# Fax



## DIVISION OF ONCOLOGY DRUG PRODUCTS

**Center for Drug Evaluation and Research, HFD-150**
**Parklawn Building**
**5600 Fishers Lane, Rockville, MD 20857**


| | | | |
|---|---|---|---|
| **To:** | Ronald Falcone, Ph.D. | **From:** | Amy Baird, CSO |
| **Fax:** | 302-886-2822 | **Fax:** | (301) 827-4590 |
| **Phone:** | 302-886-2715 | **Phone:** | (301) 594-5779 |
| **Pages (including cover):** | 2 | **Date:** | March 11, 2003 |

**Re:** NDA 21-399 Iressa. Submission dated February 25, 2003, requesting a meeting.

☐ **Urgent** ✔ **For Review** ☐ **Please Comment** ☐ **Please Reply** ☐ **Please Recycle**



• **Comments:**

Your request for a meeting has been scheduled, see the attached. Please call should you have any questions.

Thank you,

Amy Baird

**Date:** April 8, 2003

**Time:** 4:30pm EST

**Place:** Woodmont Office Complex 2
1451 Rockville Pike
Rockville, MD
Conference Room G

**FDA Attendees:**

Richard Pazdur, M.D., Division Director, DODP
Grant Williams, M.D., Deputy Director, DODP
Martin Cohen, M.D., Clinical Reviewer, DODP
Ann Farrell, M.D., Acting Clinical Team Leader, DODP
Richard Lostritto, Ph.D., Chemistry Team Leader, DNDCI
Chengyi Liang, Ph.D., Chemistry Reviewer, DNDCI
David Morse, Ph.D., Supervisory Pharmacologist, DODP
William McGuinn, Ph.D., Pharmacology Reviewer, DODP
Gang Chen, Ph.D., Statistical Team Leader, DODP
Rajeshwari Sridhara, Ph.D., Statistical Reviewer, DODP
Atiqur Rahman, Ph.D., Biopharmaceutical Team Leader, DODP
Sophia Abraham, Ph.D., Biopharmaceutical Reviewer, DODP
Amy Baird, Project Manager, DODP

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/s/

Amy Baird
3/11/03 02:15:16 PM
CSO

# Fax



## DIVISION OF ONCOLOGY DRUG PRODUCTS

**Center for Drug Evaluation and Research, HFD-150**
**Parklawn Building**
**5600 Fishers Lane, Rockville, MD 20857**


| | | | |
|---|---|---|---|
| **To:** | Maureen Morgan/Ronald Falcone, Ph.D. | **From:** | Amy Baird, CSO |
| **Fax:** | 302-886-2822 | **Fax:** | (301) 827-4590 |
| **Phone:** | 302-886-2715 | **Phone:** | (301) 594-5779 |
| **Pages (including cover):** | 1 | **Date:** | March 10, 2003 |
| **Re:** | NDA 21-399 Iressa. Request for information. | | |

✔ **Urgent** ☐ **For Review** ☐ **Please Comment** ✔ **Please Reply** ☐ **Please Recycle**



• **Comments:**

Per the Iressa review team, please provide demographic information (sex, smoking status, histology, and race) corresponding to the results from the two phase III trials (0014 and 0017) and the ASCO abstracts recently described by AstraZeneca. Please call should you have any questions.

Thank you,

Amy Baird

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/s/

Amy Baird
3/10/03 04:18:04 PM
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# Fax


## DIVISION OF ONCOLOGY DRUG PRODUCTS

**Center for Drug Evaluation and Research, HFD-150**
**Parklawn Building**
**5600 Fishers Lane, Rockville, MD 20857**


| | |
|---|---|
| **To:** Ronald Falcone, Ph.D. | **From:** Amy Baird, CSO |
| **Fax:** 302-886-2822 | **Fax:** (301) 827-4590 |
| **Phone:** 302-886-2715 | **Phone:** (301) 594-5779 |
| **Pages (including cover):** 2 | **Date:** January 15, 2003 |
| **Re:** NDA 21-399 Iressa. Telephone conference held January 13, 2003. | |

☐ **Urgent** ☐ **For Review** ☐ **Please Comment** ✔ **Please Reply** ☐ **Please Recycle**



- **Comments:**

Pursuant to the telephone conference held January 13, 2003, please submit the following:

1. Updated report of all pulmonary SAEs associated with Iressa including those from Japan, from the ongoing Iressa trials (including INTACT 1 and 2), and the expanded access. The report should be similar to the format of the update you submitted on October 18, 2002, with an attempt to include additional information such as incidence, severity, reversibility, duration, dose/timing, time to onset, previous medication, prior radiation, etc. For the INTACT 1 and 2 trials, please include a report describing the adverse reactions in this study (a study report if available) and narrative descriptions for all severe pulmonary adverse events.

2. AstraZeneca stated in the telephone conference that expert panels had been convened to analyze pulmonary adverse events occurring in Japan. Please submit these analyses and the data analyzed. Please address issues such as incidence, severity, reversibility, duration, dose/timing, time to onset, previous medication, prior radiation, etc

3. Written statement as to how AstraZeneca ensures receipt of data on adverse events from patients entered onto the expanded access protocol... particularly patients that may have permanently discontinued therapy because of an adverse event.

4. We discussed during the conference the possibility that chemotherapy may have abrogated Iressa ILD toxicity in the Iressa trials. Please provide your thoughts on this.

5. You briefly discussed why there is a difference in ILD rates between the U.S and Japan. Please provide this explanation in writing.

6. Please analyze the number of patients and the Iressa-exposure time from US trials, from expanded access, from the Japanese experience.

Please call should you have any questions.

Thank you,

Amy Baird

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/s/

Amy Baird
1/15/03 02:16:40 PM
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# FAX

**FOOD AND DRUG ADMINISTRATION**
**DIVISION OF ONCOLOGY DRUG PRODUCTS**
Center for Drug Evaluation and Research, HFD-150
5600 Fishers Lane, Rockville, MD 20857

| | |
|---|---|
| **To:** Ronald Falcone | **From:** Christy Cottrell for Amy Baird |
| **Fax:** (302) 886-2822 | **Fax:** (301) 594-0499 |
| **Phone:** (302) 886-2715 | **Phone:** (301) 594-5761 |
| **Pages, including cover sheet:** 3 | **Date:** ~~1-8-02~~ 1/8/03 |

**Re:** NDA 21-399 for Iressa



Ron,

Please refer to your pending NDA 21-399 for Iressa. Attached is a courtesy copy of the Extension of User Fee Goal Date letter.

If you have any questions, please contact Amy Baird at (301) 594-5779.

