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September 28, 2010
By email to gerry.roy@oig.hhs.gov

Mr. Gerry Roy
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Subject: Alleged regulatory violations by managers in the FDA's Center for Devices and Radiological Health: A new investigation

Dear Mr. Roy:

We want to thank you for meeting with us two months ago to discuss the untenable situation in the FDA's Center for Devices and Radiological Health (CDRH). During our July 17 meeting, it was apparent that you were dissatisfied and concerned about last year's investigation of wrongdoing in CDRH conducted by the Inspector General's Office of Investigations (OI). This investigation, which was triggered by whistleblowers' allegations of wrongdoing in CDRH, took place between May 2009 and December 2009 (the "2009 investigation") and was completed a few months before you became director of OI.

The 2009 investigation was seriously flawed. The focus of that investigation was solely on criminal matters, despite the fact that the CDRH whistleblowers alleged wrongdoing that was mainly non-criminal in nature. We remain gravely concerned that current FDA leadership is hiding behind the seemingly favorable outcome of the 2009 investigation and is using this outcome as an excuse for not taking the necessary corrective actions. The result: tragic injuries and deaths caused by defective medical devices. The approval by FDA of these defective devices was and continues to be enabled by the wrongdoing never addressed by the 2009 investigation.

We previously discussed these subjects in detail in a draft memo we sent on June 21, 2010, to Roberta Baskin, Senior Communications Advisor to the Inspector General. A copy is appended to the present letter. In this memo we relate the story of four devices that were approved for marketing or are on their way to approval, despite strong contrary recommendations by the FDA's own expert reviewers – physicians and scientists – recommendations arising from their concerns about the efficacy or safety of the devices.

At the July 27 meeting in your office we discussed several subjects:

- o Allegations of misconduct. Whistleblowers have alleged for more than two years that managers in the FDA's Center for Devices and Radiological Health (CDRH) engaged in serious wrongdoing, including regulatory violations and retaliation. We believe the allegations are valid.
- o Investigation by Office of Investigations (OI). In response to the allegations, the OI conducted the 2009 investigation. During the July 27 meeting, we said that this investigation – whose conclusions are entirely favorable to management – was fundamentally flawed and that it did not deal with the alleged regulatory violations, including the retaliation against whistleblowers. We also noted that top FDA leadership is using the investigation's favorable – but seriously flawed – conclusions to mislead Congress and the public about the practices condemned by the whistleblowers.
- o Corrective measures. We believe your office should take specific measures to deal with the flawed investigation of 2009 and should stop the improper use by senior FDA officials of the investigation's conclusions. Such measures by your office are needed as a way of compelling senior FDA officials to correct past regulatory violations within CDRH and put an end to continuing violations.

You said during the July 27 meeting that you would examine the problems we brought to your attention. Specifically, you said that you would talk to your investigators about beginning a new investigation.

We are writing to ask about a new investigation – specifically, to ask if it has actually begun.

If a new investigation has begun, we want to make absolutely clear what our concerns are, so that the mistakes of the 2009 investigation are not repeated.

**Types of violations investigated: criminal and non-criminal violations**

In the OI's previous investigation, which ended in late 2009, the investigators (Special Agents) excluded precisely the kinds of violations alleged by the CDRH whistleblowers. The results of the investigation are summarized in two documents prepared in the Office of Investigations: the *Investigative Memorandum* of February 4 and the letter of February 23 to Dr. Joshua Sharfstein. (There are links to both documents in the draft memo of June 21 appended to the present letter.)

According to the letter sent to Dr. Sharfstein, the investigators found that many issues were "management decisions, administrative in nature, and outside the scope of the criminal investigation" and that the investigation "failed to find any evidence of criminal activity on the part of FDA employees."

The restriction of the investigation to criminal activity – for which the investigators say they found no evidence – apparently occurred about halfway through the period of the investigation. (See the appended memo of June 21 for further comments on this change in the focus of the investigation.)

At the July 27 meeting we criticized the decision to focus the 2009 investigation narrowly on criminal activity. The CDRH whistleblowers had filed complaints about many specific instances of managerial misconduct. They alleged that managers had violated FDA regulations and had retaliated against them, but these allegations – of non-criminal wrongdoing – were virtually ignored in the two documents cited above.

We expect that this omission will be corrected – that the new investigation will deal with the violations of regulations and other acts of non-criminal misconduct that were alleged by the CDRH whistleblowers. This will presumably include possible violations of 21 CFR 10.70, "Documentation of significant decisions in administrative file." The violation of this regulation by managers was common and harmful, as well as particularly easy for an investigator to verify.

