in Wales, to protect the health of the public. To do this, PHW will:

ACTION: Work collaboratively with agencies working within Wales to identify opportunities for, and then to develop services to integrate the use of pathogen genomic data into routine environmental health activities.

ACTION: Establish and develop collaborations relating to the use of genomics as part of ONE Health work with other human, plant and animal health agencies operating across the UK.

ACTION: Share data with collaborating organisations in academia and industry to generate insights that can be used for the development of new services or direct public health action.

2.1.8 Objective 8: UK-wide pathogen genomics and bioinformatics collaboration and co-creation

The UK is host to a range of world leading genomics capabilities, with accredited services in existence or development within all the nations of the UK. As the nations of the UK develop their individual genomics capabilities, opportunities present themselves for collaboration, co-creation, and co-delivery across the UK. The benefits of UK-wide collaboration are clear - in some cases, work can be undertaken on a 'once for the UK basis', with services being delivered either in a federated way or by a nominated public health agency, depending upon the service requirements. In other cases, collaboration may allow savings in terms of development time, with protocols and software being shared across the UK to enable all the public health agencies and diagnostic laboratories to work from the same analysis process, ensuring standardisation and equivalence of data/results. Lastly, where developments are undertaken on a per-UK nation-basis, there is an opportunity to develop standardised frameworks to demonstrate equivalence of results, complete with suitable platforms for data sharing and collaborative data analysis. The genomics work undertaken in the UK in response to the SARS-CoV-2 pandemic was recognised internationally as the best response of its type in the world and demonstrates the potential when the UK public health agencies and academia work together collaboratively towards a common goal. To develop the UK-wide pathogen genomics ecosystem and develop pathogen genomics capability across the UK PHW will;

ACTION: Support efforts within the UK, particularly as part of the UK Health Protection Oversight Group, to achieve better strategic alignment amongst pathogen genomics services in the UK.

ACTION: Develop routes for sharing of pathogen genomics expertise and knowledge between staff in the four nations public health agencies.

ACTION: Build links across the four nations public health agencies to improve the sharing of data, bioinformatics software and laboratory approaches, to support standardisation and collaboration.

2.1.9 Objective 9: International collaboration to develop standards and best practice for Pathogen Genomics

Unlike human genomics, best practice in pathogen genomics is still largely undocumented and not fully defined/agreed across the field. Recent years have seen the establishment of multiple networks to develop, document and agree on best practice and standards for pathogen genomics.

ACTION: PHW and GPW will engage with international organisations to support the development of standards for pathogen genomics.

ACTION: PHW will, where appropriate and compliant with the law, contribute pathogen genomic data and insight derived from data to international resources.

2.1.10 Objective 10: Develop collaborative relationships with industry

Within Wales, there are several companies that provide products that are essential both for PHW and the All-Wales Medical Genomics Service. Following the successful co-location of key GPW stakeholders at the new Canolfan Iechyd Genomig Cymru, there are opportunities to develop partnerships with industry, to support the development of genomics services in Wales and attract inward investment into Wales.

Throughout the pandemic Wales benefited from good relationships with key suppliers, and as we move forward there are opportunities to develop commercial partnerships with companies across a range of areas of activity, to support our service development and to deliver economic benefits to our communities.

ACTION: PHW and GPW will seek to develop collaborations with industry, to support service development and delivery, and potentially attract investment to Wales.

2.1.11 Objective 11: collaborative development of new services working across Genomics Partnership Wales

It is increasingly clear that 'microbial genomics' approaches will have a role in understanding, detecting and preventing non-infectious diseases. Over the next ten years, microbial genomics will also play an increasingly important role as part of the diagnostic and patient management pathway for a range of diseases, beyond those currently perceived to be 'infectious disease'.

There are a number of published papers that have identified host genetic markers that relate to severity or probability of infection for certain organisms, and by using an understanding of a host's genomics, guidance can be improved, and antimicrobial treatments made more effective and precise.

Looking beyond infectious disease, evidence of the role of microorganisms in cancer (either as an indicator or cause) is building, particularly with respect to colorectal cancer and stomach cancer; where opportunities for prevention exist. The effectiveness of the HPV vaccination programme demonstrates the potential value of understanding where the triggers of a non-infectious disease are a microorganism that can be prevented. It is likely that as healthcare data becomes more accessible and available, many new links between chronic disease and infectious disease will come to light. It is therefore extremely important that we build links between subject matter experts in these different areas of practice, to ensure that we are in the best position possible to prevent disease in the future.

As well as certain organisms having a causative role in cancer and other chronic diseases, some members of the gut microbiome have been shown to impact the effectiveness of

immune checkpoint inhibitors in cancer treatments, meaning that it is likely that in future, profiling of an individual's microbiome will form part of personalized cancer treatments; with tools such as FMT being used to alter a patient's microbiome to improve treatment effectiveness.

Lastly, with the advent of pharmacogenomics, there are opportunities to improve the selection of treatments against pathogens, taking into account a host's own genome.

These potential service areas are not something that may be expected to be delivered within the next 3-5 years, however, genomics moves quickly, and as the evidence develops, we must be prepared to act rapidly. The unique setup in Wales – with the co-location of the Pathogen Genomics Unit, Wales Gene Park and All Wales Medical Genomics service provides opportunities for collaboration, co-creation and co delivery that are unique in the UK. Beyond then three partners based in the same building, the wider HEI ecosystem in Wales and the wider UK provides a fertile ground for ideas to grow. Recognising this, the GPW partners will work to;

ACTION: Identify how pathogen genomics diagnostics could be used within the SWAN clinic, and develop services

ACTION: Evaluate where pathogen genomic tests have a role in the diagnosis and management of chronic diseases.

ACTION: Ensure pathogen genomics forms a part of pharmacogenomics services as they develop in Wales.

ACTION: Generate evidence to support the implementation of tests that consider host genomic markers that relate to infection alongside microbial diagnostics.

ACTION: Work with GPW partners to assess laboratory technologies to improve services.