Thanks,

Christy Cottrel for Amy Baird

# Fax



## DIVISION OF ONCOLOGY DRUG PRODUCTS

**Center for Drug Evaluation and Research, HFD-150**
**Parklawn Building**
**5600 Fishers Lane, Rockville, MD 20857**


| | | | |
|---|---|---|---|
| **To:** | Ronald Falcone, Ph.D. | **From:** | Amy Baird, CSO |
| **Fax:** | 302-886-2822 | **Fax:** | (301) 827-4590 |
| **Phone:** | 302-886-2715 | **Phone:** | (301) 594-5779 |
| **Pages (including cover):** | 1 | **Date:** | December 23, 2002 |

**Re:** NDA 21-399 Iressa. Specifically, your submission dated November 27, 2002, which is in response to the FDA facsimile of November 22, 2002.

✔ **Urgent** ☐ **For Review** ☐ **Please Comment** ✔ **Please Reply** ☐ **Please Recycle**



• **Comments:**

Per the request of the review team, please provide the database from the expanded access trial with the fields identified in attachment #2 of your November 27 correspondence. Also provide the safety database for the INTACT I and II trials as SAS transport files. The documentation needs to be included with the INTACT data. The Division would like to receive this information as soon as possible. Please call should you have any questions.

Thank you,

Amy Baird

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/s/

Amy Baird
12/23/02 02:06:17 PM
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# Fax


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**Center for Drug Evaluation and Research, HFD-150**
**Parklawn Building**
**5600 Fishers Lane, Rockville, MD 20857**

| | |
|---|---|
| **To:** Ronald Falcone, Ph.D. | **From:** Amy Baird, CSO |
| **Fax:** 302-886-2822 | **Fax:** (301) 827-4590 |
| **Phone:** 302-886-2715 | **Phone:** (301) 594-5779 |
| **Pages (including cover):** 2 | **Date:** November 22, 2002 |

**Re:** NDA 21-399 Iressa. Telephone conference held November 20, 2002 at 5:00pm.

☐ **Urgent** ☐ **For Review** ☐ **Please Comment** ✔ **Please Reply** ☐ **Please Recycle**



• **Comments:**

Pursuant to the telephone conference held November 20, 2002, please submit the following:

1. The Division would like to review all serious adverse event data for both the Expanded Access Protocols and the INTACT 1 and INTACT 2 trials. This data is to include the underlying investigator data that is sent to AZ. However, please first provide a list of the fields from the ——— ' safety database and AstraZeneca's database. Once this information is submitted, the Division will determine what exact safety information is necessary for further review.

2. Please also provide any efficacy data from the Expanded Access Trial, for e.g., whether the patient responded or had symptom benefit.

3. Provide a timeline indicating when Japan first notified AZ of ILD cases and all subsequent discussions/meetings thereafter. With this submission, please include information regarding the numerator and denominator for the ILD cases at the following time periods: end of August, mid September, and September 24, 2002.

4. The following was not addressed in the telephone conference of November 20, 2002, but nonetheless should be addressed. As we carefully consider the risk versus benefit of Iressa in refractory patients, we are evaluating both the pulmonary toxicity and the precision of our response rate estimate. We have evaluated the database and the narratives you have provided. We note that several of the responders appear to have received chemotherapy within several weeks prior to entering this study. We want to be certain that none of the tumor responses attributed to Iressa were caused by recent chemotherapy. The following are cases that we would like to evaluate more closely:

   2090/0037
   2090/0048
   2255/0338

   Please provide a careful analysis of this issue in these patients, and support this with documentation, including:

   Last chemotherapy regimen, date of first dose, date of last dose
   Date of radiologic exam documenting progression on chemotherapy
   Date of baseline radiologic exam for Iressa evaluation
   Date of radiologic exam documenting first Iressa response

   As soon as possible after submitting the above analysis, provide radiologic reports and films/scans documenting tumor progression on the last chemotherapy regimen (include baseline and progression films/scans).

Please call should you have any questions.

Thank you,

Amy Baird

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/s/

Amy Baird
11/22/02 12:32:50 PM
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**Center for Drug Evaluation and Research, HFD-150**
**Parklawn Building**
**5600 Fishers Lane, Rockville, MD 20857**

| | |
|---|---|
| **To:** Ronald Falcone, Ph.D. | **From:** Amy Baird, CSO |
| **Fax:** 302-886-2822 | **Fax:** (301) 827-4590 |
| **Phone:** 302-886-2715 | **Phone:** (301) 594-5779 |
| **Pages (including cover):** 1 | **Date:** November 18, 2002 |
| **Re:** NDA 21-399 Iressa. Request for additional information. | |

☐ **Urgent** ☐ **For Review** ☐ **Please Comment** ✔ **Please Reply** ☐ **Please Recycle**



- **Comments:**

Per the request of the clinical and statistical teams, please provide the following information.

Regarding studies 0014 and 0017, why were some patients censored for progression on day 1 [pfs=1]?

Please provide the CRFs of patients who died within 30 days of treatment for both studies 0014 and 0017. Also, along with these CRFs, please list of the cause of death.

Please call should you have any questions.

Thank you,

Amy Baird

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/s/

Amy Baird
11/18/02 02:15:26 PM
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**Center for Drug Evaluation and Research, HFD-150**
**Parklawn Building**
**5600 Fishers Lane, Rockville, MD 20857**

| | | | |
|---|---|---|---|
| **To:** | Leonid Freytor | **From:** | Amy Baird, CSO |
| **Fax:** | 302-886-2822 | **Fax:** | (301) 594-0498 |
| **Phone:** | 302-886-2510 | **Phone:** | (301) 594-5771 |
| **Pages (including cover):** | 1 | **Date:** | October 16, 2002 |

**Re:** NDA 21-399 Iressa. Specifically, your facsimile dated October 7, 2002, regarding interstitial pneumonitis occurrences.

✔ **Urgent** ☐ **For Review** ☐ **Please Comment** ✔ **Please Reply** ☐ **Please Recycle**



• **Comments:**

In your facsimile dated October 7, 2002, you reported a total of 91 events in relation to interstitial lung disorders. Please provide a summary report on the onset of these events to include information such as how many days into therapy the event occurred, prior therapies, how the diagnosis was made, whether it was considered serious/life-threatening, treatment patients received, outcome of the patient, and dechallenge/rechallenge information. Also, please provide available case report forms and MedWatch forms (if case report forms are not available) in this report.

Please call should you have any questions.

