FDA RESPONSE:

The modified — method is acceptable as long as it provides needed resolution of all the impurities above 0.1% and the impurities are identified. The Division asked to submit an IND amendment for the new — method and to make sure that the method is stability indicating.

2. Cubist plans to modify the existing manufacturing process for bulk daptomycin currently being used by — to produce clinical supplies. These changes have been outlined in the meeting package and will be submitted as an IND amendment. **Does FDA agree that the proposed comparability testing for bulk daptomycin and daptomycin drug product outlined in the meeting package is adequate to qualify material produced by the modified manufacturing process thereby allowing the material to be used in the Phase 3 clinical trials?**

FDA RESPONSE:

The comparability protocol for — versus — appears to be acceptable, but the acceptance criteria for the sameness should be provided and justified. In addition, the impurity profiles of the drug substance before and after the change should be included.

3. Due to limitations for purification capacity at — , Cubist needs to manufacture bulk daptomycin at — for commercial manufacturing. — process will be submitted in the NDA as the sole manufacturer of bulk daptomycin. **Is the comparability testing between the bulk material produced at — and — adequate to support an NDA? Is the comparability testing of the daptomycin drug product produced using material produced at — and — adequate to support an NDA?**

FDA RESPONSE:

The plan for bridging studies for the change in the manufacturing site from — to — acceptable for submission in the NDA. The division's understanding is that — material will not be used in the clinical studies for NDA submission. The data and acceptance criteria will be reviewed to determine acceptance of the drug substance from the new site. Also, the data for the drug product manufactured from the new source of the drug substance will be reviewed in the NDA.

4. Primary drug product stability data for the NDA will be generated using bulk daptomycin produced at — and drug product produced by the commercial drug product manufacturer (either Abbott — . Please be aware that the manufacturing procedures to produce bulk drug are essentially the

same between — and the commercial supplier — **Is the proposed approach of using — bulk drug for primary drug product stability studies acceptable providing the equivalence between bulk material produced by — and — is established?**

FDA RESPONSE:
Primary drug product stability data for the NDA will be acceptable if comparability is demonstrated between the drug substance batches manufactured at — (clinical site) and at — (proposed commercial site).

5. Abbott will produce — daptomycin vials in — — with varying capacities. For the primary stability studies, — will operate at — — capacity. **Does the FDA agree with the proposed primary stability plan outlined in the meeting package?**

   FDA RESPONSE:
   This is acceptable.

6. Since daptomycin is produced using a — process, the firm claims that FDA guidelines permit identification of impurities which occur at 0.3% or greater. Cubist plans to identify any impurity in the bulk daptomycin that is present at this level. **Is this acceptable to the FDA?**

   FDA RESPONSE:
   The acceptance criteria of 0.3% limit referenced in the "Guide for Inspection on Fermentation of Bulk Drug Substance" are contingent on review of the impurity profile data and methods for optimized process.

Agreements: See discussion/recommendation section

Issues Requiring Further Discussion: See discussion/recommendation section

Enclosure: None

Action Items: None

Minutes Preparer: Jose R. Cintron, R.Ph., M.A.
Senior Regulatory Management Officer

Chairs Concurrence: Dr. Chi Wan Chen,
Office Director, DNDC-III

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/s/

Chi Wan Chen
7/24/02 02:50:26 PM

MEMORANDUM OF TELECON

DATE: April 29, 2003 **TIME:** 1:15 PM **LOCATION:** S-348

APPLICATION NUMBER: NDA 21-572

DRUG NAME: CIDECIN® (daptomycin for injection)

BETWEEN:
Name:

David Schubert	Vice President, Regulatory Affairs and Quality
Judy Newberne	Director, Regulatory Affairs

Representing: Cubist Pharmaceuticals, Inc.

AND
Name:

Janice Soreth, MD	Director, DAIDP
David Ross, MD, PhD	Medical Team Leader
Susan Thompson, MD	Medical Officer
Sumathi Nambiar, MD, MPH	Medical Officer
LT Daniel Nguyen, RPh	Regulatory Health Project Manager

Representing: Division of Anti-Infective Drug Products, HFD-520

BACKGROUND:

On April 10, 2003 the Division informed the sponsor of the discrepancies in the data sets for study 9801. The Division emphasized the importance of resolving these discrepancies. This teleconference was held to further discuss action plans in addressing the discrepancies within the data sets.

MEETING OBJECTIVE(S):

To clarify action plans in resolving data set issues discovered by the Division.

DISCUSSION AND RECOMMENDATIONS:

The sponsor conveyed the following to the Division:

1. The sponsor will provide a written response outlining their understanding of the problem with the data sets.
2. The sponsor will inform the Division of which data sets are involved.
3. The sponsor will explain how the individual data sets, and ISS and ISE data sets were derived.
4. The sponsor will provide a time frame for submission of corrected data sets.

ACTION ITEMS:

- The sponsor will comply with the requests within the Discussion and Recommendation section after consulting with the contractor who constructed the data sets.
- Further discussion of data set issues will be addressed in a face-to-face meeting to be arranged between the sponsor and the Agency.

LT Daniel Nguyen, RPh
Regulatory Health Project Manager
Minutes Recorder

David Ross, MD, PhD
Medical Team Leader

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/s/

Daniel Nguyen
5/29/03 10:26:41 AM
CSO
04-29-03 Telecon
Please sign off

Frances LeSane
5/29/03 10:29:33 AM
CSO

David Ross
5/29/03 10:33:46 AM
MEDICAL OFFICER

Janice Soreth
5/29/03 01:05:55 PM
MEDICAL OFFICER

MEMORANDUM OF TELECON

DATE: April 10, 2003

NDA/IND: NDA 21-572

DRUG: Cidecin

BETWEEN:

David Schubert	Vice President, Regulatory Affairs and Quality
Judy Newberne	Director, Regulatory Affairs
Meri Bloom	Manager, Regulatory Affairs
Ed Campanaro	Executive Director, Clinical Operations
Conni Otradovec	Director, Biostatistics
Bobbi Lemay	Biostatistician
Jeff Alder	Senior Director, Pharmacology
Grace Thorne	Director, Microbiology
Barry Eisenstein	Executive VP, Research and Development
Frank Tally	Executive VP, Scientific Affairs and Chief Scientific Officer

PHONE: 1-888-742-8686

REPRESENTING: Cubist Pharmaceuticals, Inc.

AND Representatives of Division of Anti-Infective Drug Products, HFD-520

David Ross	Medical Team Leader
Albert Sheldon	Microbiology Team Leader
Peter Coderre	Microbiology Reviewer
Raquel Peat	Regulatory Health Project Manager

SUBJECT: To discuss submission of microbiology and clinical data for NDA 21-572, Cidecin.

DISCUSSION AND RECOMMENDATIONS: A summary of discussions and conclusions reached at the teleconference are listed below:

1. *Concentration of free calcium in blister fluid and extracellular space of tissue fluids:* The Agency request the calcium concentrations in animal models that mimic human infections.

2. The Agency requested that an analysis of efficacy results for Studies 9801 and 9901, for both EOT and TOC responses, in which sponsor overrides of the evaluability/outcome algorithm are not performed. In addition, clinical questions about discrepancy in the datasets for study 9801 will be sent via email. The Agency emphasized the importance of resolving these discrepancies to ensure that there are not more general issues with the accuracy of the datasets.

AGREEMENTS (DECISIONS) REACHED:

1. The sponsor agreed to submit a response addressing clinical and microbiology questions.

/S/

Minutes Prepared by: LTJG Raquel Peat, M.S., M.P.H.

/S/

Chair Concurrence: David Ross, M.D., Ph.D.

ATTACHMENT: Questions and comments emailed to sponsor on April 10, 2003.

----Original Message----
From: Peat, Raquel
Sent: Thursday, April 10, 2003 1:42 PM
To: David Schubert (E-mail)
Subject: NDA 21,572, Cidecin
Importance: High

Follow up questions from our teleconference that was held today:

Clinical Comments:

Please clarify the following for study 9801:

- Patient number 001600042: Though the patient is reported to have missed the test of cure (TOC) visit, the CLINRESP dataset has visit number 4, i.e. the TOC visit, listed as '6/9/99'. Although the patient satisfies criteria 7 and 10 for evaluability in Table 16.2.3.5, in the STATUS dataset the value for criterion 7 is '0' and for criterion 10 the value is 'missing'.

- Patient number 0144100044: The CLINRESP dataset lists end of therapy (EOT) visit date as '5/13/00', and TOC visit date as 'missing'. However, in Table 16.2.3.5 in the final study report, the patient is not listed as having satisfied criterion 10. If the TOC visit is missing, per the algorithm provided, the patient should be classified as non-evaluable, since at the EOT visit the investigator had classified the patient as 'improved'. However, the sponsor's outcome for this patient is 'cure'.

The 2 examples were found by chance, it is important to understand how they came about and whether they reflect more general problems in the accuracy of the datasets.

- Page 78 of the final study report states that a total of 102 subjects in the daptomycin group and 103 in the comparator group underwent a surgical procedure related to the infection site during the study. In Table 11-6 only 44 patients in the daptomycin arm and 47 patients in the comparator arm are listed has having had a surgical intervention. Please clarify the reason for this difference.

Microbiology Comments:

- What is the concentration of free calcium in blister fluid? In the extracellular space of skin tissues around epithelial cells?

LTJG Raquel Peat, M.S., M.P.H., USPHS
Regulatory Health Project Manager
Division of Anti-Infective Drug Products
Center for Drug Evaluation and Research
Food and Drug Administration
9201 Corporate Boulevard, HFD-520
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/s/

Raquel Peat
5/2/03 12:56:23 PM
CSO
4/10/03 Telecon
ready for sign off

David Ross
5/5/03 04:48:32 PM
MEDICAL OFFICER

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Office of Drug Safety

Memo

To: Janice Soreth, M.D.
Director, Division of Anti-Infective Drug Products
HFD-520

From: Alina R. Mahmud, R.Ph.
Team Leader, Division of Medication Errors and Technical Support
HFD-420

Through: Carol Holquist, R.Ph.
Deputy Director, Division of Medication Errors and Technical Support
HFD-420

Jerry Phillips, R.Ph.
Associate Director, Office of Drug Safety
HFD-400

CC: Raquel Peat
Project Manager
HFD-520

Date: September 17, 2003

Re: ODS Consult 03-0233-1; Cubicin (Daptomycin for Injection); NDA 21-572.

DMETS reviewed the proprietary name, Cubicin, on August 25, 2003, and found the unacceptable due to potential for with Ambien, Calcium, Librium, and Eulexin (see ODS consult 03-0233). However, the application was approved on September 12, 2003 with the proprietary name Cubicin.

