CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

22-023

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

Department of Health and Human Services Food and Drug Administration	Form Approved: OMB No. 0910-0513 Expiration Date: 07/31/06
PATENT INFORMATION SUBMITTED WITH THE FILING OF AN NDA, AMENDMENT, OR SUPPLEMENT	NDA NUMBER 22-023
For Each Patent That Claims a Drug Substance (Active Ingredient), Drug Product (Formulation and Composition) and/or Method of Use	NAME OF APPLICANT / NDA HOLDER MERCK & CO., INC.

The following is provided in accordance with Section 505(b) and (c) of the Federal Food, Drug, and Cosmetic Act.

TRADE NAME (OR PROPOSED TRADE NAME) (TRADENAME)	
ACTIVE INGREDIENT(S) Fosaprepitant Dimeglumine	STRENGTH(S) 115 mg/vial
DOSAGE FORM Injectable; IV	

This patent declaration form is required to be submitted to the Food and Drug Administration (FDA) with an NDA application, amendment, or supplement as required by 21 CFR 314.53 at the address provided in 21 CFR 314 53(d)(4). Within thirty (30) days after approval of an NDA or supplement, or within thirty (30) days of issuance of a new patent. a new patent declaration must be submitted pursuant to 21 CFR 314.53(c)(2)(ii) with all of the required information based on the approved NDA or supplement. The information submitted in the declaration form submitted upon or after approval will be the *only* information relied upon by the FDA for listing a patent in the Orange Book.

For hand-written or typewriter versions (only) of this report: If additional space is required for any narrative answer (i.e.. one that does not require a "Yes" or "No" response), please attach an additional page referencing the question number.

FDA will not list patent information if you submit an incomplete patent declaration or the patent declaration indicates the patent is not eligible for listing.

For each patent submitted for the pending NDA, amendment, or supplement referenced above, you must submit all the information described below. If you are not submitting any patents for this pending NDA, amendment or supplement, complete above section and sections 5 and 6.

1. GENERAL

a. United States Patent Number 5,691,336	b. Issue Date of Patent November 25, 1997	c. Expiration Date of Patent March 4, 2014
d. Name of Patent Owner MERCK & CO., INC.	Address *(of Patent Owner)* P.O. BOX 2000, RY 60-30	
	City/State RAHWAY, NEW JERSEY	
	ZIP Code 07065-0907	FAX Number *(if available)* 732-594-4720
	Telephone Number 732-594-3904	E-Mail Address *(if available)*
e. Name of agent or representative who resides or maintains a place of business within the United States authorized to receive notice of patent certification under section 505(b)(3)and (j)(2)(B) of the Federal Food, Drug, and Cosmetic Act and 21 CFR 314.52 and 314 95 (if patent owner or NDA applicant/holder does not reside or have a place of business within the United States)	Address *(of agent or representative named in 1.e.)*	
	City/State	
	ZIP Code	FAX Number *(if available)*
	Telephone Number	E-Mail Address *(if available)*

f. Is the patent referenced above a patent that has been submitted previously for the approved NDA or supplement referenced above?	☐ Yes	☒ No
g. If the patent referenced above has been submitted previously for listing. is the expiration date a new expiration date?	☐ Yes	☐ No

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

2. Drug Substance (Active Ingredient)

2.1 Does the patent claim the drug substance that is the active ingredient in the drug product described in the pending NDA, amendment, or supplement?	☒ Yes	☐ No
2.2 Does the patent claim a drug substance that is a different polymorph of the active ingredient described in the NDA, amendment, or supplement? See Attachment #1	☐ Yes	☐ No
2.3 If the answer to question 2.2 is "Yes," do you certify that, as of the date of this declaration, you have test data demonstrating that a drug product containing the polymorph will perform the same as the drug product described in the NDA? The type of test data required is described at 21 CFR 314.53(b).	☐ Yes	☐ No
2.4 Specify the polymorphic form(s) claimed by the patent for which you have the test results described in 2.3		
2.5 Does the patent claim only a metabolite of the active ingredient pending in the NDA or supplement? (Complete the information in section 4 below if the patent claims a pending method of using the pending drug product to administer the metabolite.)	☐ Yes	☒ No
2.6 Does the patent claim only an intermediate?	☐ Yes	☒ No
2.7 If the patent referenced in 2.1 is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.)	☐ Yes	☐ No

3. Drug Product (Composition/Formulation)

3.1 Does the patent claim the drug product, as defined in 21 CFR 314.3, in the pending NDA, amendment, or supplement?	☒ Yes	☐ No
3.2 Does the patent claim only an intermediate?	☐ Yes	☒ No
3.3 If the patent referenced in 3.1 is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.)	☐ Yes	☐ No

4. Method of Use

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

4.1 Does the patent claim one or more methods of use for which approval is being sought in the pending NDA, amendment, or supplement?	☐ Yes	☒ No
4.2 Claim Number (*as listed in the patent*)	Does the patent claim referenced in 4.2 claim a pending method of use for which approval is being sought in the pending NDA, amendment, or supplement? ☐ Yes ☐ No	
4.2a If the answer to 4.2 is "Yes," identify with specificity the use with reference to the proposed labeling for the drug product.	Use: (*Submit indication or method of use information as identified specifically in the proposed labeling*)	

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5. No Relevant Patents

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

6. Declaration Certification

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

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

6.2 Authorized Signature of NDA Applicant/Holder or Patent Owner (*Attorney, Agent, Representative or other Authorized Official*) (*Provide information below*)	Date Signed
J. Eric Thies	March 6, 2006

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

Check applicable box and provide information below.

☐ NDA Applicant/Holder	☐ NDA Applicant's/Holder's Attorney, Agent (Representative) or other Authorized Official
☐ Patent Owner	☒ Patent Owner's Attorney, Agent (Representative) or Other Authorized Official

Name Merck & Co., Inc	
Address P.O. Box 2000, RY60-30	City/State Rahway, NJ
ZIP Code 07065-0907	Telephone Number (732) 594-3904
FAX Number *(if available)* (732) 594-4720	E-Mail Address *(if available)*

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FORM FDA 3542a
TRADEMARK (Fosaprepitant dimeglumine)
NDA No. 22-023
US Patent No. 5,691,336

ATTACHMENT 1

Item 2.2 and 2.3:

The claims of Patent No. 5,691,336 are not limited to any particular polymorphic form of the drug substance. The patent claims encompass all polymorphic forms of the drug substance described in the NDA for which approval is being sought to the extent that they exist. Because the patent is submitted for listing on that basis, no testing of other polymorphic forms of the drug substance is required, and Questions 2.2 and 2.3 are accordingly left blank.

Department of Health and Human Services Food and Drug Administration	Form Approved: OMB No. 0910-0513 Expiration Date: 07/31/06
PATENT INFORMATION SUBMITTED WITH THE FILING OF AN NDA, AMENDMENT, OR SUPPLEMENT	NDA NUMBER 22-023
For Each Patent That Claims a Drug Substance (Active Ingredient), Drug Product (Formulation and Composition) and/or Method of Use	NAME OF APPLICANT / NDA HOLDER MERCK & CO., INC.

The following is provided in accordance with Section 505(b) and (c) of the Federal Food, Drug, and Cosmetic Act.

TRADE NAME (OR PROPOSED TRADE NAME) (TRADENAME)	
ACTIVE INGREDIENT(S) Fosaprepitant Dimeglumine	STRENGTH(S) 115 mg/vial
DOSAGE FORM Injectable; IV	

This patent declaration form is required to be submitted to the Food and Drug Administration (FDA) with an NDA application, amendment, or supplement as required by 21 CFR 314.53 at the address provided in 21 CFR 314.53(d)(4). Within thirty (30) days after approval of an NDA or supplement, or within thirty (30) days of issuance of a new patent, a new patent declaration must be submitted pursuant to 21 CFR 314.53(c)(2)(ii) with all of the required information based on the approved NDA or supplement. The information submitted in the declaration form submitted upon or after approval will be the *only* information relied upon by the FDA for listing a patent in the Orange Book.

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FDA will not list patent information if you submit an incomplete patent declaration or the patent declaration indicates the patent is not eligible for listing.

For each patent submitted for the pending NDA, amendment, or supplement referenced above, you must submit all the information described below. If you are not submitting any patents for this pending NDA, amendment or supplement, complete above section and sections 5 and 6.

1. GENERAL

a. United States Patent Number	b. Issue Date of Patent	c. Expiration Date of Patent
5,716,942	February 10, 1998	February 10, 2015

d. Name of Patent Owner		
MERCK & CO., INC.	Address *(of Patent Owner)* P.O. BOX 2000, RY 60-30	
	City/State RAHWAY, NEW JERSEY	
	ZIP Code 07065-0907	FAX Number *(if available)* 732-594-4720
	Telephone Number 732-594-3904	E-Mail Address *(if available)*

e. Name of agent or representative who resides or maintains a place of business within the United States authorized to receive notice of patent certification under section 505(b)(3)and (j)(2)(B) of the Federal Food, Drug, and Cosmetic Act and 21 CFR 314.52 and 314.95 (if patent owner or NDA applicant/holder does not reside or have a place of business within the United States)		
	Address *(of agent or representative named in 1.e.)*	
	City/State	
	ZIP Code	FAX Number *(if available)*
	Telephone Number	E-Mail Address *(if available)*

f. Is the patent referenced above a patent that has been submitted previously for the approved NDA or supplement referenced above?	☐ Yes	☒ No
g. If the patent referenced above has been submitted previously for listing, is the expiration date a new expiration date?	☐ Yes	☐ No

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

2. Drug Substance (Active Ingredient)

2.1 Does the patent claim the drug substance that is the active ingredient in the drug product described in the pending NDA, amendment, or supplement?	☐ Yes	☒ No
2.2 Does the patent claim a drug substance that is a different polymorph of the active ingredient described in the NDA, amendment, or supplement?	☐ Yes	☒ No
2.3 If the answer to question 2.2 is "Yes," do you certify that, as of the date of this declaration, you have test data demonstrating that a drug product containing the polymorph will perform the same as the drug product described in the NDA? The type of test data required is described at 21 CFR 314.53(b).	☐ Yes	☐ No
2.4 Specify the polymorphic form(s) claimed by the patent for which you have the test results described in 2.3		
2.5 Does the patent claim only a metabolite of the active ingredient pending in the NDA or supplement? (Complete the information in section 4 below if the patent claims a pending method of using the pending drug product to administer the metabolite.)	☐ Yes	☒ No
2.6 Does the patent claim only an intermediate?	☐ Yes	☒ No
2.7 If the patent referenced in 2.1 is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.)	☐ Yes	☐ No

3. Drug Product (Composition/Formulation)

3.1 Does the patent claim the drug product, as defined in 21 CFR 314.3, in the pending NDA, amendment, or supplement?	☐ Yes	☒ No
3.2 Does the patent claim only an intermediate?	☐ Yes	☒ No
3.3 If the patent referenced in 3.1 is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.)	☐ Yes	☐ No

4. Method of Use

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

4.1 Does the patent claim one or more methods of use for which approval is being sought in the pending NDA, amendment, or supplement?	☒ Yes	☐ No
4.2 Claim Number (*as listed in the patent*) 1	Does the patent claim referenced in 4.2 claim a pending method of use for which approval is being sought in the pending NDA, amendment, or supplement? ☒ Yes	☐ No

4.2a If the answer to 4.2 is "Yes," identify with specificity the use with reference to the proposed labeling for the drug product	Use: (*Submit indication or method of use information as identified specifically in the proposed labeling*) TRADENAME, in combination with other antiemetic agents, is indicated for the: prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of highly emetogenic cancer chemotherapy including high-dose cisplatin; prevention of nausea and vomiting associated with initial and repeat courses of moderately emetogenic cancer chemotherapy.

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4. Method of Use (continued)

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

4.1 Does the patent claim one or more methods of use for which approval is being sought in the pending NDA, amendment, or supplement?	☒ Yes ☐ No
4.2 Claim Number (*as listed in the patent*) 19	Does the patent claim referenced in 4.2 claim a pending method of use for which approval is being sought in the pending NDA. amendment, or supplement? ☒ Yes ☐ No
4.2a If the answer to 4.2 is "Yes," identify with specificity the use with reference to the proposed labeling for the drug product.	Use: (*Submit indication or method of use information as identified specifically in the proposed labeling*) TRADENAME, in combination with other antiemetic agents, is indicated for the: prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of highly emetogenic cancer chemotherapy including high-dose cisplatin; prevention of nausea and vomiting associated with initial and repeat courses of moderately emetogenic cancer chemotherapy.

4. Method of Use (continued)

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

4.1 Does the patent claim one or more methods of use for which approval is being sought in the pending NDA, amendment, or supplement?	☒ Yes ☐ No
4.2 Claim Number (*as listed in the patent*) 20	Does the patent claim referenced in 4.2 claim a pending method of use for which approval is being sought in the pending NDA. amendment, or supplement? ☒ Yes ☐ No
4.2a If the answer to 4.2 is "Yes," identify with specificity the use with reference to the proposed labeling for the drug product.	Use: (*Submit indication or method of use information as identified specifically in the proposed labeling*) TRADENAME, in combination with other antiemetic agents, is indicated for the: prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of highly emetogenic cancer chemotherapy including high-dose cisplatin; prevention of nausea and vomiting associated with initial and repeat courses of moderately emetogenic cancer chemotherapy.

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5. No Relevant Patents

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

6. Declaration Certification

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

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

6.2 Authorized Signature of NDA Applicant/Holder or Patent Owner (*Attorney, Agent, Representative or other Authorized Official*) (*Provide Information below*)	Date Signed
J. Eric Thies	March 6, 2006

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

Check applicable box and provide information below.

☐ NDA Applicant/Holder	☐ NDA Applicant's/Holder's Attorney, Agent (Representative) or other Authorized Official
☐ Patent Owner	☒ Patent Owner's Attorney, Agent (Representative) or Other Authorized Official
Name Merck & Co., Inc	
Address P.O. Box 2000, RY60-30	City/State Rahway, NJ
ZIP Code 07065-0907	Telephone Number (732) 594-3904
FAX Number *(if available)* (732) 594-4720	E-Mail Address *(if available)*

Computer generated form "Patent Submission with NDA" (Miscellaneous folder) Merck & Co. Inc 10/26/2005

Department of Health and Human Services Food and Drug Administration	Form Approved: OMB No 0910-0513 Expiration Date: 07/31/06
PATENT INFORMATION SUBMITTED WITH THE FILING OF AN NDA, AMENDMENT, OR SUPPLEMENT	NDA NUMBER 22-023
For Each Patent That Claims a Drug Substance (Active Ingredient), Drug Product (Formulation and Composition) and/or Method of Use	NAME OF APPLICANT / NDA HOLDER MERCK & CO., INC.

The following is provided in accordance with Section 505(b) and (c) of the Federal Food, Drug, and Cosmetic Act

TRADE NAME (OR PROPOSED TRADE NAME) (TRADENAME)	
ACTIVE INGREDIENT(S) Fosaprepitant Dimeglumine	STRENGTH(S) 115 mg/vial
DOSAGE FORM Injectable; IV	

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For each patent submitted for the pending NDA, amendment, or supplement referenced above, you must submit all the information described below. If you are not submitting any patents for this pending NDA, amendment or supplement, complete above section and sections 5 and 6.

1. GENERAL

a. United States Patent Number 5,538,982	b. Issue Date of Patent July 23, 1996	c. Expiration Date of Patent July 23, 2013
d. Name of Patent Owner GlaxoSmithKline	Address *(of Patent Owner)* 980 Great West Road	
	City/State Brentford, Middlesex	
	ZIP Code TW8 9GS United Kingdom	FAX Number *(if available)*
	Telephone Number 44 (0)208-047-5000	E-Mail Address *(if available)*
e. Name of agent or representative who resides or maintains a place of business within the United States authorized to receive notice of patent certification under section 505(b)(3)and (j)(2)(B) of the Federal Food, Drug, and Cosmetic Act and 21 CFR 314.52 and 314.95 (if patent owner or NDA applicant/holder does not reside or have a place of business within the United States) GlaxoSmithKline	Address *(of agent or representative named in 1.e)* Corporate Intellectual Property Dept., Five Moore Drive	
	City/State Research Triangle Park, North Carolina	
	ZIP Code 27709	FAX Number *(if available)*
	Telephone Number 919-483-9000	E-Mail Address *(if available)*

f. Is the patent referenced above a patent that has been submitted previously for the approved NDA or supplement referenced above?	☐ Yes	☒ No
g. If the patent referenced above has been submitted previously for listing, is the expiration date a new expiration date?	☐ Yes	☐ No

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

2. Drug Substance (Active Ingredient)

2.1 Does the patent claim the drug substance that is the active ingredient in the drug product described in the pending NDA, amendment, or supplement?	☐ Yes	☒ No
2.2 Does the patent claim a drug substance that is a different polymorph of the active ingredient described in the NDA, amendment, or supplement?	☐ Yes	☒ No
2.3 If the answer to question 2.2 is "Yes," do you certify that, as of the date of this declaration, you have test data demonstrating that a drug product containing the polymorph will perform the same as the drug product described in the NDA? The type of test data required is described at 21 CFR 314.53(b).	☐ Yes	☐ No
2.4 Specify the polymorphic form(s) claimed by the patent for which you have the test results described in 2.3		
2.5 Does the patent claim only a metabolite of the active ingredient pending in the NDA or supplement? (Complete the information in section 4 below if the patent claims a pending method of using the pending drug product to administer the metabolite.)	☐ Yes	☒ No
2.6 Does the patent claim only an intermediate?	☐ Yes	☒ No
2.7 If the patent referenced in 2.1 is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.)	☐ Yes	☐ No

3. Drug Product (Composition/Formulation)

3.1 Does the patent claim the drug product, as defined in 21 CFR 314.3, in the pending NDA, amendment, or supplement?	☐ Yes	☒ No
3.2 Does the patent claim only an intermediate?	☐ Yes	☒ No
3.3 If the patent referenced in 3.1 is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.)	☐ Yes	☐ No

4. Method of Use

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

4.1 Does the patent claim one or more methods of use for which approval is being sought in the pending NDA, amendment, or supplement?	☒ Yes	☐ No
4.2 Claim Number (*as listed in the patent*) 1	Does the patent claim referenced in 4.2 claim a pending method of use for which approval is being sought in the pending NDA, amendment, or supplement? ☒ Yes	☐ No

4.2a If the answer to 4.2 is "Yes," identify with specificity the use with reference to the proposed labeling for the drug product.	Use: (*Submit indication or method of use information as identified specifically in the proposed labeling*) TRADENAME, in combination with other antiemetic agents, is indicated for the: prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of highly emetogenic cancer chemotherapy including high-dose cisplatin; prevention of nausea and vomiting associated with initial and repeat courses of moderately emetogenic cancer chemotherapy.

