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Ospidéal Ollscoile Chorcaí
Cork University Hospital

Molecular Virology

Diagnostics & Research Laboratory

Service Users Manual

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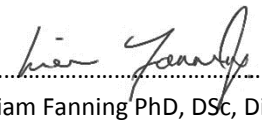
Foreword

The Molecular Virology Diagnostics and Research Laboratory (MVDRL) provides a diagnostic and clinical liaison virology service for clinicians investigating hepatitis B virus (HBV), hepatitis C virus (HCV), and human immunodeficiency virus (type 1) (HIV-1). The main focus of the laboratory's work is to provide specialist molecular virology diagnostic services. In 2017, over 4,000 patient samples were sent for testing to the MVDRL which reflects the value of the services offered. Requests for this service can only be made through a relevant hospital consultant. The tests available and specific requirements for specimen collection and delivery are outlined in this document.

The MVDRL is committed to providing the highest quality diagnostic and consultative services for all its users.



Liam Fanning PhD, DSc, Director, MVDRL.

May 2018

1 Introduction

1.1 Overview

This manual is designed to give an overview of the services and tests provided by the Molecular Virology Diagnostics and Research Laboratory (MVDRL). Included is a brief description of the laboratory, our location for delivery of specimens, key contact personnel, hours of service, instructions for completion of test request and report forms (TRRF) and instructions for collection and transportation of specimens to the laboratory. A number of molecular virology diagnostic tests are performed routinely. The MVDRL refers some specialised molecular testing to external laboratories and this manual includes the requirements for those tests. Requests for this service can only be made by hospital consultants or their designee.

This manual details the following:

- Available tests.
- Request forms and specimen containers required.
- Information necessary in the labelling of forms and containers.
- Requirements for the collection and delivery of specimens to the laboratory.

The laboratory requires that all test requests are made with the correct form. Completion of all sections of the request form is required. Test specimens must be collected as described herein and delivered to the laboratory within the assigned time requirements so that the best possible service can be delivered. Test requests may be rejected if acceptance criteria are not adhered to.

The quality of information provided to the laboratory directly impacts the quality of the service provided. Provision of the correct test sample with legible and appropriate clinical details on the sample tube facilitates an efficient processing and turn-around of the test request.

The information in this manual is subject to change and will be updated regularly to reflect the most up to date services available.

1.2 Disclaimer

This user manual has been prepared by the MVDRL and every care has been taken to ensure the contents are accurate and current at time of completion. **Users of the service should only use this manual as a guide to the testing procedures described herein and not as a complete or authoritative statement of testing available**.

Turn-around times described herein are from the date of receipt at the laboratory to the reports issuing date in calendar days. The turn-around times are median days typically achieved by the laboratory. Listed turn-around times are subject to change but the laboratory is committed to delivering a quality and timely service.

The MVDRL shall not be liable to users of the manual nor to any other person, firm, company or other body for any loss, direct, indirect, or consequential, in contract or in tort of for any negligent misstatement or omission contained herein, by reason of, arising from or in relation to any such user, other person, company or body relying or acting upon or purporting to rely or act upon any matter contained in this manual.

2 General information

2.1 Laboratory address

Full name and address: Molecular Virology Diagnostic and Research Laboratory
Department of Medicine
Clinical Sciences Building
University College Cork
Cork University Hospital
Wilton
Cork

The MVDRL is located in the Department of Medicine, University College Cork (UCC), on the first floor of the Clinical Sciences Building (CSB), Cork University Hospital (CUH). The CSB can be accessed in CUH via the connecting corridor from Outpatients. Turn right through the double doors at CUH Laboratory Reception and follow the corridor around to the left until you reach the CSB foyer. The entrance to the Department of Medicine is up the stairs on the right. The laboratory is located in room 1.10. The CSB can also be accessed from the back of the CUH campus using the Services Delivery/Staff Car Park entrance.

2.2 Hours of service

Routine hours:

Monday to Thursday	09:00-17.00	**Deadline for sample reception:**	**16.30**
Friday	09:00-16.00	**Deadline for sample reception:**	**15.30**
Saturday & Sunday	Closed		
Bank & Public Holidays	Closed (including Christmas Public Sector Holiday period)		

An out of hours' service is not available for testing, however, urgent samples will be accepted out of hours by CUH Laboratory Specimen receipt**.**

2.3 General MVDRL contact details

Website: www.ucc.ie/en/meddept/people/liam-fanning/mvdrl/

General enquiries:

Laboratory staff:	CUH internal line dial:	22552
	External line dial:	021-4922552

Any general queries related to service provision should be directed to Laboratory Staff using the contact details provided here. Results will only be reported in hard-copy format as soon as they have been authorised, see **Section 3, Communication of Results**. Enquiries regarding the interpretation of results and associated medical advice should be made through the Laboratory Director. Additional contact details are provided in Table 1.