This memo is in response to a request from the Division of Anti-Infective Drug Products (HFD-520), the Division of Medication Errors and Technical Support (DMETS) conducted a review of the proposed risk management plan for the approved product Cubicin. The sponsor contends that they will manage any risk associated with possible confusion of proprietary name with other medications through education, fair balanced promotion and surveillance.

1. Sponsor's RMP proposal:

We will educate health care professionals, particularly pharmacists, on the proper use of Cubicin. The package insert will be the primary basis for education concerning the product and management of risk. The unique features of Cubicin, such as once daily dosing, will help clearly differentiate Cubicin from other medications. The dosing of for Cubicin is on a weight basis and requires reconstitution (with normal saline) and instillation of proper dose to a secondary I.V. bag. This multiple step process lends itself to several checks by the health care professions to ensure that the proper medication and dose is being prepared. This multiple step process lends itself to several checks by the health care professions to ensure that the proper medication and dose is being prepared. This is quite unlike Cleocin or clindamycin phosphate.

DMETS' response:

DMETS acknowledges that the package insert provided with Cubicin instructs practitioners on the proper use; however, labels and labeling, will not prevent the misinterpretation of a prescription due to look-alike and/or sound-alike similarities. Once a prescription is read as a drug other than the intended drug product, in this case Cubicin, dosing and reconstitution instructions contained within the package insert will not prevent a medication error from occurring. Therefore, the package insert should not be used as the primary basis for educating health care practitioners, especially pharmacists. Rather, health care practitioners should be educated in proactive manner with mailings of "Dear Healthcare Practitioner" letters, detailed by company sales representatives at the launch of the product, etc.

Additionally, the sponsor only references the currently marketed drug product, Cleocin, as having a potential for confusion with Cubicin. DMETS refers the sponsor to ODS consult 03-0233 where the drug products Ambien, Calcium, Librium, and Eulexin are identified as having the potential for confusion with Cubicin. DMETS recommends that the sponsor acknowledge the potential for confusion with these products as well.

2. Sponsor's RMP proposal:

Cubist is willing to submit all medication error reports relating to proprietary name confusion, both potential and actual, that occur with Cubicin for a period of one year following the date of approval. All actual and potential errors will be submitted as a 15-day reports regardless of the patient outcome. Cubist agrees to evaluate these data with FDA and, if warranted, implement interventions to further minimize risk of medication errors.

DMETS' Comment:

DMETS commends the sponsor for taking the initiative in monitoring and reporting medication errors pertaining to Cubicin; however, DMETS recommends that the sponsor continue this practice for a period of three years rather than one year. A time-period of one year does not provide the Agency with a true depiction of the potential for medication errors as it may take practitioners some time after the launch of the product to begin prescribing.

DMETS would be willing to meet with the Division for further discussion, if needed. If you have further questions or need clarification, please contact Sammie Beam, Project Manager, at 301-827-3242.

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/s/

Alina Mahmud
9/22/03 09:57:20 AM
DRUG SAFETY OFFICE REVIEWER

Carol Holquist
9/22/03 10:05:08 AM
DRUG SAFETY OFFICE REVIEWER

Jerry Phillips
9/22/03 01:12:54 PM
DRUG SAFETY OFFICE REVIEWER

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CONSULTATION RESPONSE
Division Of Medication Errors and Technical Support
Office of Drug Safety
(DMETS; HFD-420)

DATE RECEIVED: Aug 20, 2003	DUE DATE: Aug 30, 2003	ODS CONSULT: 03-0233

TO:

Janice Soreth, M.D.
Director, Division of Anti-Infective Drug Products
HFD-520

THROUGH:

Raquel Peat
Project Manager, Division of Anti-Infective Drug Products
HFD-520

PRODUCT NAME:	**NDA SPONSOR:**
Cubicin (Daptomycin for Injection) 500 mg/vial and 250 mg/vial **NDA #:** 21-572	Cubist Pharmaceuticals, Inc.

SAFETY EVALUATOR: Alina R. Mahmud, R.Ph.

SUMMARY: In response to a consult from the Division of Anti-Infective Drug Products (HFD-520), the Division of Medication Errors and Technical Support (DMETS) conducted a review of the proposed proprietary name "Cubicin" to determine the potential for confusion with approved proprietary and established names as well as pending names.

RECOMMENDATIONS:

1. DMETS does not recommend the use of the proprietary name, Cubicin.

2. DDMAC finds the proprietary name, Cubicin, acceptable from a promotional perspective.

/S/

Carol Holquist, RPh
Deputy Director,
Division of Medication Errors and Technical Support
Office of Drug Safety
Phone: 301-827-3242 Fax: 301-443-9664

/S/

Jerry Phillips, RPh
Associate Director
Office of Drug Safety
Center for Drug Evaluation and Research
Food and Drug Administration

Division of Medication Errors and Technical Support
Office of Drug Safety
HFD-420; Parklawn Rm. 6-34
Center for Drug Evaluation and Research

PROPRIETARY NAME REVIEW

DATE OF REVIEW: August 25, 2003

NDA NUMBER: 21-572

NAME OF DRUG: Cubicin (Daptomycin for Injection)
500 mg/vial and 250 mg/vial

NDA SPONSOR: Cubist Pharmaceuticals, Inc.

I. INTRODUCTION

This consult was written in response to a request from the Division of Anti-Infective Drug Products (HFD-520), for assessment of the tradename "Cubicin", regarding potential name confusion with other proprietary or established drug names. Additionally, an independent trademark evaluation summary conducted by ——— was submitted in support of the proposed proprietary name Cubicin.

Cubicin is the second proposed proprietary name for this application. The sponsor had initially submitted the name "Cidecin" for review. DMETS found "Cidecin" unacceptable from a safety perspective on May 28, 2003 (see ODS consult 03-0001).

PRODUCT INFORMATION

Cubicin (Daptomycin for Injection) is indicated for the treatment of complicated skin and skin structure infections . A Cubicin dose of 4 mg/kg should be administered over a 30 minute period by intravenous infusion in 0.9% Sodium Chloride Injection, USP once every 24 hours for 7-14 days. Patients with a creatinine clearance of less than or equal to 40 mL/min should receive a 4 mg/kg dose every 48 hours. Cubicin will be supplied in single-use vials containing either 250 mg or 500 mg daptomycin as a sterile, lyophilized powder. The contents of a 250 mg vial should be reconstituted with 5 mL of 0.9% sodium chloride injection, USP. The contents of a 500 mg vial should be reconstituted with 10 mL of 0.9% sodium chloride injection, USP. Reconstituted Cubicin should be further diluted with 0.9% sodium chloride injection, USP to be administered by intravenous infusion over a period of 30 minutes.

RISK ASSESSMENT

The DMETS medication error staff conducted a search of several standard published drug product reference texts[1] as well as several FDA databases[2] for existing drug names which sound-alike or look-alike to "Cubicin" to a degree where potential confusion between drug names could occur under the usual clinical practice settings. The Saegis[3] Pharma-In-Use database was searched for drug names with potential for confusion. An Expert Panel discussion was conducted to review all findings from the searches. In addition, DMETS conducted three prescription analysis studies, to simulate the prescription ordering process.

A. EXPERT PANEL DISCUSSION

An Expert Panel discussion was held by DMETS to gather professional opinions on the safety of the proprietary name, Cubicin. Potential concerns regarding drug marketing and promotion related to the proposed name were also discussed. This group is composed of DMETS Medication Errors Prevention Staff and representation from the Division of Drug Marketing, Advertising, and Communications (DDMAC). The group relies on their clinical and other professional experiences and a number of standard references when making a decision on the acceptability of a proprietary name.

1. Five product names were identified in the Expert Panel Discussion (EPD) that were thought to have potential for confusion with Cubicin. One product name, Kinesid, was identified following a search in the POCA[4] (Phonologic and Orthographic Computer Analysis) database. The drug product, Calcium, was identified in DMETS' prescription studies. These products are listed in Table 1, along with the dosage forms available and usual FDA-approved dosage.

2. DDMAC did not have concerns about the name, Cubicin, with regard to promotional claims.

Table 1. Potential sound-alike and look-alike names identified by DMETS Expert Panel

Product Name	Dosage form(s), Generic name	Usual dose*	Look-alike or Sound-alike
Cubicin	Daptomycin for Injection 500 mg/vial and 250 mg/vial Single Use Vial	4 mg/kg IV every 24 hours ESRD patients: 4 mg/kg IV every 48 hours.	
Coumadin	Warfarin Sodium Tablets, USP 1 mg, 2 mg, 2.5 mg, 3 mg, 4 mg, 5 mg, 6 mg, 7.5 mg, and 10 mg. Warfarin Sodium Powder for Injection, Lyophilized 5.4 mg	The dosage and administration of must be individualized for each patient according to the particular patient's PT/INR response to the drug. The dosage should be adjusted based upon the patient's PT/INR.	Sound-alike

[1] Facts and Comparisons. 2003, Facts and Comparisons, St. Louis, MO. http://www.efactsweb.com/index.asp MICROMEDEX Integrated Index, 2003, MICROMEDEX, Inc., 6200 South Syracuse Way, Suite 300, Englewood, Colorado 80111-4740, which includes all products/databases within ChemKnowledge, DrugKnowledge, and RegsKnowledge Systems and PDR Physician's Desk Reference (Medical Economics Company Inc. 2003).

[2] The Division of Medication Errors and Technical Support [DMETS] database of Proprietary name consultation requests, New Drug Approvals 98-03, and the electronic online version of the FDA Orange Book.

[3] Data provided by Thomson & Thomson's SAEGIS ™ Online Service, available at www.thomson-thomson.com

[4] POCA (Phonologic and Orthographic Computer Analysis) database owned by the Division of Medication Error and Technical Support.