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4. Method of Use (continued)

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

4.1 Does the patent claim one or more methods of use for which approval is being sought in the pending NDA, amendment, or supplement?		☒ Yes ☐ No
4.2 Claim Number (*as listed in the patent*) 2	Does the patent claim referenced in 4.2 claim a pending method of use for which approval is being sought in the pending NDA. amendment, or supplement?	☒ Yes ☐ No
4.2a If the answer to 4.2 is "Yes," identify with specificity the use with reference to the proposed labeling for the drug product.	Use: (*Submit indication or method of use information as identified specifically in the proposed labeling*) TRADENAME. in combination with other antiemetic agents, is indicated for the: prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of highly emetogenic cancer chemotherapy including high-dose cisplatin; prevention of nausea and vomiting associated with initial and repeat courses of moderately emetogenic cancer chemotherapy	

4. Method of Use (continued)

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

4.1 Does the patent claim one or more methods of use for which approval is being sought in the pending NDA, amendment, or supplement?		☒ Yes ☐ No
4.2 Claim Number (*as listed in the patent*) 3	Does the patent claim referenced in 4.2 claim a pending method of use for which approval is being sought in the pending NDA, amendment. or supplement?	☒ Yes ☐ No
4.2a If the answer to 4.2 is "Yes," identify with specificity the use with reference to the proposed labeling for the drug product.	Use: (*Submit indication or method of use information as identified specifically in the proposed labeling.*) TRADENAME. in combination with other antiemetic agents, is indicated for the: prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of highly emetogenic cancer chemotherapy including high-dose cisplatin; prevention of nausea and vomiting associated with initial and repeat courses of moderately emetogenic cancer chemotherapy	

4. Method of Use (continued)

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

4.1 Does the patent claim one or more methods of use for which approval is being sought in the pending NDA, amendment, or supplement?		☒ Yes ☐ No
4.2 Claim Number (*as listed in the patent*) 4	Does the patent claim referenced in 4.2 claim a pending method of use for which approval is being sought in the pending NDA. amendment, or supplement?	☒ Yes ☐ No
4.2a If the answer to 4.2 is "Yes," identify with specificity the use with reference to the proposed labeling for the drug product	Use: (*Submit indication or method of use information as identified specifically in the proposed labeling*) TRADENAME. in combination with other antiemetic agents, is indicated for the: prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of highly emetogenic cancer chemotherapy including high-dose cisplatin; prevention of nausea and vomiting associated with initial and repeat courses of moderately emetogenic cancer chemotherapy	

4. Method of Use (continued)

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

4.1 Does the patent claim one or more methods of use for which approval is being sought in the pending NDA, amendment, or supplement?		☒ Yes ☐ No
4.2 Claim Number (*as listed in the patent*) 5	Does the patent claim referenced in 4.2 claim a pending method of use for which approval is being sought in the pending NDA, amendment. or supplement?	☒ Yes ☐ No
4.2a If the answer to 4.2 is "Yes," identify with specificity the use with reference to the proposed labeling for the drug product.	Use: (*Submit indication or method of use information as identified specifically in the proposed labeling*) TRADENAME. in combination with other antiemetic agents. is indicated for the: prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of highly emetogenic cancer chemotherapy including high-dose cisplatin; prevention of nausea and vomiting associated with initial and repeat courses of moderately emetogenic cancer chemotherapy.	

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4. Method of Use (continued)			
Sponsors must submit the information in section 4 separately for each patent claim claiming a method of using the pending drug product for which approval is being sought. For each method of use claim referenced, provide the following information:			
4.1 Does the patent claim one or more methods of use for which approval is being sought in the pending NDA, amendment, or supplement?		☒ Yes	☐ No
4.2 Claim Number (*as listed in the patent*) 6	Does the patent claim referenced in 4.2 claim a pending method of use for which approval is being sought in the pending NDA, amendment, or supplement?	☒ Yes	☐ No
4.2a If the answer to 4.2 is "Yes," identify with specificity the use with reference to the proposed labeling for the drug product.	Use: (*Submit indication or method of use information as identified specifically in the proposed labeling.*) TRADENAME, in combination with other antiemetic agents, is indicated for the: prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of highly emetogenic cancer chemotherapy including high-dose cisplatin; prevention of nausea and vomiting associated with initial and repeat courses of moderately emetogenic cancer chemotherapy.		

Computer generated form "Patent Submission with NDA" (Miscellaneous folder) Merck & Co., Inc 10/29/2005

5. No Relevant Patents

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

6. Declaration Certification

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

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

6.2 Authorized Signature of NDA Applicant/Holder or Patent Owner (*Attorney, Agent, Representative or other Authorized Official*) (*Provide information below*)	Date Signed
J. Eric Thies	March 6. 2006

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

Check applicable box and provide information below.

☐ NDA Applicant/Holder	☒ NDA Applicant's/Holder's Attorney, Agent (Representative) or other Authorized Official
☐ Patent Owner	☐ Patent Owner's Attorney, Agent (Representative) or Other Authorized Official

Name Merck & Co., Inc	
Address P.O. Box 2000, RY60-30	City/State Rahway, NJ
ZIP Code 07065-0907	Telephone Number (732) 594-3904
FAX Number *(if available)* (732) 594-4720	E-Mail Address *(if available)*

Computer generated form "Patent Submission with NDA" (Miscellaneous folder) Merck & Co., Inc 10/26/2005

EXCLUSIVITY SUMMARY

NDA # 22-023 (Type 2) SUPPL # HFD # 180

Trade Name Emend

Generic Name fosaprepitant dimeglumine

Applicant Name Merck & Co, Inc.

Approval Date, If Known PDUFA date is January 27, 2008

PART I IS AN EXCLUSIVITY DETERMINATION NEEDED?

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

a) Is it a 505(b)(1), 505(b)(2) or efficacy supplement?

YES ☒ NO ☐

If yes, what type? Specify 505(b)(1), 505(b)(2), SE1, SE2, SE3,SE4, SE5, SE6, SE7, SE8

505(b)(1)

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

YES ☒ NO ☐

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

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

Fosaprepitant dimeglumine, a white to off-white amorphous powder, is a prodrug of aprepitant that is freely soluable in water. When administred intravenously it rapidly converts to aprepitant. Because the administration of fosaprepitant dimeglumine (I.V.) is different than that of aprepitant (oral capsules) clinical data is necessary.

d) Did the applicant request exclusivity?

YES ☐ NO ☒

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

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

YES ☐ NO ☒

If the answer to the above question in YES, is this approval a result of the studies submitted in response to the Pediatric Written Request?

IF YOU HAVE ANSWERED "NO" TO ALL OF THE ABOVE QUESTIONS, GO DIRECTLY TO THE SIGNATURE BLOCKS AT THE END OF THIS DOCUMENT.

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

YES ☐ NO ☒

IF THE ANSWER TO QUESTION 2 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8 (even if a study was required for the upgrade).

PART II FIVE-YEAR EXCLUSIVITY FOR NEW CHEMICAL ENTITIES
(Answer either #1 or #2 as appropriate)

1. Single active ingredient product.

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

YES ☒ NO ☐

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

#(s).

NDA# 21-549 Emend (aprepitant) Capsules: 40, 80, and 125 mg

NDA#

NDA#

2. Combination product.

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

YES ☐ NO ☒

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

NDA#

NDA#

NDA#

IF THE ANSWER TO QUESTION 1 OR 2 UNDER PART II IS "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8. (Caution: The questions in part II of the summary should only be answered "NO" for original approvals of new molecular entities.)
IF "YES," GO TO PART III.

PART III THREE-YEAR EXCLUSIVITY FOR NDAs AND SUPPLEMENTS

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

1. Does the application contain reports of clinical investigations? (The Agency interprets "clinical investigations" to mean investigations conducted on humans other than bioavailability studies.) If

the application contains clinical investigations only by virtue of a right of reference to clinical investigations in another application, answer "yes," then skip to question 3(a). If the answer to 3(a) is "yes" for any investigation referred to in another application, do not complete remainder of summary for that investigation.

YES ☒ NO ☐

IF "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8.

2. A clinical investigation is "essential to the approval" if the Agency could not have approved the application or supplement without relying on that investigation. Thus, the investigation is not essential to the approval if 1) no clinical investigation is necessary to support the supplement or application in light of previously approved applications (i.e., information other than clinical trials, such as bioavailability data, would be sufficient to provide a basis for approval as an ANDA or 505(b)(2) application because of what is already known about a previously approved product), or 2) there are published reports of studies (other than those conducted or sponsored by the applicant) or other publicly available data that independently would have been sufficient to support approval of the application, without reference to the clinical investigation submitted in the application.

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

YES ☒ NO ☐

If "no," state the basis for your conclusion that a clinical trial is not necessary for approval AND GO DIRECTLY TO SIGNATURE BLOCK ON PAGE 8:

NOTE ON QUESTION 2a): Study 07L1 is a clinical study that provided essential support to the safety of Emend. Although efficacy endpoints were measured, the study failed to meet the efficacy endpoints. Therefore, the study only supported safety and not efficacy.

Since Study 07L1 does not support efficacy, we do not consider it essential for approval of exclusivity purposes.

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

YES ☐ NO ☒

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

YES ☐ NO ☐

If yes, explain:

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

YES ☐ NO ☒

If yes, explain:

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

See PART III, Question 2a)

Studies comparing two products with the same ingredient(s) are considered to be bioavailability studies for the purpose of this section.

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

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

Investigation #1 YES ☐ NO ☐

Investigation #2 YES ☐ NO ☐

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

Question #3) is being answered as Not Applicable (N/A). The clinical study was a safety study/failed efficacy study -- efficacy was demonstrated due to the pK study alone.

b) For each investigation identified as "essential to the approval", does the investigation duplicate the results of another investigation that was relied on by the agency to support the

effectiveness of a previously approved drug product?

Investigation #1 YES ☐ NO ☐

Investigation #2 YES ☐ NO ☐

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

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

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

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

Investigation #1

IND # YES ☐ ! NO ☐
! Explain:

Investigation #2

IND # YES ☐ ! NO ☐
! Explain:

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

Investigation #1	!
	!
YES ☐	! NO ☐
Explain:	! Explain:

Investigation #2	!
	!
YES ☐	! NO ☐
Explain:	! Explain:

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

YES ☐ NO ☐

If yes, explain:

Name of person completing form: Jagjit Grewal, M.P.H.
Title: Regulartory Project Manager
Date: January 17, 2008

Name of Office/Division Director signing form: Joyce Korvick, M.D., M.P.H.
Title: Deputy Division Director

Form OGD-011347; Revised 05/10/2004; formatted 2/15/05

APPEARS THIS WAY ON ORIGIN

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

/s/

Joyce Korvick
1/25/2008 06:36:06 PM

Pediatric Research and Equity Act Deferrals

Product name and active ingredient/ dosage form:

IND/NDA/BLA #: 22-023 Supplement Type: Supplement Number:

HFD: 180

Sponsor: Merck & Co., Inc.

Indication(s): Two Indications
(NOTE: If the drug is approved for or you are seeking approval for more than one indication, address the following for each indication.)

- Indication #1: EMEND For Injection, in combination with other antiemetic agents, is indicated for the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of highly emetogenic cancer chemotherapy including high-dose cisplatin.

1. Deferral specifics
   a. Pediatric age group(s) included in deferral: 6 months to 17 years

   b. Reason(s) for requesting deferral of pediatric studies (address each age group separately and for each age group — choose all that apply):
      - ☒ Adult studies completed and ready for approval
      - ☐ Additional safety or effectiveness data needed (**describe**)
      - ☐ Other (**specify**)

   c. Pediatric age group(s) not included in deferral: 0 to < 6 months

   d. Reason(s) for not including the pediatric age group(s) listed in letter c in the deferral request (address each excluded age group separately and for each such age group — choose all that apply):
      - ☐ Adequate pediatric labeling exists
      - ☐ Studies completed in the specified age group
      - ☒ Requesting a partial waiver
      - ☐ Other (**specify**)

   2. The law requires that certain criteria be met BEFORE a deferral is granted. the applicant must submit—
      "(I) certification of the grounds for deferring the assessments;
      "(II) a description of the planned or ongoing studies;
      "(III) evidence that the studies are being conducted or will be conducted with due diligence and at the earliest possible time; **and**
      "(IV) a timeline for the completion of such studies.

Has the Sponsor submitted these (if yes, this should be reviewed at the same time as the deferral)? Yes, submission dated 1/22/08.

3. Has a pediatric plan been submitted to the Agency? Note: Pediatric plans MUST be reviewed by the Pediatric Review Committee (PeRC)
   - If so, provide date:
     Submission dated 1/22/08.
   - If not, provided projected date pediatric plan is to be submitted

3. Timeline for the completion of studies
   Proposed submission of studies by June 30, 2011

4. Has a Written Request been issued?
   No.

- Indication #2: EMEND For Injection, in combination with other antiemetic agents, is indicated for the prevention of nausea and vomiting associated with initial and repeat courses of moderately emetogenic cancer chemotherapy.

1. Deferral specifics
   a. Pediatric age group(s) included in deferral: 6 months to 17 years

   b. Reason(s) for requesting deferral of pediatric studies (address each age group separately and for each age group — choose all that apply):
      - ☒ Adult studies completed and ready for approval
      - ☐ Additional safety or effectiveness data needed (**describe**)
      - ☐ Other (**specify**)

   c. Pediatric age group(s) not included in deferral: 0 to < 6 months

   d. Reason(s) for not including the pediatric age group(s) listed in letter c in the deferral request (address each excluded age group separately and for each such age group — choose all that apply):
      - ☐ Adequate pediatric labeling exists
      - ☐ Studies completed in the specified age group
      - ☒ Requesting a partial waiver
      - ☐ Other (**specify**)

   2. The law requires that certain criteria be met BEFORE a deferral is granted. the applicant must submit—
      "(I) certification of the grounds for deferring the assessments;
      "(II) a description of the planned or ongoing studies;
      "(III) evidence that the studies are being conducted or will be conducted with due diligence and at the earliest possible time; **and**

"(IV) a timeline for the completion of such studies.

Has the Sponsor submitted these (if yes, this should be reviewed at the same time as the deferral)? Yes, submission dated 1/22/08.

3. Has a pediatric plan been submitted to the Agency? Note: Pediatric plans MUST be reviewed by the Pediatric Review Committee (PeRC)
   - If so, provide date
     Submission dated 1/22/08.
   - If not, provided projected date pediatric plan is to be submitted

3. Timeline for the completion of studies
   Proposed submission of studies by June 30, 2011

4. Has a Written Request been issued?
   No

APPEARS THIS WAY ON ORIGINAL

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

/s/

Jagjit S Grewal
1/25/2008 12:04:40 PM
CSO

Joyce Korvick
1/25/2008 06:35:44 PM
MEDICAL OFFICER

PEDIATRIC PAGE

(Complete for all filed original applications and efficacy supplements)

NDA/BLA #: 22-023 **Supplement Type (e.g. SE5):** _____ **Supplement Number:** _____

Stamp Date: March 31, 2006 (original); July 27, 2007 (Class 2 Resubmission) **PDUFA Goal Date:** January 27, 2008

HFD 180 **Trade and generic names/dosage form:** Emend (fosaprepitant dimeglumine) I.V 115 mg

Applicant: Merck & Co. Inc **Therapeutic Class:** Antiemetic

Does this application provide for new active ingredient(s), new indication(s), new dosage form, new dosing regimen, or new route of administration? *

- ☒ **Yes. Please proceed to the next question.**
- ☐ **No. PREA does not apply. Skip to signature block.**

** SE5, SE6, and SE7 submissions may also trigger PREA. If there are questions, please contact the Rosemary Addy or Grace Carmouze.*

Indication(s) ***previously approved*** **(please complete this section for supplements only):**_____

Each indication covered by current application under review must have pediatric studies: ***Completed, Deferred, and/or Waived.***

Number of indications for this application(s): 2

Indication #1: EMEND For Injection, in combination with other antiemetic agents, is indicated for the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of highly emetogenic cancer chemotherapy including high-dose cisplatin.

Is this an orphan indication?

- ☐ **Yes. PREA does not apply. Skip to signature block.**
- ☒ **No. Please proceed to the next question.**

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

- ☐ **Yes: Please proceed to Section A.**
- ☒ **No: Please check all that apply:** X **Partial Waiver** X **Deferred** ____ **Completed**

NOTE: More than one may apply

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

Section A: Fully Waived Studies

Reason(s) for full waiver:

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

☐ **Other:**_____

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

Section B: Partially Waived Studies

Age/weight range being partially waived (fill in applicable criteria below):

Min____ **kg**____ **mo.** 0 **yr.**____ **Tanner Stage**____
Max____ **kg**____ **mo.** <6 months **yr.**____ **Tanner Stage**____
Reason(s) for partial waiver:

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

b(4)

b(4)

The PPSR and WR are currently pending.

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

Section C: Deferred Studies

Age/weight range being deferred (fill in applicable criteria below):

Min ____	**kg**____	**mo.** 6 months	**yr.**____	**Tanner Stage**____
Max____	**kg**____	**mo.**____	**yr.** 17 years	**Tanner Stage**____

Reason(s) for deferral:

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

Date studies are due (mm/dd/yy): June 30, 2011

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

Section D: Completed Studies

Age/weight range of completed studies (fill in applicable criteria below):

Min ____	**kg**____	**mo.**____	**yr.**____	**Tanner Stage**____
Max____	**kg**____	**mo.**____	**yr.**____	**Tanner Stage**____

Comments:

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

This page was completed by:

{See appended electronic signature page}

Regulatory Project Manager

FOR QUESTIONS ON COMPLETING THIS FORM CONTACT THE PEDIATRIC AND MATERNAL HEALTH STAFF at 301-796-0700

(Revised: 10/10/2006)

Attachment A

(This attachment is to be completed for those applications with multiple indications only.)

Indication #2: EMEND For Injection, in combination with other antiemetic agents, is indicated for the prevention of nausea and vomiting associated with initial and repeat courses of moderately emetogenic cancer chemotherapy.

Is this an orphan indication?

- ☐ **Yes. PREA does not apply. Skip to signature block.**
- ☒ **No. Please proceed to the next question.**

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

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

Section A: Fully Waived Studies

Reason(s) for full waiver:

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

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

Section B: Partially Waived Studies

Age/weight range being partially waived (fill in applicable criteria below)::

Min	**kg**	**mo. 0**	**yr.**	**Tanner Stage**
Max	**kg**	**mo. <6 months**	**yr.**	**Tanner Stage**

Reason(s) for partial waiver:

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

If studies are deferred, proceed to Section C. If studies are completed, proceed to Section D. Otherwise, this Pediatric Page is

complete and should be entered into DFS.

Section C: Deferred Studies

Age/weight range being deferred (fill in applicable criteria below):

Min ____	**kg**____	**mo.** 6 months	**yr.**____	**Tanner Stage**____
Max____	**kg**____	**mo.**____	**yr.** 17 years	**Tanner Stage**____

Reason(s) for deferral:

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

Date studies are due (mm/dd/yy): June 30, 2011

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

Section D: Completed Studies

Age/weight range of completed studies (fill in applicable criteria below):

Min ____	**kg**____	**mo.**____	**yr.**____	**Tanner Stage**____
Max____	**kg**____	**mo.**____	**yr.**____	**Tanner Stage**____

Comments:

If there are additional indications, please copy the fields above and complete pediatric information as directed. If there are no other indications, this Pediatric Page is complete and should be entered into DFS.

