Michelle W. Kloss, Ph.D.
Senior Director
Regulatory Affairs

DESK COPY

Merck & Co., Inc.
BLA-20
P.O. Box 4
West Point PA 19486-0004
Tel 610 397 2905
Fax 610 397 2516

May 16, 2001

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

MERCK

c/o
Central Document Room
Food and Drug Administration
Center for Drug Evaluation and Research
12229 Wilkins Avenue
Rockville, MD 20852

Dear Dr. Soreth:

NDA 21-337: INVANZ™ (Ertapenem Sodium)

Response to FDA Request For Information

Reference is made to pending New Drug Application (NDA) cited above for INVANZ™ submitted as an electronic archive on November 30, 2000 and to a April 25, 2001 facsimile communication from Ms. Maureen Dillon Parker (FDA) to Dr. Michelle Kloss (MRL, a Division of Merck & Co., Inc.) requesting additional Case Report Forms (CRFs) and source documentation for certain patients in Protocols 017 and 023. Additional reference is made to a May 4, 2001 telephone conversation between Ms. Dillon Parker and Dr. Kloss during which this April 25, 2001 request was discussed and the Agency was informed of the anticipated timelines for submission of the requested CRFs; during this conversation, MRL agreed to submit, per the Agency's request, written documentation summarizing these anticipated submission timelines. Final reference is made to a May 7, 2001 submission which provided, in follow-up to a May 4, 2001 Agency request, this written summary of anticipated submission timelines for the requested CRF and source documentation.

With this submission, as outlined in the May 7, 2001 communication cited above, MRL is providing all the domestic patient CRFs for Protocols 017 and 023 that were requested in the April 25, 2001 facsimile communication cited above. All information is in an electronic format as indicated in the Table of Contents for this submission.

This response is formatted as required in Title 21 paragraph 314.50 of the Code of Federal Regulations and is being submitted in accordance with the January 1999, *Guidance for Industry – Providing Regulatory Submissions in Electronic Format – NDAs*. As an attachment to this letter, Merck Research Laboratories (MRL), a division of Merck & Co., Inc., is providing one Compact Disk (CD) which contains the response. All documents requiring signatures for certification are included as paper for archival purposes.

We have taken precautions to ensure that the contents of this CD are free of computer viruses (Norton Anti-Virus 4.0, Symantec Corp., 1991-1997) and we authorized the use of anti-virus software, as appropriate.

A list of reviewers from the Division of Anti-Infective Drug Products who should be provided access to this electronic submission on their desktops may be obtained from Ms. Maureen Dillon Parker, Regulatory Project Manager, Division of Anti-Infective Drug 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, nor any future communications in regard to it, public without first obtaining the written permission of Merck & Co., Inc.

Please direct questions or need for additional information to Michelle W. Kloss, Ph.D. (610-397-2905) or, in my absence, to Bonnie J. Goldmann, M.D. (610-397-2383).

Sincerely yours,

Michelle W. Kloss

Michelle W. Kloss, Ph.D.
Senior Director, Regulatory Affairs

Enclosure: CD

Federal Express

Desk Copy (Cover letter): Ms. Maureen Dillon Parker, Regulatory Project Manager
HFD-520, Room S306

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Michelle W. Kloss, Ph.D.
Senior Director
Regulatory Affairs

Merck & Co., Inc.
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May 21, 2001

DESK COPY

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

c/o Central Document Room
Food and Drug Administration
Center for Drug Evaluation and Research
12229 Wilkins Avenue
Rockville, MD 20852

Dear Dr. Soreth:

NDA 21-337: INVANZ™ (Ertapenem Sodium)

AMENDMENT TO PENDING NEW DRUG APPLICATION

Reference is made to the pending New Drug Application (NDA) cited above for INVANZ™ submitted as an electronic archive on November 30, 2000. Reference is also made to an August 17, 1999 FDA/Merck teleconference meeting during which it was agreed that Merck would provide, in lieu of site-specific stability data, Certificates of Analyses for three validation batches of ertapenem drug substance and three validation batches of drug product three months prior to the user fee goal (PDUFA) date for NDA 21-337. Additional reference is made to April 20, 2000 and April 24, 2000 FDA/Merck teleconference meetings, held in follow-up to a proposal for Agency concurrence submitted on April 14, 2000, during which it was agreed that the Certificates of Analyses cited above would be accompanied by a memo certifying that validation of ertapenem drug substance and product had been completed successfully. Final reference is made to a May 7, 2001 submission which provided a proposal for Agency concurrence regarding a revised submission timeline for the Certificates of Analyses for the validation batches of drug product and to a May 16, 2001 teleconference meeting between FDA and Merck to discuss this revised submission timeline proposal. During this May 16, 2001 teleconference meeting, the Agency was informed that the Certificates of Analyses for three validation batches of ertapenem drug substance would be submitted by June 1, 2001 and that the Certificates of Analyses for three validation batches of drug product would be submitted on August 30, 2001.

In accordance with the May 16, 2001 teleconference meeting discussions cited above, with this submission and as indicated on the attached Form FDA 356h, we are providing three Certificates of Analyses containing the release data for the manufacturing process validation batches for ertapenem sodium, manufactured at Merck Manufacturing Division facility located in Danville, Pennsylvania. Included in this submission is a memo certifying that validation of ertapenem drug substance has been completed successfully. All information is in an electronic format as indicated in the Table of Contents for this amendment.

This amendment is formatted as required in Title 21 paragraph 314.50 of the Code of Federal Regulations and is being submitted in accordance with the January 1999, *Guidance for Industry – Providing Regulatory Submissions in Electronic Format – NDAs.* As an attachment to this letter, Merck Research Laboratories (MRL), a division of Merck & Co., Inc., is providing one Compact Disk (CD) which contains the amendment. 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. We have taken precautions to ensure that the contents of this CD are free of computer viruses (Norton Anti-Virus 4.0, Symantec Corp., 1991-1997) and we authorized the use of anti-virus software, as appropriate.

A list of reviewers from the Division of Anti-Infective Drug Products who should be provided access to this electronic submission on their desktops may be obtained from Ms. Maureen Dillon Parker, Regulatory Project Manager, Division of Anti-Infective Drug Products.

Pursuant to 21 CFR 314.50, a complete field copy of this amendment has been submitted to the FDA Philadelphia District Office.

We consider the filing of this amendment to be a confidential matter, and request that the Food and Drug Administration not make its content, nor any future communications in regard to it, public without first obtaining the written permission of Merck & Co., Inc.

Questions concerning this amendment should be directed to Michelle W. Kloss, Ph.D. (610-397-2905) or, in my absence, to Bonnie J. Goldmann, M.D. (610-397-2383).

Sincerely yours,

Michelle W. Kloss

Michelle W. Kloss, Ph.D.
Senior Director, Regulatory Affairs

Q:\maione\mk826\nda amendment\bulk coas

Enclosure: CD

Federal Express

Desk Copies/att:

Ms. Maureen Dillon Parker, Regulatory Project Manager
HFD-520, Room S-306,
Federal Express #2

Dr. B. Vithal Shetty, HFD-520, Room N-356
Federal Express #2

Philadelphia District Office, FDA
Federal Express #3

Michelle W. Kloss, Ph.D.
Senior Director
Regulatory Affairs

Merck & Co., Inc.
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P.O. Box 4
West Point PA 19486-0004
Tel 610 397 2905
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DESK COPY

May 24, 2001

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

c/o Central Document Room
Food and Drug Administration
Center for Drug Evaluation and Research
12229 Wilkins Avenue
Rockville, MD 20852

Dear Dr. Soreth:

NDA 21-337: INVANZ™ (Ertapenem Sodium)

RESPONSE TO FDA REQUEST FOR INFORMATION

Reference is made to the Original NDA for INVANZ™ cited above submitted as an electronic archive on November 30, 2000. Reference is also made to a May 3, 2001 facsimile communication from Ms. Maureen Dillon Parker (FDA) to Dr. Michelle Kloss (MRL, a Division of Merck & Co., Inc.) which requested that MRL review Case Report Forms (CRFs) for Protocol 017, submit corrected data for "Anatomic Site Code", submit new data sets that include this variable, and submit revised analyses in the Clinical Study Report that are dependent on this variable.

With this submission, we are providing the information requested by the Agency in the May 3, 2001 communication cited above. The data on primary site of infection were reviewed for all patients enrolled in Protocol 017 and corrected as appropriate. This involved review of information from the PD CRF with comments, the AP1 CRF with comments, and the SCON information, including both operative note and investigator summary of case. From a review of a total of 665 CRFs in Protocol 017, 54 corrections were made to the "anatomic site code". Displays and analyses that are affected by these data corrections are included in this submission; these include demographic display tables and by anatomic site outcomes analysis tables. It is noteworthy that the changes that resulted from this review of Protocol 017 CRFs were minor and did not alter any of the study conclusions.

The information included in this submission is contained on one Compact Disk (CD). All documents requiring signatures for certification are included as paper for archival purposes.

