Approval Package for:

APPLICATION NUMBER:
ANDA 63-014

Name: Penicillin G Sodium for Injection, USP

Sponsor: Marsam Pharmaceuticals, Inc.

Approval Date: September 13, 1988
## CENTER FOR DRUG EVALUATION AND RESEARCH

**APPLICATION NUMBER:**
ANDA 63-014

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APPLICATION NUMBER:
ANDA 63-014

APPROVAL LETTER
Our Reference: 63-014

Marsam Pharmaceuticals, Inc.
Attention: Howard C. Zell, Ph.D.
Building 31, Olney Avenue
P.O. Box 1022
Cherry Hill, N.J. 08034

Dear Dr. Zell:

Reference is made to your Abbreviated Antibiotic Drug Application for
Penicillin G Sodium for Injection, U.S.P.

Please also refer to your additional submission dated September 2, 1988.

We have completed our review of the application and it is approved.

An expiration date of twenty-four (24) months should be used on each batch of
the drug to be manufactured and packaged as described in the application.

Place drug samples from the first three production batches into your stability
program and test each batch at three (3) month intervals during the first year
of aging, at six (6) month intervals during the second year, annually
thereafter. As the data become available they should be furnished to this
office at six (6) month intervals throughout the authorized shelf life of the
subject drug.

For Initial Campaigns: We request that you submit, in duplicate, any proposed
advertising or promotional copy which you intend to use in your immediate
advertising or promotional campaigns. Please submit all proposed materials in
draft or mock-up form, not final printed. Submit both copies together with a
copy of the proposed or final printed labeling to the Division of Drug
Advertising and Labeling (HFD-240). Also, please do not use Form FD-2253 for
this submission.

For Subsequent Campaigns: We call your attention to regulation 21 CFR
314.81(b)(3) which requires that all material for any subsequent advertising
or promotional campaigns at the time of their initial use be submitted to our
Division of Drug Advertising and Labeling (HFD-240) with a completed Form
2253. A copy of Form FD-2253 is enclosed for your convenience.
Please be reminded that since you are manufacturing the subject drug for the first time, that 21 CFR 314.81 requires that certain records and reports be submitted following approval of the application.

The application should be kept up to date by submitting supplements whenever changes are contemplated in the manufacturing and/or laboratory procedures, controls, packaging, labeling, source of antibiotics, etc.

Sincerely yours,

Marvin Seife, M.D.
Director
Division of Generic Drugs
Office of Drug Standards
Center for Drugs and Biologics

HFD-235
HFD-235/OD
HFD-83
R/D JSinger 9/3/88
R/D init JHarrison 9/3/88
HFD-230/Dr. Seife 9/13/88
9-11-88 bcw 5084d
CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:
ANDA 63-014

LABELING
**SQUIBB Marsam**

1 box • 10 vials  
NDC 0003-0668-05

5,000,000 units per vial  
PENICILLIN G SODIUM  
for INJECTION USP

Caution: Federal law prohibits dispensing without prescription

---

**PENICILLIN G SODIUM** for INJECTION USP

Each vial provides 5,000,000 units penicillin G sodium with approx.
140 mg citrate buffer (composed of sodium citrate and not more than
4.6 mg citric acid). One million units penicillin contains approx.
2.0 mEq sodium.

Sterile • For Intramuscular or Intravenous drip use

**PREPARATION OF SOLUTION:** Add 23 mL, 18 mL, 8 mL, or 3 mL
diluent to provide 200,000 u, 250,000 u, 500,000 u, or 1,000,000 u
per mL, respectively.

Sterile solution may be kept in refrigerator 1 week without significant
loss of potency.

Store at room temperature prior to constitution

© 1986 Squibb-Marsam, Inc.

Mfd. for Squibb-Marsam, Inc., Cherry Hill, NJ 08034

by Marsam Pharmaceuticals Inc.
Cherry Hill, NJ 08034

C5347 66805
CAUTION: Federal law prohibits dispensing without prescription.

