Exposing Corruption Exploring Solutions
Project On Government Oversight

January 13, 2011
To: Kathleen.Sebelius@hhs.gov

The Honorable Kathleen Sebelius
Secretary, U.S. Department of Health and Human Services
200 Independence Avenue, SW
Washington, D.C. 20201

Subject: Unsafe medical devices: The FDA's Center for Devices and Radiological Health and HHS Inspector General are failing to protect the public

Dear Secretary Sebelius:

In recent years the FDA's Center for Devices and Radiological Health (CDRH) has improperly approved the marketing of medical devices that do not meet the FDA's own standards for efficacy and safety. Some of the unlucky patients who received these defective devices have been seriously harmed by them.

This is not an isolated problem, but a systemic one that has endangered the health and safety of Americans. Among the devices that should not have been approved for marketing are:

- A computer-aided detection system for breast cancer (*NY Times*, Jan. 12, 2009)
- A device used to monitor hemodialysis (*NY Times*, Aug. 20, 2010)
- Pediatric feeding tubes (*NY Times*, Aug. 20, 2010)
- A device surgically implanted in the knee (*Wall Street Journal*, March 6, 2009)
- A device surgically implanted for urinary incontinence in women (*NY Times*, May 4, 2009)

The broad underlying problem is managerial misconduct. When CDRH managers fail to heed the advice of their own medical and scientific experts within CDRH, they often overrule these experts by circumventing the FDA's regulations. A group of the CDRH experts were concerned about the managers' violations of regulations and the harmful effect of these violations on patients' health and safety. When they reported their complaints within the FDA, they were largely ignored. They then took their complaints outside the agency, writing to members of Congress and the President. The whistleblowers'

letters, with detailed allegations of managerial misconduct in CDRH, became widely known.[1]

Investigations by the Office of Investigations, OIG

The HHS Office of Investigations in the Office of the Inspector General (OIG) has dealt with the whistleblowers' allegations of managerial misconduct on two occasions: in an investigation from May to December 2009 and in a "Special Inquiry" from August to October 2010.

The results of the 2009 investigation (announced in February 2010 by the Office of Investigations in an *Investigative Memorandum* and a letter) were surprising. Specifically, the findings were limited to an investigation of *criminal* wrongdoing. (The investigators stated that they found none.) The investigation ignored the possibility of non-criminal wrongdoing, including non-criminal retaliation, which had been almost exclusively the complaint of the whistleblowers in their referral to the Office of Investigations.

The findings of the 2009 investigation, highly favorable to CDRH, conflicted sharply with conclusions reached about a year previously by the House Committee on Energy and Commerce and described in a news release:

> This Committee has been provided with compelling evidence to support the charges that senior managers within CDRH "ordered, intimidated and coerced FDA experts to modify their scientific reviews, conclusions and recommendations in violation of the law."

In July 2010 we met with Mr. Gerry Roy, Deputy Inspector General for Investigations. Our purpose was to express our concern about the two related issues: the wrongdoing that was continuing unchecked within CDRH, and the failure by the Office of Investigations (led by Mr. Roy's predecessor) to properly investigate that wrongdoing in 2009. On September 28, 2010, we wrote Mr. Roy to review our July meeting with him and to inquire about any

[1] The CDRH physicians and scientists presented their concerns in an October 2008 letter to Representative John Dingell, reported by the *New York Times* (Nov. 17, 2008). The letter to Representative Dingell (Oct. 14, 2008) and two subsequent letters – to Mr. John Podesta, on the Obama transition team (Jan. 7, 2009), and to President Obama (April 2, 2009) – are posted online with the names of the whistleblowers redacted. Subsequently, three of the whistleblowers (Dr. Robert Smith, Dr. Julian Nicholas, and Dr. Gamal Akabani) identified themselves in statements describing the problems in CDRH and criticizing the FDA's failure to correct them. They are quoted in articles on or about March 28, 2010 (*N.Y. Times*, Associated Press in print publications and posted by Fox News and MSNBC); August 20 (*N.Y. Times*); September 28 (Associated Press in print publications and posted by Salon.com and Huffington Post; *Wall Street Journal*); October 14 (*N.Y Times*, *Washington Post*); and November 9 (Associated Press in Bloomberg Businessweek, Salon.com, and elsewhere). The three whistleblowers who identified themselves publicly were, in essence, fired by the FDA through the simple stratagem of not renewing their contracts, which in previous years had been renewed routinely. A fourth CDRH whistleblower has been fired in this way within the last month. She had been employed since 1996 as a reviewer in the Radiation Branch of the Office of Device Evaluation in CDRH.