Michelle W. Kloss, Ph.D.
Senior Director
Regulatory Affairs

Merck & Co., Inc.
BLA-20
P.O. Box 4
West Point PA 19486-0004
Tel 610 397 2905
Fax 610 397 2516

ELECTRONIC COPY

May 25, 2001

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

c/o Central Document Room
Food and Drug Administration
Center for Drug Evaluation and Research
12229 Wilkins Avenue
Rockville, MD 20852

Dear Dr. Soreth:

NDA 21-337: INVANZ™ (Ertapenem Sodium)

RESPONSE TO FDA REQUEST FOR INFORMATION

Reference is made to the pending NDA for INVANZ™ cited above submitted as an electronic archive on November 30, 2000. Reference is also made to a May 23, 2001 facsimile communication from Dr. Janice Pohlman (FDA) to Dr. Michelle Kloss (MRL, a Division of Merck & Co., Inc.) providing 3 comments on Merck Protocol 016 (Skin and Skin Structure Infection) and to a telephone conversation the same day between representatives FDA and MRL to discuss these 3 comments. During this conversation, MRL provided verbal responses to comments #1 and #3 of the facsimile communication cited above and it was agreed that MRL would provide written documentation in response to comment #2 once additional information was received from the Agency. Further reference is made to an additional May 23, 2001 facsimile communication from Dr. Pohlman to Dr. Kloss providing, in follow-up to the telephone conversation, this additional information regarding comment #2. Final reference is made to a May 24, 2001 telephone conversation between representatives of FDA and MRL during which MRL provided confirmation of its May 23, 2001 verbal responses to Comments #1 and #3.

With this submission, MRL is providing a complete response to comment #2 of the Agency's May 23, 2001 facsimile communication cited above. All information is in an electronic format as indicated in the Table of Contents for this submission.

This response is formatted as required in Title 21 paragraph 314.50 of the Code of Federal Regulations and is being submitted in accordance with the January 1999, *Guidance for Industry – Providing Regulatory Submissions in Electronic Format – NDAs*. As an attachment to this letter, Merck Research Laboratories (MRL), a division of Merck & Co., Inc., is providing one Compact Disk (CD) which contains the response. 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. We have taken precautions to ensure that the contents of this CD are free of computer viruses (Norton Anti-Virus 4.0, Symantec Corp., 1991-1997) and we authorized the use of anti-virus software, as appropriate.

All electronic archival information is contained on one CD. We have taken precautions to ensure that the contents of the CDs and diskette are free of computer viruses (Norton Anti-Virus 4.0, Symantec Corp., 1991-1997) and we authorized the use of anti-virus software, as appropriate.

A list of reviewers from the Division of Anti-Infective Drug Products who should be provided access to this electronic submission on their desktops may be obtained from Ms. Maureen Dillon Parker, Regulatory Project Manager, Division of Anti-Infective Drug 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, nor any future communications in regard to it, public without first obtaining the written permission of Merck & Co., Inc.

Please direct questions or need for additional information to Michelle W. Kloss, Ph.D. (610-397-2905) or, in my absence, Bonnie J. Goldmann, M.D. (610-397-2383).

Sincerely yours,

Michelle W. Kloss

Michelle W. Kloss, Ph.D.
Senior Director, Regulatory Affairs

Enclosure: CD

Federal Express #1

Desk Copy: Ms. Maureen P. Dillon Parker, Regulatory Project Manager (cover letter)
HFD-520, Room S306
Fax/Federal Express #2
Dr. Janice Pohlman (cover letter)
HFD-520, Room S312
Fax/Federal Express #2

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Michelle W. Kloss, Ph.D.
Senior Director
Regulatory Affairs

DESK COPY

Merck & Co., Inc.
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May 29, 2001

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

c/o Central Document Room
Office of Drug Evaluation IV (CDER)
Food and Drug Administration
9201 Corporate Boulevard
Rockville, MD 20850

Dear Dr. Soreth:

NDA 21-337: INVANZ™ (Ertapenem Sodium)

GENERAL CORRESPONDENCE

Reference is made to the pending NDA cited above and to a May 16, 2001 teleconference meeting between representatives of FDA and Merck which was held to discuss a revised timeline proposal for Agency concurrence regarding the submission of the drug product validation documentation (Certificates of Analysis) to this NDA.

With this submission, we are providing a summary of this May 16, 2001 meeting as minutes from the teleconference meeting. We would also appreciate receiving the Agency's minutes from this meeting once they become available.

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 January 1999, *Guidance for Industry – Providing Regulatory Submissions in Electronic Format – NDAs.* As an attachment 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. We have taken precautions to ensure that the contents of this CD are free of computer viruses (Norton Anti-Virus 4.0, Symantec Corp., 1991-1997) and we authorized the use of anti-virus software, as appropriate.

A list of reviewers from the Division of Anti-Infective Drug Products who should be provided access to this electronic submission on their desktops may be obtained from Ms. Maureen Dillon Parker, Regulatory Project Manager, Division of Anti-Infective Drug 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, nor any future communications in regard to it, public without first obtaining the written permission of Merck & Co., Inc.

Please direct questions or need for additional information to Michelle W. Kloss, Ph.D. at (610) 397-2905 or, in my absence, Bonnie J. Goldmann, M.D. at (610) 397-2383.

Sincerely,

Michelle W. Kloss

Michelle W. Kloss, Ph.D.
Senior Director
Regulatory Affairs

Enclosure: CD
Federal Express #1

Desk copy/att.: Ms. Maureen Dillon-Parker, Regulatory Project Manager
HFD-520, Room S306
Federal Express #2

Desk copy/att: Dr. B. Vithal Shetty
HFD-520, Room N356
Federal Express #2

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Michelle W. Kloss, Ph.D.
Senior Director
Regulatory Affairs

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P.O. Box 4
West Point PA 19486-0004
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DESK COPY

May 29, 2001

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

c/o Central Document Room
Food and Drug Administration
Center for Drug Evaluation and Research
12229 Wilkins Avenue
Rockville, MD 20852

Fax 5/31/01

Dear Dr. Soreth:

NDA 21-337: INVANZ™ (Ertapenem Sodium)

RESPONSE TO FDA REQUEST FOR INFORMATION

Reference is made to the pending NDA for INVANZ™ cited above submitted as an electronic archive on November 30, 2000. Reference is also made to a May 11, 2001 facsimile communication from Ms. Maureen Dillon Parker (FDA) to Dr. Michelle Kloss (MRL, a Division of Merck & Co., Inc.) which requested the submission of the balance of Case Report Forms (CRFs) for Protocol 016 and also provided comments from the Biopharmaceutical Reviewer regarding Protocol 028 and Protocol 015.

With this submission, we are providing the balance of CRFs for Protocol 016 as requested by the Agency in the May 11, 2001 communication cited above. Please note that the information requested by the Agency for Protocol 028 and Protocol 015 will be provided shortly in a subsequent submission.

This response is formatted as required in Title 21 paragraph 314.50 of the Code of Federal Regulations and is being submitted in accordance with the January 1999, *Guidance for Industry Providing Regulatory Submissions in Electronic Format – NDAs*. As an attachment to this letter, Merck Research Laboratories (MRL), a division of Merck & Co., Inc., is providing one DLT Tape 20/40 which contains the response. All documents requiring signatures for certification are included as paper for archival purposes.

We have taken precautions to ensure that the contents of this tape are free of computer viruses (Norton Anti-Virus 4.0, Symantec Corp., 1991-1997) and we authorized the use of anti-virus software, as appropriate.

A list of reviewers from the Division of Anti-Infective Drug Products who should be provided access to this electronic submission on their desktops may be obtained from Ms. Maureen Dillon Parker, Regulatory Project Manager, Division of Anti-Infective Drug 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, nor any future communications in regard to it, public without first obtaining the written permission of Merck & Co., Inc.

Please direct questions or need for additional information to Michelle W. Kloss, Ph.D. (610-397-2905) or, in my absence, Bonnie J. Goldmann, M.D. (610-397-2383).

Sincerely yours,

Michelle W. Kloss

Michelle W. Kloss, Ph.D.
Senior Director, Regulatory Affairs

Enclosure: DLT Tape

Federal Express #1

Desk Copy: Ms. Maureen P. Dillon Parker, Regulatory Project Manager (cover letter)
HFD-520, Room S306
Federal Express #2

Dr. Janice Pohlman (cover letter)
HFD-520, S312
Federal Express #2

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Michelle W. Kloss, Ph.D.
Senior Director
Regulatory Affairs

Merck & Co., Inc
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P.O. Box 4
West Point PA 19486-0004
Tel 610 397 2905
Fax 610 397 2516

May 31, 2001

DESK COPY

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

c/o Central Document Room
Food and Drug Administration
Center for Drug Evaluation and Research
12229 Wilkins Avenue
Rockville, MD 20852

Dear Dr. Soreth:

NDA 21-337: INVANZ™ (Ertapenem Sodium)

RESPONSE TO FDA REQUEST FOR INFORMATION

Reference is made to the pending NDA for INVANZ™ cited above submitted as an electronic archive on November 30, 2000. Reference is also made to a May 11, 2001 facsimile communication from Ms. Maureen Dillon Parker (FDA) to Dr. Michelle Kloss (MRL, a Division of Merck & Co., Inc.) which requested the submission of the balance of Case Report Forms (CRFs) for Protocol 016 and also provided comments from the Biopharmaceutical Reviewer regarding Protocol 028 and Protocol 015. Further reference is made to a May 29, 2001 submission providing the balance of CRFs for Protocol 016.

With this submission, we are providing the information for Protocol 028 requested by the Agency in the May 11, 2001 communication cited above. Please note that the information requested by the Agency for Protocol 015 will be provided shortly in a subsequent submission.