PENICILLIN G SODIUM FOR INJECTION USP

DESCRIPTION
Penicillin G Sodium for Injection is crystalline penicillin G sodium as a sterile powder. The preparation contains approximately 28 mg citrate buffer (composed of sodium citrate and not more than 0.92 mg citric acid) and 2.0 mEq sodium per million units of penicillin.

CLINICAL PHARMACOLOGY
Penicillin G is bactericidal against penicillin-susceptible microorganisms during the stage of active multiplication. It acts by inhibiting biosynthesis of cell-wall mucopeptide. It is not active against the penicillinase-producing bacteria, which include many strains of staphylococci. Penicillin G is highly active in vitro against staphylococci (except penicillinase-producing strains), streptococci (groups A, C, G, H, L, and M) and pneumococci. Other organisms susceptible in vitro to penicillin G are N. gonorrhoeae, Corynebacterium diptheriae, Bacillus anthracis, Clostridium, Actinomyces bovis, Streptobacillus moniliformis, Listeria monocytogenes, and Leptospira; Treponema pallidum is extremely susceptible. Some species of gram-negative bacilli are susceptible to moderate to high concentrations of penicillin G obtained with intravenous administration. These include most strains of Escherichia coli; all strains of Proteus mirabilis, Salmonella, and Shigella; and some strains of Enterobacter aerogenes (formerly Aerobacter aerogenes) and Alcaligenes faecalis.

Susceptibility plate testing: If the Kirby-Bauer method of disc susceptibility is used, a 10 u penicillin disc should give a zone greater than 28 mm when tested against a penicillin-susceptible bacterial strain.

Aqueous penicillin G is rapidly absorbed following both intramuscular and subcutaneous injection. Approximately 60 percent of the total dose of 300,000 u is excreted in the urine within this five-hour period. Therefore, high and frequent doses are required to maintain the elevated serum levels desirable in treating certain severe infections in individuals with normal kidney function. In neonates and young infants and in individuals with impaired kidney function, excretion is considerably delayed.

INDICATIONS AND USAGE
Penicillin G Sodium for Injection is indicated in the treatment of severe infections caused by penicillin G-susceptible microorganisms when rapid and high penicillinemia is required. Therapy should be guided by bacteriological studies, including susceptibility tests, and by clinical response.

The following infections will usually respond to adequate dosage:
Streptococcal infections. Note: streptococci in groups A, C, G, H, L, and M are very susceptible to penicillin G. Some group D organisms are susceptible to the high serum levels obtained with aqueous penicillin G. Aqueous penicillin G sodium is the penicillin dosage form of...
choice for bacteremia, empyema, severe pneumonia, pericarditis, endocarditis, meningitis, and other severe infections caused by susceptible strains of the gram-positive species listed above.

Pneumococcal Infections; Staphylococcal Infections—penicillin G-susceptible; Anthrax; Actinomycosis; Clostridial Infections (including tetanus); Diphtheria (to prevent the carrier state); Erysipelasoid endocarditis (Erysipelothrix rhusiopathiae); Vincent's gingivitis and pharyngitis (fusospirochetal); Severe infections of the oropharynx (Note: necessary dental care should be accomplished in infections involving gum tissue) and lower respiratory tract and genital area infections due to F. nucleatum spirochetes; Gram-negative bacillary Infections (bacteremias)—(E. coli, E. aerogenes, A. falcogenes, Salmonella, Shigella and P. mirabilis); Listeria Infections (L. monocytogenes); Meningitis and endocarditis; Pasteurella Infections (P. multocida); Bacteremia and meningitis; Rat-bite fever (S. minus or S. moniliformis); Gonococcal endocarditis and arthritis (N. gonorrhoeae); Syphilis (T. pallidum) including congenital syphilis; Meningococcal meningitis.

