DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

SEP 7 2001

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Mr. Arthur J. Ward
TCI AJW Technology Consultants, Inc.
962 Allegro Lane
Apollo Beach, Florida 33572

Re: Docket No. 01P-0068

Dear Mr. Ward:

You submitted a citizen petition on February 8, 2001, on behalf of Medicap, Ltd., requesting that the Food and Drug Administration revoke the ban on prosthetic hair fibers, 21 C.F.R. §895.101. You state that Medicap has provided information demonstrating that it has developed a product that warrants revoking the ban and establishing an appropriate device classification.[1] We have reviewed the information in your petition and we are denying the petition for the reasons explained here.

I. Background on Banning a Device

FDA' s authority to ban a device comes from section 516 of the Federal Food, Drug, and Cosmetic Act (the Act) (21 U.S.C. 360f). Subsection (a) of that section sets forth the criteria for banning a device as follows:

Whenever the Secretary finds, on the basis of all available data and information, that –

(1) a device intended for human use presents substantial deception or an unreasonable and substantial risk of illness or injury; and
(2) in the case of substantial deception or an unreasonable and substantial risk of illness or injury which the Secretary determined could be corrected or eliminated by labeling or change in labeling and with respect to which the Secretary provided written notice to the manufacturer specifying the deception or risk of illness or injury, the labeling or change in labeling to correct the deception or eliminate or reduce such risk, and the period within which such labeling or change in labeling was to be done, such labeling or change in labeling was not done within such period; he may initiate a proceeding to promulgate a regulation to make such device a banned device.

1 Because the information you submit pertains only to your client's specific device, known as Biofibre, and in fact seeks to distinguish it from other types of prosthetic hair fibers, your petition is facially insufficient to justify revocation of the ban as to the whole category of devices which it addresses. In light of your approach, FDA construes your petition to seek the alternative relief of amending the ban to exempt Biofibre alone from its coverage, and evaluates whether you have provided the necessary evidence to sustain this narrower relief.

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See also 21 C.F.R. § 895.20. FDA regulations implementing this provision and listing devices that have been banned are found in 21 C.F.R. part 895.

In accordance with these statutory and regulatory provisions, in 1983 FDA instituted a ban on prosthetic hair fibers intended for implantation into the human scalp after a careful review of scientific and manufacturing data, reports in medical literature, consumer complaints, and in consultation with the appropriate classification panel. After evaluating information from all of these sources, FDA determined that prosthetic hair fibers present a substantial deception and an unreasonable and substantial risk of illness or injury; that the deception or risk cannot be corrected or eliminated by labeling or a change in labeling; and that the deception or risk associated with use of the device represents an unreasonable, direct, and substantial danger to the health of individuals. In particular, FDA concluded that prosthetic hair fibers are inherently dangerous when used in the manner recommended or suggested in their labeling, and that adequate directions cannot be written to assure safe and effective use, either by lay persons or by physicians. See 48 FR 25127 (June 3, 1983). Accordingly, FDA published an immediately-effective proposed rule in the June 3, 1983, Federal Register, detailing its findings and banning prosthetic hair fibers under section 516 of the Act. See 48 FR 25126 (June 3, 1983); see also 49 FR 1177 (Jan. 10, 1984) (notice of final rule on same).

Your petition seeks to revoke the rule promulgated as just described. In order for a regulation banning a device to be amended or revoked, the Commissioner must find that "the conditions that constituted the basis for the regulation banning the device are no longer applicable." 21 C.F.R. § 895.21(h). As explained in detail below, the information submitted in support of your petition does not permit the Commissioner to make this finding. First, the flaws and inadequacies in your data make it an unreliable basis for such a determination. Second, even assuming that the information you provide is accurate, it reveals a risk of illness or injury that is substantial and unreasonable in light of the benefits of your device and cannot be corrected by labeling, a fundamental condition that constituted a sufficient basis for the original ban.

II. The Data Submitted by MEDICAP is flawed.

Your petition presents data intended to demonstrate that, for Biofibre, the health risks underlying the original determination to ban prosthetic hair -- including infection, foreign body reaction, and related sequelae -- are reduced to acceptable levels. However, there are numerous problems with these data that prevent FDA from relying on them as a basis for amending the ban.

Because of numerous problems, FDA is unable to conclude that the preclinical data you have submitted are accurate and relevant to the device you intend to market. For example, although nylon is a generic name for a material with many possible formulations, you do not specify the particular nylon used in your product. In addition, you state that the fibers are dyed to match the recipient's hair color, but you do not specify the manner in which the dye is incorporated into the fibers. And although you performed some biocompatibility testing, since you did not identify the nature of the fibers and the dyes that were used in the clinical study, FDA is unable to determine if your biocompatibility testing reflects the same device for which you have submitted clinical data.

