

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

21-669

**ADMINISTRATIVE and CORRESPONDENCE
DOCUMENTS**



21 CFR 314.50(i)(1)(ii)

September 19, 2003

Ms. Maureen Dillon-Parker
Food and Drug Administration
Center for Drug Evaluation and Research
Division of Anti-Infective Drug Products, HFD-520
Attention: Division Document Room, N115
9201 Corporate Blvd
Rockville, Maryland 20857

Re: NDA N21-669

Dear Ms. Dillon-Parker:

Reference is made to NDA N21-669 submitted by Sage Products. Reference is also made to a September 12, 2003 voicemail from Maureen Dillon-Parker of FDA to Ajay Chawla of Sage Products and subsequent telephone conversation between Ms Dillon-Parker and Mr. Chawla. Our understanding from Ms. Dillon-Parker is that FDA is considering treating NDA N21-669 as an application submitted under section 505(b)(2) of the Federal, Food, Drug, and Cosmetic Act ("FDCA"). FDA has therefore requested that Sage Products provide patent certification information in accordance with FDCA 505(b)(2) and 21 C.F.R. § 314.50(i). This letter responds to that request.

In the opinion and to the best knowledge of Sage Products, there are no patents that claim the drug or drugs on which investigations that are relied upon in this application were conducted or that claim a use of such drug or drugs.

Thank you for your attention to this NDA.

Sincerely yours,

Tom Keaty
Product Development Manager
Sage Products, Inc

Department of Health and Human Services Food and Drug Administration		Form Approved: OMB No. 0910-0513 Expiration Date: 7/31/06 See OMB Statement on Page 3.	
PATENT INFORMATION SUBMITTED WITH THE FILING OF AN NDA, AMENDMENT, OR SUPPLEMENT <i>For Each Patent That Claims a Drug Substance (Active Ingredient), Drug Product (Formulation and Composition) and/or Method of Use</i>		NDA NUMBER N21-669	NAME OF APPLICANT / NDA HOLDER Sage Products, Inc.
<i>The following is provided in accordance with Section 505(b) and (c) of the Federal Food, Drug, and Cosmetic Act.</i>			
TRADE NAME (OR PROPOSED TRADE NAME)			
ACTIVE INGREDIENT(S) Chlorhexidine Gluconate	STRENGTH(S) 2% weight-by-weight		
DOSAGE FORM Topical via nonwoven cloth			
This patent declaration form is required to be submitted to the Food and Drug Administration (FDA) with an NDA application, amendment, or supplement as required by 21 CFR 314.53 at the address provided in 21 CFR 314.53(d)(4). Within thirty (30) days after approval of an NDA or supplement, or within thirty (30) days of issuance of a new patent, a new patent declaration must be submitted pursuant to 21 CFR 314.53(c)(2)(ii) with all of the required information based on the approved NDA or supplement. The information submitted in the declaration form submitted upon or after approval will be the <i>only</i> information relied upon by FDA for listing a patent in the Orange Book.			
For hand-written or typewriter versions (only) of this report: If additional space is required for any narrative answer (i.e., one that does not require a "Yes" or "No" response), please attach an additional page referencing the question number.			
FDA will not list patent information if you submit an incomplete patent declaration or the patent declaration indicates the patent is not eligible for listing.			
For each patent submitted for the pending NDA, amendment, or supplement referenced above, you must submit all the information described below. If you are not submitting any patents for this pending NDA, amendment, or supplement, complete above section and sections 5 and 6.			
1. GENERAL			
a. United States Patent Number	b. Issue Date of Patent	c. Expiration Date of Patent	
d. Name of Patent Owner	Address (of Patent Owner)		
	City/State		
	ZIP Code	FAX Number (if available)	
	Telephone Number	E-Mail Address (if available)	
e. Name of agent or representative who resides or maintains a place of business within the United States authorized to receive notice of patent certification under section 505(b)(3) and (j)(2)(B) of the Federal Food, Drug, and Cosmetic Act and 21 CFR 314.52 and 314.95 (if patent owner or NDA applicant/holder does not reside or have a place of business within the United States)	Address (of agent or representative named in 1.e.)		
	City/State		
	ZIP Code	FAX Number (if available)	
	Telephone Number	E-Mail Address (if available)	
f. Is the patent referenced above a patent that has been submitted previously for the approved NDA or supplement referenced above?		<input type="checkbox"/> Yes	<input type="checkbox"/> No
g. If the patent referenced above has been submitted previously for listing, is the expiration date a new expiration date?		<input type="checkbox"/> Yes	<input type="checkbox"/> No

For the patent referenced above, provide the following information on the drug substance, drug product and/or method of use that is the subject of the pending NDA, amendment, or supplement.

2. Drug Substance (Active Ingredient)

2.1 Does the patent claim the drug substance that is the active ingredient in the drug product described in the pending NDA, amendment, or supplement? Yes No

2.2 Does the patent claim a drug substance that is a different polymorph of the active ingredient described in the pending NDA, amendment, or supplement? Yes No

2.3 If the answer to question 2.2 is "Yes," do you certify that, as of the date of this declaration, you have test data demonstrating that a drug product containing the polymorph will perform the same as the drug product described in the NDA? The type of test data required is described at 21 CFR 314.53(b). Yes No

2.4 Specify the polymorphic form(s) claimed by the patent for which you have the test results described in 2.3.

2.5 Does the patent claim only a metabolite of the active ingredient pending in the NDA or supplement? (Complete the information in section 4 below if the patent claims a pending method of using the pending drug product to administer the metabolite.) Yes No

2.6 Does the patent claim only an intermediate? Yes No

2.7 If the patent referenced in 2.1 is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.) Yes No

3. Drug Product (Composition/Formulation)

3.1 Does the patent claim the drug product, as defined in 21 CFR 314.3, in the pending NDA, amendment, or supplement? Yes No

3.2 Does the patent claim only an intermediate? Yes No

3.3 If the patent referenced in 3.1 is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.) Yes No

4. Method of Use

Sponsors must submit the information in section 4 separately for each patent claim claiming a method of using the pending drug product for which approval is being sought. For each method of use claim referenced, provide the following information:

4.1 Does the patent claim one or more methods of use for which approval is being sought in the pending NDA, amendment, or supplement? Yes No

4.2 Claim Number (as listed in the patent) | Does the patent claim referenced in 4.2 claim a pending method of use for which approval is being sought in the pending NDA, amendment, or supplement? Yes No

4.2a If the answer to 4.2 is "Yes," identify with specificity the use with reference to the proposed labeling for the drug product. Use: (Submit indication or method of use information as identified specifically in the proposed labeling.)