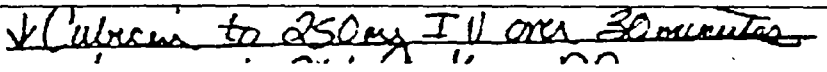
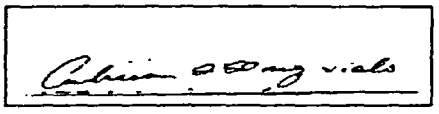
Product Name	Dosage form(s), Generic name	Usual dose*	Look-alike or Sound-alike
Cubicin	Daptomycin for Injection 500 mg/vial and 250 mg/vial Single Use Vial	4 mg/kg IV every 24 hours ESRD patients: 4 mg/kg IV every 48 hours.	
Quelicin	Succinylcholine Chloride Injection 20 mg/mL and 50 mg/mL	*Short surgical procedures:* Initial dose: 0.6 mg/kg IV. Maintenance dose: may range from 0.3 to 1.1 mg/kg. *Long surgical procedures:* Average rate for an adult ranges between 2.5 and 4.3 mg/min. Solutions containing 0.1% to 0.2% (1 to 2 mg/ml) are commonly used for continuous IVdrip. *Prolonged muscular relaxation:* Prolonged muscular relaxation may be achieved with intermittent IV injections. Give an initial dose of 0.3 to 1.1 mg/kg then give 0.04 to 0.07 mg/kg at appropriate intervals to maintain the required degree of relaxation.	Sound-alike
Ambien	Zolpidem Tartrate Tablets 5 mg and 10 mg	10 mg immediately before bedtime.	Look-alike
Kinesed	Phenobarbital, Hyoscyamine Sulfate, Atropine Sulfate, Hyoscine Sulfate	*This preparation is no longer marketed.*	Sound-alike
Cleocin	Clindamycin HCl Capsules 75 mg, 150 mg, 300 mg Clindamycin Palmitate Oral solution 75 mg/5 mL Clindamycin Phosphate Injection 150 mg/mL Cream 2% Suppository 100 mg Gel, Lotion, Topical Solution, Topical Suspension - 10 mg	Oral: 150 mg to 450 mg every 6 hours IM/IV: 600 mg to 4.8 grams/day in 2 to 4 divided doses Peds one month and older: 350 mg to 450 mg/m2/day Neonates less than one month 15 to 20 mg/kg/day in 3 to 4 divided doses Topical: apply twice daily	Sound-alike
Calcium	Variety of Calcium salts and preparations	Varies according to patient needs.	Look-alike
Cubicin	Herbal supplement	Used in the treatment of prostate cancer.	Look-alike, Sound-alike

* Frequently used, not all inclusive

B. PRESCRIPTION ANALYSIS STUDIES

1. Methodology for **Cubicin** studies

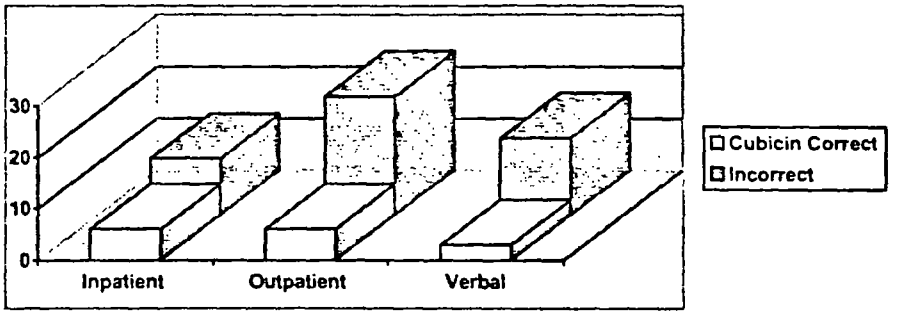
Studies were conducted within FDA for the proposed proprietary name to determine the degree of confusion of Cubicin with other U.S. drug names due to similarity in visual appearance with handwritten prescriptions or verbal pronunciation of the drug name. These studies employed a total of 128 health care professionals (nurses, pharmacists, and physicians). This exercise was conducted in an attempt to simulate the prescription ordering process. DMETS staff members wrote inpatient and outpatient prescriptions for Cubicin, each consisting of a combination of marketed and unapproved drug products. These written prescriptions were optically scanned and one prescription was delivered via e-mail to each study participant. In addition, one DMETS staff member recorded a verbal outpatient prescription that was then delivered to a group of study participants via telephone voicemail. Each reviewer was then requested to provide an interpretation of the prescription via e-mail.

HANDWRITTEN PRESCRIPTIONS	VERBAL PRESCRIPTION
Cubicin	
Inpatient: 	
Outpatient: 	*Verbal:* Dispense four vials of Cubicin, two hundred and fifty milligrams. The home nurse will be administering these."

2. Results for **Cubicin** studies

Results of these exercises are summarized below:

Study	No. of participants	# of responses	"Cubicin" response	Other response
Written: Inpatient	43	17 (40%)	6 (35%)	11 (65%)
Written Outpatient	41	23 (56%)	0 (0%)	23 (100%)
Verbal:	44	18 (41%)	3 (17%)	15 (83%)
Total:	128	58 (73%)	9 (16%)	49 (84%)



When examining the interpretations from the written inpatient prescriptions, 11 of 17 (65%) respondents interpreted the name incorrectly. In addition, all 23 respondents (100%) from the written outpatient prescriptions interpreted the name incorrectly. Incorrect responses included *Cabicin (4), Cabicur, Cubiis (2), Cubirin, Cubricin, Cubiia, Cibium, Cubrium (3), Culiris, Cabrica (2), Cabris, Cubrius, Cabica, Cabiun, Cubrien, Cubrism, Cubrisi, Cubien, Cubrison, and Cubiin. Two respondents provided the interpretation Ambien which is the name of a currently marketed drug product. Two additional participants commented that the name looks "strikingly" and "a lot" like Ambien. One respondent provided the interpretation "Calcium" which is the name of a currently marketed over-the counter vitamin and prescription drug product.*

Among the verbal outpatient Cidecin prescriptions, 15 of 18 (83%) respondents interpreted the name incorrectly. However, many of the misinterpretations were phonetically equivalent to "Cubicin". These included Cubisan (2), Cubisin (3), Cubisan, Cubacin, Cubison (3), Tubersyn, Juvicen, Quebecin, Cubeson, and Qubicin. None of the interpretations are similar to a currently marketed drug product.

C. SAFETY EVALUATOR RISK ASSESSMENT

1. Sound-alike, Look-alike Names

In reviewing the proprietary name "Cubicin", the primary concerns raised were related to look-alike and/or sound-alike names that are currently available in the U.S. marketplace: Coumadin, Cleocin, Quelicin, Ambien, Calcium, and Kinesed. Upon further review, DMETS discovered that Kinesed is no longer marketed, thus this name will not be discussed below. Additionally, the Expert Panel identified the name of an herbal supplement as Cubicin, which is identical to the proposed proprietary name. A search of online references and textbooks did not reveal a product with the name of Cubicin. The name Cubicin appears on the following website: http://www.dotpharmacy.com/uprostat.html.

Prescription studies were conducted to simulate the prescription ordering process. In this case, there was confirmation that Cubicin could be confused with Ambien and Calcium. Two respondents from the written outpatient prescription study provided the interpretation Ambien which is the name of a currently marketed drug product. Two additional participants commented that the name looks "strikingly" and "a lot" like Ambien. One respondent provided the interpretation "Calcium" which is the name of a currently marketed over-the counter and presciption drug product. Although there are limitations to the predictive value of these studies, primarily due to sample size, we have acquired safety concerns due to the positive interpretation with this drug product. A

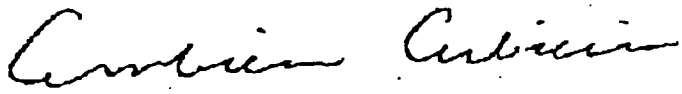
positive finding in a study with a small sample size may indicate a high risk and potential for medication errors when extrapolated to the general U.S. population.

Coumadin has potential for sound-alike confusion with Cubicin. Coumadin contains warfarin and is indicated for the prophylaxis and/or treatment of venous thrombosis and its extension, and pulmonary embolism. Coumadin is also indicated for the prophylaxis and/or treatment of the thromboembolic complications associated with atrial fibrillation and/or cardiac valve replacement. Lastly, Coumadin is indicated to reduce the risk of death, recurrent myocardial infarction, and thromboembolic events such as stroke or systemic embolization after myocardial infarction. Coumadin and Cubicin contain three syllables and share a similar prefix sound ("ku-"). The second syllable "ma" in Coumadin vs. "bi" in Cubicin is somewhat distinguishable. Although the last syllable "din" vs. "cin" end with "in", this suffix is distinguishable in sound due to the first letter difference. Coumadin and Cubicin overlap in dosage form; however, the drug products differ in dosage strength, dose and storage (room temperature vs. refrigeration). Additionally, PT/INR levels must be assessed frequently for patients on Coumadin. Given these differences and the lack of convincing sound-alike potential, the likelihood for confusion is minimal.

Quelicin has potential for sound-alike confusion with Cubicin. Quelicin contains succinylcholine chloride and is indicated as an adjunct to general anesthesia to facilitateendotracheal intubation, and to induceskeletal muscle relaxation during surgery or mechanical ventilation. Quelicin and Cubicin each contain three syllables and share the suffix "cin". However, the first and second syllable distinguishes one name from the other. Quelicin and Cubicin overlap in dosage form (injection) and route of administration (intravenous). Additionally, the products share a numerically similar dose (0.4 mg/kg vs. 4 mg/kg) and strength (50 mg/mL vs. 500 mg/vial). The products differ with respect to other characteristics such as storage (room temperature vs. refrigeration) and preparation (reconstituted vs. ready for injection). Additionally, Quelicin is to be used only if skilled in the management of artificial respiration and when facilities are instantly available for tracheal intubation and for providing adequate ventilation of the patient, including the administration of oxygen under positive pressure and the elimination of carbon dioxide. The clinician must be prepared to assist or control respiration. DMETS believes that the potential for confusion is minimal especially since the products lack strong sound-alike potential.

Ambien and Cubicin were found to have look-alike potential. In fact, two study participants from the written outpatient study misinterpreted Cubicin as Ambien while two other participants noted the similarity in appearance. Ambien is the proprietary name for zolpidem and is indicated for the short-term treatment of insomnia. When scripted, the first letter "A" in Ambien vs. "C" in Cubicin may look similar if the letter "A" is not fully looped. The remaining letters in each name look almost identical when scripted (see writing on page 8). Ambien and Cubicin differ in dosage form, route of administration, strength, dose, and storage (room temperature vs. refrigeration). Ambien is recommended for use at bedtime whereas Cubicin can be given at any time during a 24-hour peroid. It is likely that Ambien and Cubicin may be concomitantly prescribed for a hospitalized patient. In this case, it is possible that upon a D/C order for Ambien or Cubicin, the wrong medication is discontinued. As a result, the patient may inadvertently miss a dose of Cubicin which may affect the patient's recovery from the infection. In the event that Ambien is inadvertently discontinued instead of Cubicin, the

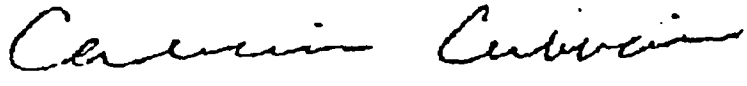
patient will remain untreated for insomnia and receive an extra dose of Cubicin. In either case, the potential for confusion is likely.



