

FDA Review

HUMAN & ANIMAL DRUGS • BIOLOGICS • MEDICAL DEVICES

Incorporating DICKINSON's FDA and DICKINSON's FDA INSPECTION

A monthly newsletter focusing on early drug/device/biologic regulatory policy, compliance and field enforcement, and personnel developments inside the Food and Drug Administration.
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TOBACCO RULE COULD DRAIN FDA's FIELD

Last week's startling White House decision to let FDA regulate cigarettes and smokeless tobacco products as "restricted devices" will have profound, transforming effects on the agency and its culture if it is consummated after the 90-day regulatory comment period ends 11/9. Because they are not protected by user fees, medical device manufacturers in particular stand to lose in any siphoning of agency resources to meet the enormous compliance and enforcement burden that will engulf FDA under the terms of its 8/11 proposed rule. And siphoning is what it will likely take, since few believe Congress will appropriate funds

(cont. p. 23)

"Perverted" FDA: officials under criminal probe

FDA's Office of Internal Affairs last week began a criminal investigation of a small device manufacturer's allegations that, over a four-year period, Seattle District and Rockville CDRH officials conducted an illegal campaign against it — including a corrupt advisory committee meeting last October — on behalf of a small group of medical critics of its products. "What we can do is help you understand how

perverted the FDA and its processes have become," co-owner Roland Jankelson told a congressional hearing 7/25, two weeks before FDA criminal investigators

(cont. p. 20)

Hidden FDA letters released: 32 drug ad. violations

For years, CDER's Division of Drug Marketing, Advertising and Communications (DDMAC) has been enforcing its regulations out of the public eye, through a series of letters that, because they aren't labeled "Warning Letter," don't come to light in the routine Warning Letter postings displayed in the agency's Freedom of Information office.

Now, pursuant to an FOI request we filed last January, 32 sets of two-way correspondence exchanges between DDMAC and drug companies have been disclosed for the first time; the three-inch-thick release, including photocopies of subject ads., covers the period 10/1/94 through 12/31/94 and took FDA eight months to assemble and disgorge. Companies and products cited in the 32 FDA complaints are listed alphabetically in the box on page 3. Because the sets of correspondence show both sides of each

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further response of 8/29/94 may have crossed in the mail. In addition to providing a point-by-point reply to each of the FDA-483 deficiencies, Taylor's letter advised that both CDER and CVM had advised in a letter of 8/17/94 that the WFI system change would be considered as a "change being affected" for all appropriate NDAs, ANDAs and NADAs.

Comment: It is interesting to note that Taylor's meeting with FDA at the Rockville, MD, offices was held during the midst of the Chicago District inspection, but apparently did not include Chicago District representatives even though it discussed the feed water to the WFI system which was "the focus" of the Chicago District inspection. Such an omission is not in the best interests of a firm that wants to establish good rapport and communication with the local district office. This is especially important, since obviously the district office has substantial impact on the scheduling and outcome of pre-approval inspections. In those instances where firms feel the need to consult with the Centers, most especially with ongoing inspectional findings, it is usually best, to say the least, to keep the local district office fully advised and to invite their participation as well as the respective Center compliance office.

—Rudolf Apodaca

PERVERTED (from p. 1)

appeared at his Tukwila, WA, facility to begin an objective examination of the possibility that FDA employees had violated the law. "I ask that you give no credence to assurances from the Commissioner that adequate changes have been, or are being, made from within the agency. Our experience indicates the following:

"1. The FDA does not have regard for the legal rights which most of us take for granted, and which are fundamental to our freedoms in this country.

"2. The FDA will not punish wrong-doing within its ranks.

"3. The Office of Chief Mediator and Ombudsman is not an efficient deterrent to FDA misbehavior. In fact, we feel that the unwillingness of the Office of Chief Mediator and Ombudsman to act in our case, or, if it should act in the future, its delay in taking action, is a

significant additional part of the FDA's misbehavior in our case."

thick file ...

Jankelson, who with his brother Robert, heads a 25-year-old small manufacturer of electronic dental measurement instruments, Myo-Tronics, Inc., presented the House Commerce subcommittee on oversight and investigations with a half-inch-thick file of company-FDA correspondence and exhibits to document his charges. FDA officials named in the allegations are: Joseph R. Baca and Richard Andros (Seattle District Office), Carolyn A. Tylenda (executive secretary, CDRH Dental Products Panel), and D. Gregory Singleton (CDRH Division of General and Restorative Devices). The dissident professional group that opposes the Myo-Tronics technology is the American Association of Dental Research (AADR).