Prevention of bacterial endocarditis (Patients unable to take oral antibiotics)—Although no controlled clinical efficacy studies have been conducted, aqueous crystalline penicillin G for injection (except penicillin G procaine suspension) has been suggested by the American Heart Association and the American Dental Association for prophylaxis against bacterial endocarditis in patients with congenital heart disease or rheumatic or other acquired valvular heart disease when they undergo dental procedures and surgical procedures of the upper respiratory tract. Since it may happen that alpha hemolytic streptococci relatively resistant to penicillin may be found when patients are receiving continuous oral penicillin for secondary prevention of rheumatic fever, prophylactic agents other than penicillin may be chosen for these patients and prescribed in addition to their continuous rheumatic fever prophylactic regimen. NOTE: When selecting antibiotics for the prevention of bacterial endocarditis the physician or dentist should read the full Joint statement of the American Heart Association and the American Dental Association.¹

CONTRAINDICATIONS
Contraindicated in patients with a history of hypersensitivity to any penicillin.

WARNINGS
Serious and occasional fatal hypersensitivity (anaphylactoid) reactions have been reported in patients on penicillin therapy. Although anaphylaxis is more frequent following parenteral administration, it has occurred in patients on oral penicillins. These reactions are more apt to occur in individuals with a history of sensitivity to multiple allergens.

There have been well-documented reports of individuals with a history of penicillin hypersensitivity who have experienced severe hypersensitivity reactions when treated with cephalosporins. Before therapy with a penicillin, careful inquiry should be made concerning previous hypersensitivity reactions to penicillins, cephalosporins, and other allergens. If an allergic reaction occurs, the drug should be discontinued and the patient treated with the usual agents, e.g., pressor amines, antihistamines, and corticosteroids. Serious anaphylactoid reactions are not controlled by antihistamines alone, and require such emergency measures as the immediate use of epinephrine, aminophylline, oxygen, and Intravenous corticosteroids.

PRECAUTIONS
Penicillin should be used with caution in individuals with histories of significant allergies and/or asthma.

In prolonged therapy with penicillin and particularly with high dosage schedules, periodic evaluation of the renal and hematopoietic systems is recommended.

In streptococcal infections, therapy must be sufficient to eliminate the organism (10 days minimum); otherwise the sequelae of streptococcal disease may occur. Cultures should be taken following the completion of
treatment to determine whether streptococci have been eradicated.

In high doses (above 10 million u), Intravenous aqueous penicillin G sodium should be administered slowly because of the adverse effects of electrolyte imbalance from the sodium content of the penicillin. The patient's renal, cardiac and vascular status should be evaluated and if impairment of function is suspected or known to exist, a reduction in the total dosage should be considered. Frequent evaluation of electrolyte balance, and renal and hematopoietic function is recommended during therapy when high doses of Intravenous aqueous penicillin G sodium are used.

Prolonged use of antibiotics may promote overgrowth of nonsusceptible organisms, including fungi. Should superinfection occur, appropriate measures should be taken. Indwelling intravenous catheters encourage superinfections and should be avoided whenever possible.

Therapy of susceptible infections should be accompanied by any indicated surgical procedures. In suspected staphylococcal infections, proper laboratory studies, including susceptibility tests, should be performed.

When treating gonococcal infections in which primary or secondary syphilis may be suspected, proper diagnostic procedures, including darkfield examinations, should be done. In all cases in which concomitant syphilis is suspected, monthly serological tests should be made for at least four months. All cases of penicillin-treated syphilis should receive clinical and serological examinations every six months for at least two or three years.

Any entry into the container to effect solution of the powder or withdrawal of contents must be accomplished with strict aseptic technique and sterile equipment.

ADVERSE REACTIONS

Penicillin is a substance of low toxicity but does possess a significant index of sensitization.

The hypersensitivity reactions reported are skin rash-E ranging from maculopapular eruptions to exfoliative dermatitis, urticaria; and serum sickness-like reactions including chills, fever, edema, arthralgia, and prostration. Severe and occasionally fatal anaphylaxis has occurred (see WARNINGS).

Hemolytic anemia, leukopenia, thrombocytopenia, neuropathy, and nephropathy are rarely observed adverse reactions and are usually associated with high intravenous dosage. Urticaria, other skin rashes, and serum sickness-like reactions may be controlled by antihistamines and, if necessary, corticosteroids. Whenever such reactions occur, penicillin should be discontinued unless, in the opinion of the physician, the condition being treated is life-threatening and amenable only to penicillin therapy. High dosage of penicillin G sodium may result in congestive heart failure due to high sodium intake.