Thank you,

Amy Baird

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/s/

Amy Baird
10/16/02 03:48:07 PM
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**Parklawn Building**
**5600 Fishers Lane, Rockville, MD 20857**


| | | | |
|---|---|---|---|
| **To:** | Ronald Falcone, Ph.D. | **From:** | Amy Baird, CSO |
| **Fax:** | 302-886-2822 & 302. 886. 4606 8 | **Fax:** | (301) 594-0498 |
| **Phone:** | 302-886-2715 | **Phone:** | (301) 594-5771 |
| **Pages (including cover):** | 2 | **Date:** | October 11, 2002 |
| **Re:** | NDA 21-399 Iressa. CMC request for information. | | |

✔ **Urgent** ☐ **For Review** ☐ **Please Comment** ✔ **Please Reply** ☐ **Please Recycle**



• **Comments:**

**Please disregard previous FDA fax dated 10-11-02 containing request for commitment on CMC deficiencies.** Please refer to the telephone conference held October 4, 2002, between AstraZeneca and members of the FDA Iressa review team. During the telephone conference we discussed deficiencies pertaining to the drug product along with timelines for AZ to respond to these deficiencies. We had also mentioned that comments regarding the drug substance would be forthcoming. On the following page are the deficiencies pertaining to both drug product and substance. Please provide a written commitment via facsimile to respond to these deficiencies in the agreed upon time.

Thank you,

/S/

Amy Baird

**Drug Product**

1. Provide acceptance criteria and test results for all drug excipients. To be provided on or before November 1, 2002.

2. Provide test code numbers for in-house test methods. To be provided on or before November 1, 2002.

3. Include water content and microbial testing on drug product stability at least until a significant body of data is gathered post-approval on the commercial scale and sized brown drug product tablets. This stability data will be collected for the first 10 commercial batches to be submitted to the NDA via supplementary new correspondence. It will be decided if further stability data is needed once commercial batch data has been submitted and reviewed. AZ will submit this information as soon as feasible.

4. Provide the acceptance criteria and test results for the 75 cc — bottle seal liner. To be provided within 30 days post approval.

**Drug Substance**

1. Please commit to add the melting range to the tests and specifications for each intermediate — and to report melting point data in the first post-approval Annual Report to this NDA.

2. Please provide your in-house test method codes or the corresponding USP monograph designations for the drug substance tests. To be provided within 30 days post approval.

3. Please provide the — test conditions for the drug substance. To be provided within 30 days post approval.

4. Please provide the source(s) of drug substance packaging materials along with verification that these materials comply with 21CFR food additive regulations. Please include any relevant Drug Master File references (with appropriate letters of authorization) which may apply. To be provided within 30 days post approval.

5. Overall, the description of the drug substance manufacturing process is clear. However, some procedure ranges — are too broadly stated. Please describe more precise criteria for these reaction parameters in the first Annual Report to the approved NDA.

# MESSAGE CONFIRMATION

10/11/02 16:42

| DATE | S.R-TIME | DISTANT STATION ID | MODE | PAGES | RESULT | |
|---|---|---|---|---|---|---|
| 10/11 | 00'50" | 8862822 | CALLING | 02 | OK | 0000 |

10/11/02 16:40 NO.004 D01

# Fax


## DIVISION OF ONCOLOGY DRUG PRODUCTS

**Center for Drug Evaluation and Research, HFD-150**
**Parklawn Building**
**5600 Fishers Lane, Rockville, MD 20857**

| | | | |
|---|---|---|---|
| **To:** | Ronald Falcone, Ph.D. | **From:** | Amy Baird, CSO |
| **Fax:** | 302-886-2822 4 302. 886. 4668 | **Fax:** | (301) 594-0498 |
| **Phone:** | 302-886-2715 | **Phone:** | (301) 594-5771 |
| **Pages (including cover):** | 2 | **Date:** | October 11, 2002 |
| **Re:** | NDA 21-399 Iressa. CMC request for information. | | |

✔ **Urgent** ☐ **For Review** ☐ **Please Comment** ✔ **Please Reply** ☐ **Please Recycle**

# MESSAGE CONFIRMATION

10/11/02 16:30
ID=FDA-DODP

| DATE | S.R-TIME | DISTANT STATION ID | MODE | PAGES | RESULT | |
|---|---|---|---|---|---|---|
| 10/11 | 00'50" | 913028864668 | CALLING | 02 | OK | 0000 |

10/11/02 16:29 FDA-DODP → 913028864668 NO.158 P01

# Fax


## DIVISION OF ONCOLOGY DRUG PRODUCTS

**Center for Drug Evaluation and Research, HFD-150**
**Parklawn Building**
**5600 Fishers Lane, Rockville, MD 20857**


| | | | |
|---|---|---|---|
| **To:** | Ronald Falcone, Ph.D. | **From:** | Amy Baird, CSO |
| **Fax:** | 302-886-2822 4·302.886.4668 | **Fax:** | (301) 594-0498 |
| **Phone:** | 302-886-2715 | **Phone:** | (301) 594-5771 |
| **Pages (including cover):** | 2 | **Date:** | October 11, 2002 |
| **Re:** | NDA 21-399 Iressa. CMC request for information. | | |

✔ **Urgent** ☐ **For Review** ☐ **Please Comment** ✔ **Please Reply** ☐ **Please Recycle**

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## DIVISION OF ONCOLOGY DRUG PRODUCTS

**Center for Drug Evaluation and Research, HFD-150**
**Parklawn Building**
**5600 Fishers Lane, Rockville, MD 20857**


| | | | |
|---|---|---|---|
| **To:** | Ronald Falcone, Ph.D. | **From:** | Amy Baird, CSO |
| **Fax:** | 302-886-2822 & 302. 886. 4618 | **Fax:** | (301) 594-0498 |
| **Phone:** | 302-886-2715 | **Phone:** | (301) 594-5771 |
| **Pages (including cover):** | 2 | **Date:** | October 11, 2002 |
| **Re:** | NDA 21-399 Iressa. CMC request for information. | | |

✔ **Urgent** ☐ **For Review** ☐ **Please Comment** ✔ **Please Reply** ☐ **Please Recycle**



• **Comments:**

Please refer to the telephone conference held October 4, 2002, between AstraZeneca and members of the FDA Iressa review team. During the telephone conference we discussed deficiencies pertaining to the drug product along with timelines for AZ to respond to these deficiencies. We had also mentioned that comments regarding the drug substance would be forthcoming. On the following page are the deficiencies pertaining to both drug product and substance. Please provide a written commitment via facsimile to respond to these deficiencies in the agreed upon time.

Thank you,

/S/

Amy Baird

**Drug Product**

1. Provide acceptance criteria and test results for all drug excipients. To be provided on or before November 1, 2002.

2. Provide test code numbers for in-house test methods. To be provided on or before November 1, 2002.

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**Drug Substance**

1. Please commit to add the melting range to the tests and specifications for each intermediate — and to report melting point data in the first post-approval Annual Report to this NDA.

2. Please provide your in-house test method codes or the corresponding USP monograph designations for the drug substance tests. To be provided on or before November 1, 2002.