We consider it essential that the Office of Investigations evaluate all the most serious instances of alleged misconduct, even if the individual offender has left the FDA and is now beyond the reach of ordinary disciplinary action.[1]

**Retaliation**

The *Investigative Memorandum* and the letter to Dr. Sharfstein state that investigators found no evidence of retaliation. Because the investigation was limited to criminal activity, the investigators must have been referring here to *criminal* retaliation (a rarely prosecuted crime); they chose to ignore the abundant evidence of non-criminal retaliation. The new investigation will presumably seek evidence of non-criminal retaliation and other prohibited personnel practices.

We believe that a fair and honest investigation by your office will confirm the occurrence of many acts of managerial retaliation against CDRH physicians and scientists. The acts of retaliation took place before, during, and after the previous investigation, and we believe there is substantial evidence that they are continuing. It has now fallen to your office to ensure that all physicians and scientists in CDRH are able to identify, without fear of retaliation, those medical devices they consider unsafe.

Three of the whistleblowers are no longer working at the FDA as expert advisors to CDRH. They were forced to leave because their contracts (with a term of two years or less) were not renewed. It is clearly contrary to the public interest to use contract non-renewal as a way for CDRH managers to rid themselves of skilled and hard-to-replace physicians or scientists who have raised concerns as whistleblowers. The evidence shows that this is what happened to the three experts whose contracts were not renewed.

[1] Dr. Donna-Bea Tillman, former head of the Office of Device Evaluation, left the FDA in March 2010. Allegations of serious managerial violations by Dr. Tillman are described in the draft memo of June 21 appended to the present letter.

**The pace of the new investigation**

The DHHS Office of Investigations completed its previous investigation of the CDRH whistleblowers' allegations nine months ago. Since then, unsafe devices, improperly approved or cleared by CDRH managers, have remained on the market, as we discuss in the appended memo of June 21. Senior FDA officials and CDRH managers appear to be exploiting the findings of the 2009 investigation. In particular, they appear to be using the investigation's written conclusions, which are entirely favorable to CDRH management, as justification for ignoring what seems to us to be obvious managerial misconduct.

The leaders of the FDA bear primary responsibility for the resulting threat to patients' health and safety. However, the FDA leaders' actions have been abetted by the findings of the 2009 investigation. It's long past time to identify and stop the managerial violations in CDRH.

This is why we would like to see the new investigation conducted expeditiously and reported publicly as soon as possible. Meanwhile, we hope you are able to devise some way – either by repudiating the 2009 investigation or through another approach – of quickly lessening the continuing harmful impact of the 2009 investigation.

We want to thank you again for your efforts and for the unusual courtesy and care with which you conducted your meeting with us. We would be glad to meet with you at any time.

Sincerely,

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Appended document: Draft memo of June 21, "DHHS Inspector General's sham investigation of wrongdoing at the FDA." Sent on June 21, 2010, by email to Roberta Baskin.

Draft of June 21 by NF, Project On Government Oversight

**DHHS Inspector General's sham investigation of wrongdoing at the FDA**

**Summary.** An *Investigative Memorandum* issued four months ago by the Office of the Inspector General of DHHS announced the results of an investigation of alleged misconduct in the Food and Drug Administration. The memorandum concluded that in the investigation, no evidence of the alleged misconduct was found. But information obtained by the Project On Government Oversight contradicts this conclusion on many grounds.

In December 2008 a senior FDA official asked the Inspector General to investigate possible misconduct in the FDA's Center for Devices and Radiological Health (CDRH). The resulting four-page *Investigative Memorandum* issued on February 4, 2010, by the OIG came to a conclusion favorable to CDRH and the FDA:

> No evidence of prohibited personnel practices; retaliation or violations of law were discovered during the investigation. No other investigative steps are required therefore this case is closed. [This passage is copied verbatim from page 4 of the *Investigative Memorandum*.]

We believe that this conclusion by the IG's office is wrong. We are aware of well-documented information – summarized below – that serious misconduct actually occurred in CDRH, despite the memorandum's claims, to the contrary, that no evidence of the alleged misconduct was found. Specifically, repeated actions by CDRH managers, in violation of FDA regulations and over the protests of CDRH physicians and scientists, led the FDA to put its stamp of approval on devices that were ineffective or unsafe or both. These devices were put on the market and are still being used. In some cases it is possible to trace a link between hazards disregarded by the FDA and subsequent deaths.

We at POGO intend to pursue this issue. We believe that Inspector General Daniel Levinson should publicly repudiate and retract the *Investigative Memorandum*. Similarly, he should withdraw written statements with conclusions parallel to those in the *Investigative Memorandum*; these are statements made a few weeks later in a letter sent on February 23 by an OIG official to Joshua Sharfstein, Principal Deputy Commissioner of the FDA. The OIG should notify those on Capitol Hill (and elsewhere) to whom the letter was sent about the reversal. In addition, Dr. Sharfstein should be asked to publicly acknowledge the FDA's recognition of the new circumstances.

