Piramal
Pharma Solutions

CELL BASED POTENCY ASSAY

Piramal is the World-Leader in the development and validation of Cell Based Potency (Killing) Assays.

Here we describe the development of our thaw for use cell based assay format.

PIRAMAL'S THAW-FOR-USE CELL BASED ASSAY

PROBLEM

The thaw for use cell based assay format offers several advantages in the planning and scheduling of assays and can also provide a more consistent cell response over that of cultured cells. For early phase studies the transfer of cell based assay require a limited time period of cell culture to generate the research master and working cell banks generating approximately 50 vials of each. During the cell culture period cells can be sacrificed to optimise the dose dilutional series that defines the activity of the drug. An eleven points geometric dilutional series with thee points on each asymptote and 5 points on the slope is the preferred format, although other formats also work. In transferring from a cultured to a thaw for use format, the cell density, cell recovery time and drug exposure time were optimised.

A multiple plate format allows for greater randomisation, increased replication and an increase in the number of test samples that can be analysed together. A multiple plate format offers several advantages (i.e. testing stability samples in the same assay) over that of a single plate format where reference and test dilutional series are analysed either in duplicate of triplicate.

APPLICATION

The key elements in the validation of bioassays are defined in ICH Q2R1 guidelines, the United States and European Pharmacopeia monographs and the FDA and EMA Bioanalytical guidelines.

For qualification a minimum of six events was performed by two operators in a design

that investigated the repeatability, intermediate precision, linearity and the bias (relative accuracy) of the method. Five mock potency samples; 50%, 71%, 100%, 141% and 200% were prepared for these studies and analysed against an independent sample prepared at 100% (reference). Similarity between the reference preparation and test preparation is performed using the unconstrained curves and Parallel line analysis was conducted using Softmax pro software. Specificity and interference were investigated in the target cell line and in a negative cell line. The non-specific toxicity is typically 1000 fold less than the targeted response. The relative potency data is log transformed and calculations performed according to . The intermediate precision data will be used to estimate the format variability and to predict the variability for different assay formats; typically increased precision is achieved by independent runs.

OUTCOME

Robustness studies are conducted using Design of Experiment software, in a factorial design that investigates those parameters that may impact the assay system suitability criteria or the relative potency measurement. The factorial design permits key interactions to be identified and will confirm if the allowed timings or cell density ranges are appropriate.

Validation is conducted using Design of Experiment software in a factorial design incorporating the degree of independent runs required to generate the reportable value.

Piramal Pharma Solutions is a contract development and manufacturing organization (CDMO), offering end-to-end development and manufacturing solutions across the drug life cycle. We serve our clients through a globally integrated network of facilities in North America, Europe and Asia. This enables us to offer a comprehensive range of services including Drug Discovery Solutions, Process & Pharmaceutical Development services, Clinical Trial Supplies and Commercial supply of APIs and Finished dosage forms. We also offer specialized services like development and manufacture of Highly Potent APIs, Antibody Drug Conjugation and are well versed in technologies such as Bio-catalysis, Route Scouting etc. Our capability as an integrated service provider & experience with various technologies enables us to serve Innovator and Generic companies worldwide.

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