progress by his office. Our letter discussed in detail the shortcomings of the 2009 investigation.

Given a public statement made by Mr. Roy, it is clear the 2009 investigation was drastically limited – limited to the investigation of *criminal* wrongdoing. According to a September 28 Associated Press article by Matthew Perrone, Mr. Roy said, "The original intent of the investigation was to look at criminal matters and our agents did that." This statement, taken together with two other documents (here and here) released soon after the investigation was completed, indicate that the 2009 investigation – from start to finish – was limited to criminal wrongdoing.

Investigation number 2: Special Inquiry, recently completed

The Office of Investigations did not conduct a new investigation, but instead initiated a "Special Inquiry." According to the *Investigative Memorandum* of October 2010, the findings of the Special Inquiry were based on the "case file and all reports and evidence contained therein" – in other words, the findings of the recent Special Inquiry in September 2010 were based exclusively or almost exclusively on documentation gathered during the 2009 investigation. But the 2009 investigation was looking for the wrong things: criminal violations rather than administrative wrongdoing (i.e. alleged violations of FDA regulations and whistleblower retaliation).

Given the facts on which the Special Inquiry was based, the conclusions of the Special Inquiry – described in the *Investigative Memorandum* of October 14, 2010, issued by the Office of Investigations and a November 5, 2010 email, sent by CDRH Director Dr. Jeffrey Shuren to members of CDRH – should come as no surprise. The Special Inquiry found there was no evidence of wrongdoing of the sort alleged by the whistleblowers, and with the additional finding that there was no evidence of retaliation against the whistleblowers.

This raises an obvious question. How could an exclusively criminal investigation (in 2009) provide a sound basis for the main conclusion of the October 2010 *Investigative Memorandum*, namely, the conclusion that within CDRH there were no regulatory violations or retaliation, both of which are non-criminal in nature? We believe that indeed there is no sound documentary basis for this conclusion.

Failure to interview the whistleblowers

The apparent lack of supporting documentation, just described, is compounded by another failure to gather evidence during the Special Inquiry that ended in October 2010.

The agent conducting the Special Inquiry apparently failed to interview any of the CDRH whistleblowers. We consider this an inexplicable and unacceptable omission. The interviews should have been conducted with the whistleblowers who are still employed by

the FDA as well as those no longer employed by the federal government because the FDA refused to renew their contracts. As we understand it, *none of the seven CDRH whistleblowers still employed by the FDA were interviewed by the agent of the Office of Investigations during the Special Inquiry*, and indeed none were ever contacted by the agent to set up an interview as part of the Special Inquiry.[2]

The consequences of unchecked wrongdoing in CDRH

We consider it almost certain that serious violations of FDA regulations by CDRH managers actually occurred as alleged by the CDRH whistleblowers. (One easily checked example is the FDA's mishandling of the ReGen knee implant device as described by Alicia Mundy in the *Wall Street Journal*, March 6, 2009, and in a September 2009 report by the FDA.) The Office of Inspector General has facilitated this destructive process within CDRH by essentially giving the agency cover to continue to operate in an improper manner.

We suggest you look at the article by Jeanne Lenzer and Shannon Brownlee, "Why the FDA can't protect the public," in the November 6 *British Medical Journal* and especially that you examine the accompanying editorial, "Regulation of devices," by Jerry Avorn, Professor of Medicine at Harvard Medical School. Dr. Avorn writes:

> These methodological concerns [related to the clinical testing of devices] have combined with an increasingly powerful and assertive medical device industry and (in the US) a long standing crisis of organisation and leadership in the branch of the FDA that oversees these products. As a result, the standards for device approval and surveillance have fallen far below those for drugs, and even those that would be dictated by common sense.