According to Jankelson's House testimony, the FDA actions against Myo-Tronics began 8/91, when "two FDA inspectors appeared at the company's door, flashed their FDA Inspector badges, and initiated a series of events that defy belief." Although the company has no proof, it suspects that members of AADR who have been denigrating the technology in Myo-Tronics' products since 1986 had a hand in "stimulating" FDA's inspection. After a 20-day inspection, Myo-Tronics was told that its four devices were no longer covered by the 510(k)s since there had been departures from previous labeling.

"Overnight, in the FDA's view, the company had gone from one with an exemplary record of over 20 years duration, to one illegally marketing its products," Jankelson told the subcommittee hearing.

"This occurred without the FDA ever once questioning the safety or efficacy of these instruments" which, Jankelson testified, have been awarded approval seals by the American Dental Association (ADA). However, although it disagreed with the basis of the FDA findings, to avoid a costly legal dispute Myo-Tronics agreed to remove some claims and filed new 510(k)s in May, 1992. But the agency had, in response to post-generic drug scandal complaints from the same House subcommittee (albeit under the direction then of Democrat John D. Dingell), imposed a "no

return phone calls" policy in CDRH, which impeded Myo-Tronics' efforts to respond to reviewer questions about the 510(k)s. One letter from CDRH in August, 1992, objected to six label claims, and the company replied promptly pointing out that the claims were from old labeling no longer in use. A second letter four months later (12/9/92) took exception to five different claims and asked Myo-Tronics to direct any questions to Louis Havlinka at (301) 427-1090; for a week, the company left seven messages on Havlinka's recorder, none of which was answered, and then it replied in writing (12/23/92). Continued efforts to communicate with FDA were made in 1993, including unsuccessful attempts through Jeff Gibbs at Hyman, Phelps & McNamara.

then seizure ...

No further communication from FDA was received by either the company or Gibbs until 8/9/93, when a Seattle District investigator arrived with two U.S. marshals and seized inventory of two products, including "Export" and "Demonstration Only" models along with those for domestic sale. FDA's rationale: after being advised in the original Warning Letter that the products were no longer covered by their 510(k)s, the company should have immediately stopped shipping, even though advised by counsel that this was not necessary.

"Again, rather than fight, we chose to cooperate with FDA," Jankelson told the subcommittee. But this did no good.

After "an agonizing period of negotiation with a belligerent and unresponsive FDA," Myo-Tronics entered into a consent decree under which it agreed to abandon five product claims it had used since before 1976 (but for which it could not find documentary proof of such pre-Amendments, grandfathered use) and to discontinue shipments until revised 510(k)s were approved. For its part, FDA agreed to complete the reviews in 60 days. But FDA reneged — after publishing a sales-crushing report of the settlement in *FDA Consumer* (insurance consultants clipped it to deny patient and medical practitioner reimbursement claims), it "lost" one of the four 510(k)s, and took 830 days to complete the promised reviews. "Myo-Tronics could have filed contempt charges against FDA," attorney Gibbs would later write

Congress, but instead, "the company gave FDA extra time in which to complete its review."

corrupt advisors ...

But FDA wasn't done with Myo-Tronics yet. "The next attack occurred in October, 1994," Jankelson told the subcommittee. Then, FDA convened the CDRH Dental Products Advisory Panel to illegally up-classify Myo-Tronics' products to Class III (PMA required), under chairman Charles Bertolami, a former director of a trade rival, Arthrotek Inc. of Ontario, CA, and co-inventor of a patent that Arthrotek had unsuccessfully asserted against Myo-Tronics for the products under review. Without revealing that Myo-Tronics' products, and similar ones made by another firm, BioResearch, were the only ones to be dealt with by the panel on a very loosely-defined agenda ("muscle monitor devices," a term that could cover over 30 other types of products as well), FDA then appointed a notorious opponent of Myo-Tronics' products and AADR member, State University of New York at Buffalo professor Norman Mohl, as the panel's expert advisor.

Not only did FDA conceal until the morning of the hearing its choice of old foe Bertolami to chair the hearing, but FDA (or one of its "special government employees" on the panel) allegedly leaked Myo-Tronics' presentation in advance to a witness who testified against the company's products.

Myo-Tronics and BioResearch got another shock when they saw the witness list: three well-known political opponents of their technology, who had earlier fought unsuccessfully to get the American Dental Association to rescind its approval seals from the firms' products. Although they represented a single organization and should have shared one 20-minute slot, FDA gave them three separate 20-minute slots to attack the products.

Inevitable result ...