AMBIEN CUBICIN

Cleocin has potential for sound-alike confusion with Cubicin. These names contain the same number of syllables and the same ending sound "-CIN". Although Cleocin has a different dosing schedule and different dosage strengths, both medications are indicated to treat infections. The products differ in storage requirements as well. Cleocin is available in various dosage formulations, including an injectable formulation. The likelihood for confusion between Cleocin and Cubicin is minimized by the dissimilarity of the "CLEO-" and "CUBI-" portions of the names.

Calcium has the potential to look similar to Cubicin (see writing sample below). In fact, one study participant from the written outpatient prescription study provided the interpretation Calcium. Calcium is available by prescription and as an over-the-counter drug product (depending on salt). Calcium is available as a solid oral dosage form or as a parenteral drug product. Calcium and Cubicin may overlap in strength (250 mg and 500 mg), dosage form (injection), route of administration (intravenous), and dosing regimen (once daily). Furthermore, confusion and error may occur if a D/C order for either Cubicin or Calcium is scripted and the incorrect medication is discontinued because of the similarities in name. The inadvertent administration of Calcium, such as calcium chloride may result in harmful and life-threatening consequences. DMETS believes that the potential for confusion between Cubicin and Calcium is likely.



CALCIUM CUBICIN

2. —— Analysis

At the request of Cubist Pharmaceuticals, Inc., —— —— evaluated "Cubicin" using the model of analysis, which is a modification of the Failure Mode and Effects Analysis (FMEA). The participants in the —— safety evaluation are healthcare practitioners who are interested in medication safety and medication error prevention. Practicing pharmacists, nurses, and physicians have voluntarily enrolled with —— to participate when needed in naming, packaging and labeling review projects. Trademarks are given an overall rating using a five-point scale, with 1 being the poorest and 5 being the best (1-2 being highly vulnerable, 2.5-3.5 being moderately vulnerable, and 4-5 having low vulnerability).

—— determined that Cubicin has a moderate vulnerability rating of 3.5. According to ——., a trademark rated as moderately vulnerable may be considered for use with medical products. However, this use should be examined carefully in light of the information revealed in the report submitted by —— The names Ambien, Larium and Eulexin were identified as having a potential for look-alike confusion with the proposed proprietary name Cubicin. Refer to Table 2 below for a comparison of these drug products with Cubicin. A risk assessment for these names is provided below.

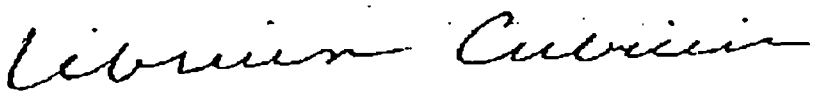
Table 2. Potential sound-alike and look-alike names identified by Cidecin Prescription Studies

Product Name	**Dosage form(s), Generic name**	**Usual dose**	**Look-alike or Sound-alike**
Cidecin	**Daptomycin for Injection 500 mg/vial and 250 mg/vial Single Use Vial**	**4 mg/kg IV every 24 hours ESRD patients: 4 mg/kg IV every 48 hours**	
Ambien	Zolpidem Tartrate Tablets 5 mg and 10 mg	10 mg immediately before bedtime.	Look-alike
Librium	Chlordiazepoxide Hydrochloride Capsules 5 mg, 10 mg, and 25 mg Powder for Injection 100 mg/ampule	5 mg to 25 mg three to four times daily. Dosage is individualized based on patient's disease state and age.	Look-alike
Eulexin	Flutamide Capsules 125 mg	Two capsules 3 times a day at 8-hour intervals for a total daily dosage of 750 mg.	Look-alike

Ambien was also identified by DMETS as having the potential for confusion with Cubicin as the names are almost identical in appearance to each other when scripted. —— identified Ambien as having a moderate look-alike similarity to Cubicin. —— states that if confused, the risk of harm is moderate due to the sedation associated with Ambien. DMETS believes that although the likelihood for dispensing error between Cubicin and Ambien is minimal, the potential for error and harm does exist if a D/C order for either Ambien or Cubicin is placed for a patient taking these medications concomitantly. As a result, the patient may inadvertently miss a dose of Cubicin which may affect the patient's recovery from the infection. In the event that Ambien is inadvertently discontinued instead of Cubicin, the patient will remain untreated for insomnia and receive an extra dose of Cubicin. In either case, the potential for confusion is likely.

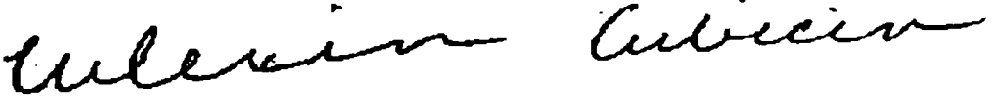
Librium has the potential to look similar to Cubicin. Librium contains chlordiazepoxide and is indicated to treat anxiety disorders and alcohol withdrawal. Librium is available as capsules and powder for injection. The "L" in Librium vs. the "C" in Cubicin look similar when scripted as do the remaining letters (see writing sample on page 10). Librium and Cubicin share an overlapping dosage form (for injection), route of administration (intravenous), and storage (refrigeration). The drug products also share a numerically similar strength (25 mg of Librium vs. 250 mg of Cubicin). This confusion may be further perpetuated if the dose of Librium is scripted with a trailing zero (e.g.

25.0 mg). DMETS believes that the potential for confusion is likely given the similarities. Librium is categorized as category D. The risk associated with the inadvertent substitution of Librium is high especially if Librium is administered to a pregnant woman.



LIBRIUM CUBICIN

Eulexin has the potential to look similar to Cubicin. Eulexin contains flutamide and is indicated for the treatment of prostate cancer. Eulexin and Cubicin share similarly scripted letters "E" vs. "C", "l" vs. "b", "e" vs. "i", and "x" vs. "c". Additionally, the names contain the letters "u" and "in" in the same position (see writing sample below). The drug products differ in dosage form, route of administration, strength, dosing regimen, and storage (room temperature vs. refrigeration). However, Eulexin and Cubicin share a similar dose of 250 mg. Confusion and error may surface if an inpatient order for Eulexin or Cubicin is written with a dose of 250 mg at 7 a.m. In this case, it is possible for the either one to be dispensed in place of the other due to its similarity in dose and look-alike potential. The consequence of Eulexin inadvertently dispensed instead of Cubicin may include hepatoxicity as Eulexin is highly toxic to the liver. Therefore, DMETS believes that the potential for risk and harm is high.



EULEXIN CUBICIN

III. COMMENTS TO THE SPONSOR

In reviewing the proprietary name "Cubicin", the primary concern for name confusion include the currently marketed drug products Ambien, Calcium, Librium, and Eulexin. Additionally, the Expert Panel identified the name of an herbal supplement as Cubicin, which is identical to the proposed proprietary name. A search of online references and textbooks did not reveal a product with the name of Cubicin. The name Cubicin appears in the following website: http://www.dotpharmacy.com/uprostat.html.

Ambien and Cubicin were found to have look-alike potential. In fact, two study participants from the written outpatient study misinterpreted Cubicin as Ambien while two other participants noted the similarity in appearance. Ambien is the proprietary name for zolpidem and is indicated for the short-term treatment of insomnia. When scripted, the first letter "A" in Ambien vs. "C" in Cubicin may look similar if the letter "A" is not fully looped. The remaining letters in each name look almost identical when scripted (see writing on page 11). Ambien and Cubicin differ in dosage form, route of administration, strength, dose and storage (room temperature vs. refrigeration). Ambien is recommended for use at bedtime whereas Cubicin can be given at any time during a 24-hour peroid. It is likely that Ambien and Cubicin may be concomitantly prescribed for a hospitalized patient. In this case, it is possible that upon a D/C order for

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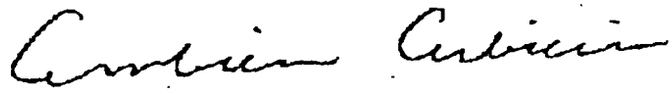
AMBIEN CUBICIN



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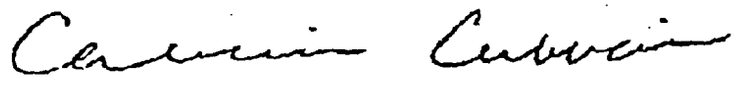

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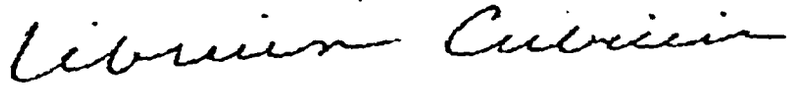

LIBRIUM CUBICIN

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EULEXIN CUBICIN

IV. RECOMMENDATIONS

A. DMETS does not recommend use of the proprietary name, Cubicin.

B. DDMAC finds the proprietary name, Cubicin, acceptable from a promotional perspective.

DMETS would appreciate feedback of the final outcome of this consult (e.g., copy of revised labels/labeling). We are willing to meet with the Division for further discussion as well. If you have any questions concerning this review, please contact Sammie Beam at 301-827-3242.

Alina R. Mahmud, R.Ph.
Team Leader
Division of Medication Errors and Technical Support
Office of Drug Safety

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

/s/

Alina Mahmud
8/27/03 11:29:32 AM
PHARMACIST

Jerry Phillips
8/27/03 12:26:36 PM
DIRECTOR

CONSULTATION RESPONSE
Division Of Medication Errors and Technical Support
Office of Drug Safety
(DMETS; HFD-420)

DATE RECEIVED: MAR-6-2003	DUE DATE: MAY-6-2003	ODS CONSULT: 03-0001

TO:

Janice Soreth, M.D.
Director, Division of Anti-Infective Drug Products
HFD-520

THROUGH:

Raquel Peat
Project Manager, Division of Anti-Infective Drug Products
HFD-520

PRODUCT NAME:	**NDA SPONSOR:**
Cidecin (Daptomycin for Injection) 500 mg/vial and 250 mg/vial **NDA #:** 21-572	Cubist Pharmaceuticals, Inc.

SAFETY EVALUATOR: Marci Lee, PharmD

SUMMARY: In response to a consult from the Division of Anti-Infective Drug Products (HFD-520), the Division of Medication Errors and Technical Support (DMETS) conducted a review of the proposed proprietary name "Cidecin" to determine the potential for confusion with approved proprietary and established names as well as pending names.

RECOMMENDATIONS:

1. DMETS does not recommend the use of the proprietary name, Cidecin.

2. DMETS recommends implementation of the labeling revisions outlined in section III of this review to minimize potential errors with the use of this product.