This response is formatted as required in Title 21 paragraph 314.50 of the Code of Federal Regulations and is being submitted in accordance with the January 1999, *Guidance for Industry - Providing Regulatory Submissions in Electronic Format – NDAs.* As an attachment to this letter, Merck Research Laboratories is providing one Compact Disk (CD) which contains the response. 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. We have taken precautions to ensure that the contents of this CD are free of computer viruses (Norton Anti-Virus 4.0, Symantec Corp., 1991-1997) and we authorized the use of anti-virus software, as appropriate.

A list of reviewers from the Division of Anti-Infective Drug Products who should be provided access to this electronic submission on their desktops may be obtained from Ms. Maureen Dillon Parker, Regulatory Project Manager, Division of Anti-Infective Drug 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, nor any future communications in regard to it, public without first obtaining the written permission of Merck & Co., Inc.

Please direct questions or need for additional information to Michelle W. Kloss, Ph.D. (610-397-2905) or, in my absence, Bonnie J. Goldmann, M.D. (610-397-2383).

Sincerely yours,

Michelle W. Kloss

Michelle W. Kloss, Ph.D.
Senior Director, Regulatory Affairs

Enclosure: CD

Federal Express #1

Desk Copy: Ms. Maureen P. Dillon Parker, Regulatory Project Manager (cover letter)
HFD-520, Room S306
Federal Express #2

Dr. Charles Bonapace (cover letter)
HFD-880, Room S355
Federal Express #3

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Michelle W. Kloss, Ph.D.
Senior Director
Regulatory Affairs

DESK COPY

Merck & Co., Inc.
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PO Box 4
West Point PA 19486-0004
Tel 610 397 2905
Fax 610 397 2516

June 5, 2001

Ms. Maureen Dillon Parker
Division of Anti-Infective Drug Products
HFD-520, Room S306
Office of Drug Evaluation IV (CDER)
Food and Drug Administration
9201 Corporate Boulevard
Rockville, MD 20850

MERCK

Dear Ms. Dillon Parker:

NDA 21-337: INVANZ™ (Ertapenem Sodium)

RESPONSE TO FDA REQUEST FOR DESK COPY COMPACT DISK (CD)

Reference is made to the pending New Drug Application cited above for INVANZ™ submitted as an electronic archive on November 30, 2000 and to a May 16, 2001 submission providing domestic Case Report Forms (CRFs) for Protocol 017 and Protocol 023 in response to the Agency's request of April 25, 2001. Reference is also made to a June 3, 2001 facsimile communication from Ms. Maureen Dillon Parker (FDA) to Dr. Michelle Kloss (MRL, a Division of Merck & Co., Inc.) requesting a desk copy on Compact Disk (CD) of the May 16, 2001 submission as well as a desk copy on CD of the submission of international CRFs for Protocol 017 and Protocol 023.

With this letter, we are providing a desk copy of the May 16, 2001 submission on CD as requested in the June 3, 2001 facsimile communication cited above. We plan to submit the international CRFs for Protocol 017 and 023 during the week of June 4, 2001; per the Agency's June 3, 2001 request, this subsequent submission will also include an additional CD as desk copy.

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, nor any future communications in regard to it, public without first obtaining the written permission of Merck & Co., Inc.

Please direct questions or need for additional information to Michelle W. Kloss, Ph.D. (610-397-2905) or, in my absence, to Bonnie J. Goldmann, M.D. (610-397-2383).

Sincerely,

Michelle W. Kloss

Michelle W. Kloss, Ph.D.
Senior Director, Regulatory Affairs

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Federal Express
File Copy: NDA 21-337, HFD-520, Room S306
Federal Express #1

Michelle W. Kloss, Ph.D.
Senior Director
Regulatory Affairs

Merck & Co., Inc.
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DESK COPY

June 6, 2001

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

c/o Central Document Room
Food and Drug Administration
Center for Drug Evaluation and Research
12229 Wilkins Avenue
Rockville, MD 20852

Dear Dr. Soreth:

NDA 21-337: INVANZ™ (Ertapenem Sodium)

RESPONSE TO FDA REQUEST FOR INFORMATION

Reference is made to the pending NDA for INVANZ™ cited above, submitted as an electronic archive on November 30, 2000. Reference is also made to a May 16, 2001 facsimile communication from Ms. Maureen Dillon Parker (FDA) to Dr. Michelle Kloss (MRL, a Division of Merck & Co., Inc.) providing Pharmacology/Toxicology Reviewer comments on this NDA.

With this submission, MRL is providing a complete response to the Agency's May 16, 2001 facsimile communication cited above. All information is in an electronic format as indicated in the Table of Contents for this submission.

This response is formatted as required in Title 21 paragraph 314.50 of the Code of Federal Regulations and is being submitted in accordance with the January 1999, *Guidance for Industry – Providing Regulatory Submissions in Electronic Format – NDAs.* As an attachment to this letter, Merck Research Laboratories (MRL), a division of Merck & Co., Inc., is providing one Compact Disk (CD) which contains the response. 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. We have taken precautions to ensure that the contents of this CD are free of computer viruses (Norton Anti-Virus 4.0, Symantec Corp., 1991-1997) and we authorized the use of anti-virus software, as appropriate.

This response is formatted as required in Title 21 paragraph 314.50 of the Code of Federal Regulations and is being submitted in accordance with the January 1999, *Guidance for Industry – Providing Regulatory Submissions in Electronic Format – NDAs.*

All electronic archival information is contained on one CD. We have taken precautions to ensure that the contents of the CDs and diskette are free of computer viruses (Norton Anti-Virus 4.0, Symantec Corp., 1991-1997) and we authorized the use of anti-virus software, as appropriate.

A list of reviewers from the Division of Anti-Infective Drug Products who should be provided access to this electronic submission on their desktops may be obtained from Ms. Maureen Dillon Parker, Regulatory Project Manager, Division of Anti-Infective Drug 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, nor any future communications in regard to it, public without first obtaining the written permission of Merck & Co., Inc.

We trust that the information provided in this submission adequately addresses the Agency's request and that the information will facilitate the Agency's review of the application. Please direct questions or need for additional information to Michelle W. Kloss, Ph.D. (610-397-2905) or, in my absence, Bonnie J. Goldmann, M.D. (610-397-2383).

Sincerely yours,

Michelle W. Kloss

Michelle W. Kloss, Ph.D.
Senior Director, Regulatory Affairs

Enclosure: CD

Federal Express #1

Desk Copy: Ms. Maureen P. Dillon Parker, Regulatory Project Manager (cover letter)
HFD-520, Room S306
Federal Express #2

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Michelle W. Kloss, Ph.D.
Senior Director
Regulatory Affairs

DESK COPY

Merck & Co., Inc.
BLA-20
P.O. Box 4
West Point PA 19486-0004
Tel 610 397 2905
Fax 610 397 2516

June 8, 2001

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

c/o Central Document Room
Food and Drug Administration
Center for Drug Evaluation and Research
12229 Wilkins Avenue
Rockville, Maryland 20852

Dear Dr. Soreth:

NDA 21-337: INVANZ™ (Ertapenem Sodium)

RESPONSE TO FDA REQUEST FOR INFORMATION

Reference is made to the pending New Drug Application (NDA) cited above for INVANZ™ submitted as an electronic archive on November 30, 2000 and to an April 25, 2001 facsimile communication from Ms. Maureen Dillon Parker (FDA) to Dr. Michelle Kloss (MRL, a Division of Merck & Co., Inc.) requesting additional Case Report Forms (CRFs) and source documentation for certain patients in Protocols 017 and 023. Additional reference is made to a May 4, 2001 telephone conversation between Ms. Dillon Parker and Dr. Kloss during which this April 25, 2001 request was discussed and the Agency was informed of the anticipated timelines for submission of the requested CRFs; during this conversation, MRL agreed to submit, per the Agency's request, written documentation summarizing these anticipated submission timelines. Reference is also made to a May 7, 2001 submission which provided, in follow-up to the May 4, 2001 Agency request, this written summary of anticipated submission timelines for the requested CRF and source documentation. Final reference is made to a May 16, 2001 submission which provided all the domestic patient CRFs for Protocols 017 and 023 that were requested in the April 25, 2001 facsimile communication.

With this submission, as outlined in the May 7, 2001 communication cited above, MRL is providing all the international patient CRFs and source documentation for Protocols 017 and 023 that were requested in the April 25, 2001 facsimile communication cited above. It should be noted that patient AN 7646 was assigned an allocation number, but never received drug, therefore the CRF for this patient is provided with this submission, but the source documentation is not available. The patient CRF is provided, but source document is not available. Additionally, please note that due to the size of the submission, MRL will provide the desk copy as requested in the June 3, 2001 facsimile from Ms. Dillon Parker to Dr. Kloss, for use by the Medical Reviewer in a subsequent submission. All information is in an electronic format as indicated in the Table of Contents for this submission.

This response is formatted as required in Title 21 paragraph 314.50 of the Code of Federal Regulations and is being submitted in accordance with the January 1999, *Guidance for Industry – Providing Regulatory Submissions in Electronic Format – NDAs.* As an attachment to this letter, Merck Research Laboratories (MRL), a division of Merck & Co., Inc., is providing a DLT Tape which contain the response. All documents requiring signatures for certification are included as paper for archival purposes.

