CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

63-165/s-3,s-5,s-6

CHEMISTRY REVIEW(S)

AADA 63-165/S-003, S-005, S-006

NAME AND ADDRESS OF APPLICANT:
Adria Laboratories
Attn: Frederick L. Grab, Ph.D.
P.O. Box 16529
Columbus, OH 43216-6529

PURPOSE OF AMENDMENT/SUPPLEMENT
The supplemental applications provide for:
S-003: for additional dosage strengths of 75 mg/vial and 100 mg/vial,
S-005: alternate use of a continuous processing vial preparation, filling, capping and rinsing manufacturing line,
S-006: labeling for the new fill sizes.

DATE(S) OF SUBMISSION(S)
March 28, 1991
May 23, 1991
May 11, 1993 (covered by this review)

PHARMACOLOGICAL CATEGORY
Antitumor Agent

TRADE NAME
Adriamycin PFS™

NONPROPRIETARY NAME
Doxorubicin Hydrochloride Injection USP

DOSAGE FORM
SVP (SVS)

POTENCY
2 mg/mL - 10, 20, 50, 75, 100, 200 mg/vial

RX OR OTC
℞

SAMPLES
N/A

RELATED IND/NDA/DMF
50-629
50-467
62-057
62-206

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Contain Trade Secret,

Commercial/Confidential

Information and are not

releasable.

Chem Review

6/9/93

AADA 63-165/S-003

NAME AND ADDRESS OF APPLICANT:
Adria Laboratories
Attn: Warren L. Meyers
P.O. Box 16529
Columbus, OH 43216-6529

PURPOSE OF AMENDMENT/SUPPLEMENT
The supplemental application provides for additional dosage strengths 75 mg/vial and 100 mg/vial.

DATE(S) OF SUBMISSION(S)
March 28, 1991

PHARMACOLOGICAL CATEGORY
Antitumor Agent

TRADE NAME
Adriamycin PFS™

NONPROPRIETARY NAME
Doxorubicin Hydrochloride Injection USP

DOSAGE FORM
SVP

POTENCY
2 mg/mL - 10, 20, 50, (75, 100 - proposed), 200 mg/vial

RX OR OTC
℞

SAMPLES
N/A

RELATED IND/NDA/DMF
50-629
50-467
62-057

STERILIZATION
N/A

LABELING

BIOEQUIVALENCY STATUS
N/A

ESTABLISHMENT INSPECTION
N/A

Page(s) 1

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Chem Review

Components / controls

5/22/92

Deficiency
Drug Master File references with accompanying authorization should be provided for all packaging components. Also included should be a listing of the components with the corresponding vendor commodity numbers, and page references to the DMFs to permit access to technical information contained therein. Also include the specification documentation for each packaging component.

STABILITY
No batches were manufactured and no stability was generated.
Deficiency
Please provide stability data and batch records from one lot of each proposed fill size (15 - 20% of the maximum proposed batch size).

REMARKS AND CONCLUSION

RECALLS | Reviewer: Eric P. Duffy | Date Completed

ORDER OF REVIEW
The application submission covered by this review was taken in the date order of receipt YES

1/22/92

AADA 63-165/S-005

NAME AND ADDRESS OF APPLICANT:
Adria Laboratories
Attn: Warren L. Meyers
P.O. Box 16529
Columbus, OH 43216-6529

PURPOSE OF AMENDMENT/SUPPLEMENT
The supplemental application provides for alternate use of a continuous processing vial preparation, filling, capping and rinsing manufacturing line.

DATE(S) OF SUBMISSION(S)
May 23, 1991

PHARMACOLOGICAL CATEGORY
Antitumor Agent

TRADE NAME
Adriamycin PFS™

NONPROPRIETARY NAME
Doxorubicin Hydrochloride Injection USP

DOSAGE FORM
SVP

POTENCY
2 mg/mL - 10, 20, 50, 200 mg/vial

RX OR OTC
℞

SAMPLES
N/A

RELATED IND/NDA/DMF

STERILIZATION
N/A ← validation reqd.

LABELING
N/A

BIOEQUIVALENCY STATUS
N/A

ESTABLISHMENT INSPECTION

Page(s) 1

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Chem Rev.