3. Please provide the — test conditions for the drug substance. To be provided on or before November 1, 2002.

4. Please provide the source(s) of drug substance packaging materials along with verification that these materials comply with 21CFR food additive regulations. Please include any relevant Drug Master File references (with appropriate letters of authorization) which may apply. To be provided on or before November 1, 2002.

5. Overall, the description of the drug substance manufacturing process is clear. However, some procedure ranges — are too broadly stated. Please describe more precise criteria for these reaction parameters in the first Annual Report to the approved NDA.

# MESSAGE CONFIRMATION

10/11/02 14:39

| DATE | S.R-TIME | DISTANT STATION ID | MODE | PAGES | RESULT | |
|---|---|---|---|---|---|---|
| 10/11 | 00'50" | 8862822 | CALLING | 02 | OK | 0000 |

10/11/02 14:35 NO.002 P01

# Fax


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**Center for Drug Evaluation and Research, HFD-150**
**Parklawn Building**
**5600 Fishers Lane, Rockville, MD 20857**

| | | | |
|---|---|---|---|
| **To:** | Ronald Falcone, Ph.D. | **From:** | Amy Baird, CSO |
| **Fax:** | 302-886-2822 & 302. 886. 4618 | **Fax:** | (301) 594-0498 |
| **Phone:** | 302-886-2715 | **Phone:** | (301) 594-5771 |
| **Pages (including cover):** | 2 | **Date:** | October 11, 2002 |
| **Re:** | NDA 21-399 Iressa. CMC request for information. | | |

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# MESSAGE CONFIRMATION

10/11/02 14:25
ID=FDA-DODP

| DATE | S.R-TIME | DISTANT STATION ID | MODE | PAGES | RESULT | |
|---|---|---|---|---|---|---|
| 10/11 | 00'50" | 913028864668 | CALLING | 02 | OK | 0000 |

10/11/02 14:24 FDA-DODP → 913028864668 NO.154 P01

# Fax


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**Center for Drug Evaluation and Research, HFD-150**
**Parklawn Building**
**5600 Fishers Lane, Rockville, MD 20857**

| | | | |
|---|---|---|---|
| **To:** | Ronald Falcone, Ph.D. | **From:** | Amy Baird, CSO |
| **Fax:** | 302-886-2822 ✓ 302.886.4668 | **Fax:** | (301) 594-0498 |
| **Phone:** | 302-886-2715 | **Phone:** | (301) 594-5771 |
| **Pages (including cover):** | 2 | **Date:** | October 11, 2002 |
| **Re:** | NDA 21-399 Iressa. CMC request for information. | | |

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## DIVISION OF ONCOLOGY DRUG PRODUCTS

**Center for Drug Evaluation and Research, HFD-150**
**Parklawn Building**
**5600 Fishers Lane, Rockville, MD 20857**


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| **Fax:** | 302-886-2822 | **Fax:** | (301) 594-0498 |
| **Phone:** | 302-886-2715 | **Phone:** | (301) 594-5771 |
| **Pages (including cover):** | 1 | **Date:** | October 3, 2002 |
| **Re:** | NDA 21-399 Iressa. FDA Request for Information. | | |

✔ **Urgent** ☐ **For Review** ☐ **Please Comment** ✔ **Please Reply** ☐ **Please Recycle**



- **Comments:**

Per the pharm/tox team, please provide the source (study and page number) for the following statement.

Under the PREGNANCY section of the Iressa labeling:

---

Please respond with this information as soon as possible and do not hesitate to call should you have any questions.

Thank you,

S
0

Amy Baird

# MESSAGE CONFIRMATION

10/03/02 16:54

| DATE | S.R-TIME | DISTANT STATION ID | MODE | PAGES | RESULT | |
|---|---|---|---|---|---|---|
| 10/03 | 00'30" | 8862822 | CALLING | 01 | OK | 0000 |

10/03/02 16:53 NO.013 D01

# Fax


## DIVISION OF ONCOLOGY DRUG PRODUCTS

**Center for Drug Evaluation and Research, HFD-150**
**Parklawn Building**
**5600 Fishers Lane, Rockville, MD 20857**

| | | | |
|---|---|---|---|
| **To:** | Ronald Falcone, Ph.D. | **From:** | Amy Baird, CSO |
| **Fax:** | 302-886-2822 | **Fax:** | (301) 594-0498 |
| **Phone:** | 302-886-2715 | **Phone:** | (301) 594-5771 |
| **Pages (including cover):** | 1 | **Date:** | October 3, 2002 |
| **Re:** | NDA 21-399 Iressa. FDA Request for Information. | | |

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## DIVISION OF ONCOLOGY DRUG PRODUCTS

**Center for Drug Evaluation and Research, HFD-150**
**Parklawn Building**
**5600 Fishers Lane, Rockville, MD 20857**


| | | | |
|---|---|---|---|
| **To:** | Ronald Falcone, Ph.D. | **From:** | Amy Baird, CSO |
| **Fax:** | 302-886-2822 | **Fax:** | (301) 594-0498 |
| **Phone:** | 302-886-2715 | **Phone:** | (301) 594-5771 |
| **Pages (including cover):** | 1 | **Date:** | October 3, 2002 |
| **Re:** | NDA 21-399 Iressa. FDA Request for Information. | | |

✔ **Urgent** ☐ **For Review** ☐ **Please Comment** ✔ **Please Reply** ☐ **Please Recycle**



• **Comments:**

The Division has recently received 6 new Iressa interstitial pneumonitis adverse event reports. Please provide the number of interstitial pneumonitis occurrences (numerator and denominator) so that we may determine the appropriate language for the label. Please call should you have any questions.

Thank you.

/S/

Amy Baird

# MESSAGE CONFIRMATION

10/03/02 17:14

| DATE | S.R-TIME | DISTANT STATION ID | MODE | PAGES | RESULT | |
|---|---|---|---|---|---|---|
| 10/03 | 00'29" | 8862822 | CALLING | 01 | OK | 0000 |

10/03/02 17:13 NO.014 P01

# Fax


## DIVISION OF ONCOLOGY DRUG PRODUCTS

Center for Drug Evaluation and Research, HFD-150
Parklawn Building
5600 Fishers Lane, Rockville, MD 20857

| | | | |
|---|---|---|---|
| **To:** | Ronald Falcone, Ph.D. | **From:** | Amy Baird, CSO |
| **Fax:** | 302-886-2822 | **Fax:** | (301) 594-0498 |
| **Phone:** | 302-886-2715 | **Phone:** | (301) 594-5771 |
| **Pages (including cover):** | 1 | **Date:** | October 3, 2002 |

**Re:** NDA 21-399 Iressa. FDA Request for Information.

✔ **Urgent** ☐ **For Review** ☐ **Please Comment** ✔ **Please Reply** ☐ **Please Recycle**

# Fax



## DIVISION OF ONCOLOGY DRUG PRODUCTS

**Center for Drug Evaluation and Research, HFD-150**
**Parklawn Building**
**5600 Fishers Lane, Rockville, MD 20857**


| | | | |
|---|---|---|---|
| **To:** | Ronald Falcone, Ph.D. | **From:** | Amy Baird, CSO |
| **Fax:** | 302-886-2822 & 302.886.4668 | **Fax:** | (301) 594-0498 |
| **Phone:** | 302-886-2715 | **Phone:** | (301) 594-5771 |
| **Pages (including cover):** | 1 | **Date:** | October 1, 2002 |
| **Re:** | NDA 21-399 Iressa. FDA Request for Information. | | |

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- **Comments:**

Per the biopharm team, please provide the following information.