In any event, your preclinical testing is incomplete and does not appear to be sufficiently related to the device as used in humans -- as a long-term implant in the scalp. First, although you submitted results of genotoxicity testing on some fibers using the Ames test, you did not demonstrate that you performed this testing on each of the types of dyed fibers. Nor did you perform any mammalian cell mutation tests or chromosomal aberration tests, two additional tests that should be conducted with each type of dyed fiber as part of adequate biocompatibility testing. Second, you did not conduct preclinical testing with the fibers as a percutaneous device, the manner in which you propose to use it in humans. Those preclinical implantation studies that you did perform used a fused mass of fibers and not individual fibers. Consequently, their results do not represent the actual use of the device.

The clinical studies you performed are also inadequate to make a reasonable judgment about your device. Basic characteristics of your presented studies are unclear. For example, you state that you are submitting three different clinical studies, but only two studies are submitted; one of the studies is analyzed in two different time periods and then presented as a prospective and retrospective study, but the data appear to be the same. In addition, the selection and composition of the second study (503 patients) is not well defined. It is unclear if this larger study with 503 subjects also includes the subjects from the smaller study. Moreover, your data do not demonstrate that your studies are an adequate sample from which to draw meaningful regulatory conclusions. Even discounting the ambiguities described above, the number of patients studied was small. The studies were conducted outside of the United States and did not include patients that may be more typical of the U.S. population, for example skin types where keloid formation may be more prevalent. In addition, you have not addressed the prospect that differences in the practice of medicine between the locations of the clinical studies and the United States may produce significant differences in the results. Compare 21 C.F.R. § 814.15(d) (permitting approval of a PMA based solely on foreign clinical data if the foreign data are applicable to the U.S. population and U.S. medical practice).

In addition to these problems with the presentation of the overall scope of your clinical research, the presentation of the resulting data is also insufficient. Of central importance, you have not defined "serious adverse events," nor have you given examples of the type of diagnoses that would be in this category. In addition, the adverse events listed in the submission appear to be incomplete; a complete line listing of all subjects with adverse events should be provided. Without this information, FDA cannot make an independent evaluation of the risks associated with your device, a central factor in any decision to revise or revoke the ban.

Also, the histology data from both clinical and preclinical studies is unsatisfactory. Your submission does not adequately explain such basic issues as from which subjects the samples were obtained, how those subjects were selected, what the particular sites of the biopsies were and how they were chosen, how deep the biopsies were, and how much of the implant and surrounding tissue was removed. Histology protocols to assess the tissue response should have included methodology (such as plastic embedding) to ensure that the fibers were not removed in the sectioning of the tissue. Without identification of the fiber-tissue interface, the histology data are inconclusive. Moreover, your studies are insufficient to evaluate the long-term consequences of prosthetic hair implants. To assess this issue, random sampling from the study population should be done. Most experts suggest that the sample size be approximately 10% of the study population. If, as you state, you have studied about 900 subjects, then approximately 90 subjects should be randomly selected to undergo serial biopsy. The data you presented appears to have come from only four patients, and it is unclear how they were selected or if they were part of the clinical study group. In addition, the duration of sampling was only two years. This is not sufficient to evaluate the long-term effects of the implants, some of which you indicate may remain implanted for longer periods of time and the effects of which may not be manifest until after the lifetime of the implant.

For all of the reasons just explained, FDA considers the data you have supplied to be an unreliable basis for a decision to amend the ban on prosthetic hair.

III. Even if FDA relied on the data you provided, this does not establish the basis necessary to amend the ban.

Even if FDA were to accept the data you have submitted, on that evidence, FDA concludes that your device presents a substantial and unreasonable risk of illness or injury that cannot be corrected by labeling.

In judging whether the risk of illness or injury posed by a device is substantial, FDA considers whether the risk is "important, material, or significant in relation to the benefit to public health" from the marketing of the device. 21 C.F.R. § 895.21(a)(1). In making this assessment, FDA looks at all available information and data, 21 C.F.R. § 895.20, in this case including the data you submitted, the information underlying the original ban, and FDA's general knowledge of percutaneous implants and tissue reactions.