2.2 Activity under Genomics Delivery Plan for Wales, Delivery Theme 3: Research and Innovation

Pathogen genomics has a role to play as part of the Research and innovation delivery theme. This work is ongoing, but we have identified a set of areas where Pathogen genomics can contribute and produce discrete deliverables. Specifically, the GPW partners will;

ACTION: Implement measures identified in the Welsh Government Genomics Research Review to develop the Welsh Genomics research landscape.

ACTION: Work within PHW and with academic stakeholders to develop an approach to expand Pathogen Genomics research in Wales.

This work will feed into activities being undertaken by the wider GPW over the coming years and will integrate alongside plans for the development of research activity across GPW focused on other areas of interest – which are outlined in the Welsh Government Genomics Review and in the Genomics Delivery Plan for Wales.

2.3 Activity under Genomics Delivery Plan for Wales, Delivery Theme 4: Enablers

Enablers, particularly digital infrastructure, was identified within the Genomics Delivery Plan for Wales as critical for the development of genomics in Wales.

As part of these enablers, we have identified three key activities that are of specific significance to Pathogen Genomics, and which we will specifically feed into as part of wider activity within GPW. We will:

ACTION: Develop systems and opportunities for UK-wide data sharing for public health.

ACTION: Support GPW efforts to develop a digital strategy in Wales to support collaborative working with Human Genomics, as part of GPW this strategy will include elements such as:

ACTION: Develop systems and opportunities for data sharing for research within Wales and externally. This includes work such as:

Collectively, pathogen genomics activity will contribute to wider digital development activities, ensuring that Wales and the UK are able to develop systems that are fit to underpin our future genomics services and research. These activities are varied and will form part of other plans that are being developed by GPW partners in parallel with this work. One of the challenges of partnership is that there will be cases where one partner needs to move faster, or differently, to the others. We recognise this and acknowledge that particularly in the digital space, pragmatism will be required to get things done and deliver the benefits of genomics to our population. However, despite the potential challenges, our three identified core digital activities provide a statement of intent as to the range and type of work that is planned in the digital space and should serve as a notice of our commitment to work as one partnership to overcome the digital challenges that we collectively face.

3. Progress monitoring and resourcing

3.1 Monitoring performance - lines of reporting

We have identified a set of measures which include the completion of tangible activities (e.g., the launch of new services) and the development of reporting information that should enable stakeholders to understand the capabilities and performance of the Pathogen Genomics work in Wales.

These reports and management information will be presented both within PHW, where key activities will form part objectives identified within the organisational IMTP, and to the GPW Programme and Governance boards, and as part of yearly GPW reporting to Welsh Government.

3.2 Resourcing

We recognise that this work is bold and transformational and has resource implications within PHW and across the wider NHS and public health system. In many cases, what is planned could potentially be achieved through upskilling our existing workforce.

In other places we may be able to achieve our objectives through collaboration with academia and industry.

However, it is important to note that in several instances, the work that is planned will require additional investment. As such, it is important to acknowledge that resourcing will be critical in achieving our full aims and will determine the pace of change. This plan presents a comprehensive vision for advancing pathogen genomics in the Welsh NHS. Through much of the development work envisaged, the cost to carry out measures will be

identified, and at that point the value can be assessed, and funded (or not) based upon the outcome of that assessment.

In most cases, the resourcing required to achieve our objectives is not yet determined, however, we can already identify elements that will be required, some of which may be possible to provide within current resources.

1. Posts to provide expanded services - the creation of new services will require additional staff. This will be identified as part of the service development process and will form part of the decision on if a possible service moves from development into routine activity.
2. Alongside this, we will need to develop the capability for utilising health economists to calculate the value of services, and to provide accurate financial planning for services.
3. As part of planning activities more generally, it will be vital to build genomics into services from the start. In some cases - such as the introduction of new vaccine programmes - genomics will be a requirement, and planning the genomics as part of the programme from the start will come with a small cost but has the potential to realise larger savings later.
4. We need to work to ensure that our workforce is appropriate to meet our future needs, and future expansions of the service. The HEIW Strategic Genomics Workforce plan, published in 2024 outlines a set of actions to be taken system wide to support the mainstreaming of genomics in the NHS. Within the pathogen genomics space specifically, we need to ensure that the workforce plan translates into action – with appropriate resource provided to develop current staff, building on the current HEIW investment in training. Making the workforce plan a reality also needs to extend ensuring that we have the right career model for progressing staff – not just in the wet laboratory, but in technical roles (such as IT and Cybersecurity) and the dry lab (including bioinformaticians and genomic epidemiologists). Beyond that, ensuring that potential recruits at every level within the NHS have the right skills to support genomics activity remains a challenge to realise the aim of mainstreamed genomics in the NHS.
5. As genomics becomes a more significant tool in infectious disease, health protection and microbiology as areas of clinical practice, it will be important to ensure that staff are coming through the system with the required training to utilise genomic data fully. This will require specific consideration of how to provide suitable training opportunities to clinical staff, to produce the next generation of genomics-aware clinicians.

Annexe 1 – Detailed elements/information in relation to planned actions

Objective 1

ACTION: Develop additional internal structures within PHW for monitoring, management, governance, and accountability of genomics activity. These structures will form part of the Public Health Genomics Programme, with reporting both to the PHW board and to the GPW programme and governance boards. This structure will provide the framework to enable the sustainable development of public health genomics in Wales. While the Public Health Genomics Programme also has a role in other areas of activity, activities outside of the scope of Pathogen Genomics are covered separately in the Genomics Delivery Plan for Wales. In the Pathogen Genomics space, the programme's responsibilities will include;

- a. The development of a single framework for the identification and implementation of new pathogen genomic services in Wales.
- b. The development of new structures to bring together genomics staff within PHW to create communities of practice and develop a critical mass of pathogen genomics (and related) expertise in areas including Genomic Epidemiology and Data Science.
- c. The implementation of internal structures to provide clear lines of responsibility/accountability and mechanisms for reporting on pathogen genomics activity within PHW.
- d. Rather than operating as a service with duplicated roles, the Programme operates as a virtual structure across PHW, bringing together subject matter experts and other professionals together to identify, design and deliver services. To enable the growth of the genomics, we will develop and further document the modular and expandable structure we have developed, with a view towards enabling future expansion to cover new services focused on pathogens, as well as supporting the development of future services based on using human genomic data – activity that is outside the scope of this plan but will be considered within the larger Genomics Delivery Plan for Wales.
- e. Developing the core programme team to deliver key aspects of this activity.

