

Project On Government Oversight

Exposing Corruption Exploring Solutions www.POGO.org

June 10, 2009
By fax to 240-276-3943
and by email

Daniel G. Schultz, M.D., Director
Center for Devices and Radiological Health
U.S. Food and Drug Administration
9200 Corporate Boulevard, Room 100
Rockville, MD 20850

Dear Dr. Schultz:

This is a follow-up to our letter of March 17, 2009 (copy attached and also posted¹), a letter to which we have not received a reply. The main subject of the letter was the policy decision by CDRH to discontinue inspections of nonclinical laboratories – inspections covered by the Good Laboratory Practice regulation.² We asked why the decision to discontinue inspections was not announced publicly – for example, by posting on the CDRH website a notice disclosing the proposed new policy, explaining it, and inviting public comment.

In our letter we described why public notice of the proposed policy was needed:

To us it seems obvious that public notice is required, if only for ethical reasons, when a change of this nature is contemplated by a federal regulatory agency. We see no justification for failing to inform patients who volunteer for clinical trials that an important safety regulation that helped protect volunteers in the past is no longer being enforced. Similarly, the physicians caring for these patients as well as those serving on IRBs [Institutional Review Boards] deserve to be told about the lack of enforcement.

The implantation of medical devices entails some risk, and for certain Class III devices the risk of injury or death is significant. That is one reason why patients or their surrogates must give informed consent to such procedures, especially when these procedures are a part of a clinical trial. Most physicians and many laymen know that in these circumstances, *informed consent is not optional*. The ethical and legal principles underlying informed consent are discussed on the FDA website.³

¹ Letter of March 17, 2009, <http://www.pogoarchives.org/m/science/pogo-schultz-cdrh-20090317.pdf>

² As we informed you previously, the Project On Government Oversight published a report, “The FDA’s Deadly Gamble with the Safety of Medical Devices,” which was posted on February 18, 2009, on our website at <http://www.pogo.org/pogo-files/reports/public-health/safety-of-medical-devices/ph-fda-20090218.html> In the report we reviewed the history of the GLP regulation, the value of GLP inspections of nonclinical laboratories in helping ensure patient safety, the decision by CDRH officials to discontinue GLP inspections, and the objections of some CDRH personnel to this decision.

³ See, on the FDA’s website, the Declaration of Helsinki of 1983 at <http://74.125.95.132/search?q=cache:ziFxfjETkaxsJ:www.fda.gov/oc/health/helsinki83.html+site:fda.gov+%22Declaration+of+Helsinki%22&cd=1&hl=en&ct=clnk&gl=us> This is a cached file. The original file (<http://www.fda.gov/oc/health/helsinki83.html>) has been removed from the FDA website. See also the Belmont Report of 1979 at www.fda.gov/OHRMS/DOCKETS/AC/05/briefing/2005-4178b_09_02_Belmont%20Report.pdf For a statement by the FDA on informed consent, see <http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/InvestigationalDeviceExemptionIDE/ucm046766.htm>

In the letter we further described the possible effects of CDRH's unannounced decision to stop GLP inspections:

. . . patients participating in clinical trials of medical devices as well as members of IRBs charged with protecting those patients should have been informed about CDRH's decision to stop GLP inspections, but they were kept in the dark. Even now, many (perhaps almost all) these patients, physicians, and IRB members still have not been told about the new policy. Some of them would undoubtedly be dismayed to learn of the stealthy relaxation of safety standards.

We remain concerned that your policy decision to discontinue GLP inspections was not announced publicly – for example, by posting on the CDRH's website a notice disclosing the proposed new policy, explaining it, and inviting public comment.

On further reflection, do you believe that CDRH's decision to stop GLP inspections is relevant or irrelevant to the issue of informed consent of patients in clinical trials?

We again request a response to this letter. We would welcome the opportunity to meet with you if you think this would be helpful.

Sincerely,



Danielle Brian
Executive Director
Project On Government Oversight



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Attachment: Letter of March 17, 2009, from Danielle Brian and Ned Feder to Dr. Daniel G. Schultz

Copies: Commissioner Margaret A. Hamburg
Deputy Commissioner Joshua Sharfstein
Michael M. Landa, Acting Chief Counsel

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March 17, 2009

By fax to 240-276-3943

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Daniel G. Schultz, M.D.

Director

Center for Devices and Radiological Health

U.S. Food and Drug Administration

9200 Corporate Boulevard, Room 100

Rockville, MD 20850

Dear Dr. Schultz:

We are writing to ask about the failure of your office to disclose an action taken within CDRH: the decision to stop enforcing an important safety regulation.