3. DDMAC finds the proprietary name, Cidecin, acceptable from a promotional perspective.

4. DMETS recommends informing Dan Boring, Chair of the LNC and FDA representative to USAN Council of the potential for confusion between Daptomycin and Dactinomycin.

/S/

Carol Holquist, RPh
Deputy Director,
Division of Medication Errors and Technical Support
Office of Drug Safety
Phone: 301-827-3242 Fax: 301-443-9664

/S/

Jerry Phillips, RPh
Associate Director
Office of Drug Safety
Center for Drug Evaluation and Research
Food and Drug Administration

Division of Medication Errors and Technical Support
Office of Drug Safety
HFD-420; Parklawn Rm. 6-34
Center for Drug Evaluation and Research

PROPRIETARY NAME REVIEW

DATE OF REVIEW: May 28, 2003

NDA NUMBER: 21-572

NAME OF DRUG: Cidecin (Daptomycin for Injection)
500 mg/vial and 250 mg/vial

NDA SPONSOR: Cubist Pharmaceuticals, Inc.

I. INTRODUCTION

This consult was written in response to a request from the Division of Anti-Infective Drug Products (HFD-520), for assessment of the tradename "Cidecin", regarding potential name confusion with other proprietary or established drug names.

PRODUCT INFORMATION

Cidecin (Daptomycin for Injection) is indicated for the treatment of complicated skin and skin structure infections . A Cidecin dose of 4 mg/kg should be administered over a 30 minute period by intravenous infusion in 0.9% Sodium Chloride Injection, USP once every 24 hours for 7-14 days. Patients with a creatinine clearance of less than or equal to 40 mL/min should receive a 4 mg/kg dose every 48 hours. Cidecin will be supplied in single-use vials containing either 250 mg or 500 mg daptomycin as a sterile, lyophilized powder. The contents of a 250 mg vial should be reconstituted with 5 mL of 0.9% sodium chloride injection, USP. The contents of a 500 mg vial should be reconstituted with 10 mL of 0.9% sodium chloride injection, USP. Reconstituted Cidecin should be further diluted with 0.9% sodium chloride injection, USP to be administered by intravenous infusion over a period of 30 minutes.

II. RISK ASSESSMENT

The DMETS medication error staff conducted a search of several standard published drug product reference texts[1] as well as several FDA databases[2] for existing drug names which sound-alike or look-alike to "Cidecin" to a degree where potential confusion between drug names could occur under the usual clinical practice settings. The Saegis[3] Pharma-In-Use database was searched for drug names with potential for confusion. An Expert Panel discussion was conducted to review all findings from the searches. In addition, DMETS conducted three prescription analysis studies, to simulate the prescription ordering process.

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[1] Facts and Comparisons, 2003, Facts and Comparisons, St. Louis, MO. http://www.efactsweb.com/index.asp MICROMEDEX Integrated Index, 2003, MICROMEDEX, Inc., 6200 South Syracuse Way, Suite 300, Englewood, Colorado 80111-4740, which includes all products/databases within ChemKnowledge, DrugKnowledge, and RegsKnowledge Systems and PDR/Physician's Desk Reference (Medical Economics Company Inc, 2003).

[2] The Division of Medication Errors and Technical Support [DMETS] database of Proprietary name consultation requests, New Drug Approvals 98-03, and the electronic online version of the FDA Orange Book.

[3] Data provided by Thomson & Thomson's SAEGIS ™ Online Service, available at www.thomson-thomson.com

A. EXPERT PANEL DISCUSSION

An Expert Panel discussion was held by DMETS to gather professional opinions on the safety of the proprietary name, Cidecin. Potential concerns regarding drug marketing and promotion related to the proposed name were also discussed. This group is composed of DMETS Medication Errors Prevention Staff and representation from the Division of Drug Marketing, Advertising, and Communications (DDMAC). The group relies on their clinical and other professional experiences and a number of standard references when making a decision on the acceptability of a proprietary name.

1. Ten product names were identified in the Expert Panel Discussion (EPD) that were thought to have potential for confusion with Cidecin. These products are listed in Table 1, along with the dosage forms available and usual FDA-approved dosage.

2. DDMAC did not have concerns about the name, Cidecin, with regard to promotional claims.

Table 1. Potential sound-alike and look-alike names identified by DMETS Expert Panel

Product Name	**Dosage form(s), Generic name**	**Usual dose***	**Look-alike or Sound-alike**
Cidecin	**Daptomycin for Injection 500 mg/vial and 250 mg/vial Single Use Vial**	**4 mg/kg IV every 24 hours ESRD patients: 4 mg/kg IV every 48 hours**	
Dactinomycin (established name)	Powder for Injection, lyophilized 0.5 mg	Not to exceed 15 mcg/kg or 400 to 600 mcg/m2 daily IV for 5 days Adults: 0.5 mg/day IV for max of 5 days Children: 0.015 mg/kg/day IV for 5 days OR 2.5 mg/m2 IV over 1 week	Look-alike and Sound-alike
Cytoxan	Cyclophosphamide Tablets 25 mg, 50 mg Powder for injection 100 mg	IV: 40 mg – 50 mg/kg in divided doses over 2 to 5 days OR 10 to 15 mg/kg every 7 to 10 d OR 3 to 5 mg/kg twice weekly Oral: 1 to 5 mg/kg/day	Sound-alike
Cytadren	Aminoglutethimide 250 mg tablets	250 mg 4 times daily	Sound-alike
Cleocin	Clindamycin HCl Capsules 75 mg, 150 mg, 300 mg Clindamycin Palmitate Oral solution 75 mg/5 mL Clindamycin Phosphate Injection 150 mg/mL Cream 2% Suppository 100 mg Gel, Lotion, Topical Solution, Topical Suspension - 10 mg	Oral: 150 mg to 450 mg every 6 hours IM/IV: 600 mg to 4.8 grams/day in 2 to 4 divided doses Peds one month and older: 350 mg to 450 mg/m2/day Neonates less than one month 15 to 20 mg/kg/day in 3 to 4 divided doses Topical: apply twice daily	Sound-alike

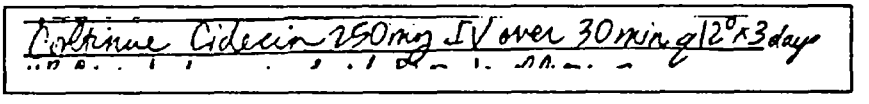
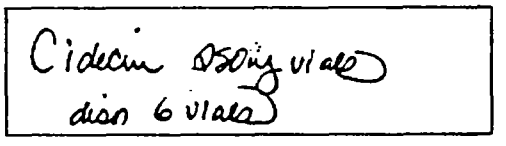
Ceftin	Cefuroxime Axetil Tablets 125 mg, 250 mg, 500 mg Suspension 125 mg/5 mL 250 mg/5 mL Powder for injection 750 mg, 1.5 grams, 7.5 grams Injection (premix) 750 mg and 1.5 grams	Adults Oral: 250 mg – 500 mg twice daily for 10 days Peds Oral 125 mg to 250 mg twice daily for 10 d Age 3 mos to 12 yrs Oral 20 mg – 30 mg/kg/day divided into two doses Adults IM/IV 750 mg to 1.5 gram IM/IV every 8 hours for 5 to 10 days	Sound-alike
Lidocaine (established name)	Injection 300 mg/3 mL 1%, 2%, 4%, 10%, 20%, 0.2%, 0.4%, 0.8%, 0.5% Various strengths mixed with epinephrine 2% cream and gel 2.5 % topical liquid 2% viscous 2.5 % ointment 2% topical solution 5% transdermal patch	Injectable local anesthetic Max 4.5 mg/kg/dose IM 300 mg Peds IV Load 1 mg/kg, CIV 20-50 mcg/kg/min Adult IV: 1-1.5 mg/kg bolus over 2-3 min and repeat in 5-10 min for total load up to 3 mg/kg; CIV 1-4 mg/min Dose varies for local anesthesia.	Look-alike
Codeine (established name)	Codeine Sulfate Tablets 15 mg, 30 mg, 60 mg Codeine Phosphate Oral solution 15 mg/5 mL 500 mL and UD 5 mL Injection 30 mg, 60 mg 1 mL vials and 1 mL tubex	Adults: 15 mg – 60 mg every 4 – 6 hours PO, IM, IV or SC. Peds one year and older: 0.5 mg/kg or 15 mg/m2 every 4-6 hours SC, IM or PO. Age 6-12 years: 5 mg – 10 mg every 4-6 hours (daily max is 60 mg) Age 2-6 years: 2.5 mg – 5 mg PO every 4 to 6 hours (daily max is 30 mg)	Look-alike
Indocin	Indomethacin Capsules 25 mg, 50 mg SR Capsules 75 mg Oral suspension 25 mg/5 mL Suppositories 50 mg	25 mg PO 2 or 3 times daily OR 75 mg SR capsule once daily 75 mg to 150 mg daily in 3 or 4 divided doses for 7 – 10 d (bursitis) 50 mg 3 times daily until pain is tolerable (acute gouty arthritis)	Look-alike
Staticin	Erythromycin 1.5 % solution (60 mL)	Apply morning and evening.	Sound-alike
Pitocin	Oxytocin 10 units/mL	Initial 1 to 2 mU/min IM: 10 units after delivery of placenta IV infusion: 10 to 40 units to a max of 40 units to 1000 mL and titrate for effect	Sound-alike

* Frequently used, not all inclusive

B. PRESCRIPTION ANALYSIS STUDIES

1. Methodology for **Cidecin** studies

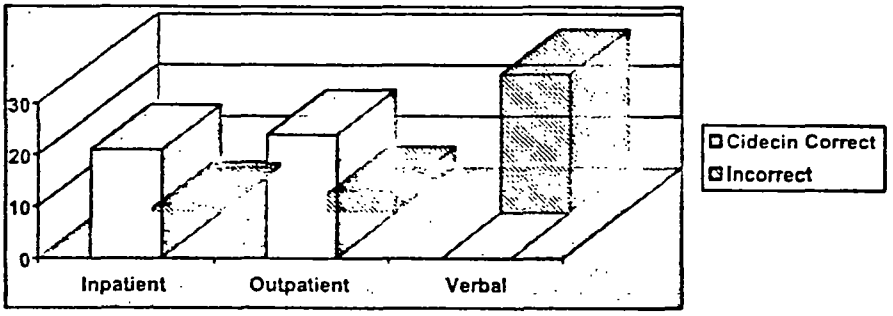
Studies were conducted within FDA for the proposed proprietary name to determine the degree of confusion of Cidecin with other U.S. drug names due to similarity in visual appearance with handwritten prescriptions or verbal pronunciation of the drug name. These studies employed a total of 105 health care professionals (nurses, pharmacists, and physicians). This exercise was conducted in an attempt to simulate the prescription ordering process. DMETS staff members wrote inpatient and outpatient prescriptions for Cidecin, each consisting of a combination of marketed and unapproved drug products. These written prescriptions were optically scanned and one prescription was delivered via e-mail to each study participant. In addition, one DMETS staff member recorded a verbal outpatient prescription that was then delivered to a group of study participants via telephone voicemail. Each reviewer was then requested to provide an interpretation of the prescription via e-mail.