And the inevitable happened. Trade rivals made hay with the panel's damaging recommendation, feeding it to insurance consultants who in turn used it to help companies deny patients' claims for therapy that uses the devices. A second, extraordinary meeting of the panel two months later to repudiate the October proceedings did little to halt the com-

panies' sales decline; Myo-Tronics had to lay off half of its 27-person workforce. A British peer-reviewed professional journal even turned down an independent review of the technology in Myo-Tronics' products on the basis that they had been seized by FDA.

Letters by CDRH device evaluation director Susan Alpert invalidating the October results and promising not to reconvene the panel until an internal investigation of conflict-of-interest issues and other problems with the hearing had been completed did little to assuage the companies' wounds. Myo-Tronics and BioResearch felt they had been so severely damaged they could have nothing more to lose if they took their fight to Capitol Hill.

But still they clung to their fading hopes that FDA's own internal system would eventually bring them justice — they appealed through attorney Gibbs 1/31 to Ombudsman and Chief Mediator Amanda B. Pedersen.

Her investigation continues, but she apparently provided Myo-Tronics with so little feedback that by 6/27 Jankelson accused Pedersen of not taking his concerns seriously and threatened to take his case to the Hill — a step that BioResearch president Jim Ramsey had already taken two weeks earlier.

Even as Myo-Tronics was waiting on the results of Pedersen's investigation, it seems the people inside FDA who were hounding the company had one more shot to fire. Last March, Jankelson told the subcommittee, "we learned that the FDA was considering the imposition of civil penalties. In fact we now know that civil penalties were recommended by the Seattle District Office in August 1992, and in June, 1994. In the words of one District FDA official: 'the company needs to be punished'."

But the Capitol Hill static that Myo-Tronics and Gibbs had generated was becoming too much.

A 4/20 letter to Myo-Tronics from Gibbs reported on a conversation that day with District Director Roger Lowell in which Lowell said the District was withdrawing its request for civil penalties. "He based this change in position on the history between FDA and Myo-Tronics — there has been 'too much going on.' Mr. Lowell could not have been more definitive." Looking back, Myo-Tronics CEO Bill Trimmingham wishes the company had taken FDA to court rather than sign the consent decree — "We paid a terrible price for that." All companies with products pending at FDA might draw another lesson as well: the crucial impor-

THE CALENDAR

MEETINGS	SPONSOR	DATE	LOCATION	PHONE
Project Mgmt & Finance: A Collaboration	DIA	Aug 28-29	Marriott, Denver CO	(215) 628-2288
Preparing for FDA Pre-Approval Inspection	PDA	Aug 30-31	Radisson, Montreal	(301) 986-0293
Cleaning Validation	PDA	Aug 30-31	Radisson, Montreal	(301) 986-0293
Val of Computerized Systems	PDA	Aug 30-31	Radisson, Montreal	(301) 986-0293
Microbiological QA for Pharm. Prod.	PDA	Aug 30-31	Radisson, Montreal	(301) 986-0293
Pharm Water System Design & Val	PDA	Sep 6-7	Caribe Hilton, San Juan, PR	(301) 986-0293
Using Disinfectants in Parenteral Facilities	PDA	Sep 6-7	Caribe Hilton, San Juan, PR	(301) 986-0293
Cleanroom Management	PDA	Sep 6-7	Caribe Hilton, San Juan, PR	(301) 986-0293
Planning & Management of Validation	PDA	Sep 7	Caribe Hilton, San Juan, PR	(301) 986-0293
Market & Advertise Drugs, Devices & Biologics	FDLI	Sep 7	Wash Vista Hotel, Wash, DC	(202) 371-1420
Steam-In-Place Technology	PDA	Sep 8	Caribe Hilton, San Juan, PR	(301) 986-0293
Aseptic Processing Val Trends & Issues	PDA	Sep 8	Caribe Hilton, San Juan, PR	(301) 986-0293
Regulatory Perspectives of Pharm Labels	PDA	Sep 8	Caribe Hilton, San Juan, PR	(301) 986-0293
Troubleshooting Pharm Water System	PDA	Sep 8	Caribe Hilton, San Juan, PR	(301) 986-0293
Basic Training in Clinical Monitoring	PERI	Sep 12-15	Georgetown Univ., Wash DC	(703) 276-0178
Pharmacokinetic Concepts in Drug Dvlp	PERI	Sep 17-20	Marriott, Arlington, VA	(703) 276-0178
Qualit of Pharm Mfg/Research Facility	PERI	Sep 23-29	Inter-Continental, Chicago	(703) 276-0178
Executive Officers Conference	NABP	Sep 30-Oct	Loews L'enfant Plaza Hotel	(708) 688-6227
Val of Computerized Systems	PDA	Sep 6-7	Hilton, San Juan, PR	(301) 986-0293
LAL Test Technology & Workshop	PDA	Sep 7-8	Hilton, San Juan, PR	(301) 986-0293
Developing Validation Protocols	PDA	Sep 8	Hilton, San Juan, PR	(301) 986-0293
PDA/FDA Joint Conference	PDA/FDA	Sep 18-20	Hyatt, Bethesda, MD	(301) 986-0293
19th Annual Conference	RAPS	Sep 18-20	Hilton, Washington, DC	(301) 770-2920
Clinical Trial Materials: Partnership for 90s	DIA	Sep 20-22	Hyatt, Chicago, IL	(215) 628-2288
Pharm Water System Design & Validation	PDA	Oct 16-17	Desmond Hotel, Malvern, PA	(301) 986-0293
Val of Computerized Systems in Pharm Industry	PDA	Oct 16-17	Desmond Hotel, Malvern, PA	(301) 986-0293

