

June 28, 2002



GlaxoSmithKline

5728 02 JUL -2 10:27

Management Dockets
Dockets Management Branch
Food and Drug Administration
HFA-305, Room 1-23
5630 Fishers Lane, Rm 1061
Rockville, MD 20852

GlaxoSmithKline
PO Box 13398
Five Moore Drive
Research Triangle Park
North Carolina 27709
Tel. 919 483 2100
www.gsk.com

Re: Comments on FDA Proposed Use of Rapid Response Surveys to Obtain Data on Safety Information to Support Quick-Turnaround Decision Making [Docket 02N-0131]

Dear Sir or Madam::

Enclosed please find comments from GlaxoSmithKline in response to FDA's proposed use of rapid response surveys to obtain data on safety information to support quick-turnaround decision-making. Public comment regarding the FDA proposal was solicited in its notice in the Federal Register on April 30, 2002, Vol. 67, No. 83, pages 21253 to 21255 (Docket No. 02N-0131).

These comments are provided in duplicate. If you have any questions regarding these comments, please contact me at (919) 483-6733.

Sincerely,

A handwritten signature in cursive script that reads "June Almenoff".

June S. Almenoff, M.D., Ph.D.
Director, Pharmacovigilance and Risk Management
Global Clinical Safety and Pharmacovigilance

02N-0131

C2

**Comments on FDA Proposed Use of Rapid Response Surveys to Obtain Data on Safety Information to Support Quick-Turnaround Decision Making
[Docket 02N-0131]**

On April 30, 2002, FDA issued a Federal Register Notice Entitled, "Agency Information Collection Activities; Proposed Collection; Comment Request; Generic FDA Rapid Response Surveys" (FR Vol.67, No. 83, 21253 to 21255). In association with its request for OMB approval, the notice solicits public comments on the use of rapid response surveys to obtain data on safety information to support quick-turnaround decision making about potential safety problems or risk management solutions from health care professionals, hospitals and other user-facilities (e.g., nursing homes, etc.), consumers, manufacturers of biologics, drugs and medical devices, distributors, and importers when FDA must quickly determine whether or not a problem with a biologic, drug, or medical device impacts the public health. We note that FDA has invited comment on four specific aspects to the proposal. Below we have provided our responses to each:

- 1) *FDA has asked whether the proposed collection of information is necessary for the proper performance of FDA's functions, including whether the information will have practical utility.*

Although the Federal register provided few details regarding how FDA intends to utilize the rapid response surveys, we envision one scenario in which such an approach may provide utility; public health emergencies that are confined to specific geographic areas such as tampering or product contamination. However, these types of situations often require intensive investigation that might extend beyond the scope of a survey. Surveys might also be valuable tools to assess whether there is improper prescribing of a product in the medical community. Finally, surveys are an excellent vehicle for assessing prescriber attitudes and knowledge. The information obtained could enhance FDA's understanding of the medical community's opinions, and this could help to guide the agency in risk management or risk intervention planning.

In our view, the proposal for rapid response surveys has limited practical utility as a tool for assessing the post marketing safety profile of drugs, vaccines, and/or devices. The survey size (50-200 respondents) is extremely small and thus not powered to detect rare, serious events. Any common adverse events that these surveys might detect would be more reliably characterized in clinical trials or post marketing safety studies, hence this approach would be unlikely to provide new information. To this end, it would be helpful if the agency could provide more specific information about the types of measurements that would be made as well as specific descriptions of the program objectives that are under consideration. Furthermore, it would be of interest to know whether there are precedents and/or preliminary data to support or validate the utility of this approach as an adjunct to other post-marketing safety surveillance methods.

Because the Federal Register Notice provides very little specific information regarding the proposed surveys we feel it is difficult for the public to provide

meaningful comment on whether the proposed collection of information is necessary or will have practical utility or achieve the intended goals. Accordingly, we suggest that prior to implementing such an approach FDA provide a more detailed description of its proposal to use rapid response surveys and allow further public comment after providing information that address the following questions/comments:

- Under what circumstances does the Agency envision the quick surveys should be utilized? Would there be standard criteria or would the “rapid response surveys” be utilized on an “as-needed” basis?
- It would be helpful if the Agency could provide more specific information about the types of measurements it envisions and specific descriptions of the program objectives that are under consideration.
- What is the nature of the “vital information” the Agency anticipates will be obtained from this source of data collection e.g. will the surveys seek information about adverse events associated with drug or device use, information regarding “real-world” use in relation to the intended use as described by the product labeling, or the feasibility of risk interventions that are being considered to address a safety issue?
- How will the Agency select participants for the surveys and ensure that participants are representative of the group targeted for input? FDA has noted that some respondents would be contacted more than once per year. Under what circumstances would the Agency contact a participant more than once?
- With regard to an assessment of post-marketing safety, what is the Agency’s view of the relative role of data derived from the surveys in relation to data from controlled clinical studies, epidemiology studies, and spontaneous medical event reports? We are concerned that small, voluntary surveys will be associated with selection bias and provide results that essentially represent testimonial evidence.
- The proposed survey size (50-200) is extremely small and thus not powered to detect new or rare serious adverse events. More frequent adverse events would be more reliably characterized in clinical trials or post marketing safety studies. Therefore it is unlikely that the use of the surveys would provide new information regarding adverse events. We believe that the safety results derived from rapid response surveys should not be used for regulatory decision making unless the information has been corroborated by more scientifically robust data.
- Does FDA intend the primary use of the surveys to support development of a specific research proposal rather than as a means to collect evidence based data that would be used as part of the assessment of the safety profile?
- We believe that the FDA should expeditiously communicate survey results with the company whose product is being investigated, and permit that company to respond to these results, especially if regulatory actions are anticipated. Accordingly, we request the Agency describe how it plans to involve the input of the sponsor in the design and assessment of the rapid response surveys.

2) *FDA has invited comment on the accuracy of FDA's estimate of the burden of the proposed collection of information, including the validity of the methodology and assumptions used.*

We have no comment on FDA's estimate of the proposed annual reporting burden as described in table 1 on page 21254.

3) *FDA has invited comment on ways to enhance the quality, utility and clarity of the information to be collected.*

- We believe that if this program is pursued, FDA should collaborate with other government agencies, academic, and industry experts that have extensive experience in the design, execution and interpretation of surveys for public health decision making.
- Sponsors are experts with regard to their products. In the event that FDA plans to implement a rapid response survey, the company will likely have valuable perspectives and information that could enhance the quality of information collected. Accordingly, we suggest that the product's sponsor should be consulted if FDA is considering use of a survey.
- The potential biases and limitations of the survey instrument must be clearly understood so that critical decision making is not influenced by potentially spurious data. If the surveys are to be used for regulatory decision making, FDA should provide evidence that the survey methodology has been validated and is not confounded by issues such as selection bias.
- The Agency should develop clear definitions and guidelines for what constitutes the type of situation for which these surveys would be appropriate.
- Surveys directed to consumers or other non-medical personnel may provide insight about drug utilization or awareness of benefit/risk messages but may provide medically unreliable data. Accordingly, the recipients of the survey need to be carefully tailored to the type of information to be collected and the intended respondents.
- Any adverse events described by a given respondent should represent only the personal experience of that respondent and not include anecdotes that the respondent may have heard.
- The proposed sample size of 50- 200 respondents might not adequately cover diverse geographic regions and practice settings, so it will be important to analyze the representativeness of these samples.

4) *The Agency has invited comment on ways to minimize the burden of the collection of information on respondents, including the use of automated collection techniques, when appropriate, and other forms of information technology.*

A decision to use automated collection techniques should be influenced by the type of information collected. We believe that automated information collection would not generally be an appropriate source of information for adverse medical events. We

believe that such information would best be collected either in person or through a telephone interview by staff with appropriate training. Automated information collection techniques might be valuable for gathering information about prescriber attitudes and knowledge of safety issues that might guide the Agency in its decisions about risk management proposals.

FROM

GLAXO WELLCOME INC

5 MOORE DR

RESEARCH TRIANGLE NC 27709

Mirk Buringatner 919.483.3073

TO Food and Drug Administration

5630 Fishers Lane, Rm 1061

Rockville MD 20852

Dockets Mgmt Branch 301.827.2120



001 (9/97) S-05 PACKAGE LABEL

United States Shipping

Complete applicable white sections of the U.S. Airbill. Sign and date the Airbill at the Sender's Signature line. Please press hard to remove the protective covering from back of Airbill. Attach this Airbill to envelope within dotted lines shown. When using a Drop Box — follow special instructions on the Drop Box.

International Shipping

Includes Canada & Puerto Rico. To help ensure legibility of this multiple-part form, please type in complete applicable sections of the International Express Airbill. Sign and date the Airbill at the Sender's Signature line. Attach Airbill and necessary documentation in plastic sleeve. Seal sleeve. Tear off backing of plastic sleeve.

F GLAXO WELLCOME
R LIBRA DOORS 13-15
O DURHAM NC 27713
M USA GLAXOSMITHKLINE
919 483 6561

SEQ. NO. 39

| | |
|--------------|-------|
| WEIGHT (LBS) | 1-E |
| PIECES | 1 |
| ZIP CODE | 20852 |
| MD | |
| FDA | USA |

BILLING REF 8142

EXP

SERVICES

ORIGIN BDC

SHIPMENT NO. 3496209522

SHIP DATE 07/01/02

229602964E
229602964E



Ship # 03496209522

Ref: 8142

Svc: EXP

Ship Date: 07/01/02

Wt: 1-E

Chg: \$4.85 Bill To: SENDER

MLDA 4X

Zip: 20852

Desc: