

THERAPEUTIC DRUG MONITORING (TDM) FREQUENTLY ASKED QUESTIONS

This is the first time I've used TDM. What are the key sample handling issues?

1. Blood samples should be obtained using EDTA or lithium heparin collection tubes.
2. The blood should be centrifuged within 4h of collection. This means that pre and post samples can be sent to the lab together. After centrifugation, plasma should be placed in a plain tube, ideally 1.5 ml screw top tubes (~48 mm x 13mm) as these are optimal for freezer racking.
3. Ensure that the Test Request Form is completed fully especially the dose, time since last dose and the drug to be analysed.

What type of samples should I collect for TDM?

We need plasma samples. Blood should be collected into EDTA or lithium heparin, centrifuged and the plasma separated.

What colour tubes should I use?

The colour of the tubes depends upon the manufacturer:

1. Sarstedt Monovettes are orange for lithium heparin and red/pink for EDTA.
2. BD Vacutainers are green for lithium heparin and lavender/pink for EDTA.

How much plasma do I need?

- | | |
|------------------|--------------------------|
| 1 or 2 drugs: | At least 1 ml of plasma. |
| 3 or more drugs: | At least 2 ml of plasma |
| PI + NNRTI: | At least 2 ml of plasma |

If volumes are likely to be a problem (e.g. for paediatric patients), 0.5 ml of plasma may be sufficient; however, this may only be enough for a single drug and may not allow for repeat analysis.

The blood has not been spun-down within 4h. Can it still be used for assays?

If it is spun within 12h of collection, the sample might still be suitable for analysis.

You should consider sending the sample but indicate the delay in spinning on the Test Request Form. Note that after 12h there is a risk of levels being lower due to degradation. This may cause problems if the concentration is at either end of the normal range.

At what time should the samples be collected?

Trough levels are utilised to determine whether the drug is within the desired target range (i.e. to check for efficacy) and we will usually provide an interpretation of the trough level.

Peak samples are not routinely required but may be useful in certain situations; for example, if the patient is experiencing toxicity on a particular drug. For most antiretroviral drugs there is no defined toxicity level. We can, however, provide information on where a patient's level falls compared to population PK data.

In certain situations it can be difficult to collect trough samples. In the case of efavirenz, etravirine and nevirapine, we can project trough concentrations using mean population half-life data on samples collected >4h post-dose. In the case of the PI regimens listed below, we can use population PK (percentile) data for samples taken >4 h post-dose to predict whether the trough is likely to be above or below the target value:

- Darunavir/r
- Fosamprenavir/r
- Atazanavir/r
- Atazanavir (unboosted)
- Lopinavir
- Saquinavir/r

Please note that this is not 100% accurate and a trough sample is preferable. For drug regimens not listed above, a true trough sample is required.

What is a trough sample?

A trough sample is collected at the end of the dosing interval, just before the next dose is due. The actual time depends on how often the patient is taking the drug.

For a twice daily regimen it is 12 h post dose (we can utilise samples taken between 10-14 hours); for a once daily regimen it is 24 h post dose (we can utilise samples taken between 20-28 hours). If a patient is coming to clinic for TDM in the morning, it is important that they do not take their morning tablets, but bring them to take after the blood sample has been collected.

I suspect that the patient is non-adherent. When should I take a sample?

TDM can be used to assess patient adherence to some antivirals but will only indicate if the most recent dose has been taken. As with all TDM samples, it is important to accurately record on the Test Request Form the 'hours post-dose of sample' and the 'sample time' columns for a relevant interpretation to be provided.

How should samples be sent?

Samples can be sent by DX (Hays) or by First Class post in appropriate packaging (often the laboratory spinning the blood will know how to package the samples). There is no need to pack samples on dry ice, even if they have been frozen prior to sending. Samples can also be sent in safe boxes. These provide leak-proof and tamper-proof packaging, pre-paid with First Class postage or special delivery, and are available from the Royal Mail on 08450 762000.

The patient is coming in on a Friday. What should I do with the samples?

Once the plasma has been separated (do not freeze the blood), the sample should be frozen over the weekend at -20°C or lower (i.e. wherever there is room!) and sent to us on Monday. The sample can thaw out in transit. There is no need to pack on ice.

The blood has been frozen. Can plasma be obtained?

No. Blood haemolyses when frozen and plasma cannot be obtained.

How much will it cost?

The cost is from £75 + VAT per drug per sample. NHS hospitals can claim the VAT back. Some drugs are covered by company schemes.

Which drugs are covered by drug company schemes?

Please check www.lab21.com for the latest information on pharmaceutical company sponsorship schemes. Where sponsorship is available, invoices will be sent directly to the pharmaceutical company.

For which drugs is TDM available?

Please check www.lab21.com for the latest information.

Do you measure NRTI levels?

We have assays for both tenofovir and lamivudine as part of our routine service.

Requests for assays of other NRTIs may be available by special arrangement but these are currently for research purposes only and may be subject to different turnaround times and charges.

What about enfuvirtide ?

We are able to receive samples for enfuvirtide assay by prior arrangement only, as this is subject to special shipping and handling arrangements (dry ice). The clinical target has not yet been defined, but TDM will allow you to compare the result with plasma levels seen in other patients.

Please check www.lab21.com for the latest information.

Where can I obtain a Test Request Form?

We are able to provide you with a Test Request Form as a PDF file personalised with your clinic and contact details (email your details to: info@lab21.com). Alternatively, you may download a standard PDF form from our web-site.

Delivery Instructions

1st Class post: Lab21 Ltd
184 Cambridge Science Park
Cambridge CB4 0GA

DX: Lab21, DX 6055300
Cambridge 94 CB

Contact Details

Telephone: 01223 395 450
Fax: 01223 395 451
Email: info@lab21.com
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