How were plasma samples analyzed that had ZD1839 concentrations higher than 100 ng/ml when the calibration curve is up to 100 ng/ml only?

Please call should you have any questions.

Thank you,

/S/

Amy Baird

# MESSAGE CONFIRMATION

10/01/02 15:05

| DATE | S.R-TIME | DISTANT STATION ID | MODE | PAGES | RESULT | |
|---|---|---|---|---|---|---|
| 10/01 | 00'28" | 8862822 | CALLING | 01 | OK | 0000 |

10/01/02 15:01 NO.005 P01

Fax


**DIVISION OF ONCOLOGY DRUG PRODUCTS**
Center for Drug Evaluation and Research, HFD-150
Parklawn Building
5600 Fishers Lane, Rockville, MD 20857


| | | | |
|---|---|---|---|
| **To:** | Ronald Falcone, Ph.D. | **From:** | Amy Baird, CSO |
| **Fax:** | 302-886-2822 & 302.886.4668 | **Fax:** | (301) 594-0498 |
| **Phone:** | 302-886-2715 | **Phone:** | (301) 594-5771 |
| **Pages (including cover):** | 1 | **Date:** | October 1, 2002 |
| **Re:** | NDA 21-399 Iressa. FDA Request for Information. | | |

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## DIVISION OF ONCOLOGY DRUG PRODUCTS

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**Parklawn Building**
**5600 Fishers Lane, Rockville, MD 20857**


| | |
|---|---|
| **To:** Ronald Falcone, Ph.D. | **From:** Amy Baird, CSO |
| **Fax:** 302-886-2822 & 302.886.4608 | **Fax:** (301) 594-0498 |
| **Phone:** 302-886-2715 | **Phone:** (301) 594-5771 |
| **Pages (including cover):** 1 | **Date:** September 30, 2002 |
| **Re:** NDA 21-399 Iressa. FDA Request for Information. | |

✔ **Urgent** ☐ **For Review** ☐ **Please Comment** ✔ **Please Reply** ☐ **Please Recycle**



• **Comments:**

Per the biopharm team, please provide a response to the following.

Have you assessed the pharmacokinetics of O-desmethyl ZD1839 (M523595) in Trial 32 in patients with hepatic impairment in addition to the parent drug?

The Iressa review team will need a response to this question as soon as possible. Please call should you have any questions.

Thank you,

/S/

Amy Baird

# MESSAGE CONFIRMATION

09/30/02 16:54

| DATE | S.R-TIME | DISTANT STATION ID | MODE | PAGES | RESULT | |
|---|---|---|---|---|---|---|
| 09/30 | 00'29" | 8862822 | CALLING | 01 | OK | 0000 |

09/30/02 16:53 NO.003 P01

# Fax


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**Center for Drug Evaluation and Research, HFD-150**
**Parklawn Building**
**5600 Fishers Lane, Rockville, MD 20857**


| | | | |
|---|---|---|---|
| **To:** | Ronald Falcone, Ph.D. | **From:** | Amy Baird, CSO |
| **Fax:** | 302-886-2822 & 302.886.4068 | **Fax:** | (301) 594-0498 |
| **Phone:** | 302-886-2715 | **Phone:** | (301) 594-5771 |
| **Pages (including cover):** | 1 | **Date:** | September 30, 2002 |
| **Re:** | NDA 21-399 Iressa. FDA Request for Information. | | |

✔ **Urgent** ☐ **For Review** ☐ **Please Comment** ✔ **Please Reply** ☐ **Please Recycle**

# MESSAGE CONFIRMATION

09/30/02 16:42
ID=FDA-DODP

| DATE | S.R-TIME | DISTANT STATION ID | MODE | PAGES | RESULT | |
|---|---|---|---|---|---|---|
| 09/30 | 00'30" | 913028864668 | CALLING | 01 | OK | 0000 |

09/30/02 16:41 FDA-DODP → 913028864668 NO.098 P01

Fax


## DIVISION OF ONCOLOGY DRUG PRODUCTS

Center for Drug Evaluation and Research, HFD-150
Parklawn Building
5600 Fishers Lane, Rockville, MD 20857

| | | | |
|---|---|---|---|
| **To:** | Ronald Falcone, Ph.D. | **From:** | Amy Baird, CSO |
| **Fax:** | 302-886-2822 & 302. 886. 4608 | **Fax:** | (301) 594-0498 |
| **Phone:** | 302-886-2715 | **Phone:** | (301) 594-5771 |
| **Pages (including cover):** | 1 | **Date:** | September 30, 2002 |
| **Re:** | NDA 21-399 Iressa. FDA Request for Information. | | |

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**Parklawn Building**
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|---|---|
| **To:** Ronald Falcone, Ph.D. | **From:** Amy Baird, CSO |
| **Fax:** 302-886-2822 | **Fax:** (301) 594-0498 |
| **Phone:** 302-886-2715 | **Phone:** (301) 594-5771 |
| **Pages (including cover):** 1 | **Date:** July 5, 2002 |
| **Re:** NDA 21-399 Iressa. Request for information from clinical team. | |

☐ **Urgent** ☐ **For Review** ☐ **Please Comment** X **Please Reply** ☐ **Please Recycle**



• **Comments:**

Per the clinical review team, please respond to the following:

The clinical team is trying to determine clinical benefit of Iressa treatment with regard to amelioration of specific pulmonary symptoms including shortness of breath, cough and ease of breathing in studies 39 and 16.

We would appreciate you performing an analysis that looks at patients with a 2 point or greater improvement, from baseline or from the nadir value, of each of these symptoms, lasting 4 or more weeks, for the entire study population. For each available data point from these patients we would like to know concomitant medications, including dose and schedule, so that we can determine whether concomitant medication might have contributed to symptom improvement. Also, please identify the subset of patients who have at baseline at least a 2-point abnormality in one of these scales so we can determine the denominator of patients who could possible show a 2-point improvement.

