Evaluating Multiple Technology Platforms to Meet Challenges of Developing a Ligand Binding Assay to Support Clinical Trials Conducted in Adult or Pediatric Populations
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Purpose
Measuring total target levels during a clinical trial is a powerful parameter that allows better understanding of pharmacokinetic (PK)/pharmacodynamics (PD) relationships. When conducting a trial in adults versus children, the characteristics of this type of assay can be very different. The assay sensitivity, throughput and especially sample volume availability are bioanalytical factors that often change. To support a monoclonal antibody targeting a circulating inflammatory cytokine in development for a pediatric indication, it was necessary to evaluate a range of technology platforms to achieve the optimum ligand binding assay capable of measuring total target levels in adult or pediatric serum samples.

Methods
A panel of anti-target antibodies was initially screened in an ELISA-based format and an assay developed with a sensitivity of 0.7 ng/mL. In order to improve sensitivity and to reduce sample volume by automating the assay, the same panel of anti-target antibodies was re-screened on the Gyrolab, Mesoscale and immune-PCR based technology platforms to select the most appropriate antibody reagents and the best assay format.

Results
Different antibody reagents were found to be suitable on the 3 platforms. Although it was possible to develop an assay on the Gyrolab and Mesoscale platforms, it was not possible to continue with the immune-PCR based technology due to a selectivity issue. On the immune-PCR based technology >50% of normal serum samples tested showed an abnormal endogenous level of cytokine which was considered an artefact.

Using the Gyrolab and Mesoscale technologies, an improved assay sensitivity was achieved over the ELISA assay, i.e., 0.2 ng/mL and 0.05 ng/mL, respectively. The assays run with these two technologies had a similar minimal required dilution and comparable assay run time of 4h. A sample volume of 25 microlitres was considered to be acceptable for serum samples coming from either adult or pediatric populations.

Conclusion
Having a choice of antibody reagents and assay technology platforms is crucial in order to deliver the most suitable assay for clinical sample testing activities. We successfully developed Gyrolab and Mesoscale assays which were suitable to measure total target levels in all patient samples tested (adult and pediatric).