The Jarisch-Herxheimer reaction has been reported in patients treated for syphilis.

DOSEAGE AND ADMINISTRATION

Penicillin G Sodium for Injection may be given intramuscularly or by continuous intravenous drip.

The usual dosage recommendation is as follows:

Severe infections due to susceptible strains of streptococci, pneumococci, and staphylococci: 200,000 to 400,000 units every 4 hours.

Diphtheria—adjunctive therapy to antitoxin: 20,000 units/10 kg of body weight daily.

Anthrax: a minimum of 5 million units of penicillin G sodium daily for five to seven days after the last dose of a primary anthrax vaccine.

Clostridial infections (as adjunctive therapy to antitoxin): 20 million units/10 kg of body weight daily.

Fusobacterium and Bacteroides infections: 50 million units/10 kg of body weight daily.

The usual dosage is 10 million units every 4 hours, given intravenously or intramuscularly.

The Jarisch-Herxheimer reaction has been reported in patients treated for syphilis.
Preparation of Solutions
Solutions of penicillin should be prepared as follows:
Loseen powder: Hold vial horizontally and rotate it while
slowly directing the stream of diluent against the wall of
the vial. Shake vial vigorously after all the diluent has
been added. Depending on the route of administration,
use Sterile Water for Injection USP, Isotonic Sodium
Chloride Injection USP, or Dextrose Injection USP. NOTE:
Penicillins are rapidly inactivated in the presence of car-
bohydrate solutions at alkaline pH.
Reconstitute with 23 mL, 18 mL, 8 mL, or 3 mL diluent
to provide concentrations of 200,000 u, 250,000 u, 500,000
u, or 1,000,000 u per mL, respectively.

HOW SUPPLIED
Penicillin G Sodium for Injection USP is available in vials
providing 5 million u of crystalline penicillin G sodium.

Storage
The dry powder is relatively stable and may be stored at
room temperature without significant loss of potency.
Sterile solutions may be kept in the refrigerator one week
without significant loss of potency. Solutions prepared
for Intravenous infusion are stable at room temperature
for at least 24 hours.

REFERENCE
1. American Heart Association: Prevention of bacterial
Penicillin G Sodium for Injection, U.S.P.
Marsam Pharmaceuticals Inc.

Material Reviewed:  A-002 dated September 2, 1988
Exhibit Sample Testing Results dated August 30, 1988

1. Final Printed Labeling – satisfactory.

Recommendation – The application may be approved.

John M. Singer
Penicillin G Sodium for Injection, U.S.P.
Marsam Pharmaceuticals Inc.

Material Reviewed: A-001 dated June 23, 1988
A-002 dated July 8, 1988

Applicant's submissions respond to our not approvable letter dated June 29, 1988.

1. Stability Data - satisfactory.

   The applicant has submitted room temperature and accelerated stability data from three batches of drug product (#8803007, #8803008 and #8803009) stored in the market container/closure system for three months. Assays are satisfactory.

   Expiration Dating Period - 24 months.

2. Explanation for the following filling operation terms: [Redacted]

   Satisfactory.

3. Precautions to insure sterility operations - satisfactory.

4. Final Printed Labeling - to be submitted at a later date.

Recommendation - the application remains not approvable due to #4.

John M. Singer
Manufacturing and Control Review

Abbreviated Antibiotic Drug Application #63-014

Date of Application: May 24, 1988
Date of Receipt: May 27, 1988

Applicant: Marsam Pharmaceuticals, Inc.
Building 31
Olney Ave.
P.O. Box 1022
Cherry Hill, N.J. 08034

Product: Penicillin G Sodium for Injection

Product is eligible for marketing when it meets the specifications prescribed by 21 CFR 440.281b.

