Log Increases in Commercial Production of Animal Vaccines Using Corning® CellSTACK® Culture Chambers

Customer Application Note

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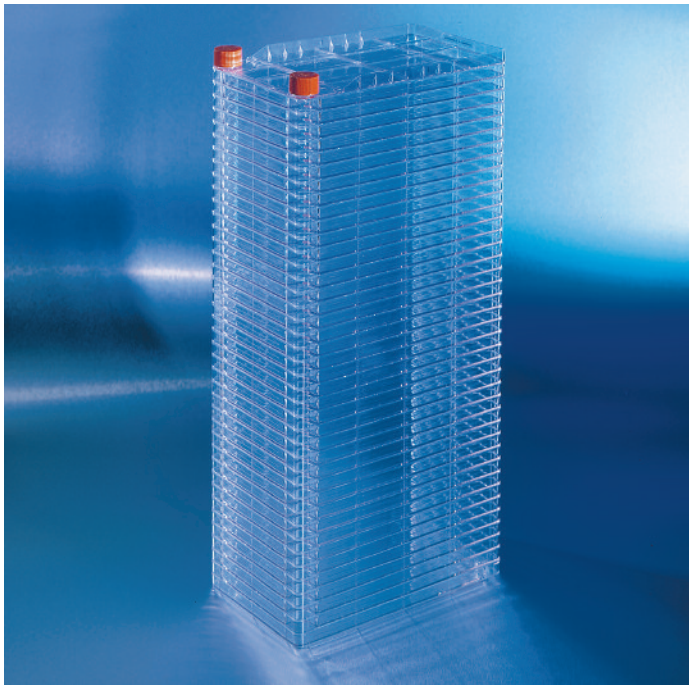
Commercial scale production of human and animal vaccines is most commonly performed in adherent based cultures due to the needs of the production systems used such as Vero, HEK and BHK-21 cells. Traditional methodologies have most often employed reusable glass systems such as Roux bottles or roller bottles. More recently, large scale vaccine producers have begun to embrace disposable technologies, such as Corning CellSTACK Culture Chambers, to reduce costs, such as cleaning and validation of reusable glass vessels and to improve yields of active product as replacements of these glass systems. This study demonstrates the significant impact on overall vaccine production by showing a greater than one log increase in vaccine production for two different animal vaccines over Roux bottle production. Importantly, it also demonstrates the substantial advantages of Corning CellSTACK Culture Chambers by their significant reduction in time and cost over the reuse of glass vessels.



Corning CellSTACK-40 Culture Chamber

Introduction

PRONABIVE, (Mexico City, Mexico) is an industry leader in producing biological products to treat a variety of animal diseases. It is the main supplier of veterinary products to the Address General of Health Animal (DGSA) of Secretary of Agriculture Cattle Ranch Development Rural Fishing and Feeding (SAGARPA).

One of the primary goals of PRONABIVE is to protect the cattle industry within Mexico. At the moment, it produces, commercializes, designs and develops biological products and chemical treatments for veterinary use. It is certified under ISO 9001:2000/NMX-CC-9001-IMNC which enables its clients to receive the best and most price competitive products on the market. PRONABIVE seeks to improve the animal health, especially cattle, in Mexico, Central and South America.

PRONABIVE has many large scale production requirements of its biological products including producing lots of 350,000 doses or more. Production of this many doses in a single lot required 1450 Roux bottles, which was very labor intensive, time consuming and costly. To increase efficiency and reduce costs, a switch was made to perform production in disposable stacked culture chamber units. The work described in this report is for the use of Corning CellSTACK Culture Chambers for large-scale production of bovine and canine rabies vaccine. This work is the result of numerous productions runs over more than 3 years.

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Materials and Methods

For each cell line used, cells were scaled up in Corning® T-flasks and CellSTACK®-10 culture chambers for inoculation into the CellSTACK-40 chamber. To inoculate each CellSTACK-40 chamber, 5.13 x 10^6 cells were combined with the appropriate virus and seeded in a CellSTACK-40 chamber in a volume of 10 liters of culture medium. At the end of the incubation period, the medium was collected for processing of virus and a fresh 10 liters of medium was added. This step was repeated one to two more times, depending on the virus-producing system.

Results

As shown in Figure 1, the production of bovine rabies vaccine was substantially increased in the Corning CellSTACK-40 chamber over the equivalent surface area of Roux bottles. Specifcally, there was 15.6 times as much vaccine produciton per cm^2 in the Corning CellSTACK-40 chamber compared to the equivalent surface area of Roux bottles. The CellSTACK chamber produced 987.4 active particles/cm^2 compared to 63.3 active particles per cm^2 for the Roux bottles. Therefore, utilizing a single CellSTACK-40 chamber is equivalent to using greater than 2,200 Roux bottles. Importantly, this relationship holds over a second harvest (Fig 1).

The data for production of canine rabies vaccine is strikingly similar. In this case, the production of active particles from the CellSTACK chamber is 12.6 times greater than the equivalent surface area of Roux bottles (Fig. 2) and, as the case for the bovine rabies vaccine, the substantial increase in vaccine production for canine rabies is maintained in several subsequent harvests.