August 1995

Dickinson's FDA REVIEW: Page 23

tance of being fully familiar with the membership of FDA advisory committees, including their individual disclosure statements which are obtainable under FOI.

Comment: The Myo-Tronics case is a rare public example of the kind of worst-case FDA scenario that regulated companies usually only whisper among themselves about — and then only behind locked doors with the lights out on Saturday nights during electrical failures when they've had too much to drink and their judgment is impaired. That such things can occur at all is a testament to the conspiracy of silence that exists on both sides of the regulatory fence. FDA employees who may know or suspect that something is wrong among some of their colleagues all subscribe to the culture of blind loyalty to the organization, which in turn is fed by a real fear for their own prospects for future career advancement if they were to break ranks and tell what they know. Rogue activities find institutional shelter this way.

As for industry, it is a rare company indeed that will step forward as Myo-Tronics has done and name names in public. Many in other companies will be wondering what its FDA future holds now. As Roland Jankelson told Congress: This is not the way American government is supposed to be.

TOBACCO (from p. 1)

adequate to cover the task FDA has set itself. Although there is no cost estimate yet available, some idea of the size of that task may be garnered from FDA's own assessment in the proposed rule: "Perhaps the most significant effect of the proposed rule with regard to potential legal liability is that manufacturers, as well as retailers and distributors, could be held responsible for violations of the regulations. As with other violative manufacturer activities under the act, such a finding could result in various sanctions, including: fines, injunctions, civil money penalties, product seizure and prosecution."

FDA clearly sees its role as extending to directly cover 2.4 million tobacco retailers, a reach it now asserts only for far fewer food stores and (rarely) pharmacies.

Another measure of the size of its prospective task came in an FDA estimate that the proposed

regulation would cost industry 1.2 million hours of resources each year to maintain records and send information to FDA. All this would have to be reviewed in the agency, a task the proposal would give to the Center for Drug Evaluation and Research (CDER), notwithstanding FDA's decision to use the medical device laws and regulations to regulate cigarettes and smokeless tobacco. CDER not only has the pharmacologic expertise to deal with the health issues raised by nicotine, but its drug-review resources from user fees by law can't be siphoned off to regulate tobacco. In the absence of new funds from Congress for tobacco regulation, FDA would have to drain every other area of its responsibilities to fund even a modest start on this new endeavor.

hit the field ...

Since most of the new activities to be brought in by the tobacco regulation would involve FDA's field (e.g., liaising with states, prosecuting retail violations, monitoring sporting events for illegal tobacco sponsorships, etc.), it may be device manufacturers waiting for preapproval inspections who would feel the resource-drain most. Not far behind might be drug advertisers waiting for various clearances — the proposed rule would require the use of resources by CDER to review some 2,000 new cigarette and smokeless tobacco labels, as well as an unknown volume of advertising campaigns, plus mandatory industry-funded anti-tobacco educational messages directed at young people, all of which would be required to bear FDA-mandated wordings.

The proposal would force tobacco companies to place the description, "A Nicotine-Delivery Device" beside the product's established name and include a "brief statement" on all advertising, such as: "About 1 out of 3 kids who become smokers will die from their smoking."

In the proposal, FDA declared that "a cigarette is analogous to a metered-dose inhaler." It based its decision to use device authorities rather than drug authorities on statutory practicalities — the subject products could remain on the market, whereas the drug route would have required safety-effectiveness approvals of NDAs and ANDAs for each cigarette and smokeless tobacco product. That would have required

2
ALLEGATIONS OF FDA ABUSES OF AUTHORITY

HEARINGS
BEFORE THE
SUBCOMMITTEE ON
OVERSIGHT AND INVESTIGATIONS
OF THE
COMMITTEE ON COMMERCE
HOUSE OF REPRESENTATIVES
ONE HUNDRED FOURTH CONGRESS
FIRST SESSION

