

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*

**21-074**

**CHEMISTRY REVIEW(S)**

DIVISION OF ANTI-INFECTIVE DRUG PRODUCTS  
Review of Chemistry, Manufacturing and Controls

AUG 17 2000

NDA #: 21-074

CHEM.REVIEW #: 3

REVIEW DATE: 15-AUG-2000

<u>SUBMISSION/TYPE</u>	<u>DOCUMENT DATE</u>	<u>CDER DATE</u>	<u>ASSIGNED DATE</u>
ORIGINAL	25-JUNE-99	29-JUNE-99	30-JUNE-99
BC <sup>1</sup>	22-FEB-00	24-FEB-00	01-MAR-00
BC <sup>2</sup>	29-FEB-00	03-MAR-00	09-MAR-00
NC <sup>3</sup>	14-FEB-00	16-MAR-00	09-MAR-00
BC <sup>4</sup>	19-APR-00	04-MAY-00	09-MAY-00
BC <sup>5</sup>	22-JUNE-00	23-JUNE-00	27-JUNE-00
BC <sup>6</sup>	26-JUNE-00	28-JUNE-00	07-JULY-00



<sup>3</sup> Response to Tradename OPDRA's consult.

<sup>4</sup> Response to Chemistry Comments of April 5, 2000 fax.

<sup>5</sup> Amendment to correct container/closure information.

<sup>6</sup> Response to not-approvable letter.

NAME & ADDRESS OF APPLICANT

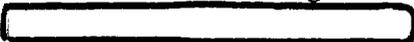
3M HEALTH CARE  
3M Center  
Saint Paul, MN 55144-1000  
612 733 1110

CONTACT

Suzanne Danielson, RAC  
Regulatory Affairs Manager  
3M Center, Building 275-3E-08  
St. Paul, MN 55144-1000

DRUG PRODUCT NAME

Proprietary: Avagard™ -CHG Hand Prep  
Established: 1% Chlorhexidine gluconate, 61% Ethyl Alcohol Antiseptic Hand Preparation  
Laboratory Code Name: HPD-5a  
Chemical type: 3 S

PHARMACOLOGICAL CATEGORY/INDICATION: Antimicrobial skin cleansing lotion as a surgical hand scrub, healthcare personnel hand wash, 



DOSAGE FORM: lotion

STRENGTHS: 1% CHG, 61% Ethyl alcohol

ROUTE OF ADMINISTRATION: Topical

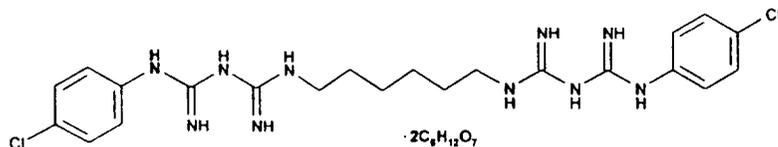
DISPENSED: \_\_\_\_\_ R<sub>x</sub>    X OTC

**CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA,  
MOLECULAR WEIGHT**

1,1'-Hexamethylenebis [5-(4-chlorophenyl) biguanide] di-D-gluconate

MF: C<sub>22</sub>H<sub>30</sub>Cl<sub>2</sub>N<sub>10</sub> · 2C<sub>6</sub>H<sub>12</sub>O<sub>7</sub>, MW: 897.8

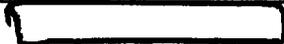
CAS # 18472-51-0



**SUPPORTING DOCUMENTS**

See previous reviews

**RELATED DOCUMENTS**



**CONSULTS**

The Methods Validation has been completed.

**REMARKS/COMMENTS:**

This review covers the Amendment to correct container/closure information, response to not-approvable letter, Methods Validation report and follow-up to other CMC comments of new and previous correspondence as listed above.

**CONCLUSIONS & RECOMMENDATIONS:**

The Applicant has notified the Agency of its intent to file an amendment to correct all deficiencies site. Follow up comments have been generated as a result of review of above correspondence and are listed in Section H of this review.

/S/

Milton J. Sloan, Ph. D., Review Chemist

cc: Org. NDA 21-074  
HFD-520/Division File  
HFD-560/Division File  
HFD-520/DKatague/Team Leader  
HFD-520/Sloan/Chem  
HFD-520/Bostwick/MO  
HFD-520/Seethaler/Pharm-Tox  
HFD-520/Sheldon/Micro  
HFD-520/Rochester/Stat  
HFD-520/DillionParker/PM /S/ 8/17/00  
HFD-830/C-wChen/ONDCIII/Div. Dir.

