CENTER FOR DRUG EVALUATION AND RESEARCH

Application Number 21-007
21-039

ENVIRONMENTAL ASSESSMENT and/or FONSI

REVIEW

OF

ENVIRONMENTAL ASSESSMENT

FOR

NDA 21-007

Agenerase™ (amprenavir) Soft Gelatin Capsules

and

NDA 21-039

Agenerase™ (amprenavir) Oral Solution

Division of Antiviral Drug Products (HFD-530)

Center for Drug Evaluation and Research

Date Completed: January 7, 1999

SUMMARY

A FONSI is recommended.

Amprenavir is expected to enter predominantly into the aquatic environment. The material is not expected to adsorp strongly to soil or sediment. An aquatic EIC of — ppb is estimated based on the highest annual use estimate of — The concentration in the aquatic environment would be expected to be significantly lower than the EIC because of dilution. No rapid degradation mechanism has been identified, therefore the toxicity to environmental organisms has been assessed. There is > 1000 fold difference between the EC_{50} s for activated sludge respiration inhibition/daphnia magna — Based on this information adverse environmental impacts are not expected.

Organism/Test	EC_{50}	NOEC
Activated Sludge Respiration Inhibition (30 minutes & 3 hours)	> 1000 ppm	N/A
Daphnia magna (48 hrs)	> 51 ppm	51 ppm

ENVIRONMENTAL ASSESSMENT

1. **Date:**

EA dated: 6/18/1998 (NDA 21-007)
9/2/1998 (NDA 21-039)
1/5/99 (amendments)

CSO: Melissa Truffa

2. **Name of applicant/petitioner:**

Glaxo Wellcome Inc.

ADEQUATE

3. **Address:**

Five Moore Drive
Research Triangle Park, NC 27709

ADEQUATE

4. **Description of the proposed action:**

a. **Requested Approval:**

The applicant is requesting approval to market Amprenavir Soft Gelatin Capsules (50 mg and 150 mg) packaged in HDPE bottles and Amprenavir Oral Solution (15 mg/mL) in HDPE bottles.

ADEQUATE

b. **Need for Action:**

The product is indicated for the treatment of HIV infection.

ADEQUATE

c. **Expected Locations of Use (Drug Product):**

The drug product is expected to be used in hospitals, clinics and private residences throughout the United States.

ADEQUATE

d. **Disposal Locations:**

Disposal at hospitals/pharmacy/clinics will be in accordance with their procedures. A community's solid waste management system will typically be used for material disposed of from home use. Solid waste management systems may include landfills, incineration and recycling. Minimal quantities of the unused drug could be disposed of in the sewer system.

ADEQUATE

5. **Identification of chemical substances that are the subject of the proposed action:**

Drug Substance: amprenavir (Agenerase™)

Chemical Name: (3*S*)-tetrahydro-3-furyl *N*-[(1*S*, 2*R*)-3-(4-amino-*N*-isobutylbenzenesulphonamido)-1-benzyl-2-hydroxypropyl]carbamate

CAS #: 161814-49-9

Molecular Weight: 505.64

Molecular Form.: $C_{25}H_{35}N_3O_6S$

Structural Form.: Provided on page 3 of the EA.

ADEQUATE

6. **Environmental Issue:**

a. **Identification of Substances of Interest:**

The applicant has identified several structurally related substances that might enter the environment in addition to the active ingredient. Testing was done only for the active ingredient since the SRSs are more polar than amprenavir and therefore

should be less harmful to organisms.

ADEQUATE

b. Environmental Fate of Released Substances:

Test	Result
Water solubility	59 mg/L @ pH 5, 20C 66 mg/L @ pH 7, 20C 68 mg/L @ pH 9, 20C
Log Octanol/Water Partition Coefficient	2.4 @ pH 6
Vapor pressure	$<10^{-8}$ torr @ 25C
pK_a	2.05
Hydrolysis	$t_{1/2}$ > 1 year
Aerobic Aquatic Biodegradation	> 28 days (no significant mineralization at 28 days)
Aerobic Soil Biodegradation	> 64 days (no significant mineralization at 64 days)
Sorption/Desorption silty clay loam clay loam sandy loam	 34-38% (s), 31-33% (d), K_{oc} 190 @ pH 4.9 78-79% (s), 18-19% (d), K_{oc} 460 @ pH 6.0 48-52% (s), 33-36% (d), K_{oc} 180 @ pH 8.2

Based on the test data the drug is expected to enter the aquatic environment. It is not expected to adsorb strongly to soil/sediment nor is it expected to bioconcentrate. No rapid environmental depletion mechanism has been identified.