HANDWRITTEN PRESCRIPTIONS	VERBAL PRESCRIPTION
Cidecin	
Inpatient: 	
Outpatient: 	*Verbal:* "... Please dispense six vials of Cidecin, two hundred and fifty milligrams. The home nurse will be administering these."

2. Results for **Cidecin** studies

Results of these exercises are summarized below:

Study	No. of participants	# of responses	"Cidecin" response	Other response
Written: Inpatient	31	22 (71%)	21 (95%)	1 (5%)
Written Outpatient	39	28 (72%)	24 (86%)	4 (14%)
Verbal:	35	27 (77%)	0 (0%)	27 (100%)
Total:	105	77 (73%)	45 (58%)	32 (42%)



When examining the interpretations from the written inpatient prescriptions, 21 of the 22 (95%) respondents interpreted the name correctly. In addition, 24 of 28 respondents (86%) from the written outpatient prescriptions interpreted the name correctly. The misinterpretation from the inpatient study was C*idercin.* Other incorrect responses included *Cidacin, Cidencin* and *Cidexin.* None of the misinterpretations represent names of currently marketed drug products.

Among the verbal outpatient Cidecin prescriptions, all of the respondents interpreted the name incorrectly. However, many of the misinterpretations were phonetically equivalent to "Cidecin". These included *Cytosan, Cytosen, Cytosin, Cytosyn, Cytocyn, Cidocin, Citosan, Cytazin, Cytocen,* and *Cytocin.* Other misinterpretations included *Cytosine, Cidexin, Cydecine* and *Cytocine.* "Cytosine" is the name of a nucleic acid and is also used to make "Cytosine Arabinoside", which is commonly known in the US marketplace as Cytosar-U or "Ara-C", which is an antineoplastic agent. One respondent noted concern for sound-alike similarity between Cidecin and Cytovene. Cytovene (ganciclovir) is an antiviral agent.

C. SAFETY EVALUATOR RISK ASSESSMENT

Although several names were identified in the initial analysis of the name (See Table 1), the primary concern for name confusion was Cytovene, which already exists in the US marketplace. Other concerns included potential for confusion with *Dactinomycin* and the medical term "Cytosine". Following review of the names identified by the expert panel, it was determined there would be minimal risk due to several differentiating factors.

Prescription studies were conducted to simulate the prescription ordering process. In this case, there was no confirmation that Cidecin could be confused with the proprietary or established names identified by the expert panel. However, the studies identified two additional names of concern, Cytosine and Cytovene. These names are listed with dosage forms available and usual FDA-approved dosage in Table 2 on page 7.

Table 2. Potential sound-alike and look-alike names identified by Cidecin Prescription Studies

Product Name	Dosage form(s), Generic name	Usual dose	Look-alike or Sound-alike
Cidecin	**Daptomycin for Injection 500 mg/vial and 250 mg/vial Single Use Vial**	**4 mg/kg IV every 24 hours ESRD patients: 4 mg/kg IV every 48 hours**	
Cytosine	Medical term for pyrimidine found in nucleic acids. Related to cytarabine known as Cytosar-U in the US. Cytarabine Powder for Injection 100 mg, 500 mg, 1 g, 2 g Injection (as Tarabine) 20 mg/mL	100 mg/m2/day CIV for days 1 to 7 OR 100 mg/m2 IV every 12 hours day 1 – 7 OR 3 g/m2 IV over 2 hours every 12 hours for 4 to 12 doses OR 5 – 75 mg/m2 once daily for 4 days to once every 4 days	Sound-alike
Cytovene	Ganciclovir Capsules 250 mg, 500 mg Powder for Injection, lyophilized 500 mg/vial	Induction 5 mg/kg IV over 1 h every 12 hours for 14 to 21 days Maintenance IV: 5 mg/kg IV infusion over 1 h once daily, 7 days per week or 6 mg/kg once daily, 5 days per week. PO: 1000 mg 3 times daily with food or 500 mg 6 times daily every 3 h with food	Sound-alike

Cytovene has potential for sound-alike confusion with Cidecin. The beginning letters "CYTO-" sound similar to "CIDE-". In addition the names both end with the "N" sound. The medication names also have the same number of syllables, which also contributes to their sound-alike similarity. Cytovene is an antiviral agent indicated for the treatment of cytomegalovirus (CMV) infections such as CMV retinitis. Both Cidecin and Cytovene are available as 500 mg in a 10 mL vial. There is also overlap between the oral capsule dosage strengths for Cytovene and the dosage strengths for Cidecin. Both medications are used on an episodic basis and both can be used for a treatment course of 14 days. Cytovene dosing includes induction therapy followed by maintenance dosing. Due to the toxicity associated with Cytovene, there is a warning that intravenous ganciclovir is to be used only for the treatment of CMV retinitis in immunocompromised patients and for the prevention of CMV disease in transplant patients at risk for CMV disease. Practitioners could expect an order for Cidecin or Cytovene from a specialist in infectious diseases. DMETS anticipates that confusion and errors are likely to occur between these products due to their similar sound and overlapping characteristics.

Dactinomycin has potential for look-alike and sound-alike confusion with *Daptomycin*, which is the established name for Cidecin. *Dactinomycin* is indicated for treatment of various types of tumors and can be administered alone or in combination with other antineoplastic agents. *Dactinomycin* carries the warning that it is extremely corrosive to soft tissue. If extravasation occurs during IV use, severe damage to soft tissues will occur. There is no overlap of dosage strengths or dosage ranges for these medications, however both are available as lyophilized powder for injection. In addition, both are administered once daily for a course of several days. *Dactinomycin* can be administered for a maximum of five days. DMETS anticipates that confusion and errors are likely to occur between these products due to their look-alike and sound-alike similarity.

daptomycin dactinomycin

Cytosine has potential for sound-alike similarity to Cidecin. The names have the same number of syllables and the letters "CYTO-" and "CIDE-" sound similar. In addition, the ending sounds "-SINE" and "-CIN" are very similar. Cytosine is the name of a nucleic acid and is also used to make "Cytosine Arabinoside", which is commonly known in the US marketplace as Cytosar-U or "Ara-C", which is an antineoplastic agent. Although the name similarity is indirectly related to a drug product, the opportunity for medication errors exists. Cytarabine (Cytosar-U) is available as a powder for injection in various dosage strengths including 500 mg, similar to Cidecin. Cytarabine is indicated for the treatment of various types leukemia. Cytarabine is administered for a course of seven days, which is also similar to Cidecin. There is no overlap of the dosing between these medications and the cytarabine order would likely come from a different type of specialist. These factors may help to prevent confusion between Cidecin and cytarabine.

Cytoxan has potential for sound-alike confusion with Cidecin. Both names have three syllables and end with the "N" sound. In addition, "CYTO-" and "CIDE-" have a similar sound in the beginning of the names. Cytoxan is indicated for the treatment of various types of cancer and is often used in combination with other antineoplastic agents. Cytoxan is available as 25 mg and 50 mg oral tablets. There is also a powder for injection formulation that contains 100 mg of Cytoxan. Therefore, there is some indirect similarity in the dosage strengths. Although the dosing for Cytoxan varies, there are some regimens that have dosage ranges, which overlap with the dosing for Cidecin. One Cytoxan regimen is a course of 7 to 10 days, similar to Cidecin. Another Cytoxan regimen calls for 3 mg to 5 mg/kg to be administered twice weekly. Although the frequency is different, the mg/kg range includes the Cidecin dose of 4 mg/kg.

Additionally, Cytoxan, Cytosar-U, Cytarabine and Cytovene are currently included in a list of names published by the United States Pharmacopeia (USP), which are known to cause confusion and medication errors. This publication is called the *USP Quality Review* and can be found at http://www.usp.org/frameset.htm?http://www.usp.org/reporting/review/rev_076c.htm. The title of the list is "Use Caution – Avoid Confusion".

DMETS conducted a search of the AERS and DQRS databases for reports of medication errors between Cytovene and Cytosar. One report describes how a pharmacist accidentally prepared an infusion of Cytovene instead of Cytosar. The report indicates that the drug names contributed to this confusion. The infusion was administered to the patient. The outcome of this error is unknown. The report also states that the products were stored in close proximity since both are cytotoxic, which is another contributing factor to this medication error scenario.

Another report describes how a nurse that speaks English as a second language has an accent such that the "X" and "S" characteristic of her first language make it difficult to understand "Cytoxan", pronounced as "Cytosan" and Cytosar.

DMETS anticipates that confusion and errors are likely to occur between these products due to their sound-alike similarity.

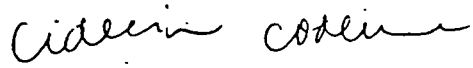
Cytadren has potential for sound-alike confusion with Cidecin. The beginning sounds of "CYTA-" and "CIDE-" are similar and both end with the "N" sound. Cytadren has a different indication, different dosing schedule and a different route of administration. The only overlapping characteristic with Cidecin is that the tablet strength of Cytadren is 250 mg. Due to many different characteristics, DMETS anticipates that these product names can coexist safely in the marketplace.

Cleocin has potential for sound-alike confusion with Cidecin. These names have the same number of syllables and the same ending sound "-CIN". Although Cleocin has a different dosing schedule and different dosage strengths, both medications are indicated to treat infections. Cleocin is available is various dosage formulations, including an injectable formulation. It is also possible that these medications would be stored near each other on a pharmacy shelf. The likelihood for confusion between Cleocin and Cidecin is minimized by the dissimilarity of the "CLEO-" and "CIDE-" portions of the names.

Ceftin has potential for sound-alike confusion with Cidecin. Although Ceftin is only available as an oral tablet or suspension, there is an injectable form of the product with a different name, Zinacef. Both Ceftin and Cidecin are used to treat infections. Ceftin is available as 250 mg and 500 mg tablets, which overlaps with the dosage strengths for Cidecin. Although the dosing schedules differ, both products are administered for a course of several days. While DMETS acknowledges there are some similar characteristics, the sound of these names is different enough to distinguish them.