The crisis of leadership in CDRH has enabled managerial wrongdoing to continue largely unchecked. Clearly some unit of the federal government should take steps to discourage the officially tolerated violations that have led, within CDRH, to standards for device approval far below those dictated by common sense.

We look forward to your comments on the issues raised in this letter. The pattern of regulatory violations in CDRH is not a mere technicality of little consequence – it's a matter of great concern on several grounds. First, there is the anguish of patients suffering from the effects of unsuitable or unsafe devices and burdened by the unnecessary medical costs of such devices. Second, the medical device market, valued at $100 billion or more annually in the U.S., depends on the manufacture of devices that are safe and effective. The FDA should not give the manufacturers of shoddy or unsafe (and thus cheaper)

[2] Of the three CDRH whistleblowers no longer employed by the government at that time, the agent contacted one, who referred the agent to his attorney. In the end, the agent did not interview the former whistleblower. It is unclear who was responsible for the failure to set up an interview.

medical devices a commercial advantage over manufacturers who set high standards for themselves.

Given the magnitude of the various problems in the FDA and the OIG, we request that you direct your office to examine, starting from scratch, the allegations of the CDRH whistleblowers. Some specific issues to be examined are described in an Appendix to this letter. The findings of the examination by your staff should be made public.

The actions of the current leaders in the FDA, CDRH, and the Office of the Inspector General have discredited these components of DHHS. And now their actions have begun to discredit the DHHS itself and the current administration, both of which seem unwilling to tackle the failures of leadership in the FDA, CDRH, and the OIG. A thorough and unbiased examination of these problems, with the findings made public, would be a good first step toward correcting the problems. We stand ready to meet with you and your staff and to help in any other way that we can.

Sincerely,

Danielle Brian
Executive Director
Project On Government Oversight

Ned Feder, M.D.
Staff Scientist
Project On Government Oversight
1100 G Street, NW
Washington, DC 20005
Phone: 202-347-1122
nfeder@pogo.org

cc:

Mr. Daniel R. Levinson, Office of the Inspector General, DHHS
Mr. Gerry Roy, Deputy Inspector General for Investigations, OIG, DHHS
Dr. Margaret Hamburg, Commissioner, Food and Drug Administration
Dr. John Taylor, Chief Counselor to the Commissioner, FDA
Dr. Jeffrey E. Shuren, Director, Center on Devices and Radiological Health, FDA
Mr. Mark Jones, Executive Director, Council of the Inspectors General on Integrity and Efficiency

APPENDIX

In their allegations made to officials in CDRH and to the DHHS Office of the Inspector General, the CDRH whistleblowers described specific violations by managers – violations that occurred during the review of specific, named medical devices. Some details are spelled out in the comments printed below. The occurrence of many of the violations should be fairly easy for your staff to verify through an examination of the administrative file for these devices.

In addition, your staff should have little difficulty in deciding whether the whistleblowers' complaints and disclosures of these and other violations were connected in some way to subsequent job-related adverse actions taken against them and then deciding, further, whether the adverse actions probably constituted acts of reprisal for the disclosures.

Four medical devices

We comment here on four specific devices that were approved by the FDA for marketing or are on their way to approval, despite strong contrary recommendations by reviewers in the FDA arising from their concerns about the efficacy and/or safety of the devices. The first and second are radiological devices. In all four cases there were apparent violations of regulations during the review process. In some cases there was retaliation against physicians and scientists who opposed approval by their managers in CDRH.

A specific regulation was apparently violated again and again in the review of the four devices. It is 21 CFR 10.70, "Documentation of significant decisions in administrative file." When a manager fails to file the required documents in the FDA's Administrative File or tampers with that file, it is a violation of 21 CFR 10.70. This violation may have a covert objective: when a manager proceeds without filing proper documentation of his or her reasons for overruling the reviewers, this shortcut facilitates the manager's approval of a device for marketing.