JULY 25, NOVEMBER 15, AND DECEMBER 5, 1995

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M-D-D-I REPORTS - "The Gray Sheet"

October 20, 1997

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DENTAL PRODUCTS ADVISORY PANEL CHAIR RESIGNS FOLLOWING RELEASE OF IG PROBE; NOV. 3-4 PANEL MEETING WILL REVISIT UNCLASSIFIED MUSCLE MONITORING DEVICES

Charles Bertolami, DDS, University of San Francisco voluntarily resigned as chairman of FDA's Dental Products Advisory Panel following an investigation by the HHS Office of the Inspector General, according to a letter from FDA Deputy Commissioner for External Affairs Sharon Smith Holston to Rep. Joe Barton (R-Tex.). Manufacturers' complaints regarding the panel chair's failure to abide by appropriate procedure at the Dental Panel's Oct. 13, 1994 meeting on muscle monitoring devices prompted the investigation.

In addition, the term of a non-voting panel consultant who participated in the meeting as a discussion leader "expired and has not been renewed," an employee was "verbally admonished" by Office of Device Evaluation Director Susan Alpert, and another employee was required to submit "a written statement...acknowledging inappropriate conduct, which will remain in official agency files (maintained by FDA's Division of Employee and Labor Management Relations) for a period of four years," the July 17 letter states.

In October 1994, the panel unanimously recommended that electromyographs (EMG) used to diagnose temporomandibular disorders and oral-facial pain be placed in *Class III* ("The Gray Sheet" Oct. 17, 1994, p. 5). Following the decision, Tukwila, Washington-based Myo-tronics, a manufacturer of EMG devices, alleged that the agenda had been fixed because the *Federal Register* notice announcing the meeting failed to specify that jaw tracking, stimulating and sonographic devices would be discussed and included in the panel's recommendations. Myo-tronics also protested the participation of Bertolami, whose patented technology was the subject of infringement suits filed against the company in May 1990. Milwaukee-based BioResearch, another EMG manufacturer, voiced similar complaints.

FDA later overturned the panel's classification decision in December 1994, explaining in a *Federal Register* notice that the previous meeting was "flawed" and "and should not [have been] the basis for decisions made about the use of these devices." The agency expressed concern that "all interested parties may not have received adequate notice of the devices to be discussed at the meeting" ("The Gray Sheet" July 31, 1995, p. 6).

An investigation was begun by the FDA Office of the Chief Mediator in conjunction with the FDA Ombudsmen's Office in response to a 33-page letter of complaint filed in January 1995 by the Washington D.C. law firm of Hyman, Phelps, & McNamara on behalf of Myo-tronics and BioResearch. In July 1995 Myo-tronics President Roland Jankelson testified at a hearing before Rep. Barton's House Commerce/Oversight Subcommittee on allegations of FDA retaliation that the FDA's Office of Internal Affairs planned to conduct its own inquiry.

The Dental Products Panel will re-examine unclassified muscle monitoring devices for the first time since October 1994 at a scheduled Nov. 3 meeting. FDA says it is trying to clear up the backlog on unclassified devices.

Myo-Tronics' complaints against FDA date back to 1992, when it sought 510(k) clearance for its *K6-1 Mandibular Kinesiograph*. Delayed review of the 510(k) provided the agency with the opportunity to initiate seizure of the product in August 1993 and to impose a consent decree in February 1994, the firm alleged.

The 510(k) claimed substantial equivalence to its pre-1976 predecessor, the *K5-R Mandibular Kinesiograph*. A May 29 supplemental IG report explains that the company reported submitting an affidavit because it did not have on hand any independently verifiable pre-amendment sales literature to support their position that the claims it was making for its product were pre-amendment. FDA Chief Reviewer Greg Singleton admitted that Myo-tronics' affidavit swearing substantial equivalence to the pre-1976 Amendments device was included in the initial 510(k) he received, but "did not give the document much weight because it was from the present employee of a company he did not trust."

Myo-tronics claims it later sent Singleton the predicate sales materials he requested, but Singleton testified the IG that he never received it. The IG report states: "In summary, the evidence shows that Dr. Singleton received the predicate sales material on three different occasions." It also notes that his testimony is "in contradiction to the information in the files, including memos to the file drafted by Dr. Singleton in which he admits receiving and discounting the information." Singleton was dismissed from the agency in a "quick and discreet" manner, FDAers say.