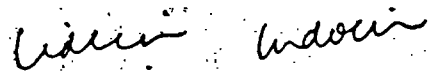
Lidocaine has potential for look-alike similarity to Cidecin. The letters "LIDO-" and "CIDE-" can look similar and the endings contain many of the same letters, "C", "I" and "N". While lidocaine is available in many formulations, there are some injectable formulations. Lidocaine is available in dosage strengths that differ from Cidecin. The indications for lidocaine differ from Cidecin. DMETS anticipates that these product names can coexist safely in the marketplace.

Codeine has potential for look-alike confusion with Cidecin. Codeine is a schedule II controlled substance and has a different indication from Cidecin. There are no overlapping dosage strengths between these products. DMETS anticipates that these product names can coexist safely in the marketplace.



Staticin has potential for sound-alike confusion with Cidecin. Staticin is a topical erythromycin product used to treat acne. Despite the name similarity, these products differ in the dosage formulation, dosage strengths and dosing schedule. DMETS anticipates that these product names can coexist safely in the marketplace.

Indocin has potential for look-alike and sound-alike confusion with Cidecin. The letters "IND-" can be mistaken for "CID-" and the endings "-OCIN" and "-ECIN" can also look similar. The similar sound comes from these ending sounds. Indocin has a different indication, different dosage formulation, and a different dosing schedule. DMETS anticipates that these product names can coexist safely in the marketplace.



III. COMMENTS TO THE SPONSOR

In reviewing the proprietary name "Cidecin", the primary concern for name confusion was Cytovene, which already exists in the US marketplace. Other concerns included potential for confusion with *Dactinomycin*, and Cytoxan.

Cytovene has potential for sound-alike confusion with Cidecin. The beginning letters "CYTO-" sound similar to "CIDE-". In addition the names both end with the "N" sound. The medication names also have the same number of syllables, which also contributes to their sound-alike similarity. Cytovene is an antiviral agent indicated for the treatment of cytomegalovirus (CMV) infections such as CMV retinitis. Both Cidecin and Cytovene are available as 500 mg in a 10 mL vial. There is also overlap between the oral capsule dosage strengths for Cytovene and the dosage strengths for Cidecin. Both medications are used on an episodic basis and both can be used for a treatment course of 14 days. Cytovene dosing includes induction therapy followed by maintenance dosing. Due to the toxicity associated with Cytovene, there is a warning that intravenous ganciclovir is to be used only for the treatment of CMV retinitis in immunocompromised patients and for the prevention of CMV disease in transplant patients at risk for CMV disease. Practitioners could expect an order for Cidecin or Cytovene from a specialist in infectious diseases. DMETS anticipates that confusion and errors are likely to occur between these products due to their similar sound and overlapping characteristics.

Dactinomycin has potential for look-alike and sound-alike confusion with *Daptomycin*, which is the established name for Cidecin. *Dactinomycin* is indicated for treatment of various types of tumors and can be administered alone or in combination with other antineoplastic agents. *Dactinomycin* carries the warning that it is extremely corrosive to soft tissue. If extravasation occurs during IV use, severe damage to soft tissues will occur. There is no overlap of dosage strengths or dosage ranges for these medications, however both are available as lyophilized powder for injection. In addition, both are administered once daily for a course of several days. *Dactinomycin* can be administered for a maximum of five days. DMETS anticipates that confusion and errors are likely to occur between these products due to their look-alike and sound-alike similarity.

daptomycin dactinomycin

Cytoxan has potential for sound-alike confusion with Cidecin. Both names have three syllables and end with the "N" sound. In addition, "CYTO-" and "CIDE-" have a similar sound in the beginning of the names. Cytoxan is indicated for the treatment of various types of cancer and is often used in combination with other antineoplastic agents. Cytoxan is available as 25 mg and 50 mg oral tablets. There is also a powder for injection formulation that contains 100 mg of Cytoxan. Therefore, there is some indirect similarity in the dosage strengths. Although the dosing for Cytoxan varies, there are some regimens that have dosage ranges, which overlap with the dosing for Cidecin. One Cytoxan regimen is a course of 7 to 10 days, similar to Cidecin. Another Cytoxan regimen calls for 3 mg to 5 mg/kg to be administered twice weekly. Although the frequency is different, the mg/kg range includes the Cidecin dose of 4 mg/kg.

Additionally, Cytoxan, Cytosar-U, Cytarabine and Cytovene are currently included in a list of names published by the United States Pharmacopeia (USP), which are known to cause confusion and medication errors. This publication is called the *USP Quality Review* and can be found at http://www.usp.org/frameset.htm?http://www.usp.org/reporting/review/rev_076c.htm. The title of the list is "Use Caution – Avoid Confusion".

DMETS anticipates that confusion and errors are likely to occur between these products due to their sound-alike similarity.

In review of the container labels, carton labeling and insert labeling of Cidecin, DMETS has attempted to focus on the safety issues relating to possible medication errors. DMETS has identified the following areas of possible improvement, which might minimize potential user error.

A. GENERAL COMMENTS

1. Ensure that the container and carton designs for the 250 mg and the 500 mg vials are adequately differentiated from each other to prevent medication errors between these dosage strengths.

2. Relocate the dosage strength "250 mg" so that it appears underneath the established name and express this information as "250 mg/vial".

3. Relocate the route of administration to appear prominently on the principal display panel.

4. If space permits, include the reconstitution instructions and resultant concentration per milliliter. For example:

   "Reconstitute each vial with XX mL of 0.9% Sodium Chloride Injection, USP. Once reconstituted, each mL contains XX mg of Daptomycin."

B. CARTON LABELING

1. Clarify the statement regarding salt content of Cidecin. There is potential for confusion with the following statement on side face 2 of the carton:

   "CIDECIN® (daptomycin for injection) contains approximately 900 mg/g of daptomycin for intravenous use following reconstitution with 0.9% sodium chloride injection, USP. Sodium hydroxide, used to adjust pH, may be present in trace amounts.

2. Include the directions for reconstitution and resulting concentration per mL.

C. INSERT LABELING

Include a statement regarding the salt content of Cidecin in the DESCRIPTION section of the insert labeling.

IV. RECOMMENDATIONS

A. DMETS does not recommend use of the proprietary name, Cidecin.

B. DMETS recommends implementation of the labeling revisions described in Section III.

C. DDMAC finds the proprietary name, Cidecin, acceptable from a promotional perspective.

D. DMETS recommends informing Dan Boring, Chair of the LNC and FDA representative to USAN Council of the potential for confusion between Daptomycin and Dactinomycin.

DMETS would appreciate feedback of the final outcome of this consult (e.g., copy of revised labels/labeling). We are willing to meet with the Division for further discussion as well. If you have any questions concerning this review, please contact Sammie Beam at 301-827-3242.

/S/

Marci Lee, PharmD
Safety Evaluator
Division of Medication Errors and Technical Support (DMETS)

Concur: /S/

Denise Toyer, PharmD Date
Team Leader
Division of Medication Errors and Technical Support
Office of Drug Safety

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

/s/

Marci Ann Lee
6/12/03 09:24:43 AM
PHARMACIST

Denise Toyer
6/12/03 09:26:53 AM
PHARMACIST

Carol Holquist
6/12/03 01:16:09 PM
PHARMACIST

Jerry Phillips
6/12/03 01:34:07 PM
DIRECTOR

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

REQUEST FOR CONSULTATION

TO (Division/Office):	FROM:
DSI, HFD-47 Brenda Friend and Ni Aye Khin	HFD-520 Susan Thompson and Raquel Peat

DATE	IND NO.	NDA NO.	TYPE OF DOCUMENT	DATE OF DOCUMENT
February 20, 2003		21-572	New NDA	20 December 2002

NAME OF DRUG	PRIORITY CONSIDERATION	CLASSIFICATION OF DRUG	DESIRED COMPLETION DATE
Cidecin®	YES	cyclic lipopeptide	ASAP

NAME OF FIRM: Cubist Pharmaceuticals, Inc.

REASON FOR REQUEST

I. GENERAL

- ☐ NEW PROTOCOL
- ☐ PROGRESS REPORT
- ☐ NEW CORRESPONDENCE
- ☐ DRUG ADVERTISING
- ☐ ADVERSE REACTION REPORT
- ☐ MANUFACTURING CHANGE/ADDITION
- ☐ MEETING PLANNED BY
- ☐ PRE-NDA MEETING
- ☐ END OF PHASE II MEETING
- ☐ RESUBMISSION
- ☐ SAFETY/EFFICACY
- ☐ PAPER NDA
- ☐ CONTROL SUPPLEMENT
- ☐ RESPONSE TO DEFICIENCY LETTER
- ☐ FINAL PRINTED LABELING
- ☐ LABELING REVISION
- ☐ ORIGINAL NEW CORRESPONDENCE
- ☐ FORMULATIVE REVIEW
- OTHER *(SPECIFY BELOW)*:

II. BIOMETRICS

STATISTICAL EVALUATION BRANCH	STATISTICAL APPLICATION BRANCH
☐ TYPE A OR B NDA REVIEW ☐ END OF PHASE II MEETING ☐ CONTROLLED STUDIES ☐ PROTOCOL REVIEW ☐ OTHER (SPECIFY BELOW):	☐ CHEMISTRY REVIEW ☐ PHARMACOLOGY ☐ BIOPHARMACEUTICS ☐ OTHER (SPECIFY BELOW):

III. BIOPHARMACEUTICS

- ☐ DISSOLUTION
- ☐ BIOAVAILABILITY STUDIES
- ☐ PHASE IV STUDIES
- ☐ DEFICIENCY LETTER RESPONSE
- ☐ PROTOCOL-BIOPHARMACEUTICS
- ☐ IN-VIVO WAIVER REQUEST

IV. DRUG EXPERIENCE

- ☐ PHASE IV SURVEILLANCE/EPIDEMIOLOGY PROTOCOL
- ☐ DRUG USE e.g. POPULATION EXPOSURE, ASSOCIATED DIAGNOSES
- ☐ CASE REPORTS OF SPECIFIC REACTIONS (List below)
- ☐ COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP
- ☐ REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY
- ☐ SUMMARY OF ADVERSE EXPERIENCE
- ☐ POISON RISK ANALYSIS

V. SCIENTIFIC INVESTIGATIONS

X☐ CLINICAL	☐ PRECLINICAL

COMMENTS/SPECIAL INSTRUCTIONS:

DSI inspection requested for the following sites from Cubist's Daptomycin complicated skin and skin infection study 9801:

- Site 66 Francis D. Pien, M.D., Straub Clinic and Hospital, 8885 King St, Honalulu, HI 96813
- Site 168 Raymond E. Tidman M.D., 2855 Old Hwy 5, 101 Burns Professional Building, Blue Ridge, GA 30513

SIGNATURE OF REQUESTER	METHOD OF DELIVERY (Check one)
R. Peat, E. DuvallMiller and S. Thompson	X E-MAIL and DFS ☐ HAND
SIGNATURE OF RECEIVER	SIGNATURE OF DELIVERER

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/s/

Susan Thompson
2/21/03 11:33:03 AM

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

REQUEST FOR CONSULTATION

TO *(Division/Office)*:
Office of Drug Safety, HFD-420
ParkJawn Building, Room 6-34

FROM:
HFD-520
Raquel Peat

DATE	IND NO.	NDA NO.	TYPE OF DOCUMENT	DATE OF DOCUMENT
December 30,2002		21-572	New NDA	20 December 2002

NAME OF DRUG	PRIORITY CONSIDERATION	CLASSIFICATION OF DRUG	DESIRED COMPLETION DATE
Cidecin®		cyclic lipopeptide	ASAP

NAME OF FIRM: Cubist Pharmaceuticals, Inc.