Device number 1. Breast cancer detection

Device. This breast cancer computer-aided detection (CAD) device is made by the company iCAD, Inc. This device is supposed to highlight regions within a mammogram that indicate to a radiologist that a cancer may be present, leading to a biopsy, additional imaging, or other intervention. Some of the problems with the review of this device were described in the *New York Times* of January 12, 2009, "In F.D.A. Files, Claims of Rush to Approve Devices," by Gardiner Harris.

According to internal documents obtained and cited by the *Times*, the whistleblowers protested that the manufacturer, iCAD, "never tested the device by the intended users (i.e. radiologists) under the intended conditions of use. This is the most basic and fundamental requirement of all F.D.A. submissions."

Over the objections of the FDA's experts on this type of device, senior FDA managers approved iCAD's device for marketing. This breast cancer CAD device is now being sold and used for the diagnosis of breast cancer.

The review in CDRH and the disapproval by experts. Data submitted by the manufacturer was reviewed three times, over a period of 16 months, by expert physicians and scientists in the Office of Device Evaluation of CDRH. On various occasions there were between three and eight of these experts. On each occasion they unanimously recommended disapproval of the device for marketing.

To this day, there is uncertainty over the efficacy and safety of the CAD breast cancer detection device.

Final approval. The person who finally approved the device for marketing was a senior manager, Dr. Donna-Bea Tillman, head of the Office of Device Evaluation. In September 2007 Dr. Tillman had agreed with the expert reviewers that the device should not be approved for marketing. Later, however, beginning in December 2007 and culminating in a final approval decision in April 2008, she changed her position and approved the device, over the objections of the medical and scientific experts, while giving little or no explanation in the Administrative File for the change in her position. Thus there was apparently no basis on file (i.e., no new data in the Administrative File after the experts' third Not Approvable letter) for the reversal of her position.

Between the disapproval and the approval, several events occurred:

- o Dr. Tillman apparently had private communications with the vice-president of iCAD without including any members of the review team and without informing them at the time that these private communications had occurred.
- o She apparently failed to file a record of these communications in the Administrative File shortly after they occurred, as is required of such communications. When she received new information from the manufacturer, she failed to show this information to the reviewers, as is required. The new information is also supposed to be incorporated promptly into the Administrative File, but it wasn't. Instead, it was put into the Administrative File after the decision was made to approve the device for marketing. This violation is both serious and easily verified.
- o She apparently failed to use the device's final labeling that was prepared by FDA's own experts. The accuracy of such final labeling is crucial.
- o In internal documents obtained by the *Times*, Congressman Christopher Shays is described as having called an FDA supervisor about iCAD's device. A company, Fujifilm, whose own device was to work in conjunction with iCAD's device, is in his congressional district.

When Dr. Tillman overruled the scientific and medical experts and approved the device, she apparently failed to place the proper documents in the Administrative File in a timely

fashion as required by 21 CFR 10.70. Specifically, *after* she approved the device, she apparently placed a crucial document, the Decision Memo, in the Administrative File. In this case, the Decision Memo would have explained Dr. Tillman's reasons for overruling the FDA experts. (Such documents are required to be placed in the Administrative File before the Labeling Review and before the FDA issues a legal "Order" approving the device for manufacturing.) The Decision Memo is supposed to be shown to the reviewers when it is filed, which allows them to contribute their views and possibly present an objection to the final decision.

These various regulatory violations contributed substantially to the FDA's ability to overrule the reviewers' recommendation and approve the device for marketing. If Dr. Tillman had complied with 21 CFR 10.70, it is likely she would have been unable to approve the device for marketing. In that case, the device would not be in use now.

Dr. Tillman subsequently left the FDA under a cloud. Despite her departure, we consider it essential that your office conduct interviews and examine the CDRH files in order to establish whether the alleged misconduct actually occurred (as we believe it did) – even if Dr. Tillman has left the FDA and is now beyond the reach of ordinary disciplinary action.

Device number 2. CT colonography

Device. This is a software device that processes CT images of the colon to provide a three-dimensional display or image of the inside of the colon. The image resembles that seen on direct inspection in ordinary colonoscopy. Ideally, colonic polyps or cancers would be seen equally well with both techniques.

