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A TIME FOR CHANGE IN ADVERTISING AND PROMOTION REGULATION

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The election of a Republican Congress in November 1994 signaled a change in how the country views the role of the Federal Government. The Food and Drug Administration (FDA) will be a principal target for regulatory reform. The Republicans see the mission of the FDA as proactive, advancing the availability of new medical products, not just protecting the public from unsafe or ineffective ones. The main focus will be on the drug and device approval processes. The FDA approval processes have faced debate and controversy numerous times in the past three decades. Major change is unlikely; continued incremental change will likely be the result of 1995's debates in Congress. This will also be a time to look at how information systems about drugs are functioning. The world is a much different place than it was when the 1962 Drug Amendments were passed. There are four incremental changes proposed. They do not fundamentally alter how FDA goes about regulating advertising and promotion. They are intended to make the system more rational and open.

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THIS IS A TIME FOR debating change at the Food and Drug Administration. The election of a Republican Congress in November 1994 signaled a change in how the country views the role of the Federal Government. The new Republican Congress has indicated that one of its principal targets for regulatory reform is the FDA.

The new prevailing view among the Republicans is that the FDA must see its mission as advancing the availability of new medical products, not just protecting the public from unsafe or ineffective ones. According to the new thinking, Congress over the past 40 years fostered an attitude that the worst thing FDA could do was approve a drug that later needed to be removed from the market. The Republican attitude seems to be that there should also be a price for failing to approve a safe and effective new drug or for delaying approval so as to deny patients access to better outcomes.

The main focus of attention from the new Congress will be the drug and device approval processes. The discussion thus far has ranged widely. Groups on the left are trying to frame the issue by advocating that, in fact, the system needs to be made even more rigorous. The extreme advocates of change from the right want the FDA abolished and replaced by a privatized system of product review. As is customary in Washington, the battle ultimately will be fought on the middle ground.

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Every think tank in Washington, including some that were virtually unknown before November 1994, is studying the FDA's approval processes. During 1995, their proposals will hit the news media.

This is hardly the first time that the approval processes at FDA have been the subject of so much debate and controversy. The 1962 Drug Amendments, of course, represented the most dramatic actual change. In the late 1970s legislation was introduced to change the drug approval process. In the early 1980s there was what is called the investigational new drug-new drug application (IND-NDA) rewrite, which the FDA promised would solve all problems. In the late 1980s, the AIDS groups brought substantial public pressure on FDA, leading to changes in the regulations to permit earlier access to certain products.

The FDA was also the subject of a lot of study before that. Most recently, there was the Edwards Report and the Lasagna Report, based on studies by committees chaired by former FDA Commissioner Charles Edwards and Tufts Dean Louis Lasagna. The think tanks can pull these and other major studies off the shelf and find recommendations that are still current, but that were never implemented. In fact, in 1992, the Council on Competitiveness, chaired by then Vice President Quayle, sought to consolidate all of the reports.

As of this writing, there is a period of rhetoric, of attacking the FDA. The rhetoric will at some point die down and serious attention will have to be paid to what is good about the system, and what does not work.

Even the most hardened of critics will agree that the system does work to assure that drugs are tested and carefully reviewed before approval. The process has assured every American that a drug, in all likelihood, will perform as described in the labeling. Most people will agree that more postmarketing surveillance needs to be done so that more can systematically be learned about a drug after it is on the market and exposed to thousands and hundreds of thousands of patients.

Agreement will be reached that the fundamental objectives set forth in the Food, Drug & Cosmetic Act remain sound, and that the review of drugs and devices before marketing is a proper function of the Federal Government. The nation does want safe and effective drugs and devices, properly tested and promoted. Few people really want to repeal the effectiveness amendments.

There have been discussions of privatization before. No one, thus far, has been able to develop a reliable and credible approach for privatizing the system, although certainly some aspects of the review process could well be performed more efficiently and with higher credibility by the private sector, and perhaps some of what FDA does now, such as the chemistry review, can be completely overhauled.

Thus, while the goals of Federal regulation are not likely to be altered, there certainly is a lot of room for improvement in the processes themselves. There is growing consensus that the process by which safe and effective drugs and services is achieved is very expensive, extraordinarily cumbersome, extremely frustrating, and increasingly placing American research at a competitive disadvantage. This is what needs to be dealt with.

The author predicts that the most likely outcome of this current debate will be:

1. No major legislation will be passed in 1995 or 1996, though many bills will be introduced, and
2. Continued incremental change in the process will occur.

If the changes are not significant enough to satisfy the new Republican majority, then serious legislation will be more likely in the next Congress.

