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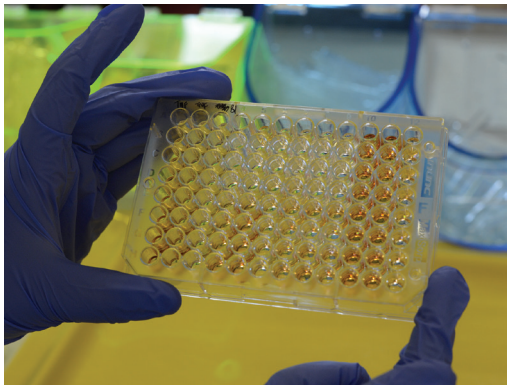
# Infliximab Therapeutic Drug Monitoring

*Serum infliximab and total anti-infliximab antibodies*

## Clinical Biochemistry



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## Sending Specimens for Analysis

**Sample requirements:** 0.5 mL of serum can be used for both infliximab drug levels and anti-infliximab antibody analysis.

- The clotted blood sample should be separated within 4 hours of collection.
- Please store serum at –20 °C prior to dispatch. Samples may be sent at ambient temperature by first class post to the address on the back of this leaflet.
- Separated serum is stable for 3 days at room temperature and at least 5 days at 4 °C.
- To aid interpretation of results, it is essential that the following information is included on the request form:
  - Infusion dosing interval
  - Number of infusions to date
  - Reason for request, i.e., not responding
  - Primary diagnosis

## Sample timing

A TROUGH level sample should be taken just before the next infusion is given (minimum of 6 weeks post previous infusion). To allow steady state concentrations of infliximab to establish, it is advised that the samples are only collected from patients on maintenance infliximab therapy.

**Note:** The Infliximab test detects Remicade® as well as biosimilars Remsima® and Infelctra®.

**Caution:** The Infliximab test may detect other anti-TNF alpha drugs.

## City Hospital Infliximab TDM Service

### Infliximab TDM testing strategy

Our strategy is that all samples for Infliximab TDM will be first analysed for infliximab drug levels. If the infliximab levels are below the therapeutic cut-off of 1 µg/mL, the sample will be analysed for anti-infliximab antibodies.

### Serum infliximab assay

We measure serum infliximab using an inhouse ELISA method. The between batch CV's are: <10 % at the lower reporting limit, <6 % at 1.5 µg/mL and <10 % at 4.0 µg/mL. The assay has been validated against a commercial kit. Our assay measures total infliximab levels (bound & unbound), which is unaffected by TNFα concentrations.

***Therapeutic ranges***

We suggest a cut-off for a therapeutic trough infliximab level of >1.0 µg/mL in a patient on maintenance dose infusions.[1]

***Reporting range***

Our reporting limits are as follows:
Lower limit: <0.4 µg/mL; Upper limit: >10.0 µg/mL

### Anti-infliximab antibodies assay

We test for total anti-infliximab antibodies using a commercial kit and report quantitative results. Measuring total antibodies avoids problems with false negative results in patients with a detectable infliximab concentration.

***Reference ranges***

Negative: <10 AU/ml; Borderline Positive: 10-20 AU/ml; Positive: >20 AU/ml.

***Reporting ranges***

Reporting limits are as follows:
Lower limit: <5 AU/ml; Upper limit: >450

## Infliximab background

Infliximab (Remicade®) is a chimeric humanmouse monoclonal antibody directed against tumour necrosis factor-alpha (TNF-α), approved for use in the treatment of various chronic inflammatory diseases including rheumatoid arthritis, severe crohn's disease and ankylosing spondylitis. The drug is administered as an infusion with a dosing interval ranging from 2 to 16 weeks.

Infusion of a standard dose of infliximab leads to highly variable inter-individual serum drug concentrations partly due to the development of anti-infliximab antibodies, which bind to infliximab leading to loss of therapeutic effect. Serum trough drug levels have been shown to correlate with clinical response and duration of effect. Furthermore, infliximab is associated with serious side effects with increasing number of infusions and cost is also a significant issue.

## Indications for therapeutic drug monitoring of infliximab

The main indication for undertaking infliximab TDM is lack of clinical response to the drug. A trough serum infliximab concentration of < 1 µg/mL, in a patient on maintenance infliximab, indicates sub-therapeutic levels. If anti-infliximab antibodies are present, further drug dose increases / infusion interval decreases are less likely to be effective and a change in drug therapy should be considered. In patients with low levels of infliximab but absent antibodies, a dose increase / infusion interval decrease may improve response and here it may be useful to remeasure the serum infliximab levels prior to the next infusion.

Positive anti-infliximab antibodies are also associated with an increased risk of infusion reactions and in such patients, concomitant immunosuppressive therapy to reduce the risk might be considered.