

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

103471

MICROBIOLOGY REVIEW

Betaseron PLA92-0495

Molecular Biology issues

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Product description

Betaseron is a recombinant human interferon- β (MW 18,500D) produced in *E.coli*. It differs from native human Ifn- β in several aspects:

1. the protein is not glycosylated
2. it lacks the N-terminal methionine
3. the cysteine at position 17 is replaced with serine to facilitate proper folding of the recombinant protein.

The specific activity of Betaseron is _____ I/ mg of Ifn- β ser17 measured in human fibroblasts by vesicular stomatitis virus challenge.

***E.coli* host and Master and Working Cell Bank characterization**

The *E.coli* host strain used for production of Betaseron is *E.coli* K-12 (known as MM294) which has no special nutritional requirement except thiamine. The variant used in production of Betaseron, MM294-1, was derived from MM294 that had been transformed with the interferon- β plasmid pSY2501 (described below).

000064

Genetic Stability of the Betaseron Production Culture

The PLA for Betaseron (submitted June 16, 1992) contains genetic stability test procedures and data in Vol. 2, Section 3.4.6, pages 134- 140. This report, entitled Genetic Stability of the Production Culture after Extended Fermentation, gives a detailed description of the test procedures used to verify the stability and integrity of the Ifn- β ser17 production clone, pSY2501.

000065