Data were generated in accordance with GMPs/GLPs using EATAD and/or OECD procedures. The test reports are provided. The testing was scientifically sound and adequate. An additional report is provided for the UV/visible absorption spectra of the drug demonstrates that the drug absorbs light in the far UV spectral region only and therefore photolysis is not expected to occur (wavelength maximum at 263 nm). This information was not included in the EA text. Additionally the fate and effects table included in the FOI EA does not provide sufficient information for a reader to understand the test results without the laboratory reports. For example, the vapor pressure is listed but the temperature at which this was determined is not included. The applicant was asked via a t-con (12/30/98) to provide a revised table that includes additional

details. This revised table was provided on January 5, 1999.

ADEQUATE

c. Environmental Concentrations:

The expected environmental introduction concentration for amprenavir products is — ppm based on a — forecast of a maximum quantity per year of —

ADEQUATE

d. Environmental Effects:

Organism/Test	EC_{50}	NOEC
Activated Sludge Respiration Inhibition (30 minutes & 3 hours)	> 1000 ppm	N/A
Daphnia magna (48 hrs)	> 51 ppm (EC_{50})	51 ppm

Test reports are provided for the effects tests. Standard test methods were used. The testing was scientifically sound and adequate. The daphnia test concentration was limited due to the solubility of the compound.

7. Mitigation measures:

No adverse environmental effects have been identified and therefore no mitigation measures are needed.

ADEQUATE

8. Alternatives to the proposed action:

No adverse environmental effects have been identified and therefore no alternatives are considered.

ADEQUATE

9. List of preparers, & their qualifications (expertise, experience, professional disciplines) and consultants:

The preparer is identified and a brief description of their qualifications provided.

ADEQUATE

10. References:

References are provided.

ADEQUATE

Appendices:

Confidential appendices containing production estimates and test reports are provided.

ADEQUATE.

The EA is appropriately identified with confidential and nonconfidential sections.

Endorsements:

/S/ /S/

HFD-357/NBSagey

HFD-800/EBSheinin 1-8-99

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Copy to NDA 21-039/through MTruffa/HFD-530
EA File 21-007
EA File 21-039

APPEARS THIS WAY
ON ORIGINAL

ENVIRONMENTAL ASSESSMENT

AND

FINDING OF NO SIGNIFICANT IMPACT

FOR

NDA 21-039

Agenerase™ (amprenavir) Oral Solution

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Antiviral Drug Products (HFD-530)

FINDING OF NO SIGNIFICANT IMPACT

NDA 21-039

Agenerase™ (amprenavir) Oral Solution

The National Environmental Policy Act of 1969 (NEPA) requires all Federal agencies to assess the environmental impact of their actions. FDA is required under NEPA to consider the environmental impact of approving certain drug product applications as an integral part of its regulatory process.

The Food and Drug Administration, Center for Drug Evaluation and Research has carefully considered the potential environmental impact of this action and has concluded that this action will not have a significant effect on the quality of the human environment and that an environmental impact statement, therefore, will not be prepared.

In support of their new drug application for amprenavir oral solution, Glaxo Wellcome Inc. has prepared an environmental assessment (attached) in accordance with 21 CFR Part 25 which evaluates the potential environmental impact of the use and disposal from use of the product. Amprenavir is a chemically synthesized drug which is indicated in the treatment of HIV infection.

Amprenavir is expected to enter the aquatic environment from use. It is not expected to adsorb strongly to soil or sediment. No rapid environmental degradation mechanism has been identified. As the drug is expected to persist in the environment for some time, the toxicity of amprenavir to environmental organisms was characterized. The results indicate that the compound is not expected to be toxic to organisms at expected environmental concentrations.