**DIVISION OF ANTI-INFECTIVE DRUG PRODUCTS**  
**Review of Chemistry, Manufacturing and Controls**

**NDA #:** 21-074      **CHEM.REVIEW #:** 4      **REVIEW DATE:** 21-MAR-2001

<u>SUBMISSION/TYPE</u>	<u>DOCUMENT DATE</u>	<u>CDER DATE</u>	<u>ASSIGNED DATE</u>
ORIGINAL	25-JUN-99	29-JUN-99	30-JUN-99
BC <sup>1</sup>	22-FEB-00	24-FEB-00	01-MAR-00
BC <sup>2</sup>	29-FEB-00	03-MAR-00	09-MAR-00
NC <sup>3</sup>	14-FEB-00	16-MAR-00	09-MAR-00
BC <sup>4</sup>	19-APR-00	04-MAY-00	09-MAY-00
BC <sup>5</sup>	22-JUN-00	23-JUN-00	27-JUN-00
BC <sup>6</sup>	26-JUN-00	28-JUN-00	07-JULY-00
MR <sup>7</sup>	17-OCT-00	19-OCT-00	09-NOV-00
BC <sup>8</sup>	21-FEB-01	23-FEB-01	05-MAR-01
BC <sup>9</sup>	14-MAR-01	15-MAR-01	20-MAR-01



- <sup>3</sup> Response to Tradename OPDRA's consult.
- <sup>4</sup> Response to Chemistry Comments of April 5, 2000 fax.
- <sup>5</sup> Amendment to correct container/closure information.
- <sup>6</sup> Response to not-approvable letter.
- <sup>7</sup> General Correspondence to provide plans for amendment and teleconference request.
- <sup>8</sup> Response to not-approvable letter.
- <sup>9</sup> Stability data update (see Memo in Attachment 2).

**NAME & ADDRESS OF APPLICANT**

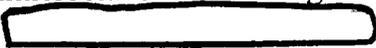
3M HEALTH CARE  
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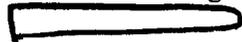
**CONTACT**

Suzanne Danielson, RAC  
Regulatory Affairs Manager  
3M Center, Building 275-3E-08  
St. Paul, MN 55144-1000

**DRUG PRODUCT NAME**

Proprietary: Avagard™ -CHG Hand Prep  
Established: 1% Chlorhexidine gluconate, 61% Ethyl Alcohol Antiseptic Hand Preparation  
Laboratory Code Name: HPD-5a  
Chemical type: 3 S

**PHARMACOLOGICAL CATEGORY/INDICATION:** Antimicrobial skin cleansing lotion as a surgical hand scrub, healthcare personnel hand wash, 



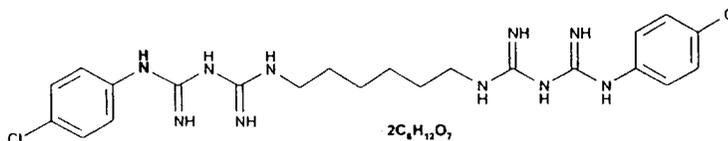
**DOSAGE FORM:** lotion

**STRENGTHS:** 1% CHG, 61% Ethyl alcohol

**ROUTE OF ADMINISTRATION:** Topical  
**DISPENSED:**                    \_\_\_ R<sub>x</sub>      X   OTC

**CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA,  
MOLECULAR WEIGHT**

1,1'-Hexamethylenebis [5-(4-chlorophenyl) biguanide] di-D-gluconate  
MF: C<sub>22</sub>H<sub>30</sub>Cl<sub>2</sub>N<sub>10</sub> · 2C<sub>6</sub>H<sub>12</sub>O<sub>7</sub>, MW: 897.8  
CAS # 18472-51-0



**SUPPORTING DOCUMENTS**

See previous reviews.

**RELATED DOCUMENTS**

[Redacted]

**CONSULTS**

The Methods Validation has been completed. The analytical methods and results will be formally submitted to the file for regulatory upon approval. Comments on the final printed labeling are deferred to the Division of Over-the-Counter Drug Products

**REMARKS/COMMENTS:**

This review covers the response to not-approvable letter and follow-up to other CMC comments of new and previous correspondence as listed above.

**CONCLUSIONS & RECOMMENDATIONS:**

The Applicant has provided updated stability data for the 500-mL [Redacted] and 0.5 oz presentation to support the proposed expiration date of 24 months. The reviewer recommends approval of this NDA.

  /  S  /    
Milton J. Sloan, Ph. D., Review Chemist

cc:    Org. NDA 21-074  
      HFD-520/Division File  
      HFD-560/Division File  
      HFD-520/DKatague/Team Leader */S/ 3/21/01*  
      HFD-520/Sloan/Chem  
      HFD-520/Bostwick/MO  
      HFD-520/Seethaler/Pharm-Tox  
      HFD-520/Sheldon/Micro  
      HFD-520/Rochester/Stat  
      HFD-520/DillionParker/PM  
      HFD-830/C-wChen/ONDCIII/Div. Dir.