Please call should you have any questions.

Thank you,

/S/
Amy Baird

# MESSAGE CONFIRMATION

07/05/02 10:42

| DATE | S.R-TIME | DISTANT STATION ID | MODE | PAGES | RESULT | |
|---|---|---|---|---|---|---|
| 07/05 | 00'33" | 8862822 | CALLING | 01 | OK | 0000 |

07/05/02 10:41 NO.248 001

# Fax


## DIVISION OF ONCOLOGY DRUG PRODUCTS

**Center for Drug Evaluation and Research, HFD-150**
**Parklawn Building**
**5600 Fishers Lane, Rockville, MD 20857**


| | | | |
|---|---|---|---|
| **To:** | Ronald Falcone, Ph.D. | **From:** | Amy Baird, CSO |
| **Fax:** | 302-886-2822 | **Fax:** | (301) 594-0498 |
| **Phone:** | 302-886-2715 | **Phone:** | (301) 594-5771 |
| **Pages (including cover):** | 1 | **Date:** | July 5, 2002 |

**Re:** NDA 21-399 Iressa. Request for information from clinical team.

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# FAX

**FOOD AND DRUG ADMINISTRATION**
**DIVISION OF ONCOLOGY DRUG PRODUCTS**
Center for Drug Evaluation and Research, HFD-150
5600 Fishers Lane, Rockville, MD 20857

| | |
|---|---|
| **To:** Ronald Falcone, Ph.D. | **From:** Amy Baird, CSO |
| **Fax:** 302-886-2822 | **Fax:** (301) 594-0498 |
| **Phone:** 302-886-2715 | **Phone:** (301) 594-5771 |
| **Pages, including cover sheet:** 1 | **Date:** 6-19-02 |

**Re: NDA 21-399 Iressa.**



**COMMENTS:**

Per the clinical reviewer assigned to Iressa, see below.

All submitted CT scans for studies 39 and 16 have been reviewed.

Regarding study 39, all responders had scans available and all responses were confirmed.

Regarding study 16, no scans were available for patient's 601/0007, 819/0008, and 819/0009. Only visit #1 scans were available for 259/0001 and only visit #10 scans were available for 916/0006. Patient 818/0003 was missing the visit #1 (baseline) scans. The reviewer felt that patients 415/0004 and 805/0009 had stable disease rather than partial response. These scans will be reviewed with a consultant radiologist.

Thank you,

/S/

Amy Baird

# MESSAGE CONFIRMATION

06/19/02 14:50

| DATE | S.R-TIME | DISTANT STATION ID | MODE | PAGES | RESULT | |
|---|---|---|---|---|---|---|
| 06/19 | 00'31" | 8862822 | CALLING | 01 | OK | 0000 |

06/19/02 14:49 NO.168 P01

# FAX

**FOOD AND DRUG ADMINISTRATION**
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Center for Drug Evaluation and Research, HFD-150
5600 Fishers Lane, Rockville, MD 20857

| | |
|---|---|
| **To:** Ronald Falcone, Ph.D. | **From:** Amy Baird, CSO |
| **Fax:** 302-886-2822 | **Fax:** (301) 594-0498 |
| **Phone:** 302-886-2715 | **Phone:** (301) 594-5771 |
| **Pages, including cover sheet:** 1 | **Date:** 6-19-02 |

**Re: NDA 21-399 Iressa.**

# FAX

**FOOD AND DRUG ADMINISTRATION**
**DIVISION OF ONCOLOGY DRUG PRODUCTS**
Center for Drug Evaluation and Research, HFD-150
5600 Fishers Lane, Rockville, MD 20857

| | |
|---|---|
| **To:** Ronald Falcone, Ph.D. | **From:** Amy Baird, CSO |
| **Fax:** 302-886-2822 | **Fax:** (301) 594-0498 |
| **Phone:** 302-886-2715 | **Phone:** (301) 594-5771 |
| **Pages, including cover sheet:** 1 | **Date:** 4-16-02 |

**Re: NDA 21-399 Iressa.**



**COMMENTS:**

Please clarify the following:

In using the dataset RS00075 (study 39), the clinical reviewer is getting a large discrepancy from the reported results regarding refractoriness/intolerance to prior docetaxel/platinum therapy. Using codes 1 and 9 in the WDREAS variable we come up with only 139 out of 216 ITT patients who are doubly refractory/intolerant. The number of doubly refractory patients goes down further if we exclude patients who were declared as having progressive disease after less than 30 days of treatment. We assume that you agree that codes 2 through 8 do not indicate progression (refractoriness)?

Thank you,

/S/

Amy Baird

# MESSAGE CONFIRMATION

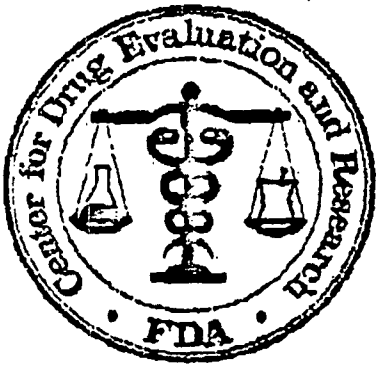
04/16/02 10:52

| DATE | S.R-TIME | DISTANT STATION ID | MODE | PAGES | RESULT | |
|---|---|---|---|---|---|---|
| 04/16 | 00'31" | 8862822 | CALLING | 01 | OK | 0000 |

04/16/02 10:51 NO.013 P01

# FAX


**FOOD AND DRUG ADMINISTRATION**
**DIVISION OF ONCOLOGY DRUG PRODUCTS**
Center for Drug Evaluation and Research, HFD-150
5600 Fishers Lane, Rockville, MD 20857


| | |
|---|---|
| **To:** Ronald Falcone, Ph.D. | **From:** Amy Baird, CSO |
| **Fax:** 302-886-2822 | **Fax:** (301) 594-0498 |
| **Phone:** 302-886-2715 | **Phone:** (301) 594-5771 |
| **Pages, including cover sheet:** 1 | **Date:** 4-16-02 |

**Re: NDA 21-399 Iressa.**



COMMENTS

# FAX

**FOOD AND DRUG ADMINISTRATION**
**DIVISION OF ONCOLOGY DRUG PRODUCTS**
Center for Drug Evaluation and Research, HFD-150
5600 Fishers Lane, Rockville, MD 20857

| | |
|---|---|
| **To:** Ronald Falcone, Ph.D. | **From:** Amy Baird, CSO |
| **Fax:** 302-886-2822 | **Fax:** (301) 594-0498 |
| **Phone:** 302-886-2715 | **Phone:** (301) 594-5771 |
| **Pages, including cover sheet:** 1 | **Date:** 3-19-02 |

**Re: NDA 21-399 Iressa.**



**COMMENTS:**

Per the clinical reviewer, please clarify prior docetaxel treatment for study 39 patient 2256/250. In dataset RS00075 it indicates that the patient started docetaxel 10-20-97 and completed it 11-17-00 but the DURATION variable indicates a one month treatment duration. Which is correct? If more than one dose of docetaxel was administered please provide dates and doses.