ACTION: The development of a working model for the PHW Public Health Genomics Programme to provide a new point of integration with GPW and Welsh Government to support:

- a. Coordinating and overseeing clinical pathogen genomics activity in Wales
- b. Planning strategically around workforce development within PHW
- c. Planning strategically to support the development of digital infrastructure within PHW and across GPW
- d. Realising opportunities for collaborative working within PHW and across GPW to reduce costs and share practice.
- e. Realising opportunities for research collaborations with academia and industry.

- f. Supporting the integration of Welsh pathogen genomics activity into UK-wide biosecurity initiatives, such as the UKMFC.

Anticipated Timeframe for delivery: workplans and structures for the core operational units will be complete by the middle of the 26/27 financial year, with public facing materials describing the structures, responsibilities and activities of the Programme and its constituent units available over the same timescale.

Objective 2

ACTION: Improve Mycobacterial services through collaboration and development, including:

- a) Collaborative development of updated bioinformatics pipelines with the other UK Public Health Agencies.
- b) Engagement with UKHSA with respect to reporting of clusters and development of a UK-wide system for cluster identification.
- c) Assessment of current sequencing service and evaluation of other technologies (e.g., MALDI-TOF, use of culture free genomic approaches) to reduce turnaround time and failure rates.
- d) Development of genomics analysis approaches to enable the delivery of other Mycobacterial services using genomic data in Wales (e.g., subspeciation of *M. abscessus*)

ACTION: Improve *C. difficile* service through the development of tools for local management of IP&C and to improve surveillance including;

- a. Development of a system for integrating epidemiological information (e.g., patient ward stays, treatment etc) and genomic data to support IP&C.
- b. Development of systems to utilise genomic data as part of surveillance reporting.
- c. Development of a core genome MLST service to enable data sharing and international investigation of *C. difficile* transmission.
- d. Collaboration on a UK-wide level to develop systems for tracking *C. difficile* clusters across the UK.

ACTION: Develop and implement standardised software platforms for cluster tracking, covering:

- a. Multiple workstreams need a platform for visualising clusters of cases across Wales, the system will need to display both genomic and other metadata.
- b. The system will need to be online, and accessible to NHS colleagues in Wales.
- c. The system will also need to be accessible to colleagues outside of the NHS and outside of Wales to support other services that are provided.

ACTION: Achieve improvements to existing service through developing underpinning service elements, covering:

- a. Reducing turnaround times through the provision of increased automation and development of more effective processes covering sample logistics, sample handling and bioinformatics processing.
- b. Increasing data use from existing services through engagement across the healthcare system to identify questions that could be answered using genomic data that is already routinely generated.
- c. Implementation, and support of standards-based systems to enable pathogen genomic data reuse within the healthcare system.
- d. Improving sequencing process through optimisations to laboratory processes to make sequencing kits and other chemicals go further.
- e. Improving bioinformatics process through improvements to bioinformatics pipelines including refactoring of code and optimisation of software.
- f. Develop and implement a plan to bring sequencing into the PHW regional microbiology laboratories, moving sequencing closer to patients, and enabling the local delivery of some services and capabilities. This work will also include work to ensure that pathogen genomics in Wales is resilient, as part of future Wales' planning for emergencies.

Anticipated Timeframe for delivery: This work is continuous and should be factored into existing roadmaps for service development immediately. Given that the activities within this objective are continuous, the Public Health Genomics Programme will be expected to report progress against this objective on a yearly basis going forward, with service status, and service improvement activities forming KPIs for the genomics activity in PHW.

Objective 3

ACTION: identify and implement measures for improved pandemic preparedness following the COVID-19 pandemic, including implementing recommendations from the COVID-19 Inquiry.

- a. As part of PHW organisational and governmental responses to the COVID-19 enquiry, we will reflect on our experiences during the pandemic and will identify responses to recommendations that are relevant to genomics, bringing forward implementation plans with tangible deliverables as the outputs of the inquiry develop. This activity will be reported via GPW, as well as forming part of organisational pandemic plans within PHW.

ACTION: Implementation of metagenomics and rapidly-deployable sequencing services in Wales to support our pandemic and threat preparedness. This covers;

- a. The ability to identify any given pathogen without needing to know what might be in the sample to start with. The development of a new metagenomics service to enable the characterisation of unknown pathogens in patient samples is a key capability in Wales' future pandemic preparedness. Metagenomics is an approach that enables the examination of all the genomic information in a sample, which allows the identification of pathogens without knowing specifically what pathogen is present at the start. It is a key tool for characterising pathogen X and in some

circumstances is the fastest method to positively identify the presence of an infecting organism. Had such a service been available in 2020, we may have been able to identify cases of SARS-CoV-2 in some hospital settings earlier. Metagenomics would also have enabled a more rapid analysis of both Mpox and Adenovirus samples in 2022/23. As a stepping stone towards a full metagenomics service, PHW will implement a viral panel sequencing capability, which would enable the sequencing of any of several hundred viral species (including a wide range of viruses including Mpox, Measles), Under this objective PHW will then move to implement a metagenomics service, providing a generic tool to characterise microorganisms in a sample, which could be used for pathogen detection or microbiome profiling. Once this capability is in place, there is the potential for additional services to be developed using the same underlying approach, including close-to-patient services for rapid pathogen identification.

- b. Building on the pandemic-era introduction of sequencing approaches based on tools that could be applied to many different pathogens, such as the ARTIC amplification scheme. Recognising that standardisation reduces costs and turnaround times, and that the ARTIC method can rapidly be applied to a new pathogen (as it was for SARS-CoV-2), a key area of activity for PHW will be to undertake work to standardise analysis approaches to simplify adding in new pathogens (e.g., expanding use of ARTIC schemes for viruses). Combined with PHW's existing modular sequencing platform in Wales, this will place us in a better place to respond to new threats, and to scale up activity rapidly in any future pandemic.