The Inspector General should then initiate a new investigation with safeguards to ensure that the biased approach and misjudgments of the first investigation are not repeated. If the IG's current position – that no evidence of the alleged misconduct was found – is allowed to stand, it will be in essence a license for continued misconduct within CDRH and the FDA as a whole.

We note that in May 2009, the Office of the Inspector General in the Defense Department repudiated and withdrew a report issued four months previously. As described in the *New York Times*, some members of Congress had called that report a whitewash, and a DOD internal review had concluded that it did not meet accepted quality standards. Evidently the IG of the DOD weighed the temporary embarrassment of withdrawing a fallacious report against the long-lasting embarrassment of defending it. Perhaps he was also swayed by considerations of fairness and justice. POGO will proceed on the expectation that the HHS Inspector General will become convinced that these principles apply as well to the memorandum describing the results of the OIG investigation.

**Background**

The health of almost all of us depends at some point in our lives on the safety and effectiveness of diagnostic imaging devices (X-ray machines, CT scanners, and MRI scanners, for example) or radiation-emitting devices used for therapy. In recent years, a group of about a dozen scientists and physicians in CDRH observed what they considered to be serious, systematic violations of the FDA's regulatory procedure for approving these devices for marketing – violations that they believed had led to the FDA's approval of unsafe devices endangering the public's health. After trying unsuccessfully to correct the violations by working within the FDA, these federal employees turned for help outside the agency – i.e., they became whistleblowers.

The violations and other deficiencies noted by the whistleblowers are instances of a long-standing problem at the FDA. Disputes within the FDA over safety generally arise from a conflict between FDA office managers and their subordinates, many of whom are physicians and scientists with far more specialized training than their manager-supervisors. It is common knowledge that managers are under pressure from manufacturers and senior FDA officials (and sometimes members of Congress) to approve new devices as quickly as possible. It is also common knowledge that managers may depend for their promotions on building a record of fast approvals. Objections by physicians and scientists who are reviewers can slow or stop the approval process.

The CDRH whistleblowers spelled out their concerns about the safety and effectiveness of medical devices in public letters sent to Congressman John Dingell (Oct. 14, 2009) [Correction added later: Oct. 14, 2008], Mr. John Podesta, then a member of the Obama transition team (Jan. 12, 2009), and President Obama (April 2, 2009).

The names of those signing the letters were redacted in the versions posted online. The complaints by the CDRH whistleblowers finally led FDA officials to request an investigation by the Inspector General. The OIG responded to this request and described the outcome of its investigation in its *Investigative Memorandum* of February 4, 2010. The main conclusions of this memorandum were repeated in the letter sent on February 23 by an OIG official to Dr. Sharfstein.

**A central, pervasive deficiency: The focus of the *Investigative Memorandum* on criminal violations**

The *Investigative Memorandum* may have been corrupted in a fundamental way by its focus on violations of the law, as distinct from non-criminal wrongdoing. The latter includes violations of federal regulations and serious mismanagement by HHS employees in the performance of their official duties – both of which are under the statutory authority of the Inspector General, even when criminal conduct is not involved. Indeed both types of non-criminal wrongdoing have been the subject of reports by the Inspector General in recent years.

In the present case, the almost exclusive focus of the OIG's investigation on violations of the law – on criminal wrongdoing – is in sharp contrast to the kind of non-criminal wrongdoing that greatly concerned the whistleblowers and led them to seek an investigation.

Moreover, it was this kind of non-criminal wrongdoing that two senior FDA officials specifically asked the IG to investigate:

- On December 3, 2008, William McConagha, the Assistant Commissioner for Accountability and Integrity, sent the IG a letter of referral in which he listed seven categories of allegations to be investigated. They included such actions as failure by CDRH managers to follow regulations and failure to provide proper documentation in the FDA's Administrative File. None of the allegations directly involved violations of criminal law (i.e., violations of criminal law were not the direct target of the allegations).
- Documents provided to POGO from congressional sources reveal that FDA Principal Deputy Commissioner Joshua Sharfstein was intimately involved in the FDA's May 2009 request for an investigation by the OIG. Emails between Dr. Sharfstein and the whistleblowers in April and May 2009, as well as Meeting Minutes, confirm that Dr. Sharfstein had told whistleblowers he specifically requested an investigation that was not limited to, and not even focused on, criminal violations. Rather, at the beginning of the OIG's investigation, Dr. Sharfstein indicated that he asked the OIG to investigate wrongdoing of all kinds, including violations of FDA regulations, mismanagement, ethical violations, and non-criminal retaliation. In addition, Dr. Sharfstein forwarded to the OIG a large number of emails with attached documents in which the CDRH whistleblowers reported non-criminal wrongdoing on a massive scale.