Table 1. List of Contacts

Position	Name	Phone	Email
Director	Dr Liam Fanning	021-49**22554**	l.fanning@ucc.ie
Virology Associate	Mr John Levis	021-49**22552**	j.levis@ucc.ie
Quality Manager	Dr Kevin Hegarty	021-4901267	k.hegarty@ucc.ie

2.4 Summary of services available

Section 9, Test Directory, provides a detailed description of all diagnostic services available in the MVDRL. In summary, the molecular virology diagnostic services provided and guidelines for sample collection and processing are:

HBV	HCV	HIV-1[a]
•Viral load & genotyping •Plasma or serum •Minumum requirement of 6ml whole blood (2 mL separated sample)	•Viral load & genotyping •Serum only •Minumum requirement of 6ml whole blood (2 mL separated sample)	•Viral load & resistance profiling (by referral) •Plasma only •Minumum 6ml whole blood (2 mL separated sample) for viral load •Minimum of 18 mL whole blood (6 mL seperated sample) for resistance[b]

[a]Requests for a HIV-1 resistance profile can only be fulfilled if the patients' viral load at time of request is at least between 200 and 500 cp/mL. The Laboratory Director is available to discuss the suitability of performing resistance profiling on a case-by-case basis. [b]If viral load of the patient is unknown at the time of resistance request, send a minimum of 18 mL whole blood (6 mL separated sample) as the laboratory must measure the viral load prior to dispatching samples for resistance profiling.

2.5 Population served

Molecular virology services through the MVDRL are open to Hospital Consultants in both Cork and Kerry to meet the needs of the population of the Health Service Executive Southern Area. Test samples from other regions are accepted for testing providing the test request has been made through the correct channels, i.e. a Hospital Consultant. Unfortunately, requests from general practitioners (GP) will not be accepted. GP service requests must be made through correct channels, i.e. through referral with a hospital consultant.

2.6 Test Request and Report Forms (TRRF)

Tests requests* should only be made using official, virus specific, MVDRL TRRFs. Correct and up-to-date TRRFs are available on the MVDRL website (www.ucc.ie/en/meddept/people/liam-fanning/mvdrl/) under "Molecular Virology Diagnostic Testing". TRRFs are available at scheduled CUH clinics or batches of current TRRFs are available upon request.

***Please note**: by submitting any request form (MVDRL or otherwise) it is expected that the consent of the patient was obtained by the requesting clinician for the testing process to be engaged.

Completing the TRRF:

- The patient identification section of the TRRF must be completed with care. The information on the TRRF must match the information on the specimen blood tube. Bar-coded addressograph labels are the preferred format for completion of the patients' demographic details.
- The TRRF must include appropriate information including medication as certain substances can interfere with *in-vitro* diagnostic procedures, see **Section 2.9**.
- Contact details of the requesting clinician must be provided to validate the test request and so that the results generated can be returned without delay.

The quality of information provided to the laboratory directly impacts the quality of the service provided. Provision of legible and appropriate clinical details on the request form facilitates an efficient processing and turn-around of the test request.

Urgent Requests: if a test request is urgent, please indicate this on the TRRF by writing "URGENT" in the top right hand corner of the form.

2.6.1 Acceptance criteria for TRRFs

Essential information required includes:

1. Patients Medical Record Number (MRN/APX).
2. Patients full name (surname and forename).
3. Patients date of birth (DOB).
4. Requesting clinician(s).
5. Relevant clinical details including anti-viral therapies.
    a. Please indicate if the patient is currently taking heparin as this medication can interfere with *in-vitro* diagnostic testing procedures, see **Section 2.9**.

Additional appropriate information if available:

1. Any extra relevant clinical information.
    a. Include antibody/antigen status where relevant.
2. Change to patient's name or address.

2.7 General guidelines for specimen collection

In general, samples for viral load assessment should be collected following standard phlebotomy procedures and **sent to the laboratory within 6 hours of venipuncture**.