This page was completed by:

{See appended electronic signature page}

Regulatory Project Manager

FOR QUESTIONS ON COMPLETING THIS FORM CONTACT THE PEDIATRIC AND MATERNAL HEALTH STAFF at 301-796-0700

(Revised: 10/10/2006)

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

/s/

Joyce Korvick
1/25/2008 06:34:49 PM

Jagjit S Grewal
1/25/2008 11:58:18 AM

Tradename (Fosaprepitant Dimeglumine)
Module 1.3.3 - Debarment Certification

As required by §306(k)(1) of 21 U.S.C. 335a(k)(1), we hereby certify that, in connection with this application, Merck & Co., Inc. did not and will not use in any capacity the services of any person debarred under subsections 306(a) or (b) of the Act.

Vijay K. Tammara, Ph.D.
Director
Regulatory Affairs

March 31, 2006
Date

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

CERTIFICATION: FINANCIAL INTERESTS AND ARRANGEMENTS OF CLINICAL INVESTIGATORS

Form Approved: OMB No. 0910-0396
Expiration Date: February 28, 2006.

TO BE COMPLETED BY APPLICANT

With respect to all covered clinical studies (or specific clinical studies listed below (if appropriate)) submitted in support of this application, I certify to one of the statements below as appropriate. I understand that this certification is made in compliance with 21 CFR part 54 and that for the purposes of this statement, a clinical investigator includes the spouse and each dependent child of the investigator as defined in 21 CFR 54.2(d).

Please mark the applicable checkbox.

☑ (1) As the sponsor of the submitted studies, I certify that I have not entered into any financial arrangement with the listed clinical investigators (enter names of clinical investigators below or attach list of names to this form) whereby the value of compensation to the investigator could be affected by the outcome of the study as defined in 21 CFR 54.2(a). I also certify that each listed clinical investigator required to disclose to the sponsor whether the investigator had a proprietary interest in this product or a significant equity in the sponsor as defined in 21 CFR 54.2(b) did not disclose any such interests. I further certify that no listed investigator was the recipient of significant payments of other sorts as defined in 21 CFR 54.2(f).

Clinical Investigators		
	See Tables C-1 and C-2	
	Fosaprepitant dimeglumine	

☐ (2) As the applicant who is submitting a study or studies sponsored by a firm or party other than the applicant, I certify that based on information obtained from the sponsor or from participating clinical investigators, the listed clinical investigators (attach list of names to this form) did not participate in any financial arrangement with the sponsor of a covered study whereby the value of compensation to the investigator for conducting the study could be affected by the outcome of the study (as defined in 21 CFR 54.2(a)); had no proprietary interest in this product or significant equity interest in the sponsor of the covered study (as defined in 21 CFR 54.2(b)); and was not the recipient of significant payments of other sorts (as defined in 21 CFR 54.2(f)).

☐ (3) As the applicant who is submitting a study or studies sponsored by a firm or party other than the applicant, I certify that I have acted with due diligence to obtain from the listed clinical investigators (attach list of names) or from the sponsor the information required under 54.4 and it was not possible to do so. The reason why this information could not be obtained is attached.

NAME	TITLE
Donald M. Hill	Controller, MRL Financial Services
FIRM/ORGANIZATION Merck & Co., Inc.	
SIGNATURE Donald M. Hill	DATE 3/02/06

Paperwork Reduction Act Statement

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Department of Health and Human Services
Food and Drug Administration
5600 Fishers Lane, Room 14C-03
Rockville, MD 20857

Created by: PSC Media Arts (301) 443-1696

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Form Approved: OMB No. 0910-0396
Expiration Date: February 28, 2006

DISCLOSURE: FINANCIAL INTERESTS AND ARRANGEMENTS OF CLINICAL INVESTIGATORS

TO BE COMPLETED BY APPLICANT

The following information concerning See Table D-1 (*Name of clinical investigator*), who participated as a clinical investigator in the submitted study Fosaprepitant dimeglumine (*Name of clinical study*), is submitted in accordance with 21 CFR part 54. The named individual has participated in financial arrangements or holds financial interests that are required to be disclosed as follows:

Please mark the applicable checkboxes.

☐ any financial arrangement entered into between the sponsor of the covered study and the clinical investigator involved in the conduct of the covered study, whereby the value of the compensation to the clinical investigator for conducting the study could be influenced by the outcome of the study;

☐ any significant payments of other sorts made on or after February 2, 1999 from the sponsor of the covered study such as a grant to fund ongoing research, compensation in the form of equipment, retainer for ongoing consultation, or honoraria;

☐ any proprietary interest in the product tested in the covered study held by the clinical investigator;

☑ any significant equity interest as defined in 21 CFR 54.2(b), held by the clinical investigator in the sponsor of the covered study.

Details of the individual's disclosable financial arrangements and interests are attached, along with a description of steps taken to minimize the potential bias of clinical study results by any of the disclosed arrangements or interests.

NAME	TITLE
Donald M. Hill	Controller, MRL Financial Services
FIRM/ORGANIZATION: Merck & Co., Inc.	
SIGNATURE: Donald M. Hill	DATE: 3/3/06

Paperwork Reduction Act Statement

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number. Public reporting burden for this collection of information is estimated to average 4 hours per response, including time for reviewing instructions, searching existing data sources, gathering and maintaining the necessary data, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information to:

Department of Health and Human Services
Food and Drug Administration
5600 Fishers Lane, Room 14-72
Rockville, MD 20857

Financial Disclosure Information

A. Introduction

In compliance with the U.S. Food and Drug Administration's regulation, *Financial Disclosure by Clinical Investigators,* published 02-Feb-1998 and revised 31-Dec-1998, the following sections detail the requested information concerning the financial interests of and compensation to investigators participating in the covered clinical studies presented in this application.

Investigators meeting the definition of Clinical Investigator (Part 54.2(d)) were requested to complete and return questionnaires related to their financial interest in Merck & Co., Inc. (hereinafter referred to as "Merck") and proprietary interest in the test product. In compliance with the regulatory requirement for the Sponsor to demonstrate "due diligence" (21 CFR Part 54.4), multiple requests for this information were made, when possible, to Clinical Investigators who did not respond. Please note that Merck has not entered into any financial arrangement with our clinical investigators whereby the value of the compensation to the investigator could be affected by the outcome of the study (21 CFR 54.2(a)). Merck Corporate Finance conducted an internal search for all payments that met the definition of "significant payments of other sorts" (21 CFR 54.2(f)) and reported the information, as appropriate. "Significant payments of other sorts" are calculated cumulatively when an investigator is involved in more than one protocol in a submission.

Data from the Clinical Studies outlined in Table A-1 are presented in this application. A summary of the non-covered clinical studies are outlined in Table A-2. The following trials are considered covered clinical studies for the purpose of financial disclosure:

A Two-Part, Placebo-Controlled, In-Clinic Study to Explore the Preliminary Safety, Tolerability, and Efficacy of Intravenous L-758,298 (An NK1 Receptor Antagonist Prodrug of L-754,430) in the Acute Treatment of Migraine (Protocol 003)

For this clinical protocol, the First Patient In (FPI) was 21-Mar-1996 and the Last Patient Out (LPO) was 08-Aug-1996. In compliance with the Financial Disclosure requirements, "significant payments of other sorts" information is not required for this protocol because the completion of the trial (defined as the "Last Patient Out" date) and the one-year period following completion of the trial occurred prior to the February 2, 1999 implementation date for "significant payments of other sorts." The cut-off date for financial information provided by the investigators was 31-Jan-2006.

A Double-Blind, Randomized, Active-Agent (Ondansetron)-Controlled, Single IV Dose Study to Investigate the Safety, Tolerability, Pharmacokinetics, and Efficacy of L-758,298 in Cisplatin-Induced Emesis (Protocol 004)

For this clinical protocol, the First Patient In (FPI) was 16-Apr-1996 and the Last Patient Out (LPO) was 01-Jul-1997. In compliance with the Financial Disclosure requirements, "significant payments of other sorts" information is not required for this protocol because the completion of the trial (defined as the "Last Patient Out" date) and the one-year period following completion of the trial occurred prior to the February 2, 1999 implementation date for "significant payments of other sorts." The cut-off date for financial information provided by the investigators was 31-Jan-2006.

A Double-Blind, Randomized, Active-Agent (Ondansetron Plus Dexamethasone)-Controlled Single IV Dose Study to Investigate the Safety, Tolerability, Plasma Concentrations, and Efficacy of L-758,298 Plus Dexamethasone in Cisplatin-Induced Emesis (Protocol 007)

For this clinical protocol, the First Patient In (FPI) was 20-Jun-1997 and the Last Patient Out (LPO) was 20-Apr-1998. In compliance with the Financial Disclosure requirements, "significant payments of other sorts" information has been reviewed for the time period of 02-Feb-1999 through 20-Apr-1999 and included, as appropriate. The cut-off date for financial information provided by the investigators was 31-Jan-2006.

A Randomized, 3-Part, Intravenous Study of the Safety, Tolerability, Bioequivalence, and Drug Interaction Potential of Final Market Image Formulations of L-758,298 in Young Healthy Subjects (Protocol 012)

For this clinical protocol, the First Patient In (FPI) was 31-Jan-2005 and the Last Patient Out (LPO) was 01-Dec-2005. In compliance with the Financial Disclosure requirements, "significant payments of other sorts" information has been reviewed for the time period of 31-Jan-2005 through 31-Aug-2005 and included, as appropriate. The cut-off date for financial information provided by the investigators was 31-Jan-2006.

A Randomized, Double-Blind, Active Comparator-Controlled, Parallel-Group Study Conducted Under In-House Blinding Conditions, to Examine the Safety and Tolerability of IV MK-0517 for the Prevention of Postoperative Nausea and Vomiting (PONV) (Protocol 015)

For this clinical protocol, the First Patient In (FPI) was 02-Aug-2005 and the Last Patient Out (LPO) was 29-Nov-2005. In compliance with the Financial Disclosure requirements, "significant payments of other sorts" information has been reviewed for the time period of 02-Aug-2005 through 31-Aug-2005 and included, as appropriate. The cut-off date for financial information provided by the investigators was 31-Jan-2006.

Table A-1 Summary of Covered Clinical Trials as Defined by 21 CFR 54.2(e)

Protocol Number	Protocol Title	FPI	LPO	"Payments of Other Sorts" Range
003	A Two-Part, Placebo-Controlled, In-Clinic Study to Explore the Preliminary Safety, Tolerability, and Efficacy of Intravenous L-758,298 (An NK1 Receptor Antagonist Prodrug of L-754,430) in the Acute Treatment of Migraine	21-Mar-1996	08-Aug-1996	N/A
004	A Double-Blind, Randomized, Active-Agent (Ondansetron)-Controlled, Single IV Dose Study to Investigate the Safety, Tolerability, Pharmacokinetics, and Efficacy of L-758,298 in Cisplatin-Induced Emesis	16-Apr-1996	01-Jul-1997	N/A
007	A Double-Blind, Randomized, Active-Agent (Ondansetron Plus Dexamethasone)-Controlled Single IV Dose Study to Investigate the Safety, Tolerability, Plasma Concentrations, and Efficacy of L-758,298 Plus Dexamethasone in Cisplatin-Induced Emesis	20-Jun-1997	20-Apr-1998	02-Feb-1999 Through 20-Apr-1999
012	A Randomized, 3-Part, Intravenous Study of the Safety, Tolerability, Bioequivalence, and Drug Interaction Potential of Final Market Image Formulations of L-758,298 in Young Healthy Subjects	31-Jan-2005	01-Dec-2005	31-Jan-2005 Through 31-Aug-2005
015	A Randomized, Double-Blind, Active Comparator-Controlled, Parallel-Group Study Conducted Under In-House Blinding Conditions, to Examine the Safety and Tolerability of IV MK-0517 for the Prevention of Postoperative Nausea and Vomiting (PONV)	02-Aug-2005	29-Nov-2005	02-Aug-2005 Through 31-Aug-2005

Table A-2 - The following trial is considered a non-covered clinical study for the purpose of financial disclosure:

Table A-2 Summary of Non-Covered Clinical Trial1 CFR 54.2(e)	
Protocol Number	**Protocol Title**
011	A Single Intravenous Rising-Dose Study of the Safety, Tolerability, and Pharmacokinetics of a New Formulation of L-758,298 in Young Healthy Subjects

Table A-3 details the total number of investigators in each of the categories that require reporting as defined in 21 CFR 54.2(a,b,c,f). As it is possible for an investigator to meet the definition for more than one category, the number of investigators in each sub-category may not add up to the total number of investigators.

Table A- 3 Summary of Investigators that Meet the Definition of "Clinical Investigator"		
Investigator Category	**Total Number**	**Comments**
Grand Total Number of Investigators/ Subinvestigators per Protocol and Site	207	Table B-1
Total Number of Investigators/ Subinvestigators Who Are Certified Regarding an Absence of Financial Arrangements per Protocol and Site	164	Table C-1
Total Number of Investigators/ Subinvestigators Not Providing Information and Not Certified per Protocol and Site	42	Table C-2 Investigators no longer at site, unable to obtain information (n=19). Investigators not returning requested information (n=23).
Total Number of Investigators/ Subinvestigators Not Certified Due to "Significant Payments of Other Sorts" or Equity Interest per Protocol and Site	1	Table D-1 Details of payments and equity are listed for the investigators for the protocol in which they participated.
Total Number of Investigators/ Subinvestigators Receiving Payments Based on the Outcome of the Study per Protocol and Site	0	Merck has not entered into any financial arrangements with our clinical investigators whereby the value of the compensation to the investigator could be affected by the outcome of the study.
Total Number of Investigators/ Subinvestigators with Proprietary Interest in the Test Product or Company per Protocol and Site	0	

13 Page(s) Withheld

X Trade Secret / Confidential (b4)

_____ Draft Labeling (b4)

_____ Draft Labeling (b5)

_____ Deliberative Process (b5)

b(6)

ACTION PACKAGE CHECKLIST

BLA # NDA # **22-023** **Cycle I Submission (3/31/06)** **Class II Resubmission (7/27/07)**	BLA STN# NDA Supplement #	If NDA, Efficacy Supplement Type
Proprietary Name: Emend Established Name: fosaprepitant dimeglumine Dosage Form: 115 mg, I.V.		Applicant: Merck & Co., Inc.
RPM: Jagjit Grewal	Division: Gastroenterology Products (HFD-180)	Phone # 301-796-0846

NDAs: NDA Application Type: ☒ 505(b)(1) ☐ 505(b)(2) Efficacy Supplement: ☐ 505(b)(1) ☐ 505(b)(2) (A supplement can be either a (b)(1) or a (b)(2) regardless of whether the original NDA was a (b)(1) or a (b)(2). Consult page 1 of the NDA Regulatory Filing Review for this application or Appendix A to this Action Package Checklist.)	505(b)(2) NDAs and 505(b)(2) NDA supplements: Listed drug(s) referred to in 505(b)(2) application (NDA #(s), Drug name(s)): Provide a brief explanation of how this product is different from the listed drug. ☐ If no listed drug, check here and explain: **Review and confirm the information previously provided in Appendix B to the Regulatory Filing Review. Use this Checklist to update any information (including patent certification information) that is no longer correct.** ☐ Confirmed ☐ Corrected Date:

❖ User Fee Goal Date ❖ Action Goal Date (if different)	January 27, 2008 January 25, 2008
❖ Actions	
• Proposed action	☒ AP ☐ TA ☐ AE ☐ NA ☐ CR
• Previous actions *(specify type and date for each action taken)*	☐ None Approvable action taken on 5/3/07
❖ Advertising *(approvals only)* Note: If accelerated approval (21 CFR 314.510/601.41), advertising must have been submitted and reviewed *(indicate dates of reviews)*	☒ Requested in AP letter ☐ Received and reviewed

❖ Application Characteristics

Review priority: ☒ Standard ☐ Priority
Chemical classification (new NDAs only):

NDAs, BLAs and Supplements:
☐ Fast Track
☐ Rolling Review
☐ CMA Pilot 1
☐ CMA Pilot 2

☐ Orphan drug designation

NDAs: Subpart H
☐ Accelerated approval (21 CFR 314.510)
☐ Restricted distribution (21 CFR 314.520)
Subpart I
☐ Approval based on animal studies

BLAs: Subpart E
☐ Accelerated approval (21 CFR 601.41)
☐ Restricted distribution (21 CFR 601.42)
Subpart H
☐ Approval based on animal studies

NDAs and NDA Supplements:
☐ OTC drug

Other: Prodrug of the currently approved product aprepitant (NDA 21-549).

Other comments:

❖ Application Integrity Policy (AIP)	
• Applicant is on the AIP	☐ Yes ☒ No
• This application is on the AIP	☐ Yes ☒ No
• Exception for review *(file Center Director's memo in* Administrative Documents *section)*	☐ Yes ☐ No
• OC clearance for approval *(file communication in* Administrative Documents *section)*	☐ Yes ☐ Not an AP action

❖ Public communications (approvals only)	
• Office of Executive Programs (OEP) liaison has been notified of action	☒ Yes ☐ No
• Press Office notified of action	☒ Yes ☐ No
• Indicate what types (if any) of information dissemination are anticipated	☐ None ☐ FDA Press Release ☐ FDA Talk Paper ☐ CDER Q&As ☒ Other: FDA Note to Correspondents