1/2 Components/Composition:

<table>
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<tr>
<th>Sterile Penicillin G Sodium, U.S.P.</th>
<th>UNITS PER VIAL</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>5,000,000</td>
</tr>
</tbody>
</table>

Applicant obtains Sterile Penicillin G Sodium, U.S.P. from the following FDA approved sources:

1)

2)

3. Manufacturing process:

A. Manufacturing facility location

Marsam Pharmaceuticals Inc.
Building 31
Olney Ave.
P.O. Box 1022
Cherry Hill, N.J. 08034

B. Raw material controls - satisfactory. The applicant performs adequate testing of the active ingredient. It meets the specifications listed in 21 CFR 440.1081a.

C. Description of facility and equipment - Satisfactory.
D. Personnel - Satisfactory.

E. Description of Batch numbering system - Satisfactory.

F. Filling Instructions - satisfactory.
   Description of filling equipment - satisfactory.

G. Master formula record - satisfactory.
   5 mm units/50 mL ____________________________ vials
   (b)(4) (b)(4)

H. Batch records - satisfactory.
   The applicant has submitted the following batch records:
   #8803007 ____________________________ vials
   (b)(4)
   #8803008 ____________________________ vials
   (b)(4)
   #8803009 ____________________________ vials
   (b)(4)

I. Sterility Control - Unsatisfactory. The applicant did not contain precautions to insure the sterility of the drug product ____________________________ Other controls are satisfactory.
   (b)(4)

4. Quality Control:

A. Analytical Procedures - satisfactory.

B. Standards for acceptance of each lot of the finished drug - satisfactory.
   The standards are the same as those listed in 21 CFR 440.281b and the USP.

C. Container/closure system - satisfactory.
   The applicant proposes to use 50 mL Type II fling vials. They are manufactured by ____________________________ The stopper is a 20 mm gray stopper manufactured by the ____________________________ The vial seal is made of aluminum with a flip-off button. It is manufactured by ____________________________
   Container Closure controls - satisfactory.

D. Stability testing protocol - satisfactory
   Stability commitment - satisfactory.
   Stability data - Unsatisfactory.
The applicant has submitted room temperature and accelerated stability data from three batches of drug product (lots #8803007, #8803008 and #8803009) stored in the 50 mL container/closure system for one month.

Review is deferred pending receipt of three month data.

Reconstitution study data - satisfactory.

E. Expiration Dating Period - Applicant requests 24 months. We cannot set an expiration dating period due to the lack of and data.

F. Labeling - satisfactory. The applicant has revised approved labeling from #60-363.

G. The drug product is Rx.

H. Bioavailability - not required since the drug product is administered IM or IV.

I. Consulting laboratory: (b)(4)

J. Exhibit Samples - sent to FDA laboratory on June 8, 1988.

Recommendation - the application is not approvable at this time due to the following deficiencies:

1. The application did not contain room temperature and accelerated stability data from three batches of drug product stored in the container/closure system for three months (assays at 0, 1, 2 and 3 months).

2. The application did not adequately explain the following terms under (b)(4)

3. The application did not contain a description of the precautions to insure the sterility of the drug product (b)(4) operations.

John M. Singer
John M. Singer
APPLICATION NUMBER:
ANDA 63-014

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS
NOTICE OF APPROVAL
NEW DRUG APPLICATION OR SUPPLEMENT

TO:  Press Relations Staff (HPA-40)

FROM:  Bureau of Drugs

ATTENTION
Forward original of this form for publication only after approval letter has been issued and the date of approval has been entered above.

TYPE OF APPLICATION
☑ ORIGINAL NDA  ☐ SUPPLEMENT TO NDA  ☐ ABBREVIATED ORIGINAL NDA  ☐ SUPPLEMENT TO ANDA

CATEGORY
☑ HUMAN  ☐ VETERINARY

TRADE NAME (or other designated name) AND ESTABLISHED OR NONPROPRIETARY NAME (if any) OF DRUG
Penicillin G Sodium

DOSAGE FORM
for injection

HOW DISPENSED
Rx
☐ OTC

ACTIVE INGREDIENT(S) (as declared on label. List by established or nonproprietary name(s) and include amount(s), if amount is declared on label.)
Penicillin G sodium 5,000,000 units