5. No Relevant Patents

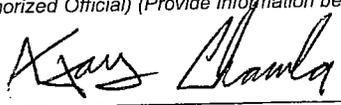
For this pending NDA, amendment, or supplement, there are no relevant patents that claim the drug substance (active ingredient), drug product (formulation or composition) or method(s) of use, for which the applicant is seeking approval and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner of the patent engaged in the manufacture, use, or sale of the drug product. Yes

6. Declaration Certification

6.1 The undersigned declares that this is an accurate and complete submission of patent information for the NDA, amendment, or supplement pending under section 505 of the Federal Food, Drug, and Cosmetic Act. This time-sensitive patent information is submitted pursuant to 21 CFR 314.53. I attest that I am familiar with 21 CFR 314.53 and this submission complies with the requirements of the regulation. I verify under penalty of perjury that the foregoing is true and correct.

Warning: A willfully and knowingly false statement is a criminal offense under 18 U.S.C. 1001.

6.2 Authorized Signature of NDA Applicant/Holder or Patent Owner (Attorney, Agent, Representative or other Authorized Official) (Provide Information below)



Date Signed

09/17/2003

NOTE: Only an NDA applicant/holder may submit this declaration directly to the FDA. A patent owner who is not the NDA applicant/holder is authorized to sign the declaration but may not submit it directly to FDA. 21 CFR 314.53(c)(4) and (d)(4).

Check applicable box and provide information below.

NDA Applicant/Holder

NDA Applicant's/Holder's Attorney, Agent (Representative) or other Authorized Official

Patent Owner

Patent Owner's Attorney, Agent (Representative) or Other Authorized Official

Name

Ajay Chawla

Address

3909 Three Oaks Road

City/State

Cary, IL

ZIP Code

60014

Telephone Number

(815) 455-4700

FAX Number (if available)

(815) 444-5710

E-Mail Address (if available)

achawla@sageproducts.com

The public reporting burden for this collection of information has been estimated to average 9 hours per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

Food and Drug Administration
CDER (HFD-007)
5600 Fishers Lane
Rockville, MD 20857

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.

EXCLUSIVITY SUMMARY for NDA # 21-669 SUPPL # —

Trade Name 2% Chlorhexidine gluconate* Generic Name Cloth, *(equivalent to 500mg chlorhexidine gluconate per cloth)
Applicant Name Sage Products, Inc. HFD- 520

Approval Date

PART I: IS AN EXCLUSIVITY DETERMINATION NEEDED?

1. An exclusivity determination will be made for all original applications, but only for certain supplements. Complete Parts II and III of this Exclusivity Summary only if you answer "YES" to one or more of the following questions about the submission.

a) Is it an original NDA? YES / X / NO / ___ /

b) Is it an effectiveness supplement? YES / ___ / NO / X /

If yes, what type (SE1, SE2, etc.)?

c) Did it require the review of clinical data other than to support a safety claim or change in labeling related to safety? (If it required review only of bioavailability or bioequivalence data, answer "NO.")

YES / X / NO / ___ /

If your answer is "no" because you believe the study is a bioavailability study and, therefore, not eligible for exclusivity, EXPLAIN why it is a bioavailability study, including your reasons for disagreeing with any arguments made by the applicant that the study was not simply a bioavailability study.

If it is a supplement requiring the review of clinical data but it is not an effectiveness supplement, describe the change or claim that is supported by the clinical data:

d) Did the applicant request exclusivity?

YES /___/ NO /X/

If the answer to (d) is "yes," how many years of exclusivity did the applicant request?

e) Has pediatric exclusivity been granted for this Active Moiety?

YES /___/ NO /X/

IF YOU HAVE ANSWERED "NO" TO ALL OF THE ABOVE QUESTIONS, GO DIRECTLY TO THE SIGNATURE BLOCKS ON Page 9.

2. Has a product with the same active ingredient(s), dosage form, strength, route of administration, and dosing schedule previously been approved by FDA for the same use? (Rx to OTC Switches should be answered No - Please indicate as such).

YES /___/ NO /X/

If yes, NDA # _____ Drug Name

IF THE ANSWER TO QUESTION 2 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON Page 9.

3. Is this drug product or indication a DESI upgrade?

YES /___/ NO /X/

IF THE ANSWER TO QUESTION 3 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON Page 9 (even if a study was required for the upgrade).

PART II: FIVE-YEAR EXCLUSIVITY FOR NEW CHEMICAL ENTITIES

(Answer either #1 or #2, as appropriate)

1. Single active ingredient product.

Has FDA previously approved under section 505 of the Act any drug product containing the same active moiety as the drug under consideration? Answer "yes" if the active moiety (including other esterified forms, salts, complexes, chelates or clathrates) has been previously approved, but this particular form of the active moiety, e.g., this particular ester or salt (including salts with hydrogen or coordination bonding) or other non-covalent derivative (such as a complex, chelate, or clathrate) has not been approved. Answer "no" if the compound requires metabolic conversion (other than deesterification of an esterified form of the drug) to produce an already approved active moiety.

YES /___/ NO /___/

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA #

NDA #

NDA #

2. Combination product.

If the product contains more than one active moiety (as defined in Part II, #1), has FDA previously approved an application under section 505 containing any one of the active moieties in the drug product? If, for example, the combination contains one never-before-approved active moiety and one previously approved active moiety, answer "yes." (An active moiety that is marketed under an OTC monograph, but that was never approved under an NDA, is considered not previously approved.)

YES /X/ NO /___/

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA # 20-832 Chlorhexidine Gluconate 2%

NDA #

NDA #

IF THE ANSWER TO QUESTION 1 OR 2 UNDER PART II IS "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON Page 9. IF "YES," GO TO PART III.

PART III: THREE-YEAR EXCLUSIVITY FOR NDA'S AND SUPPLEMENTS

To qualify for three years of exclusivity, an application or supplement must contain "reports of new clinical investigations (other than bioavailability studies) essential to the approval of the application and conducted or sponsored by the applicant." This section should be completed only if the answer to PART II, Question 1 or 2, was "yes."

1. Does the application contain reports of clinical investigations? (The Agency interprets "clinical investigations" to mean investigations conducted on humans other than bioavailability studies.) If the application contains clinical investigations only by virtue of a right of reference to clinical investigations in another application, answer "yes," then skip to question 3(a). If the answer to 3(a) is "yes" for any investigation referred to in another application, do not complete remainder of summary for that investigation.

YES / X / NO / ___ /

IF "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON Page 9.

2. A clinical investigation is "essential to the approval" if the Agency could not have approved the application or supplement without relying on that investigation. Thus, the investigation is not essential to the approval if 1) no clinical investigation is necessary to support the supplement or application in light of previously approved applications (i.e., information other than clinical trials, such as bioavailability data, would be sufficient to provide a basis

for approval as an ANDA or 505(b)(2) application because of what is already known about a previously approved product), or 2) there are published reports of studies (other than those conducted or sponsored by the applicant) or other publicly available data that independently would have been sufficient to support approval of the application, without reference to the clinical investigation submitted in the application.

For the purposes of this section, studies comparing two products with the same ingredient(s) are considered to be bioavailability studies.

- (a) In light of previously approved applications, is a clinical investigation (either conducted by the applicant or available from some other source, including the published literature) necessary to support approval of the application or supplement?

