Issues with transferring Gyros preclinical assays to clinical

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Consult the doctor

Background to the issue

Gyros platform

1. Excellent platform for Ligand binding
    1. Quick, fully automated, very consistent, requires small sample and reagent volumes and experience in GSK is it either works or doesn't
    2. Extensively used across GSK in discovery and preclinical development
2. When transferring to clinical we struggle with lower limit of quantification (LLQ) and specificity
    1. Typically looking for an order of magnitude reduction in LLQ
    2. Typically move from recombinant protein to Anti-ID approach (reagent supply consistency)
    3. However also have issues transferring identical preclinical assay to clinical (affinity and specificity)
    4. Stability of Alex Fluor 647 detector reagents
        1. Supply in house as labelling Anti-ID

Discusion

1. Do other companies have these issue's?
    1. Transferring assays
        1. Typical LLQs across the industry (GSK human 10ng/mL)
        2. The use of Anti-ID
        3. Transferring Identical preclinical assays to clinical
        4. What assay format have the highest success rate for assay transfers?
2. Stability with detector reagents
    1. In house labelled or commercially sourced?
    2. What Fluorophores are used?

Possible solutions/ideas

1. Gyros appears sensitive to reagent quality due to short interaction time
2. Better anti-ID affinity and specificity
    1. Stringent selection criteria (mAb)
    2. Phage library derived antibodies
    3. Affinity maturation
3. Detector
    1. Better fluorophores e.g. Quantum dots