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Do Not Duplicate

The IG also found evidence that the Myo-tronics 510(k)'s affidavit was not processed under standard FDA operating protocols. IG notes that "in the normal course of events, an affidavit would be sent to the" Office of Compliance in FDA's Center for Devices and Radiological Health "once it was received by the Office of Device Evaluation," and OC would be responsible for determining if "more information was needed or if the affidavit was strong enough to substantiate the claims as pre-Amendment." However, the investigation found that "in this instance, the affidavit was seemingly not sent to the Office of Compliance for more than a year after its receipt and when it was sent it was sent as part of a [non-substantially equivalent] package for review and concurrence."

IG highlights the finding that a separate affidavit from an independent purchaser which "validates the existence of a Myo-tronics, Inc. sales brochure prior to May 1976" was not included in the 510(k) administrative file. "This brochure included product claims consistent with most of the product claims in question in 1992," IG says, emphasizing that it "is particularly significant because it came directly to the FDA from an independent source who was in a position to know of pre-amendment claims made by Myo-tronics, Inc., and the affidavit verifies that the brochure had been in commerce pre-May 1976."

➤ FDA plans to use the Myo-tronics incident "as a 'case study' in roundtable discussions with executive secretaries of FDA's medical device and other advisory committees," Holston says in her letter to Rep. Barton. It also will be cited in training sessions for product reviewers and newly appointed committee members "to educate them on the boundary between appropriate conduct and conduct that is either inappropriate or can be construed as such."

FDA forwarded a letter to industry on Sept. 18 specifying that devices considered by the Dental panel "will include, but will not be limited to devices such as muscle monitoring devices, jaw tracking devices, TENS devices and ultrasound devices" (see *In Brief* p. 2). Panel recommendations, the letter continued, "will assist FDA in developing a comprehensive strategy for subsequent device classification efforts."

Myo-tronics' Jankelson responded to FDA's notice of the upcoming panel meeting by contacting FDA and requesting a roster of panel members. In an Oct. 9 letter addressed to ODE Dental Devices Branch Chief Susan Runner, ODE Dental, Infection Control and General Hospital Devices Director Timothy Ulatowski, and ODE Dental Reviewer Pamela Scott, Jankelson stated he was concerned that "individuals who were very much involved" in the planning of the October 1994 meeting "are the same individuals who are in charge of decisions regarding the upcoming panel meeting."

Citing the previous "egregious misconduct" of FDA employees who allegedly "rigged" the panel "in order to serve the agenda of an outside group," Jankelson said it was crucial that the list "be made available to [Myo-tronics] immediately so that the legitimacy of the current process is not clouded even further."

ODE's Division of Dental Infection Control says the list is being finalized and is not ready for public release. Myo-tronics says it intends to revisit the issues raised in Jankelson's letter at the Nov. 3 meeting if it does not receive a response. The company also says it will file suit against the agency if it does not believe the panel members possess the adequate level of expertise.

Nov. 4 panel discussion will focus on reclassification of coated and uncoated endosseous dental implant (EDI) devices and the classification of oral appliances for the treatment of obstructive sleep apnea and snoring. The meeting may extend to Nov. 5, if necessary, FDA says.

In light of new data for uncoated and coated EDIs, FDA is asking the panel to reconsider downclassifying the devices, agency staffers say. At a 1991 Dental Products meeting, panel members recommended downclassifying only uncoated screw type implants made of commercially pure titanium: all blade, solid cylinder and hollow cylinder forms of EDIs remain in *Class III* ("The Gray Sheet" Jan. 6, 1997, p. 7)

The Dental Implant Manufacturer's Association says it plans to make a presentation to the panel. DIMA submitted a petition in 1989 seeking downclassification for coated and uncoated screw-type, blade, cylinder and screw-type/cylinder EDIs in response to FDA's proposal in 1989 to require PMAs for the devices.

"comprehensively regulated by FDA" — as no doubt they are more than cosmetics. call to order...

On the horrors of federally unregulated cosmetics, however, Kennedy brought forward graphs, pictures, patient histories, all the results of countless hours of diligent staff work. When fellow senators saw what he was about, so many turned to private conversations in the chamber that the chair had to call for order. Section 761 would not apply to state initiatives or referenda prior to 8/1 — that is to say, it leaves untouched California's 1986 "Proposition 65," requiring clear warnings of carcinogens or reproductive toxins on any product. As for other states, which are said to have done nothing in the field, preemption would occur only when and if FDA does act. The section, Jeffords said, would assure that then FDA would have "the authority to provide uniformity."

Absent anyone actually doing anything about cosmetics (apart from California), the debate had the sound of pure theory.

There was more — a hypothetical risk that a device section might provide cigarette manufacturers with an opportunity for evasion through "creative labeling" (notwithstanding an express disclaimer of applicability to tobacco), an objection to eliminating the requirement of environmental impact statements in FDA approvals ("an assault on the basic environmental protections," declaimed Kennedy), and amendments from Dick Durbin (R-IL) to keep some post-market device surveillance mandatory and to specify tighter conflict-of-interest rules for third-party reviewers. The real questions now, however, are whether the substantive compromises will hold in the House, and whether the pettifoggish objections will pop up as in the Senate.