YES / X / NO / ___ /

If "no," state the basis for your conclusion that a clinical trial is not necessary for approval **AND GO DIRECTLY TO SIGNATURE BLOCK ON Page 9:**

- (b) Did the applicant submit a list of published studies relevant to the safety and effectiveness of this drug product and a statement that the publicly available data would not independently support approval of the application?

YES / ___ / NO / X /

- (1) If the answer to 2(b) is "yes," do you personally know of any reason to disagree with the applicant's conclusion? If not applicable, answer NO.

YES / ___ / NO / X /

If yes, explain:

(2) If the answer to 2(b) is "no," are you aware of published studies not conducted or sponsored by the applicant or other publicly available data that could independently demonstrate the safety and effectiveness of this drug product?

YES /___/ NO /X/

If yes, explain:

(c) If the answers to (b)(1) and (b)(2) were both "no," identify the clinical investigations submitted in the application that are essential to the approval:

Investigation #1, Study # 01-109381-11

Investigation #2, Study # 020125

Investigation #3, Study # 500-102

3. In addition to being essential, investigations must be "new" to support exclusivity. The agency interprets "new clinical investigation" to mean an investigation that 1) has not been relied on by the agency to demonstrate the effectiveness of a previously approved drug for any indication and 2) does not duplicate the results of another investigation that was relied on by the agency to demonstrate the effectiveness of a previously approved drug product, i.e., does not redemonstrate something the agency considers to have been demonstrated in an already approved application.

(a) For each investigation identified as "essential to the approval," has the investigation been relied on by the agency to demonstrate the effectiveness of a previously approved drug product? (If the investigation was relied on only to support the safety of a previously approved drug, answer "no.")

Investigation #1 YES /___/ NO /X/

Investigation #2 YES /___/ NO /X/

Investigation #3 YES /___/ NO /X/

If you have answered "yes" for one or more investigations, identify each such investigation and the NDA in which each was relied upon:

NDA # _____ Study #
NDA # _____ Study #
NDA # _____ Study #

- (b) For each investigation identified as "essential to the approval," does the investigation duplicate the results of another investigation that was relied on by the agency to support the effectiveness of a previously approved drug product?

Investigation #1 YES /___/ NO /X/
Investigation #2 YES /___/ NO /X/
Investigation #3 YES /___/ NO /X/

If you have answered "yes" for one or more investigations, identify the NDA in which a similar investigation was relied on:

NDA # _____ Study #
NDA # _____ Study #
NDA # _____ Study #

- (c) If the answers to 3(a) and 3(b) are no, identify each "new" investigation in the application or supplement that is essential to the approval (i.e., the investigations listed in #2(c), less any that are not "new"):

Investigation #__, Study #
Investigation #__, Study #
Investigation #__, Study #

4. To be eligible for exclusivity, a new investigation that is essential to approval must also have been conducted or sponsored by the applicant. An investigation was "conducted or sponsored by" the applicant if, before or during the conduct of the investigation, 1) the applicant was the sponsor of the IND named in the form FDA 1571 filed with the Agency, or 2) the applicant (or its predecessor in interest) provided substantial support for the study. Ordinarily, substantial support will mean providing 50 percent or more of the cost of the study.

(a) For each investigation identified in response to question 3(c): if the investigation was carried out under an IND, was the applicant identified on the FDA 1571 as the sponsor?

Investigation #1 ~~#3~~ !
IND # 64143 YES / X / ! NO / ___ / Explain:
! ! ! ! !

Investigation #2 !
IND # _____ YES / ___ / ! NO / ___ / Explain:
! ! ! ! !

(b) For each investigation not carried out under an IND or for which the applicant was not identified as the sponsor, did the applicant certify that it or the applicant's predecessor in interest provided substantial support for the study?

Investigation #1 !
YES / ___ / Explain _____ ! NO / ___ / Explain _____

_____ ! ! ! ! !

Investigation #2 !
YES / ___ / Explain _____ ! NO / ___ / Explain _____

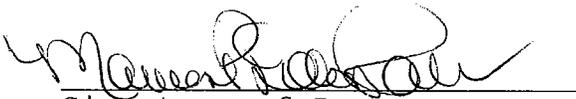
_____ ! ! ! ! !

(c) Notwithstanding an answer of "yes" to (a) or (b), are there other reasons to believe that the applicant should not be credited with having "conducted or sponsored" the study? (Purchased studies may not be used as the basis for exclusivity. However, if all rights to the drug are purchased (not just studies on the drug), the applicant may be considered to have sponsored or conducted the studies sponsored or conducted by its predecessor in interest.)

YES / /

NO / /

If yes, explain: _____



Signature of Preparer

4/25/05
Date

Title: *Chief, Project Management Staff*
Project manager for NDA 21-669

Signature of Office or Division Director

Date



4/27/05

cc:

Archival NDA

HFD- /Division File

HFD- /RPM

HFD-610/Mary Ann Holovac

HFD-104/PEDS/T.Crescenzi

*← Copy 4/27/05
Sent*

Form OGD-011347

Revised 8/7/95; edited 8/8/95; revised 8/25/98, edited 3/6/00

PEDIATRIC PAGE

(Complete for all filed original applications and efficacy supplements)

NDA # : 21-669 Supplement Type (e.g. SE5): NA Supplement Number: NA

Stamp Date: Orig - 9/4/03 Resubmission- 10/25/04 Action Date: Orig- 7/4/04 Resubmission 4/25/05

HFD-520 Trade and generic names/dosage form: 2% Chlorhexidine gluconate* Cloth, *(equivalent to 500 mg chlorhexidine gluconate per cloth)

Applicant: Sage Products, Inc. Therapeutic Class: 4020400

Indication(s) previously approved: None

Each approved indication must have pediatric studies: Completed, Deferred, and/or Waived.

Number of indications for this application(s): 1

Indication #1: Patient Preoperative Skin Preparation

Is there a full waiver for this indication (check one)?

Yes: Please proceed to Section A.

No: Please check all that apply: Partial Waiver Deferred Completed

NOTE: More than one may apply

Please proceed to Section B, Section C, and/or Section D and complete as necessary.

Section A: Fully Waived Studies

Reason(s) for full waiver:

- Products in this class for this indication have been studied/labeled for pediatric population
- Disease/condition does not exist in children
- Too few children with disease to study
- There are safety concerns
- Other: _____

If studies are fully waived, then pediatric information is complete for this indication. If there is another indication, please see Attachment A. Otherwise, this Pediatric Page is complete and should be entered into DFS.

Section B: Partially Waived Studies

Age/weight range being partially waived:

Min _____	kg _____	mo. <u><2</u>	yr. _____	Tanner Stage _____
Max _____	kg _____	mo. _____	yr. _____	Tanner Stage _____

Reason(s) for partial waiver:

- Products in this class for this indication have been studied/labeled for pediatric population
- Disease/condition does not exist in children
- Too few children with disease to study
- There are safety concerns
- Adult studies ready for approval
- Formulation needed
- Other: _____

If studies are deferred, proceed to Section C. If studies are completed, proceed to Section D. Otherwise, this Pediatric Page is complete and should be entered into DFS.