NAME OF APPLICANT (Include City and State)
Monsanto Pharmaceuticals Inc.
Building 31, Alhambra Ave.
P.O. Box 1522
Cherry Hill, N. J. 08034

PRINCIPAL INDICATION OR PHARMACOLOGICAL CATEGORY
Antibiotic

COMPLETE FOR VETERINARY ONLY

ANIMAL SPECIES FOR WHICH APPROVED

COMPLETE FOR SUPPLEMENT ONLY

CHANGE APPROVED TO PROVIDE FOR

FORM PREPARED BY

DATE 9/9/68

FORM APPROVED BY

DATE 9/13/68

FORM FD 15-2 (2/75) PREVIOUS EDITION MAY BE USED UNTIL SUPPLY IS EXHAUSTED.
Memorandum

Date: August 30, 1988

From: Chief, Antimicrobial Drugs Branch
       HFD-473

Subject: Forms 62-991 and 63-014; Penicillin G Potassium and Penicillin G Sodium for Injection, USP; Marsam Pharmaceuticals Inc.

To: John M. Singer
    HFD-235

These two applications are reported jointly here because of the many common elements within them: the products differ only in the metal ion form and the variety of dosage levels.

These applications adequately describe the composition of these products. The raw materials for each are obtained from FDA approved sources as adequate raw materials controls appear to be operative. The manufacturing process is essentially the same for potassium penicillin and sodium penicillin. The compendial testing of the finished product and material is all performed by in-house Marsam personnel except for the pyrogens tests. There are no outstanding comments of the finished product.

The batch numbers for commercial batches of these products are seven digit numbers in which: A letter and a hyphenated digit suffix are used as required to indicate separate production runs of this type. Products that carry the Squibb-Marsam labeling encode the same information alphanumerically.

Adequate protocols for accelerated (37-400C/75% RH) and long term (RT) stability studies are described. Summaries of test results up through one month's storage under both conditions in the market packages were submitted for three batches of each product. These data are insufficient to justify the 24 month expiry period requested for these products. Presumably, additional data have been submitted to you.

ADB received exhibit samples from the same batches used in the stability studies. All of these batches were manufactured in February and March 1988 and were therefore about 5-6 months old at the time of ADB's tests and assays. Each batch of the Pen G K product was manufactured from a separate batch 8803007 and 8803008 of the Pen G Na product were made from The manufacture of each of these batches was completed on separate
days. There was no indication of maximum batch sizes, but since no 

is involved, ADB is not greatly concerned over their size 
since the most likely manufacturing 

batches. The samples were 

examined for conformance to USP XXI and CFR physicochemical 

specifications. All of the test results are satisfactory and the 

individual assay values are in close agreement. All except one of ADB's 

averaged potency values are lower than Marmam's and lower than the claimed 

formulation. These data are tabulated in the attached Chemistry 

Review Notes.

ADB finds these application to be incomplete on account of their 

insufficient stability data. These applications are satisfactory 

otherwise and ADB would concur in their approval provided that 
satisfactory additional stability data have been received.

Joseph H. Graham, Ph.D.

co: HFD-470 (Overpeck)
    HFD-473 (Chem. Sec.; R/P)
    HFD-333 (Geissel)

JHG/ymb
0208Y
RE: Form 62-991
Penicillin G Potassium for Injection, USP
Submitted by Marsam Pharmaceuticals Inc.

This applicant requests approval to market its generic penicillin G potassium for injection, USP in 4 different configurations (1,000,000 units/20ml vial, 5,000,000 units/50ml vial, 10,000,000 units/50ml vial, & 20,000,000 units/100ml vial).

The active ingredient, penicillin G potassium for injection, as raw material comes from (b)(4).

Raw materials, check tests on raw materials, manufacturing process, release tests on finished products, and stability study programs are adequately described. Stability data on exhibit samples are submitted. An expiry date of 24 months is proposed.

Three exhibit samples (M10580-M10582) submitted were tested and found to be within the limits specified in 21 CFR 440.280b & USP XXI. Test data from the company and FDA laborato ries are tabulated in Table I.