At U.S. hospitals and clinics, empty or partially empty packages will be disposed of according to hospital/clinic procedures. From home use, empty or partially empty containers will typically be disposed of by a community's solid waste management system which may include landfills, incineration and recycling, while minimal quantities of unused drug may be disposed of in the sewer system.

The Center for Drug Evaluation and Research has concluded that the product can used and disposed of without any expected adverse environmental effects. Adverse effects are not anticipated upon endangered or threatened species or upon property listed in or eligible for listing in the National Register of Historic Places.

1/7/99 /s/

DATE PREPARED BY
Nancy B. Sager
Environmental Officer
Center for Drug Evaluation and Research

1-8-99 /s/

DATE CONCURRED
Eric B. Sheinin, Ph.D.
Director, Office of New Drug Chemistry
Center for Drug Evaluation and Research

Attachment: Environmental Assessment

APPEARS THIS WAY
ON ORIGINAL

cc: Original to NDA 21-039 through PM: MTruffa/HFD-530
HFD-357/EA File
HFD-357/Docket File
HFD-205/FOI copy

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ON ORIGINAL

ENVIRONMENTAL ASSESSMENT

FOR

AMPRENAVIR ORAL SOLUTION, 15 MG/ML

APPEARS THIS WAY
ON ORIGINAL

1. DATE

September 2, 1998

2. APPLICANT

Glaxo Wellcome Inc.

3. ADDRESS

Five Moore Drive
Research Triangle Park, NC 27709

4. DESCRIPTION OF THE PROPOSED ACTION

4.a. Requested Approval

Glaxo Wellcome Inc has filed NDA 21-039 pursuant to Section 505(b) of the Food, Drug and Cosmetic Act for Amprenavir Oral Solution, 15 mg/mL. The product will be packaged in opaque, white, round 240-mL bottles constructed of high-density polyethylene resin. An EA has been submitted pursuant to 21 CFR Part 25.

4.b. Need for Action

Amprenavir is indicated for the treatment of HIV infection.

4.c. Locations of Use

Amprenavir Oral Solution, 15 mg/mL will be dispensed by pharmacies and used in hospitals, clinics and private residences throughout the United States.

4.d. Disposal Sites

At United States hospitals, pharmacies and clinics, empty or partially empty packages will be disposed of according to hospital, pharmacy, or clinic procedures. In the home, empty or partially empty containers will typically be disposed of by the community's solid waste management system. Solid waste management systems may include landfills, incineration and recycling. Minimal quantities of the unused drug could be disposed of in the sewer system.

5. IDENTIFICATION OF CHEMICAL SUBSTANCES

5.a. Nomenclature

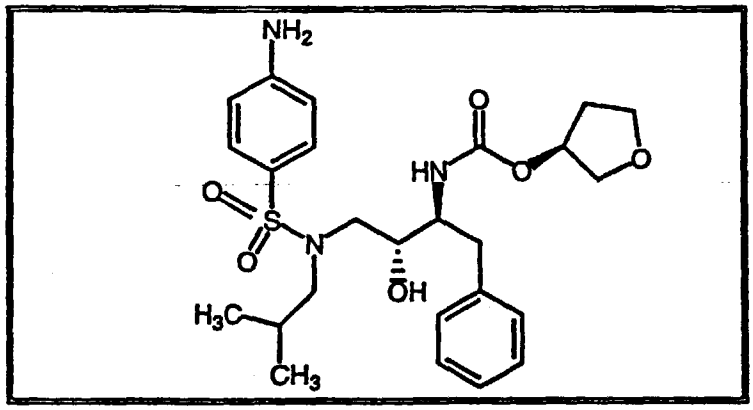
5.a.i.	**Established Name**	amprenavir
5.a.ii.	**Proprietary Name**	Agenerase™
5.a.iii.	**Chemical Name (IUPAC)**	(3*S*)-tetrahydro-3-furyl *N*-[(1*S*,2*R*)-3-(4-amino-*N*-isobutylbenzenesulphonamido)-1-benzyl-2-hydroxypropyl]carbamate

