ONE HUNDRED EIGHTH CONGRESS

U.S. House of Representatives
Committee on Energy and Commerce
Washington, DC 20515–6115

JOE BARTON, TEXAS
CHAIRMAN

December 3, 2004

Lester M. Crawford, D.V.M., Ph.D.
Acting Commissioner
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857

Dear Dr. Crawford:

On November 18, 2004, you testified before the Subcommittee on Health and Subcommittee on Oversight and Investigations in a joint hearing entitled "Flu Vaccine: Protecting High-Risk Individuals and Strengthening the Market." We now request your response to several additional questions (attached).

Because we wish to include the questions and responses in the printed record of this hearing, please respond no later than Friday, December 17, 2004. Please fax and e-mail the responses. The faxed response should be directed to Eugenia Edwards, Committee on Energy and Commerce majority staff, at (202) 226-2447, and Voncille Hines, Committee on Energy and Commerce minority staff, at (202) 225-5288. The e-mail copy of the response should be in MS Word format and directed to Eugenia Edwards (Eugenia.Edwards@mail.house.gov) and Voncille Hines (Voncille.Hines@mail.house.gov). Due to the uncertainties of postal deliveries on Capitol Hill, your response should not be sent through the postal service.

If you have any questions, please contact John Ford, Minority Counsel with the Committee on Energy and Commerce, at (202) 226-3400.

Sincerely,

JOHN D. DINGELL
RANKING MEMBER

Attachment

cc: The Honorable Joe Barton, Chairman
Committee on Energy and Commerce

The Honorable Michael Bilirakis, Chairman
Subcommittee on Health

The Honorable Sherrod Brown, Ranking Member
Subcommittee on Health

The Honorable Greg Walden, Vice Chairman
Subcommittee on Oversight and Investigations

The Honorable Peter Deutsch, Ranking Member
Subcommittee on Oversight and Investigations

Questions for Lester M. Crawford, D.V.M., Ph.D.
Acting Commissioner
Food and Drug Administration
from the Honorable John D. Dingell
Committee on Energy and Commerce
regarding the November 18, 2004, Subcommittee on Health and Subcommittee on Oversight and Investigations
Hearing entitled "Flu Vaccine: Protecting High-Risk Individuals and Strengthening the Market"

1. Does the Administration have plans to submit legislation aimed at assuring an adequate and reliable supply of flu vaccines? If so, please describe the basic features of the legislation. If not, please explain.

2. Does FDA need any additional authority or resources in order to do its job of vaccine facility oversight? If so, please give details. If not, please explain.

3. In hindsight, is there anything you would have done differently with respect to the Chiron facility in England? Looking forward, are there any lessons learned from what has happened at the Chiron facility?

4. Please discuss in detail the substance and timing of any proposed or anticipated changes in the good manufacturing practices requirements that apply to manufacturers of flu vaccines. Specifically, how might these differ from current GMPs? Also, please indicate how these changes may affect the adequacy and reliability of the flu vaccine supply in the future.

5. One comment we heard at the hearing was that it is important for additional vaccine production capacity to be based in the United States and not somewhere else. According to this view, this is important for annual influenza vaccines, and especially important in the context of a pandemic. Do you agree? Please explain. If you agree, what policies do you think are needed to achieve that goal?

6. Can you explain in detail how the Administration's $100 million request for flu vaccine activities will be spent? Did you provide input into this request? If so, what amount did you recommend?

Questions for Lester M. Crawford, D.V.M., Ph.D.
Acting Commissioner
Food and Drug Administration
from the Honorable Edward J. Markey
Committee on Energy and Commerce
regarding the November 18, 2004, Subcommittee on Health and
Subcommittee on Oversight and Investigations
Hearing entitled "Flu Vaccine: Protecting High-Risk Individuals and Strengthening the Market"

1. Dr. Crawford, in your testimony you asserted that in June 2003, the Chiron plant was given a clean bill of health. You stated, "The 2003 production was perfectly alright. Nothing went wrong in 2003. That's the misconception that the newspaper got." However, the FDA Establishment Inspection Report, dated June 2002-October 2003, and the FDA 2003 Inspection Observation Findings, dated June 10, 2003, explicitly states that there were in fact multiple deficiencies in the manufacturing process at the Chiron plant. Indeed, the report – a copy of which is attached -- lays out 20 separate areas in which the FDA staff found deficiencies on the part of the manufacturer.

    a. Please explain how you reconcile the findings of multiple deficiencies made in this report with your testimony that the Chiron plant had a clean bill of health in 2003.
    b. For each of the deficiencies identified in this report, please indicate: 1) whether Chiron objected to the observation made by the FDA staff, and if so, when such objection was made, 2) whether the FDA staff withdrew the observation following such objection (and if so, why), 3) whether Chiron implemented corrective action to address the deficiency identified by the FDA staff, 4) if corrective action was implemented, the date upon which such action occurred, 5) the date upon which the FDA staff concurred that the deficiency had, in fact, been corrected by Chiron's corrective action, and, 6) if corrective action was not taken, the reason why it was not taken and what response the FDA staff undertook in response to the failure of the manufacturer to take the corrective action.