Discussion

This study describes the significant increase in effective vaccine production using a disposable stacked cell culture system, the Corning CellSTACK Culture Chamber, over a traditional reusable glass system using Roux bottles. There are a number of factors that make using Corning CellSTACK chambers a significantly greater production system than Roux bottles.

First is the overall efficiency of vaccine production itself. As shown in this study, the production of active vaccine particles is 12 to 16 times greater per cm^2 in the CellSTACK chambers over the Roux bottles. The mechanism for this is not clear. However, it may be due to the absorptive properties of glass versus plastic. It may also be due to the substantial reduction in handling between the two systems. A single CellSTACK-40 chamber has a growth area of 25,440 cm^2; this is the equivalent of 145 plastic or Roux culture bottles (175 to 180 cm^2 cell growth area each). The advantage of having such a large growth area in a single unit allows users to make single manipulations of large numbers of cells, thereby reducing the risk of contamination by manipulation of hundreds if not thousands of individual bottles. It also allows users to develop a "closed" system of tubing allowing easy seeding and harvesting of the chamber without exposing the chamber to the external environment. In a production setting, this is important, as these manipulations can then be performed outside a tissue culture hood or clean room.

Secondly, there are also other advantages that help reduce time and cost of production. When considering the environmental impact of water consumption and waste discharge for cleaning and validating this number of Roux bottles, it is clear that using a disposable system is much more beneficial

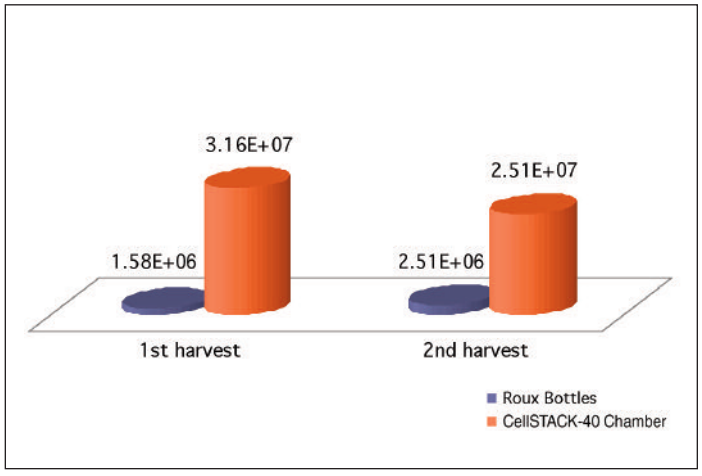

Figure 1. Bovine Rabies Vaccine Titer (Acatlan strain)

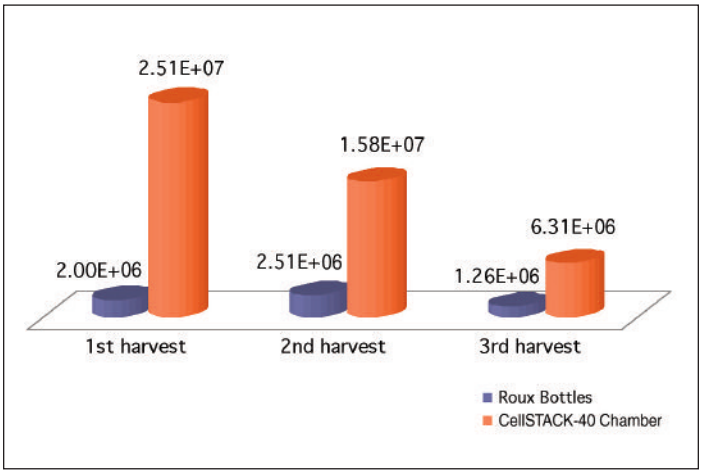

Figure 2. Canine Rabies Vaccine Titer (PV strain)

to the local environment. This is further improved when considering that for both vaccines, there is at least a one log increase in production using the Corning® CellSTACK®-40 chamber over the Roux bottles. Also, there is no turnaround time to clean, sterilize and validate reusable glass vessels when using disposable plastic systems, thereby increasing throughput of the production area dramatically. In fact, with the right vaccine, production of a single facility or suite can be increased nearly 20 times by switching from reusable glass to Corning CellSTACK Culture Chambers.

Summary

The benefits of using Corning CellSTACK culture chambers for vaccine production over a reusable glass system include:

- Greater than ten times (1.0 log) increase in vaccine production per cm^2
- Entire production process can be "closed" with the use of aseptic connections available for use with Corning CellSTACK culture chambers
  - Decreased risk of bacterial contamination
  - Decreased requirement for calibrations and verifications of product
- Amount of support materials is substantially decreased
- Easier to monitor single or few vessels versus hundreds or thousands of bottles
- Elimination of water needs for cleaning
- Increased safety for workers with removal of glass vessels
- Greater homogeneity from one vessel versus hundreds or thousands of bottles to enhance the consistency of production lots
- Reduction in need for preventive or corrective maintenance services
- Best handling of 20 liters or more volume of production for rapid industrial cell growth
- Efficient consumption and diminishing production costs

Bibliography

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Kuchler, R.J. Biochemical Methods in Cell Culture and Virology. Dowden, Hutchinson & Ross, Inc. Pennsylvania, USA. 1977.

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