We have taken precautions to ensure that the contents of the tape are free of computer viruses (Norton Anti-Virus 4.0, Symantec Corp., 1991-1997) and we authorized the use of anti-virus software, as appropriate.

A list of reviewers from the Division of Anti-Infective Drug Products who should be provided access to this electronic submission on their desktops may be obtained from Ms. Maureen Dillon Parker, Regulatory Project Manager, Division of Anti-Infective Drug 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, nor 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 Michelle W. Kloss, Ph.D. (610-397-2905) or, in my absence, to Bonnie J. Goldmann, M.D. (610-397-2383).

Sincerely yours,

Bonnie Goldmann for
Michelle W. Kloss, Ph.D.
Senior Director, Regulatory Affairs

Enclosure: DLT Tape

Courier

Desk Copy: Ms. Maureen Dillon Parker, Regulatory Project Manager (cover letter)
HFD-520, Room S306
Courier

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Michelle W. Kloss, Ph.D.
Senior Director
Regulatory Affairs

Merck & Co., Inc.
BLA-20
P.O. Box 4
West Point PA 19486-0004
Tel 610 397 2905
Fax 610 397 2516

June 8, 2001

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

c/o Central Document Room
Food and Drug Administration
Center for Drug Evaluation and Research
12229 Wilkins Avenue
Rockville, MD 20852

MERCK

Dear Dr. Soreth:

NDA 21-337: INVANZ™ (Ertapenem Sodium)

RESPONSE TO FDA REQUEST FOR INFORMATION

Reference is made to the pending New Drug Application (NDA) cited above for INVANZ™ submitted as an electronic archive on November 30, 2000 in which Case Report Forms (CRFs) were provided in Item 12. Reference is also made to a January 18, 2001 submission providing additional CRFs in response to a December 15, 2000 FDA request. Further reference is made to a May 4, 2001 telephone conversation between Ms. Maureen Dillon Parker (FDA) and Dr. Michelle Kloss (MRL, a Division of Merck & Co., Inc.) during which the Agency was informed that MRL had recently discovered that the SCON forms (which contained the operative summaries and narratives) had inadvertently not been attached to the domestic patient CRFs for Protocols 017 and 023 previously provided to the Agency in the submissions cited above. During this conversation, it was agreed that MRL would resubmit, as soon as possible, CRFs including the SCON page attachment to replace those previously submitted CRFs that lacked this attachment. Further reference is made to a May 7, 2001 communication which provided, per the Agency's May 4, 2001 request, a summary of anticipated submission timelines for the outstanding CRF documentation for this NDA.

As indicated on the attached Form FDA 356h and per the May 4, 2001 telephone conversation cited above, we are providing replacement CRFs for the Protocol 017 and Protocol 023 domestic patient CRFs that were previously provided to the Agency; these replacement CRFs include the SCON page attachment which was inadvertently omitted from the previously submitted CRFs. All information is in an electronic format as indicated in the Table of Contents for this response; a listing of the replacement CRFs is included in this submission.

This response is formatted as required in Title 21 paragraph 314.50 of the Code of Federal Regulations and is being submitted in accordance with the January 1999, *Guidance for Industry – Providing Regulatory Submissions in Electronic Format – NDAs*. As an attachment to this letter, Merck Research Laboratories (MRL), a division of Merck & Co., Inc., is providing one Compact Disk (CD) which contains the response. All documents requiring signatures for certification are included as paper for archival purposes.

ORIGINAL

We have taken precautions to ensure that the contents of this CD are free of computer viruses (Norton Anti-Virus 4.0, Symantec Corp., 1991-1997) and we authorized the use of anti-virus software, as appropriate.

A list of reviewers from the Division of Anti-Infective Drug Products who should be provided access to this electronic submission on their desktops may be obtained from Ms. Maureen Dillon Parker, Regulatory Project Manager, Division of Anti-Infective Drug Products.

We consider the filing of this response to be a confidential matter, and request that the Food and Drug Administration not make its content, nor any future communications in regard to it, public without first obtaining the written permission of Merck & Co., Inc.

MRL sincerely apologizes for any inconvenience this inadvertent oversight may have caused the Agency. Questions concerning this submission should be directed to Michelle W. Kloss, Ph.D. (610-397-2905) or, in my absence, to Bonnie J. Goldmann, M.D. (610-397-2383).

Sincerely yours,

Bonnie J. Goldmann for

Michelle W. Kloss, Ph.D.
Senior Director, Regulatory Affairs

Enclosure: CD

Courier

Desk Copy: Ms. Maureen Dillon Parker, Regulatory Project Manager (cover letter)
HFD-520, Room S-306
Courier

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Michelle W. Kloss, Ph.D.
Senior Director
Regulatory Affairs

DESK COPY

Merck & Co., Inc.
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West Point PA 19486-0004
Tel 610 397 2905
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June 12, 2001

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

c/o Central Document Room
Food and Drug Administration
Center for Drug Evaluation and Research
12229 Wilkins Avenue
Rockville, MD 20852

Dear Dr. Soreth:

NDA 21-337: INVANZ™ (Ertapenem Sodium)

RESPONSE TO FDA REQUEST FOR INFORMATION

Reference is made to the pending NDA for INVANZ™ cited above, submitted as an electronic archive on November 30, 2000. Reference is also made to a May 11, 2001 facsimile communication from Ms. Maureen Dillon Parker (FDA) to Dr. Michelle Kloss (MRL, a Division of Merck & Co., Inc.) which requested the submission of the balance of Case Report Forms (CRFs) for Protocol 016 and also provided comments from the Biopharmaceutical Reviewer regarding Protocol 028 and Protocol 015. Further reference is made to a May 29, 2001 submission providing the balance of CRFs for Protocol 016 and to a May 31, 2001 submission providing information for Protocol 028.

With this submission, we are providing the information for **Protocol 015,** along with the assay validation information, requested by the Agency in the May 11, 2001 communication cited above.

This response is formatted as required in Title 21 paragraph 314.50 of the Code of Federal Regulations and is being submitted in accordance with the January 1999, *Guidance for Industry – Providing Regulatory Submissions in Electronic Format – NDAs.* As an attachment to this letter, Merck Research Laboratories is providing one Compact Disk (CD) which contains the response. 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. We have taken precautions to ensure that the contents of this CD are free of computer viruses (Norton Anti-Virus 4.0, Symantec Corp., 1991-1997) and we authorized the use of anti-virus software, as appropriate.

A list of reviewers from the Division of Anti-Infective Drug Products who should be provided access to this electronic submission on their desktops may be obtained from Ms. Maureen Dillon Parker, Regulatory Project Manager, Division of Anti-Infective Drug 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, nor any future communications in regard to it, public without first obtaining the written permission of Merck & Co., Inc.

Please direct questions or need for additional information to Michelle W. Kloss, Ph.D. (610-397-2905) or, in my absence, Bonnie J. Goldmann, M.D. (610-397-2383).

Sincerely yours,

Michelle W. Kloss

Michelle W. Kloss, Ph.D.
Senior Director, Regulatory Affairs

Enclosure: CD

Federal Express #1

Desk Copy: Ms. Maureen P. Dillon Parker, Regulatory Project Manager (cover letter)
HFD-520, Room S306
Federal Express #2

Dr. Charles Bonapace (cover letter)
HFD-880, Room S355
Federal Express #3

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Michelle W. Kloss, Ph.D.
Senior Director
Regulatory Affairs

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June 14, 2001

Ms. Maureen Dillon Parker
Division of Anti-Infective Drug Products
HFD-520, Room S306
Office of Drug Evaluation IV (CDER)
Food and Drug Administration
9201 Corporate Boulevard
Rockville, MD 20850

MERCK

Dear Ms. Dillon Parker:

NDA 21-337: INVANZ™ (Ertapenem Sodium)

RESPONSE TO FDA REQUEST FOR DESK COPY COMPACT DISK (CD)

Reference is made to the pending New Drug Application cited above for INVANZ™ submitted as an electronic archive on November 30, 2000 and to a June 8, 2001 submission providing international patient Case Report Forms (CRFs) and source documentation for Protocol 017 and Protocol 023 in response to the Agency's request of April 25, 2001. Reference is also made to a June 3, 2001 facsimile communication from Ms. Maureen Dillon Parker (FDA) to Dr. Michelle Kloss (MRL, a Division of Merck & Co., Inc.) requesting a desk copy on Compact Disk (CD) of the submission of international CRFs for Protocol 017 and Protocol 023.

Due to the size of the June 8, 2001 submission, MRL was not able to provide the desk copy at that time; therefore with this letter, we are providing a desk copy of the June 8, 2001 submission on CD (2) as requested in the June 3, 2001 facsimile communication cited above. We apologize for any inconvenience this delay may have caused the Agency.

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, nor any future communications in regard to it, public without first obtaining the written permission of Merck & Co., Inc.

Please direct questions or need for additional information to Michelle W. Kloss, Ph.D. (610-397-2905) or, in my absence, to Bonnie J. Goldmann, M.D. (610-397-2383).