Section C: Deferred Studies

Age/weight range being deferred:

Min _____ kg _____ mo. _____ yr. _____ Tanner Stage _____
Max _____ kg _____ mo. _____ yr. _____ Tanner Stage _____

Reason(s) for deferral:

- Products in this class for this indication have been studied/labeled for pediatric population
- Disease/condition does not exist in children
- Too few children with disease to study
- There are safety concerns
- Adult studies ready for approval
- Formulation needed

Other: _____

Date studies are due (mm/dd/yy): _____

If studies are completed, proceed to Section D. Otherwise, this Pediatric Page is complete and should be entered into DFS.

Section D: Completed Studies

Age/weight range of completed studies:

Min _____ kg _____ mo. _____ yr. _____ Tanner Stage _____
Max _____ kg _____ mo. _____ yr. _____ Tanner Stage _____

Comments:

If there are additional indications, please proceed to Attachment A. Otherwise, this Pediatric Page is complete and should be entered into DFS.

This page was completed by:

{See appended electronic signature page}

Regulatory Project Manager

cc: NDA 21-669
HFD-960/ Grace Carmouze

FOR QUESTIONS ON COMPLETING THIS FORM CONTACT THE DIVISION OF PEDIATRIC DRUG DEVELOPMENT, HFD-960, 301-594-7337.

(revised 12-22-03)

**This is a representation of an electronic record that was signed electronically and
this page is the manifestation of the electronic signature.**

/s/

Peter Kim
4/21/05 09:54:00 AM

Jean Mulinde
4/21/05 01:28:55 PM

Maureen Dillon-Parker
4/20/05 04:26:50 PM
NDA 21-669; Pediatric Page

Orig

PEDIATRIC PAGE

(Complete for all filed original applications and efficacy supplements)

NDA #: 21-669 Supplement Type (e.g. SE5): NA Supplement Number: NA

Stamp Date: September 4, 2003 Action Date: July 4, 2004

HFD-520 Trade and generic names/dosage form: CHG Antiseptic Cloths (chlorhexidine gluconate, 2%)

Applicant: Sage Products, Inc. Therapeutic Class: 4020400

Indication(s) previously approved:

Each approved indication must have pediatric studies: Completed, Deferred, and/or Waived.

Number of indications for this application(s): 1

Indication #1: Patient Preoperative Skin Preparation

Is there a full waiver for this indication (check one)?

- Yes: Please proceed to Section A.
- No: Please check all that apply: Partial Waiver Deferred Completed
 NOTE: More than one may apply
 Please proceed to Section B, Section C, and/or Section D and complete as necessary.

Section A: Fully Waived Studies

Reason(s) for full waiver:

- Products in this class for this indication have been studied/labeled for pediatric population
- Disease/condition does not exist in children
- Too few children with disease to study
- There are safety concerns
- Other: _____

If studies are fully waived, then pediatric information is complete for this indication. If there is another indication, please see Attachment A. Otherwise, this Pediatric Page is complete and should be entered into DFS.

Section B: Partially Waived Studies

Age/weight range being partially waived:

Min _____	kg _____	mo. <u><2</u>	yr. _____	Tanner Stage _____
Max _____	kg _____	mo. _____	yr. _____	Tanner Stage _____

Reason(s) for partial waiver:

- Products in this class for this indication have been studied/labeled for pediatric population
- Disease/condition does not exist in children
- Too few children with disease to study
- XX There are safety concerns
- Adult studies ready for approval
- Formulation needed
- Other: _____

New Drug Application N21-669
Sage Products, Inc.

Section 8.0: Clinical Data and Statistical Evaluation

8.10 DEBARMENT CERTIFICATION

The services of any person debarred under FD&C Act 306 (a) or (b) were not used in any capacity in connection with this application.

USER FEE PAYMENT & PDUFA/FDAMA VALIDATION SHEET

Must be completed for ALL original NDAs, efficacy supplements and initial rolling review submissions

NDA # 21-669 SUPP TYPE & # N-Doc Division 520 UFID # _____

Applicant Name: SABE PRODUCTS INC. Drug Name: 2% Pre-op Prep (Enbrenexidine Gluconate)

For assistance in filling out this form see the Document Processing Manual for complete instructions and examples.

1. Was a Cover Sheet submitted?
 Yes No

2. Firm in Arrears?
 Yes No

3. Bundling Policy Applied Appropriately? Refer to Draft "Guidance for Industry: Submitting Separate Marketing Applications and Clinical Data for Purposes of Assessing User Fees"
<http://www.fda.gov/cder/guidance>
 Yes No (explain in comments)

4. Administrative Split? (list all NDA#s and Divisions)

NDA #/Doc Type	Div.	Fee? (Y/N)

5. Type 6?
 Yes No
 Type 6 to which other application?
 NDA # _____ Supp Type & # _____

6. Clinical Data Required for Approval? (Check one)
 Yes*
 Yes, by reference to another application
 NDA # _____ Supp Type & # _____
 No

* Yes if NDA contains study or literature reports of what are explicitly or implicitly represented by the application to be adequate and well-controlled trials. Clinical data do not include data used to modify the labeling to add a restriction that would improve the safe use of the drug (e.g., adding an adverse reaction, contraindication or warning to the labeling).

7. 505(b)(2) application? (NDA original applications only) Refer to Draft "Guidance for Industry Applications Covered by Section 505(b)(2)"
<http://www.fda.gov/cder/guidance>
 Yes No To be determined

8. Subpart H (Accelerated Approval/Restricted Distribution)?
 Yes No To be determined

9. Exclusion from fees? (Circle the appropriate exclusion. For questions, contact User Fee staff)
List of exclusions:
 2 - No fee - administrative split
 4 - No fee - 505b2
 7 - Supplement fee - administrative split
 9 - No fee Subpart H supplement- confirmatory study
 11 - No fee Orphan Exception
 13 - No fee State/Federal exemption from fees

10. Waiver Granted?
 Yes (letter enclosed) No
 Select Waiver Type below: Letter Dates Sept 5, 2003
 Small Business Barrier-to-Innovation
 Public Health Other (explain)

11. If required, was the appropriate fee paid?
 Yes No

12. Application Review Priority
 Priority Standard To be determined

13. Fast Track/Rolling Review Presubmission?
 Yes No

Comments


 PM Signature/Date

This form is the initial data extraction of information for both User Fee payment and PDUFA/FDAMA data elements. The information entered may be subject to change due to communication with the User Fee staff. This form will not reflect those changes. Please return this form to your submission room for processing.

