SIMILARITY ASSESSMENT OF REFERENCE REMICADE™ -INFLIXIMAB- AND ITS MARKETED BIOSIMILAR INFLECTRA™ BY MEANS OF AGGREGATES PROFILE OVER TIME AND FREEZE/THAW STRESS

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Objective:

To evaluate the similarity between reference **Remicade™** and its marketed biosimilar **Inflectra™** by means of tracking the aggregate contain in several solutions prepared in conditions for hospital use, in a stability study over time stored at 4 ºC. Similarity of both reconstituted medicines regarding aggregate contain when subjected to freeze (-20 ºC)/thaw cycles was also assessed.

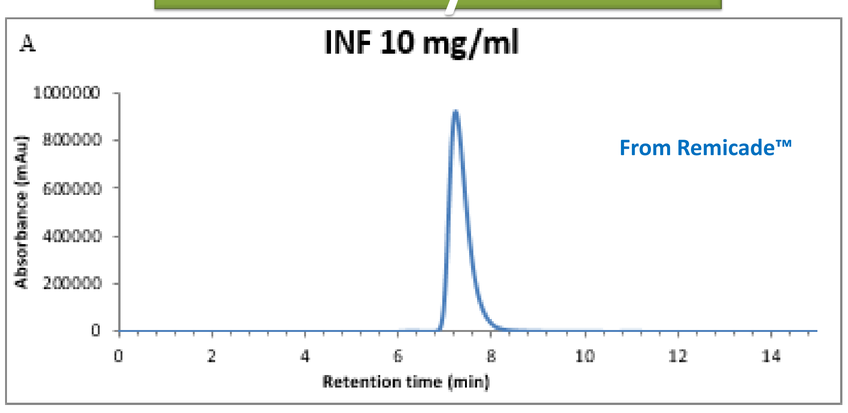
Background:

Inflectra™ (infliximab) product monograph indicates slightly higher aggregate proportions than the reference product **Remicade™**.

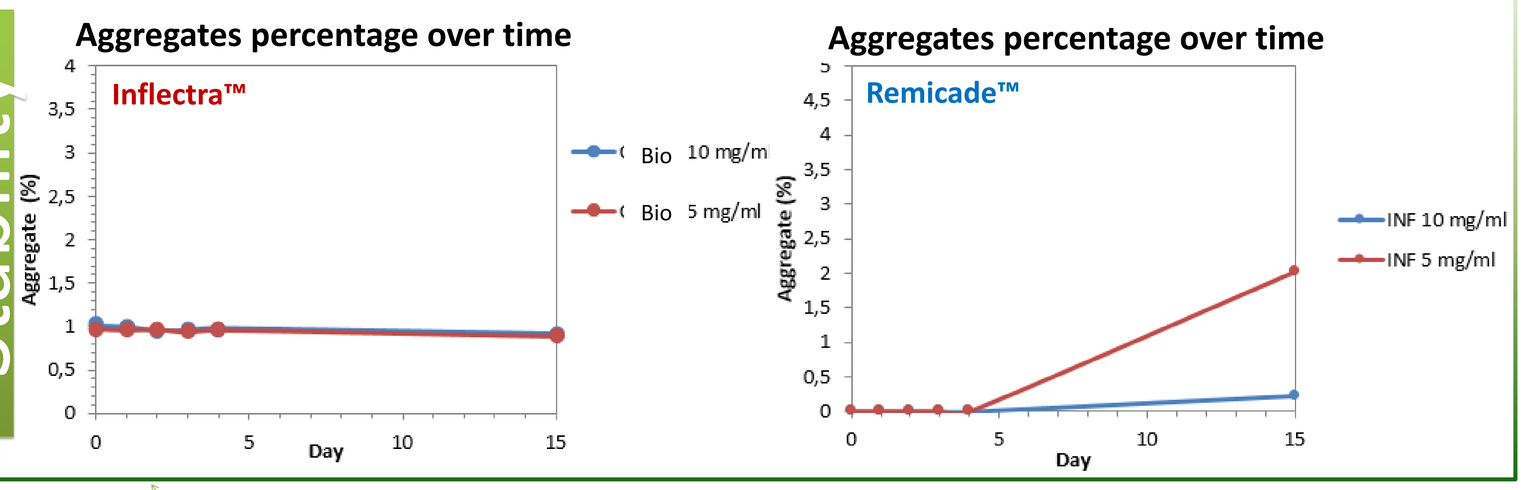
Materials and methods:

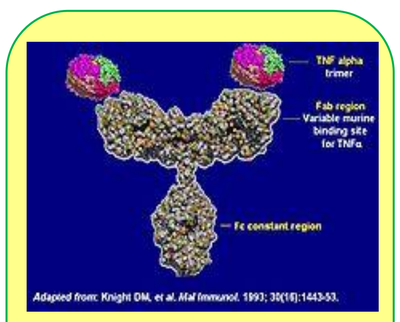
Two vials of **Remicade™** and two vials of **Inflectra™** were used for the study. Three concentrations, i.e. 10 mg/mL –reconstituted sample with water-, 5 mg/mL and 2 mg/mL –in NaCl 0.9 %-, were assessed. The aggregates profile of the INF samples was obtain by Size Exclusion High Performed Liquid Chromatography with Diode Array Detection (SE-HPLC-DAD) method previously developed for that purpose. INF samples from the two medicines were analyzed right after the solutions (both reconstituted and diluted) were prepared; the chromatographic aggregate profiles recorded were compared with those obtained in successive days analyzing the samples stored refrigerated at 4 ºC up to 15 days and the samples stored frozen at -20 ºC in several cycles of freeze/thaw.

Day 0



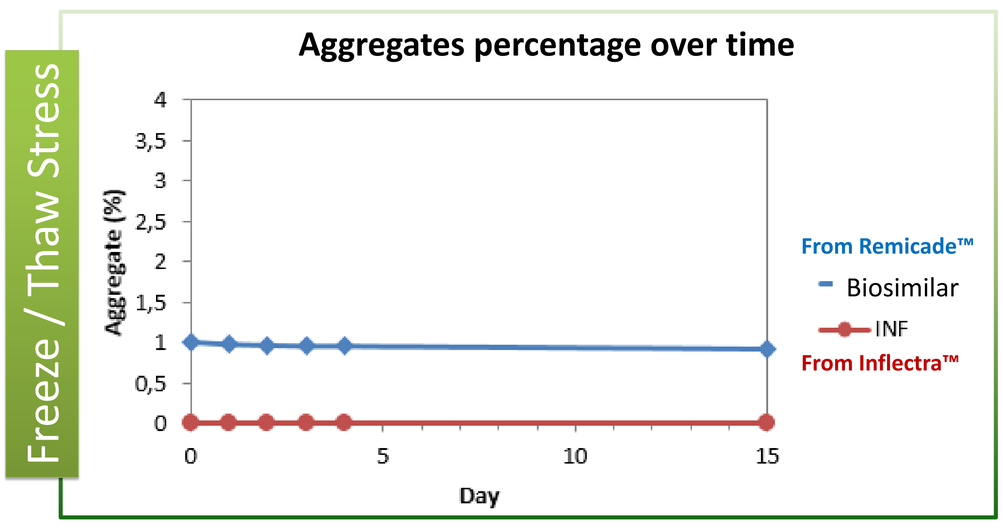
Stability





From: http://es.wikipedia.org/wiki/Infliximab

Freeze / Thaw Stress



Results:

Aggregate chromatographic profiles clearly indicates the presence of aggregates in reconstituted (10 mg/ml) and diluted at 5 mg/ml Inflectra™ samples as natural infliximab aggregates. No aggregates were detected in the dilution at 2 mg/ml that could be explained by the dilution process itself. All these aggregate chromatographic profiles from Inflectra™ samples were unchanged over the checked time (15 days), and for the freeze (-20 ºC)/thaw cycles (5) of the reconstituted samples. In the case of Remicade™, no aggregates were detected in the chromatographic profiles until day 15 where low proportion was noticed; and no aggregates were detected for the reconstituted samples after the 5 cycles of freeze (-20 ºC)/thaw.

Conclusion:

REMICADE® and its biosimilar INFLECTRA® show slight differences regarding their aggregates contain, with natural aggregates in INFLECTRA® that persists in dilutions up to 5 mg/ml and along time when stored at 4 ºC. Inflectra™ seems to be more stable regarding the aggregation process, since the aggregation profiles remain unchanged over the checked time. Remicade™ suffers some degradation that lead to form aggregates at 15th day after solutions preparation. No new aggregation was induced in both medicines after five cycles of freeze / thaw. Therefore, and despite the initial higher contain in aggregates in Inflectra, in use-stabilities of the biosimilar and reference medicine are similar.

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