The actual investigation by the OIG took place from May or June to December 2009. In September 2009. the first investigator was replaced by another investigator. At that point, according to reliable sources, the change in the nature of the investigation was striking – a transformation from what had appeared to be a real investigation to one that was not.

The whistleblowers' concern proved valid. The *Investigative Memorandum* deals almost exclusively with violations of law; it concludes there were none. The OIG's letter of February 23, 2010, to Dr. Sharfstein stated that many of the issues in contention within

CDRH were "outside of the scope of a criminal investigation," as indeed they were. Thus many of the very issues that concerned the whistleblowers and senior FDA officials were ignored in the *Investigative Memorandum*.

It is clear that some person or persons in OIG made a decision to shift the investigation quietly from an investigation of the type of alleged wrongdoing requested by senior FDA officials, based on the whistleblowers' concerns, to an investigation of criminal wrongdoing. Whether this decision was the result of faulty reasoning or malfeasance is a matter for others outside POGO to determine.

* * *

We next describe 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 violations of regulations during the review process. In some cases there was retaliation against reviewers 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.

The whistleblowers repeatedly and explicitly called violations of 21 CFR 10.70 (as well as other regulatory violations) to the attention of the OIG investigator. A competent investigator from the OIG should have been able to obtain without difficulty the evidence that would establish a violation of this regulation.

**Device number 1. Breast cancer detection.**

Some of the problems with the review of this device were described in the *New York Times* of January 12, 2009.

Device. This breast cancer computer-aided detection (CAD) device is made by the company iCAD. 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 or other intervention.

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 disapproved the device for marketing.

To this day, there is uncertainty over the efficacy and safety of the CAD breast cancer detection device. A recent article in the medical literature summarizes why this is so; see the Postscript at the end of this document.

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 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:

- She 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.
- She 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.
- She failed to use the device's final labeling that was prepared by FDA's own experts. The accuracy of such final labeling is crucial.
- 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 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 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.

Retaliation

[NOTE added on Sept. 26. In the original version of the June 21 memorandum (which POGO sent to the HHS Office of the Inspector General) there were two paragraphs here, totaling about 300 words, in which specific details of retaliation against two named CDRH scientists were described. In the current version of this memorandum, which is being posted on POGO's website, these paragraphs have been deleted to protect these scientists, who still work at FDA, from further retaliation.]

**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 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, 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 majority 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 violations of 21 CFR 10.70 during the review. For example, managers 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.

The February 23, 2010, OIG letter to Dr. Sharfstein 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 and the claim that all relevant information was reviewed – argues strongly against the trustworthiness of the investigator and the validity of the investigation.

Another retaliation in CDRH

Dr. Gamal Akabani was also 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 threats. In a final and particularly reprehensible threat, a manager, after inquiring about Dr. Akabani's family, 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 were clearly a reference to federal health insurance for their serious medical conditions; his wife was 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.

**Device number 3. Hemodialysis device.**

Device. The Edwards hemodialysis device: 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, 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.

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 violations of 21 CFR 10.70 during the review. These included the 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 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 solution to this problem is obvious: a requirement by the FDA that feeding tubes have connectors that are incompatible with the connectors used 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 tampering with the Administrative File. Specifically, the review memorandum from the FDA's pediatrician was excluded from the Administrative File, and a description of his consulting was erased from the electronic records.

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## Postscript

**More on CAD breast cancer detection devices: The FDA's low standards of approval**

To this day there is uncertainty over the efficacy and safety of these devices. This is the subject of an article this month in *Archives of Internal Medicine*, "A Call for Evidence of Benefits Outweighing Harms Before Implementing New Technologies," by Karla Kerlikowske (June 14, 2010).

A crucial determination -- the value or lack of value of CAD devices for breast cancer detection – was not established by adequate data when the FDA first approved these devices, and it has still not been established:

> Although it has been 12 years since the FDA approved CAD, there is not agreement on whether there is benefit in CAD use when interpreting mammography. . . .

In the eyes of some in the medical community, the FDA itself has not been sufficiently skeptical about the value of devices such as the CAD breast cancer detection device:

> Health care providers and individuals cannot presume that newer technologies are better than existing ones without actual data to that effect. Health care providers should not adopt new technologies without first demanding scientific evidence beyond that required for FDA approval. . . .

Physicians and scientists in CDRH who, as reviewers of a device, insist on adequate data before approving the device for marketing should be rewarded for their efforts, not overruled and subjected to retaliation. The problem is not within the FDA alone. The Inspector General bears a large part of the responsibility. The OIG's *Investigative Memorandum* of February 4, 2010, if allowed to stand, ensures that current practices within CDRH will continue.