ACTION: Develop our collaborative links with academia and industry to enhance our preparedness and ability to respond to urgent threats. This includes;

- a. The pandemic evidenced the critical role for academics in driving the research response to the pandemic, working in close collaboration with public health. The development of pathogen genomics research collaborations that are integrated into service delivery is a critical requirement for future pandemic response, and so we will undertake engagement work and stakeholder analysis to develop a plan for collaborations with academics that are focused on delivering public health research as a part of service delivery. This work will then feed into the development of networks of partners that can be activated in the case of a major incident or threat, improving our future ability to respond to pandemics or other major incidents. Activities under this objective will be complimentary to those under the research theme but will be focused on service needs.
- b. Over the course of the pandemic Wales benefited from significant support from suppliers including New England Biolabs, Illumina and IDT who worked with PHW to ensure that sequencing supplies were available, to provide an uninterrupted genomics service both for SARS-CoV-2 and other clinical services. PHW also supplied sequence data and other information to diagnostic manufacturers such as Seegene, to support improving diagnostic tests, based on observed patterns of mutations in viral populations. Collectively, the pandemic has seen the benefits of close working with suppliers, and with the move to Canolfan Iechyd Genomig Cymru, there are opportunities for further engagement with commercial organisations to

bring economic and other benefits to Wales. As part of pandemic preparedness, PHW will work with their suppliers to ensure that Wales is in the best place when a pandemic occurs again and will build on our existing relationships to create new opportunities as part of wider GPW efforts to bring economic investment to Wales.

ACTION: Develop the ability of genomic data to be generated and used across PHW and ensure that knowledge gained from the development and operation of genomics services is retained. Key activities to embed genomics as part of our overall preparedness include;

- a. As part of recovering from the pandemic, a significant amount of knowledge and experience has been gained around rapidly scaling up PHW's sequencing services. It is vital that this is recorded, and that mechanisms are put in place to accurately track available capacity; to highlight issues so these can be managed effectively over time. Collectively, this should enable the development of a scale-up plan for genomics - which encompasses the baseline capability within PHW, combined with capacity available through the All-Wales Medical Genomics Service, Wales Gene Park and the academic sector - which can be enacted in the case of a future pandemic.
- b. Developing services and other activities that will enable sequencing to be established in the PHW regional laboratories will significantly enhance our resilience and preparedness. Linking this capacity to services will ensure that staff have the skills to support scale up if required. As part of the development of sequencing capability within the PHW regional microbiology labs, we will also develop a plan to enable the activation of this capacity to support a future pandemic response, and to enhance the resilience of our sequencing capability.

ACTION: Contribute our expertise and engage with UK Government initiatives relating to Biological Security, in particular the UK Microbial Forensics consortium, to support the development of UK capabilities that will detect and respond to future threats.

- a. Pandemics are not the only threats that the UK faces in the biological space. With an increasingly unstable world, the UK government has recognised the risk of threats from both state and non-state actors using biological agents to cause harm to the country. Our experience in Wales places us in an excellent position to contribute to biological security work in the UK, particularly the UK Microbial Forensics Consortium (UKMFC), where the Welsh experience of developing modular, ISO accredited genomics services is likely to be invaluable in developing UK capability in this area. We recognise the importance of working with UK-wide partners on biosecurity, and PHW specifically, and GPW more generally, will aim to be fully engaged with relevant Biological Security initiatives. In particular, as part of this work, the PenGU will operate as part of the UKMFC laboratory network, supporting the development of an initial operating capability.

Anticipated Timeframe for delivery: We will actively contribute to the UKMFC throughout the 26/27 FY and will actively support its plans to establish an initial operating capability in the UK. For the metagenomics and standardisation of analysis approaches work, scoping work/prelim service development will take place in 26/27, followed by service workup in 27/28. We will begin by developing a panel-based system that provides targeted sequencing of a large panel of pathogens, before moving on to deploying a full Metagenomics service.

We will aim for our panel-based service to be operational by the end of 26/27, with a full metagenomics service minimum viable product being ready for testing in 28/29. The development of partnerships and collaboration with industry and academia will be an ongoing activity, which should be reported on by the Public Health Genomics Programme as part of GPW on a yearly basis. Implementation and reporting of pandemic preparedness measures will form part of PHW EPRR planning processes.

Objective 4

ACTION: Develop and aim to introduce genomics into routine *Cryptosporidium* and *Toxoplasma* outbreak characterisation work, based at the UK Reference Laboratory in Swansea. Wales hosts an internationally recognised reference laboratory focused on parasites, with key expertise in *Cryptosporidium* and *Toxoplasma*, hosted by PHW in their Swansea regional laboratory. The *Cryptosporidium* reference laboratory provides services for public health professionals across the UK, as well as for the water industry. Genomics potentially offers advantages over current methods that are used to identify if cases belong to a single outbreak. The introduction of genomics into *Cryptosporidium* and *Toxoplasma* work would be world leading and would build on established Welsh expertise in this area.

ACTION: Scope potential fungal genomics services, and develop an implementation plan where appropriate to be taken forward for new Mycology Genomics Services in Wales. Wales has a global reputation in Mycology and is an active participant in European research and public health networks. With increasing rates of resistance to anti-fungal agents, and increased threats from climate change, developing capabilities to introduce genomics into routine service is going to become increasingly critical. We will work with the Mycology team within PHW to scope initial potential services, including the use of metataxonomics and whole genome sequencing, where genomics could add value and contribute to better patient outcomes.