Biased advisors: FDA slaps staffers as probes continue

Whenever companies come away from an FDA advisory panel with less than they wanted, there is a temptation to think the panel was rigged. In 1994 the Dental Products Advisory Panel of the Center for Devices and

Radiological Health (CDRH) assessing a Myo-Tronics Inc. dental measuring device was indeed rigged, and this past July FDA deputy commissioner for external affairs Sharon Smith Holston told House Commerce oversight and investigations chairman Joe Barton (R-TX) — who is investigating at least two other CDRH panels for similar concerns — about actions taken to remedy the situation. Omitting individuals' names, she said FDA has:

- Verbally admonished General and Restorative Devices reviewer D. Gregory Singleton, who left the agency 8/1;
- Disciplined panel executive secretary Carolyn A. Tyenda by inserting a confession of "inappropriate conduct" into her record for four years (she left the agency two years ago);
- Accepted the "voluntary" resignation of panel chairman Charles Bertolami, a former marketplace competitor of Myo-Tronics who had brought an unsuccessful lawsuit against the company over the products being reviewed;
- Elected not to renew the appointment of non-voting panel consultant and discussion leader Norman Mohl, whom Myo-Tronics identified as a well-known opponent of its technology.

Holston told Barton Myo-Tronics will get a new review by a reconvened panel when

FDA DOUBLE STANDARD IS REAL

FDA director of employee relations Kathy Vengazo confirmed to *FDA Review* that because of conflicting statutes the agency does have a double standard when punishing internal vs. external wrongdoers.

Under the Food, Drug and Cosmetic Act, industry wrongdoers may be publicly identified in an explicit Warning Letter that may, as in Myo-Tronics' case, be falsely based — and may suffer immediate financial harm as a result.

Under the Civil Service Reform and Privacy Acts, FDA wrongdoers on the other hand are protected from public exposure even after they have left the agency and died — unless they lose a formal appeal after a hearing, which seldom happens because most cases are settled informally.

For its monetary losses, moreover, Myo-Tronics has no practical legal recourse.

FDA's investigations into all allegations are completed. In the meantime, she asked Barton not to release her letter.

Myo-Tronics co-owner Roland Jankelson, who got a copy of the heavily-purged letter under FOI late last month, denounced FDA's actions as inadequate.

"They are still crawling under a rock," Jankelson said. "What were the acts of misbehavior? Do they acknowledge there was something wrong? Do they admit that their seizure of our products was wrong? It's far short of an agency coming clean." FDA's illegal actions against his company, including a Singleton-orchestrated Seattle District attempt to impose \$2 million in civil monetary penalties, cost Myo-Tronics millions of dollars and were all made possible by the culture change the former Commissioner **David Kessler** encouraged, Jankelson charged.

other cases ...

FDA's Office of Internal Affairs is currently investigating two other allegations of compromised panel integrity at CDRH — the turn-down of a Biocontrol non-invasive glucose monitor by the Clinical Devices and Clinical Toxicology Advisory Panel last year, and the seating a few months before of a voting member of the Ophthalmic Devices Advisory Panel who allegedly had a relationship with Summit Technology and who unsuccessfully opposed the approval of rival Visx Inc.'s excimer laser, a subject tangential to a larger scandal now known as "Lasergate."

Almost a re-run of Myo-Tronics' panel experience occurred in the **Biocontrol** case last year, when the panel was — as Biocontrol tells it — overwhelmed by conflicted trade opponents and condemned its Diasensor 1000 glucose monitor. The company says it was refused additional time to present its case and was herded into what turned out to be an ambush by a CDRH hand-picked panel whose composition and real agenda was so confused in a flurry of rapidly changing rosters that Biocontrol was left guessing until the morning it convened — and then the prepara-

tions were so rushed that several members claimed they did not have the full 30 days required in regulations to familiarize themselves with the issues. One panelist did not get his kit of materials until the morning of the hearing, several others not until a few days before. Not only did members have alleged conflicts of interest, two reportedly holding briefs for competitor companies, but they were allowed to overwhelm deliberations and assure a turn-down of the application, according to Biocontrol.

As in the Myo-Tronics experience, this result was aided by the complexity of the technology at issue. For Biocontrol it was a novel statistical efficacy-measuring technology, the Clarke Error Grid, that most panelists said they did not understand.

