

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

74-890

APPLICATION NUMBER:

ADMINISTRATIVE DOCUMENTS

DIVISION REVIEW SUMMARY

ANDA: 74-890

DRUG PRODUCT: Cimetidine

FIRM: Torpharm Inc.

DOSAGE FORM: Tablet

STRENGTHS: 200 mg, 300 mg, 400 mg and 800 mg

CGMP STATEMENT/EIR UPDATE STATUS: Pending

BIO INFORMATION: Acceptable by H. Nguyen 9/30/96.

VALIDATION - (DESCRIPTION OF DOSAGE FORM SAME AS FIRM'S):
The firm will perform the following tests on the finished product:

Tests	Specifications
Appearance	
Identification	
Dissolution (USP)	2S tablets less than 400 mg
Content Uniformity	
Assay-HPLC (USP)	
Avg. Tablet Weight	300 mg

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Where:

- CM RC3 N"Carbamy;-N-methyl-N'-(2-5-methyl-imidazole-4-yl)-methylthio)ethyl)Guanidine dihydrochloride
- CM RC4 N"-Cyano-N-methyl-N'-(2-5-methyl-imidazole-4-yl)-methylsulphonyl)ethyl)guanidine
- CM RC5 4-Methyl-5-hydroxymethyl imidazole
- CM RC6 4-methyl-5-2 aminoethyl-thiomethyl-imidazol dihydrochloride
- CM RC7 N-Cyano-N' (2-5-methyl-1H-imidazol-4-yl)methyl)thioo)ethyl-S-methylisothiourea
- CM RC8 N-cyano-N'-N"-dimethyl guanidine
- CM RC9 Bis(2-N"cyano'N"-methyl guanidinyl)ethyl)disulfide

*Revised, new method.

STABILITY-

The firm's stability protocol is included on page 5617.

*The Related Compounds testing was recently revised. See March 98 amendment. For abbreviations, see under Finished Product Specifications.

A post approval commitment is included on page 5630. The firm requests a 24 month expiration dating period based on the accelerated data provided.

The firm included accelerated data for all container closure combinations:

	200 mg Lot #50066A, Lot #50066B, Lot #50066C,
	300 mg Lot #50067A, Lot #50067B, Lot #50067C,
	400 mg Lot #50071A, Lot #50071B, Lot #50071C.
	800 mg Lot #50043A, Lot #50043B, Lot #50043C

LABELING-The labeling review was found acceptable 5/22/97.

STERILIZATION VALIDATION - Not Applicable

SIZE OF BIO BATCHES-

A description of the manufacturing process is included on pages 3180-3182 with a flow chart. Cimetidine Tablets are manufactured by [redacted]. The process is divided into stages: [redacted]. The processes and equipment used to manufacture the biobatches are functionally equivalent to the proposed scale-up processes and equipment. The Master batch records are included on pages 3184-3314. The production batch size is [redacted] of the granulation. A [redacted] is used. The proposed number of tablets are: [redacted]

The executed batch records are included on pages 3336-4339. The common granulation lots used for the exhibit batches were all kg. The granulation (Lots #50038 and 50059) was used for the mg strength to manufacture the [redacted] t #50061). The final coated batch is Lot #50066. This lot was packaged into 3 containers giving lots 50066A, 50066B and 50066C.

For the 300 mg strength, the lot was manufactured by lot #50059. The uncoated cores [redacted] lot # is 50062. The coated lot # is 50067. # packaging configurations yielded lots #50067A, 50067B, and 50067C.

For the 400 mg strength, the lot was manufactured using tablet [redacted] lot #50060. The uncoated cores [redacted] ere lot #50063, and the coated lot # was 50071. The 3 packaging configurations yielded lot #s 50071A, 50071B and 50071C.

For the 800 mg strength, the lot was manufactured from [redacted] lots #50037 and 50038. The uncoated cores were lot #50042. The coated lot was #50043 with 4 packaging configurations, Lot #50043A, 50043B, 50043C and 50043D.

The reconciliation data are included on pages 3324-3330. The packaging information is included on pages 3332-3335. All lots include packaging records as well. For the 200 mg lots: A (100's) 107 units, B 100's 107 units and C (1000's) 105 units were packaged. For the 300 mg lots: A (100s) 90 units, B (100s) 90 units and C (1000s) 89 units were packaged. For the 400 mg lots A (60s) 169 units, B (60s) 169 units and C (500s) 167 units were packaged. For the 800 mg lot A (30s) 179 units, B (30s) 179 units and C (500s) 179 units were packaged.

SIZE OF STABILITY BATCHES- same as above

PROPOSED PRODUCTION BATCH- The Master batch records are included on pages 3184-3314. The production batch size is of the granulation. A common granulation is used. The proposed number of tablets are:

RECOMMENDATION: The application is approvable.

SIGNATURE: *Karen Bernard* DATE: *10/6/98*