ACTION: Extend anaerobic genomics in Wales as part of the UK Anaerobe Reference Unit beyond *C. difficile*, to develop accredited genomic services for other anaerobic pathogens, and to support the development of a Faecal Microbiota Transplant (FMT) bank for Wales. This work covers;

- a. Wales hosts the UK Anaerobe Reference Unit, which provides reference services for anaerobic bacteria for the UK healthcare and public health system. This is an area where Wales has an established international reputation. At the present time, anaerobic bacterial characterisation uses a range of approaches but does not include genomics. We will work with the UK ARU to develop a set of accredited genomics services as part of their reference activities, which will be global firsts-of-their-kind. This work will secure the future of the UK ARU as well as providing benefits to clinical and public health users – and their patients – across the UK.
- b. Develop the required genomics capabilities to support the establishment of a Faecal Microbiota Transplant (FMT) bank for Wales. Genomics is an essential tool required for the development of a safe FMT bank. FMT as an approach can provide an effective treatment to persistent *C. difficile* infection, as well as potentially being useful for treating chronic conditions such as Chron's disease. FMT may also offer potential as a tool to displace

resistant bacteria from some patient groups (e.g., cancer patients – work that could be undertaken in partnership with the Velindre NHS Trust) where the risk of developing a resistant infection is high (e.g., following antimicrobial prophylaxis and chemotherapy). FMT banks are increasingly being established globally, and with Wales' expertise in Anaerobes, we are well placed to bring this approach into the Welsh NHS.

ACTION: Audit current genomic services in Wales, and examine the cost and performance of the services provided, to identify if there is a case for repatriation into Wales. Where better value would be provided through repatriation, we will begin the process of developing the services to make this happen.

Wales already makes use of a number of pathogen genomics or genetics services provided by external providers. These services, which in some cases represent a considerable cost to the Welsh NHS, are potential sources of savings and service improvements. Services focused on 16S/18S characterisation are one area where opportunities exist, while other services may also benefit from repatriation of sequencing into Wales. Other areas where improvements may be possible include examining the generation and use of data for Hepatitis C outbreak characterisation, and the generation and use of data for gastrointestinal pathogen outbreak identification. As part of this work, PHW will perform an audit of current pathogen genomics services that are undertaken by external providers at a cost to the NHS in Wales. This audit will include an options appraisal (e.g., performing sequencing in Wales instead, or identifying models that allow fewer samples to be sequenced) that could decrease cost and improve turnaround times. Based upon the opportunities identified, we expect to repatriate a number of services to Wales, making use of our existing laboratory and sequencing capacity within PHW to provide better value for money to the taxpayer.

Anticipated Timeframe for delivery: This work will be preceded by the development of a standardised system for identifying and commissioning the development work for new pathogen genomics services, complete with a review board which will make recommendations to inform which services should be developed. This process will also include the completion of an audit of current genomics services that are provided by suppliers outside of the Welsh NHS, with a view to reviewing if these could be provided within PHW at a lower cost. The review process will be established by the end of 26/27, and an initial audit will also have been completed by the end of the 26/27 financial year. The first new proposed pathogen genomics services will commence their development by the start of the 27/28 financial year. By 2030, we anticipate having new genomics services across at least two of the areas of activity identified, subject to any required funding.

Objective 5

ACTION: Engage with stakeholders across the NHS, academia, industry and charities to identify key microbiological services that need transformation, and where genomics could play a key role.

- a. This will include engagement with key clinical networks, patient groups, and Welsh Government to identify areas where genomics could create new opportunities to deliver transformational services. Based upon this work, PHW will develop a list of potential services, prioritised based upon clinical

need and patient benefit, for consideration for development and commissioning.

ACTION: Undertake preliminary work to identify how genomics could be used for STI diagnostics and health protection. The preliminary analysis will be followed by the development of an implementation plan for putting STI genomics into service in Wales.

- a. Opportunities exist to introduce genomics to improve the detection of drug resistant STIs, and to improve transmission detection/tracking and targeted public health action. The use of genomics may enable a re-imagining of how the STI service is delivered, ensuring more patients receive the right treatment first time, and bringing down the rates of STIs in Wales. This work will be broad and will take in a range of options; we already operate an HIV service but believe that there may be significant opportunities to improve care by extending genomic services to cover blood borne viruses more generally. Alongside this, the development of services/use of genomics to characterise Gonorrhoea, *Mycoplasma genitalium*, candidiasis and bacterial vaginosis offer significant opportunities to improve the care that is provided to people in Wales, building on the strengths of genomics to provide rapid results for clinical action.

ACTION: Identify current evidence gaps and needs with respect to the use of metataxonomics and metagenomics in clinical service. Alongside this work, PHW will develop its capacity to perform close to patient sequencing with a view to enabling metagenomics in hospitals in Wales. This work would include;

- a. Developing evidence and scope out the use of metataxonomics as a tool for patient management. Metataxonomics - which characterises the mix of microbial species in a sample - has been identified as a possible tool to examine changes in the gut or lung that could benefit a range of patient groups. Metataxonomics is relatively inexpensive, and so as evidence grows as to its potential clinical utility, it is possible that Wales could develop a service that would generate more clinically actionable information, particularly for the management of vulnerable patient groups such as those with CF or neonates.
- b. Developing Wales' capacity to perform close to patient sequencing. Close to patient sequencing offers opportunities to rapidly identify infecting organisms in patients in ICU, particularly those with sepsis or bacteraemia. Using genomics, recent work has demonstrated that the infecting organism and its drug resistances can be identified within 6 hours of a sample being taken, using close-to-patient meta genomic sequencing. This technology is currently being evaluated in England, and in Wales we should develop evidence for the application of this approach, before, if the results are positive, hosting a trial within at least one Welsh hospital, where a more complete service can be worked up and tested. This service would be placed based on need - in a hospital where rates of resistance are high in sepsis or bacteraemia patients. By 2035, we would anticipate having this capability embedded and operational in every Welsh acute care hospital.

Timeframe for delivery: Collectively this objective is focused on work that is cutting edge, and yet to be 'ready for service'. It reflects our desire to identify where genomics could revolutionise how we provide care, and where it could have a major impact on our patients. Over the course of 26/27 and 27/28, we will complete the scoping and planning for this

work, with an aim to begin bringing trials and evidence generation online in 27/28 and 28/29, funding permitting. This work will then lead to the development of services, with the expectation that accredited services will be in place for one or more of the targeted areas by 2030.

Objective 6

ACTION: Develop and further embed the use of genomic data as part of surveillance systems in Wales.