Ordinary colonoscopy has been used for many years for screening purposes – for examining the general population of asymptomatic individuals. There are extensive published studies showing that ordinary colonoscopy as a screening procedure has reduced the incidence and effects of colorectal cancer.

The issue for the FDA. The FDA has approved the use of the new procedure, CT colonography, in patients with specific indications (such as evidence of gastrointestinal bleeding). However, the FDA has not cleared the procedure for screening asymptomatic individuals in the general population. This is a major public health issue, and it still hasn't been resolved. Although there are advantages to CT colonography (the patient's comfort without sedation, for example), there are also risks: the increased incidence of radiation-induced cancer in the population subjected to screening, as well as the increased risk for those patients who require a dual procedure, namely, a follow-up of ordinary colonoscopy if the CT colonography discloses a polyp.

Physicians *are allowed* to perform CT colonography for screening. This so-called off-label use of the device is performed on the physician's own initiative. But the manufacturer of the CT colonography device is *not allowed to promote or label the device for screening*

unless and until the manufacturer has shown the FDA that the device is safe and effective for screening and the FDA approves it for that use. The manufacturer has requested clearance of the CT colonography device for screening (through a 510(k) request). Clearance is being considered by the FDA (according to the FDA website), but it has not been granted. The issue is unresolved.

The review team, consisting of physicians experienced in this area and a statistician, examined the data submitted by the manufacturer. The experts concluded that the data and the methodology were unacceptable. They further concluded that the device should not be approved for marketing. The device remains under review.

There were several apparent violations of 21 CFR 10.70 during the review. For example, managers apparently failed to document properly in the Administrative File the private meetings and conversations they had with the manufacturer.

Retaliation

Dr. Julian Nicholas is an unusually skilled and experienced gastroenterologist, an expert of the kind that the FDA needs. He had a flawless record of performance for his three years working for the FDA, as reflected in his personnel evaluations. From May to August 2009, Dr. Nicholas resisted approval of the CT colonography device. Three months later he was warned (indirectly, through comments made to his CDRH colleagues) that there would no longer be funding for his position. Then he himself was told that there would be no funding when his current contract expired. (He had been working for several years under six-month contracts, routinely renewed each time.) A high-level investigation at the FDA concluded that the non-renewal of Dr. Nicholas's contract was unjustified, and he was offered a renewal. However, when he asked how he would be protected from future retaliation, the offer was withdrawn. Within the Gastroenterology Branch at that time, Dr. Nicholas was the only gastroenterologist specializing in issues affecting adults rather than with those affecting pediatric patients. Dr. Nicholas is currently a physician at Scripps Health in San Diego.

In a December 2009 letter to you, Dr. Nicholas described CDRH's flawed review of the CT colonography device and the subsequent retaliation he experienced. There is a link to this letter on the Pharmalot website. We understand that Dr. Nicholas has received no reply from your office.

The February 23, 2010, OIG letter to Dr. Sharfstein (on the subject of the 2009 investigation) contains this pair of statements: that there was a "review of all relevant information" and that the investigators found "no evidence of . . . retaliation." In view of the failure to interview Dr. Nicholas, the claim that all relevant information was reviewed is unsupportable. This contradiction within the OIG letter to Dr. Sharfstein on the most obvious elements in any investigation of retaliation – namely, the decision not to gather

certain crucial information combined with the claim that all relevant information was reviewed – argues strongly against the validity of the 2009 investigation.

Another retaliation in CDRH

Dr. Gamal Akabani was also apparently threatened with non-renewal of his contract if he continued to oppose the approval of radiological devices. Though he was not part of the review team for CT colonography, he is a recognized expert on radiation-emitting devices that include those used for radiation therapy of cancer. The *New York Times* has reported on the FDA's premature approval of many such devices – devices with design flaws that have led to more than a thousand reports of errors in radiation dosage in the last ten years, leading in some cases to serious injury or death because of overdosage. On many occasions in 2007 and 2008 Dr. Akabani was approached by his manager-supervisors to change his review memos when he identified problems with devices under review.