❖ Exclusivity	
• NDAs: Exclusivity Summary (approvals only) *(file Summary in* Administrative Documents *section)*	☒ Included
• Is approval of this application blocked by any type of exclusivity?	☒ No ☐ Yes
• NDAs/BLAs: Is there existing orphan drug exclusivity for the "same" drug or biologic for the proposed indication(s)? *Refer to 21 CFR 316.3(b)(13) for the definition of "same drug" for an orphan drug (i.e., active moiety). This definition is NOT the same as that used for NDA chemical classification.*	☒ No ☐ Yes If, yes, NDA/BLA # and date exclusivity expires:
• NDAS: Is there remaining 5-year exclusivity that would bar effective approval of a 505(b)(2) application? *(Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval.)*	☒ No ☐ Yes If yes, NDA # and date exclusivity expires:
• NDAs: Is there remaining 3-year exclusivity that would bar effective approval of a 505(b)(2) application? *(Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval.)*	☒ No ☐ Yes If yes, NDA # and date exclusivity expires:
• NDAs: Is there remaining 6-month pediatric exclusivity that would bar effective approval of a 505(b)(2) application? *(Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval.)*	☒ No ☐ Yes If yes, NDA # and date exclusivity expires:
❖ Patent Information (NDAs and NDA supplements only)	
• Patent Information: Verify that form FDA-3542a was submitted for patents that claim the drug for which approval is sought. If the drug is an old antibiotic, skip the Patent Certification questions.	☒ Verified ☐ Not applicable because drug is an old antibiotic.
• Patent Certification [505(b)(2) applications]: Verify that a certification was submitted for each patent for the listed drug(s) in the Orange Book and identify the type of certification submitted for each patent.	21 CFR 314.50(i)(1)(*i*)(A) ☐ Verified 21 CFR 314.50(i)(1) ☐ (ii) ☐ (iii)
• [505(b)(2) applications] If the application includes a **paragraph III** certification, it cannot be approved until the date that the patent to which the certification pertains expires (but may be tentatively approved if it is otherwise ready for approval).	☐ No paragraph III certification Date patent will expire
• [505(b)(2) applications] For **each paragraph IV** certification, verify that the applicant notified the NDA holder and patent owner(s) of its certification that the patent(s) is invalid, unenforceable, or will not be infringed (review documentation of notification by applicant and documentation of receipt of notice by patent owner and NDA holder). *(If the application does not include any paragraph IV certifications, mark "N/A" and skip to the next section below (*Summary Reviews*)).*	☐ N/A (no paragraph IV certification) ☐ Verified
• [505(b)(2) applications] For **each paragraph IV** certification, based on the questions below, determine whether a 30-month stay of approval is in effect due to patent infringement litigation. Answer the following questions for **each** paragraph IV certification: (1) Have 45 days passed since the patent owner's receipt of the applicant's	☐ Yes ☐ No

notice of certification? (Note: The date that the patent owner received the applicant's notice of certification can be determined by checking the application. The applicant is required to amend its 505(b)(2) application to include documentation of this date (e.g., copy of return receipt or letter from recipient acknowledging its receipt of the notice) (see 21 CFR 314.52(e))).	
*If "**Yes,**" skip to question (4) below. If "**No,**" continue with question (2).*	
(2) Has the patent owner (or NDA holder, if it is an exclusive patent licensee) submitted a written waiver of its right to file a legal action for patent infringement after receiving the applicant's notice of certification, as provided for by 21 CFR 314.107(f)(3)?	☐ Yes ☐ No
*If "**Yes,**" there is no stay of approval based on this certification. Analyze the next paragraph IV certification in the application, if any. If there are no other paragraph IV certifications, skip to the next section below (*Summary Reviews*).* *If "**No,**" continue with question (3).*	
(3) Has the patent owner, its representative, or the exclusive patent licensee filed a lawsuit for patent infringement against the applicant? (Note: This can be determined by confirming whether the Division has received a written notice from the (b)(2) applicant (or the patent owner or its representative) stating that a legal action was filed within 45 days of receipt of its notice of certification. The applicant is required to notify the Division in writing whenever an action has been filed within this 45-day period (see 21 CFR 314.107(f)(2))).	☐ Yes ☐ No
*If "**No,**" the patent owner (or NDA holder, if it is an exclusive patent licensee) has until the expiration of the 45-day period described in question (1) to waive its right to bring a patent infringement action or to bring such an action. After the 45-day period expires, continue with question (4) below.*	
(4) Did the patent owner (or NDA holder, if it is an exclusive patent licensee) submit a written waiver of its right to file a legal action for patent infringement within the 45-day period described in question (1), as provided for by 21 CFR 314.107(f)(3)?	☐ Yes ☐ No
*If "**Yes,**" there is no stay of approval based on this certification. Analyze the next paragraph IV certification in the application, if any. If there are no other paragraph IV certifications, skip to the next section below (*Summary Reviews*).* *If "**No,**" continue with question (5).*	
(5) Did the patent owner, its representative, or the exclusive patent licensee bring suit against the (b)(2) applicant for patent infringement within 45 days of the patent owner's receipt of the applicant's notice of certification? (Note: This can be determined by confirming whether the Division has received a written notice from the (b)(2) applicant (or the patent owner or its representative) stating that a legal action was filed within 45 days of receipt of its notice of certification. The applicant is required to notify the Division in writing whenever an action has been filed within this 45-day period (see 21 CFR 314.107(f)(2)). If no written notice appears in the NDA file, confirm with the applicant whether a lawsuit was commenced	☐ Yes ☐ No

within the 45-day period). *If "**No**," there is no stay of approval based on this certification. Analyze the next paragraph IV certification in the application, if any. If there are no other paragraph IV certifications, skip to the next section below (*Summary Reviews*).* *If "**Yes**," a stay of approval may be in effect. To determine if a 30-month stay is in effect, consult with the Director, Division of Regulatory Policy II, Office of Regulatory Policy (HFD-007) and attach a summary of the response.*	
[redacted]	
❖ Summary Reviews (e.g., Office Director, Division Director) *(indicate date for each review)*	Deputy Division Director: 1/25/08; 5/3/07
❖ BLA approvals only: Licensing Action Recommendation Memo (LARM) *(indicate date)*	N/A
[redacted]	
❖ Package Insert	[redacted]
• Most recent division-proposed labeling (only if generated after latest applicant submission of labeling)	N/A
• Most recent applicant-proposed labeling (only if subsequent division labeling does not show applicant version)	January 25, 2008
• Original applicant-proposed labeling	March 31, 2006
• Other relevant labeling (e.g., most recent 3 in class, class labeling), if applicable	Label for aprepitant included
❖ Patient Package Insert	[redacted]
• Most-recent division-proposed labeling (only if generated after latest applicant submission of labeling)	N/A
• Most recent applicant-proposed labeling (only if subsequent division labeling does not show applicant version)	January 25, 2008
• Original applicant-proposed labeling	March 31, 2006
• Other relevant labeling (e.g., most recent 3 in class, class labeling), if applicable	PPI from aprepitant included
❖ Medication Guide	[redacted]
• Most recent division-proposed labeling (only if generated after latest applicant submission of labeling)	N/A
• Most recent applicant-proposed labeling (only if subsequent division labeling does not show applicant version)	N/A
• Original applicant-proposed labeling	N/A
• Other relevant labeling (e.g., most recent 3 in class, class labeling)	N/A
❖ Labels (**full color** carton and immediate-container labels)	[redacted]
• Most-recent division-proposed labels (only if generated after latest applicant submission)	N/A
• Most recent applicant-proposed labeling	January 25, 2008
❖ Labeling reviews and minutes of any labeling meetings *(indicate dates of reviews and meetings)*	☒ DMETS 12/7/06; 1/3/08 ☐ DSRCS ☒ DDMAC 12/7/06 ☐ SEALD ☒ Other reviews CMC 1/28/08 ☐ Memos of Mtgs

❖ Administrative Reviews (RPM Filing Review/Memo of Filing Meeting; ADRA) *(indicate date of each review)*	RPM Filing Review: 9/29/06
❖ NDA and NDA supplement approvals only: Exclusivity Summary *(signed by Division Director)*	☒ Included
❖ AIP-related documents • Center Director's Exception for Review memo • If AP: OC clearance for approval	
❖ Pediatric Page (all actions)	☒ Included
❖ Debarment certification (original applications only): verified that qualifying language was not used in certification and that certifications from foreign applicants are cosigned by U.S. agent. *(Include certification.)*	☒ Verified, statement is acceptable
❖ Postmarketing Commitment Studies	☐ None
• Outgoing Agency request for post-marketing commitments *(if located elsewhere in package, state where located)*	Email dated 1/16/08
• Incoming submission documenting commitment	1/25/08
❖ Outgoing correspondence (letters including previous action letters, emails, faxes, telecons)	Filing communication: 6/15/06 Information Request: 8/17/06 Information Request: 11/7/06 Tcon Meeting Minutes: 11/16/06 Information Request: 12/5/06 PDUFA Goal Extension: 1/18/07 Information Request: 1/24/07 Information Request: 2/2/07 Information Request: 10/18/07 DDMAC Proposed Ad Launch Comments: 11/26/07 Tcon Meeting Minutes: 11/26/07 Resubmission Ack: 1/7/08 Label Changes Fax: 1/18/08 PMC Agreement: 1/23/08
❖ Internal memoranda, telecons, email, etc.	N/A
❖ Minutes of Meetings	
• Pre-Approval Safety Conference *(indicate date; approvals only)*	N/A
• Pre-NDA/BLA meeting *(indicate date)*	☒ No mtg See Meeting Minutes for IND 48,924 dated 1/12/06
• EOP2 meeting *(indicate date)*	☒ No mtg
• Other (e.g., EOP2a, CMC pilot programs)	Type C meeting for tradename advice: 8/3/06
❖ Advisory Committee Meeting	☒ No AC meeting
• Date of Meeting	N/A
• 48-hour alert or minutes, if available	N/A
❖ Federal Register Notices, DESI documents, NAS/NRC reports (if applicable)	N/A
❖ CMC/Product review(s) *(indicate date for each review)*	4/16/07; 12/13/07
❖ Reviews by other disciplines/divisions/Centers requested by CMC/product reviewer *(indicate date for each review)*	☒ None
❖ BLAs: Product subject to lot release (APs only)	☐ Yes ☐ No

❖ Environmental Assessment (check one) (original and supplemental applications)	
• ☒ Categorical Exclusion *(indicate review date)(all original applications and all efficacy supplements that could increase the patient population)*	From CMC review 4/16/07 (found satisfactory March 2007)
• ☐ Review & FONSI *(indicate date of review)*	
• ☐ Review & Environmental Impact Statement *(indicate date of each review)*	
❖ NDAs: Microbiology reviews (sterility & apyrogenicity) *(indicate date of each review)*	3/27/07; 12/17/07 ☐ Not a parenteral product
❖ Facilities Review/Inspection	
❖ NDAs: Facilities inspections (include EER printout)	Date completed: 5/10/06 ☒ Acceptable ☐ Withhold recommendation

❖ BLAs: Facility-Related Documents • Facility review *(indicate date(s))* • Compliance Status Check (approvals only, both original and supplemental applications) *(indicate date completed, must be within 60 days prior to AP)*	☐ Requested ☐ Accepted ☐ Hold
❖ NDAs: Methods Validation	☒ Completed: 7/27/07 ☐ Requested ☐ Not yet requested ☐ Not needed
[illegible]	
❖ Pharm/tox review(s), including referenced IND reviews *(indicate date for each review)*	1/17/07; 1/18/08
❖ Review(s) by other disciplines/divisions/Centers requested by P/T reviewer *(indicate date for each review)*	☒ None
❖ Statistical review(s) of carcinogenicity studies *(indicate date for each review)*	☒ No carc NAI
❖ ECAC/CAC report/memo of meeting	N/A
❖ Nonclinical inspection review Summary (DSI)	☒ None requested

❖ Clinical review(s) *(indicate date for each review)*	4/25/07; 1/16/08
❖ Financial Disclosure reviews(s) or location/date if addressed in another review	- See application - See page 16 of 32 in Clinical review dated 4/25/07
❖ Clinical consult reviews from other review disciplines/divisions/Centers *(indicate date of each review)*	☐ None QTc – complete 4/24/07 DCRP – complete 12/17/07
❖ Microbiology (efficacy) reviews(s) *(indicate date of each review)*	☒ Not needed
❖ Safety Update review(s) *(indicate location/date if incorporated into another review)*	N/A
❖ Risk Management Plan review(s) (including those by OSE) *(indicate location/date if incorporated into another review)*	N/A
❖ Controlled Substance Staff review(s) and recommendation for scheduling *(indicate date of each review)*	☒ Not needed
❖ DSI Inspection Review Summary(ies) *(include copies of DSI letters to investigators)*	☐ None requested
• Clinical Studies	N/A
• Bioequivalence Studies	12/8/06
• Clin Pharm Studies	N/A
❖ Statistical Review(s) *(indicate date for each review)*	☒ None NAI
❖ Clinical Pharmacology review(s) *(indicate date for each review)*	☐ None 4/30/07; 1/25/08

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

/s/

Jagjit S Grewal
2/21/2008 11:05:00 AM

Grewal, Jagjit

From: Andrew, Nicholas W. [nicholas_andrew@merck.com]
Sent: Monday, January 21, 2008 10:28 AM
To: Grewal, Jagjit
Subject: RE: NDA 22-023 Emend - Postmarketing Commitment

Jagjit,

Merck agrees to a postmarketing commitment for NDA 22,023 to further characterize the effects of fosaprepitant on blood pressure. To address this commitment, Merck plans to provide a comprehensive review of the blood pressure data from our clinical programs with aprepitant and fosaprepitant. The analysis will be provided by [redacted] and will include available data from approximately 3265 patients exposed to either fosaprepitant (N≈275) or aprepitant (N≈2990), regardless of dose, in completed clinical studies, the clinical study reports for which were submitted previously to FDA. This analysis will include ~475 patients/subjects enrolled in Phase I Clinical Pharmacology studies, ~1800 patients in Phase II and III CINV and PONV clinical studies with blood pressure measurements within a 24-hour dosing period, and ~990 patients with blood pressure measurements while being dosed at steady state (e.g., in the discontinued depression development program). b(4)

Kind Regards,

Nick Andrew

Merck Research Laboratories

Worldwide Regulatory Affairs

Phone 732-594-5585

Fax 732-594-5235

From: Grewal, Jagjit [mailto:Jagjit.Grewal@fda.hhs.gov]
Sent: Wednesday, January 16, 2008 5:35 PM
To: Andrew, Nicholas W.
Cc: Grewal, Jagjit
Subject: NDA 22-023 Emend - Postmarketing Commitment

Nick,

As discussed in this afternoon's teleconference, please confirm Merck's agreement with the Agency's requested Phase IV postmarketing commitment to better characterize the effects of fosaprepitant upon blood pressure.

Additionally, we will await Merck's outline of the data to be provided in support of this postmarketing commitment. Thank you.

Jagjit Grewal, MPH
Regulatory Project Manager
Division of Gastroenterology Products
CDER/OND/ODE III
Food & Drug Administration

Phone: (301) 796-0846
Fax: (301) 796-9905
Email: Jagjit.Grewal@fda.hhs.gov

Notice: This e-mail message, together with any attachments, contains information of Merck & Co., Inc. (One Merck Drive, Whitehouse Station, New Jersey, USA 08889), and/or its affiliates (which may be known outside the United States as Merck Frosst, Merck Sharp & Dohme or MSD and in Japan, as Banyu - direct contact information for affiliates is available at http://www.merck.com/contact/contacts.html) that may be confidential, proprietary copyrighted and/or legally privileged. It is intended solely for the use of the individual or entity named on this message. If you are not the intended recipient, and have received this message in error, please notify us immediately by reply e-mail and then delete it from your system.

"EMF <fda.hhs.gov>" made the following annotations.

This message was sent by Merck across the Internet in encrypted format and was succe

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/s/

Jagjit S Grewal
1/23/2008 03:53:32 PM
CSO

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Drug Evaluation ODE III

FACSIMILE TRANSMITTAL SHEET

DATE: January 18, 2008

To: Nicholas Andrew Associate Director MRL Regulatory Affairs	**From:** Jagjit Grewal, MPH Regulatory Project Manager
Company: Merck Research Laboratories	Division of Gastroenterology Products
Fax number: (732) 594-5235	**Fax number:** 301-796-9905
Phone number: (732) 594-5585	**Phone number:** 301-796-0846

Subject: NDA 22-023 Labeling Change Recommendations

Total No. of pgs including cover: 27

DOCUMENT TO BE MAILED? NO

Please find enclosed the FDA's recommendations for changes to the proposed labeling for NDA 22-023. Feel free to contact me with any questions.

Enclosed:

1) Annotated PI Labeling (18 pages)
2) Annotated PPI Labeling (3 pages)
3) FDA Recommendations for Proposed Carton Labels (1 pages summary)
4) Annotated Proposed Trade Carton 115mg-IV Vial, 1x (2 pages)
5) Annotated Proposed Trade Carton 115mg-IV Vial, 10x (2 pages)

THIS DOCUMENT IS INTENDED ONLY FOR THE USE OF THE PARTY TO WHOM IT IS ADDRESSED AND MAY CONTAIN INFORMATION THAT IS PRIVILEGED, CONFIDENTIAL, AND PROTECTED FROM DISCLOSURE UNDER APPLICABLE LAW.

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26 Page(s) Withheld

_____ Trade Secret / Confidential (b4)

X Draft Labeling (b4)

X Draft Labeling (b5)

_____ Deliberative Process (b5)

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/s/

Jagjit S Grewal
1/18/2008 11:50:53 AM
CSO

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 22-023

Merck & Co., Inc.
Attention: Nicholas Andrew
Associate Director, MRL Regulatory Affairs
P.O. Box 1000, UG2CD-48
North Wales, PA 19454

Dear Mr. Andrew:

We acknowledge receipt on July 27, 2007 of your July 27, 2007 resubmission to your new drug application for Emend (fosaprepitant dimeglumine) for Injection, 115 mg.

We consider this a complete, class 2 response to our May 3, 2007 action letter. Therefore, the user fee goal date is January 27, 2008.

All applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred. We note that you have not fulfilled the requirements. We acknowledge receipt of your request for a waiver of pediatric studies for this application. Once the application has been filed we will notify you whether we have waived the pediatric study requirement for this application.

If you have any question, call Jagjit Grewal, Regulatory Project Manager, at (301) 796-0846.

Sincerely,

{See appended electronic signature page}

Brian Strongin, R.Ph., M.B.A.
Chief, Project Management Staff
Division of Gastroenterology Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

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/s/

Brian Strongin
1/7/2008 01:06:48 PM

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

IND 48,924
NDA 22-023

Merck & Co., Inc.
Attention: Vijay Tammara, Ph.D.
Director, Regulatory Affairs
P.O. Box 1000, UG2CD-48
North Wales, PA 19454-1099

Dear Dr. Tammara:

We refer to your February 28, 2006 correspondence, received March 1, 2006 requesting a type C meeting (teleconference) to discuss the Division's February 1, 2006 letter containing tradename advice for fosaprepitant dimeglumine for injection.

The date scheduled for this meeting was to have been July 6, 2006.

We further refer to our conversations and emails of July 6, 2006 to discuss your response to our July 5, 2006 email which contained our pre-meeting draft responses.

We also refer to your letter submitted July 6, 2006 containing your responses to our July 5, 2006 email and July 6, 2006 pre-meeting clarifying conversations.

We acknowledge your decision to accept our written and agreed-upon responses in lieu of the July 6, 2006 teleconference.

Therefore, the attached responses, represent the official minutes of the scheduled and canceled July 6, 2006 teleconference.

If you have any questions, call me at 301-796-0991.

Sincerely,

{See appended electronic signature page}

Betsy Scroggs, Pharm. D.
Regulatory Health Project Manager
Division of Gastroenterology Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

Enclosure:

IND 48,924 Fosaprepitant Dimeglmine
NDA 22-023

Background: Fosaprepitant dimeglumine for injection, a pro-drug of aprepitant (EMEND™), is a neurokinin (NK-1) receptor antagonist investigated for use in chemotherapy-induced nausea and vomiting (CINV). EMEND® is approved for use in post-operative nausea and vomiting (PONV) and moderately and highly emetogenic chemotherapy-induced nausea and vomiting (CINV/MEC) and (CINV/HEC) respectively.

NDA 21-549 for EMEND® (aprepitant) Capsules, 80 mg and 125 mg was approved March 26, 2003 for use in CINV/HEC.

NDA 21-549/S-008 was approved October 28, 2005 for use in CINV/MEC.

NDA 21-549/S-010 was approved June 30, 2006 for the treatment of post-operative nausea and vomiting (PONV).

Under IND 48,924 (fosaprepitant dimeglumine) the firm submitted a February 28, 2006 meeting request to discuss FDA's February 1, 2006 requested tradename advice.

NDA 22-023, for fosaprepitant dimeglumine was submitted March 31, 2006.

The date scheduled for the requested meeting under IND 48,924 was to have been July 6, 2006. The firm canceled the meeting based on FDA's emailed July 5, 2006 pre-meeting draft responses and the July 6, 2006 clarifying emails and telephone conversations between Dr. Tammara and Dr. Scroggs. The firm followed with a July 6, 2006 submission containing the agreed-upon responses and canceled the meeting.

The following discussion points are listed in a question and answer format.