5.b. CAS Registry Number 161814-49-9

5.c. Molecular Formula $C_{25}H_{35}N_3O_6S$

5.d. Molecular Weight 505.64

5.e. Structural Formula



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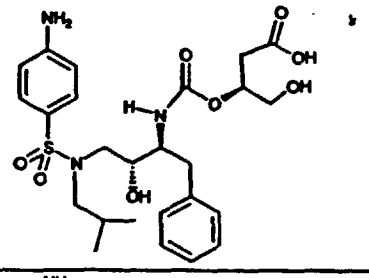
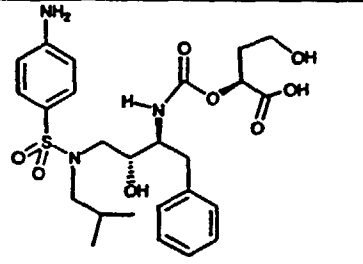
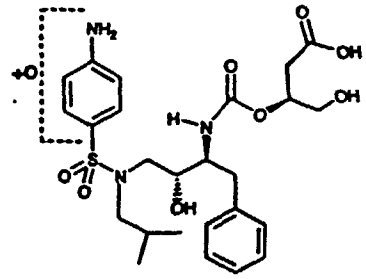
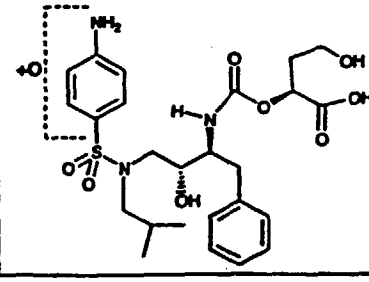
ON ORIGINAL

6. ENVIRONMENTAL ISSUES

6.a. Identification of Substances of Interest

The requested approval could potentially result in emissions to the environment of the drug substance and structurally related substances (SRSs). Information identifying the drug substance can be found in Section 5 above. Information on potential predominant SRSs is as follows:

Name	CAS #	Chemical Structure
(3*R*)-3-[((1*S*,2*S*)-3-[[(4-aminophenyl)sulfonyl](isobutyl)amino]-1-benzyl-2-hydroxypropylamino)carbonyl]oxy-4-hydroxybutanoic acid	N/A	BD/8064/120/2 
(3*R*)-3-[((1*S*,2*S*)-2-[[(4-aminophenyl)sulfonyl](isobutyl)amino]-1-benzyl-2-hydroxypropylamino)carbonyl]oxy-4-hydroxybutanoic acid	N/A	 GW513607A
(3*R*)-3-[((1*S*,2*S*)-3-[[(4-amino-3-hydroxyphenyl)sulfonyl](isobutyl)amino]-1-benzyl-2-hydroxypropylamino)carbonyl]oxy-4-hydroxybutanoic acid	N/A	
(3*R*)-3-[((1*S*,2*S*)-2-[[(4-amino-3-hydroxyphenyl)sulfonyl](isobutyl)amino]-1-benzyl-2-hydroxypropylamino)carbonyl]oxy-4-hydroxybutanoic acid	N/A	

Environmental fate and effects studies were conducted on only the drug substance because all of the predominant SRSs are more polar than the drug substance and therefore have less potential to harm the environment. In addition, none of the predominant SRSs will be present in the environment at levels greater than one part per billion. A summary of the results of the environmental fate and effects studies conducted on the drug substance can be found in Table 1. Complete test reports can be found in Confidential Appendix 2.

6.b. Environmental Fate of Released Substances

Based on the results of the environmental fate tests conducted (Table 1), amprenavir will partition into the aquatic environmental compartment. The water solubility is significantly greater than the expected introduction concentration (EIC). Partitioning into the terrestrial and atmospheric compartments is expected to be minimal. The K_{oc} is less than 1000 and the vapor pressure is less than 10^{-8} torr. Amprenavir is not expected to significantly bioconcentrate, $\log_{10}P_{ow} = 2.4$. No significant environmental depletion is expected.