Sincerely,

Michelle W. Kloss, Ph.D.
Senior Director, Regulatory Affairs

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Federal Express
File Copy: NDA 21-337, HFD-520, Room S306
Federal Express #1

Michelle W. Kloss, Ph.D.
Senior Director
Regulatory Affairs

Merck & Co., Inc.
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DESK COPY

June 19, 2001

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

c/o Central Document Room
Food and Drug Administration
Center for Drug Evaluation and Research
12229 Wilkins Avenue
Rockville, MD 20852

Dear Dr. Soreth:

NDA 21-337: INVANZ™ (Ertapenem Sodium)

RESPONSE TO FDA REQUEST FOR INFORMATION

Reference is made to the pending NDA for INVANZ™ cited above, submitted as an electronic archive on November 30, 2000. Reference is also made to a June 8, 2001 facsimile communication from Ms. Maureen Dillon Parker (FDA) to Dr. Michelle Kloss (MRL, a Division of Merck & Co., Inc.) which requested Case Report Form (CRF) culture result sheets (CR1) for selected patients who participated in Protocols 018 and 020. Further reference is made to the June 12, 2001 facsimile communication from Dr. Kloss to Ms. Dillon Parker providing the requested CR1 form and related Investigator Clinical Data Verification Forms (ICDVFs).

With this submission, we are providing the official submission of the June 12, 2001 facsimile containing the CR1 pages and related ICDVFs, as requested by the Agency in the June 8, 2001 communication cited above.

This response is formatted as required in Title 21 paragraph 314.50 of the Code of Federal Regulations and is being submitted in accordance with the January 1999, *Guidance for Industry – Providing Regulatory Submissions in Electronic Format – NDAs.* As an attachment to this letter, Merck Research Laboratories is providing one Compact Disk (CD) which contains the response. All documents requiring signatures for certification are included as paper for archival purposes.

We have taken precautions to ensure that the contents of this CD are free of computer viruses (Norton Anti-Virus 4.0, Symantec Corp., 1991-1997) and we authorized the use of anti-virus software, as appropriate.

A list of reviewers from the Division of Anti-Infective Drug Products who should be provided access to this electronic submission on their desktops may be obtained from Ms. Maureen Dillon Parker, Regulatory Project Manager, Division of Anti-Infective Drug 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, nor any future communications in regard to it, public without first obtaining the written permission of Merck & Co., Inc.

Please direct questions or need for additional information to Michelle W. Kloss, Ph.D. (610-397-2905) or, in my absence, Bonnie J. Goldmann, M.D. (610-397-2383).

Sincerely yours,

Michelle W. Kloss, Ph.D.
Senior Director, Regulatory Affairs

Enclosure: CD

Federal Express #1

Desk Copy: Ms. Maureen P. Dillon Parker, Regulatory Project Manager (cover letter)
HFD-520, Room S306
Fax/Federal Express #2

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Michelle W. Kloss, Ph.D.
Senior Director
Regulatory Affairs

Merck & Co., Inc.
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June 20, 2001

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

c/o Central Document Room
Food and Drug Administration
Center for Drug Evaluation and Research
12229 Wilkins Avenue
Rockville, MD 20852

Dear Dr. Soreth:

NDA 21-337: INVANZ™ (Ertapenem Sodium)

RESPONSE TO FDA REQUEST FOR INFORMATION

Reference is made to the pending NDA for INVANZ™ cited above submitted as an electronic archive on November 30, 2000. Reference is also made to a June 19, 2001 facsimile communication from Ms. Maureen Dillon Parker (FDA) to Dr. Michelle Kloss (MRL, a Division of Merck & Co., Inc.) which requested the Case Report Form (CRF) for patient AN 3323 (Study 020-028).

With this submission, we are providing the CRF for AN 3323 requested in the June 19, 2001 communication cited above and the related Investigator Clinical Data Verification Forms (ICDVFs).

This response is formatted as required in Title 21 paragraph 314.50 of the Code of Federal Regulations and is being submitted in accordance with the January 1999, *Guidance for Industry – Providing Regulatory Submissions in Electronic Format – NDAs.* As an attachment to this letter, Merck Research Laboratories is providing one Compact Disk (CD) which contains the response. All documents requiring signatures for certification are included as paper for archival purposes.

We have taken precautions to ensure that the contents of this CD are free of computer viruses (Norton Anti-Virus 4.0, Symantec Corp., 1991-1997) and we authorized the use of anti-virus software, as appropriate.

A list of reviewers from the Division of Anti-Infective Drug Products who should be provided access to this electronic submission on their desktops may be obtained from Ms. Maureen Dillon Parker, Regulatory Project Manager, Division of Anti-Infective Drug 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, nor any future communications in regard to it, public without first obtaining the written permission of Merck & Co., Inc.

Please direct questions or need for additional information to Michelle W. Kloss, Ph.D. (610-397-2905) or, in my absence, Bonnie J. Goldmann, M.D. (610-397-2383).

Sincerely yours,

Michelle W. Kloss

Michelle W. Kloss, Ph.D.
Senior Director, Regulatory Affairs

Enclosure: CD

Federal Express #1

Desk Copy: Ms. Maureen P. Dillon Parker, Regulatory Project Manager (cover letter)
HFD-520, Room S306
Fax/Federal Express #2

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Michelle W. Kloss, Ph.D.
Senior Director
Regulatory Affairs

DESK COPY

Merck & Co., Inc.
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June 22, 2001

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

c/o Central Document Room
Food and Drug Administration
Center for Drug Evaluation and Research
12229 Wilkins Avenue
Rockville, MD 20852

Dear Dr. Soreth:

NDA 21-337: INVANZ™ (Ertapenem Sodium)

RESPONSE TO FDA REQUEST FOR INFORMATION

Reference is made to the pending NDA for INVANZ™ cited above submitted as an electronic archive on November 30, 2000. Reference is also made to a May 11, 2001 facsimile communication from Ms. Maureen Dillon Parker (FDA) to Dr. Michelle Kloss (MRL, a Division of Merck & Co., Inc.) requesting individual patient information for Protocol 028. Further reference is made to a May 31, 2001 submission which provided the total plasma concentration requested and a commitment to submit the unbound plasma data as soon as it became available.

With this submission, we are providing preliminary, unaudited unbound plasma concentration data for Protocol 028 as requested by the Agency in the May 11, 2001 communication cited above. This submission thus completes MRL's response to the Agency comments regarding Protocol 028 cited in the May 11, 2001 communication cited above.

This response is formatted as required in Title 21 paragraph 314.50 of the Code of Federal Regulations and is being submitted in accordance with the January 1999, *Guidance for Industry – Providing Regulatory Submissions in Electronic Format – NDAs.* As an attachment to this letter, Merck Research Laboratories is providing one Compact Disk (CD) which contains the response. 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. We have taken precautions to ensure that the contents of this CD are free of computer viruses (Norton Anti-Virus 4.0, Symantec Corp., 1991-1997) and we authorized the use of anti-virus software, as appropriate.

A list of reviewers from the Division of Anti-Infective Drug Products who should be provided access to this electronic submission on their desktops may be obtained from Ms. Maureen Dillon Parker, Regulatory Project Manager, Division of Anti-Infective Drug 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, nor any future communications in regard to it, public without first obtaining the written permission of Merck & Co., Inc.

Please direct questions or need for additional information to Michelle W. Kloss, Ph.D. (610-397-2905) or, in my absence, Bonnie J. Goldmann, M.D. (610-397-2383).

Sincerely yours,

Michelle W. Kloss

Michelle W. Kloss, Ph.D.
Senior Director, Regulatory Affairs

Enclosure: CD

Federal Express #1

Desk Copy: Ms. Maureen P. Dillon Parker, Regulatory Project Manager (cover letter)
HFD-520, Room S306
Fax/Federal Express #2

Dr. Charles Bonapace (cover letter)
HFD-880, Room S355
Federal Express #3

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Michelle W. Kloss, Ph.D.
Senior Director
Regulatory Affairs

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June 22, 2001

DESK COPY

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

c/o Central Document Room
Food and Drug Administration
Center for Drug Evaluation and Research
12229 Wilkins Avenue
Rockville, MD 20852

Dear Dr. Soreth:

NDA 21-337: INVANZ™ (Ertapenem Sodium)

RESPONSE TO FDA REQUEST FOR INFORMATION

Reference is made to the pending NDA for INVANZ™ cited above submitted as an electronic archive on November 30, 2000. Reference is also made to a [redacted] facsimile communication from Ms. Maureen Dillon Parker (FDA) to Dr. Michelle Kloss (MRL, a Division of Merck & Co., Inc.) which requested additional information for patient AN 6281 (Study 018).

With this submission, we are providing the information for patient AN 6281 requested by the Agency in the June 12, 2001 communication cited above.

This response is formatted as required in Title 21 paragraph 314.50 of the Code of Federal Regulations and is being submitted in accordance with the January 1999, *Guidance for Industry – Providing Regulatory Submissions in Electronic Format – NDAs.* As an attachment to this letter, Merck Research Laboratories is providing one Compact Disk (CD) which contains the response. 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. We have taken precautions to ensure that the contents of this CD are free of computer viruses (Norton Anti-Virus 4.0, Symantec Corp., 1991-1997) and we authorized the use of anti-virus software, as appropriate.

A list of reviewers from the Division of Anti-Infective Drug Products who should be provided access to this electronic submission on their desktops may be obtained from Ms. Maureen Dillon Parker, Regulatory Project Manager, Division of Anti-Infective Drug 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, nor any future communications in regard to it, public without first obtaining the written permission of Merck & Co., Inc.