This period of examination of FDA processes is also an opportune time to look

at how information systems about drugs are functioning. It is known that advertising and promotional issues will be examined by Capitol Hill because the former counsel to the Washington Legal Foundation (WLF) is now counsel to the new Republican chairman of the House Health Subcommittee. WLF, of course, was the organization that filed the First Amendment petition in 1993 and the lawsuit in 1994 that challenged FDA's proposed policy on industry-sponsored continuing medical education programs and other symposia.

The present approach to regulation of drug advertising and promotion derives from the 1962 Drug Amendments. In 1962, in legislation passed in the wake of the Thalidomide episode, the Congress included in the Drug Amendments a provision that placed prescription drug advertising under FDA's jurisdiction. The legislative history of that provision indicates that the Congress was concerned about abuses in the way that drug companies were advertising their products.

The world at the time was much simpler. The advertising amendments were passed in an era that was precomputer, precable TV, premanaged care—when most Americans had a family doctor who made house calls and who was paid directly by the consumer. Prescription drug information for consumers was nonexistent, and many if not most consumers accepted their prescriptions without question or understanding.

The advertising provision in the Drug Amendments was extraordinarily simple. It consists of a single paragraph. It basically calls for the generic name and the drug's "formula" to be included in drug advertising and "other descriptive printed matter," and for a brief summary of prescribing information to be provided. It specifically excludes preclearance of advertising, except in extraordinary circumstances.

There was no mention in the law about press releases, letters to formularies, television advertising, video news releases, faxed information, or information transmitted over the Internet. The complex web of regulations and policies, some of which are not even written, that do apply to these modern methods of communications has evolved over the years in response to what has occurred in the marketplace, based on FDA's view that its mandate to control drug information was broad and that limiting the amount of information available about certain aspects of drug research and new uses for existing drugs served the best interests of the public health.

At one point FDA was out-of-date with regard to understanding how Americans were getting their drug information. The agency has made significant strides in closing that gap of understanding.

But the effect of the present "cobbled together" system of regulation has been to create an information system that satisfies no one. Patient understanding of prescription drugs remains low, as reflected in the high noncompliance rate consistently observed.

The most knowledgeable resources about drugs, the companies that research and make them, are severely restricted in what they can say publicly about their products and ongoing research. The FDA has established very firm limits on information flow from companies, and permits only authorized information to reach physicians and patients from them. Even information that is completely accurate and that would undeniably benefit patients cannot be generally disseminated if it is not approved by the government.

Because the government regulates only what drug companies can disseminate, but not what journals or other sources of information can say, the information environment is even more confusing. Every week information about drugs is seen on television or in newspapers, reporting on the latest study or the latest hazard, but FDA does not limit, nor should it, this information, even though the medical journals, or consumer organizations, or any-

one else, have their own self-interest in the publicity derived.

In principle, the author is a believer in incremental change, and therefore proposes some modest changes in the present system of regulating medical advertising and promotion that would help bring better information into the marketplace:

1. *The single most important issue in the area of advertising and promotion is the communication of "off-label" data* —A careful balance must be achieved. If *any* new information about a marketed drug can be communicated, then there is a strong possibility that even greater confusion will result, as physicians and patients will be unable to discern the valid from the frivolous. Continued incentives must also be provided for companies to submit supplemental applications to the FDA to change the labeling; if the wide and continuous dissemination of "off-label" information were permitted, there would not be much incentive to seek formal labeling changes.

   Part of the solution is to permit the dissemination to physicians of legitimate "off label" data for approved drugs with the clear proviso that the information always be accompanied by a clear statement that the indication is not approved by FDA or that the research has not been reviewed by the agency. The statement could also say that an application is pending before the FDA, if that is the case.

   The question is how to define "legitimate" "off-label" uses. Rather than leave this to the discretion of the FDA, it is proposed that "legitimate" be defined as information about the drug that is included in the various drug compendia or in peer-reviewed medical literature. This would also apply to combinations of approved drugs, such as cancer drugs which are commonly used in unapproved combinations.

   Inclusion of information in the compendia, or acceptance of a drug's use based on a peer-reviewed and published study, is now sufficient for many insurance companies to reimburse. It should, therefore, be information that can legitimately be disseminated to health professionals.

   In addition, it should be acceptable for companies to compile peer-reviewed information and compendial information about "off-label" uses and provide them to physicians, even on an unsolicited basis, so long as the package of materials is not misleading or promotional, and so long as there is clear disclosure that the indication is not approved.

   There should be provision for patients to receive similar packets of information from drug companies on request. Patients with serious or life-threatening diseases should not have to go through medical texts and computer systems to locate information that companies can readily compile and make available.