Please do not hesitate to call should you have any questions.

Thank you,

/S/

Amy Baird

# MESSAGE CONFIRMATION

03/19/02 16:54

| DATE | S.R-TIME | DISTANT STATION ID | MODE | PAGES | RESULT | |
|---|---|---|---|---|---|---|
| 03/19 | 00'29" | 8862822 | CALLING | 01 | OK | 0000 |

03/19/02 16:48 NO.049 001

# FAX

**FOOD AND DRUG ADMINISTRATION**
**DIVISION OF ONCOLOGY DRUG PRODUCTS**
Center for Drug Evaluation and Research, HFD-150
5600 Fishers Lane, Rockville, MD 20857

| | |
|---|---|
| **To:** Ronald Falcone, Ph.D. | **From:** Amy Baird, CSO |
| **Fax:** 302-886-2822 | **Fax:** (301) 594-0498 |
| **Phone:** 302-886-2715 | **Phone:** (301) 594-5771 |
| **Pages, including cover sheet:** 1 | **Date:** 3-19-02 |

**Re: NDA 21-399 Iressa.**

# FAX

**FOOD AND DRUG ADMINISTRATION**
**DIVISION OF ONCOLOGY DRUG PRODUCTS**
Center for Drug Evaluation and Research, HFD-150
5600 Fishers Lane, Rockville, MD 20857

| | |
|---|---|
| **To:** Ronald Falcone, Ph.D. | **From:** Amy Baird, CSO |
| **Fax:** 302-886-2822 | **Fax:** (301) 594-0498 |
| **Phone:** 302-886-2715 | **Phone:** (301) 594-5771 |
| **Pages, including cover sheet:** 1 | **Date:** 3-6-02 |

**Re: NDA 21-399 Iressa.**



**COMMENTS:**

The DDEMOG dataset for trial 16 does not include the dataset variables that are listed in the .pdf definitions of the dataset nor are they comparable to those in the DDEMOG dataset of trial 39. Please provide the corrected dataset as soon as possible.

Also, regarding the patient demographics study 39 (Dataset ISE-DDEMOG).

1. Does DXSTAG refer to stage at diagnosis or stage at entry onto study 39? We are assuming the former but want to make sure. If so, for patients with diagnosis stages I-IIIB when did disease progress to stage IV?
2. Please provide information as to prior surgery and/or radiation therapy and time of treatment.
3. Provide information on specific chemotherapy regimens that patients received and dates that a treatment regimen started and stopped.
4. Provide documentation that patients were indeed refractory to prior chemotherapy.

Please do not hesitate to call should you have any questions.

Thank you,

/S/

Amy Baird

# MESSAGE CONFIRMATION

03/06/02 10:01
ID=FDA-DODP

| DATE | S.R-TIME | DISTANT STATION ID | MODE | PAGES | RESULT | |
|---|---|---|---|---|---|---|
| 03/06 | 00'33" | 8862822 | CALLING | 01 | OK | 0000 |

03/06/02 10:00 FDA-DODP → 913028862822 NO.007 P01

# FAX

**FOOD AND DRUG ADMINISTRATION**
**DIVISION OF ONCOLOGY DRUG PRODUCTS**
Center for Drug Evaluation and Research, HFD-150
5600 Fishers Lane, Rockville, MD 20857

| | |
|---|---|
| **To:** Ronald Falcone, Ph.D. | **From:** Amy Baird, CSO |
| **Fax:** 302-886-2822 | **Fax:** (301) 594-0498 |
| **Phone:** 302-886-2715 | **Phone:** (301) 594-5771 |
| **Pages, including cover sheet:** 1 | **Date:** 3-6-02 |

**Re: NDA 21-399 Iressa.**

# FAX

**FOOD AND DRUG ADMINISTRATION**
**DIVISION OF ONCOLOGY DRUG PRODUCTS**
Center for Drug Evaluation and Research, HFD-150
5600 Fishers Lane, Rockville, MD 20857

| | |
|---|---|
| **To:** Ronald Falcone, Ph.D. | **From:** Amy Baird, CSO |
| **Fax:** 302-886-2822 | **Fax:** (301) 594-0498 |
| **Phone:** 302-886-2715 | **Phone:** (301) 594-5771 |
| **Pages, including cover sheet:** 1 | **Date:** 2-26-02 |

**Re: NDA 21-399 Iressa.**



**COMMENTS:**

In reviewing the adverse events in phase 1 multiple dose trials, the clinical reviewer is unable to confirm your numbers for all adverse events (diarrhea, asthenia, anorexia, abdominal pain, headache, pharyngitis, constipation, dry mouth and anemia) and is also unable to confirm your numbers for drug related adverse events in the phase 1 population.

Is it possible that the reason why our numbers do not correspond is that you are counting individuals who have an adverse event recorded prior to the first day of treatment? Not counting these individuals might be okay if the adverse event was of short duration, i.e., ending within a day or two of the start of treatment. If the adverse event is of longer duration or if the stop (end) date the adverse event is not recorded then the adverse event should be counted as the study drug might have contributed to the total duration of the AE.

Please respond.

Thank you,

/S/

Amy Baird

# MESSAGE CONFIRMATION

02/26/02 10:40

| DATE | S.R-TIME | DISTANT STATION ID | MODE | PAGES | RESULT | |
|---|---|---|---|---|---|---|
| 02/26 | 00'33" | 8862822 | CALLING | 01 | OK | 0000 |

02/26/02 10:38 NO.042 P01

# FAX

**FOOD AND DRUG ADMINISTRATION**
**DIVISION OF ONCOLOGY DRUG PRODUCTS**
Center for Drug Evaluation and Research, HFD-150
5600 Fishers Lane, Rockville, MD 20857

| | |
|---|---|
| **To:** Ronald Falcone, Ph.D. | **From:** Amy Baird, CSO |
| **Fax:** 302-886-2822 | **Fax:** (301) 594-0498 |
| **Phone:** 302-886-2715 | **Phone:** (301) 594-5771 |
| **Pages, including cover sheet:** 1 | **Date:** 2-26-02 |

**Re: NDA 21-399 Iressa.**

# FAX

**FOOD AND DRUG ADMINISTRATION**
**DIVISION OF ONCOLOGY DRUG PRODUCTS**
Center for Drug Evaluation and Research, HFD-150
5600 Fishers Lane, Rockville, MD 20857

| | |
|---|---|
| **To:** Ronald Falcone, Ph.D. | **From:** Amy Baird, CSO |
| **Fax:** 302-886-2822 | **Fax:** (301) 594-0498 |
| **Phone:** 302-886-2715 | **Phone:** (301) 594-5771 |
| **Pages, including cover sheet:** 1 | **Date:** 2-21-02 |

**Re: IND [redacted] Iressa.**



**COMMENTS:**

In regards to the ISS submitted for NDA 21-399, the clinical reviewer is unable to reproduce your numbers in Table 15 (drug related AE's with an incidence of >=5%-Trial 39). There are minor differences in Table 16 as well as minor differences in Table 21 (FDA numbers have 1 patient more for several categories), minor differences in Table 22 (FDA numbers have 1 patient more for several categories) and Table 23 (considerable differences especially for diarrhea). Please confirm that AstraZeneca numbers are correct for the ISS.