Please direct questions or need for additional information to Michelle W. Kloss, Ph.D. (610-397-2905) or, in my absence, Bonnie J. Goldmann, M.D. (610-397-2383).

Sincerely yours,

Michelle W. Kloss

Michelle W. Kloss, Ph.D.
Senior Director, Regulatory Affairs

Enclosure: CD

Federal Express #1

Desk Copy: Ms. Maureen P. Dillon Parker, Regulatory Project Manager (cover letter)
HFD-520, Room S306
Fax/Federal Express #2

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Michelle W. Kloss, Ph.D.
Senior Director
Regulatory Affairs

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July 3, 2001

Central Document Room
Food and Drug Administration
Center for Drug Evaluation and Research
12229 Wilkins Avenue
Rockville, MD 20852

MERCK

NDA 21-337: INVANZ™ (Ertapenem Sodium)

Response to FDA Request for Information

Reference is made to the pending New Drug Application (NDA) cited above for INVANZ™ submitted as an electronic archive on November 30, 2000. Reference is also made to a February 28, 2001 Agency facsimile communication from Ms. Maureen Dillon-Parker (FDA) to Dr. Michelle Kloss (MRL, a Division of Merck & Co., Inc.) which requested information regarding the results of Protocol 029 and to a March 22, 2001 submission of a summary of the preliminary, unaudited results for Protocol 029 as a complete response to this Agency request. Further reference is made to a July 2, 2001 teleconference meeting between representatives from FDA and MRL during which the Agency requested information regarding the timeline for submission of the Clinical Study Report (CSR), along with SAS transport files, for Protocol 029. Final reference is made to a telephone conversation on July 2, 2001 between Ms. Frances LeSane and Dr. Jean Mulinde (FDA) and Dr. Michelle Kloss (MRL) during which the Agency was informed of MRL's timeline for submission of the Protocol 029 CSR, in follow-up to the teleconference meeting cited above.

With this submission, in follow-up to the March 22, 2001 submission and the June 2, 2001 conversations cited above, MRL is providing the CSR for Protocol 029 along with all SAS transport files. In addition, we are providing a desk copy on CD for use by the Medical Reviewer. All information is in an electronic format as indicated in the Table of Contents for this submission.

This response is formatted as required in Title 21 paragraph 314.50 of the Code of Federal Regulations and is being submitted in accordance with the January 1999, *Guidance for Industry – Providing Regulatory Submissions in Electronic Format – NDAs*. As an attachment to this letter, Merck Research Laboratories (MRL), a division of Merck & Co., Inc., is providing one Compact Disk (CD) which contains the response. All documents requiring signatures for certification are included as paper for archival purposes. A Review copy of the CSR are also being submitted in hard copy as described in the Statement of Organization following the cover letter.

We have taken precautions to ensure that the contents of this CD are free of computer viruses (Norton Anti-Virus 4.0, Symantec Corp., 1991-1997) and we authorized the use of anti-virus software, as appropriate.

A list of reviewers from the Division of Anti-Infective Drug Products who should be provided access to this electronic submission on their desktops may be obtained from Ms. Maureen Dillon-Parker, Regulatory Project Manager, Division of Anti-Infective Drug 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, nor 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 Michelle W. Kloss, Ph.D. (484-344-2905) or, in my absence, to Bonnie J. Goldmann, M.D. (484-344-2383).

Sincerely,

Michelle W. Kloss

Michelle W. Kloss, Ph.D.
Senior Director, Regulatory Affairs

Enclosure: CD

Hand Deliver

Desk Copy: Ms. Maureen Dillon Parker, Regulatory Project Manager (cover letter +CD)
HFD-520, Room S306
Hand Deliver #2

Q:\malone\mk826\nda amendment\P029 CSR

Michelle W. Kloss, Ph.D.
Senior Director
Regulatory Affairs

Merck & Co., Inc.
BLA-20
P.O. Box 4
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Tel 484 344 2905
Fax 484 344 2516

July 6, 2001

MERCK

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

c/o Central Document Room
Food and Drug Administration
Center for Drug Evaluation and Research
12229 Wilkins Avenue
Rockville, MD 20852

Dear Dr. Soreth:

NDA 21-337: INVANZ™ (Ertapenem Sodium)

RESPONSE TO FDA REQUEST FOR INFORMATION

Reference is made to the pending NDA for INVANZ™ cited above, submitted as an electronic archive on November 30, 2000. Reference is also made to a June 22, 2001 facsimile communication from Ms. Maureen Dillon-Parker (FDA) to Dr. Michelle Kloss (MRL, a Division of Merck & Co., Inc.) providing Pharmacology/Toxicology reviewer comments on the NDA. Further reference is made to a July 2, 2001 teleconference meeting between representatives of FDA and MRL held at MRL's request in order to obtain further clarification from the Agency regarding Comments #2, #3 and #4 of the facsimile communication. During this teleconference meeting discussion, Dr. Ken Seethaler (Pharmacology/Toxicology Reviewer) indicated that he would consult his supervisor further regarding these comments and it was agreed that MRL would provide its responses to these specific comments in writing to facilitate Dr. Seethaler's consultation.

With this submission, MRL is providing a summary of its responses to Comments #2, #3, and #4 as agreed during the July 2, 2001 teleconference cited above. All information is in an electronic format as indicated in the Table of Contents for this submission.

This response is formatted as required in Title 21 paragraph 314.50 of the Code of Federal Regulations and is being submitted in accordance with the January 1999, *Guidance for Industry – Providing Regulatory Submissions in Electronic Format – NDAs*. As an attachment to this letter, Merck Research Laboratories (MRL), a division of Merck & Co., Inc., is providing one Compact Disk (CD) which contains the response. All documents requiring signatures for certification are included as paper for archival purposes.

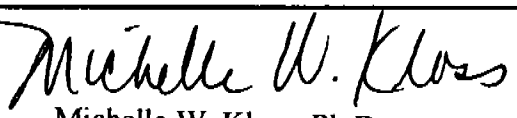
We have taken precautions to ensure that the contents of this CD are free of computer viruses (Norton Anti-Virus 4.0, Symantec Corp., 1991-1997) and we authorized the use of anti-virus software, as appropriate.

A list of reviewers from the Division of Anti-Infective Drug Products who should be provided access to this electronic submission on their desktops may be obtained from Ms. Maureen Dillon-Parker, Regulatory Project Manager, Division of Anti-Infective Drug 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, nor any future communications in regard to it, public without first obtaining the written permission of Merck & Co., Inc.

Questions concerning this amendment should be directed to Michelle W. Kloss, Ph.D. (484-344-2905) or, in my absence, to Bonnie J. Goldmann, M.D. (484-344-2383).

Sincerely yours,



Michelle W. Kloss, Ph.D.
Senior Director, Regulatory Affairs

Enclosure: CD

Federal Express #1

Desk Copy: Ms. Frances LeSane, Supervisory Regulatory Project Manager (cover letter)
HFD-520, Room N355
Fax/Federal Express #2

Ms. Maureen Dillon-Parker, Regulatory Project Manager (cover letter)
HFD-520, Room S306
Fax/Federal Express #2

Dr. Ken Seethaler (cover letter)
HFD-520, Room N357
Fax/Federal Express #2

Michelle W. Kloss, Ph.D.
Senior Director
Regulatory Affairs

Merck & Co., Inc.
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P.O. Box 4
West Point PA 19486-0004
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Fax 484 344 2516

DESK COPY

July 13, 2001

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

c/o Central Document Room
Food and Drug Administration
Center for Drug Evaluation and Research
12229 Wilkins Avenue
Rockville, MD 20852

Dear Dr. Soreth:

NDA 21-337: INVANZ™ (Ertapenem Sodium)

RESPONSE TO FDA REQUEST FOR INFORMATION

Reference is made to the pending NDA for INVANZ™ cited above, submitted as an electronic archive on November 30, 2000. Reference is also made to a June 22, 2001 facsimile communication from Ms. Maureen Dillon Parker (FDA) to Dr. Michelle Kloss (MRL, a Division of Merck & Co., Inc.) providing Pharmacology/Toxicology reviewer comments on the NDA. Further reference is made to a July 2, 2001 teleconference meeting between representatives of FDA and MRL held at MRL's request in order to obtain further clarification from the Agency regarding Comments #2, #3 and #4 of the facsimile communication; at this teleconference meeting, it was agreed that MRL would provide written responses to Comments #2, #3 and #4 in advance of the responses to the other Agency comments cited in the facsimile communication in order to facilitate Dr. Ken Seethaler's (Pharmacology/Toxicology Reviewer) consultation with his supervisor regarding these comments. Final reference is made to a July 6, 2001 submission which provided MRL's responses to Comments #2, #3 and #4.

With this submission, per the agreements reached at the teleconference meeting cited above, MRL is providing responses to the Agency's remaining comments (Comments #1, #5 and #6) in the June 22, 2001 facsimile communication cited above. MRL has thus provided a complete response to all the Agency comments noted in the June 22, 2001 facsimile communication. All information is in an electronic format as indicated in the Table of Contents for this submission.

This response is formatted as required in Title 21 paragraph 314.50 of the Code of Federal Regulations and is being submitted in accordance with the January 1999, *Guidance for Industry – Providing Regulatory Submissions in Electronic Format – NDAs.* As an attachment to this letter, Merck Research Laboratories (MRL), a division of Merck & Co., Inc., is providing one Compact Disk (CD) which contains the response. All documents requiring signatures for certification are included as paper for archival purposes.