The following are the preferred specimen collection tubes (Vacuette®), however, suitable alternative tubes are accepted once they meet the criteria of the specimen required:

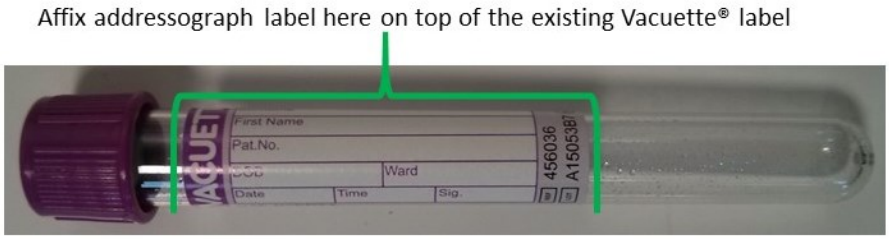
- 6 mL purple/lavender cap ethylene diamine tetra-acetic acid (EDTA) Vacuettes® for plasma collection.
- 9 mL pink cap Vacuette® with Z-clot activators for serum collection.
- For paediatric samples, use equivalent micro-tubes for plasma (EDTA) or serum (clot activators) collection.
    - Sample volume; at least 1.0 mL, preferably 2.0 mL.

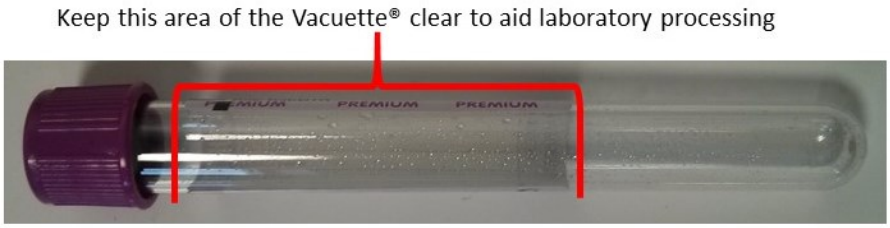
Refer to the **Test Directory, Section 9** of this user manual, for a list of test services available, the sample type required, time-line for delivery of samples from time of venipuncture and other relevant information regarding specimen collection.

2.7.1 Acceptance criteria for sample containers

Bar-coded addressograph labels are the preferred format for labelling of blood collection tubes.

- Care must be taken when attaching the addressograph label to the tube so that the label free side of the tube remains uncovered.
- **Please trim the addressograph label so that it covers only the prefixed label on the tube**:





- Inaccurate separation of plasma from white blood cells and other blood components can cause aberrant HIV results. Pealing or removing stickers post centrifugation can disturb the separated layers. Therefore, laboratory scientists performing the separation must have a clear view of the separated layers within the tube.
- Handwritten tube labels, with clear and legible script, are accepted.

Essential information required on the sample container includes:

1. Surname
2. First name
3. Patients MRN/APX
4. Patients DOB.
5. Date and time of specimen collection.
6. Identity of person taking sample e.g. phlebotomists initials.
7. Sample type (details on prefixed manufacturers label are suitable for this purpose).

2.8 Transportation of (suspected) infectious material

The MVDRL is a Biosafety Level 2 Laboratory. Specimens sent to the laboratory for testing must be considered as Biological Substance, Category B (UN 3373). Specimens that meet the criteria of UN 3373 are substances which are known or are reasonably expected to contain pathogens which can cause disease in humans or animals. The transport of specimens to the laboratory must be done in such a way as to minimise the risk of infection to those who may come into contact with the specimens.

2.8.1 General guidelines

As a general rule, all laboratory specimens should be treated as potentially infectious and standard precautions applied. Infection control guidelines for dealing with biological spills should be followed in the event of leakage or spillage of a specimen during handling or transport.

- The correct specimen container and laboratory request form must always be used when sending specimens to the laboratory.
- The primary specimen container must be suitable, closed correctly and **not externally contaminated**.

- The primary container and the accompanying request form must be correctly labelled so that the associated risk can be readily assessed if required, see **Sections 2.6 and 2.7**.
- Any evidence of contamination on the request form or the external surface of any specimen container or packaging will result in specimen rejection and immediate disposal.
    - The requestor will be notified in the event of a specimen rejection because of a contamination event.

2.8.2 On-campus transportation

The following are guidelines for transportation of specimens to the laboratory from within the CUH campus:

- Specimens must be placed in a biohazard bag that is correctly sealed.
- The accompanying request form must only be placed in the document slot out of direct contact with the primary specimen container.
- Specimens must never be sent in paper carrier bags.
- Under no circumstances should primary specimens be transported to the laboratory without suitable secondary packaging (i.e. plastic biohazard bag).
- Specimens must be handed directly to laboratory staff where practicable and not left outside the laboratory door unattended.

2.8.3 Off-campus transportation

UN 3373 describes the Internationally recognized packaging requirements for Biological Substance, Category B. The requirements of UN 3373 must be adhered to when samples are being shipped/couriered to the laboratory from locations external to the CUH campus. Those who prepare and ship specimens fitting the criteria for UN 3373 are required to know the requirements for proper transport, see **Appendix 1**.

