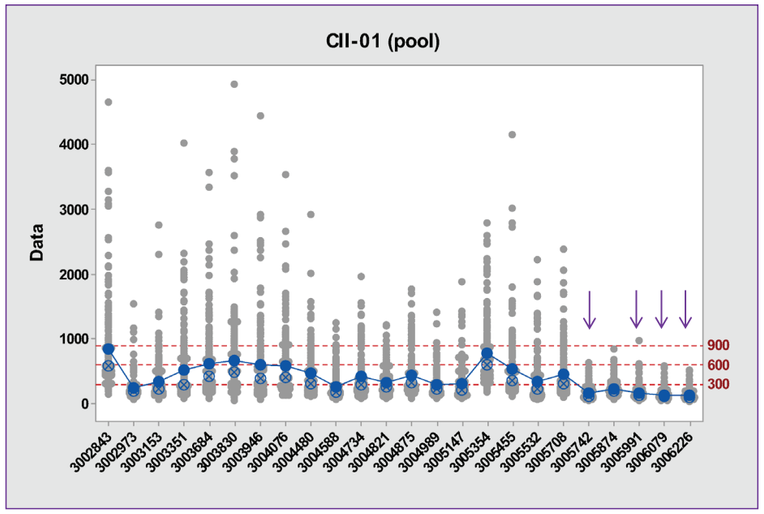
b) Plot of individual background values for the 180 non-transfused male samples on CII-01 beads as a representative of other class II beads. Mean values are connected by a blue line. Median values are shown as circled with X.



Conclusions:

Optimization of the LIFECODES LifeScreen Deluxe assay reduced background signals, especially in class II beads. This will result in lower false positive rates and better lot to lot reproducibility. This optimization will also be applied to LIFECODES Class I and II ID assays to further improve the performance of LIFECODES antibody screening products. This white paper summarizes the data illustrating the improved performance of the LIFECODES LifeScreen Deluxe assay.

Challenges still exist to determine true positive and negative results due to the limitation of both cell based assays and bead based assays. This is a continuous challenge, and a focus for continued innovation to assist transplant laboratories. As an assay manufacturer, we are dedicated to providing products with accurate and consistent performance which is critical for the transplant community to improve transplant outcomes. As demonstrated by the LIFECODES LifeScreen Deluxe optimization program, Immucor is continuously and diligently working toward improved product performance.

References

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IMMUCOR

Optimized LIFECODES® LifeScreen Deluxe:
Continuous Quality Improvement

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Optimized LIFECODES® LifeScreen Deluxe: Continuous Quality Improvement

Introduction:

The presence or absence of HLA-specific antibodies has a role in determining the survival of transplant allografts (1). Exposure to foreign HLA antigens leads to the production of HLA antibodies in approximately 33% of patients awaiting transplant (2, 3). The LIFECODES LifeScreen Deluxe assay is a qualitative Luminex® xMAP bead based immunoassay that detects class I and class II HLA antibodies in serum samples.

The LIFECODES LifeScreen Deluxe assay is composed of unique beads coated with affinity purified class I and class II HLA antigens. An anti-Human IgG antibody conjugated to phycoerythrin is used as a reporter and analyzed on the Luminex instrument. The signal intensity from each bead is compared to the signal intensity of a negative control bead to determine the presence or absence of HLA antibodies.

Immucor has recently completed a significant investment to reduce the background signal and improve lot to lot reproducibility for the LIFECODES LifeScreen Deluxe Class II antigens. The optimization included a thorough assessment of the systems and process controls used to manufacture the LIFECODES LifeScreen Deluxe assay, and resulted in the implementation of a new cell growth system used to grow and harvest antigens.

This white paper summarizes the internal data generated as part of the optimization program. The LIFECODES LifeScreen Deluxe optimization program was successful in reducing background signals and false positive rates for Class II beads, as well as improving lot to lot consistency. Because of the success obtained with Class II, Immucor has already applied this technology to the Class I antigens to release a fully optimized LIFECODES LifeScreen Deluxe assay.

Materials And Methods:

The LIFECODES LifeScreen Deluxe assay was performed according to the product insert.

Different lots of LIFECODES LifeScreen Deluxe were tested with a panel of sera collected from 180 non-transfused males for this study.

Results:

Figure 1 shows the historical background MFI data for class I and class II beads spanning lots released from August 2015 to January 2018. Each production lot of LIFECODES LifeScreen Deluxe was tested with a panel of sera collected from 180 non-transfused males. Background MFIs (mean values of 180 non transfused male) for class I (figure 1a) beads show relatively low and stable background below or around 300 MFI (figure 1a, purple line). Background MFIs for class II (figure 1b) beads show high MFI in lots released between August 2015 (lot 3002843) and August 2017 (lot 3005708), especially for the CII-02 beads, which represent the DR51 CREG.