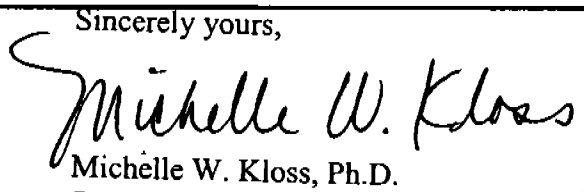
We have taken precautions to ensure that the contents of this CD are free of computer viruses (Norton Anti-Virus 4.0, Symantec Corp., 1991-1997) and we authorized the use of anti-virus software, as appropriate.

A list of reviewers from the Division of Anti-Infective Drug Products who should be provided access to this electronic submission on their desktops may be obtained from Ms. Maureen Dillon Parker, Regulatory Project Manager, Division of Anti-Infective Drug 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, nor any future communications in regard to it, public without first obtaining the written permission of Merck & Co., Inc.

Questions concerning this amendment should be directed to Michelle W. Kloss, Ph.D. (484-344-2905) or, in my absence, to Bonnie J. Goldmann, M.D. (484-344-2383).

Sincerely yours,



Michelle W. Kloss, Ph.D.
Senior Director, Regulatory Affairs

Enclosure: CD

Hand Deliver

Desk Copy: Ms. Maureen Dillon Parker, Regulatory Project Manager (cover letter)
HFD-520, Room S306
Hand-Deliver

Desk Copy w/att: Dr. Ken Seethaler
HFD-520, Room N357
Hand-Deliver

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Michelle W. Kloss, Ph.D.
Senior Director
Regulatory Affairs

DESK COPY

Merck & Co., Inc.
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July 16, 2001

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

c/o Central Document Room
Food and Drug Administration
Center for Drug Evaluation and Research
12229 Wilkins Avenue
Rockville, MD 20852

Dear Dr. Soreth:

NDA 21-337: INVANZ™ (Ertapenem Sodium)

AMENDMENT TO PENDING NEW DRUG APPLICATION

Reference is made to the pending New Drug Application (NDA) cited above for INVANZ™ submitted as an electronic archive on November 30, 2000. Reference is also made to a May 7, 2001 submission of a background document that provided notification of Merck's intent to file a CMC amendment to the NDA cited above to update Reference C-2 of the CMC information

Further reference is made to a May 16, 2001 teleconference meeting between representatives of FDA and Merck during which the content and timeline for this upcoming CMC amendment was discussed.

With this submission, in follow-up to the May 7, 2001 background document and to the May 16, 2001 teleconference meeting cited above, we are providing an amendment to the pending NDA cited above. This amendment describes a modification to the information submitted in Reference [C-2] of the CMC section in the pending NDA in support of the

This amendment is formatted as required in Title 21 paragraph 314.50 of the Code of Federal Regulations and is being submitted in accordance with the January 1999, *Guidance for Industry – Providing Regulatory Submissions in Electronic Format – NDAs.* As an attachment to this letter, Merck Research Laboratories (MRL), a division of Merck & Co., Inc., is providing one Compact Disk (CD) which contains the amendment. 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. We have taken precautions to ensure that the contents of this CD are free of computer viruses (Norton Anti-Virus 4.0, Symantec Corp., 1991-1997) and we authorized the use of anti-virus software, as appropriate.

A list of reviewers from the Division of Anti-Infective Drug Products who should be provided access to this electronic submission on their desktops may be obtained from Ms. Maureen Dillon Parker, Regulatory Project Manager, Division of Anti-Infective Drug Products.

Pursuant to 21 CFR 314.50, a complete field copy of this amendment has been submitted to the FDA Philadelphia District Office.

We consider the filing of this amendment to be a confidential matter, and request that the Food and Drug Administration not make its content, nor any future communications in regard to it, public without first obtaining the written permission of Merck & Co., Inc.

Questions concerning this amendment should be directed to Michelle W. Kloss, Ph.D. (484-344-2905) or, in my absence, to Bonnie J. Goldmann, M.D. (484-344-2383).

Sincerely,

Sonia L. Gordon for mwk

Michelle W. Kloss, Ph.D.
Senior Director, Regulatory Affairs

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Enclosure: CD

Hand Deliver

Desk Copy: Ms. Maureen Dillon Parker, Regulatory Project Manager (cover letter)
HFD-520, Room S306
Hand Deliver

Desk Copy/att: Dr. Vithal Shetty
HFD-520, Room N356
Hand Deliver

Desk Copy/att: Philadelphia District Office, FDA
Food and Drug Administration
U.S. Custom House Room 900
2nd & Chestnut Streets
Philadelphia, PA 19106-2973
Federal Express

Michelle W. Kloss, Ph.D.
Senior Director
Regulatory Affairs

Merck & Co., Inc.
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July 17, 2001

DELIVERY COPY

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

c/o Central Document Room
Food and Drug Administration
Center for Drug Evaluation and Research
12229 Wilkins Avenue
Rockville, MD 20852

Dear Dr. Soreth:

NDA 21-337: INVANZ™ (Ertapenem Sodium)

RESPONSE TO FDA REQUEST FOR INFORMATION

Reference is made to the pending NDA for INVANZ™ cited above submitted as an electronic archive on November 30, 2000. Reference is also made to a July 6, 2001 facsimile communication from Ms. Maureen Dillon Parker (FDA) to Dr. Michelle Kloss (MRL, a Division of Merck & Co., Inc.) which provided Clinical Reviewer requests for additional information regarding Protocol 017.

With this submission, we are providing the requested Case Report Forms (CRFs) for patients AN 5698 and AN 0511 in response to Comment #1 in the July 6, 2001 communication cited above. Please note that MRL's responses to the remaining comments cited in the July 6, 2001 communication will be submitted shortly under separate cover.

This response is formatted as required in Title 21 paragraph 314.50 of the Code of Federal Regulations and is being submitted in accordance with the January 1999, *Guidance for Industry – Providing Regulatory Submissions in Electronic Format – NDAs.* As an attachment to this letter, Merck Research Laboratories is providing one Compact Disk (CD) which contains the response. 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. We have taken precautions to ensure that the contents of this CD are free of computer viruses (Norton Anti-Virus 4.0, Symantec Corp., 1991-1997) and we authorized the use of anti-virus software, as appropriate.

A list of reviewers from the Division of Anti-Infective Drug Products who should be provided access to this electronic submission on their desktops may be obtained from Ms. Maureen Dillon Parker, Regulatory Project Manager, Division of Anti-Infective Drug 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, nor any future communications in regard to it, public without first obtaining the written permission of Merck & Co., Inc.

Please direct questions or need for additional information to Michelle W. Kloss, Ph.D. (484-344-2905) or, in my absence, Bonnie J. Goldmann, M.D. (484-344-2383).

Sincerely yours,

Tonia L Jodrow for MWK

Michelle W. Kloss, Ph.D.
Senior Director, Regulatory Affairs

Enclosure: CD

Federal Express #1

Desk Copy: Ms. Maureen P. Dillon Parker, Regulatory Project Manager (cover letter)
HFD-520, Room S306
Federal Express #2

Q:\kane\mk826\nda amendments\06Jul01_CRFs

Michelle W. Kloss, Ph.D.
Senior Director
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DESK COPY

July 18, 2001

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

c/o Central Document Room
Food and Drug Administration
Center for Drug Evaluation and Research
12229 Wilkins Avenue
Rockville, MD 20852

Dear Dr. Soreth:

NDA 21-337: INVANZ™ (Ertapenem Sodium)

RESPONSE TO FDA REQUEST FOR INFORMATION

Reference is made to the pending NDA for INVANZ™ cited above, submitted as an electronic archive on November 30, 2000. Reference is also made to a July 11, 2001 telephone conversation between Ms. Maureen Dillon Parker (FDA) and Dr. Michelle Kloss (MRL, a Division of Merck & Co., Inc.) and a July 12, 2001 facsimile communication from Ms. Dillon Parker to Dr. Kloss which requested clarification regarding the evaluability of Patient AN 0437 in Protocol 017. The July 12, 2001 facsimile communication also provided Agency comments on Protocol 036.

With this submission, in response to the Agency request for Protocol 017 cited above, we are providing the Case Report Form (CRF) for patient AN 0437; a summary of the evaluability of Patient AN 0437 is provided below. Please note that MRL's responses to the remaining Agency comments regarding Protocol 036 cited in the July 12, 2001 communication will be submitted shortly under separate cover.

Patient AN #017-038-437 is per protocol clinically evaluable and per protocol microbiologically evaluable. The patient had an empyema of the gallbladder with choledocholithiasis and cholangitis. When the evaluability of this patient was initially considered on May 22, 2000, the patient was not considered per protocol evaluable because the reviewer did not differentiate between simple cholecystitis (i.e. not a complicated intraabdominal infection) and empyema of the gallbladder with cholangitis (i.e. a complicated intraabdominal infection); evaluability exclusions, both specifically pertaining to the baseline diagnosis, were recorded as "disease definition not met (3)" and "baseline/intercurrent medical events (8)". The patient evaluability was subsequently assessed by the medical monitor on June 8, 2000 and the patient was classified as per protocol evaluable because the patient did have a complicated intraabdominal infection.