As FDA indicated in promulgating the ban, implanted foreign objects carry an inherent risk of infection, inflammatory reaction, and rejection. Percutaneous implants, such as prosthetic hair fibers, increase the risk of infection because they provide an open communication between the outside environment and the underlying tissues, allowing penetration of bacteria. With prosthetic hair fibers particularly, the open channel surrounding the implanted fiber results even where the device is sterile prior to implantation, and even where the implantation surgery is performed by trained physicians using appropriate surgical techniques. Because the hair fibers are anchored only in soft tissue, they are subject to constant movement, which prevents the surrounding tract from ever healing completely or forming a tight seal around the implant. In addition, the scalp is particularly susceptible to infection because it is difficult to keep clean. This infection risk is further exacerbated because the intended application of prosthetic hair fibers requires the implantation of hundreds, if not thousands, of separate fibers, multiplying the number of potential points of entry by pathogens. Where such penetration does occur, the spectrum of infection can range from simple cellulitis (infection of the superficial skin or scalp) to more serious infections such as infections of the bone (osteomyelitis) or systemic infections with organ involvement.

Besides infection, foreign body reaction is a natural response to any implanted material. Indeed, in investigating products while considering whether to institute the ban, FDA found that all materials then available, including ones such as polyester that are generally regarded as biocompatible, resulted in severe foreign body reactions when implanted in the scalp. See 48 FR 25127. Acute inflammation from implanted foreign fibers can produce scarring, see 48 FR 25128, which may include keloid formation in certain populations. Chronic infection and inflammation can result in permanent tissue changes and predispose one to serious risks such as cancer. Compare 48 FR 25133.

You contend that Biofibre implantation does not result in infection and foreign body reactions like those found by FDA prior to 1983. To ensure the success of the procedure and reduce complications, your clinical studies relied on strict patient selection, strict surgical technique adherence, close patient follow-up, and other burdensome requirements for patients, including prescribed pre- and post- implant use of topical antibiotics and topical steroids, daily use of particular shampoos, and avoidance of such common conditions as exposure to heat, sunlight, and acidic conditions (which may include sweat). But even among patients adhering to these measures, the published studies

you provided demonstrate serious infection rates of 1.0% in the 196-patient prospective study and 3.8% in the 503-patient retrospective study.[2] A further 11.2% of the participants in the 196-patient study experienced inflammation reactions and mild infections, which researchers attributed to poor post-procedure care. The percentages of total unspecified adverse events were 13.8% in the 196-patient prospective study and 20.1% in the 503-patient retrospective study. These data suggest that despite the elaborate care protocol specified by your labeling, as well as the other restrictions on use on which you rely to make Biofibre safe, a significant risk of adverse events, particularly infection, remains. Moreover, the adverse events patients experienced under a very rigorous compliance regime suggest that if there is less vigilance outside the controlled environment of the study, even more serious adverse events, similar to those experienced in the years before the ban, may result.

Based on the available information in your petition, then, it appears that Biofibre continues to manifest risks of infection and foreign body reaction similar to those that FDA identified as resulting from other percutaneous prosthetic hair implants in instituting the ban regulation. The risks presented by Biofibre are likewise unreasonable in light of the limited public health benefits that the product provides. Your own studies demonstrate that Biofibre provides only a non-permanent mitigation of baldness: under conditions that you consider normal and acceptable, including the elaborate care protocol described above, average hair fall results in a loss of between 10% and 30% of fibers annually. In light of the modest benefits your device is intended to provide -- the cosmetic simulation of natural hair for a limited, though indefinite period -- the demonstrated risks are very substantial.[3]

Finally, the risk of illness or injury you have identified is not alleviated by the labeling provided. As already noted, even among carefully selected patient populations who were instructed in accordance with the thorough protocol included in your labeling, as many as one-fifth of patients experienced some form of infection or inflammation. Moreover, since these serious health risks result from Biofibre's nature as a percutaneous implant, as with the original ban, FDA concludes that no labeling change can alleviate its concerns.

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[2] For purposes of this portion of the response, FDA accepts the characterization of adverse events as "serious" or "mild" as provided by the studies you submitted. As already explained, however, one failing in your supporting evidence is that your submission does not provide sufficiently detailed information to permit FDA to make its own assessment of the seriousness of the adverse events.

[3] If FDA were conducting a risk-benefit analysis of Biofibre in the course of considering a PMA, it would do so in a context recognizing the risk-benefit profiles of several readily available alternative products for mitigating baldness, including autologous hair transplants, medications, and hairpieces.

IV. Conclusion.

For the reasons stated above, FDA finds that Medicap has not met the burden of establishing that the conditions that serve as a basis for the regulation banning the implantation of prosthetic hair fibers are inapplicable to Biofibre, and therefore denies your petition to revoke that regulation as it applies to Biofibre. In the event that Medicap develops new information in the future that may meet this burden, it may submit a new petition for FDA consideration. If you have any questions regarding this response, please contact Mr. Anthony D. Watson, Division of General, Restorative, and Neurological Devices at (301) 594-3090.

Sincerely yours,

Linda S. Kahan
Deputy Director
Center for Devices
and Radiological Health

cc: Isabella Ruoli, Medicap Ltd.