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**TESTIMONY  
of the  
AMERICAN COLLEGE of CARDIOLOGY  
for the  
FOOD and DRUG ADMINISTRATION's  
Public Hearing  
on  
OVER-THE-COUNTER DRUGS**

Thursday, June 29, 2000  
10:40 a.m.

Presented by

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00N-1256

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Good morning. I am Dr. Edward Frohlich and I am pleased to speak on behalf of the American College of Cardiology (ACC) this morning. I am a Fellow of the ACC, as well as a Master of the American College of Physicians. I have also served as a member on the Board of Trustees at the ACC. I am currently the Alton Ochsner Distinguished Scientist of the Ochsner Medical Foundation in New Orleans and am Editor-in-Chief of *Hypertension*, an official scientific journal of the American Heart Association.

The ACC appreciates this opportunity to offer its comments regarding the Food and Drug Administration's (FDA) approach to regulating over-the-counter (OTC) drug products. The ACC is a 25,000-member non-profit professional medical society and teaching institution whose mission is to foster optimal cardiovascular care and disease prevention through professional education, promotion of research, leadership in the development of standards and guidelines, and the formulation of health care policy. The ACC represents more than 90 percent of the cardiologists practicing in the United States.

Our interest and concern about the FDA's regulation of OTC drug products grows out of our primary responsibility as cardiovascular physicians to ensure that patients have the best care available to them – care that is safe, effective, appropriate, and comprehensive – and that today is provided with that responsibility clearly in mind. We are advocates of good drug therapy because we know that, when appropriately utilized, they

can substantially improve patient outcomes. Within that framework, we propose guidelines for the FDA to consider when evaluating applications for OTC status.

We believe that the FDA's current approach to regulating OTC drug products works to ensure that such products are safe and effective and offers safeguards to ensure that consumers receive care that is appropriate and comprehensive. We agree that it is appropriate for the FDA to examine its overall philosophy and approach to regulating OTC drug products in "light of the continuously changing health care environment, including the growing self-care movement." Furthermore, we find that the FDA's current approach ensures that "consumers [have] easy access to certain drugs that can be used safely for conditions that consumers can self-treat without the help of a health care practitioner" and is the correct approach to regulating OTC drug products.

The FDA's current regulations are necessary to fulfill the statutory mandate of the Federal Food, Drug, and Cosmetic Act, requiring a prescription for a drug which, "because of its toxicity or other potentiality for harmful effect, or the method of its use, or the collateral measures necessary to its use, is not safe for use except under the supervision of a practitioner licensed by law to administer such a drug." 21 U.S.C. § 353(b)(1). The FDA's current regulations for OTC drugs define "safety," for OTC use, to mean "a low incidence of adverse reactions or significant side effects under adequate directions for use and warnings against unsafe use as well as low potential for abuse which may result from abuse under conditions of widespread availability." § 330.10(a)(4)(i). "Effectiveness" is defined to mean "a reasonable expectation that, in a

significant proportion of the target population, the pharmacological effect of the drug, when used under adequate directions for use and warnings against unsafe use, will provide clinically significant relief of the type claimed.” § 330.10(a)(4)(ii). Finally, the “benefit-to-risk ratio of a drug shall be considered in determining safety and effectiveness.” § 330.10(a)(4)(iii).

The ACC has developed a set of guidelines that we believe are appropriate for FDA application for OTC drug products, especially the cardiovascular drugs. We believe that our guidelines are consistent with the FDA’s regulations. The following summarizes areas of general agreement between the ACC and the FDA:

- **Low Side-Effect Profile**

Like the FDA’s regulations, we believe that drugs made available for OTC use should have a “low incidence of side effects.” **We add that, where side effects exist in an OTC drug, they should generally be of the type which can be monitored without physician assistance or testing.** Non-steroidal anti-inflammatory drugs, for example, typically cause stomach upset prior to gastric ulceration. Likewise, antihistamines will cause drowsiness that is readily detectable to the consumer without any sophisticated monitoring needed. We further believe that side effects which can only be detected by laboratory tests or physician monitoring compromise consumer safety by going undetected until they become severe or life-threatening. Thus, drugs with such side effects should not be available for OTC use.

▪ **Low Potential for Harm Due to Abuse**

The FDA's regulations state that an OTC drug should have a "low potential for harm which may result from abuse under conditions of widespread availability." We agree that the potential *for harm, if abused*, should be low. **We would add, however, that drugs which have great potential *for abuse* should not be available OTC, even if the harm from abuse is not great.** Such a drug would not be a good OTC candidate because it would not be used according to "adequate directions for use and warnings against unsafe use" and, hence, would not provide the type of relief claimed.

An example of abuse of an OTC drug might be use for fraudulent purposes. It is conceivable that certain drugs may be taken over a short duration to achieve a clinical endpoint in order to mask a clinical condition (e.g., Federal Aviation Administration (FAA) licensure or approval for insurance). Antihypertensive agents, for example, may lower blood pressure rapidly allowing a person with hypertension to appear normotensive for an FAA license, insurance, or employment. Such fraud has costs beyond the immediate incident; such as higher insurance premiums for all or danger to the public safety in case of the pilot who is not on a regular treatment program yet passes the FAA examination.

