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FILE NOTE

APPLICATION FOR REGISTRATION
TEICOPLANIN
'TARGOCID' POWDER FOR INJECTION IN VIALS
100, 200 AND 400 mg PLUS WATER FOR INJECTION
MARION MERRELL DOW AUSTRALIA PTY LTD

Correspondence: Company letters of 12 March 1991, 29 July 1991, and 12 September 1992. Company reply of 1 December 1992 to TGA's letter of 25 August 1992. Company reply of 29 April 1993 to TGA's letter of 12 February 1993.

EVALUATION OF COMPANY RESPONSES

RAW MATERIAL SPECIFICATIONS

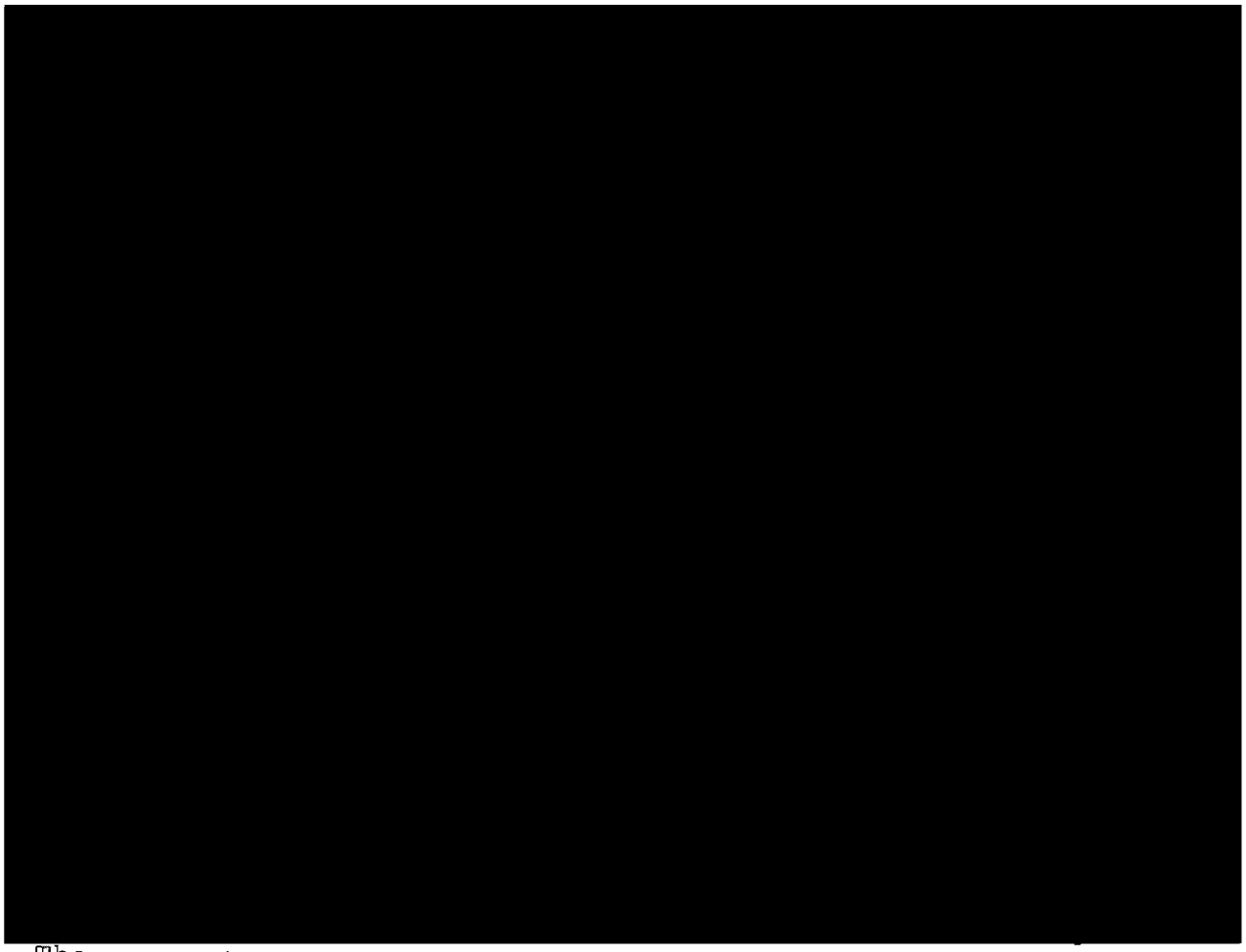
The company's responses to the composition and water content questions (below) have indicated the difficulties controlling the quality of this substance.

7.2 Composition

[redacted]

SUMMARY OF COMPANY'S PROPOSED LIMITS

COMPONENT	RAW MATERIAL		FINAL PRODUCT	
	% release	% expiry	% release	% expiry
[redacted]				



These specification limits should be put to the company.

TO BE RESOLVED

7.3 Water Content

The company was asked to tighten the moisture content limits from 15 to 12% for the raw material.

The company's reply is that this is impractical. However, the data submitted for 32 batches manufactured for the current process shows that most would meet the 12% limit. It would seem that the drum drying process is not well controlled and that moisture contents between 5 and 12% are achievable. Pushing the drying by this process to moisture contents of less than 5%, however, leads to degradation.

Alternative drying processes such as freeze drying as used for the finished product are certainly more gentle.

It would be preferable for the specification limit to be reduced to 12% but it is not worth pursuing further and the company's limit should be accepted at this stage.

ACCEPTABLE

STABILITY STUDIES

9.1 The company claim that their estimations for teicoplanin activity presented in the 24 month stability data for 3 recent batches are based on the assumption that moisture content remains unchanged over the storage period. However, the company specifications require that the microbiological assay result be expressed on an anhydrous, salt and and solvent free basis. Therefore, it should be noted that potencies calculated after storage on an "as is" basis will differ from those calculated by the method of the company specifications.

[redacted]

ACCEPTABLE

FORMULATED PRODUCTS

11.2 The company have agreed to tighten the release specification for water content to NMT 1.5% to ensure that a shelf life limit of NMT 2.5% can be met. They state that their previous response inadvertently contained a confusing statement.

ACCEPTABLE

11.3 Fiducial limits for the teicoplanin content of the finished products as determined by microbiological assay.

The company have accepted the proposed specification limits as follows:

Presentation	[redacted]	Release %	Expiry %
100mg vials		LFLE NLT 95 UFLE NGT 130	LFLE NGT 130 UFLE NLT 95
200mg vials		LFLE NLT 95 UFLE NGT 115	LFLE NGT 115 UFLE NLT 95
400mg vials		LFLE NLT 95 UFLE NGT 120	LFLE NGT 120 LFLE NLT 95

ACCEPTABLE

The company have stated that only the entire vials contents method will be used for teicoplanin assay. However, it should be confirmed that any weight fill variation will be compensated by taking an average fill and expressing the results in terms of labelled claim.

TO BE RESOLVED

LABELLING MATTERS

14 The company have agreed to include the proposed warning statement "WARNING SPECIAL RECONSTITUTION PROCEDURES APPLY. SEE PRODUCT INFORMATION" on the cartons and labels.

ACCEPTABLE

RECOMMENDATIONS

Several matters still remain to be resolved and will be raised with the company in a separate letter.

The approval for registration is not recommended until these matters have been resolved.

[redacted]
Antibiotics Section
TGAL

10 June 1993