CC: original archival file
 HFD-007

Processor Name & Date

QC Name & Date



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-669

Sage Products, Inc.
Attention: Ajay Chawla
Quality Assurance Compliance Manager
3909 Three Oaks Road
Cary, Illinois 60013

Dear Mr. Chawla:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for [REDACTED] (chlorhexidine gluconate 2% solution).

We also refer to your December 10, 2004, correspondence, received December 13, 2004, requesting a meeting to discuss the review status of your pending NDA.

Based on the statement of purpose, objectives, and proposed agenda, we consider the meeting a type C meeting as described in our guidance for industry titled *Formal Meetings with Sponsors and Applicants for PDUFA Products* (February 2000). The meeting is scheduled for:

Date: Monday, February 7, 2005
Time: 11:30am – 12:30pm
Location: 9201 Corporate Boulevard
Rockville, Maryland 20850

CDER invited participants:

Division of Anti-Infective Drug Products

Janice Soreth, MD, Director
Peter Kim, MD, Clinical Reviewer
David Bostwick, Clinical Reviewer
Milton Sloan, Ph.D., Chemistry Reviewer
James Vidra, Ph.D., Chemistry Team Leader
Thamban Valappil, Ph.D., Statistical Reviewer
Daphne Lin, Ph.D., Statistical Team Leader
Chuck Bonapace, Ph.D., Biopharmaceutical Reviewer
Venkatswar Jarugula, Ph.D., Biopharmaceutical Team Leader
Amy Ellis, Ph.D., Pharmacology Reviewer
Robert Osterberg, Ph.D., Pharmacology Team Leader
Peter Coderre, Ph.D., Microbiology Reviewer
Fred Marsik, Ph.D., Microbiology Team Leader (acting)
Maureen Dillon-Parker, Project Manager

Division of Over the Counter Drug Products

Charles Ganley, M.D., Director

Curtis Rosebraugh, M.D., Deputy Director

Tia Frazier, RN, Project Manager

Debbie Lumpkins, Team Leader

Michelle Jackson, Ph.D., Interdisciplinary Scientist

Walter Ellenberg, Chief, Project Manager (acting)

Andrea Leonard Segal, MD, Clinical Team Leader

Susan Johnson, Interdisciplinary Scientist

Please have all attendees bring photo identification and allow 15-30 minutes to complete security clearance. If there are additional attendees, email that information to me at dillonparker@cder.fda.gov so that I can give the security staff time to prepare temporary badges in advance. Upon arrival at FDA, give the guards either of the following numbers to request an escort to the conference room: Maureen Dillon-Parker #301-827-2125; the division secretary, Lorraine Meaney #301-827-2120.

Provide any additional background information for this meeting (three copies to the NDA and 23 desk copies to me) at least two-weeks prior to the meeting. If the materials presented in the information package are inadequate to justify holding a meeting, or if we do not receive the package by January 24, 2005 we may cancel or reschedule the meeting.

If you have any questions, call Maureen Dillon-Parker, Regulatory Project Manager, at (301) 827-2125.

Sincerely,

{See appended electronic signature page}

Frances V. LeSane
Chief, Project Management Staff
Division of Anti-Infective Drug Products
Office of Drug Evaluation IV
Center for Drug Evaluation and Research

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/s/

Judith Milstein
12/27/04 04:24:57 PM
Judith Milstein for Frances V. LeSane



RECEIVED
OCT 27 2004
MEGA/CDER

October 21, 2004

Ms Maureen Dillon-Parker
Food and Drug Administration
Center for Drug Evaluation and Research
Division of Anti-Infective Drug Products, HFD-520
Attention: Division Document Room, N115
9201 Corporate Blvd
Rockville, Maryland 20850

RE: NDA 21-669

Dear Ms. Dillon-Parker,

Please find enclosed the chemistry, packaging and labeling information as requested in your Approvable Action Letter dated 07/01/2004.

If there are any additional comments or questions, please feel free to contact me at (815) 455-4700 ext. 1182.

Sincerely,

A handwritten signature in black ink that reads "Ajay Chawla". The signature is fluid and cursive, with the first name and last name clearly distinguishable.

Ajay Chawla
Compliance Manager
Sage Products, Inc.
3909 Three Oaks Road
Cary, Illinois 60013
Phone: (815) 455-4700 ext 1182
Fax: (815) 444-5235
achawla@sageproducts.com

NDA 21-669

Sage Products, Inc.

2% CHG Pre-Op Prep (Antiseptic Cloth)

Healthcare Antiseptic: Patient Preoperative Skin Preparation

INFORMATION REQUEST

1. The Applicant must submit an assessment as required in The Pediatric Research Equity Act of 2003. The Applicant should provide, as soon as possible, a plan to assess the safety and effectiveness of the drug product for the claimed indications in all relevant pediatric subpopulations. If the Applicant believes that the disease and the effects of the drug are sufficiently similar in adults and pediatric patients, then they should provide a detailed explanation (supported by literature or available data) for the specific pediatric age groups for which they believe such an approach is applicable. For other pediatric age groups the Applicant should provide a pediatric plan for studies which will be conducted and may wish to submit a request for DEFERRAL for submission of study results until a specified date after approval of the drug so that availability for use in adult populations will not be delayed. Alternately, the Applicant may submit a request for a WAIVER/PARTIAL WAIVER for consideration, as the Applicant believes appropriate.
2. A Curriculum Vitae for [REDACTED] should be provided. (Principal Investigator for the third efficacy study, [REDACTED] -500-102)

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/s/

Maureen Dillon-Parker
5/25/04 03:02:57 PM
CSO
Fax 5-18-04; NDA 21-669

MEMORANDUM

**DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH**

CLINICAL INSPECTION SUMMARY

DATE: May 18, 2004
TO: Maureen Parker-Dillon, Regulatory Project Manager
Peter Kim, M.D., Medical Officer, Clinical Reviewer
Jean Mulinde, M.D., Medical Team Leader
Division of Anti-Infective Drug Products, HFD-520
THROUGH: Leslie K. Ball, M.D., Chief
Good Clinical Practice Branch II, HFD-47
Division of Scientific Investigations
FROM: Brenda R. Friend, R.Ph., J.D.
Good Clinical Practice Branch II, HFD-47
Division of Scientific Investigations
SUBJECT: Evaluation of Clinical Inspections
NDA: 21-669
APPLICANT: Sage Products, Inc.
DRUG: 2% CHG Pre-Op Prep (chlorhexidine gluconate, 2%)
CHEMICAL CLASSIFICATION: Type 3
THERAPEUTIC CLASSIFICATION: Standard Review
INDICATIONS: Patient pre-operative skin preparation
CONSULTATION REQUEST DATE: January 8, 2004
GOAL DATE TO PROVIDE
INSPECTION SUMMARY REPORT: May 15, 2004
ACTION GOAL DATE: June 15, 2004

I. BACKGROUND

Chlorhexidine gluconate (CHG) has antibacterial activity, related to its physical properties whereby the di-cation binds to negatively charged bacterial membranes. After binding, the hydrophobic portion of the molecule interacts with the cell wall, disrupting its integrity. At low concentrations, CHG interferes with cell membrane function and acts as a bacteriostatic agent. At high concentrations, the cell membrane becomes leaky, causing irreversible damage and cell death. Numerous topical solutions are currently marketed with CHG as the active ingredient with concentrations ranging from 0.5% to 4%. The sponsor, Sage Products, Inc., has requested the use of 2% CHG Pre-Op Prep as an [REDACTED]. The NDA was supported by the pivotal protocol: [REDACTED]-01-109381-11 entitled "Determination of the Antimicrobial Efficacy of a Chlorhexidine Gluconate Impregnated Cloth Wipe as a Patient Preoperative Skin Preparation."

