APPENDIX 4
Therapeutic Drug Level Monitoring

General Principles

- Only clinically relevant tests should be performed; **do not** perform tests that cannot be interpreted or do not assist patient management. Random levels that do not conform to the timings indicated below are not clinically useful.
- 'Peak' levels refer to the highest blood concentration of a drug after administration
- 'Trough' levels refer to the lowest blood concentration of a drug after administration
- 'Steady-state' refers to the situation reached when the intake of a drug equals that of its removal from the body
- Blood samples should be collected only after the drug concentration has reached steady-state i**.e. at least 4 half-lives at a constant dosing regimen.** Levels close to steady state may be reached earlier if a loading dose has been administered. Drugs with long half-lives may be monitored before steady-state has been achieved to ensure patients with impaired metabolism or renal excretion are not at risk of developing toxicity at the initial dosage regimen
- Drug concentrations may be requested for any of the following reasons:
    - Suspected toxicity
    - Lack of response
    - To assess patient compliance
    - To assess therapy following a change in dosage regimen
    - A change in clinical state of the patient
    - Potential drug interaction due to a change in other medications
    - Where manifestations of toxicity and disease are similar
- To interpret a result, the details of the dosage regime (dose and duration) must be known
- For patients suspected of symptoms of drug toxicity, the best time to take the blood specimen is when the symptoms are occurring
- If there is a question as to whether an adequate dose of the drug is being achieved, it is usually best to obtain trough levels (rather than peak) as these are less influenced by absorption and distribution problems. However, for some drugs where toxicity is a concern (such as gentamicin), peak levels may be requested
- A range of drug concentrations is usually targeted rather than a specific value as the effect of a drug at a known concentration may vary greatly between individuals
- Trough levels are usually obtained at the end of the dosage interval i.e. immediately before the next dose is due to be given
- Peak levels are usually obtained:
    - 30 minutes after an intravenous dose (if given by infusion, 30 minutes after the infusion has been stopped); aminoglycoside antibiotics (gentamicin, tobramycin) given by bolus should have their levels checked 30 minutes post dose to avoid the distribution phase
    - one hour after an intramuscular dose
    - one to two hours after oral dosing
    - slow release drugs may not produce peak levels for several hours after ingestion

Drug	Timing of blood sample	Vacutainer tube	Therapeutic Range
Carbamazepine	Sample immediately before next dose (trough)	**Red or Yellow**	16-50 micmol/L
Clozapine	Sample immediately before next dose (trough) or at anytime if toxicity suspected	**Red**	Trough 1000 nmol/L; Toxicity >2000 nmol/L
Cyclosporin	Sample immediately before next dose *(C0)* or exactly 2 hours post dose *(C2)*	**Purple**	**See drug monograph for interpretation**
Digoxin	Sample 8-24 hours post dose	**Red or Yellow**	0.6-2.0 nmol/L
Gentamicin	Sample trough level 2-4 hours before next dose is due	**Yellow or Red (Green for paeds)**	**See drug monograph for interpretation**
Lithium	Sample 12 hours post dose	**Yellow**	0.6-1.2 mmol/L
Phenobarbitone	Sample immediately before next dose (trough)	**Yellow, Red or Green**	65-130 micmol/L
Phenytoin	Sample at least 12 hours post dose (trough)	**Yellow**	Trough 40-80 micmol/L
Theophylline	For i/v infusion, sample at any time	**Yellow, Red or Green**	55-110 micmol/L
Tobramycin	- Trough: immediately before next dose - Peak: 30 mins post dose	**Red or Yellow**	Trough <1mg/L Peak 20-30mg/L
Vancomycin	- Sample daily in routine morning bloods, beginning **day after** starting infusion	**Red, Yellow or Purple**	18-25mg/L **See drug monograph**

All table data taken from the CCDHB Laboratory Test Database (January 2013)

For Paracetamol toxicity see ***APPENDIX 3***

References

1. Gross AS. Best practice in therapeutic drug monitoring. Br J Clin Pharmacol 1998;46(2):95–9
2. Birkett DJ. Therapeutic drug monitoring. Austr Prescr 1997;20:9-11
3. Kang JS, Lee MH. Overview of therapeutic drug monitoring. Korean J Intern Med 2009;24(1):1–10