Thank you,

/S/

Amy Baird

# MESSAGE CONFIRMATION

02/21/02 09:12

| DATE | S.R-TIME | DISTANT STATION ID | MODE | PAGES | RESULT | |
|---|---|---|---|---|---|---|
| 02/21 | 00'30" | 8862822 | CALLING | 01 | OK | 0000 |

02/21/02 09:11 NO.020 001

# FAX

**FOOD AND DRUG ADMINISTRATION**
**DIVISION OF ONCOLOGY DRUG PRODUCTS**
Center for Drug Evaluation and Research, HFD-150
5600 Fishers Lane, Rockville, MD 20857

| | |
|---|---|
| **To:** Ronald Falcone, Ph.D. | **From:** Amy Baird, CSO |
| **Fax:** 302-886-2822 | **Fax:** (301) 594-0498 |
| **Phone:** 302-886-2715 | **Phone:** (301) 594-5771 |
| **Pages, including cover sheet:** 1 | **Date:** 2-21-02 |

**Re:** IND [redacted] Iressa.

# FAX

**FOOD AND DRUG ADMINISTRATION**
**DIVISION OF ONCOLOGY DRUG PRODUCTS**
Center for Drug Evaluation and Research, HFD-150
5600 Fishers Lane, Rockville, MD 20857

| | |
|---|---|
| **To:** Ronald Falcone, Ph.D. | **From:** Amy Baird, CSO |
| **Fax:** 302-886-2822 | **Fax:** (301) 594-0498 |
| **Phone:** 302-886-2715 | **Phone:** (301) 594-5771 |
| **Pages, including cover sheet:** 2 | **Date:** 2-21-02 |

**Re: IND [redacted] Iressa.**



**COMMENTS:**

In reviewing the adverse events for Trial 0039, the clinical reviewer has noted some discrepancies between our analysis and AstraZeneca's analysis. The clinical reviewer has asked that you explain why there are differences. See the attached table. Please call should you have any questions.

Thank you,

/S/

Amy Baird

| Adverse Event | Number of Patients 250 mg/day (n=102) | FDA #'s | 500 mg/day (n=114) | FDA #'s |
|---|---|---|---|---|
| Diarrhea | 58 (56.9) | 60 | 85 (74.6) | 86 |
| Rash | 49 (48.0) | 50 | 63 (55.3) | 63 |
| Asthenia | 29 (28.4) | 34 | 41 (36.0) | 46 |
| Dyspnea | 29 (28.4) | 31 | 26 (22.8) | 30 |
| Nausea | 27 (26.5) | 28 | 31 (27.2) | 34 |
| Acne | 26 (25.5) | 28 | 38 (33.3) | 38 |
| Anorexia | 24 (23.5) | 25 | 31 (27.2) | 34 |
| Pain | 23 (22.5) | 24 | 15 (13.2) | 20 |
| Cough Increased | 22 (21.6) | 24 | 23 (20.2) | 25 |
| Vomiting | 22 (21.6) | 23 | 21 (18.4) | 23 |
| Dry Skin | 17 (16.7) | 17 | 30 (26.3) | 30 |
| Peripheral edema | 15 (14.7) | 16 | 11 (9.6) | 13 |
| Chest Pain | 14 (13.7) | 15 | 15 (13.2) | 15 |
| Back Pain | 14 (13.7) | 14 | 13 (11.4) | 14 |
| Constipation | 13 (12.7) | 13 | 8 (7.0) | 9 |
| Weight Loss | 12 (11.8) | | 12 (10.5) | |
| Pharyngitis | 11 (10.8) | | 16 (14.0) | |
| Pruritus | 11 (10.8) | | 10 (8.8) | |
| Sinusitis | 11 (10.8) | | 4 (3.5) | |
| Abdominal Pain | 10 (9.8) | | 14 (12.3) | |
| Fever | 8 (7.8) | | 12 (10.5) | |
| Dehydration | 5 (4.9) | | 13 (11.4) | |

# MESSAGE CONFIRMATION

02/21/02 08:50

| DATE | S.R-TIME | DISTANT STATION ID | MODE | PAGES | RESULT | |
|---|---|---|---|---|---|---|
| 02/21 | 00'42" | 8862822 | CALLING | 02 | OK | 0000 |

02/21/02 08:49 NO.019 P01

# FAX

**FOOD AND DRUG ADMINISTRATION**
**DIVISION OF ONCOLOGY DRUG PRODUCTS**
Center for Drug Evaluation and Research, HFD-150
5600 Fishers Lane, Rockville, MD 20857

| | |
|---|---|
| **To:** Ronald Falcone, Ph.D. | **From:** Amy Baird, CSO |
| **Fax:** 302-886-2822 | **Fax:** (301) 594-0498 |
| **Phone:** 302-886-2715 | **Phone:** (301) 594-5771 |
| **Pages, including cover sheet:** 2 | **Date:** 2-21-02 |

**Re:** IND [redacted] Iressa.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-399

AstraZeneca Pharmaceuticals LP
Attention: Ronald Falcone, Ph.D.
Regulatory Affairs Director
1800 Concord Pike
P.O. Box 8355
Wilmington, DE 19803-8355

Dear Dr. Falcone:

Please refer to your August 2, 2002 new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for IRESSA® (gefitinib).

On December 26, 2002, we received your December 24, 2002, major amendment to this application. The receipt date is within 3 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 5, 2003.

If you have any questions, call Amy Baird, Consumer Safety Officer, at (301) 594-5779.

Sincerely,

/S/

*{See appended electronic signature page}*

Dotti Pease
Chief, Project Management Staff
Division of Oncology Drug Products
Office of Drug Evaluation I
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/

Amy Baird
1/8/03 09:27:25 AM
Signing for Dotti Pease

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

/s/

Christy Cottrell
1/8/03.09:41:37 AM
CSO