cobra:bio

Expertise
Experience
Excellence

DNA Products:

Production of Clinical Grade DNA from an Unstable Plasmid

Background

A US non-government organization in collaboration with a Swedish University required 1g of plasmid for a Phase I clinical trial to demonstrate proof of concept in humans. It was anticipated that the pDNA would be used for Phase I trials, after which the plasmid would be modified as it was not the optimal vector.

Objectives

As this product would not proceed beyond Phase I, our objectives were to identify a clone that would be stable and to design a fermentation strategy that would maintain stability during manufacturing, rather than redesign the vector for improved stability.

Challenge

Once the plasmid was received, Cobra performed a genetic stability study to ensure plasmid loss or structural rearrangement would not occur during the cGMP manufacture. The study would also ensure that the plasmid was viable for commercial scale manufacture. However, the study revealed a deletion product that could potentially prevent the program from continuing.

Method / Solution

A stable clone could not be isolated from the original plasmid, so three further plasmids were evaluated. Multiple clones were screened using shake flask experiments to identify more stable versions and to identify the point at which the deletion was occurring. One of the three plasmids produced clones that were shown to be stable using mock 50L fermenter cell banking conditions. The stable clone was used to produce two cGMP cell banks.

After cell bank testing was completed, the preferred clone was selected to produce DNA for the toxicology studies. The cGMP manufacture was completed and produced the required amount of material within specification and containing no deletion products.

Benefit

Cobra succeeded in producing clinical grade DNA from unstable vectors so that the customer could proceed with a Phase I study. Cobra worked closely with the client to rapidly identify and isolate a clone that did not produce deletion products. Using this collaborative approach, Cobra met the original anticipated timeline.