Metagenomics User Handbook

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1. Introduction

1.1 General Information

Synnovis is a partnership between Guy's and St Thomas' NHS Foundation Trust, King's College Hospital NHS Foundation Trust, and SYNLAB UK & Ireland, integrated pathology service across South East London. The collaboration combines clinical and scientific expertise from the NHS with the innovation, investment, and efficiency of a leading diagnostics organisation.

Synnovis provides pathology services to a population of over two million people and supports multiple hospital sites, including King's College Hospital Denmark Hill, Princess Royal University Hospital (PRUH), Guy's Hospital, St Thomas' Hospital, and Evelina London Children's Hospital, as well as numerous GP practices and community healthcare settings.

In recent years, Synnovis has expanded its scope beyond conventional diagnostics to include advanced molecular and genomic technologies. Building on this strategy, a new Pathogen Genomics Unit has been established within the Infection Sciences Division to enhance the detection and characterisation of infectious agents using Next Generation Sequencing (NGS) technologies.

This unit incorporates Oxford Nanopore Technologies (ONT) platforms to enable rapid, comprehensive identification of bacteria, fungi, and DNA and RNA viruses directly from clinical specimens.

A novel in-house metagenomics method, developed collaboratively by Synnovis and Guy's & St Thomas' NHS Foundation Trust (GSTT), has been implemented for clinical diagnostic use following extensive validation. This pioneering workflow includes human DNA depletion, total nucleic acid extraction, sequencing, and bioinformatics interpretation, allowing clinicians to obtain actionable results within hours, even for complex or culture-negative infections.

The Synnovis Pathogen Genomics Unit is fully integrated with clinical microbiology and infectious diseases teams, ensuring results are interpreted in the clinical context and directly inform patient management.

This Handbook includes information on:

- Contact details for key staff
- Service levels and hours of operation
- Location of services
- Types of investigation offered
- Types of specimens required and collection conditions.
- Instructions for collecting specimens with a particular emphasis on safety and maintenance of sample validity.

Should any service user have any queries in connection with any aspect of the Pathogen Genomics Unit, contact should be made with the relevant departmental senior staff, the Consultant Clinical Scientist, Operations Manager, Service Delivery Manager or the Department's Quality Manager.

This Metagenomics User Handbook should be user-friendly and intuitive. Suggestions for improving the content for the next edition are welcome.

1.2 Pathology Laboratory

The Infection Sciences Laboratory department includes the following specialties:

- Microbiology
- Virology
- Pathogen Genomics

Access to all areas of the Infection Sciences department is restricted to authorised staff only. All entrances into the department are secured by digi-lock or proximity pass access.

1.3 Key personnel and contact details

For Metagenomics Results phone Customer Services on: 0204 513 7300?

Clinical Lead		
Dr Adela Alcolea-Medina Consultant Clinical Scientist Adela.medina@synnovis.co.uk / adela.medina@nhs.net 02071887188 (Ext 58947)		
Metagenomics Core Laboratory Scientific Staff		
Name	**Designation**	**Contact details**
Dr Ronan Doyle	Clinical Bioinformatician	Ronan.doyle@synnovis.co.uk Ronan.doyle2@nhs.net 02071887188 (Ext 58947)
Duty Metagenomics (for clinical advice) Mon-Fri 9:00-5:30		02071887188 (Ext 58947)

Biochemistry Core Laboratories Operations Staff		
Name	**Designation**	**Contact details**
Gillian Maloney	Service Delivery Manager	Gillian.maloney@synnovis.co.uk
Lisa Bryan	Microbiology Operations Manager	Lisa.Bryan@synnovis.co.uk
Natasha Odubade	Infection Sciences Quality Manager	Natasha.odubade@synnovis.co.uk

Postal addresses:

Infection Diseases 5th Floor, North Wing

St Thomas' Hospital

Westminster Bridge Road

London SE1 7EH

2. Laboratory Service

The Metagenomics Unit provides unbiased metagenomic sequencing for the detection of bacteria, fungi, DNA and RNA viruses directly from clinical specimens.

This is a validated clinical diagnostic service for testing respiratory samples, enabling the rapid detection of pathogens from complex or culture-negative infections.

The service uses validated human DNA depletion and nucleic acid extraction pipelines, followed by Oxford Nanopore long-read sequencing and automated bioinformatic analysis for taxonomic classification and pathogen identification.

2.1 Normal laboratory opening times

Monday - Friday: 09:00 – 17:30

The Central Specimen reception at St Thomas' Hospital is open 24h and 7 days a week for specimen drop off.

Samples received before **8:00 am** are processed the same day. Sequencing runs may continue beyond standard hours at the discretion of the duty Clinical Scientist to ensure completion of ongoing analyses.