Despite written assurances to Biocontrol by CDRH director **Bruce Burlington** that the panel was unlikely to delve into statistics, 60% of the session was devoted to the grid and its statistical fundamentals. As in the Myo-Tronics case, Biocontrol alleges that the panel's adverse finding was pre-ordained by CDRH's failure to adequately plumb conflicts of interest among panel members, forcing the company to submit its product to the panel before it was ready, concealing the makeup and the agenda of the panel until the company had little chance to respond to either, and otherwise assertively misleading the sponsor about the likely substance of the proceedings. In Biocontrol's case, this rather black-and-white picture is muddled by the company's failure to present adequate clinical effectiveness data — only eight subjects — and its refusal to accede to informal FDA requests that it withdraw the 510(k) application (although written CDRH advice to the company assured it that its data were adequate for panel review).

Lasergate ...

FDA's third investigation of an allegedly compromised advisory committee has since been overshadowed by the associated, infamous "Lasergate" leakage Thanksgiving, 1995, to a trade competitor, Summit Tech-



FOOD AND DRUG ADMINISTRATION

Office of Internal Affairs
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Rockville MD 20852

Attachment (5)
Ref. #3

MEMORANDUM OF TELEPHONIC INTERVIEW

Case Number: 95-OIA-970-074

Case Title: FDA Retaliation

Person Interviewed: Dr. Charles Green, D.D.S.

Date of Interview: August 26, 1996

Place of Interview: Office of Internal Affairs, Rockville, Md.

Interviewed By: S/A Leon C. Drezek & S/A Matthew Kochanski, HHS-OIG

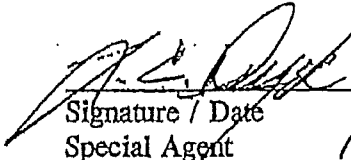
On August 26, 1996, Dr. Charles Green, Northwestern University, Chicago, IL., was telephonically interviewed by the undersigned and provided the following information:

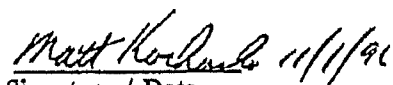
Dr. Green indicated that he, along with Dr. James Lund, provided testimony in person before the October, 1994 Dental Advisory Panel that was considering the classification of "Muscle Monitor Devices". In addition, Dr. Green stated that he personally read into the record of the panel meeting, a letter authored by Dr. John Rugh which was also offered as testimony before the panel. Dr. Green characterized the testimony he and Drs. Lund and Rugh provided as strongly advocating a recommendation that the FDA place muscle monitor devices into Class III, requiring that clinical studies be performed to scientifically prove the safety and efficacy of the devices. Dr. Green stated that he, Dr. Lund, Dr. Rugh and Dr. Norman Mohl, who served as the panel's special consultant, share the same views regarding muscle monitor devices, and the need for clinical studies to scientifically show safety and efficacy.

Dr. Green was queried about a luncheon meeting that he attended with FDA officials including Drs. Tylanda and Singleton, in April, 1994, during a conference on Temporomandibular Joint disorders (TMJ). Dr. Green recalled that Dr. Mohl set up the luncheon meeting with the FDA officials to introduce him (Green) and others who shared their views on the devices to the FDA personnel. Dr. Green stated that in addition, the luncheon meeting provided the group an opportunity to inform the FDA officials concerning the work that the Neuroscience Group of the professional association, the International Association of Dental Research (IADR) had been doing concerning muscle monitor devices. Dr. Green stated that the non-FDA dentists were all members of the

IADR, as well as members of the American Academy of Oralfacial Pain (AAOP), and reiterated that they all held views that he characterized as anti-muscle monitor devices. Dr. Green stated that the FDA officials were briefed on a position paper that the neuroscience group of the IADR had developed that contained strongly negative views towards the devices. Dr. Green opined that the FDA officials present during the luncheon were fully aware of his own, Dr. Mohl's and others, negative views concerning the devices.

Concerning an organized letter writing campaign to FDA regarding the devices, Dr. Green stated that he is aware that one or two professional organizations urged their membership to write to FDA to indicate anti-device views, but he knew of no additional specifics regarding this. Concerning the devices, Dr. Green indicated that the devices have been used in dental research since the 1950's, but that the clinical utility of the devices has not been scientifically proven. As a result, Dr. Green and others believe that the FDA should call for full clinical studies to scientifically establish safety and efficacy. Dr. Green denied that anyone involved with the October, 1994 Dental Advisory Panel had "leaked" any information to him, and that he never received or reviewed copies of any proprietary Myo-tronics, Inc. documents the company submitted to FDA for the panel meeting.

 9/3/96
Signature / Date
Special Agent

 11/1/96
Signature / Date
Special Agent