As you may know, the Project On Government Oversight has recently published a report, "The FDA's Deadly Gamble with the Safety of Medical Devices," posted on February 18 on our website at <http://www.pogo.org/pogo-files/reports/public-health/safety-of-medical-devices/ph-fda-20090218.html>

In the report we describe the decision by top management of CDRH to discontinue the GLP inspections of nonclinical laboratories. (The number of GLP inspections in 2005, 2006, 2007, and 2008 was 33, 21, 7, and 1, respectively.) This decision almost guarantees that some manufacturers will inaccurately claim (in an IDE application, for example) that their devices were tested in GLP-compliant facilities, knowing that their claim is very unlikely to be challenged by CDRH.

As you know, every Warning Letter for GLP noncompliance represents a lab facility caught in the act of violating an important safety regulation. Such letters were sent to delinquent laboratories and manufacturers in the past, but no longer. Thus, from now on, patients in clinical trials may suffer the consequences of the lack of GLP inspections.

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In response to an inquiry, a member of your staff wrote to POGO on your behalf: “If you know of any specific instances that indicate a link between GLP non-compliance and significant public health issues either in the premarket or postmarket area, you may submit such information to us for review” (letter of May 27, 2008, reproduced in Appendix C of our report). It’s a surprising statement. Surely CDRH should not be waiting for allegations from outsiders like POGO before taking the obvious, long-established, customary step – inspections to monitor GLP compliance.

The purpose of the present letter is to ask: Why was the new policy not launched in plain view? As the Director of CDRH you could have posted a notice on the CDRH website disclosing the proposed new policy, explaining it, and inviting public comment. Members of the Society of Quality Assurance were astonished when they learned about the new policy as an almost incidental part of a presentation by a CDRH employee at an SQA meeting in May 2007.

Members of SQA are only a tiny fraction of the many thousands who are affected by the nonclinical testing of medical devices. Until our report was published a few weeks ago and reported in the press, CDRH’s shutdown of GLP inspections was almost unknown. Patients and physicians had no way of knowing about the decision quietly made by CDRH management. Specifically, patients participating in clinical trials of medical devices as well as members of IRBs charged with protecting those patients should have been informed about CDRH’s decision to stop GLP inspections, but they were kept in the dark. Even now, many (perhaps almost all) these patients, physicians, and IRB members still have not been told about the new policy. Some of them would undoubtedly be dismayed to learn of the stealthy relaxation of safety standards.

To us it seems obvious that public notice is required, if only for ethical reasons, when a change of this nature is contemplated by a federal regulatory agency. We see no justification for failing to inform patients who volunteer for clinical trials that an important safety regulation that helped protect volunteers in the past is no longer being enforced. Similarly, the physicians caring for these patients as well as those serving on IRBs deserve to be told about the lack of enforcement.

The limited resources of CDRH may explain the decision to terminate GLP inspections. That’s one possibility. However, a less benign explanation is also possible. An article in *Circulation* in 2004 indicates that the design and nonclinical testing of a new device may cost \$10 to \$20 million and take two to three years.* Thus manufacturers have a strong financial incentive to pressure you and others in CDRH to cut back on GLP inspections. For this reason it was all the more important to explain your policy decision publicly and in advance.

* Aaron V. Kaplan, et al. “Medical device development: From prototype to regulatory approval.” *Circulation*. 2004; 109: 3068-3072. One of the nine authors is David A. Feigal, your predecessor as Director of CDRH.

A lack of openness in CDRH has led to mistakes or disasters in the past and is almost sure to do so in the future. An article entitled, "Political lobbying drove FDA process," in the March 6 *Wall Street Journal*, describes a recent example of missteps (or worse) behind the closed doors of the FDA. In a letter to the Acting Commissioner of the FDA on the same day, Senator Charles Grassley sought further information about the problems within CDRH described in the *Wall Street Journal* article.

We request a prompt reply to our question: Why was your policy decision to discontinue GLP inspections not announced publicly – for example, by posting a notice on the CDRH website disclosing the proposed new policy, explaining it, and inviting public comment?

Soon after the transmission of the present letter to your office we will post a copy of it on POGO's website. We will post your reply as soon as we receive it. We also welcome comments from those to whom we have sent a copy of this letter (see below).

Sincerely,



Danielle Brian
Executive Director
Project On Government Oversight



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