   There is continued legitimacy to prohibiting outright promotion directly to consumers of indications not approved by FDA. If significant research appears in a peer-reviewed journal, however, the FDA should recognize the company's legitimate right to publicize that research within a limited window of time.

   A related issue is reimbursement policy for "off-label" uses. Insurance companies have discretion in what they will and will not reimburse when a drug is used outside of labeling. For consumers, this is often a point of negotiation with the insurance company. It would help if FDA declared its comfort with a policy that permits reimbursement for compendia-approved indications or for well-recognized uses, even when such uses are not in the labeling.

   Some people would advocate going a step further, and would urge that provision be made to include in a drug's offi-

cial labeling certain "off-label" uses. Richard M. Cooper, former Chief Counsel of FDA, advocated this in a recent article in the *Food and Drug Law Journal* (1). There is merit to this suggestion but there is a concern that it would take too long for the agency to come up with appropriate standards. Mr. Cooper also made a number of other suggestions for dealing with the promotion of "off-label" uses that merit attention, including permitting limited promotion while an NDA supplement is pending,

2. *Eliminate the brief summary requirement in print ads, whether for the physician or the consumer*—If ever there was a wasteful requirement, this is it. One advertising executive estimated about two years ago that inclusion of the brief summary in advertising costs $80 million a year. The author would have guessed the amount to be much higher.

   But in a time when every physician has access to a *Physician's Desk Reference* (PDR) or to a computerized version of it, it hardly makes sense to require the brief summary to be included with advertising. For consumers, the brief summaries that appear are difficult if not impossible to read. FDA has, in effect, made a mockery of the requirement by permitting the brief summary to be unreadable.

   One replacement for the brief summary is to require ads to carry a brief "major statement" of contraindications, warnings, and serious side effects and adverse reactions. The "major statement" could be included in a box in the corner of each ad, in a typeface large enough to read. This "major statement" would enable companies to save millions of dollars in advertising costs and also communicate more of the most important information in a concentrated way. Deleting the brief summary requirements would require a change in the law, as the Food, Drug & Cosmetic Act specifically requires that a brief summary be included in advertising,

3. *FDA communication of its policies and decisions to the world*—The traditional way for FDA to announce policy is through the *Federal Register*. The administrative process is very clear. As is well-known, FDA has not issued any final regulations in the advertising and promotion area for decades. The only regulation that has been proposed was the one that appeared in the *Federal Register* on November 27, 1992, on continuing promotion of unapproved uses through symposia, and that proposal has been challenged by the Washington Legal Foundation.

   The FDA's policies are communicated in a number of informal ways:

   - Letters to all NDA and abbreviated new drug application (ANDA) holders,
   - Policies announced from podiums,
   - Articles in the major medical journals, and
   - Through enforcement actions in warning letters.

   From talking with many people in the industry, it is known that a lot of uncertainty remains about what FDA policies are, and how they are applied. There is one simple way that FDA can enhance an understanding of its policies, and that is to make available publicly all the notice of violation letters it issues.

   Notices of violation are letters that are sent to companies when the violations are not worthy of a warning letter. The author does not know how many are issued each year, but at one point there were a few hundred. By making warning letters public, FDA would provide considerable guidance to companies seeking to learn what FDA views as violative. It would also open the regulatory process to greater scrutiny, and

4. *FDA should open up still further its processes for policy development*—The

agency has made great strides in this regard. It has met privately with a number of industry organizations on a variety of matters. It has held a two-day public meeting on pharmacoeconomics. More meetings are needed, and the author is pleased that FDA has agreed to sponsor more later in 1995.

Most importantly, in developing new policies, FDA must be open-minded about the role of industry efforts. FDA's view is that companies cannot be trusted to disseminate balanced information and that physicians, other health professionals, and patients cannot handle certain kinds of information. The information world and medical practice are different today than they were in 1962; the policies now being developed must reflect those changes and the current complexity of information transfer. Further, FDA must recognize that it performs its best service by creating a way for information to be communicated, rather than just creating barriers. The present policies are based on laws that never contemplated the present information and medical environments, and on FDA's view that companies cannot be trusted to issue accurate and honest information.

CONCLUSIONS

These proposals are modest and incremental. They do not fundamentally alter how FDA goes about regulating advertising and promotion. They are intended to make the system more rational and open, and service the needs of physicians and patients, and hopefully lead to more informed drug use.

REFERENCE

1. Cooper RM. Unapproved Uses of Drugs: An Analysis and Some Proposals. *Food Drug Law J.* 1994; 49(4)533-539.