▪ **Clinically Significant Relief**

FDA's regulations define "effectiveness" as "the demonstration that, in a significant proportion of the target population, the pharmacological effect of the drug . . . will provide clinically significant relief of the type claimed." **Since OTC drugs**

are usually available in the lowest possible therapeutic dose, doses which are sub-therapeutic in a significant proportion of the target population should not be made available for OTC use. This is especially true for drugs in which the "relief of the type claimed" is something which cannot be readily assessed by the consumer. Thus, if a drug's claimed relief requires a laboratory test or some other technical intervention, consumers may easily believe that they are "relieved" when, in fact, they are not. Furthermore, a high risk patient taking an OTC drug for such a "silent" condition, is at greater risk for disease progression.

Thus, the following is an important guideline that the ACC would add to the FDA's regulations:

- **Existence of Symptoms**

The prescription drugs which the FDA has thus far changed to OTC status are used to relieve symptoms that a consumer experiences. For example, *nonsteroidal anti-inflammatory drugs* (NSAID) alleviate pain and when the consumer uses an over-the-counter NSAID he or she knows whether it is effective based on whether or not the pain is relieved. Likewise, *H2 blockers* are used to relieve heartburn and their effectiveness is known to the consumer based on relief of their symptoms. Other examples include *steroid creams* for relief of a rash and *antihistamines* taken to relieve symptoms of hay fever or urticaria.

**The ACC believes that the relief of symptoms should be an important requirement for any OTC product.** If a currently available OTC drug does not relieve a symptom, the consumer is more likely to seek the advice of a health care provider for relief. If "relief" requires a laboratory test to ascertain, the consumer does not know whether he or she is, in fact, relieved.

Such a guideline is especially important for cardiovascular drugs which often treat conditions for which there are no associated symptoms with which a consumer can assess the drug's efficacy. The risk of sub-therapeutic dosage or sub-optimal therapeutic endpoint is increased in a drug which requires monitoring to assess its effectiveness. High-risk consumers and those with established disease are especially vulnerable and we believe that management of these patients should *always* be supervised by a physician. It is, therefore, of vital importance that, if drugs used for treating such "silent" conditions are made available over the counter, important information must be provided to consumers regarding all risk factors and their appropriate management. Information about what constitutes high risk and that warns high risk consumers that OTC dosages may not be effective must also be part of the drug's labeling.

**We propose that medical specialty societies participate in the preparation of guidelines for patients who would use over-the-counter drugs.** Such guidelines are appropriately developed by physicians with input from patients and can include

information on when the taking of an OTC drug may, or may not, be benefited by physician supervision.

Furthermore, if physician monitoring of symptoms and laboratory values is necessary to assess a consumer's "relief" by an OTC drug, we do not recognize the advantage of the drug's OTC status -- if the consumer must go to a physician for appropriate monitoring, where is the benefit to the consumer? Risks will increase if OTC drugs are taken without appropriate monitoring and consumer access may actually be hampered when drugs that are available OTC are no longer covered by health insurance or plans. Likewise, access to generic drugs may be affected by OTC switches.

Finally, we believe that drugs that do not relieve symptoms, but instead require some other intervention to assess their effectiveness, do not qualify for OTC use based on Congress' mandate that drugs requiring "collateral measures necessary to [their] use" be available by prescription only. Laboratory determinations and professional supervision for follow-up constitute such "collateral measures," making drugs requiring such monitoring unacceptable for OTC use.

### **Conclusion**

We understand, however, that the FDA is considering changing its criteria for OTC status -- considering drugs that treat "acute" conditions as well as conditions which are chronic and often multifactorial in nature. We understand that OTC status may

increase access to certain drugs which are safe and, therefore, reach populations which have not previously benefited from certain therapies. We applaud such efforts to increase access to appropriate drugs and therapies. However, we also believe that the FDA must carefully consider OTC status for drugs which treat conditions such as those described above. Coronary artery disease is an excellent example of a chronic disease that is multifactorial in nature and often without symptoms until well-advanced. Physicians treating such patients address *all* risk factors and institute and monitor therapies beyond pharmacological therapies. Physicians advise on lifestyle changes including diet, smoking, exercise, and other interventions, as well as monitor the response to such therapies. In some cases, such lifestyle changes eliminate the need for certain pharmacological therapy – and have benefits beyond the specific condition for which they were instituted. These collateral benefits should also be taken into account when OTC switches are considered for drugs treating conditions such as these.

The ACC neither recommends nor opposes OTC status for any particular drug with this testimony. We believe that such switches should be based on sound evidence that consumers will benefit and that all benefits and risks be considered. We also believe that consumer education is of paramount importance if these new classes of drugs are to become available OTC.

I look forward to working further with the FDA as it continues to review its regulatory approach for over-the-counter drugs. I am happy to discuss any questions you may have.