2.2 Out of hours service

There is not out of hours service for the metagenomics service.

3. Use of the Laboratory

3.1 Patient Identification and Specimen Labelling

Either an Epic Beaker or a paper-based request must accompany all specimens sent to the laboratory. It should clearly state the following information. Those in bold are a minimum requirement and without them the sample could be discarded or delayed:

- **Patient name**
- **Hospital number/NHS number**
- **Date of birth (age if DOB not known)**
- **Sex**
- **Ward or Address for report**

- **Requesting Medical Officer/GP name and number**
- **Date and time specimen taken**
- **Tests required**

Other useful data:

- Contact number or bleep for requesting clinician
- Patient address
- All relevant clinical details.

It is the responsibility of the person collecting the sample to ensure it is correctly labelled.

Under no circumstances is it possible to change the details once the sample has been sent to the laboratory.

The following will be rejected:

- Unlabelled specimens
- Inadequate patient information
- Mismatched samples and forms
- Grossly leaking specimens
- Low volume samples (<500 ul)

Specimens are accepted only when they are correctly labelled and collected as per instructions provided within this handbook and other related policies to ensure validity of the results.

The department will strictly enforce this policy. The requested analyses will **NOT** be performed on any samples where there is any discrepancy with patient identification.

3.2 Urgent tests

Only samples for which clinical details have been discussed and agreed with the Clinical Scientist in charge of the Metagenomics Service will be accepted for urgent testing.

Urgent samples can only be processed **after 08:00**, once authorisation has been obtained from the duty Clinical Scientist.
Samples received before 12:00 (midday) will be prioritised for same-day processing, and preliminary results will be reported by the evening of the same day.

Samples received **after 12:00** will be processed on the same working day, with results reported the following morning**.**

This approach ensures the appropriate prioritisation of clinically urgent cases while maintaining the integrity of the validated workflow and quality assurance processes.

Clinicians requesting urgent metagenomic testing must:

- Provide full clinical details on the request form (or via Epic Beaker)
- Discuss the case with the duty Clinical Scientist before sample dispatch
- Ensure the sample is clearly marked as **"URGENT – AGREED WITH METAGENOMICS TEAM"**

Any samples received without prior discussion or appropriate labelling will be processed under the routine turnaround schedule**.**

3.3 Transportation of Specimens

Metagenomic specimens must be transported in a manner that **preserves nucleic acid integrity**, particularly **RNA**, which is highly susceptible to degradation.

Samples must be **kept at refrigerated temperature (2–8 °C) at all times** from the point of collection until receipt in the laboratory. Exposure to room temperature, heat, or freezing conditions prior to processing is strictly prohibited, as this may compromise RNA quality and overall diagnostic accuracy.

If transport delays are anticipated, samples should be stored at **2–8 °C** and delivered to the laboratory as soon as possible. Ideally, samples should arrive within **24 hours of collection**.

When receiving samples from external institutions or laboratories, it is the responsibility of the sender to ensure that:

- Samples are packaged and transported in accordance with **UN3373** and **IATA Packing Instruction 650**.
- Packaging maintains **refrigerated temperature (2–8 °C)** throughout transit.
- All accompanying documentation is complete and securely attached.
- Courier or transport arrangements guarantee temperature control and prevent unnecessary agitation or delays.

Any specimens received outside the required temperature range, or found to be leaking or otherwise compromised.

3.3.1 Primary receptacle

- The **primary receptacle** must be a **watertight, leak-proof tube or container** containing the specimen.

- Each receptacle must be clearly labelled with **two patient identifiers**, **specimen type**, and **collection date/time**.

- The container must be sealed tightly and wrapped with sufficient **absorbent material** to contain the entire sample volume in the event of leakage.
- Samples should be maintained at **2–8 °C** from the time of collection. Use of refrigerated transport boxes or insulated carriers with cool packs is recommended.

3.3.2 Secondary packaging

- The **secondary packaging** must be **durable, watertight, and leak-proof**, enclosing the primary receptacle(s).
- Each sample should be placed in an individual plastic **biohazard "kangaroo" bag** with a separate pocket for request forms.
- Request forms (electronic or paper) must not be placed in the same compartment as the specimen to avoid contamination.
- Bags must be sealed securely (do not use staples, pins, or paperclips).
- Multiple primary containers may be included in a single secondary package provided they are properly cushioned and separated to avoid breakage.
- The secondary packaging should also contain **temperature-stabilising materials** (e.g. gel packs) to maintain 2–8 °C conditions during transit.