- a. Embed genomics as part of surveillance of Acute Respiratory Infections and as part of the Welsh WHO National Influenza Centre, encompassing our existing Influenza and SARS-CoV-2 services, with an expectation that target viruses will be added into surveillance efforts based upon the prioritisation process developed as part of objective 4, while also utilising viral panel and metagenomics sequencing capabilities developed as part of the planned pandemic preparedness activities under objective 3. As part of this work PHW will undertake work to identify what 'normal' looks like in human pathogen populations, to support future incident and threat response.
- b. Exploit genomic data that already generated. Genome data is routinely generated for Welsh patients for organisms including gastrointestinal pathogens (sequencing/analysis currently performed by UKHSA under an MOU) and Non-tuberculous Mycobacteria (sequencing/analysis currently performed by PHW). The data generated by these, and other, services could be used for pathogen genomic monitoring but is not currently fully exploited. PHW will undertake work to identify potential uses of this already-generated data, to improve Wales' current surveillance systems. As part of this work, PHW will also examine other pathogen genomic services operating in the UK, to identify if they may provide a route to introduce new monitoring capability in Wales at lower cost than would otherwise be the case.

ACTION: Work with partners and stakeholders to develop new sources of genomic surveillance data, and support the generation of evidence to enable their use in Public Health practice.

- a. Develop wastewater monitoring as part of the public health system. Wales built an internationally recognised wastewater monitoring system as part of the SARS-CoV-2 pandemic, which covered large parts of the population. Preliminary work has examined the potential for genomics-based wastewater monitoring to examine AMR and the spread of resistance mechanisms, conduct community surveillance of pathogens such as norovirus and monitor zoonotic pathogens in bathing water. Wastewater monitoring is already used to monitor poliovirus in some parts of the world. The pandemic wastewater-based epidemiology system was delivered by universities and relied upon genomics to characterise potential variants in the wastewater. The next step is to work out how this activity can be developed as a long-term part of the wider public health surveillance apparatus in Wales, and where it may plug current gaps or provide a cost-effective mechanism to perform community sampling of infectious diseases. The end goal of this work will be, if it is cost effective, to introduce a wastewater monitoring system in Wales, to look for key pathogens in our communities. The development of such a system has natural synergies with objective 3 and would provide a key tool in any future pandemic or major threat.

Timeframe for delivery: Efforts to exploit genomic data that are already generated will be developed through 26/27 and 27/28, as part of the activities of the Genomic Epidemiology Unit within PHW. PHW will work with Welsh Government to develop plans for wastewater to be used as part of the wider surveillance system, as well as continuing to work with Welsh Government and international partners to ensure that our respiratory infection surveillance remains as one of the best of its type in the world. This activity will generate results in 26/27, which will be included as objectives in the PHW IMTP moving forward and will form the basis of scoping activities to identify costs and scale/scope of the potential activities. We will work to develop our genomic epidemiological analysis capabilities in 26/27 and 27/28, with an aim to be moving towards accredited services, where appropriate from 28/29.

Objective 7

ACTION: Work collaboratively with agencies working within Wales to identify opportunities for, and then to develop services to integrate the use of pathogen genomic data into routine environmental health activities. This would include;

- a) Work within Wales to identify how genomics can be integrated into relevant pathogen monitoring undertaken by Welsh organisations including Natural Resources Wales and Welsh Water.
- b) Develop links with the Animal and Plant Health Agency, aiming to develop systems for data sharing to enable joint public health activities to be undertaken, particularly with respect to TB and pathogens with zoonotic potential such as Influenza.
- c) Work with environmental health colleagues to assess the utility of genomics to support work focused on examining the issue of mould in housing, and its impact on the health of individuals.

ACTION: Establish and develop collaborations relating to the use of genomics as part of ONE Health work with other human, plant and animal health agencies operating across the UK. This action potentially covers;

- a) Work with agencies across the UK to establish collaborations around ONE Health. In particular, PHW will work through the HPOG Genomics subgroup to scope potential collaborations and develop joint activities to develop ONE health genomics services in the UK.
- b) Work as part of UK-wide ONE Health collaborations, including PATH-Safe, the UK Biosecurity Network and the UK Microbial Forensics consortium. Wales will be an active contributor to these UK-wide activities. As part of this work, we will also examine the potential utility of applying genomics as part of surveillance activities such as the All-Wales Shopping Basket Sampling Program to support both wider-UK activities and provide benefits for monitoring programmes in Wales.
- c) Work with UK animal health agency colleagues and environmental health colleagues to examine how genomics can be used to support surveillance of antifungal (e.g., azole) use and rising rates of resistance.

ACTION: Share data with collaborating organisations in academia and industry to generate insights that can be used for the development of new services or direct public health action. This work could encompass;

- a) Contributing genomic data generated through the provision of clinical pathogen genomic activities to research and development activities, including those associated with developing tools for source attribution.
- b) Supporting efforts to develop research work and services focused on examining the Microbiome, the impact of environmental exposure on population health and evidence generation.

Timeline for delivery: Over the course of 26/27 and 27/28, we will develop our collaborative links across the UK, with the intention that by 28/29 Wales is contributing genomic data and expertise to ONE health initiatives across the UK. From 28/29 onward Wales will work to integrate active ONE health approaches into routine genomic epidemiological surveillance services.

Objective 8

ACTION: Support efforts within the UK, particularly as part of the UK Health Protection Oversight Group, to achieve better strategic alignment amongst pathogen genomics services in the UK.

1. Catalogue genomics services operated within the UK (both within the public and private sector), with a view to identify potential services that could be used by Wales, which would remove the need for extensive development costs in Wales.
2. Collate and advertise the capacity within Wales to offer existing services outside of the Welsh NHS. This would include planning to provide mechanisms for result reporting and test requests, systems for charging, as well as maintaining a catalogue of services that other parts of the UK or international customers may want to access.
3. Identify a set of pilot projects to develop collaboratively, to be coordinated, overseen, and managed through the HPOG Genomics subgroup.

ACTION: Develop routes for sharing of pathogen genomics expertise and knowledge between staff in the four nations public health agencies.

4. Develop operational links between bioinformatics and lab teams across the UK public health agencies, with an aim to build these communities of practice, share expertise and undertake joint analysis and development work.

ACTION: Build links across the four nations public health agencies to improve the sharing of data, bioinformatics software and laboratory approaches, to support standardisation and collaboration.