Discussion Points:

Question: Based on MRL's responses to the FDA's February 1, 2006 letter, does the Agency concur that EMEND® IV is the most appropriate trade name for Fosaprepitant Dimeglumine. b(4)

FDA Response sent to MRL via email July 5, 2006 : No. However, the following may be acceptable:

EMEND® (fosaprepitant dimeglumine for injection).

MRL Response sent to FDA via email July 6, 2006 and submitted to the NDA: MRL proposes the following:

EMEND®
(fosaprepitant dimeglumine)
for Injection

In addition, we have the following requests for information and recommendations.

1. Since Fosaprepitant Dimeglumine is given as 115 mg intravenous injection on day 1 and is followed by oral aprepitant on days 2 and 3, we have concerns about potential medication errors. Consequently, please send us a proposal for 1) a risk management plan (RMP), and 2) an educational program for healthcare professionals to be implemented at the launch of this product.

   MRL Response sent to FDA via email July 6, 2006 and submitted to the NDA:
   MRL proposes the following:

   b(4)

2. Do you have plans to develop an intravenous formulation for the day 2 and 3 (80 mg) dose as well?

   MRL Response sent to FDA via email July 6, 2006 and submitted to the NDA: b(4)

Meeting Chair: Dr. Hugo Gallo Torres
Date: August 3, 2006

Meeting Recorder: Dr. Betsy Scroggs Betsy Scroggs
Date: August 3, 2006

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/s/

Betsy Scroggs
8/3/2006 03:46:33 PM

MEMORANDUM OF MEETING MINUTES

MEETING DATE: November 9, 2007

TIME: 1:00PM - 2:00PM

LOCATION: FDA/CDER
White Oak Building #22
10903 New Hampshire Ave.
Silver Spring, MD 20993

APPLICATION: NDA 22-023

DRUG NAME: Fosaprepitant Dimeglumine for Injection

TYPE OF MEETING: Teleconference

MEETING CHAIR: Anastasia Lolas, M.S.

MEETING RECORDER: Jagjit Grewal

FDA ATTENDEES:

Anastasia Lolas, M.S.	Microbiology Reviewer
Brian Strongin, R.Ph MBA	Chief, Project Management Staff, Div. of Gastroenterology Products
Jagjit Grewal, MPH	Regulatory Project Manager, Div. of Gastroenterology Products

EXTERNAL CONSTITUENT ATTENDEES:

Nicholas Andrew	Associate Director	Regulatory Affairs
Charlotte Merritt	Senior Director	Regulatory Affairs
John Curran	Director	RAS-CMC
Cathy Hoath	Associate Director	RAS-CMC
Bret Duersch Ph. D.	Principal Analytical Chemist	Pharm. Analytical Chemistry
Cheryl Moser	Research Fellow	Pharm. Analytical Chemistry

BACKGROUND:
The agency issued a letter dated October 18, 2007 to Merck & Co., Inc, requesting data summaries of microbial studies that support a 24-hour holding time for the reconstituted and diluted product in the infusion bag. A 4-hour holding time at room temperature is acceptable without any data.

In a response letter dated November 1, 2007, Merck indicated that "Chemical stability data from reconstituted drug product support storage for up to 24 hours at room temperature. This 24 hour storage time is in accordance with USP<797> Pharmaceutical Compounding – Sterile Preparations, which states, ...in the absence of a passing sterility test, the storage periods cannot exceed the following time periods: before administration, the CSPs [compounded sterile preparations] are properly stored and are exposed for not more than 24 hours at controlled room temperature..., for not more than 3 days at a cold temperature..., and for 45 days in solid frozen state at -20°C or colder."

Subsequently, a teleconference was scheduled for November 9, 2007 between the FDA and Merck & Co., Inc. to discuss the issue further.

MEETING OBJECTIVE:
To clarify and discuss the FDA request for microbial studies that support a 24-hour holding time.

DISCUSSION POINTS:
The FDA indicated that the USP guidance represents minimal requirements. Additionally, the high potential of microorganism growth during the 24 hours allowed for storage due to the high amount of lactose in the drug product warranted a study.

Merck requested input on the type of data and study that would address the FDA's recommendation. The FDA stated that the reconstituted fosaprepitant dimeglumine intravenous solution should be inoculated with microbes and the growth is to be followed over time. The FDA would be concerned if exponential growth and proliferation was observed. It was not conveyed at this meeting the specific quantifiable limit of growth that the FDA would consider as acceptable.

Merck asked if it would be beneficial to conduct a microbial growth study at a lower storage temperature of 2°C-8°C. It was also asked what the acceptable holding time may be at this lower temperature range. The FDA responded that it may be beneficial to conduct this study, and an 8-12 hour limit was suggested noting that it is difficult to propose a limit without data.

Merck will evaluate the teleconference discussion and provide a response to the FDA within 1 week.

POST MEETING UPDATES:

- Merck submitted a response dated November 16, 2007 which indicated their plans to conduct a microbial assessment study as requested by the agency. The results from the study are expected to be provided to the FDA in mid-December. This submission also included Merck's meeting minutes of the November 9, 2007 teleconference.

- An email was sent to Merck on November 16, 2007 to clarify the FDA's position on a quantifiable limit in conducting the microbial growth studies. The agency considers as growth a 0.5 log increase.

- An email was sent to Merck on November 21, 2007 to provide additional comments regarding the agreed upon microbial growth assessment study. It was conveyed that the product solution needs to be inoculated with approximately 100 CFU and samples taken to determine microorganism numbers at initial time and after 4, 8, 12, 18, 24 and 36 hours.

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/s/

Jagjit S Grewal
11/26/2007 09:37:01 AM
CSO

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

REQUEST FOR CONSULTATION

TO *(Division/Office)*:
CDER OSE CONSULTS

FROM: Jagjit Grewal, RPM HFD-180
WO22, RM 5109
Division of Gastroenterology Products (DGP)

DATE	IND NO.	NDA NO.	TYPE OF DOCUMENT	DATE OF DOCUMENT
November 16, 2007		22-023	NDA	July 27, 2007

NAME OF DRUG	PRIORITY CONSIDERATION	CLASSIFICATION OF DRUG	DESIRED COMPLETION DATE
Fosaprepitant Dimeglumine for injection		Antiemetic	December 17, 2007

NAME OF FIRM: Merck and Company, 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)*: **Trade name review**

II. BIOMETRICS

STATISTICAL EVALUATION BRANCH

- ☐ TYPE A OR B NDA REVIEW
- ☐ END OF PHASE II MEETING
- ☐ CONTROLLED STUDIES
- ☐ PROTOCOL REVIEW
- ☐ OTHER (SPECIFY BELOW):

STATISTICAL APPLICATION BRANCH

- ☐ 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: Please review for trade name (Emend) and please review labeling. This submission dated July 27, 2007 is a resubmission and can be found in EDR at \\CDSESUB1\EVSPROD\NDA022023\0018.

The initial submission for this NDA is dated March 31, 2006 and can be found in EDR at \\CDSESUB1\EVSPROD\NDA022023\0000. DMETS previous review of this trade name by Linda Wisniewski dated December 7, 2006 found the trade name to be acceptable. The approval of this NDA was delayed beyond 90 days from DMETS intial review. Therefore, a re-eveluation of the trade name is being requested.

PDUFA DATE: 1/27/08
ATTACHMENTS: Draft Package Insert, Container and Carton Labels
CC: Archival IND/NDA 22-023
HFD-180/Division File
HFD-180/RPM

HFD-180/Reviewers and Team Leaders	
NAME AND PHONE NUMBER OF REQUESTER Jagjit Grewal (301) 796-0846	METHOD OF DELIVERY (Check one) ☒ DFS ONLY ☐ MAIL ☐ HAND
SIGNATURE OF RECEIVER	SIGNATURE OF DELIVERER

5/28/05

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/s/

Jagjit S Grewal
11/16/2007 05:34:59 PM

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

REQUEST FOR CONSULTATION

TO *(Office/Division)*: Division of Cardiovascular and Renal Products (DCRP)

FROM *(Name, Office/Division, and Phone Number of Requestor)*:
Jagjit Grewal (6-0846); HFD-180
RPM
Division of Gastroenterology Products (DGP)
WO Bldg #22 5109

DATE	IND NO.	NDA NO.	TYPE OF DOCUMENT	DATE OF DOCUMENT
November 16, 2007		22-023	NDA	July 27, 2007

NAME OF DRUG	PRIORITY CONSIDERATION	CLASSIFICATION OF DRUG	DESIRED COMPLETION DATE
Emend (fosaprepitant dimeglumine) for Injection	High	Aniemetic	December 17, 2007

NAME OF FIRM: Merck & Company, 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 2a MEETING
- ☐ END-OF-PHASE 2 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

- ☐ PRIORITY P NDA REVIEW
- ☐ END-OF-PHASE 2 MEETING
- ☐ CONTROLLED STUDIES
- ☐ PROTOCOL REVIEW
- ☐ OTHER (SPECIFY BELOW):
- ☐ CHEMISTRY REVIEW
- ☐ PHARMACOLOGY
- ☐ BIOPHARMACEUTICS
- ☐ OTHER (SPECIFY BELOW):

III. BIOPHARMACEUTICS

- ☐ DISSOLUTION
- ☐ BIOAVAILABILTY STUDIES
- ☐ PHASE 4 STUDIES
- ☐ DEFICIENCY LETTER RESPONSE
- ☐ PROTOCOL - BIOPHARMACEUTICS
- ☐ IN-VIVO WAIVER REQUEST

IV. DRUG SAFETY

- ☐ PHASE 4 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
- ☐ NONCLINICAL

COMMENTS / SPECIAL INSTRUCTIONS: Merck Research Laboratories submitted a new NDA (NDA 22-023/000, Fosaprepitant for injection) for the prevention of chemotherapy-induced nausea and vomiting. During our review of this submission dated July 27, 2007, we found that the new product (an I.V. form of Emend®) potentiated diltiazem effects on the reduction of blood pressure in hypertensive patients (Study 011, PK). In some patients, the individual systolic pressures were decreased by up to 49 mg Hg; in others, the diastolic pressures decreased by up to 28 mg Hg. According to the report, there was no clinically meaningful PR prolongation or change in heart rate. We would appreciate your comments on the blood pressure changes with the combination of fosaprepitant and diltiazem (Study 011).

The sponsor's study submission can be found in EDR at \\CDSESUB1\EVSPROD\NDA022023\0018

Additionally, a copy of the July 27, 2007 submission and clinical study synopsis will be emailed to Devi Kozeli.	
SIGNATURE OF REQUESTOR Jagjit Grewal	METHOD OF DELIVERY (Check one) ☒ DFS ☒ EMAIL ☐ MAIL ☐ HAND
PRINTED NAME AND SIGNATURE OF RECEIVER	PRINTED NAME AND SIGNATURE OF DELIVERER

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/s/

Jagjit S Grewal
11/16/2007 03:47:44 PM

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

REQUEST FOR CONSULTATION

TO *(Office/Division)*: Division of Cardiovascular and Renal Products (DCRP)	FROM *(Name, Office/Division, and Phone Number of Requestor)*: Jagjit Grewal (6-0846); HFD-180 RPM Division of Gastroenterology Products (DGP) WO Bldg #22 5109

DATE	IND NO.	NDA NO.	TYPE OF DOCUMENT	DATE OF DOCUMENT
November 16, 2007		22-023	NDA	July 27, 2007

NAME OF DRUG	PRIORITY CONSIDERATION	CLASSIFICATION OF DRUG	DESIRED COMPLETION DATE
Emend (fosaprepitant dimeglumine) for Injection	High	Aniemetic	December 17, 2007

NAME OF FIRM: Merck & Company, Inc.

REASON FOR REQUEST

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- ☐ NEW CORRESPONDENCE
- ☐ DRUG ADVERTISING
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- ☐ RESUBMISSION
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- ☐ LABELING REVISION
- ☐ ORIGINAL NEW CORRESPONDENCE
- ☐ FORMULATIVE REVIEW
- ☒ OTHER *(SPECIFY BELOW)*:

II. BIOMETRICS

- ☐ PRIORITY P NDA REVIEW
- ☐ END-OF-PHASE 2 MEETING
- ☐ CONTROLLED STUDIES
- ☐ PROTOCOL REVIEW
- ☐ OTHER (SPECIFY BELOW):
- ☐ CHEMISTRY REVIEW
- ☐ PHARMACOLOGY
- ☐ BIOPHARMACEUTICS
- ☐ OTHER (SPECIFY BELOW):

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The sponsor's study submission can be found in EDR at \\CDSESUB1\EVSPROD\NDA022023\0018

Additionally, a copy of the July 27, 2007 submission and clinical study synopsis will be emailed to Devi Kozeli.	
SIGNATURE OF REQUESTOR Jagjit Grewal	METHOD OF DELIVERY (Check one) ☒ DFS ☒ EMAIL ☐ MAIL ☐ HAND
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Jagjit S Grewal
11/16/2007 03:47:44 PM

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 22-023

INFORMATION REQUEST LETTER

Merck & Co., Inc.
Attention: Vijay Tammara, Ph.D.
Director, Regulatory Affairs
P.O. Box 1000, UG2CD-48
North Wales, PA 19454

Dear Dr. Tammara:

Please refer to your March 31, 2006 new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Emend (fosaprepitant dimeglumine) for Injection.

We also refer to your submission dated July 27, 2007.

We are reviewing the Microbiology section of your submission and have the following comments and information requests:

- The proposal to keep the reconstituted product in the infusion bag for 24 hours at room temperature is not acceptable.
- Please submit data summaries of microbial growth studies that support a 24-hour holding time.
- A 4-hour holding time at room temperature is acceptable without any data.

We request a prompt written response in order to continue our evaluation of your NDA.

If you have any questions, please call Chantal Phillips, Regulatory Project Manager, at 301-796-2259.

Sincerely,

{See appended electronic signature page}

Brian Strongin, R.Ph., M.B.A.
Chief, Project Management Staff
Division of Gastroenterology Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

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/s/

Brian Strongin
10/18/2007 04:37:28 PM

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

INFORMATION REQUEST LETTER

NDA 22-023

Merck & Co., INC
Attn: Vijay K Tammara, Ph.D.
Director, Regulatory Affairs
Sumneytown Pike, P.O. Box 4, BLA-20
West Point, PA 19486

Dear Dr. Tammara:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Fosaprepitant Dimeglumine Injection.

We are reviewing the clinical pharmacology section of your submission and have the following comments and information requests:

- Dexamethasone dose is reduced 50% when oral Emend is used for chemotherapy induced nausea and vomiting (CINV) as the latter is a CYP3A4 inhibitor. There are no data provided in your marketing application to support this dexamethasone dose when fosaprepitant I.V. 115 mg is coadministered. Please address this concern.

We request a prompt written response in order to continue our evaluation of your NDA.

As you are aware, the Prescription Drug User Fee Act Goal date is approaching. Please respond to this Information Request in a timely manner in order for us to proceed with the review of your NDA.

If you have any questions, call Giuseppe Randazzo, Project Manager, at (301) 796-0980.

Sincerely,

{See appended electronic signature page}

Joyce Korvick M.D. M.P.H.
Deputy Director
Division of Gastroenterology Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

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/s/

Joyce Korvick
2/2/2007 04:28:38 PM

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

PDUFA GOAL DATE EXTENSION

NDA 22-023

Merck & Co., Inc.
Attn: Vijay K. Tammara
Director Regulatory Affairs
Sumneytown Pike, P.O. Box 4, BLA-20
West Point, PA 19486

Dear Vijay Tammara:

Please refer to your March 31, 2006 new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Fosaprepitant Dimeglumine Injection.

On December 7, 2006, we received your December 07, 2006 major amendment to this application. The receipt date is within three months of the user fee goal date. Therefore, we are extending the goal date by three months to provide time for a full review of the submission. The extended user fee goal date is May 03, 2007.

If you have questions, call me at (301)-796-0980.

Sincerely,

{See appended electronic signature page}

Giuseppe Randazzo
Project Manager
Division of Gastroenterology Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

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/s/

Giuseppe Randazzo
1/18/2007 08:33:50 AM

MEMORANDUM

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

DATE: December 6, 2006

TO: Mary Dempsey
Office of Safety and Epidemiology (OSE)
Tel: (301) 796-0147
Room 4326

FROM: Giuseppe Randazzo
Division of Gastroenterology Products (DGP)
Tel: (301) 796-0980 Fax: (301) 796-9905
Email: Giuseppe.Randazzo@cder.fda.gov

SUBJECT: **Removal of consult request**
NDA 22-023
Emend
(fosaprepitant dimeglumine)
For Injection

On October 17, 2006 we (Division of Gastroenterology Products) submitted a consult request to Mary Dempsey at the Office of Safety and Epidemiology (OSE) to review [redacted] b(4)

[redacted] b(5)

After speaking with OSE and upon further review, DGP and OSE agree with the sponsor's statements regarding [redacted]

DGP is officially withdrawing our consult request from OSE.

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/s/

Giuseppe Randazzo
12/6/2006 02:13:07 PM
CSO

Hugo Gallo Torres
12/6/2006 02:47:03 PM
MEDICAL OFFICER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

INFORMATION REQUEST LETTER

NDA 22-023

Merck & Co., Inc.
Attention: Vijay K. Tammara
Director Regulatory Affairs
Sumneytown Pike, P.O. Box 4, BLA-20
West Point, PA 19486

Dear Vijay Tammara:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for fosaprepitant dimeglumine.

We also refer to your submission dated March 31, 2006.

We are reviewing the clinical biopharmacology sections of your submission and have the following comments and information requests. We request a prompt written response in order to facilitate our review of the QT study (P016L1) and continue our evaluation of your NDA.

Please provide two datasets, one for fosaprepitant/aprepitant and one for moxifloxacin, in the following specified formats. The datasets should be submitted as a SAS transport files (*.xpt). Please provide in a Define.pdf file a description of each data item. Additionally, be sure to maintain and flag in your datasets any measurements and/or subjects that have been **excluded from the analysis**.

The dataset should include the following column headings: Subject ID, drug, time (hours postdose), RR, QT, QTc, dQTc (baseline adjusted QTc), ddQTc (baseline-adjusted, placebo corrected QTc), drug conc, covariates (age, gender, etc). If QT measurements at each time point were obtained in duplicates or triplicates, provide the mean values. For example:

ID	Drug	Time	Dose	RR	QT	QTC		DQTC	DDQTC	CONC	Covariates
Subject #						QTcF mean	QTci mean				

Comments:

1. ID – Patient number should be numeric and unique
2. All RR, QT, QTc values should be in msec units. If measured in duplicates or triplicates, please provided the mean values here.

3. CONC- Pharmacokinetic concentration should be given in mass units/mL units. Please identify any concentrations that are below the limit of quantification.
4. Also please submit a detailed description of the column headers
5. Repeat patient specific information (covariate) at all records (Weight, Age etc.). If the covariate is time-varying (DTVC in the following), include against appropriate time record. For example:

ID	Drug	Time	.....	.....	WT	AGE	DTVC	.....
1	Moxi	0	.....	.....	70	24	19	.....
1	Moxi	0.25	.....	.....	70	24	19	.....
1	Moxi	0.5	.....	.....	70	24	22	.....

If you have any questions, call Giuseppe Randazzo, Regulatory Project Manager, at (301) 796-0980.