2. You testified that no underlying systematic problems were identified prior to 2004. You asserted that the problems that the FDA had identified in 2002 and 2003 had nothing to do with the problems that arose in 2004. However, the FDA's October 2004 report states that, "During an inspection of your firm (we) observed... Failure to adequately address root causes during failure investigations, noted during the inspection of year 2003 has not been adequately corrected. For example, the previous inspection observation noted: The most recent sterility failure Investigation #R/0198/10/04 for nine (9) filled vials of finished Fluvirin batches concluded that inadequate aseptic technique during aseptic connections was the cause. During the 2003 inspection, the firm was cited for the failure to evaluate the reduction in aseptic connection to reduce the possibility of contamination. There is no documentation that adequate corrective action has been conducted."

a. How do you reconcile this report -- by your own FDA staff -- with your assertions that this report was "referring to not to 2003 but 2002. And we did—what happened was, they made the corrections and it seemed to have happened again."?

b. How can the plant have "failed to adequately addressed root causes during failure inspections" and at the same time have "made the corrections?"

c. Doesn't the recurrence of problems which had supposedly been corrected suggest that the corrections themselves were flawed or inadequate, or that the FDA staff had erred in concluding that some corrections had been effective in addressing problems previously identified by the FDA?

d. Did the plant make some basic corrections that allowed them to preserve the 2003 production of vaccine but simultaneously fail to address the root cause of the violation?

e. What problems did the FDA find in 2001? Did the plant adequately address those problems? If so, when? If not, what is the FDA doing to ensure compliance? What were the root causes of the problems in 2001? Did the plant adequately address those root causes? If so, when? If not, what was the FDA doing to ensure compliance?

f. What problems did the FDA find in 2002? Did the plant adequately address those problems? If so, when? If not, what is the FDA doing to ensure compliance? What were the root causes of the problems in 2002? Did the plant adequately address those root causes? If so, when? If not, what is the FDA doing to ensure compliance?

g. What problems did the FDA find in 2003? Did the plant adequately address those problems? If so, when? If not, what is the FDA doing to ensure compliance? What were the root causes of the problems in 2003? Did the plant adequately address those root causes? If so, when? If not, what is the FDA doing to ensure compliance?

h. What problems did the FDA find in 2004? Did the plant adequately address those problems? If so, when? If not, what is the FDA doing to ensure compliance? What were the root causes of the problems in 2004? Did the plant adequately address those root causes? If so, when? If not, what is the FDA doing to ensure compliance?

3. You testified that "What happened (in 2004) was the same kind of (problems as in 2002) happened again… Some of the same kinds of problems did occur again in 2004." Why do you think the problems that occurred in 2004 were so similar to the problems in 2002?

4. What is the basis for your assertion that "What happened in 2002 is not relevant to 2004."? Please provide the Subcommittee a copy of all reports, memoranda, or other analyses which would substantiate your assertion. If there are none, upon what evidence is your assertion based?

5. In response to questions from Rep. Upton, you testified about the FDA's decision-making timeline verses the British timeline. You stated, "...the British made their announcement on October 5 and we had the final meeting and presentation of the data from Chiron Corporation on also Oct 5. We sent a team over on... they were functioning by October 8th and by October 15, I made the decision that it could not be used."

   a. Did the FDA have all of the same information that the British had when they made their conclusion that the vaccine was unusable on October 5th?
   b. If so, why did it take us 10 additional days to come to the same conclusion?
   c. If not, why was there a discrepancy in the information the British had versus the information that the FDA had and what information did they have that the FDA didn't?

6. In response to Rep. Eshoo's statement, "It seems that the British have beaten us to the punch on this." You responded, "No. We actually found out about it first."

   a. What did you find out before the British regulators did?
   b. When did you find out about "it"? When did the British find out about "it"?
   c. Why, if you found out about the problems before the British, did it take the FDA longer to come to the conclusion that the vaccine was unusable?

7. You testified that the FDA had inspectors in the plant on August 25th working on a new line when the FDA was informed of the problems with the vaccine.

   a. Did those FDA inspectors examine the problems with the vaccine at the plant?
   b. If so, please provide a copy of the inspection report.
   c. If not, why?