5/22/92

Mfg and Composition

The following deficiency comments should be communicated to the firm:

The application fails to contain major portions of required information, and therefore has not been comprehensively reviewed. We offer the following comments at the present time, and will offer comprehensive comment when all required information has been submitted.

1. Please provide a completed batch record, and stability data from a batch produced by the proposed alternate manufacturing process.

2. Validation of the proposed filling process should be provided.

3. Please revise your exhibit Master Batch Record to incorporate the maximum batch size.

3. Please describe any revisions to in-process control procedures.

RECOMMENDATION: NOT APPROVABLE - MAJOR

RECALLS	Reviewer	Date Completed
	Eric P. Duffy	

ORDER OF REVIEW
The application submission covered by this review was taken in the date order of receipt YES

cc:

ED. Duffy for JDH
1/22/92

AADA 63-165/S-004
NAME AND ADDRESS OF APPLICANT:
Adria Laboratories
Attn: Warren L. Meyers
P.O. Box 16529
Columbus, OH 43216-6529

PURPOSE OF AMENDMENT/SUPPLEMENT
The supplemental application provides for optional use of the facilities at Albuquerque, New Mexico (Adria SP, or Columbus, Ohio (Adria Laboratories) for testing, packaging, and labeling.

DATE(S) OF SUBMISSION(S)
May 23, 1991

PHARMACOLOGICAL CATEGORY
Antitumor Agent

TRADE NAME
Adriamycin PFS™

NONPROPRIETARY NAME
Doxorubicin Hydrochloride Injection USP

DOSAGE FORM
SVP

POTENCY
2 mg/mL - 10, 20, 50, 200 mg/vial

RX OR OTC
℞

SAMPLES
N/A

RELATED IND/NDA/DMF

STERILIZATION

LABELING

BIOEQUIVALENCY STATUS

ESTABLISHMENT INSPECTION
EER - pending (requested 5/20/92)

COMPONENTS

COMPOSITION

MANUFACTURING

CONTROLS

PACKAGING

STABILITY

REMARKS AND CONCLUSION
The firm is in the process of transfering all responsibilities for this product from Columbus OH to the manufacturing site at Albuquerque NM. This supplement provided for optional QC testing, labeling, and packaging at the Albuquerque NM facility. EER for the operations at the new facility is required.

RECOMMENDATION: APPROVABLE pending satisfactory EER acceptable 5/22/92

RECALLS

Reviewer
Eric P. Duffy

Date Completed

ORDER OF REVIEW
The application submission covered by this review was taken in the date order of receipt YES

cc:

5/20/92

AADA 63-165/S-007

NAME AND ADDRESS OF APPLICANT:
Adria Laboratories
Attn: Frederick L. Grab, Ph.D.
P.O. Box 16529
Columbus, OH 43216-6529

PURPOSE OF AMENDMENT/SUPPLEMENT
The supplemental application provides for a manufacturing rework procedure.

DATES OF SUBMISSIONS
November 3, 1992
April 29, 1993 - amendment

PHARMACOLOGICAL CATEGORY
Antitumor Antibiotic

TRADE NAME
Adriamycin PFS™

NONPROPRIETARY NAME
Doxorubicin Hydrochloride Injection USP

DOSAGE FORM
SVP

POTENCY
2 mg/mL - 10, 20, 50, 200 mg/vial

RX OR OTC
℞

SAMPLES
N/A

RELATED IND/NDA/DMF

STERILIZATION
N/A

LABELING
N/A

BIOEQUIVALENCY STATUS
N/A

ESTABLISHMENT INSPECTION
N/A

COMPONENTS
Same as approved.

COMPOSITION
Same as approved

MANUFACTURING
The supplement proposes establishing a general rework procedure for the following situations:

lot failure due to -

CONTROLS
N/A

PACKAGING
N/A

STABILITY
Stability data for the reworked Lot # DXD021 are provided:

6 months at 2° - 8° C - acceptable
[this is the recommended storage temperature]
3 months at 24° - 28° C
[94.6 % l.c. @ 3 mos/initial 106.4 % l.c.]
3 months at 33° - 37° C [60.7 % l.c. @ 3 mos]

MICROBIOLOGY
See review by KHMuhvich dated 5/11/93.