REASON FOR REQUEST

I. GENERAL

- ☐ NEW PROTOCOL
- ☐ PROGRESS REPORT
- ☐ NEW CORRESPONDENCE
- ☐ DRUG ADVERTISING
- ☐ ADVERSE REACTION REPORT
- ☐ MANUFACTURING CHANGE/ADDITION
- ☐ MEETING PLANNED BY
- ☐ PRE-NDA MEETING
- ☐ END OF PHASE II MEETING
- ☐ RESUBMISSION
- ☐ SAFETY/EFFICACY
- ☐ PAPER NDA
- ☐ CONTROL SUPPLEMENT
- ☐ RESPONSE TO DEFICIENCY LETTER
- ☐ FINAL PRINTED LABELING
- ☐ LABELING REVISION
- ☐ ORIGINAL NEW CORRESPONDENCE
- ☐ FORMULATIVE REVIEW
- X OTHER *(SPECIFY BELOW)*:

II. BIOMETRICS

STATISTICAL EVALUATION BRANCH	STATISTICAL APPLICATION BRANCH
☐ TYPE A OR B NDA REVIEW ☐ END OF PHASE II MEETING ☐ CONTROLLED STUDIES ☐ PROTOCOL REVIEW ☐ OTHER (SPECIFY BELOW):	☐ CHEMISTRY REVIEW ☐ PHARMACOLOGY ☐ BIOPHARMACEUTICS ☐ OTHER (SPECIFY BELOW):

III. BIOPHARMACEUTICS

- ☐ DISSOLUTION
- ☐ BIOAVAILABILTY STUDIES
- ☐ PHASE IV STUDIES
- ☐ DEFICIENCY LETTER RESPONSE
- ☐ PROTOCOL-BIOPHARMACEUTICS
- ☐ IN-VIVO WAIVER REQUEST

IV. DRUG EXPERIENCE

- ☐ PHASE IV SURVEILLANCE/EPIDEMIOLOGY PROTOCOL
- ☐ DRUG USE e.g. POPULATION EXPOSURE, ASSOCIATED DIAGNOSES
- ☐ CASE REPORTS OF SPECIFIC REACTIONS (List below)
- ☐ COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP
- ☐ REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY
- ☐ SUMMARY OF ADVERSE EXPERIENCE
- ☐ POISON RISK ANALYSIS

V. SCIENTIFIC INVESTIGATIONS

- ☐ CLINICAL
- ☐ PRECLINICAL

COMMENTS/SPECIAL INSTRUCTIONS:

Trade Name Review- This is an EDR submission-- http://edr/.

SIGNATURE OF REQUESTER	METHOD OF DELIVERY (Check one)
R. Peat and E. DuvallMiller	X MAIL ☐ HAND
SIGNATURE OF RECEIVER	SIGNATURE OF DELIVERER

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/s/

Beth Duvall-Miller
1/2/03 10:17:42 AM
BDM acting for FVL

FAX

Pfizer Inc
1700 Rockville Pike, Suite 500
Rockville, MD 20852
tel 301-231-5548
fax 301-231-5576
sharon.olmstead@pharmacia.com
www.pfizer.com

Date: June 17, 2003

To: Janice Soreth, MD
Fax Number: 301-827-2326
From: Sharon Olmstead

cc: Sammie Beam for Jerry Phillips
Fax Number: 301-443-9664

Pages: 11 (including cover sheet)

APPEARS THIS WAY
ON ORIGINAL

Ronald J. Garutti, MD
Vice President
Worldwide Regulatory Affairs
100 Route 206 North
Peapack, NJ 07977

June 17, 2003

Janice Soreth, MD
Director, Division of Anti-Infective Drug Products (HFD-520)
Center for Drug Evaluation and Research
Food and Drug Administration
9201 Corporate Blvd.
Rockville, MD 20850

Dear Dr. Soreth:

We would like to bring to your immediate attention a situation that could result in potentially serious medication errors due to a sound-alike/look-alike trademark under consideration in your division.

As reported in the press on February 20, 2003, FDA accepted for priority review the new drug application, CIDECIN (daptomycin) for the treatment of complicated skin infections, with an action date of June 20, 2003. Our concern stems from the similarity in sound and appearance of CIDECIN to our trademark CLEOCIN (clindamycin), an antibacterial agent approved for the treatment of serious infections caused by susceptible anaerobic infections and serious infections due to susceptible strains of streptococci, pneumococci, and staphylococci.

As an antibacterial agent, CLEOCIN labeling contains a black box warning for pseudomembranous colitis ranging in severity from mild to life threatening. The seriousness of this potential adverse event coupled with the severity of illness for our approved patient population lead us to enlist — — to conduct a special evaluation of the error potential of the name pair CIDECIN and CLEOCIN. The report confirmed our initial concerns for potential medication error problems.

As you will see from the attached electronic report, — expert group agreed with the opinion of 42 respondents regarding the high potential for confusing these two products, which may lead to medication errors. This is of particular concern given the overlapping indication of serious skin infections being sought for approval as well as those under development. Additionally, the similarity in medical specialty of infectious disease health professionals; the distribution of the products within the hospital setting; and the intravenous route of administration all contribute to the complexity for potential medication errors with these two products.

We welcome the opportunity to discuss these matters with you and the Division of Medication Errors and Technical Support.

Sincerely,

Sharon Olmstead

for Ronald J. Garutti, MD
Vice President
Worldwide Regulatory Affairs

Attachment

cc: Jerry Phillips, DMETS

Redacted 9

pages of trade

secret and/or

confidential

commercial

information

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

Form Approved: OMB No. 0910-0297
Expiration Date: February 29, 2004.

USER FEE COVER SHEET

See Instructions on Reverse Side Before Completing This Form

A completed form must be signed and accompany each new drug or biologic product application and each new supplement. See exceptions on the reverse side. If payment is sent by U.S. mail or courier, please include a copy of this completed form with payment. Payment instructions and fee rates can be found on CDER's website: http://www.fda.gov/cder/pdufa/default.htm

1. APPLICANT'S NAME AND ADDRESS

Cubist Pharmaceuticals, Inc
65 Hayden Avenue
Lexington, Massachusetts 02421

2. TELEPHONE NUMBER *(Include Area Code)*

(781) 860-8605

3. PRODUCT NAME

Daptomycin

4. BLA SUBMISSION TRACKING NUMBER (STN) / NDA NUMBER

N21-572

5. DOES THIS APPLICATION REQUIRE CLINICAL DATA FOR APPROVAL?

☒ YES ☐ NO

IF YOUR RESPONSE IS "NO" AND THIS IS FOR A SUPPLEMENT, STOP HERE AND SIGN THIS FORM.

IF RESPONSE IS "YES", CHECK THE APPROPRIATE RESPONSE BELOW:

☒ THE REQUIRED CLINICAL DATA ARE CONTAINED IN THE APPLICATION.

☐ THE REQUIRED CLINICAL DATA ARE SUBMITTED BY REFERENCE TO:

_____
(APPLICATION NO. CONTAINING THE DATA).

6. USER FEE I.D. NUMBER

4484

7. IS THIS APPLICATION COVERED BY ANY OF THE FOLLOWING USER FEE EXCLUSIONS? IF SO, CHECK THE APPLICABLE EXCLUSION.

☐ A LARGE VOLUME PARENTERAL DRUG PRODUCT APPROVED UNDER SECTION 505 OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT BEFORE 9/1/92
(Self Explanatory)

☐ A 505(b)(2) APPLICATION THAT DOES NOT REQUIRE A FEE
(See item 7, reverse side before checking box.)

☐ THE APPLICATION QUALIFIES FOR THE ORPHAN EXCEPTION UNDER SECTION 736(a)(1)(E) of the Federal Food, Drug, and Cosmetic Act
(See item 7, reverse side before checking box.)

☐ THE APPLICATION IS A PEDIATRIC SUPPLEMENT THAT QUALIFIES FOR THE EXCEPTION UNDER SECTION 736(a)(1)(F) of the Federal Food, Drug, and Cosmetic Act
(See item 7, reverse side before checking box.)

☐ THE APPLICATION IS SUBMITTED BY A STATE OR FEDERAL GOVERNMENT ENTITY FOR A DRUG THAT IS NOT DISTRIBUTED COMMERCIALLY
(Self Explanatory)

8. HAS A WAIVER OF AN APPLICATION FEE BEEN GRANTED FOR THIS APPLICATION?

☐ YES ☒ NO

(See item 8, reverse side if answered YES)

Public reporting burden for this collection of information is estimated to average 30 minutes 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:

Department of Health and Human Services
Food and Drug Administration
CBER, HFM-99
1401 Rockville Pike
Rockville, MD 20852-1448

and

Food and Drug Administration
CDER, HFD-94
12420 Parklawn Drive, Room 3046
Rockville, MD 20852

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SIGNATURE OF AUTHORIZED COMPANY REPRESENTATIVE	TITLE	DATE
	President & Chief Operating Officer	12/13/02

FORM FDA 3397 (4/01)

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Drug Evaluation IV

FACSIMILE TRANSMITTAL SHEET

DATE: March 14, 2003

To: David Schubert Vice President, Regulatory Affairs and Quality	**From:** LTJG Raquel Peat, Regulatory Health Project Manager
Company: Cubist Pharmaceuticals	Division of Division of Anti-Infective Drug Products
Fax number: 781-860-1408	**Fax number:** 301-827-2325
Phone number: 781-860-8455	**Phone number:** (301) 827-2125

Subject: NDA 21-572

Total no. of pages including cover: 4

Comments:

Information Request. Please respond either electronically or hard copy.

Document to be mailed: ☐ YES ☑ NO