In applying the correction to the database, the per protocol clinical evaluability and the per protocol microbiologic evaluability were applied. Only one of the evaluability exclusions, "disease definition not met (3)", was deleted; the other evaluability exclusion "baseline/intercurrent medical events (8)" should have been deleted but this did not occur. As a consequence, the SAS transport file containing the evaluability information in the NDA incorrectly lists an evaluability exclusion for this patient.

This response is formatted as required in Title 21 paragraph 314.50 of the Code of Federal Regulations and is being submitted in accordance with the January 1999, *Guidance for Industry – Providing Regulatory Submissions in Electronic Format – NDAs.* As an attachment to this letter, Merck Research Laboratories is providing one Compact Disk (CD) which contains the response. 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. We have taken precautions to ensure that the contents of this CD are free of computer viruses (Norton Anti-Virus 4.0, Symantec Corp., 1991-1997) and we authorized the use of anti-virus software, as appropriate.

A list of reviewers from the Division of Anti-Infective Drug Products who should be provided access to this electronic submission on their desktops may be obtained from Ms. Maureen Dillon Parker, Regulatory Project Manager, Division of Anti-Infective Drug 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, nor any future communications in regard to it, public without first obtaining the written permission of Merck & Co., Inc.

Please direct questions or need for additional information to Michelle W. Kloss, Ph.D. (484-344-2905) or, in my absence, Bonnie J. Goldmann, M.D. (484-344-2383).

Sincerely yours,

Michelle W. Kloss

Michelle W. Kloss, Ph.D.
Senior Director, Regulatory Affairs

Enclosure: CD

Federal Express #1

Desk Copy: [redacted], Regulatory Project Manager (cover letter)
HFD-520, Room S306
[redacted] Express #2

Q:\kane\mk826\nda amendments\12Jul01_CRF0437

Michelle W. Kloss, Ph.D.
Senior Director
Regulatory Affairs

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DESK COPY

July 18, 2001

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

c/o Central Document Room
Food and Drug Administration
Center for Drug Evaluation and Research
12229 Wilkins Avenue
Rockville, MD 20852

Dear Dr. Soreth:

NDA 21-337: INVANZ™ (Ertapenem Sodium)

RESPONSE TO FDA REQUEST FOR INFORMATION

Reference is made to the pending NDA for INVANZ™ cited above, submitted as an electronic archive on November 30, 2000 and to a July 10, 2001 telephone conversation between Ms. Maureen Dillon Parker (FDA) and Dr. Michelle Kloss (MRL, a Division of Merck & Co., Inc.). During this conversation, Ms. Dillon Parker requested, on behalf of the Statistical Reviewer for Protocol 017, that MRL provide a new SAS transport file that includes the variable "COMPARE" with the dataset "QEVALU" for Protocol 017.

With this submission, MRL is providing the requested SAS transport file information in response to the Agency's request communicated in the July 10, 2001 conversation cited above; the new SAS transport file is called "QEVALUC". All information is in an electronic format as indicated in the Table of Contents for this submission.

This response is formatted as required in Title 21 paragraph 314.50 of the Code of Federal Regulations and is being submitted in accordance with the January 1999, *Guidance for Industry – Providing Regulatory Submissions in Electronic Format – NDAs.* As an attachment to this letter, Merck Research Laboratories (MRL), a division of Merck & Co., Inc., is providing one Compact Disk (CD) which contains the response. All documents requiring signatures for certification are included as paper for archival purposes.

We have taken precautions to ensure that the contents of this CD are free of computer viruses (Norton Anti-Virus 4.0, Symantec Corp., 1991-1997) and we authorized the use of anti-virus software, as appropriate.

A list of reviewers from the Division of Anti-Infective Drug Products who should be provided access to this electronic submission on their desktops may be obtained from Ms. Maureen Dillon Parker, Regulatory Project Manager, Division of Anti-Infective Drug 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, nor any future communications in regard to it, public without first obtaining the written permission of Merck & Co., Inc.

Questions concerning this amendment should be directed to Michelle W. Kloss, Ph.D. (484-344-2905) or, in my absence, to Bonnie J. Goldmann, M.D. (484-344-2383).

Sincerely yours,

Michelle W. Kloss

Michelle W. Kloss, Ph.D.
Senior Director, Regulatory Affairs

Enclosure: CD

Federal Express

Desk Copy: Ms. [redacted], Regulatory Project Manager (cover letter)
HFD-520, Room S306
Federal Express #2

Q\kane\mk826\nda amendments\10Jul01_statistics

Michelle W. Kloss, Ph.D.
Senior Director
Regulatory Affairs

Merck & Co., Inc.
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P.O. Box 4
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DESK COPY

July 19, 2001

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

c/o Central Document Room
Food and Drug Administration
Center for Drug Evaluation and Research
12229 Wilkins Avenue
Rockville, MD 20852

Dear Dr. Soreth:

NDA 21-337: INVANZ™ (Ertapenem Sodium)

GENERAL CORRESPONDENCE

Reference is made to the pending New Drug Application cited above for INVANZ™ submitted as an electronic archive on November 30, 2000. Reference is also made to a July 2, 2001 teleconference meeting between the Agency and MRL held to discuss Agency comments on this pending NDA and to a July 3, 2001 submission, in follow-up to this teleconference meeting, of the Protocol 029 Clinical Study Report (CSR). Further reference is made to a series of telephone conversations on July 9, 2001, July 11, 2001, and July 13, 2001 between Ms. Maureen Dillon Parker (FDA) and Dr. Michelle Kloss (MRL, a Division of Merck & Co., Inc.) during which the Protocol 029 CSR submission and the Agency review timelines for this pending NDA were discussed. During the July 13, 2001 conversation, agreement was reached between the Agency and MRL that, in light of the July 3, 2001 submission of the Protocol 029 CSR, the user fee timeclock for the INVANZ™ NDA would be extended by 60 days, with a change in the Agency's action date for this NDA from September 30, 2001 to November 30, 2001. During the same conversation, it was agreed that the Agency would provide Merck with written notification of this revised review timeline and user fee date and, per the Agency's request, it was agreed that MRL would provide written confirmation of its agreement with this Agency decision.

With this submission, per the agreements reached during the telephone conversations cited above, MRL is providing its agreement with the Agency decision to extend the user fee date for the INVANZ™ NDA by 60 days, such that the revised user fee date for Agency action on this NDA will be November 30, 2001 rather than September 30, 2001.

All information is in an electronic format as indicated in the Table of Contents for this submission. 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 January 1999, *Guidance for Industry – Providing Regulatory Submissions in Electronic Format – NDAs.* As an attachment to this letter, Merck Research Laboratories (MRL), a division of Merck & Co., Inc., is providing one Compact Disk (CD) which contains this submission. All documents requiring signatures for certification are included as paper for archival purposes.

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A list of reviewers from the Division of Anti-Infective Drug Products who should be provided access to this electronic submission on their desktops may be obtained from Ms. Maureen Dillon Parker, Regulatory Project Manager, Division of Anti-Infective Drug 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, nor 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 Michelle W. Kloss, Ph.D. (484-344-2905) or, in my absence, to Bonnie J. Goldmann, M.D. (484-344-2383).

Sincerely,

Michelle W. Kloss

Michelle W. Kloss, Ph.D.
Senior Director, Regulatory Affairs

Enclosure: CD

Federal Express #1

[redacted]: M[redacted] Parker, Regulatory Project Manager (cover letter)
[redacted] S306

Fax/Federal Express #2

Q:\maione\mk826\nda amend\pdufa date.doc

Michelle W. Kloss, Ph.D.
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DESK COPY

July 20, 2001

Janice Soreth, M.D., Acting Director
HFD-520, Room N348

c/o Central Document Room
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Center for Drug Evaluation and Research
12229 Wilkins Avenue
Rockville, MD 20852

NDA 21-337: INVANZ™ (Ertapenem Sodium)

GENERAL CORRESPONDENCE

Reference is made to the pending NDA cited above for INVANZ™ submitted as an electronic archive on November 30, 2000 and to a July 2, 2001 teleconference meeting between representatives of FDA and MRL, a Division of Merck & Co., Inc., which was held to discuss the Agency's facsimile communication of June 22, 2001 which provided pharmacology/toxicology comments.

With this submission, we are providing a summary of this July 2, 2001 teleconference meeting as minutes from the meeting. We would also appreciate receiving the Agency's minutes from this meeting once they become available.

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 January 1999, *Guidance for Industry – Providing Regulatory Submissions in Electronic Format – NDAs.* As an attachment 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.

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A list of reviewers from the Division of Anti-Infective Drug Products who should be provided access to this electronic submission on their desktops may be obtained from Ms. Maureen Dillon Parker, Regulatory Project Manager, Division of Anti-Infective Drug 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, nor any future communications in regard to it, public without first obtaining the written permission of Merck & Co., Inc.

Please direct questions or need for additional information to Michelle W. Kloss, Ph.D. at (484) 344-2905 or, in my absence, Bonnie J. Goldmann, M.D. at (484) 344-2383.

Sincerely,

Michelle W. Kloss

Michelle W. Kloss, Ph.D.
Senior Director
Regulatory Affairs

Enclosure: CD

Federal Express

Desk Copy: [redacted] Dillon Parker, Regulatory Project Manager (cover letter)
HFD-520, Room S306
Federal Express #2

Q:maione/MK826/070201telecconmin