



National Medical Association

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L. Natalie Carroll, M.D.
President

May 20, 2003

Mark B. McClellan, M.D., Ph.D.
Commissioner
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857

Re: Artecoll

Dear Dr. McClellan:

The National Medical Association and the National Center for Policy Research for Women & Families are very concerned about the Food and Drug Administration's (FDA) policy of approving medical products as safe and effective that have not been adequately tested in African Americans and other racial and ethnic groups that are likely to use the product.

This issue recently came to public attention during the February 2003 review of a premarket approval application (PMA) for Artecoll (a permanent cosmetic treatment for facial scars and wrinkles) by the Advisory Committee of the Center for Drugs and Radiologic Health. The study sample included 115 men and women, including no African Americans and only one Asian.

In the case of Artecoll, it is possible that African Americans and Asian Americans might scar more noticeably, and autoimmune responses also might be more serious compared to Whites. The data indicating a 16% chance of an adverse reaction in the first year following permanent implantation in facial wrinkles can only be extrapolated to the White and Hispanic populations that were tested. Adverse reaction rates for African Americans and Asian Americans might be considerably higher. The Executive Clinical Summary for Artecoll noted the exclusion of subjects with known susceptibility to keloids and to subjects presenting with a history of autoimmune disease. Those exclusion criteria would exclude many, but not all African Americans and Asian Americans, and it is essential to determine whether the product is safe or effective for African Americans and Asian Americans without those known susceptibilities. Such research should be completed and reviewed by the FDA before any decision is made about approving the product, unless the product is labeled as being for whites only.

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Although the lack of racial diversity was clearly presented in the company's data to the FDA, the FDA staff did not mention it as a shortcoming in their presentations. Even after the issue was raised in a public comment period, the FDA advisory committee voted to recommend approval, requiring additional research to determine long-term safety, but none to remedy the lack of safety data for African Americans or Asian Americans.

The FDA recently issued a "Guidance for Industry on the Collection of Race and Ethnicity Data in Clinical Trials" which we believe is a step in the right direction. We are pleased that some Centers at the FDA have demonstrated that they have begun to consider this important issue. However, the FDA needs to do more if it is to protect the health and safety of all Americans.

The FDA Guidance merely encourages that manufacturers identify the Subjects in clinical trials according to race and ethnicity. It is not clear that this encouragement will even apply to the Center for Devices and Radiologic Health, which seems to think that devices implanted in the human body do not require the same careful study as drugs or biologics. More important, the guidance fails to *require* the inclusion of racial and ethnic groups in the study population, or to even encourage the use of subsamples of adequate size to ensure that subgroup analysis can provide meaningful data about safety and effectiveness for those subpopulations.

When there is reason to believe that variation among racial or ethnic groups may influence the safety or effectiveness of a medical product, including a medical device, then the burden should shift to the manufacturer to include all relevant racial or ethnic groups. It is critical that racial and ethnic subpopulations be adequately represented in clinical trials in order to ensure that the tested product is safe and effective for all the subpopulations that are likely to use that product.

We are committed to the fundamental scientific principle that clinical trials evaluating the safety and effectiveness of medical products should reflect the racial and ethnic diversity of the population that will use the medical product. We agree with former FDA Commissioner Jane Henney who said, "It is only through participation of the many populations that will ultimately receive a new product that we can ensure that the medical products we approve are appropriate, safe and effective for all Americans, and not just a narrow cut of our country's population."

The FDA, like the National Institutes of Health, should require that all studies upon which FDA approval are based, should demonstrate that the human subjects are representative of the target population intended to be treated by the medical product, including devices. The only exception to this mandatory requirement should be when the manufacturer presents compelling scientific evidence for the exclusion of a racial or ethnic population based on legitimate safety concerns, and agrees to label the product as contraindicated for that population.

Mark McClellan, M.D.

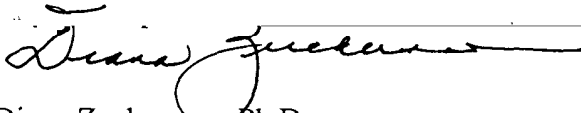
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We share your expressed concern that life-saving medical products should be made available as quickly as possible, while maintaining high standards of safety and effectiveness. This means, however, that medical products should be proven safe and effective for all Americans.

Moreover, when the benefits of a product are not life-saving, or not clearly superior to other medical products on the market, the FDA should be especially cautious, willing to delay approval until the risks are clearly established for different racial and ethnic groups.

Sincerely,



Diana Zuckerman, Ph.D.

President

National Center for Policy Research for Women & Families



L. Natalie Carroll, M.D.

President

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cc David Feigal, Jr., M.D.

Theresa A. Toigo, R.Ph., MBA