6.c. Environmental Concentrations

Estimates of environmental concentrations for the substances of interest can be found in Confidential Appendix 1.

6.d. Environmental Effects

There should be no significant adverse environmental effects from the requested approval. The results of environmental effects testing for aquatic species (Table 1) show that the *Daphnia magna* EC_{50} (>51 mg/L) divided by the maximum expected emission concentration (MEEC) (Confidential Appendix 1) is greater than 1000. In addition, the MEEC is less than the no observed effect concentration (NOEC).

7. MITIGATION MEASURES

No adverse environmental effects have been identified and therefore no mitigation measures are needed.

8. ALTERNATIVES TO THE PROPOSED ACTION

No adverse environmental effects have been identified and therefore no alternatives to the proposed action need to be considered.

Table 1 A Summary of Environmental Fate and Effects Results for Amprenavir

DATA SUMMARY TABLE					
PHYSICAL/CHEMICAL CHARACTERIZATION					
Water Solubility	**pH**	**at 20°C [1]**	**at 50°C [1]**		
	5	59 mg/L	62 mg/L		
	7	66 mg/L	66 mg/L		
	9	68 mg/L	65 mg/L		
N-octanol/water Partition Coefficient at 25°C and pH 6.		**P_{ow}**	**$\log_{10} P_{ow}$**		
		280	2.4		
Vapor Pressure at 25°C			**Torr**		
			$<10^{-8}$		
UV/Visible Absorption Spectra			**Wavelength maximum**		
			263 nm		
Dissociation Constant			**P_{ka}**		
			2.05		
Soil Sorption/Desorption	**Soil**	**pH**	**Sorption**	**Desorption**	**K_{oc}**
	silty clay loam	4.9	34% to 38%	31% to 33%	190
	clay loam	6.0	78% to 79%	18% to 19%	460
	sandy loam	8.2	48% to 52%	33% to 36%	180
DEPLETION MECHANISMS					
Hydrolysis Rate					**$T_{1/2}$>1 yr**
Aerobic Biodegradation in Water					Less than 1.5% mineralization to carbon dioxide in 28 days
Aerobic Biodegradation in Soil					Less than 1.8% mineralization to carbon dioxide in 64 days
Photodegradation – unlikely based upon the UV/visible absorption spectra					
ENVIRONMENTAL EFFECTS					
Activated Sludge Respiration Inhibition (over 30 minutes and 3 hours)					**EC_{50}**
					>1000 mg/L
Acute Toxicity to *Daphnia magna* (48 hours)				**EC_{50}**	**NOEC**
				>51 mg/L	51 mg/L

[1] Solution temperatures for the water solubility tests were held at 20 degrees centigrade and 50 degrees centigrade for the first 24 hours of the study. After 24 hours solution temperatures were maintained at 25 degrees centigrade.

9. LIST OF PREPARERS

This EA was prepared by:

Douglas S. Finan

- Manager, Environmental Affairs, Glaxo Wellcome Inc., 1991 - present
- Environmental Engineer, Glaxo Wellcome Inc., 1990 - 1991
- Environmental Engineer, North Carolina Division of Environmental Management, 1979-1990
- Environmental Specialist, Deltona Corporation, 1978-1979
- Bachelor of Science in Environmental Science & Engineering Florida Institute of Technology, 1978

10. REFERENCES

Center for Drug Evaluation and Research, "Guidance for Industry Environmental Assessment of Human Drug and Biological Applications," U.S. FDA, July 1998.

Council On Environmental Quality, "Regulations on Implementing National Environmental Policy Act Procedures," Federal Register, Vol. 43, November 29, 1978, p. 55990.

U.S. FDA, "Environmental Assessment Technical Assistance Handbook," U.S. FDA, March 1987.

U.S. FDA, "National Environmental Policy Act; Policies and Procedures; Final Rule," Federal Register, Vol. 50, April 26, 1985.