The Review Division was concerned about discrepancies found at the [REDACTED] (Clinical Investigator [REDACTED]). The positive control did not meet the log reductions, whereas other sites did not report this finding. In addition, there were more exclusions (contaminations) than at other sites and no adverse events.

II. RESULTS (by site):

NAME	CITY, STATE	ASSIGNED DATE	EIR RECEIVED DATE	CLASSIFICATION
			Pending	Pending

Protocol - -01-109381

The study was conducted in healthy volunteers 18 years of age or older as a complete block design in that each subject was tested with two products at one or more anatomical locations. The study comprised of a 14-day pretreatment phase during which standardized antimicrobial soaps, shampoos and deodorants were used; a baseline week where subjects were sampled at least 72 hours prior to the test period; and a test period where subjects were sampled for a second baseline and prepped with CHG Pre-op Prep and Hibiclens to the femoral region or abdomen.

The primary efficacy endpoint was the log₁₀ reduction of skin flora at each body site following application. Microbiological samples were to be collected at 10 ± 1 minutes post prepping, and 30 minutes and 6 hours post prepping.

A total of 69 subjects were enrolled in the study with 51 subjects completing the study. Nine subjects withdrew for personal reasons; nine subjects did not meet the inclusion/exclusion criteria.

1. Site Inspected (Mr. Mulberry, Miami, OH): Data Acceptable

- a. **What was inspected:** The study records of all 51 subjects completing the study were reviewed including the log baseline requirements for entry into the test phase of the study.
- b. **Limitations of the inspection:** None.
- c. **General observations/commentary**

The sponsor monitored this site. During the inspection and at the close of the inspection, the following observations were discussed with the clinical investigator. A 3-item 483 was issued.

- 1) Record availability: All subjects' records were available.
- 2) Protocol Deviations: No significant issues found.
- 3) Subject eligibility: No significant issues found.
- 4) Subject withdrawals: No significant issues found.
- 5) Adverse events: No significant issues found.
- 6) Informed consent/IRBs/protocol amendments: All subjects signed and dated consent forms prior to enrollment. However, there was no documentation that each subject was given a signed copy of the informed consent. In addition, a complete copy of each subject's informed consent was not maintained at the study site.
- 7) Record Keeping: There is no documentation for any of the 51 subjects completing the study that a visual examination of the anatomical testing sites was performed prior to sampling during the test period to ensure no evidence of injury or dermatoses, as required by protocol.
- 8) Drug accountability: Records were not maintained to document the number of test articles returned to the sponsor.

III. OVERALL ASSESSMENT OF FINDINGS AND GENERAL RECOMMENDATIONS

In general, the inspection of documents support that audited subjects exist, met eligibility criteria, received assigned study medication, and adequately reported adverse events. No definitive reason(s) could be identified to explain why the positive control did not meet log reductions in the abdominal and groin area test sites.

The data submitted in support of this NDA appear acceptable.

Follow-up action: None needed.

[Note: This Clinical Inspection Summary was based on a draft EIR, without exhibits, received from the FDA inspector, and a draft memorandum received from the Review Division Microbiologist. Should the final review of EIR and exhibits contain information that would significantly affect the classification or have an impact on the approval process, I will inform the Review Division.]

Brenda R. Friend, R.Ph., J.D.
Good Clinical Practice Branch II, HFD-47
Division of Scientific Investigations

CONCURRENCE:

Supervisory comments

Leslie K. Ball, M.D., Branch Chief
Good Clinical Practice Branch II, HFD-47
Division of Scientific Investigations

DISTRIBUTION:

NDA 21-669
HFD-45/Division File/Reading File
HFD-45/Program Management Staff (electronic copy)
HFD-47/Ball/Friend
HFD-47/Lackner GCPB2 Files

rd:BRF:5/5/04:5/10/04:5/18/04

O:\BRF\CIS\NDA21669 2% CHG prep.doc

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/s/

Brenda Friend
5/19/04 11:33:51 AM
CSO

Leslie Ball
5/19/04 04:51:48 PM
MEDICAL OFFICER

Regarding NDA 21-669

Regarding Safety Study: "Exclusive Repeated Insult Patch Test," Protocol No. SGNC-001, performed by [REDACTED], can you please identify where in the submission the information on racial backgrounds for all 218 subjects can be found? Alternatively, if this information has not been submitted, we request that it be provided.

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/s/

Maureen Dillon-Parker

4/8/04 01:30:36 PM

CSO

NDA 21-669; Facsimile sent 4-7-04; clinical request for information
on safety study

fax sent
2/5/04



DEPARTMENT OF HEALTH & HUMAN SERVICES
Public Health Service
Food and Drug Administration
Center for Drug Evaluation and Research

MEMORANDUM

DATE : February 3, 2004

FROM: Dr. Peter Coderre, Microbiology Reviewer, Division of Anti-Infective Drug Products

THROUGH: Dr. Albert Sheldon, Microbiology Team Leader, Division of Anti-Infective Drug Products (HFD-520)

SUBJECT: Sage 2% CHG pre-operative washcloth, NDA 21-669

TO : Maureen Dillon-Parker

At this stage in the review of this NDA, this Reviewer has detected the following deficiencies that require the Applicant's attention.

1. Over the course of the spectrum of activity studies, the Applicant provided MIC data for most of the required organisms listed in the Tentative Final Monograph. However, while the Applicant supply MIC data for *Candida* species, the Applicant did not supply separate MIC data for *Candida albicans*. This data is necessary and must be presented in a tabular format similar to previously submitted MIC data.
2. While the Applicant made reference to the use of ASTM procedures for the validation of the neutralization studies and included raw data in an appendix, the Applicant did not present the data or provide a scientific discussion of said data. Data from neutralization studies should include data from both time-kill studies and clinical simulation trials. Data should be derived from a minimum of ten participants. A recommended format for the presentation of the data is shown below.

	Plating			
Article	Time	Plate Counts	Ave. cfu/ml	% recovery
# control	30 sec.			
	30 min.			
Toxicity	30 sec.			
control	30 min.			
Bulk Drug	30 sec.			
Product	30 min.			
Vehicle	30 sec.			
	30 min.			
Active	30 sec.			
Ingredient	30 min.			

