NovoSeven® – Virus Safety

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The majority of manufacturers using mammalian cell cultures have had occasional experience with virus infection in the fermenter. Therefore, regulatory agencies around the world are increasingly concerned about this issue, although in all cases the viruses have been nonpathogenic to humans and most likely coming from raw materials (e.g. bovine serum used in the fermentation of the cells).

At Novo Nordisk we have addressed this issue by introducing a comprehensive virus programme for master cell banks, working cell banks and for cell banks established at the end of production. Additionally, we are testing the bovine serum used in the production process. To add further safety to the product, the purification process has been validated, and its capacity to eliminate potential viruses has been estimated. It is, however, also very important to stress that no material of human origin is used anywhere in the production of NovoSeven process or in the production of NovoSeven itself.

The cell banks used for production, the master cell banks and the working cell banks are all tested by a very broad range of tests. The tests are performed by an external contract house, internationally recognized for their expertise within this area, the test panel is shown in table 1.

At the end of production, cell banks are established from the production fermenters and they are also tested similarly to master and working cell banks. The bovine serum used in the production is tested according to rules published in the Federal Registry by the United States Department of Agriculture (USDA) for a broad range of viruses. Further, only serum from New Zealand and the USA where a very high veterinary standard is observed is used in the production. A quality assurance system has been established to ensure the origin of the serum, including audits of abattoirs and processing plants.

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Table 1. Testing of master cell banks (MCB) and master working cell banks (MWCB)

Name of test

Acceptance criteria

MCB

MWCB

Reverse transcriptase

XC plaque

S+L-

Cocultivation

In vivo

In vitro

MAP or HAP

Plaque assay

EM

negative negative negative not done negative negative negative negative
retrovirus and retro-virus-like particles are accepted
negative negative negative negative negative negative negative negative
retrovirus and retro-virus-like particles are accepted

Finally, validation of the purification process has been made. Taken together, the virus tests of cell banks, The result shows that a logarithm reduction factor in the range from 10 to more than 23 log units has been obtained, adding further safety to the product. intensive virus test of serum, process validation and the absence of any material of human origin assures a very high degree of safety in the NovoSeven product.

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