Number of tests = 27
Time spent = 20 hours

James R. Marsh
Review Chemist

Reviewed by
Thomas G. Alexander
Chief, Chemistry Section
<table>
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Chemistry Review Notes  
August 22, 1988

RE: Form 63-014  
Penicillin G Sodium for Injection, USP  
Submitted by Marsam Pharmaceuticals Inc.

This applicant requests approval to market its generic penicillin G sodium for injection, USP in one configuration (5,000,000 units/50 ml vial).

The active ingredient, penicillin G sodium for injection, as raw material comes from (0)(4).

Raw materials, check tests on raw materials, manufacturing process, release tests on finished products, and stability study programs are adequately described. Stability data on exhibit samples are submitted. An expiry date of 24 months is proposed.

Three exhibit samples (M10637-M10639) submitted were tested and found to be within the limits specified in 21 CFR 440.281b & USP XXI. Test data from the company and FDA laboratories are tabulated in Table I.

Number of tests = 27  
Time spent = 19 hours

Reviewed by:  
Thomas G. Alexander  
Chief, Chemistry Section

James R. Marsh  
Review Chemist

**Table I: Test Data on Penicillin G Sodium for Injection, USP  
(Form 63-014)**

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</tr>
<tr>
<td>Potency (Iodom)</td>
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<tr>
<td>90-120% LC</td>
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<tr>
<td>Avg. % LC</td>
<td>111.2</td>
<td>101.9</td>
<td>113.5</td>
</tr>
</tbody>
</table>
Our Reference: 63-014

Warren Pharmaceuticals, Inc.
Attention: Judith U. Arnoff, R.Ph.
Building 31, Olney Ave
P.O. Box 1022
Cherry Hill, N.J. 08034

Gentlemen:

Please refer to your Abbreviated Antibiotic Drug Application for Penicillin G Sodium for Injection, USP, and to your additional submissions dated June 23 and July 8, 1988.

We have completed our review of the submissions and conclude that the application remains not approvable since final printed labeling has not been submitted and exhibit sample testing has not been completed.

Please submit final printed labeling when available.

          Sincerely yours,


                                       John M. Singer
                                       Antibiotic Drug Review Branch
                                       Division of Generic Drugs

---HFD-235---
HFD-235/00
R/D JSinger
R/D init JHarrison
HFD-230/Dr. Seife
7-15-88 bcw 4807d
Marsam Pharmaceuticals, Inc.
Attention: Judith U. Arnoff, R.Ph.
Building 31, Olney Avenue
P.O. Box 1022
Cherry Hill, N.J. 08034

Gentlemen:

Please refer to you Abbreviated Antibiotic Drug Application dated May 24, 1988 for Sterile Penicillin G Sodium for Injection, U.S.P.

We have completed our review of the submission and conclude that the application is not approvable due to the following deficiencies:

1. The application did not contain room temperature and accelerated stability data from three batches of drug product stored in the container/closure system for three months (assays at 0, 1, 2 and 3 months).

2. The application did not adequately explain the following terms under (a)(4).

3. The application did not contain a description of the precautions to insure the sterility of the drug product under (a)(4) operations.

Please submit 6 copies of final printed labeling that are identical in content and format to the draft labeling.

Sincerely yours,

John M. Singer
Antibiotic Drug Review Branch
Division of Generic Drugs

HFD-235
HFD-235/DD
R/D JSinger
R/D init JP
HFD-230/Dr. Seife
6-27-88 bcw 4744d
June 8, 1988
Chemist, HFD-235

Abbreviated Antibiotic Drug Application 63-014

Director, Antimicrobial Drug Branch, HFD-473

Marsam Pharmaceuticals, Inc. has submitted an Abbreviated Antibiotic Drug Application for Penicillin G Sodium for Injection, U.S.P. Please perform the required compendial tests.

The following are being forwarded with this memo:

1. Duplicate copy of the applicant.
2. Samples with Certificates of Analysis for three batches.

If there are any questions, I may be reached at 443-4340.

John M. Singer

HFD-235/0D
R/D JSinger 6/8/88
HFD-230/Dr. Seife
6/8/88 bcw 4659d