APPENDICES

Confidential Appendix 1 - Environmental Concentrations and Assessment Factors
Confidential Appendix 2 - Environmental Fate and Effects Study Reports

ENVIRONMENTAL ASSESSMENT

AND

FINDING OF NO SIGNIFICANT IMPACT

FOR

NDA 21-007

Agenerase™ (amprenavir) Soft Gelatin Capsules

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Antiviral Drug Products (HFD-530)

FINDING OF NO SIGNIFICANT IMPACT

NDA 21-007

Agenerase™ (amprenavir) Soft Gelatin Capsules

The National Environmental Policy Act of 1969 (NEPA) requires all Federal agencies to assess the environmental impact of their actions. FDA is required under NEPA to consider the environmental impact of approving certain drug product applications as an integral part of its regulatory process.

The Food and Drug Administration, Center for Drug Evaluation and Research has carefully considered the potential environmental impact of this action and has concluded that this action will not have a significant effect on the quality of the human environment and that an environmental impact statement, therefore, will not be prepared.

In support of their new drug application for amprenavir soft gelatin capsules, Glaxo Wellcome Inc. has prepared an environmental assessment (attached) in accordance with 21 CFR Part 25 which evaluates the potential environmental impact of the use and disposal from use of the product. Amprenavir is a chemically synthesized drug which is indicated in the treatment of HIV infection.

Amprenavir is expected to enter the aquatic environment from use. It is not expected to adsorb strongly to soil or sediment. No rapid environmental degradation mechanism has been identified. As the drug is expected to persist in the environment for some time, the toxicity of amprenavir to environmental organisms was characterized. The results indicate that the compound is not expected to be toxic to organisms at expected environmental concentrations.

At U.S. hospitals and clinics, empty or partially empty packages will be disposed of according to hospital/clinic procedures. From home use, empty or partially empty containers will typically be disposed of by a community's solid waste management system which may include landfills, incineration and recycling, while minimal quantities of unused drug may be disposed of in the sewer system.

The Center for Drug Evaluation and Research has concluded that the product can used and disposed of without any expected adverse environmental effects. Adverse effects are not anticipated upon endangered or threatened species or upon property listed in or eligible for listing in the National Register of Historic Places.

1/7/99 /S/
DATE PREPARED BY
Nancy B. Sager
Environmental Officer
Center for Drug Evaluation and Research

1-9-99 /S/
DATE CONCURRED
Eric B. Sheinin, Ph.D.
Director, Office of New Drug Chemistry
Center for Drug Evaluation and Research

Attachment: Environmental Assessment

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ENVIRONMENTAL ASSESSMENT

FOR

AMPRENAVIR SOFT GELATIN CAPSULES, 50 MG AND 150 MG

APPEARS THIS WAY
ON ORIGINAL

1. DATE

June 18, 1998

2. APPLICANT

Glaxo Wellcome Inc.

3. ADDRESS

Five Moore Drive
Research Triangle Park, NC 27709

4. DESCRIPTION OF THE PROPOSED ACTION

4.a. Requested Approval

Glaxo Wellcome Inc. has filed NDA 21-007 pursuant to Section 505(b) of the Food, Drug and Cosmetic Act for Amprenavir Soft Gelatin Capsules, 50 mg and 150 mg. The capsules will be packaged in HDPE bottles. An EA has been submitted pursuant to 21 CFR Part 25.

4.b. Need for Action

Amprenavir is indicated for the treatment of HIV infection.

4.c. Locations of Use

Amprenavir Soft Gelatin Capsules, 50 mg and 150 mg will be dispensed by pharmacies and used in hospitals, clinics and private residences throughout the United States.

4.d. Disposal Sites

At United States hospitals, pharmacies and clinics, empty or partially empty packages will be disposed of according to hospital, pharmacy, or clinic procedures. In the home, empty or partially empty containers will typically be disposed of by the community's solid waste management system. Solid waste management systems may include landfills, incineration and recycling. Minimal quantities of the unused drug could be disposed of in the sewer system.