2.9 Rejection criteria for test requests

The main reasons for test delay or cancellation are:

Test request forms:

- Incomplete forms/missing labels.
- Incorrect or missing MRN/APX.
- Contaminated (unidentified staining) of TRRF.
- Incorrect or illegible "**Clinical Details**" section on TRRF.
- Illegible patient demographics.
- Illegible name of requesting clinician.

Test specimens:

- Leaking containers.
- Delay in delivery of sample to the laboratory (**>6hrs post venipuncture results in sample rejection**).
- Incorrect labelling of specimen container.
- Incorrect or missing date of venipuncture.
- Discordancy between details recorded on specimen container compared to TRRF.
- Insufficient sample for testing.
    - **Note:** Refer to **Section 9, Test Directory**, for specific details on sample volume requirements for each investigation. Larger sample volumes are required for test requests additional to the standard viral load assessment.
- Incorrect sample for requested test.
    - **Note: Section 9, Test Directory**, details the specimen type requirements for each investigation. Please refer to the Test Directory to avoid collection of samples in the incorrect preservative/anticoagulant.
- Samples which are highly haemolysed, hyperlipaemic, or which contain gross contamination.
- Heparinised samples must be avoided.

- The presence of heparin in the test sample can cause inhibition in polymerase chain reaction (PCR) assays which are routinely used in molecular diagnostics.

Note: Identifiers on the request form must match exactly the identifiers on the blood collection tube.
Note: Section 9, Test Directory, provides specific details on the types and volumes of samples required for specific test requests.
Note: Please contact the laboratory if in any doubt about specific requirements.

2.10 Specimen retention policy

In accordance with the guidelines of the Health Service Executive's "Record Retention Periods: Health Service Policy 2013", the MVDRL will retain all serum/plasma specimens for a minimum of 2 years following date of receipt unless otherwise arranged.

2.11 Policy on protection of personal information

In the course of their work, MVDRL staff are required to collect and process personal data as defined by the General Data Protection Regulations (GDPR) (EU) 2016/679. It is the policy of the MVDRL to comply with the GDPR (EU) 2016/679 in relation to all "personal data" collected and processed in the course of processing specimens received for testing. Further details on the MVDRLs data protection policy is available on the University's website (https://www.ucc.ie/en/ocla/comp/data/).

3 Communication of Results

Results are reported (hard-copy format) as soon as they are authorised. The original submitted TRRF will be returned in hard-copy format **only** to the requesting Clinician. Telephone enquiries regarding patient results are available during hours of regular service, see **Section 2.2. Hours of service**. Enquiries regarding the interpretation of results and associated medical advice should be made through the Laboratory Director.

Routine communication of results by telephone, email or text message is not standard practice in the MVDRL. However, the requirement for issuing/discussing results outside of standard practice is understood and will be considered on a case-by-case basis. Communication of results using verbal or digital format will only be considered/authorised following consultation with the Laboratory Director (or an appointed designee) and will be limited to emergency situations only.

Under no circumstances will clinical staff other than the requesting clinician or a designee of their choosing be issued reports (verbal or otherwise). Patient consent is required if a copy of the report is not going to the source of the original request. Consent to issue a copy of the report to anyone other than the requesting clinician (or designee of their choosing) needs to be provided in writing by the patient. MVDRL Consent Forms are available for download on the MVDRL website.

4 Same-day results

Processing time required for molecular testing can range from 6 to 8 hours. Therefore, users should be aware that same day turn-around is not always achievable. The testing platform used by the laboratory is a batch system where diagnostic runs are performed only when the required number of samples is available for testing. The MVDRL is committed to providing a clinically relevant service and understands that downstream clinical decisions can be dependent on molecular diagnostic results. Therefore, it is recommended that service users contact the laboratory ahead of requesting tests to discuss the possibilities of expediting testing on an individual, case-by-case basis. Therapeutic or infection control decisions should not be deferred pending laboratory results without consultation with the Laboratory Director.

5 Supplementary Testing

The MVDRL can facilitate repeat testing of samples following review of clinical details and following consultation with the Laboratory Director. Repeat testing is dependent on the quality and volume of sample that was originally submitted. Refer to **Section 9, Test Directory** for specific details on sample requirements.

6 Referral Laboratories

National Virus Reference Laboratory (NVRL)
University College Dublin,
Belfield, Dublin 4.

Virus Reference Department
PHE Colindale, 61 Colindale Ave,
London NW9 5HT, UK.