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Chem Review

Mfg process/sterility

RECOMMENDATION: APPROVAL

The following comment should be directed to the firm in the letter of approval: Please submit microbiological monitoring results from personnel in the rework area for the first production rework lot of the subject drug product. Samples should include fingertips and sleeves of gowns.

ORDER OF REVIEW
The application covered by this review was taken in date receipt order for review:

YES X NO

RECALLS	Reviewer	Date Completed
	Eric P. Duffy	

Endorsements: — DOV 1/18/93
193

AADA 63-165/S-007

NAME AND ADDRESS OF APPLICANT:
Adria Laboratories
Attn: Warren L. Meyers
P.O. Box 16529
Columbus, OH 43216-6529

PURPOSE OF AMENDMENT/SUPPLEMENT
The supplemental application provides for a manufacturing rework procedure.

DATE(S) OF SUBMISSION(S)
November 3, 1992

PHARMACOLOGICAL CATEGORY
Antitumor Antibiotic

TRADE NAME
Adriamycin PFS™

NONPROPRIETARY NAME
Doxorubicin Hydrochloride Injection USP

DOSAGE FORM
SVP

POTENCY
2 mg/mL - 10, 20, 50, 200 mg/vial

RX OR OTC
Rx

SAMPLES
N/A

RELATED IND/NDA/DMF
50-629
50-467
62-057

STERILIZATION
N/A

LABELING
N/A

BIOEQUIVALENCY STATUS
N/A

ESTABLISHMENT INSPECTION

COMPONENTS
Same as approved.

COMPOSITION
Same as approved

MANUFACTURING
The supplement proposes establishing a general rework procedure for the following situations:

lot failure due to -

Master batch records for the rework procedure are provided:

Instructions and records -

C

Page(s) 2

Contain Trade Secret, Commercial/Confidential Information and are not releasable.

Chem Rev.
Mfg / deficiencies
3/29/93

8. With respect to this rework procedure being applicable to lots where , you have not specified which would qualify a lot for rework and provided data that indicate that product degradation does not occur. In the absence of these data, or a demonstration batch the proposed rework procedure is not considered appropriate for rework due to .

9. Please provide any stability data available to date.

RECOMMENDATION: NOT APPROVABLE - MINOR

RECALLS	Reviewer	Date Completed
	Eric P. Duffy	

cc:

Endorsements: EDuffy 3/29/93

AADA 63-165/S-008

SPECIAL SUPPLEMENT - CHANGES BEING EFFECTED

NAME AND ADDRESS OF APPLICANT:
Adria Laboratories
Attn: Frederick L. Grab, Ph.D.
P.O. Box 16529
Columbus, OH 43216-6529

PURPOSE OF AMENDMENT/SUPPLEMENT
The supplemental application provides for change in the manufacturing process which calls for addition of Doxorubicin Hydrochloride USP to water for more ready dissolution.

DATES OF SUBMISSIONS
July 27, 1993

PHARMACOLOGICAL CATEGORY
Antitumor Antibiotic

TRADE NAME
Adriamycin PFS™

NONPROPRIETARY NAME
Doxorubicin Hydrochloride Injection USP

DOSAGE FORM
SVP

POTENCY
2 mg/mL - 10, 20, 50, 200 mg/vial

RX OR OTC
℞

SAMPLES
N/A

RELATED IND/NDA/DMF
50-629
50-467
62-057

STERILIZATION
N/A

LABELING
N/A

BIOEQUIVALENCY STATUS
N/A

ESTABLISHMENT INSPECTION
N/A

COMPONENTS
Same as approved.

COMPOSITION
Same as approved

MANUFACTURING

CONTROLS
N/A

PACKAGING
N/A

STABILITY
N/A

MICROBIOLOGY
N/A

REMARKS AND CONCLUSION
The revised process is acceptable.

RECOMMENDATION: APPROVAL

ORDER OF REVIEW
The application covered by this review was taken in date receipt order for review:

YES X NO

RECALLS	Reviewer	Date Completed
	Eric P. Duffy	

Endorsements:

7/93

FYI by mw/10/7/93