Sincerely,

{See appended electronic signature page}

CAPT E. Dennis Bashaw, Pharm.D.
Director, Div. of Clinical Pharmacology III
Office of Clinical Pharmacology
U.S. Food and Drug Administration

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/s/

Dennis Bashaw
12/5/2006 09:07:32 AM

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Drug Evaluation ODE III

FACSIMILE TRANSMITTAL SHEET

DATE: November 16, 2006

To: Vijay Tammara	**From:** Giuseppe Randazzo
Company Merck Co., Inc.	Division of Gastroenterology Products
Fax number: 267-305-6406	**Fax number:** 301 796 9905
Phone number: 267-305-6713	**Phone number:** 301 796 0980

Subject: NDA 22-023

Total pages with cover: 5

DOCUMENT TO BE MAILED? NO

Comments:

Dear Dr. Tammara.

The attached copy of the teleconference minutes will serve as the official meeting minutes.

If you have any questions or concerns please contact me.

Thank you
Giuseppe Randazzo

NDA 22-023

Merck & Co., Inc
Attn: Dr. Vijay Tammara
Director Regulatory Associate
PO Box 1000, UG2CD-48
North Wales PA 19454-1099

Dear Dr. Tammara:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Fosaprepitant Dimeglumine for Injection.

We also refer to the teleconference among representatives from Merck & Co., Inc. and the FDA on November 07, 2006. The purpose of the meeting was to clarify a few questions from a Chemistry, Manufacturing and Controls (CMC) perspective.

The official minutes of that meeting are enclosed. You are responsible for notifying us of any significant differences in understanding regarding the meeting outcomes.

If you have any questions, call me at (301) 796-0980.

Sincerely,

{See appended electronic signature page}

Giuseppe Randazzo
Regulatory Project Manager
Division of Gastroenterology Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

Enclosure

MEMORANDUM OF MEETING MINUTES

MEETING DATE:	November 07, 2006
TIME:	11:00 am – 12:00 pm
LOCATION:	FDA/CDER White Oak Building #22 10903 New Hampshire Ave. Silver Spring, MD 20993
APPLICATION:	NDA 22-023
DRUG NAME:	Fosaprepitant Dimeglumine for Injection
TYPE OF MEETING:	Teleconference
MEETING CHAIR:	Marie Kowblansky
MEETING RECORDER:	Giuseppe Randazzo

FDA ATTENDEES:

Marie Kowblansky, Ph.D.	Pharmaceutical Assessment Lead, **ONDQA Pre-Marketing Assessment Division II**
Julia Pinto, Ph.D.	Chemistry Reviewer, ONDQA Premarketing Assessment Division II
Giuseppe Randazzo	Regulatory Project Manager, Div. of Gastroenterology Products

EXTERNAL CONSTITUENT ATTENDEES:

Joe Arena, Ph.D.	Senior Director	Regulatory Affairs
Hite Baker	Senior Principal Engineer	Sterile Process Eng
Abizer Bookwala, M.S.	Regulatory Manager	Regulatory Affairs
William Bowen	Director	Analytical Pharm - GPC
John Curran	Director	RAS-CMC
Thomas Dowling, Ph.D.	Senior Director	Analytical API - GPC
Brett Duersch, Ph. D.	Research Fellow	Analytical Pharm - GPC
Cathy Hoath	Sr. Regulatory Scientist	RAS-CMC
Daniel Kumke	Sr. Research Fellow	Chem Process Dev- GPC
Tom Lapinas, Ph. D.	Director	New Products Mgmt
Gail Murphy, Ph. D.	Executive Director	Clinical Pharmacology
Jiri Placek, Ph. D.	Sr. Investigator	Pharm - GPC
Cindy Starbuck, Ph. D.	Director	Chem Process Dev – GPC
Vijay Tammara, Ph. D.	Director	Regulatory Affairs

BACKGROUND:
On October 17, 2006 we emailed Dr. Vijay Tammara of Merck & Co., Inc. requesting a teleconference (tcon) to clarify 2 CMC issues. Dr. Tammara asked that the tcon be delayed due to information they wish to submit in a background package. Merck submitted a general correspondence/background package on October 27, 2006 asking for FDA feedback on the following:

Merck's Research Laboratories (MRL) proposes to:

1.
2.
3.

b(4)

4.

We agreed to have the tcon on November 07, 2006.

MEETING OBJECTIVES:
The purpose of the meeting was to clarify our 2 Chemistry, Manufacturing and Controls (CMC) issues:

1.
2.

b(4)

DISCUSSION POINTS:

1.

b(4)

__1__ Page(s) Withheld

__X__ Trade Secret / Confidential (b4)

_____ Draft Labeling (b4)

_____ Draft Labeling (b5)

_____ Deliberative Process (b5)

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/s/

Giuseppe Randazzo
11/16/2006 04:40:23 PM
CSO

Marie Kowblansky
11/16/2006 05:05:50 PM
CHEMIST

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

INFORMATION REQUEST LETTER

NDA 22-023

Merck & Co., INC
Attn: Vijay K Tammara, Ph.D.
Director, Regulatory Affairs
Sumneytown Pike, P.O. Box 4, BLA-20
West Point, PA 19486

Dear Dr. Tammara:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for fosaprepitant dimeglumine.

We are reviewing the microbiology section of your submission and have the following comments and information requests. We request a prompt written response in order to continue our evaluation of your NDA.

1. Provide studies that demonstrate the integrity of the container-closure system.
2. Identify the sterilizing filters and provide a product-specific bacterial filter retention study.
3. Drug Master File —— had been found deficient. A separate letter has been sent to the DMF holder. Please coordinate your response with the DMF holder and include a statement in your response indicating that the DMF has been updated. b(4)

As you are aware, the Prescription Drug User Fee Act Goal date is approaching. Please respond to this Information requests in a timely manner in order to for us to proceed with the review of your NDA.

If you have any questions, call Giuseppe Randazzo, Project Manager, at (301) 796-0980.

Sincerely,

{See appended electronic signature page}

David Hussong, Ph.D.
Associate Director for New Drug Microbiology
New Drug Microbiology Staff
Office of Pharmaceutical Science
Center for Drug Evaluation and Research

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/s/

David Hussong
11/7/2006 05:00:22 PM

NDA REGULATORY FILING REVIEW
(Including Memo of Filing Meeting)

NDA # 22-023 Supplement # 000 Efficacy Supplement Type SE- 2

Proprietary Name: Emend (fosaprepitant dimeglumine) for Injection
Established Name: fosaprepitant dimeglumine
Strengths: 115 mg/mL reconstituted from lyophilized powder

Applicant: Merck & Co., Inc.
Agent for Applicant (if applicable):

Date of Application: March 31, 2006
Date of Receipt: April 3, 2006
Date clock started after UN: N/A
Date of Filing Meeting: June 1, 2006
Filing Date: June 16, 2006
Action Goal Date (optional): User Fee Goal Date: February 3, 2007

Indication(s) requested: Chemotherapy-induced nausea and vomiting (CINV)

Type of Original NDA: (b)(1) ☒ (b)(2) ☐
AND (if applicable)
Type of Supplement: (b)(1) ☐ (b)(2) ☐

NOTE:
(1) If you have questions about whether the application is a 505(b)(1) or 505(b)(2) application, see Appendix A. A supplement can be either a (b)(1) or a (b)(2) regardless of whether the original NDA was a (b)(1) or a (b)(2). If the application or efficacy supplement is a (b)(2), complete Appendix B.

Review Classification: S ☒ P ☐
Resubmission after withdrawal? ☐ Resubmission after refuse to file? ☐
Chemical Classification: (1,2,3 etc.) 2
Other (orphan, OTC, etc.) No

Form 3397 (User Fee Cover Sheet) submitted: YES ☒ NO ☐

User Fee Status: Paid ☒ Exempt (orphan, government) ☐
Waived (e.g., small business, public health) ☐

NOTE: *If the NDA is a 505(b)(2) application, and the applicant did not pay a fee in reliance on the 505(b)(2) exemption (see box 7 on the User Fee Cover Sheet), confirm that a user fee is not required by contacting the User Fee staff in the Office of Regulatory Policy. The applicant is required to pay a user fee if: (1) the product described in the 505(b)(2) application is a new molecular entity or (2) the applicant claims a new indication for a use that that has not been approved under section 505(b). Examples of a new indication for a use include a new indication, a new dosing regime, a new patient population, and an Rx-to-OTC switch. The best way to determine if the applicant is claiming a new indication for a use is to compare the applicant's proposed labeling to labeling that has already been approved for the product described in the application. Highlight the differences between the proposed and approved labeling. If you need assistance in determining if the applicant is claiming a new indication for a use, please contact the User Fee staff.*

- Is there any 5-year or 3-year exclusivity on this active moiety in any approved (b)(1) or (b)(2) application? YES ☒ NO ☐
  If yes, explain: Merck's Fosaprepitant is the pro-drug of Merck's Emend (aprepitant) approved March 26, 2003. CMC has decided that Fosaprepitant is a Type 2 NDA. Merck holds exclusivity on **aprepitant as an NCE until March 26, 2008 as well as an I-475 until October 28, 2008 for "prevention** of nausea and vomiting associated with initial and repeat courses of moderately emetogenic cancer chemotherapy.

Note: If the drug under review is a 505(b)(2), this issue will be addressed in detail in appendix B.

- Does another drug have orphan drug exclusivity for the same indication? YES ☐ NO ☒

- If yes, is the drug considered to be the same drug according to the orphan drug definition of sameness [21 CFR 316.3(b)(13)]?
  YES ☐ NO ☐

  If yes, consult the Director, Division of Regulatory Policy II, Office of Regulatory Policy (HFD-007).

- Is the application affected by the Application Integrity Policy (AIP)? YES ☐ NO ☒
  If yes, explain:

- If yes, has OC/DMPQ been notified of the submission? YES ☐ NO ☒

- Does the submission contain an accurate comprehensive index? YES ☒ NO ☐
  If no, explain:

- Was form 356h included with an authorized signature? YES ☒ NO ☐
  If foreign applicant, both the applicant and the U.S. agent must sign.

- Submission complete as required under 21 CFR 314.50? YES ☒ NO ☐
  If no, explain:

- Answer 1, 2, or 3 below (do not include electronic content of labeling as an partial electronic submission).

  1. This application is a paper NDA YES ☐

  2. This application is an eNDA or combined paper + eNDA YES ☐
     This application is: All electronic ☐ Combined paper + eNDA ☐
     This application is in: NDA format ☐ CTD format ☐
     Combined NDA and CTD formats ☐

     Does the eNDA, follow the guidance?
     (http://www.fda.gov/cder/guidance/2353fnl.pdf) YES ☐ NO ☐

     If an eNDA, all forms and certifications must be in paper and require a signature.

If combined paper + eNDA, which parts of the application were submitted in electronic format?

Additional comments:

3. This application is an eCTD NDA. YES ☒
If an eCTD NDA, all forms and certifications must either be in paper and signed or be electronically signed.

Additional comments:

- Patent information submitted on form FDA 3542a? YES ☒ NO ☐
- Exclusivity requested? YES, _____ Years NO ☒
NOTE: An applicant can receive exclusivity without requesting it; therefore, requesting exclusivity is not required.
- Correctly worded Debarment Certification included with authorized signature? YES ☒ NO ☐
If foreign applicant, both the applicant and the U.S. Agent must sign the certification.

NOTE: Debarment Certification should use wording in FD&C Act section 306(k)(1) i.e., "[Name of applicant] hereby certifies that it did not and will not use in any capacity the services of any person debarred under section 306 of the Federal Food, Drug, and Cosmetic Act in connection with this application." Applicant may not use wording such as "To the best of my knowledge . . . ."

- Are the required pediatric assessment studies and/or deferral/partial waiver/full waiver of pediatric studies (or request for deferral/partial waiver/full waiver of pediatric studies) included? YES ☒ NO ☐
- If the submission contains a request for deferral, partial waiver, or full waiver of studies, does the application contain the certification required under FD&C Act sections 505B(a)(3)(B) and (4)(A) and (B)? YES ☒ NO ☐
- Is this submission a partial or complete response to a pediatric Written Request? YES ☐ NO ☒

If yes, contact PMHT in the OND-IO

- Financial Disclosure forms included with authorized signature? YES ☒ NO ☐
(Forms 3454 and/or 3455 must be included and must be signed by the APPLICANT, not an agent.)
NOTE: *Financial disclosure is required for bioequivalence studies that are the basis for approval.*
- Field Copy Certification (that it is a true copy of the CMC technical section) YES ☐ NO ☒
- PDUFA and Action Goal dates correct in tracking system? YES ☒ NO ☐
If not, have the document room staff correct them immediately. These are the dates EES uses for calculating inspection dates.
- Drug name and applicant name correct in COMIS? If not, have the Document Room make the corrections. Ask the Doc Rm to add the established name to COMIS for the supporting IND if it is not already entered.
- List referenced IND numbers: IND 48,924

- Are the trade, established/proper, and applicant names correct in COMIS? YES ☒ NO ☐
  If no, have the Document Room make the corrections.

- End-of-Phase 2 Meeting(s)? Date(s) _____ NO ☒
  If yes, distribute minutes before filing meeting.

- Pre-NDA Meeting(s)? Date(s) December 13, 2005 NO ☐
  If yes, distribute minutes before filing meeting.

- Any SPA agreements? Date(s) August 10, 2005 NO ☐
  If yes, distribute letter and/or relevant minutes before filing meeting.

Project Management

- If Rx, was electronic Content of Labeling submitted in SPL format? YES ☒ NO ☐
  If no, request in 74-day letter.

- If Rx, for all new NDAs/efficacy supplements submitted on or after 6/30/06:
  Was the PI submitted in PLR format? YES ☐ NO ☐

  If no, explain. Was a waiver or deferral requested before the application was received or in the submission? If before, what is the status of the request:

- If Rx, all labeling (PI, PPI, MedGuide, carton and immediate container labels) has been consulted to DDMAC? YES ☒ NO ☐

- If Rx, trade name (and all labeling) consulted to OSE/DMETS? YES ☒ NO ☐

- If Rx, MedGuide and/or PPI (plus PI) consulted to ODE/DSRCS?
  N/A ☐ YES ☒ NO ☐

- Risk Management Plan consulted to OSE/IO? N/A ☐ YES ☒ NO ☐

- If a drug with abuse potential, was an Abuse Liability Assessment, including a proposal for scheduling submitted? NA ☒ YES ☐ NO ☐

If Rx-to-OTC Switch or OTC application:

- Proprietary name, all OTC labeling/packaging, and current approved PI consulted to OSE/DMETS? YES ☐ NO ☐

- If the application was received by a clinical review division, has DNPCE been notified of the OTC switch application? Or, if received by DNPCE, has the clinical review division been notified? YES ☐ NO ☐

Clinical

- If a controlled substance, has a consult been sent to the Controlled Substance Staff?
  YES ☐ NO ☐

Chemistry

- Did applicant request categorical exclusion for environmental assessment? YES ☒ NO ☐
  If no, did applicant submit a complete environmental assessment? YES ☐ NO ☐
  If EA submitted, consulted to EA officer, OPS? YES ☐ NO ☐
- Establishment Evaluation Request (EER) submitted to DMPQ? YES ☒ NO ☐
- If a parenteral product, consulted to Microbiology Team? YES ☒ NO ☐

ATTACHMENT

MEMO OF FILING MEETING

DATE: June 1, 2006

NDA #: 22-023

DRUG NAMES: Fosaprepitant Dimeglumine

APPLICANT: Merck & Company, Inc.

BACKGROUND: NDA 22-023 submitted March 31, 2006 for Emend (fosaprepitant dimeglumine) for **Injection is the prodrug for EMEND (aprepitant). The sought after indication is "for the prevention of acute** and delayed nausea and vomiting associated with initial and repeat courses of highly emetogenic cancer chemotherapy, including high-dose cisplatin. For the prevention of nausea and vomiting associated with initial and repeat course of moderately emetogenic cancer chemotherapy.

The firm asserts in their March 31, 2006 cover letter that the molecule is an NME, however the CMC review of May 11, 2006 states that since aprepitant is the physiologically active moiety in fosaprepitant, ONDQA classifies fosprepitant Dimeglumine as a Type II molecule.

The study title for the pivotal BE study used to bridge the oral aprepitant to I.V.

"Study Title:P012L1-MRL Clinical Study Report: A Randomized, 5-Part, Intravenous Study of the Safety, Tolerability, Bioequivalence, and Drug Interaction Potential of Final Market Image Formulations of MK-0517 **in Young Healthy Subjects (Protocol 012)."**

ATTENDEES: Betsy Scroggs, Brian E. Harvey, Joyce Korvick, Jasti Choudary, Dennis Bashaw, Sue Chih Lee, Marie Kowblansky, Melissa Furness, Stella Grosser, Wen Jen Chen, Diane Smith, Denise Toyer, **Julia Pinto, Sushanta Chakdur, Gary Della'Zanna, Hugo Gallo-Torres, Anastasias Lolas**

ASSIGNED REVIEWERS (including those not present at filing meeting) : As follows:

Discipline/Organization	Reviewer
Medical:	**Gary Della'Zanna at time of filing**
Secondary Medical:	Hugo Gallo Torres as of 9/30/2006
Statistical:	Wen Jen Chen
Pharmacology:	Sushanta Chakdur
Statistical Pharmacology:	
Chemistry:	Julia Pinto

Environmental Assessment (if needed):	Requested categorical exclusiong
Biopharmaceutical:	Sue Chih Lee
Microbiology, sterility:	Anastasias Lolas
DSI:	Ct Viswanathan
OPS:	N/A
Regulatory Project Management:	Betsy Scroggs until 9/28/2006 Giuseppe Randazzo as of 9/29/2006
Other Consults:	DMTS - Diane Smith, PM & Kristina Arnwine **Michael Brony – DDMAC** **DSRCS – Jeanine Best** OSE IO for RMP - Contact Mary Dempsey

Per reviewers, are all parts in English or English translation? YES ☒ NO ☐
If no, explain:

CLINICAL FILE ☒ REFUSE TO FILE ☐

- Clinical site audit(s) needed? YES ☐ NO ☒
  If no, explain:
- Advisory Committee Meeting needed? YES, date if known _____ NO ☒
- If the application is affected by the AIP, has the division made a recommendation regarding whether or not an exception to the AIP should be granted to permit review based on medical necessity or public health significance?
  N/A ☒ YES ☐ NO ☐

CLINICAL MICROBIOLOGY N/A ☒ FILE ☐ REFUSE TO FILE ☐

STATISTICS N/A ☒ FILE ☒ REFUSE TO FILE ☐

BIOPHARMACEUTICS FILE ☒ REFUSE TO FILE ☐

- Biopharm. study site audits(s) needed? YES ☒ NO ☐

PHARMACOLOGY/TOX N/A ☐ FILE ☒ REFUSE TO FILE ☐

- GLP audit needed? YES ☐ NO ☒

CHEMISTRY FILE ☒ REFUSE TO FILE ☐

- Establishment(s) ready for inspection? YES ☒ NO ☐
- Sterile product? YES ☒ NO ☐
  If yes, was microbiology consulted for validation of sterilization?
  YES ☒ NO ☐

ELECTRONIC SUBMISSION:
Any comments: eCTD

REGULATORY CONCLUSIONS/DEFICIENCIES:
(Refer to 21 CFR 314.101(d) for filing requirements.)