3.3.3 Outer packaging

- The **outer packaging** provides external protection and ensures compliance with transport regulations.
- It must be clearly marked with **UN3373 Biological Substance, Category B** labelling and include the sender's and recipient's contact details**.**
- The packaging must be rigid and shock-resistant, capable of withstanding handling during transit.
- For postal or external courier transport, an approved **UN3373-compliant transport box** must be used.
- For on-site or inter-hospital transfer, use a **rigid Daniels or equivalent biohazard transport container** that can be securely closed and disinfected after use.
- The outer packaging should include visible instructions indicating **"Keep Refrigerated (2–8 °C)"** and an emergency contact telephone number.

3.4 Transport of specimens by road

Metagenomics specimens are transported **only between clinical areas and laboratories within Synnovis partner hospitals**. No samples are accepted directly from General Practitioners or community settings.

Transport of these potentially infectious diagnostic specimens must comply with the **Carriage of Dangerous Goods and Use of Transportable Pressure Equipment Regulations 2009 (as amended)** and relevant **ADR** requirements. All metagenomics samples are classified as **Biological Substance, Category B (UN3373)** and must follow **IATA Packing Instruction 650**.

The following requirements apply:

- Specimens must be transported in **secure, rigid transport boxes** with a **fastened, leak-proof lid**.
- Each box must be clearly labelled with:
  - the **UN3373 diamond mark** and **biohazard warning symbol**,
  - the statement **"Biological Substance, Category B – Keep Refrigerated (2–8 °C)"**, and
  - an **emergency contact telephone number**.
- Boxes must be kept **refrigerated (2–8 °C)** throughout transport to maintain RNA stability and prevent sample degradation.
- Containers must be **placed in the boot of a car or rear compartment of a van**, separate from passengers, and **securely restrained** to prevent movement during transit.
- **Mail or other items must never be transported** in the same carrier box as specimens.
- Only **authorised hospital porters or designated courier staff** trained in specimen transport procedures may carry metagenomics samples.
- Sending departments are responsible for ensuring that the correct procedures are followed and that only **approved, correctly labelled transport boxes** are used.

This procedure ensures that all metagenomics specimens are transported safely, maintain integrity for sequencing analysis, and comply fully with national transport and biosafety regulations.

4. List of examinations performed in Pathogen Unit

At present, the Pathogen Genomics Unit provides a validated metagenomic sequencing service for the detection of pathogens in respiratory samples. This assay is designed to detect a broad range of bacterial, fungal, DNA and RNA viral pathogens directly from clinical specimens, without prior culture.

4.1 Turnaround times

Sample Type	Time Received in Laboratory	Preliminary Report Available	Final Authorised Report	Notes
Routine samples	Received before 08:00	By 15:00 same day	By 15:00 the following day	Routine testing performed in sequence with daily batch workflow.
Routine samples	Received after 08:00	By 15:00 the following working day	By 15:00 the subsequent day	Samples arriving after 08:00 are processed in the next scheduled run.
Urgent samples (agreed with Clinical Scientist)	Received before 12:00	By 17:00–18:00 same day	By 15:00 the following day	Only accepted following prior discussion and authorisation with duty Clinical Scientist.
Urgent samples (agreed with Clinical Scientist)	Received after 12:00	By 09:00 the following day	By 15:00 the subsequent day	Samples clearly labelled "URGENT – AGREED WITH METAGENOMICS TEAM."

4.2 Minimum sample volumes

Specimen Type	Minimum Volume	Storage / Transport Conditions
All samples	700 µL	Keep refrigerated (2–8 °C); **do not freeze**

4.3 Add ons

In metagenomic sequencing, the entire specimen is utilised during processing, and therefore add-on requests are not possible once a sample has entered the workflow.

If further investigation is clinically indicated, such as repeat sequencing, extended pathogen review, or confirmatory molecular testing (e.g. PCR), discuss with the Clinical Scientist to confirm the most appropriate diagnostic approach and ensure sample integrity is maintained.

5. Complaints

Formal complaints from users of the Metagenomics Service may be received through any of the following routes:

- **Synnovis Customer Services**
- **Patient Advice and Liaison Services (PALS)**
- **Directly to the Pathogen Genomics Unit or the Synnovis Quality Department**

All complaints are managed in accordance with the **Synnovis Complaints Policy** and the relevant Trust's procedures. Complaints are logged, investigated, and tracked through the QMS to ensure appropriate corrective and preventive actions are implemented.

The investigation and response process includes:

1. **Acknowledgement** of receipt of complaint.
2. **Investigation** by the relevant section lead, Quality Manager, or Service Delivery Manager.
3. **Documentation** of findings, root cause analysis, and corrective actions.
4. **Formal response** issued within the timeframe specified by Trust policy.

Complaints may be raised by:

- Hospital clinical or laboratory staff
- Referring clinicians
- Synnovis partner Trusts
- Patients, relatives, or representatives (via official Trust channels)

All complaints are reviewed during **Quality Management Review (QMR)** meetings, and trends are monitored to support continuous improvement.