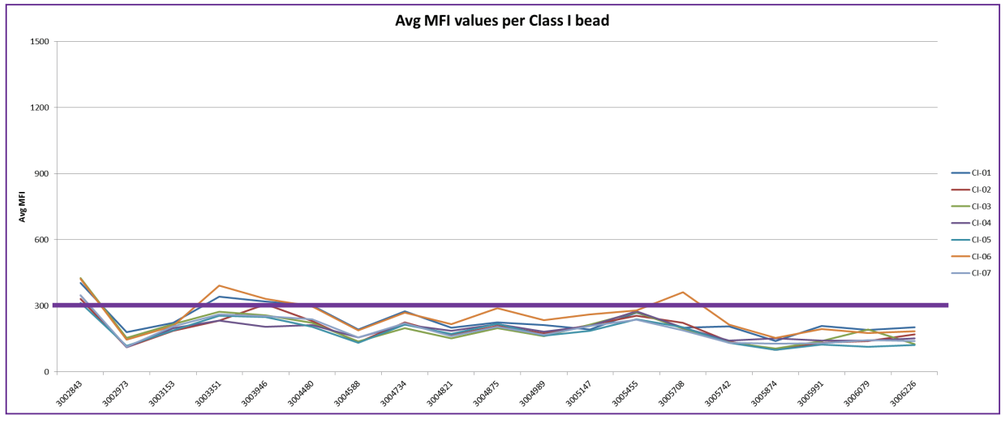
Initial updates to the manufacturing process were applied from December 2016 (lot 3004734) to August 2017 (lot 3005708) as indicated by the purple rectangle in figure 1b. The overall background MFIs were reduced in these lots compared to the lots released before December 2016. However, background MFI is still higher than 300 (figure 1, purple line) for most of the beads, especially for the CII-02 beads.

Optimized antigen production using a new cell culture system was implemented in September 2017 (lot 3005742) and was released as an RUO/PEO lot for customer evaluation (figure 1b, dotted purple arrow). This lot shows significant decrease in background MFI value compared to previous lots. After the evaluation, three IVD lots (lot 3005991, 3006079 and 3006226) with optimized antigen production were built. These lots also show the consistently low background MFI values (figure 1b, solid purple arrows).

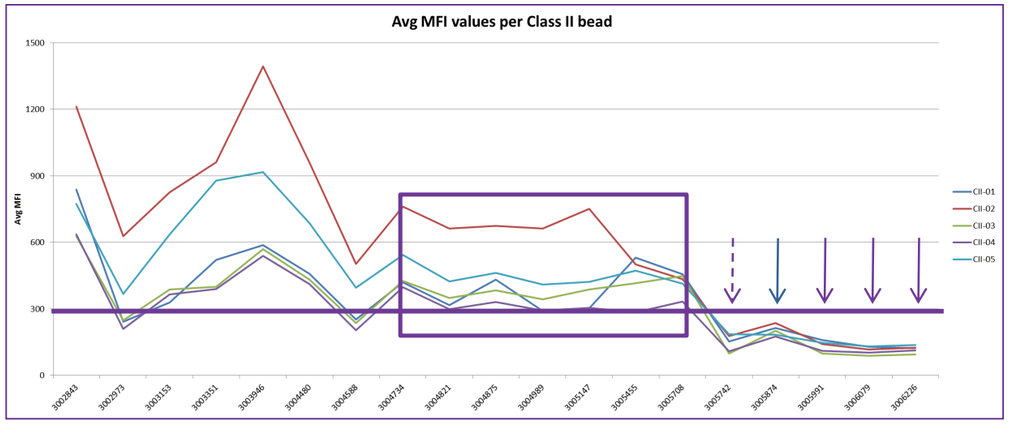
Note that lot 3005874 (figure 1b, blue arrow) was a selected lot with antigens built using the old cell culture systems that showed low background MFI. The low background MFI of this lot with old cell cultures system indicates the variability of the background MFI using the old cell culture system.

Figure 1.

a) Background MFI values for class I beads



b) Background MFI values for class II beads.



CII-02 beads showed the highest background MFI before optimizing the antigen production. The individual value plot of the CII-02 beads shows the spread of background MFI values from below 300 to up to 9000 MFI before optimizing antigen production (from lot 3002843 to lot 3005708). After optimizing antigen production, the background MFI variability is significantly reduced as shown in figure 2a (purple arrows).

As shown in figure 2b (purple arrows), the background MFI variability of other class II beads are reduced significantly (CII-01 beads are shown as an example, CII-03, 04, and 05 beads showed the similar MFI variability as CII-01 beads). These results indicate improved lot to lot consistency as a result of optimized antigen production across all class II beads.

Figure 2.

a) Plot of individual background values for the 180 non-transfused male samples on CII-02 beads. Mean values are connected by a blue line. Median values are shown as circled with X.