☐ The application is unsuitable for filing. Explain why:

☒ The application, on its face, appears to be well-organized and indexed. The application appears to be suitable for filing.

- ☒ No filing issues have been identified.
- ☐ Filing issues to be communicated by Day 74. List (optional):

ACTION ITEMS:

1. ☒ Ensure that the review and chemical classification codes, as well as any other pertinent classification codes (e.g., orphan, OTC) are correctly entered into COMIS.
2. ☐ If RTF, notify everybody who already received a consult request of RTF action. Cancel the EER.
3. ☐ If filed and the application is under the AIP, prepare a letter either granting (for signature by Center Director) or denying (for signature by ODE Director) an exception for review.
4. ☒ If filed, complete the Pediatric Page at this time. (If paper version, enter into DFS.)
5. ☒ Convey document filing issues/no filing issues to applicant by Day 74.

Betsy Scroggs, Pharm.D.
Regulatory Health Project Manager

Appendix A to NDA Regulatory Filing Review

NOTE: The term "original application" or "original NDA" as used in this appendix denotes the NDA submitted. It does not refer to the reference drug product or "reference listed drug."

An original application is likely to be a 505(b)(2) application if:

(1) it relies on published literature to meet any of the approval requirements, and the applicant does not have a written right of reference to the underlying data. If published literature is cited in the NDA but is not necessary for approval, the inclusion of such literature will not, in itself, make the application a 505(b)(2) application,
(2) it relies for approval on the Agency's previous findings of safety and efficacy for a listed drug product and the applicant does not own or have right to reference the data supporting that approval, or
(3) it relies on what is "generally known" or "scientifically accepted" about a class of products to support the safety or effectiveness of the particular drug for which the applicant is seeking approval. (Note, however, that this does not mean *any* reference to general information or knowledge (e.g., about disease etiology, support for particular endpoints, methods of analysis) causes the application to be a 505(b)(2) application.)

Types of products for which 505(b)(2) applications are likely to be submitted include: fixed-dose combination drug products (e.g., heart drug and diuretic (hydrochlorothiazide) combinations); OTC monograph deviations(see 21 CFR 330.11); new dosage forms; new indications; and, new salts.

An efficacy supplement can be either a (b)(1) or a (b)(2) regardless of whether the original NDA was a (b)(1) or a (b)(2).

An efficacy supplement is a 505(b)(1) supplement if the supplement contains all of the information needed to support the approval of the change proposed in the supplement. For example, if the supplemental application is for a new indication, the supplement is a 505(b)(1) if:

(1) The applicant has conducted its own studies to support the new indication (or otherwise owns or has right of reference to the data/studies),

(2) No additional information beyond what is included in the supplement or was embodied in the finding of safety and effectiveness for the original application or previously approved supplements is needed to support the change. For example, this would likely be the case with respect to safety considerations if the dose(s) was/were the same as (or lower than) the original application, and.

(3) **All other "criteria" are met (e.g., the applicant owns or has right of reference to the data relied** upon for approval of the supplement, the application does not rely for approval on published literature based on data to which the applicant does not have a right of reference).

An efficacy supplement is a 505(b)(2) supplement if:

(1) Approval of the change proposed in the supplemental application would require data beyond that needed to support our previous finding of safety and efficacy in the approval of the

original application (or earlier supplement), and the applicant has not conducted all of its own studies for approval of the change, or obtained a right to reference studies it does not own. For example, if the change were for a new indication AND a higher dose, we would likely require clinical efficacy data and preclinical safety data to approve the higher dose. If the applicant provided the effectiveness data, but had to rely on a different listed drug, or a new aspect of a previously cited listed drug, to support the safety of the new dose, the supplement would be a 505(b)(2),

(2) The applicant relies for approval of the supplement on published literature that is based on data that the applicant does not own or have a right to reference. If published literature is cited in the supplement but is not necessary for approval, the inclusion of such literature will not, in itself, make the supplement a 505(b)(2) supplement, or

(3) The applicant is relying upon any data they do not own or to which they do not have right of reference.

If you have questions about whether an application is a 505(b)(1) or 505(b)(2) application, consult **with your ODE's Office of Regulatory Policy representative.**

Appendix B to NDA Regulatory Filing Review
Questions for 505(b)(2) Applications

1. Does the application reference a listed drug (approved drug)? YES ☐ NO ☐

*If "**No,**" skip to question 3.*

2. Name of listed drug(s) referenced by the applicant (if any) and NDA/ANDA #(s):

3. **Is this application for a drug that is an "old" antibi**otic (as described in the draft guidance implementing the 1997 FDAMA provisions? (Certain antibiotics are not entitled to Hatch-Waxman patent listing and exclusivity benefits.)
YES ☐ NO ☐

*If "**Yes,**" skip to question 7.*

4. Is this application for a recombinant or biologically-derived product?
YES ☐ NO ☐

*If "**Yes** "contact your ODE's Office of Regulatory Policy representative.*

5. The purpose of the questions below (questions 5 to 6) is to determine if there is an approved drug product that is equivalent or very similar to the product proposed for approval that should be referenced as a listed drug in the pending application.

   (a) Is there a pharmaceutical equivalent(s) to the product proposed in the 505(b)(2) application that is already approved?
   YES ☐ NO ☐

   (***Pharmaceutical equivalents*** are drug products in identical dosage forms that: **(1)** contain identical amounts of the identical active drug ingredient, i.e., the same salt or ester of the same therapeutic moiety, or, in the case of modified release dosage forms that require a reservoir or overage or such forms as prefilled syringes where residual volume may vary, that deliver identical amounts of the active drug ingredient over the identical dosing period; **(2)** do not necessarily contain the same inactive ingredients; **and** **(3)** meet the identical compendial or other applicable standard of identity, strength, quality, and purity, including potency and, where applicable, content uniformity, disintegration times, and/or dissolution rates. (21 CFR 320.1(c))

*If "**No,**" to (a) skip to question 6. Otherwise, answer part (b and (c)).*

   (b) Is the pharmaceutical equivalent approved for the same indication for which the 505(b)(2) application is seeking approval? YES ☐ NO ☐

   (c) Is the approved pharmaceutical equivalent(s) cited as the listed drug(s)? YES ☐ NO ☐

*If "**Yes,**" (c), list the pharmaceutical equivalent(s) and proceed to question 6.*

*If "**No,**" to (c) list the pharmaceutical equivalent and contact your ODE's Office of Regulatory Policy representative.*
Pharmaceutical equivalent(s):

6. (a) Is there a pharmaceutical alternative(s) already approved? YES ☐ NO ☐

(***Pharmaceutical alternatives*** are drug products that contain the identical therapeutic moiety, or its precursor, but not necessarily in the same amount or dosage form or as the same salt or ester. Each such drug product individually meets either the identical or its own respective compendial or other applicable standard of identity, strength, quality, and purity, including potency and, where applicable, content uniformity, disintegration times and/or dissolution rates. (21 CFR 320.1(d)) Different dosage forms and strengths within a product line by a single manufacturer are thus pharmaceutical alternatives, as are extended-release products when compared with immediate- or standard-release formulations of the same active ingredient.)

*If "**No,**" to (a) skip to question 7. Otherwise, answer part (b and (c)).*

(b) Is the pharmaceutical alternative approved for the same indication for which the 505(b)(2) application is seeking approval? YES ☐ NO ☐

(c) Is the approved pharmaceutical alternative(s) cited as the listed drug(s)? YES ☐ NO ☐

*If "**Yes,**" to (c), proceed to question 7.*

NOTE: *If there is more than one pharmaceutical alternative approved, consult your ODE's Office of Regulatory Policy representative to determine if the appropriate pharmaceutical alternatives are referenced.*

*If "**No,**" to (c), list the pharmaceutical alternative(s) and contact your ODE's Office of Regulatory Policy representative. Proceed to question 7.*

Pharmaceutical alternative(s):

7. (a) Does the application rely on published literature necessary to support the proposed approval of the drug product (i.e. is the published literature necessary for the approval)?
YES ☐ NO ☐

*If "**No,**" skip to question 8. Otherwise, answer part (b).*

(b) Does any of the published literature cited reference a specific (e.g. brand name) product? Note that if yes, the applicant will be required to submit patent certification for the product, see question 12.

8. **Describe the change from the listed drug(s) provided for in this (b)(2) application (for example, "This application provides for a new indication, otitis media" or "This application provides for a change in dosage form, from capsules to solution").**

9. Is the application for a duplicate of a listed drug and eligible for approval under section 505(j) as an ANDA? (Normally, FDA may refuse-to-file such NDAs (see 21 CFR 314.101(d)(9)). YES ☐ NO ☐

10. Is the application for a duplicate of a listed drug whose only difference is that the extent to which the active ingredient(s) is absorbed or otherwise made available to the site of action less than that of the reference listed drug (RLD)? (See 314.54(b)(1)). If yes, the application may be refused for filing under 21 CFR 314.101(d)(9)). YES ☐ NO ☐

11. Is the application for a duplicate of a listed drug whose only difference is YES ☐ NO ☐

that the rate at which the product's active ingredient(s) is absorbed or made available to the site of action is unintentionally less than that of the RLD (see 21 CFR 314.54(b)(2))? If yes, the application may be refused for filing under 21 CFR 314.101(d)(9).

12. Are there certifications for each of the patents listed in the Orange Book for the listed drug(s) referenced by the applicant (see question #2)? (This is different from the patent declaration submitted on form FDA 3542 and 3542a.) YES ☐ NO ☐

13. Which of the following patent certifications does the application contain? (Check all that apply <u>and</u> identify the patents to which each type of certification was made, as appropriate.)

☐ Not applicable (e.g., solely based on published literature. See question # 7

☐ 21 CFR 314.50(i)(1)(i)(A)(1): The patent information has not been submitted to FDA. (Paragraph I certification)
Patent number(s):

☐ 21 CFR 314.50(i)(1)(i)(A)(2): The patent has expired. (Paragraph II certification)
Patent number(s):

☐ 21 CFR 314.50(i)(1)(i)(A)(3): The date on which the patent will expire. (Paragraph III certification)
Patent number(s):

☐ 21 CFR 314.50(i)(1)(i)(A)(4): The patent is invalid, unenforceable, or will not be infringed by the manufacture, use, or sale of the drug product for which the application is submitted. (Paragraph IV certification)
Patent number(s):

NOTE: *IF FILED, and if the applicant made a "Paragraph IV" certification [21 CFR 314.50(i)(1)(i)(A)(4)], the applicant must* ***subsequently*** *submit a signed certification stating that the NDA holder and patent owner(s) were notified the NDA was filed [21 CFR 314.52(b)]. The applicant must also submit documentation showing that the NDA holder and patent owner(s) received the notification [21 CFR 314.52(e)]. OND will contact you to verify that this documentation was received.*

☐ 21 CFR 314.50(i)(3): Statement that applicant has a licensing agreement with the patent owner (must also submit certification under 21 CFR 314.50(i)(1)(i)(A)(4) above).
Patent number(s):

☐ Written statement from patent owner that it consents to an immediate effective date upon approval of the application.
Patent number(s):

☐ 21 CFR 314.50(i)(1)(ii): No relevant patents.

☐ 21 CFR 314.50(i)(1)(iii): The patent on the listed drug is a method of use patent and the labeling for the drug product for which the applicant is seeking approval does not include any indications that are covered by the use patent as described in the corresponding use code in the Orange Book. Applicant must provide a statement that the method of use patent does not claim any of the proposed indications. (Section viii statement)
Patent number(s):

14. Did the applicant:

- Identify which parts of the application rely on the finding of safety and effectiveness for a listed drug or published literature describing a listed drug or both? For example, pharm/tox section of application relies on finding of preclinical safety for a listed drug.

  YES ☐ NO ☐

  *If "**Yes,**" what is the listed drug product(s) and which sections of the 505(b)(2) application rely on the finding of safety and effectiveness or on published literature about that listed drug*
  Was this listed drug product(s) referenced by the applicant? (see question # 2)

  YES ☐ NO ☐

- Submit a bioavailability/bioequivalence (BA/BE) study comparing the proposed product to the listed drug(s)?

  N/A ☐ YES ☐ NO ☐

15. (a) Is there unexpired exclusivity on this listed drug (for example, 5 year, 3 year, orphan or pediatric exclusivity)? Note: this information is available in the Orange Book.

YES ☐ NO ☐

If "Yes," please list:

Application No.	Product No.	Exclusivity Code	Exclusivity Expiration

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

/s/

Betsy Scroggs
9/29/2006 03:34:42 PM
CSO

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 22-023

INFORMATION REQUEST LETTER

Merck & Co., Inc.
Attention: Vijay Tammara, Ph.D.
Director, Regulatory Affairs
P.O. Box 1000, UG2CD-48
North Wales, PA 19454

Dear Dr. Tammara:

Please refer to your March 31, 2006 new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for FOSAPREPITANT DIMEGLUMINE.

We also refer to your submissions dated May 4 and June 2, 2006.

We are reviewing the Chemistry, Manufacturing and Controls section of your submission and have the following comments and information requests. We request a prompt written response in order to continue our evaluation of your NDA.

Drug Substance

1.

2.

3.

b(4)

4.

5.

6.

Drug Product

1.

b(4)

2.

3.

4.

If you have any questions, call Linda D. Mullins-Athey, Regulatory Health Project Manager for Quality, at 301-796-2096.

Sincerely,

{See appended electronic signature page}

Moo-Jhong Rhee, Ph.D.
Chief, Branch III
Pre-Marketing Assessment Division II
Office of New Drug Quality Assessment
Center for Drug Evaluation and Research

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

/s/

Moo-Jhong Rhee
8/17/2006 02:24:03 PM

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

REQUEST FOR CONSULTATION

TO *(Division/Office)*:
Director, Division of Medication Errors and Technical Support (DMETS), HFD-420 WO22, RM 4447

FROM: Betsy Scroggs, RHPM HFD-180
WO22, RM 5109 (301) 796-0991

DATE	IND NO.	NDA NO.	TYPE OF DOCUMENT	DATE OF DOCUMENT
7/31/2006	48,924	22-023	NDA	3/31/2006 and 7/6/2006

NAME OF DRUG	PRIORITY CONSIDERATION	CLASSIFICATION OF DRUG	DESIRED COMPLETION DATE
Fosaprepitant Dimeglumine	Medium	Antiemetic	11/1/2006

NAME OF FIRM: Merck & Co., 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)*: **Trade name review**

II. BIOMETRICS

STATISTICAL EVALUATION BRANCH

- ☐ TYPE A OR B NDA REVIEW
- ☐ END OF PHASE II MEETING
- ☐ CONTROLLED STUDIES
- ☐ PROTOCOL REVIEW
- ☐ OTHER (SPECIFY BELOW):

STATISTICAL APPLICATION BRANCH

- ☐ 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: Application: Please review for updated trade name Emend® (fosaprepitant dimeglumine) for Injection and please review labeling. PDUFA date is 2/3/2007N022023 Document: 2797344 Location: \\CDSESUB1\EVSPROD\N022023\0000 This consult request supercedes the 6/2/2006 request.

PDUFA DATE: 2/3/2007
ATTACHMENTS: Draft Package Insert, Container and Carton Labels
CC: Archival IND/NDA 22-023 Please note that the firm's July 6, 2006 updated tradename request is attached.
HFD-180/Division File
HFD-180/RPM
HFD-180/Reviewers and Team Leaders

NAME AND PHONE NUMBER OF REQUESTER
Betsy Scroggs, RHPM Thank you!

METHOD OF DELIVERY (Check one)
☒ DFS ONLY ☐ MAIL ☐ HAND

SIGNATURE OF RECEIVER

SIGNATURE OF DELIVERER

5/28/05

NDA 22-023 July 6, 2006

TRADENAME
(Fosaprepitant Dimeglumine)

Response to FDA Request for Information

Information and data submitted herein contains trade secrets, or privileged or confidential information, the property of Merck & Co., Inc. and government agencies are not authorized to make it public without written permission from Merck.

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OFFICIAL FDA Copies
not desk copies

Vijay Tammara, Ph D
Director
Regulatory Affairs

Merck & Co., Inc.
P.O Box 1000, UG2CD-48
North Wales PA 19454-1099
Tel 267 305 6713
Fax 267 305 6406
vijay_tammara@merck.com

July 6, 2006

ORIGINAL

CDER/CDR

JUL 1 2 2006 MERCK Research Laboratories

RECEIVED

Brian E. Harvey, M.D., Ph.D., Director
Food and Drug Administration
Center for Drug Evaluation and Research
Division of Gastroenterology Products
5901-B Ammendale Road
Beltsville, MD 20705-1266

RECEIVED

JUL 1 2 2006

CDER White Oak DR 1

Dear Dr. Harvey:

N-022-BL

ORIGINAL AMENDMENT

N(BL)

NDA 22-023: TRADENAME (Fosaprepitant Dimeglumine)
Response to FDA Request for Information

Reference is made to the New Drug Application cited above, and to MRL's February 28, 2006 submission (IND 48,924, Serial No. 111) requesting a Type C meeting with FDA to discuss MRL's proposed tradename of EMEND® IV, and to FDA's March 23, 2006 facsimile granting MRL a Type C meeting on July 6, 2006. Further reference is also made to a July 5, 2006 e-mail from Dr. Betsy Scroggs, Regulatory Project Manager, FDA, to Dr. Vijay Tammara, Director, Regulatory Affairs, MRL, which provided FDA's pre-meeting responses for the scheduled July 6, 2006 Type C meeting. Final reference is also made to a series of telephone conversations on July 6, 2006 between Dr. Scroggs and Dr. Tammara to discuss MRL's responses to FDA's July 5, 2006 e-mail. Based on those conversations, FDA and MRL agreed on the responses listed below, and the scheduled July 6, 2006 Type C meeting was canceled.

MRL Question (from MRL's February 28, 2006 IND submission):
Based on MRL's responses to the FDA's February 1, 2006 letter, does the Agency concur that ——— is the most appropriate trade name for Fosaprepitant Dimeglumine. b(4)

FDA Responses (from July 5, 2006 e-mail):
No. However, the following may be acceptable:

EMEND®
(fosaprepitant dimeglumine for injection).

MRL Response:
MRL proposes the following:

EMEND®
(fosaprepitant dimeglumine)
for Injection

FDA Request #1:
Since Fosaprepitant Dimeglumine is given as 115 mg intravenous injection on day 1 and is followed by oral aprepitant on days 2 and 3, we have concerns about potential medication errors. Consequently, please send us a proposal for ———

b(4)

MRL Response #1:

FDA Request #2:
Do you have plans to develop an intravenous formulation for the day 2 and 3 (80 mg) dose as well?

MRL Response #2:

b(4)

This submission is formatted as required in Title 21 paragraph 314.50 of the Code of Federal Regulations and is being submitted in accordance with the current FDA Guidance Documents for the electronic common technical document including, but not limited to the following: *Comprehensive Table of Contents Heading and Hierarchy, Study Tagging Files Specification, Organization of The Common Technical Document – Annex – Granularity Document, and the International Conference on Harmonization, ICH M2 EWG, Electronic Common Technical Document Specification.* As an enclosure to this letter, Merck Research Laboratories (MRL), a Division of Merck & Co., Inc., is providing one Compact Disk (CD) which contains the submission. All documents requiring signatures for certification are included as paper for archival purposes.

