

PRODUCTION OF LDMNPV IN THE WAVE® CELL CULTURE BIOREACTOR

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ABSTRACT

The development of bioreactor production methods for Gypchek would provide a means of production that can be scaled to a large capacity (production of 20,000 acre equivalents + per year), that is potentially at a lower cost than the current larval based production method, and would generate a product completely free of bacteria, fungi, and other viruses. Recently, a bioreactor with a completely novel design was developed and has become the bioreactor of choice by pharmaceutical companies using insect cell lines to produce proteins. This bioreactor, termed the Wave bioreactor, has several advantages compared to a stirred tank bioreactor that include an overall simpler system, elimination of down time between production runs, elimination of autoclave based sterilization, lower production costs, elimination of sheer stress, and potentially greater levels of polyhedra production. The Wave bioreactor system uses a sterile disposable plastic bag (shaped like a pillow) in place of a glass or stainless steel tank to hold the medium and insect cells. The bag is placed on a flat platform, inflated by an air pump, liquid medium and cells are added, and the platform is rocked in a front to back motion. Overall, the Wave bioreactor is a far simpler system than a stirred tank bioreactor because the tank and all stainless steel piping/fittings are eliminated.

The rocking motion of the Wave bioreactor platform creates a wave in the liquid medium that moves back and forth in the bag. The movement of liquid coupled with the large air-fluid interface area allows for significantly greater oxygen transfer than what occurs in stirred tank bioreactors. Consequently, there is no need for an agitator to mix the fluid within the Wave bag, or a sparger to bubble air/oxygen through the medium. The agitator and sparger in stirred tank bioreactors cause shear stress on the insect cells. Elimination of shear stress caused by the agitator and sparger should result in healthier cells and greater polyhedra production. Methods to produce Gypchek in the Wave bioreactor will be developed and we will determine whether the Wave or a stirred tank bioreactor is best for virus production. Results to date indicate that the Wave bioreactor virtually eliminates shear stress based on the condition of the cells. Cells in the Wave were free from granular material and vacuoles. In contrast, most of the cells within a stirred tank bioreactor contain vacuoles and granular material after 4-5 days. In addition, in contrast to a stirred tank bioreactor cells can be grown in the Wave system without pluronic F-68.