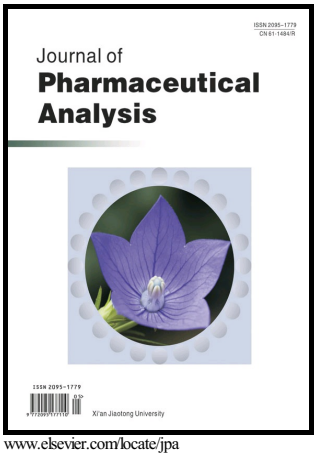
Author's Accepted Manuscript



Surrogate potency assays: Comparison of binding profiles complements dose response curves for unambiguous assessment of relative potencies

Robert Karlsson, Veronica Fridh, Åsa Frostell

PII: S2095-1779(17)30141-7
DOI: https://doi.org/10.1016/j.jpha.2017.12.008
Reference: JPHA405

To appear in: *Journal of Pharmaceutical Analysis*

Received date: 8 August 2017
Revised date: 28 November 2017
Accepted date: 21 December 2017

Cite this article as: Robert Karlsson, Veronica Fridh and Åsa Frostell, Surrogate potency assays: Comparison of binding profiles complements dose response curves for unambiguous assessment of relative potencies, *Journal of Pharmaceutical Analysis,* https://doi.org/10.1016/j.jpha.2017.12.008

Surrogate potency assays: Comparison of binding profiles complements dose response curves for unambiguous assessment of relative potencies

Robert Karlsson, Veronica Fridh, Åsa Frostell*

Purification and Analysis, GE Healthcare Life Sciences, Uppsala, Sweden.

*Corresponding author

Email: asa.frostell@ge.com

Abstract

Surface plasmon resonance (SPR) systems are widely used for detailed characterization of antibody activities including antigen and Fc-receptor binding. During later stages of development, where the focus is to ensure that established critical quality attributes (CQA) are maintained during cell culture, purification and formulation processes, analysis is simplified, and relative potencies are often determined. Here, simulation of binding data revealed that relative potency values, determined by EC50 or PLA analyses, accurately reflect changes in active concentration only if binding kinetics remain unchanged. Changes in the association rate constant shifted dose response curves, and therefore relative potencies, in the same way as changes in analyte concentration. However, for interactions characterized by stable binding, changes in the dissociation rate constant did not result in any shift, suggesting that this type of change may go unnoticed in the dose response curve. Based on these insights, EC50 and PLA analysis of dose response curves obtained with an anti-TNF-α antibody was complemented with the Biacore functionality for sensorgram comparison analysis, whereby changes in antigen and Fc-receptor binding profiles could be detected. Next, analysis of temperature