All of the information is contained on one CD and is not more than 100MB. Merck has taken precautions to ensure that the contents of the media are free of computer viruses (Symantec AntiVirus Corporate Edition, Symantec Corporation), and we authorize the use of anti-virus software, as appropriate.

A list of reviewers from the Division of Gastroenterology Products who should be provided access to this electronic submission on their desktops may be obtained from Dr. Betsy Scroggs, Regulatory Project Manager, Division of Gastroenterology Products.

We consider the information included in this submission to be a confidential matter and request that the Food and Drug Administration not make its content, or any future communications in regard to it, public without first obtaining the written permission of Merck & Co., Inc.

Questions concerning this submission should be directed to Vijay K. Tammara, Ph.D. (267-305-6713) or, in his absence, to Joseph P. Arena, Ph.D. (267-305-6772).

Sincerely,

Vijay K. Tammara, Ph.D.
Director, Regulatory Affairs

Enclosure: CD

DHL #1

Desk Copy: Dr. Betsy Scroggs, Regulatory Project Manager (cover letter)
Food and Drug Administration
Division of Gastroenterology Products FDA
Room 5109, White Oak CDER Bldg. # 22
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002
DHL #2

Q:\HIIR0517\NDA 22.023\tradename.doc

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

APPLICATION TO MARKET A NEW DRUG, BIOLOGIC, OR AN ANTIBIOTIC DRUG FOR HUMAN USE

(Title 21, Code of Federal Regulations, Parts 314 & 601)

Form Approved: OMB No. 0910-0338
Expiration Date: September 30, 2008
See OMB Statement on page 2.

FOR FDA USE ONLY

APPLICATION NUMBER

RECEIVED

JUL 12 2006

CDER White Oak DR 1

APPLICANT INFORMATION

NAME OF APPLICANT Merck & Co., Inc.	DATE OF SUBMISSION July 6, 2006
TELEPHONE NO. *(Include Area Code)* 267-305-6713	FACSIMILE (FAX) *Number (Include Area Code)* 267-305-6406
APPLICANT ADDRESS *(Number, Street, City, State, Country, ZIP Code or Mail Code, and U.S. License number if previously issued)*: PO Box 1000, UG2CD-48 North Wales, PA 19454-1099	AUTHORIZED U.S. AGENT NAME & ADDRESS *(Number, Street, City, State, ZIP Code, telephone & FAX number)* IF APPLICABLE Vijay K. Tammara, Ph.D. Director, Regulatory Affairs

PRODUCT DESCRIPTION

NEW DRUG OR ANTIBIOTIC APPLICATION NUMBER, OR BIOLOGICS LICENSE APPLICATION NUMBER *(if previously issued)* 22-023

ESTABLISHED NAME *(e.g., Proper name, USP/USAN name)* fosaprepitant dimeglumine	PROPRIETARY NAME *(trade name)* IF ANY

CHEMICAL/BIOCHEMICAL/BLOOD PRODUCT NAME *(if any)* 1-Deoxy-1-(methylamino)-D-glucitol [3-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phenyl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl] 2,5-dihydro-5-oxo-1H-1,2,4-triazol-1-yl]phosphonate (2:1) (salt)	CODE NAME *(if any)* MK-0517, L-000758298-003C

DOSAGE FORM: Lyophilized Powder	STRENGTH: 115 mg/mL	ROUTE OF ADMINISTRATION: Intravenous

(PROPOSED) INDICATION(S) FOR USE:
For the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of highly emetogenic cancer chemotherapy, including high-dose cisplatin. For the prevention of nausea and vomiting associated with initial and repeat courses of moderately emetogenic cancer chemotherapy

APPLICATION DESCRIPTION

APPLICATION TYPE *(check one)* ☒ NEW DRUG APPLICATION (21 CFR 314.50) ☐ ABBREVIATED NEW DRUG APPLICATION (ANDA, 21 CFR 314.94) ☐ BIOLOGICS LICENSE APPLICATION (21 CFR Part 601)

IF AN NDA, IDENTIFY THE APPROPRIATE TYPE ☐ 505 (b)(1) ☐ 505 (b)(2)

IF AN ANDA, OR 505(b)(2), IDENTIFY THE REFERENCE LISTED DRUG PRODUCT THAT IS THE BASIS FOR THE SUBMISSION
Name of Drug — Holder of Approved Application

TYPE OF SUBMISSION (check one) ☐ ORIGINAL APPLICATION ☐ AMENDMENT TO A PENDING APPLICATION ☐ RESUBMISSION ☐ PRESUBMISSION ☐ ANNUAL REPORT ☐ ESTABLISHMENT DESCRIPTION SUPPLEMENT ☐ EFFICACY SUPPLEMENT ☐ LABELING SUPPLEMENT ☐ CHEMISTRY MANUFACTURING AND CONTROLS SUPPLEMENT ☒ OTHER

IF A SUBMISSION OF PARTIAL APPLICATION, PROVIDE LETTER DATE OF AGREEMENT TO PARTIAL SUBMISSION:

IF A SUPPLEMENT, IDENTIFY THE APPROPRIATE CATEGORY ☐ CBE ☐ CBE-30 ☐ Prior Approval (PA)

REASON FOR SUBMISSION Response to FDA Request for Information, Re. Tradename

PROPOSED MARKETING STATUS *(check one)* ☒ PRESCRIPTION PRODUCT *(Rx)* ☐ OVER THE COUNTER PRODUCT (OTC)

NUMBER OF VOLUMES SUBMITTED 1 — THIS APPLICATION IS ☐ PAPER ☒ PAPER AND ELECTRONIC ☐ ELECTRONIC

ESTABLISHMENT INFORMATION (Full establishment information should be provided in the body of the Application.)
Provide locations of all manufacturing, packaging and control sites for drug substance and drug product (continuation sheets may be used if necessary). Include name, address, contact, telephone number, registration number (CFN), DMF number, and manufacturing steps and/or type of testing (e.g. Final dosage form, Stability testing) conducted at the site. Please indicate whether the site is ready for inspection or, if not, when it will be ready.

Cross References (list related License Applications, INDs, NDAs, PMAs, 510(k)s, IDEs, BMFs, and DMFs referenced in the current application)

CDER/CDR

JUL 10 2006

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This application contains the following items: *(Check all that apply)*	
☒	1. Index
☐	2. Labeling *(check one)* ☐ Draft Labeling ☐ Final Printed Labeling
☐	3. Summary (21 CFR 314.50 (c))
☐	4. Chemistry section
☐	A. Chemistry, manufacturing, and controls information (e.g., 21 CFR 314.50(d)(1); 21 CFR 601.2)
☐	B. Samples (21 CFR 314.50 (e)(1); 21 CFR 601.2 (a)) (Submit only upon FDA's request)
☐	C. Methods validation package (e.g., 21 CFR 314.50(e)(2)(i); 21 CFR 601.2)
☐	5. Nonclinical pharmacology and toxicology section (e.g., 21 CFR 314.50(d)(2); 21 CFR 601.2)
☐	6. Human pharmacokinetics and bioavailability section (e.g., 21 CFR 314.50(d)(3); 21 CFR 601.2)
☐	7. Clinical Microbiology (e.g., 21 CFR 314.50(d)(4))
☐	8. Clinical data section (e.g., 21 CFR 314.50(d)(5); 21 CFR 601.2)
☐	9. Safety update report (e.g., 21 CFR 314.50(d)(5)(vi)(b); 21 CFR 601.2)
☐	10. Statistical section (e.g., 21 CFR 314.50(d)(6); 21 CFR 601.2)
☐	11. Case report tabulations (e.g., 21 CFR 314.50(f)(1); 21 CFR 601.2)
☐	12. Case report forms (e.g., 21 CFR 314.50 (f)(2); 21 CFR 601-2)
☐	13. Patent information on any patent which claims the drug (21 U.S.C. 355(b) or (c))
☐	14. A patent certification with respect to any patent which claims the drug (21 U.S.C. 355 (b)(2) or (j)(2)(A))
☐	15. Establishment description (21 CFR Part 600, if applicable)
☐	16. Debarment certification (FD&C Act 306 (k)(1))
☐	17. Field copy certification (21 CFR 314.50 (k)(3))
☐	18. User Fee Cover Sheet (Form FDA 3397)
☐	19. Financial information (21 CFR Part 54)
☐	20. OTHER (Specify)

CERTIFICATION

I agree to update this application with new safety information about the product that may reasonably affect the statement of contra l nd ications, warnings, precautions, or adverse reactions in the draft labeling. I agree to submit safety update reports as provided for by regulation or as requested by FDA. If this application is approved, I agree to comply with all applicable laws and regulations that apply to approved applications, including, but not limited to the following:

1. Good manufacturing practice regulations in 21 CFR Parts 210, 211 or applicable regulations, Parts 606, and/or 820.
2. Biological establishment standards in 21 CFR Part 600.
3. Labeling regulations in 21 CFR Parts 201, 606, 610, 660, and/or 809.
4. In the case of a prescription drug or biological product, prescription drug advertising regulations in 21 CFR Part 202.
5. Regulations on making changes in application in FD&C Act Section 506A, 21 CFR 314.71, 314.72, 314.97, 314.99, and 601.12.
6. Regulations on Reports in 21 CFR 314.80, 314.81, 600.80, and 600.81.
7. Local, state and Federal environmental impact laws.

If this application applies to a drug product that FDA has proposed for scheduling under the Controlled Substances Act, I agree not to market the product until the Drug Enforcement Administration makes a final scheduling decision.
The data and information in this submission have been reviewed and, to the best of my knowledge are certified to be true and accurate.

Warning: A willfully false statement is a criminal offense, U.S. Code, title 18, section 1001.

SIGNATURE OF RESPONSIBLE OFFICIAL OR AGENT	TYPED NAME AND TITLE	DATE
	Vijay K. Tammara, Ph.D. Director, Regulatory Affairs	July 6, 2006

ADDRESS *(Street, City, State, and ZIP Code)*	Telephone Number
PO Box 1000, UG2CD-48 North Wales, PA 19454-1099	(267) 305-6713

Public reporting burden for this collection of information is estimated to average 24 hours per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research
Central Document Room
5601-B Ammendale Road
Beltsville, MD 20705-1266

Department of Health and Human Services
Food and Drug Administration
Center for Biologics Evaluation and Research (HFM-99)
1401 Rockville Pike
Rockville, MD 20852-1448

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

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/s/

Betsy Scroggs
7/31/2006 04:45:32 PM

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

REQUEST FOR CONSULTATION

TO *(Division/Office)*:	FROM:
Division of Drug Marketing, Advertising, and Communications **Attention: Dr. Michael Brony** **(301) 796-0576**	**Betsy Scroggs, Pharm.D.** **Regulatory Health Project Manager: HFD-180** **Division of Gastroenterology Products** **(301) 796-0991 ruth.scroggs@fda.hhs.gov**

DATE	IND NO.	NDA NO.	TYPE OF DOCUMENT	DATE OF DOCUMENT
7/14/2006	N/A	**22-023**	NDA labeling	**3/31/2006**

NAME OF DRUG	PRIORITY CONSIDERATION	CLASSIFICATION OF DRUG	DESIRED COMPLETION DATE
Emend IV (proposed) (fosaprepitant dimeglumine for injection)	**Medium**	Anti-emetic	**11/14/2006**

NAME OF FIRM: **MERCK & Co., 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
- ☒ Label Review

COMMENTS, CONCERNS, and/or SPECIAL INSTRUCTIONS:

Please perform a label review from the DDMAC point of view. Please complete by November 14, 2006.
Request includes PI, PPI, trade carton, and trade container.

Project Manager: Betsy Scroggs (301) 796-0991

Medical Officer: Gary Della'Zanna (301) 796-0882

Application: N022023
Document: 2797344
Location: \\CDSESUB1\EVSPROD\N022023\0000

SIGNATURE OF REQUESTER	METHOD OF DELIVERY (Check one)
Betsy Scroggs, Pharm.D.	DFS MAIL ☐ HAND
SIGNATURE OF RECEIVER	SIGNATURE OF DELIVERER

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/s/

Betsy Scroggs
7/14/2006 03:28:42 PM

DSI CONSULT

Request for Biopharmaceutical Inspections

DATE: June 7, 2006
TO: Associate Director for Bioequivalence
Division of Scientific Investigations, HFD-48

THROUGH: (Required for international inspections)
Director, Review Division, HFD-180 or
Director, Division of Pharmaceutical Evaluation, HFD-180
FROM: Betsy Scroggs, Pharm.D., Regulatory Health Project Manager, HFD-180

SUBJECT: **Request for Biopharmaceutical Inspections**
NDA 22-023
(Fosaprepitant Dimeglumine) Injection

Study/Site Identification:

As discussed with you, the following studies/sites pivotal to approval (OR, raise question regarding the quality or integrity of the data submitted and) have been identified for inspection:

Study #	Clinical Site (name, address, phone, fax, contact person, if available)	Analytical Site (name, address, phone, fax, contact person, if available)
Protocol 012	[redacted]	Eric Woolf, PhD. Department of Drug Metabolism Merck Research Laboratories West Point, PA 19486

b(4)

Goal Date for Completion:

We request that the inspections be conducted and the Inspection Summary Results be provided by **October 31, 2006**. We intend to issue an action letter on this application by **February 3, 2007**.

Should you require any additional information, please contact
Betsy Scroggs, Pharm.D., Regulatory Health Project Manager at (301) 796-0991.
Concurrence: (Optional)
Hugo Gallo-Torres, Medical Team Leader (301) 796-0894
Edward Bashaw, Division Director, Office of Clinical Pharmacology 3 (301) 796-1502

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/s/

Betsy Scroggs
7/6/2006 10:27:54 AM

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

REQUEST FOR CONSULTATION

TO *(Division/Office)*:
Director, Division of Medication Errors and Technical Support (DMETS), HFD-420
WO22, RM 4447

FROM: Betsy Scroggs, RHPM HFD-180
WO22, RM 5109
(301) 796-0991

DATE	IND NO.	NDA NO.	TYPE OF DOCUMENT	DATE OF DOCUMENT
6/1/06	48,924 for reference	22-023	NDA	3/31/2006

NAME OF DRUG	PRIORITY CONSIDERATION	CLASSIFICATION OF DRUG	DESIRED COMPLETION DATE
Fosaprepitant Dimeglumine	Medium	Antiemetic	9/3/2006

NAME OF FIRM: Merck & Co., 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)*: **Trade name review**

II. BIOMETRICS

STATISTICAL EVALUATION BRANCH	STATISTICAL APPLICATION BRANCH
☐ TYPE A OR B NDA REVIEW	☐ CHEMISTRY REVIEW
☐ END OF PHASE II MEETING	☐ PHARMACOLOGY
☐ CONTROLLED STUDIES	☐ BIOPHARMACEUTICS
☐ PROTOCOL REVIEW	☐ OTHER (SPECIFY BELOW):
☐ 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: Application: Please review for trade name [redacted] and please review labeling.
PDUFA date is 2/3/2007N022023 Document: 2797344 Location: \\CDSESUB1\EVSPROD\N022023\0000 b(4)

PDUFA DATE: 2/3/2007
ATTACHMENTS: Draft Package Insert, Container and Carton Labels
CC: Archival IND/NDA 22-023
HFD-180/Division File
HFD-180/RPM
HFD-180/Reviewers and Team Leaders

NAME AND PHONE NUMBER OF REQUESTER	METHOD OF DELIVERY (Check one)
Betsy Scroggs, RHPM	☒ DFS ONLY ☐ MAIL ☐ HAND
SIGNATURE OF RECEIVER	SIGNATURE OF DELIVERER

5/28/05

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/s/

Betsy Scroggs
6/2/2006 03:39:17 PM

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 22-023

Merck & Co., Inc.
Attention: Vijay K. Tammara, Ph.D.
Director, Regulatory Affairs
P.O.Box 1000, UG2CD-48
North Wales, Pa 19454-1099

Dear Dr. Tammara:

We acknowledge receipt on May 5, 2006 of your May 4, 2006 correspondence notifying the Food and Drug Administration that the corporate address has been changed from

P. O. BOX 4, BLA-20
West Point, PA 19486

To:

P. O. Box 1000, UG2CD-48
North Wales, PA 19454-1099

Telephone: (267) 305-6713

for the following new drug application:

NDA 22-023 for Fosaprepitant Dimeglumine.

We have revised our records to reflect this change.

Please cite the NDA number listed above at the top of the first page of all submissions to this application. Send all submissions, electronic or paper, including those sent by overnight mail or courier, to the following address:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Gastroenterology Products
5901-B Ammendale Road
Beltsville, MD 20705-1266

If you have any question, call me at (301) 796-0991.

Sincerely,

{See appended electronic signature page}

Betsy Scroggs, Pharm.D.
Regulatory Health Project Manager
Division of Gastroenterology Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

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/s/

Betsy Scroggs
5/31/2006 03:56:18 PM

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

REQUEST FOR CONSULTATION

TO *(Office/Division)*: OPS, Microbiolog Staff (HFD-805)
Attn: David Hussong (301-796-1228)
WO21 RM 3654
CC: Jim McVey, TL

FROM *(Name, Office/Division, and Phone Number of Requestor)*:
Betsy Scroggs, Pharm.D., RHPM
(301) 796-0991
WO22 RM 5109

DATE	IND NO.	NDA NO.	TYPE OF DOCUMENT	DATE OF DOCUMENT
5/17/06	48,924	22-023	Original eCDT NDA	3/31/06

NAME OF DRUG	PRIORITY CONSIDERATION	CLASSIFICATION OF DRUG	DESIRED COMPLETION DATE
Fosaprepitant Injection	Standard	Antiemetic	10/15/06

NAME OF FIRM: Merck & Co., 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 2a MEETING
- ☐ END-OF-PHASE 2 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

- ☐ PRIORITY P NDA REVIEW
- ☐ END-OF-PHASE 2 MEETING
- ☐ CONTROLLED STUDIES
- ☐ PROTOCOL REVIEW
- ☐ OTHER (SPECIFY BELOW):
- ☐ CHEMISTRY REVIEW
- ☐ PHARMACOLOGY
- ☐ BIOPHARMACEUTICS
- ☐ OTHER (SPECIFY BELOW):

III. BIOPHARMACEUTICS

- ☐ DISSOLUTION
- ☐ BIOAVAILABILTY STUDIES
- ☐ PHASE 4 STUDIES
- ☐ DEFICIENCY LETTER RESPONSE
- ☐ PROTOCOL - BIOPHARMACEUTICS
- ☐ IN-VIVO WAIVER REQUEST

IV. DRUG SAFETY

- ☐ PHASE 4 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
- ☐ NONCLINICAL

COMMENTS / SPECIAL INSTRUCTIONS: Micro consult requested for New NDA 22-023 Fosaprepitant Injection.
ONDQA Reviewer: Julia Pinto (301) 796-1733.

Application: N022023
Document: 2797344
Location: \\CDSESUB1\EVSPROD\N022023\0000

SIGNATURE OF REQUESTOR
Betsy Scroggs, Pharm.D., RHPM

METHOD OF DELIVERY (Check one)
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/s/

Betsy Scroggs
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