Peter Coderre, Microbiology Reviewer
 Division of Anti-Infective Drug Products

Albert Sheldon, Microbiology Team Leader
 Division of Anti-Infective Drug Products

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/s/

Peter Coderre
2/4/04 04:09:44 PM
MICROBIOLOGIST

Albert Sheldon
2/4/04 04:17:29 PM
MICROBIOLOGIST
review contains recommendations that need to be provided to
the commpany

Lillian Gavrilovich
2/9/04 03:35:31 PM
MEDICAL OFFICER



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-669

Sage Products, Inc.
Attention: Ajay Chawla
Product Development Compliance Manager
3909 Three Oaks Road
Cary, Illinois 60013

Dear Mr. Chawla:

We have received your new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for the following:

Name of Drug Product: 2% CHG Pre-Op Prep (chlorhexidine gluconate)

Review Priority Classification: Standard (S)

Date of Application: August 29, 2003

Date of Receipt: September 4, 2003

Our Reference Number: NDA 21-669

Unless we notify you within 60 days of the receipt date that the application is not sufficiently complete to permit a substantive review, we will file the application on November 3, 2003, in accordance with 21 CFR 314.101(a). If the application is filed, the user fee goal date will be July 4, 2004.

Please cite the NDA number listed above at the top of the first page of any communications concerning this application. Address all communications concerning this NDA as follows:

NDA 21-669

Page 2

U.S. Postal Service:

Center for Drug Evaluation and Research
Division of Anti-Infective Drug Products, HFD-520
Attention: Division Document Room
5600 Fishers Lane
Rockville, Maryland 20857

Courier/Overnight Mail:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Anti-Infective Drug Products, HFD-520
Attention: Document Room
9201 Corporate Boulevard
Rockville, Maryland 20850

If you have any questions, call Ms. Maureen Dillon-Parker, Regulatory Project Manager, at (301) 827-2125.

Sincerely,

{See appended electronic signature page}

Frances V. LeSane
Chief, Project Management Staff
Division of Anti-Infective Drug Products
Office of Drug Evaluation IV
Center for Drug Evaluation and Research

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/s/

Frances LeSane
10/17/03 02:31:54 PM



SEP 5 2003

Food and Drug Administration
Rockville MD 20857

Lori Hays
Manager, Regulatory Affairs
Sage Products Inc.
3909 Three Oaks Road
Cary, IL 60013

**RE: Sage Products Inc. Small Business Waiver Request 2003.057 for Chlorhexidine
Gluconate 2% Preoperative Skin Preparation, New Drug Application 21-669**

Dear Ms. Hays:

This responds to your July 1, 2003, letter requesting a waiver of the human drug application fee for the new drug application (NDA) for the over-the-counter chlorhexidine gluconate 2% preoperative skin preparation, under the small business waiver provision, section 736(d)(1)(D)¹ of the Federal Food, Drug, and Cosmetic Act (the Act) (Waiver Request 2003.057). For the reasons described below, the Food and Drug Administration (FDA) grants Sage Products Inc.'s (Sage's) request for a small business waiver of the application fee for NDA 21-669 for the chlorhexidine gluconate 2% preoperative skin preparation.

According to your waiver request, Sage is a small business with ~~no~~ employees and no affiliates. You note that NDA 21-669 will be Sage's first human drug application submitted to FDA for review under section 505(b) of the Act. You anticipate submission of NDA 21-669 in August 2003.

Under section 736(d)(3)(B) of the Act,² a waiver of the application fee is granted to a small business for the first human drug application that it or its affiliate³ submits to the FDA for review. The small business waiver provision entitles a small business to a waiver when the business meets the following criteria: (1) the business must employ fewer than 500 persons, including employees of its affiliates, and (2) the marketing application must be the first human drug application, within the meaning of the Act, that a company or its affiliate submits to FDA.

FDA's decision to grant Sage's request for a small business waiver for NDA 21-669 is based on the following findings. First, the Small Business Administration (SBA) determined and stated in its letter dated July 31, 2003, that Sage has fewer than 500 employees, including those of its affiliate, BioSafety Systems, Inc.

¹ 21 U.S.C. 379h(d)(1)(D).

² 21 U.S.C. 379h(d)(3)(B).

³ "The term 'affiliate' means a business entity that has a relationship with a second business entity if, directly or indirectly — (A) one business entity controls, or has the power to control, the other business entity; or (B) a third party controls, or has the power to control, both of the business entities" (21 U.S.C. 379g(9)).

Second, according to FDA records, the marketing application for NDA 21-669 is the first human drug application, within the meaning of the Act, to be submitted to FDA by Sage or its affiliates. Consequently, your request for a small business waiver of the application fee for NDA 21-669 is granted, provided that FDA receives the marketing application for chlorhexidine gluconate preoperative skin preparation no later than July 31, 2004, 1 year after the effective date of the size determination made by SBA. Please include a copy of this letter with your application.

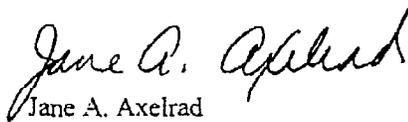
If FDA refuses to file the application or if Sage withdraws the application before it is filed by FDA, a reevaluation of the waiver may be required should the company resubmit its marketing application. If this situation occurs, Sage should contact this office approximately 90 days before it expects to resubmit its marketing application to determine whether it continues to qualify for a waiver.

We have notified the FDA Office of Financial Management (OFM) of this waiver decision and have asked them to waive the application fee for NDA 21-669. FDA records show that as of September 2, 2003, Sage's application 21-669 has not been submitted. However, FDA was notified of payment of the application fee, \$533,400, on August 28, 2003. You should receive a refund of \$533,400. If you do not receive this refund within 30 days of the date of this letter, please contact Donna Simms, OFM, at 301-827-5042.

FDA plans to disclose to the public information about its actions granting or denying waivers and reductions. This disclosure will be consistent with the laws and regulations governing the disclosure of confidential commercial or financial information.

If any billing questions arise concerning the marketing application or if you have any questions about this small business waiver, please contact Beverly Friedman, Michael Jones, or Tawni Schwerner at 301-594-2041.