5. IDENTIFICATION OF CHEMICAL SUBSTANCES

5.a. Nomenclature

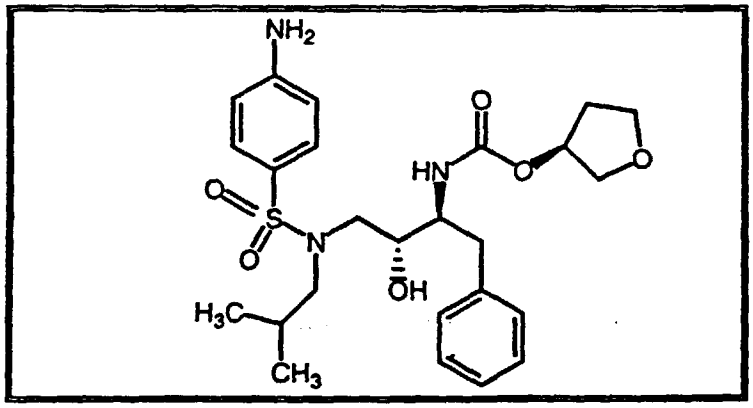
5.a.i.	**Established Name**	amprenavir
5.a.ii.	**Proprietary Name**	Agenerase™
5.a.iii.	**Chemical Name (IUPAC)**	(3*S*)-tetrahydro-3-furyl *N*-[(1*S*,2*R*)-3-(4-amino-*N*-isobutylbenzenesulphonamido)-1-benzyl-2-hydroxypropyl]carbamate

5.b. CAS Registry Number 161814-49-9

5.c. Molecular Formula $C_{25}H_{35}N_3O_6S$

5.d. Molecular Weight 505.64

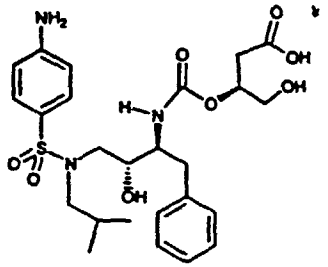
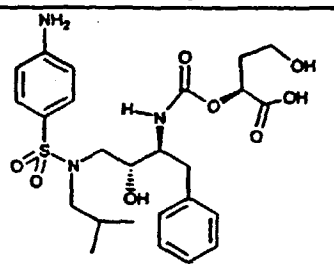
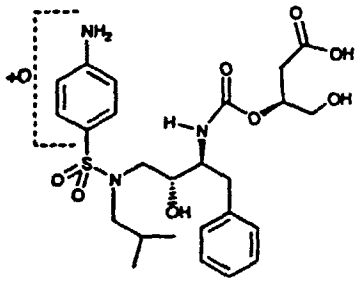
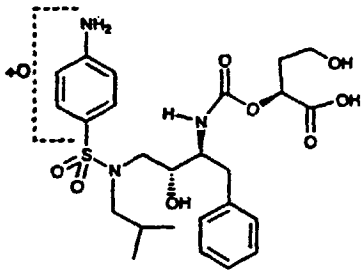
5.e. Structural Formula



6. ENVIRONMENTAL ISSUES

6.a. Identification of Substances of Interest

The requested approval could potentially result in emissions to the environment of the drug substance and structurally related substances (SRSs). Information identifying the drug substance can be found in Section 5 above. Information on potential predominant SRSs is as follows:

Name	CAS#	Chemical Structure
(3*R*)-3-[((1*S*,2*S*)-3-[[(4-aminophenyl)sulfonyl](isobutyl)amino]-1-benzyl-2-hydroxypropylamino)carbonyl]oxy-4-hydroxybutanoic acid	N/A	BD/8064/120/2 
(3*R*)-3-[((1*S*,2*S*)-2-[[(4-aminophenyl)sulfonyl](isobutyl)amino]-1-benzyl-2-hydroxypropylamino)carbonyl]oxy-4-hydroxybutanoic acid	N/A	 GW513607A
(3*R*)-3-[((1*S*,2*S*)-3-[[(4-amino-3-hydroxyphenyl)sulfonyl](isobutyl)amino]-1-benzyl-2-hydroxypropylamino)carbonyl]oxy-4-hydroxybutanoic acid	N/A	
(3*R*)-3-[((1*S*,2*S*)-2-[[(4-amino-3-hydroxyphenyl)sulfonyl](isobutyl)amino]-1-benzyl-2-hydroxypropylamino)carbonyl]oxy-4-hydroxybutanoic acid	N/A	

Environmental fate and effects studies were conducted on only the drug substance because all of the predominant SRSs are more polar than the drug substance and therefore have less potential to harm the environment. In addition, none of the predominant SRSs will be present in the environment at levels greater than one part per billion. A summary of the results of the environmental fate and effects studies conducted on the drug substance can be found in Table 1. Complete test reports can be found in Confidential Appendix 2.