Soon the objections by managers progressed to what seemed to be threats. In what appears to be a final and particularly reprehensible threat, a manager, after inquiring about Dr. Akabani's family, apparently indicated that his contract was secure, thus maintaining the welfare of his family – as long as he agreed with the actions of managers. In context, the questions by the manager about Dr. Akabani's family appeared to be a reference to federal health insurance for their serious medical conditions; his wife had been recently diagnosed with cancer, and his son has a rare syndrome with high morbidity, including blindness, and high mortality. At this point, Dr. Akabani apparently felt he had no choice but to seek a position elsewhere. In November 2008 he resigned from the FDA and became an Associate Professor in the Department of Nuclear Engineering at Texas A & M University.

We believe that retaliation against other CDRH whistleblowers occurred, but we are not including the details here. We are withholding this information in order to protect those whistleblowers from further retaliation.

Device number 3. Hemodialysis device

Device. The Edwards hemodialysis device is a device for monitoring dialysis and providing a warning. During hemodialysis, the patient's blood circulates through the dialyzer ("artificial kidney"), usually for a few hours. As the patient's blood passes through the dialyzer during this period, the patient may lose or gain fluid excessively, thus worsening the patient's medical condition. The device under review has an alarm that monitors the patient's fluid balance. The alarm is triggered when the imbalance reaches a predefined threshold.

The issue for the FDA. After the alarm sounds during a dialysis, thus warning of a medical problem, the monitor can easily be reset. The known, serious defect in this device is that during the reset, the amount of fluid imbalance is simply reset to zero – without compensating for the cumulative imbalance up to that point and without warning the

operator of the dialyzer about the cumulative imbalance. If, during successive resettings, this cumulative imbalance grows and is unrecognized, serious harm to the patient may result. The problem is well known; see *NY Times*, August 20, 2010.

Similar devices with the same defect as the Edwards hemodialysis device are known to have led to several instances of serious injury and death. Despite these instances and over the objections of an FDA reviewer, in 2007 the FDA cleared the Edwards device for marketing as requested by the manufacturer (through a 510(k) request). Three years later, in 2010, the FDA recalled the Edwards device after it had led to serious injury and death because of the defect in the alarm system.

There were several apparent violations of 21 CFR 10.70 during the review. These included the apparent failure of managers to properly document, in the Administrative File, their explanation or justification for ignoring the well-known, serious safety concerns pointed out by reviewers.

Device number 4. Pediatric feeding tubes

Device. Pediatric feeding tubes. Some pediatric patients are fed through a feeding tube that delivers semi-liquid food (puréed vegetables, for example) into the patient's upper GI tract without the need for the patient to swallow. The food passes from a food reservoir through what can be called the "reservoir tubing." The reservoir tubing, in turn, is connected to the patient's feeding tube through a connector that temporarily locks the two tubes together during a feeding.

The issue for the FDA. The typical semi-liquid food contains materials that are clearly unsuitable for intravenous administration, and therein lies the problem. The reservoir tubings made by some manufacturers have standard interlocking connectors that may accidentally be joined to a patient's intravenous tubing. When that happens, the passage of the semi-liquid food directly into the patient's blood stream is immediately harmful and may be fatal. The problem is well known; see *NY Times*, August 20, 2010, "U.S. Inaction Lets Look-Alike Tubes Kill Patients," by Gardiner Harris. The solution to this problem is obvious: a requirement by the FDA that feeding tubes have connectors that are incompatible with the connectors used routinely on intravenous tubing.

In August 2009 a manufacturer requested clearance (through a 510(k) request) for a feeding tube that had a connector of a standard type used with intravenous tubing. The FDA cleared the device for marketing in May 2010 despite the conclusion of the FDA's pediatrician and other reviewers that this feeding tube could lead to serious injury or death.

During the review of this device there was apparent tampering with the Administrative File. Specifically, the review memorandum from the FDA's pediatrician was apparently excluded from the Administrative File, and a description of his consulting was apparently erased from the electronic records.