cell banks and the preparation of each lot of assay cells under standardized conditions from an individually frozen vial. Each lot of assay cells is thus in an identical physiological condition. Assay-ready cells can be manufactured under conditions of current GMPs, and stored frozen for several years without loss of drug sensitivity.

For neutralization assays, a recommended approach for expressing data is to report results as the amount of serum required to neutralize the biological activity induced by a constant quantity of the antigen. In some instances, however, it may be necessary to use an antibody standard or a reference preparation for expressing the levels of neutralizing antibodies in the test samples relative to the amounts of the neutralizing antibodies in the reference antibody preparation. It may also be possible to express antibody levels using arbitrary units provided that the unit has been well defined for the reference material. Although this approach is not ideal (the heterogeneous nature of polyclonal antibodies is particularly problematical for this), the use of this strategy may provide relatively precise estimates of antibody levels in the test samples and can reduce variability. This situation is most likely to occur when a number of sequential samples from the same animal or patient are available, and it is hard to include all samples from all patients in the same assays for establishing a valid comparison of antibody levels between different samples/patients.

7.3.7 Biosensor-based immunoassays

This method, unlike most other platforms, does not require the use of a labeled secondary reagent. Although several types of biosensors are available, the vast majority of published biosensor data cites the use of Biacore instruments (https://www.biacore.com/lifesciences/index.html) for monitoring the immune response in preclinical phases and clinical trials. Several models of Biacore are automated and also compliant with the 21 CFR part 11 requirement, which facilitates the use of this instrument for regulatory submissions.

The Biacore utilizes SPR to detect the increase in mass on the surface of the sensor chip following binding of an antibody to the antigen immobilized on the sensor chip. This increase in mass is directly proportional to the amount of antigen-binding antibody present in the serum sample being tested. The ability of the instrument to monitor the interaction in real-time and provide a continuous signal of the events occurring on the sensor surface enables the detection of rapidly dissociating or low-affinity antibodies if these are present in the sample. The detection of low-affinity antibodies is necessary as these antibodies have the potential to neutralize the therapeutic product and may predict the generation of a later mature immune response. Furthermore, characterization of the antibodies in terms of affinities, antibody class, and subclass can also be easily performed. These attributes have contributed to the increased use and popularity of this platform in studies on immunogenicity.