### CRITICAL VALUES FOR THERAPEUTIC DRUG LEVELS

The concept of critical values for drug levels was originally developed by the late Daniel M. Baer, MD, and first published in the April 1982 issue of MLO. This table is an expanded version of that publication and newly revised for 2016-2017 by Catherine A. Hammett-Stabler, PhD, DABCC, FACB, Professor of Pathology, Director of Core Laboratories at McLaren Clinical Laboratories at UNC Medical Center in Chapel Hill, NC.

**Drug** | **Indication** | **Therapeutic Range** | **Critical Value** | **Comments**
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Aetominophen | Analgesic | 5-20 µg/mL | >200 µg/mL; drawn 4 hours after ingestion | *Determination if a concentration is toxic is dependent upon when it is drawn in relation to the time of ingestion of the dose. Multiple serum concentrations will be needed to monitor improvement and removal of drug.*

Amikacin | Antimicrobial | Peak: 15-30 µg/mL; Trough: 4-8 µg/mL | >10 µg/mL | Peak: 30 minutes after end of infusion. Trough: before next dose. Conventional dosing protocol.

Amiodarone | Antiarrhythmic | 0.5-2 µg/mL | >2.5 µg/mL | Trough concentration. Serum amiodarone levels >2.5 µg/mL had a positive predictive value of 76% for adverse drug events.

Amisulpride | Antidepressant/| 125-250 ng/mL | >500 ng/mL | Trough concentration. Life threatening cardiac toxicity and/or seizures with concentration >1000 ng/mL.

Carbamazepine | Anticonvulsant/mood stabilizer | 4-12 µg/mL | >20 µg/mL | Trough concentrations. Correlate serum concentration with clinical presentation.

Cyclosporine | Immunosuppressant | 100-400 ng/mL | >500 ng/mL | Specific concentration goal dependent upon clinical situation. For concentrations drawn with intravenous therapy, blood should be drawn from site other than that where drug is being infused. (Cyclosporine adheres to plastic). TDM levels are dependent on transplant type.

Digoxin | Inotropic, AV node blocker | 0.5-2.0 ng/mL | >2.5 ng/mL | Samples should be drawn >8 hours after last dose.

Doxepin | Antidepressant | 110-250 ng/mL | >500 ng/mL | Trough concentration.

Etoxaximide | Antiepileptic | 40-100 µg/mL | >200 µg/mL | Trough concentration.

Flecainide | Antiarrhythmic | 0.2-1.0 µg/mL | >1.0 µg/mL | Midpoint or trough concentration.

Flucytosine | Antifungal | 25-50 µg/mL | >100-200 µg/mL | Concentration should be a peak drawn 2 hours post dose.

Gentamicin | Antimicrobial | Peak: 4-10 µg/mL; Trough: <2 µg/mL | >12 µg/mL | Peak: 1 hour after infusion. Trough: before next dose. Conventional dosing protocol.

Imipramine | Antidepressant | >180-240 µg/mL | >500 ng/mL | Concentration = imipramine + desipramine (metabolite).

Lamotrigine | Anticonvulsant/mood stabilizer | 1-15 µg/mL | >20 µg/mL | Trough concentration. High concentrations generally associated with increased somnolence/confusion.

Lidocaine | Antiarrhythmic | 1.5-5 µg/mL | >6 µg/mL | Concentration can be drawn at any point (from separate IV line).

Lithium | Mood stabilizer | Acute: 1-1.6 mmol/L; Chronic: 0.6-1.2 mmol/L | >2.8 mmol/L; >5 mmol/L potentially fatal | Serum concentrations may increase in presence of hyponatremia. Concentration: 12 hours after dose.

Nortriptyline | Antidepressant/analgesic (neuropathic pain) | 50-150 ng/mL | >500 ng/mL | Trough concentration.

Phenobarbital | Antiepileptic | 15-40 µg/mL | >60 µg/mL | Trough concentration. Do not collect before steady state achieved.

Phenytoin | Antiepileptic | 10-20 µg/mL | >20 µg/mL | Trough concentrations. Tox: >20 µg/mL (lateral nystagmus), >40 µg/mL (decreased mentation). Toxicity may occur at lower concentrations in presence of hypoalbuminemia. Consider free phenytoin.

Primidone | Antiepileptic | 5-12 µg/mL | >15 µg/mL | Metabolized to Phenobarbital.

Procarbazine (PA) (metabolite: NAPA) | Antiarrhythmic | PA: 4-8 µg/mL; NAPA: 10-20 µg/mL | >10 µg/mL; >40 µg/mL | Mid-point or trough concentration. Procarbazine monitoring is particularly important in patients who might be fast acetylators (60% to 70% of northern Europeans, and 50% of black and white Americans) and in patients with renal impairment. Procarbazine and N-acetylsalicylic acid levels should always be measured on the same sample.

Prometidine | Antidepressant | 30-70 µg/mL | >500 ng/mL | Trough concentration.

Quinidine | Antiarrhythmic | 2-5 µg/mL | >6 µg/mL | Midpoint or trough concentration.

Salicylate | Analgesic, antipyretic | Anti-inflammatory | 20-100 µg/mL; 100-200 µg/mL | Vertigo, tinnitus 150-300 µg/mL; Nausea, vomiting, hyper ventilation 250-400 µg/mL; Toxicity >500 µg/mL | Serum concentration should be used in conjunction with clinical presentation to make decision on therapy. Multiple serum concentrations will be necessary to monitor improvement and removal of drug.

Sirodol | Immunosuppressant | 4-20 ng/mL | >25 µg/mL | Trough concentration. Whole blood samples. Therapeutic levels can be lower when used in combination with other immunosuppressants. Blood concentrations can be measured using immunoassay or mass spectrometry. Therapeutic levels depend on the type of transplant, time post transplant and other concomitant drug therapy.

Tacrolimus | Immunosuppressant | 5-20 ng/mL | >25 ng/mL | Whole blood samples collected as trough. Therapeutic levels can be lower when used in combination with other immunosuppressants. Bias may be present between immunoassay and LC/MS methods.

Theophylline | Bronchodilator | 10-20 µg/mL | >25 µg/mL | Pulmonary literature suggest that concentrations 5-15 mg/L may be as efficacious with less toxicity. Trough concentration dependent upon drug formulation.

Tobramycin | Antiepileptic | Peak: 4-8 µg/mL; Trough: <1.0 µg/mL | >12 µg/mL; >2 µg/mL | Conventional dosing protocol. Peak: 1 hour after end of infusion. Trough: before next dose.

Valproic acid | Antiepileptic/mood stabilizer | 50-125 µg/mL | >200 µg/mL | Toxicity may occur at lower concentrations in presence of hypoalbuminemia. Consider free valproic acid. Trough concentration preferred.

Vancomycin | Antimicrobial | Trough concentrations: General: 5-15 µg/mL; Pneumonia: 15-20 µg/mL | >30 µg/mL | Monitoring of peaks no longer recommended. Goal trough concentration dependent upon indication. Trough: before next dose.

Voriconazole | Antifungal | >1.0-5.5 µg/mL | >6 µg/mL | Trough concentration preferred. Steady state achieved after 7 days of therapy.

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Ranges are approximate and may vary with laboratory and/or assay.

Proper interpretation of therapeutic drug concentrations requires that the specimen be drawn at an appropriate time in relation to drug administration.