# The new biosimilar of infliximab SB2 can be quantified by IFX-optimized therapeutic drug monitoring assays

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## Background and Aims

SB2, a biosimilar of the originator Infliximab(IFX), has been recently approved by the European Medicines Agency (EMA) for the treatment of IBD. Therapeutic Drug Monitoring is widely used in the adjustment of IFX therapy and is expected to be used in the adjustment of biosimilars. The aim of this study was to validate utilization of IFX-optimized therapeutic drug monitoring assays for the quantification of biosimilar SB2. Moreover, the existence of IFX, CT-P13 and SB2 cross-immunogenicity was also evaluated.

## Methods

Spiking with known concentration of originator IFX, CT-P13 and SB2 were performed in donors' samples and the percentage of recovery of each assay was evaluated. Three different IFX quantification assays were evaluated: an *in-house* built method, a commercially-available ELISA assay from R-Biopharm and a point-of-care device (POC-IFX) from Buhlmann (Quantum Blue). Reactivity of SB2 to patients-extracted anti-IFX and anti-CT-P13 antibodies was quantified using the *in-house* built method.

## Results

Quantitative comparison showed an excellent ICC between the three assays when evaluating SB2, originator IFX and CT-P13. ICC was 0.986, 0.979 and 0.974 for POC IFX/*in-house* ELISA, commercial ELISA/*in-house* ELISA and commercial ELISA/POC IFX, respectively. The results show that all tested IFX-optimized assays are equally accurate in measuring SB2 levels: the intraclass correlation coefficient (ICC) between theoretical and measured concentrations varied from 0.945 to 0.983.

**Table 1 : ICC between the theoretical and measured concentrations**

| | ICC | | Difference | |
|---|---|---|---|---|
| | ICC | CI95% | Average | CI95% |
| **COMMERCIAL ELISA** | | | | |
| Spiked concentrations- IFX | 0.986 | 0.949-0.996 | -0.72 | -1.82 |
| Spiked concentrations- CT-P13 | 0.990 | 0.964-0.997 | -0.10 | -0.98 |
| Spiked concentrations- SB2 | 0.945 | 0.796-0.985 | -0.69 | -3.05 |
| **POC IFX** | | | | |
| Spiked concentrations- IFX | 0.982 | 0.932-0.995 | 0.94 | -0.23 |
| Spiked concentrations- CT-P13 | 0.985 | 0.945-0.996 | 1.33 | 0.31 |
| Spiked concentrations- SB2 | 0.983 | 0.938-0.996 | 1.28 | 0.14 |
| ***IN-HOUSE* ELISA** | | | | |
| Spiked concentrations- IFX | 0.951 | 0.818-0.987 | -1.31 | -3.54 |
| Spiked concentrations- CT-P13 | 0.920 | 0.702-0.978 | -0.46 | -3.42 |
| Spiked concentrations- SB2 | 0.972 | 0.896-0.992 | -0.39 | -1.99 |

**Table 2. ICC between the different methods.**

| | ICC | | Difference | |
|---|---|---|---|---|
| | ICC | CI95% | Average | CI95% |
| **IFX** | | | | |
| Commercial ELISA – POC IFX | 0.990 | 0.961-0.997 | 1.66 | 0.70 |
| Commercial ELISA – *in-house* ELISA | 0.978 | 0.918-0.994 | -0.59 | -2.20 |
| POC IFX – *in-house* ELISA | 0.968 | 0.881-0.991 | -2.25 | -4.08 |
| **CT-P13** | | | | |
| Commercial ELISA – POC IFX | 0.995 | 0.980-0.999 | 1.44 | 0.79 |
| Commercial ELISA – *in-house* ELISA | 0.957 | 0.839-0.988 | -0.35 | -2.61 |
| POC IFX – *in-house* ELISA | 0.936 | 0.761-0.983 | -1.79 | -4.42 |
| **SB2** | | | | |
| Commercial ELISA – POC IFX | 0.974 | 0.905-0.993 | 1.96 | 0.29 |
| Commercial ELISA – *in-house* ELISA | 0.979 | 0.922-0.994 | 0.30 | -1.32 |
| POC IFX – *in-house* ELISA | 0.986 | 0.946-0.996 | -1.66 | -2.85 |

Finally, the anti-IFX and anti-CT-P13 sera reacted almost to the same extent to SB2, originator IFX and CT-P13, with ICCs ranging from 0.986 to 0.993

**Table 3. ICC between the anti-drug reactivity of IFX and its biosimilars.**

| | ICC | | Difference | |
|---|---|---|---|---|
| | ICC | CI95% | Average | CI95% |
| **Anti-IFX serum** | | | | |
| SB2-CT-P13 | 0.988 | 0.977-0.994 | -0.83 | -1.13 |
| SB2-IFX | 0.992 | 0.984-0.996 | -1.49 | -1.77 |
| IFX-CT-P13 | 0.986 | 0.972-0.993 | 0.66 | 0.31 |
| **Anti-CT-P13 serum** | | | | |
| SB2-CT-P13 | 0.989 | 0.978-0.994 | 0.29 | 0.07 |
| SB2-IFX | 0.987 | 0.975-0.993 | -0.36 | -0.61 |
| IFX-CT-P13 | 0.993 | 0.986-0.996 | 0.65 | 0.46 |

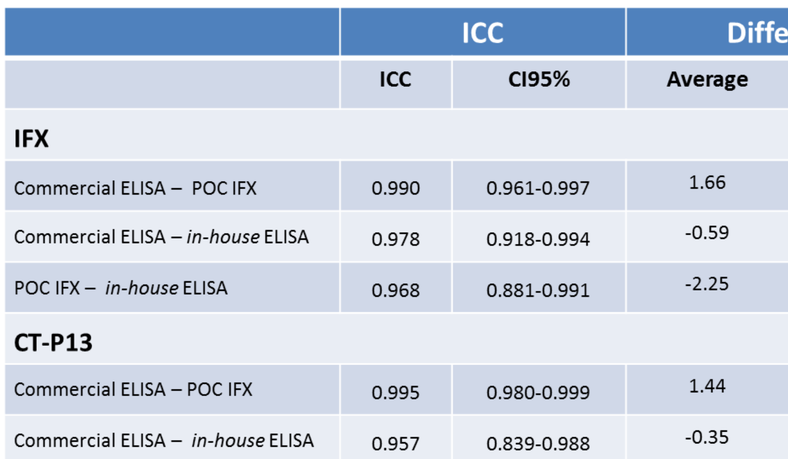


**Figure 1. Reactivity of IFX, CT-P13 and SB2 to anti-IFX and anti-CT-P13 sera**

## Conclusion

The tested assays, which were optimized to quantify IFX, can be safely used to monitor drug levels in patients medicated with IFX biosimilar SB2. Moreover, these drugs were shown to have a high cross-immunogenicity: this means that switching between them in a patient that has measurable levels of anti-drug antibodies will likely yield no clinical benefit.