5. Develop a standardised set of datasets and processes to enable Wales to select, evaluate and commission services provided by an agency or company based outside of Wales. This work will also involve the development of processes and datasets to undertake equivalence testing, to establish the comparability of performance of genomic analyses and pipelines used in different places in the UK.
6. Develop a set of shared pipelines and the establishment of joint collaboration and development environments to enable the bioinformatics teams across the UK public health agencies to undertake collaborative work.

Timeframe for delivery: Most of this work is dependent upon the development of collaborative links with the other UK public health agencies. The development of these links will grow over the course of 26/27 and 27/28, with the aim that there will be at least one collaborative development project initiated by the end of the 27/28 FY. The catalogue of services in the UK will be completed once the pathogen genomics strategies for all the four nations are published. From 27/28 onwards, we will develop processes to support standardisation and equivalence testing, which will also provide the basis for the commissioning of services provided elsewhere in the UK for Wales.

Objective 9

ACTION: PHW and GPW will engage with international organisations to support the development of standards for pathogen genomics.

1. The Public Health Alliance for Genomic Epidemiology (PHA4GE).
2. The WHO International Pathogen Surveillance Network.
3. The WHO Global Influenza Surveillance and Response System, as it expands its focus to cover other viruses and the use of genomics.
4. Networks within Europe, including as part of ESCMID and those developed by ECDC.
5. The Global Alliance for Genomic Health (GA4GH).

These activities all align with activities envisaged in Wales and provide an opportunity for Wales to contribute its expertise and perspective globally - while also providing a route for Wales to influence the development of the wider pathogen genomics field.

ACTION: PHW will, where appropriate and compliant with the law, contribute pathogen genomic data and insight derived from data to international resources.

We will also seek to contribute to UK and international activities and data sharing programmes, sharing data and insight to support the development of global knowledge. This includes;

1. Contributing data to the UK HIV sequence database, hosted by UKHSA
2. Contributing data to the WHO TB resistance catalogue
3. Sharing viral surveillance data through portals including GISAID

Timeframe for delivery: We will engage with the identified networks in 26/27 and 27/28 with an aim to joining four of the five identified networks by the end of the 27/28 financial year. We will work to develop a system to support and enable the routine release of sequence data, which will be applied on a per-organism/per-service basis. The first examples of routine data sharing will exist by 27/28.

Objective 10

ACTION: PHW and GPW will seek to develop collaborations with industry, to support service development and delivery, and potentially attract investment to Wales.

- a. Developing collaborations with reagent and equipment manufacturers - we currently make use of extensive use of equipment manufactured by Illumina, as well as reagents provided by companies including IDT and New England Biolabs. These and other companies may provide opportunities for the development of collaborative links that could be used to support service development, and which could be used to bring jobs to Wales.
- b. Developing collaborations with diagnostic manufacturers - PHW has a long-term track record of working with diagnostic manufacturers to identify issues with diagnostics and support validation of new diagnostic tests. These links may create opportunities for more extensive collaborations to be developed, which could bring benefits to Wales.
- c. Developing collaborations with vaccine development companies - Wales can generate significant amounts of pathogen sequence data, and our pathogen genomic surveillance capabilities have the potential to be of real value in the development and monitoring of vaccines. Because of the services that PHW already provides (e.g., diagnostics and the national vaccine programmes), there is a distinctive PHW offer in the vaccine space, and this is an area we will seek to develop. In collaboration across GPW, there is potential to attract companies that produce a range of vaccines (to both infectious and chronic disease), building on the growing life sciences sector in Wales and infrastructure available in the Cardiff City Region.
- d. Developing collaborations with IT - the pathogen genomics activity within Wales is dependent upon technology, and as we develop our genomics capability, we will need to build scalable data storage and analysis systems, as well as exploiting technologies such as AI to analyse our data. The cutting-edge nature of our work creates opportunities for collaboration with technology companies.

Timeframe for delivery: We plan to implement a standardised system for developing MOUs by the end of 26/27 and aim to have at least one new MOU in place with industry by the end of 28/29.

Objective 11

ACTION: Identify how pathogen genomics diagnostics could be used within the SWAN clinic, and develop services

1. Make pathogen genomics diagnostics that can characterise unusual or unexpected pathogens available as part of SWAN clinic activities.

ACTION: Evaluate where pathogen genomic tests have a role in the diagnosis and management of chronic diseases.

2. Develop metataxonomics as a tool, with a view to being able to utilise the technology alongside human genomic sequencing for the management of chronic and non-infectious disease (e.g., CF, bronchiectasis). Over the course of 26-29, this work will see the generation of evidence and evaluation of the technology, between the GPW partners.

3. Developing metagenomics as a tool for diagnosis/detection and management of cancer. There is mounting published data demonstrating the potential for metagenomics in this area, and so working to develop metagenomics across the GPW partnership will leave us well placed to transition this to service once the evidence supports it. Potential uses include diagnosis and detection of cancers that have been shown to be caused by infectious disease (stomach cancer/*H. pylori*) as well as for detecting organisms that are increasingly thought to be involved in cancer (e.g., *F. nucleatum*, associated with colorectal cancer). With the establishment of a metagenomics capability, we would also be in a position to support (once the evidence is sufficiently robust) the potential use of microbiome profiling as part of immune checkpoint inhibitor treatment selection and management, to improve the predictability of clinical response. This work could further be combined with FMT to enable the alteration of a patient's microbiome to improve likely immune checkpoint inhibitor response. PHW will develop a metagenomics service as part of Objective 3; however, under this objective, PHW will engage with Wales Gene Park and the All-Wales Medical Genomics Service to undertake the evaluation work required to enable the use of this capability for fighting cancer.

ACTION: Ensure pathogen genomics forms a part of pharmacogenomics services as they develop in Wales.

4. Integration of pathogen genomics elements into planned pharmacogenomics work (e.g., examining AMR and investigating the impact of other drugs on the host microbiome). This work is detailed as part of the Pharmacogenomics Delivery Plan. Both delivery plans were developed at the same time, and were shared between teams to avoid duplication, and ensure that activities were aligned.

