A rapid immunogenicity assay using immunochromatographic test strips is a newly developed IM assay method that requires no sample dilution and wash steps, thus, capable of detecting both high- and low-affinity ADAs. It is very tolerant of acid dissociated samples. ANP's nano intelligent detection system (NIDS)® rapid IM assay can be utilized for not only patient sample testing during clinical trials but, more importantly near-patient monitoring of immunogenic reactions, particularly after the biologic drug/biosimilar is approved (related publication). ANP offers various rapid IM assay products and services using both a handheld reader and a high throughput screening reader.

There are several challenges in detecting ADAs; for example, ADAs in an immune patient may already be bound to the biotherapeutic drug in circulating immune complexes, especially in the presence of the excess drug. Unless dissociated from these complexes, the ADA will not be detectable in any IM assay of any format. The typical approach to this challenge is to perform an acid dissociation pretreatment of the sample to liberate the ADA from the immune complexes, and then after neutralization, immediately run the IM assay. The IM assay is run immediately after neutralization to prevent the immune complexes from reforming.

Endogenous protein interferences can cause erroneous results in immunogenicity tests in whatever format. For mAbs and similar biotherapeutics that function by binding and blocking disease-associated active proteins, the drug's target molecule can create a bridging or a sandwich complex with the drug conjugate reagents in the IM assay. This leads to a false positive result in IM assays in the absence of ADA. Acid dissociation by itself will not resolve this problem. Other approaches that may work involve using a different blocking antibody that will bind interfering target proteins prior to running an immunogenicity assay. Once blocked, the target molecules can no longer form bridging complexes with the drug conjugate reagents. However, these blocking antibodies are dissociated from the target molecules upon acid dissociation, thus, removing their therapeutic effect. If added immediately after the neutralization step in the acid dissociation process, the blocker will not have enough time to bind the target proteins since the IM assay are run immediately.

For drugs where the historical data suggest a low ADA production, the studies are short, allowing a risk-based approach that the FDA allows.

4.14 Interchangeability

A biosimilar product is a biological product that is approved based on a showing that it is highly similar to an FDA-approved biological product, known as a reference product, and has no clinically meaningful differences in terms of safety and effectiveness of the reference product. Only minor differences in clinically inactive components are allowable in biosimilar products.