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File No. 86/9010
Application No. 91/156/2
Evaluation No. A030

Marion Merrell Dow Australia Pty Ltd
PO Box 237
Frenchs Forest NSW 2086

Attention: [redacted]
Quality Assurance and Technical Affairs Manager

Dear Sir

I refer to your letters of 12 March 1991, 29 July 1991, 12 September 1991, 1 December 1992 and 29 April 1993 concerning the application for registration of teicoplanin "Targocid' powder for injection (100, 200 and 400 mg strengths) presented in glass vials with ampoules of water for injection included, under the provisions of the Therapeutic Goods Act 1989.

Your additional data and responses to outstanding matters of chemistry and quality control have now been evaluated and you are required to provide the following further information under Section 31(1) of the Act to allow the Secretary to make a decision regarding your application. Your response should be provided within one month of the date of this letter.

The numbering of the following matters has been retained from those raised in TGA's letter of 25 August 1992.

MANUFACTURE OF THE RAW MATERIAL TEICOPLANIN
RAW MATERIAL SPECIFICATIONS

7.2 Composition

[redacted]

Such limits would allow for degradation in manufacture of the finished product as well as over the shelf life of the finished product.

STERILITY MATTERS

12.3 In regard to the ampoules of Water for Injection, you have acknowledged that your sterility test incubation period of 10 days is not in accordance with the 14 day incubation period specified in clause C454 of the Australian Code of GMP.

It is agreed that your present incubation period of 10 days exceeds the general requirements of the EP, USP and BP in regard to incubation periods for the membrane filtration method. However, results of tests carried out by TGAL show that approximately 15% of all positive tests show first signs of growth after the 10th day of incubation. This is found with both direct inoculation and the method of membrane filtration. Limiting incubation to 10 days will result in missing a substantial proportion of positives.

It is noted that your sterility test incubation period for antibiotic and lyophilised preparations is 14 days. You should be aware that the 14 day Sterility test incubation period is now mandatory for all goods manufactured in Australia according to determination No 1. of 1991 under Subsection 36(1) of the Therapeutic Goods Act 1989 which states that - "Subject to this determination, Therapeutic Goods must be manufactured in compliance with the Codes". It is also a requirement that therapeutic goods manufactured overseas be subject to levels of GMP equivalent to those expected of products manufactured in Australia. Sponsors of products manufactured overseas should comply with the 14 days test unless cogent reasons can be provided for non-compliance. Please comment.

SAFETY MATTERS

13.1 Please provide a general method for the Bacterial Endotoxin Test which complies with the USP XXII 1990 <85> Bacterial Endotoxins Test and the proposaed revisions in the Pharmacopial Forum Sept-Oct 1992 Vol 18, No 5.

13.2 Please provide results that show that the general method is being followed for the Water for Injection samples.

13.3 Please confirm that an Endotoxin limit of 0.25EU/ml is used.

Please address your response, quoting the above mentioned file and control number to:

Section 31 Officer
Attention [redacted]
Application Entry Cell
Drug Evaluation Branch
Therapeutic Goods Administration
PO Box 100
WODEN ACT 2606

Yours faithfully

[redacted]

Chief Scientist
Antibiotics Section
Therapeutic Goods Administration Laboratories
[redacted]
Delegate of the Secretary
10 ~~May~~ June 1993

COMPUTER UPDATED
ENTERED WTA: [redacted]
VERIFIED WTA: —
C/No: 91/186/L Date: 17/6/93

ASO5V – MIS & please make sure need correct title also part mark cpt both – [redacted]
[redacted] 16/6