ACTION: Generate evidence to support the implementation of tests that consider host genomic markers that relate to infection alongside microbial diagnostics.

5. Generation of evidence and evaluation of the potential of the use of SNP markers in humans to inform the management of patients who may have an elevated likelihood of particular types of infection. This work will build on pre-existing work and expertise within PHW focused on fungal pathogens, with the development of research and evaluation work that includes both Wales Gene Park and the All-Wales Medical Genomics Service as partners.

ACTION: Work with GPW partners to assess laboratory technologies to improve services.

6. Collaborative approaches to assessment of novel technologies (e.g., lab equipment, sequencing technologies), from both the perspective of human and pathogen genomics to support better integrated planning and value for money for the Welsh NHS.

Timeframe for delivery: There has already been engagement with the development of the Pharmacogenomics Delivery Plan, with PHW planned to own a number of actions in that plan with respect to pathogen pharmacogenomics. Building on this, by 27/28 we should have at least one joint project that will lead to the use of pathogen genomic data as part of the envisaged Welsh Pharmacogenomics service.

Theme 3 – Research

ACTION: Implement measures identified in the Welsh Government Genomics Research Review to develop the Welsh Genomics research landscape.

1. Implement plans associated with Pathogen Genomics that form part of the Welsh Government Genomics Research Review. GPW has actively participated in the development of the genomics research review, to ensure that pathogen genomics is fully represented. We will work to ensure that the potential of the vibrant pathogen genomics research landscape in Wales is realised as part of fulfilling the planned roadmap for research development in Wales through engagement across the ecosystem in Wales, including within GPW and across the wider academic and industry sectors.

ACTION: Work within PHW and with academic stakeholders to develop an approach to expand Pathogen Genomics research in Wales.

2. Support the development of a pathogen genomics research plan by PHW as part of the continued development of the Public Health Genomics programme itself, and the development of research activity within PHW. This plan will link pathogen genomics activity to the wider PHW organisational research strategy, providing a long-term framework for the development and delivery of pathogen genomics-focused research in Wales.
3. Work with academic partners in Wales and the wider UK to build pathogen genomics research collaborations. PHW will seek to engage with the other UK public health agencies and funders to develop working relationships with key groups of researchers (e.g., UKHSA HPRUs). We will do this through collaboration on grant applications, shared PhD students/studentships, collaboration agreements and pilot projects and the development of a model for undertaking pathogen genomics research that covers situations where PHW may be able to support research (such as through the provision of samples or metadata).

Theme 4 – Enablers

ACTION: Develop systems and opportunities for UK-wide data sharing for public health.

Working within PHW and with the other UK public health and animal/plant health agencies we will engage collaboratively to build platforms to support research and service activity and enable rapid data sharing for public health purposes.

- a. As part of this work, we will seek to engage the data science community within the NHS in Wales, to support the development of joined up systems that enable more effective data management.
- b. We will work with Information Governance colleagues to improve how and when we are able to share pathogen genomic data within the wider healthcare system.
- c. We will work with patients and colleagues within Wales and across the wider UK to examine issues of ethics and consent in relation to the public health uses of pathogen genomics data, and to develop robust frameworks to

inform and guide the development of new services and uses of newly generated data.

ACTION: Support GPW efforts to develop a digital strategy in Wales to support collaborative working with Human Genomics, as part of GPW this strategy will include elements such as:

- a. Building shared digital infrastructures, to remove duplication and improve the cost effectiveness of digital infrastructures for genomics. These infrastructures – and the nature of sharing - could vary significantly. Potential examples could include, for example, equipment that is shared, digital resources that can be shared (such as gateways for cloud service access), or they could also cover coordinated purchasing of equipment to realise improved discounts from suppliers and build resilience into the wider genomics system. Key in this activity is pragmatism; the principle of sharing what is possible, in a way that ensures that organisations are not compromised in providing their core business, but not sharing where this is not cost effective or does not offer sufficient benefits over the cost of doing so. It will be essential to develop processes (e.g., information governance, cybersecurity, cost sharing) to ensure that this is a viable activity, and one that can be achieved without starting from a blank sheet of paper every time such sharing is possible.
- b. Building communities of practice and developing mechanisms to share expertise in building and managing genomics digital infrastructure across organisations.
- c. Building shared approaches for sequence analysis/processing (e.g., sharing expertise relating to use of capabilities such as the Illumina DRAGEN, approaches for human read mapping – used to remove human contamination in pathogen samples - and QC processes and metrics) and data storage, including the options for secondments and staff exchange.
- d. Building systems that provide shared data storage that fit the needs of both human and pathogen genomic services.
- e. Developing shared procurement routes and common frameworks for procuring digital services for genomics, that are matched to the needs of both human and pathogen genomic services.
- f. Developing infrastructure with a view to developing compatible digital infrastructures with a supporting governance framework to enable appropriate data sharing. This, in turn, would enable the use of human and pathogen genomic data in different ways/by different organisations (e.g., using pathogen data alongside host genetic information, or the use of host genetic data for population screening purposes), unlocking benefits to our patients and population, as well as potentially creating new research opportunities for Welsh researchers.

ACTION: Develop systems and opportunities for data sharing for research within Wales and externally. This includes work such as:

- a. Developing models for sustainable data ingest of pathogen genomic data into Trusted Research Environments such as SAIL, linked to other strategic

work such as the transition to the new National Pathology LIMS in Wales and the new Health Protection system.

- b. Pioneering a model for data sharing of genomic data in Wales, with appropriate consent models - that cover consent and data sharing models for pathogen data, microbiome data and in the future, linked human host data.
- c. Contribute to the development of a GPW digital strategy which all partners are signed up to.
- d. Support the development of an archive data storage solution and system to enable the use of NHS sequencing instruments by academic researchers, such as the GPW work to enable access to the All-Wales Medical Genomics Service NovaSeqs for Wales Gene Park.
- e. Contribute to the development of a set of principles and requirements to allow the selection of cloud-based services to meet digital needs.
- f. Contribute to the development of a GPW data strategy and digital blueprint for genomics in Wales, articulating the needs of pathogen genomics as part of the broader plan.