7 Abbreviations

APX	See MRN
CSB	Clinical Sciences Building
CUH	Cork University Hospital
DOB	Date of Birth
EDTA	Ethylene diamine tetra-acetic acid
GP	General Practitioner
GDPR	General Data Protection Regulation
HBV	Hepatitis B Virus
HCV	Hepatitis C Virus
HIV	Human Immunodeficiency Virus
MRN	Medical Record Number
MVDRL	Molecular Virology Diagnostic & Research Laboratory
PCR	Polymerase Chain Reaction
RT-PCR	Reverse Transcription-Polymerase Chain Reaction
TRRF	Test Request and Report Form
UCC	University College Cork

8 Appendices

Appendix 1:

Transport Packaging requirements for UN 3373 Substances:
Any packaging for biological substances must include three components:

- A primary receptacle: the tube, vial or other container typically made of glass or rigid plastic (including the stopper, cap or other closure elements) that is in direct contact with the specimen.
- A secondary packaging (including cushioning and other materials) that fully encapsulates the primary receptacle.
- An outer packaging for shipping or transit.

In addition, one external surface of the outer packaging clearly must show the text "BIOLOGICAL SUBSTANCE, CATEGORY B." Adjacent to this, inside a diamond mark whose lines are at least 2 mm thick, must appear the text "UN 3373" in characters at least 6 mm high.

Components must meet specific requirements, including being capable of passing specific test procedures based on receptacle or packaging type. In addition, compliance with the regulations is based, in part, on overall performance; so there can be no substitutions of a component from one manufacturer with a similar – but untested – component from another manufacturer.

Refer to http://www.un3373.com/info/regulations/ for further details.

9 Test Directory

Note: All samples, regardless of requested test, **must be delivered to the laboratory within 6 hours of venipuncture** to ensure sample stability.
Note: For **paediatric samples**, use equivalent micro-tubes for plasma (EDTA) or serum (clot activators) collection. Please send at least 1.0 mL and preferably 2x 1.0mL samples.

Virus	Diagnostic Method	Specimen Required	Volume	Vacuette® Cap (preferred[1])	Testing Frequency[2]	Target Turnaround Time[2]
Hepatitis B Virus	PCR – quantitation of viral load.	Blood: EDTA Plasma (purple/lavender cap Vacuette®)	6.0 mL	 EDTA	Weekly	8 days (median time)
	Genotyping – virus resistance profile.	Blood: EDTA Plasma (purple/lavender cap Vacuette®)	6.0 mL		By arrangement	By arrangement
Hepatitis C Virus	RT-PCR – quantitation of viral load.	Blood: Clotted serum (pink cap – Vacuette®)	9.0 mL	 Serum	Weekly	4 days (median time)
	Genotyping – virus resistance profile.	Blood: Clotted serum (pink cap – Vacuette®)	9.0 mL		Bi-weekly	15 days (median time)
	Genotyping – patient/virus pharmacogenetic profiles.	Specialist tests, e.g. IL28B or Q80K. Please contact laboratory[3]	NA[3]	NA[3]	Referral by arrangement	Referral by arrangement
Human Immunodeficiency Virus Type 1	RT-PCR – quantitation of viral load.	Blood: EDTA Plasma (purple/lavender cap Vacuette®)	6.0 mL	 EDTA	Weekly	5 days (median time)
	Genotyping – virus resistance profile[4]. Recommended only in patients with ≥500 cp/mL.	Blood: EDTA Plasma (purple/lavender cap Vacuette®). Send at least 3x 6.0 mL tubes for resistance profiling[5].	3x 6.0 mL		Referral by arrangement	Referral by arrangement
	Proviral DNA Test	Specialist tests - contact laboratory[3]	NA[3]	NA[3]		

[1]These caps illustrate the preferred specimen collection tubes (Vacuette®), however, suitable alternative tubes are accepted once they meet the criteria of the specimen required. [2]Testing frequency and turnaround times are presented as median times and actual turnaround times are governed by several factors outside of the control of the MVDRL. However, the laboratory aims to process, test and issue reports as quickly as the programme for testing permits. Please contact the laboratory for more information on testing schedules. [3]Specialist pharmacogenetic tests are available through consultation with the Laboratory Director. [4]Samples with a viral load of between 200 and 500 cp/mL can be considered for resistance profiling following consultation with the Laboratory Director. [5]Send 2x 6.0 mL if present viral load of the patient is known. NA = not applicable. PCR = polymerase chain reaction. RT-PCR = reverse transcription PCR. EDTA = ethylene diamine tetra-acetic acid.