6.b. Environmental Fate of Released Substances

Based on the results of the environmental fate tests conducted (Table 1), amprenavir will partition into the aquatic environmental compartment. The water solubility is significantly greater than the expected introduction concentration (EIC). Partitioning into the terrestrial and atmospheric compartments is expected to be minimal. The K_{oc} is less than 1000 and the vapor pressure is less than 10^{-8} torr. Amprenavir is not expected to significantly bioconcentrate, $\log_{10}P_{ow} = 2.4$. No significant environmental depletion is expected.

6.c. Environmental Concentrations

Estimates of environmental concentrations for the substances of interest can be found in Confidential Appendix 1.

6.d. Environmental Effects

There should be no significant adverse environmental effects from the requested approval. The results of environmental effects testing for aquatic species (Table 1) show that the *Daphnia magna* EC_{50} (>51 mg/L) divided by the maximum expected emission concentration (MEEC) (Confidential Appendix 1) is greater than 1000. In addition, the MEEC is less than the no observed effect concentration (NOEC).

7. MITIGATION MEASURES

No adverse environmental effects have been identified and therefore no mitigation measures are needed.

8. ALTERNATIVES TO THE PROPOSED ACTION

No adverse environmental effects have been identified and therefore no alternatives to the proposed action need to be considered.

Table 1 **A Summary of Environmental Fate and Effects Results for Amprenavir**

DATA SUMMARY TABLE					
PHYSICAL/CHEMICAL CHARACTERIZATION					
Water Solubility		**pH**	**at 20°C [1]**	**at 50°C [1]**	
		5	59 mg/L	62 mg/L	
		7	66 mg/L	66 mg/L	
		9	68 mg/L	65 mg/L	
N-octanol/water Partition Coefficient at 25°C and pH 6.			**P_{ow}**	**$\log_{10} P_{ow}$**	
			280	2.4	
Vapor Pressure at 25°C				**Torr**	
				$<10^{-8}$	
UV/Visible Absorption Spectra				**Wavelength maximum**	
				263 nm	
Dissociation Constant				**P_{ka}**	
				2.05	
Soil Sorption/Desorption	**Soil**	**pH**	**Sorption**	**Desorption**	**K_{oc}**
	silty clay loam	4.9	34% to 38%	31% to 33%	190
	clay loam	6.0	78% to 79%	18% to 19%	460
	sandy loam	8.2	48% to 52%	33% to 36%	180
DEPLETION MECHANISMS					
Hydrolysis Rate					$T_{1/2}$>1 yr
Aerobic Biodegradation in Water					Less than 1.5% mineralization to carbon dioxide in 28 days
Aerobic Biodegradation in Soil					Less than 1.8% mineralization to carbon dioxide in 64 days
Photodegradation – unlikely based upon the UV/visible absorption spectra					
ENVIRONMENTAL EFFECTS					
Activated Sludge Respiration Inhibition (over 30 minutes and 3 hours)					**EC_{50}**
					>1000 mg/L
Acute Toxicity to *Daphnia magna* (48 hours)				**EC_{50}**	**NOEC**
				>51 mg/L	51 mg/L

[1] Solution temperatures for the water solubility tests were held at 20 degrees centigrade and 50 degrees centigrade for the first 24 hours of the study. After 24 hours solution temperatures were maintained at 25 degrees centigrade.

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10. REFERENCES

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APPENDICES

Confidential Appendix 1 - Environmental Concentrations and Assessment Factors
Confidential Appendix 2 - Environmental Fate and Effects Study Reports