Sincerely,



Jane A. Axelrad
Associate Director for Policy
Center for Drug Evaluation and Research

Sage Products, Inc.
Waiver Request # 2003.057
Page 3

BCC:

HFD-5 M. Jones

HFD-5 B. Friedman

HFD-5 Chronological File

HFD-5 Sage Products, Inc. waiver file

HFM-110 C. Vincent/R. Eastep

HFA-103 S. Farran (RECORD ON PAYMENT AND ARREARS LIST)

HF-20 F. Claunts

Drafted: L. Morrison 8/8/03

Reviewed: B. Friedman 8/19/03

Edited: S. O'Malley 9/2/03

Reviewed J. Axelrad

September 3, 2003

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NDA/EFFICACY SUPPLEMENT ACTION PACKAGE CHECKLIST

Supplement Information		
NDA 21-669	Efficacy Supplement Type SE- [NA]	Supplement Number [NA]
Drug: 2% Chlorhexidine gluconate* Cloth, *(equivalent to 500 mg chlorhexidine gluconate per cloth)		Applicant: Sage Products, Inc.
RPM: Maureen Dillon-Parker	HFD-520	Phone # 301-827-2161
Application Type: () 505(b)(1) (X) 505(b)(2)	Reference Listed Drug (NDA #, Drug name): NA	
❖ Application Classifications:		
• Review priority	(X) Standard () Priority	
• Chem class (NDAs only)	4020400 (3S)	
• Other (e.g., orphan, OTC)	NA	
❖ User Fee Goal Dates		
April 25, 2005 (Resubmission)		
❖ Special programs (indicate all that apply)		
(X) None Subpart H () 21 CFR 314.510 (accelerated approval) () 21 CFR 314.520 (restricted distribution) () Fast Track () Rolling Review () CMA Pilot 1 () CMA Pilot 2		
❖ User Fee Information		
• User Fee	() Paid	
• User Fee waiver	(X) Small business () Public health () Barrier-to-Innovation () Other	
• User Fee exception	() Orphan designation () No-fee 505(b)(2) () Other	
❖ Application Integrity Policy (AIP)		
• Applicant is on the AIP	() Yes (X) No	
• This application is on the AIP	() Yes (X) No	
• Exception for review (Center Director's memo)		
• OC clearance for approval		
❖ Debarment certification: verified that qualifying language (e.g., willingly, knowingly) was not used in certification & certifications from foreign applicants are cosigned by US agent.		
(X) Verified		
❖ Patent		
• Information: Verify that form FDA-3542a was submitted.	(X) Verified	
• Patent certification [505(b)(2) applications]: Verify type of certifications submitted.	21 CFR 314.50(i)(1)(i)(A) () I () II () III () IV 21 CFR 314.50(i)(1) (X) (ii) () (iii)	
• For paragraph IV certification, verify that the applicant notified the patent holder(s) of their certification that the patent(s) is invalid, unenforceable, or will not be infringed (certification of notification and documentation of receipt of notice).	() Verified	

❖ Exclusivity (approvals only)	
• Exclusivity summary	Enclosed
• Is there an existing orphan drug exclusivity protection for the active moiety for the proposed indication(s)? Refer to 21 CFR 316.3(b)(13) for the definition of sameness for an orphan drug (i.e., active moiety). This definition is NOT the same as that used for NDA chemical classification!	() Yes, Application # _____ (X) No
❖ Administrative Reviews (Project Manager, ADRA) (indicate date of each review)	Not Applicable
General Information	
❖ Actions	
• Proposed action	(X) AP () TA () AE () NA
• Previous actions (specify type and date for each action taken)	None
• Status of advertising (approvals only)	(X) Materials requested in AP letter () Reviewed for Subpart H
❖ Public communications	
• Press Office notified of action (approval only)	() Yes (X) Not applicable
• Indicate what types (if any) of information dissemination are anticipated	(X) None () Press Release () Talk Paper () Dear Health Care Professional Letter
❖ Labeling (package insert, patient package insert (if applicable), MedGuide (if applicable))	
• Division's proposed labeling (only if generated after latest applicant submission of labeling)	
• Most recent applicant-proposed labeling	Enclosed
• Original applicant-proposed labeling	Enclosed
• Labeling reviews (including DDMAC, DMETS, DSRCS) and minutes of labeling meetings (indicate dates of reviews and meetings)	Enclosed
• Other relevant labeling (e.g., most recent 3 in class, class labeling)	Enclosed (Chloraprep)
❖ Labels (immediate container & carton labels)	
• Division proposed (only if generated after latest applicant submission)	
• Applicant proposed	Enclosed
• Reviews	See OTC/MO/Chemistry/DMETS Reviews
❖ Post-marketing commitments	
• Agency request for post-marketing commitments	None
• Documentation of discussions and/or agreements relating to post-marketing commitments	None
❖ Outgoing correspondence (i.e., letters, E-mails, faxes)	Enclosed
❖ Memoranda/Telecons/Facsimiles	Enclosed
❖ Minutes of Meetings	
• EOP2 meeting (indicate date)	None
• Pre-NDA meeting (indicate date) – NDA INDEX TELECONFERENCE	July 21, 2003
• Pre-Approval Safety Conference (indicate date; approvals only)	None
• Other – CHEMISTRY	July 23, 2003; February 7, 2005

❖ Advisory Committee Meeting	
• Date of Meeting	NA
• 48-hour alert	NA
❖ Federal Register Notices, DESI documents, NAS/NRC reports (if applicable)	NA
Summary Application Review	
❖ Summary Reviews (e.g., Office Director, Division Director, Medical Team Leader) (<i>indicate date for each review</i>)	Enclosed- OTC Memo from Div Dir Dated 4-25-05
Clinical Information	
❖ Clinical review(s) (<i>indicate date for each review</i>)	6/25/04; 4/19/05
❖ Microbiology (efficacy) review(s) (<i>indicate date for each review</i>)	6/25/04; TL Memo 6/25/04
❖ Safety Update review(s) (<i>indicate date or location if incorporated in another review</i>)	NA
❖ Risk Management Plan review(s) (<i>indicate date/location if incorporated in another rev</i>)	NA
❖ Pediatric Page (separate page for each indication addressing status of all age groups)	Enclosed
❖ Demographic Worksheet (<i>NME approvals only</i>)	NA
❖ Statistical review(s) (<i>indicate date for each review</i>)	6/24/04; 4/21/05
❖ Biopharmaceutical review(s) (<i>indicate date for each review</i>)	11/7/03
❖ Controlled Substance Staff review(s) and recommendation for scheduling (<i>indicate date for each review</i>)	NA
❖ Clinical Inspection Review Summary (DSI)	
• Clinical studies	5/18/04; 6/2/04
• Bioequivalence studies	NA
CMC Information	
❖ CMC review(s) (<i>indicate date for each review</i>)	6/22/04; 6/25/04; 4/21/05
❖ Environmental Assessment	
• Categorical Exclusion (<i>indicate review date</i>)	6/25/04
• Review & FONSI (<i>indicate date of review</i>)	NA
• Review & Environmental Impact Statement (<i>indicate date of each review</i>)	6/25/04
❖ Microbiology (validation of sterilization & product sterility) review(s) (<i>indicate date for each review</i>)	NA
❖ Facilities inspection (provide EER report)	Date completed: 6/08/04 (X) Acceptable () Withhold recommendation
❖ Methods validation	() Completed (X) Requested () Not yet requested
Nonclinical Pharm/Tox Information	
❖ Pharm/tox review(s), including referenced IND reviews (<i>indicate date for each review</i>)	1/16/04
❖ Nonclinical inspection review summary	NA
❖ Statistical review(s) of carcinogenicity studies (<i>indicate date for each review</i>)	NA
❖ CAC/ECAC report	NA

NA = Not Applicable