TCI AJW TECHNOLOGY CONSULTANTS, INC.

962 Allegro Lane • Apollo Beach, FL 33572
Phone: (813) 645-2855
FAX: (813) 645-2856

January 31, 2001

Dockets Management Branch
Food and Drug Administration
Department of Health and Human Services, Rm.1-23
12420 Parklawn Dr.
Rockville, MD 20857

Dear Sir or Madam,

We are submitting the attached petition on behalf of our client:

MEDICAP srl
Via A. Lincoln
15 – 41012 Capri (MO)
Italy

under 21 CFR, Part 10, §10.30 to request the Commissioner to revoke the ban set on the Implementation of Prosthetic Hair Fibers per 48 FR 25136, June 3, 1983 as well as per 21 CFR §895.101.

We believe the information included clearly demonstrates that the Medicap Biofibre device warrants the revoking of the above ban and the establishment of an appropriate classification to enable the pre-market notification process to be initiated.

Please advise me directly if you have any questions or require any additional information. If a personal meeting would assist in your review please contact me in this matter at your earliest convenience.

Sincerely Yours,

Arthur J. Ward

Arthur J. Ward

01P-0068

CP1

January 8, 2001

Dockets Management Branch
Food and Drug Administration
Department of Health and Human Services, Rm.1-23
12420 Parklawn Dr.
Rockville, MD 20857

Dear Sir or Madam,

The undersigned submits this petition on behalf of:

MEDICAP Ltd.
15, Via A. Lincoln
41012 Carpi (MO)
Italy

under 21 CFR, Part 10, §10.30 to request the Commissioner to revoke the ban set on the Implementation of Prosthetic Hair Fibers per 48 FR 25136, June 3, 1983 as well as per 21 CFR §895.101.

A. Action Requested

We request the Commissioner revoke the Ban on Prosthetic Hair Fibers established in Section 895.101 of 21 CFR as cited below:

"Prosthetic hair fibers are devices intended for implantation into the human scalp to simulate natural hair or conceal baldness. Prosthetic hair fibers may consist of various materials; for example, synthetic fibers, such as modacrylic, polyacrylic and polyester; and natural fibers, such as processed human hair. Excluded from the banned device are natural hair transplants, in which a person's hair and its surrounding tissue are surgically removed from one location on the person's scalp and then grafted onto another area of the person's scalp."

We also request that a product classification be established to enable the appropriate pre-market notification process to be initiated.

B. **Statement of Grounds**

According to 48 FR 25136, June 3, 1983 and 21 CFR §895.101 the ban concerns fibers in polyester, modacrylic, polyacrylic and processed human hair, since:

1. They presented RISKS of illness or injury due to:
   - non biocompatibility of the fibers
   - non medical performance of the implant.

2. They presented FRAUD due to:
   - spreading of deceptive information on the efficacy of result
   - inadequate information on risks deriving from implant.

3. They did not show any benefit for public health.

From investigation carried out by FDA and from the causes which lead to the ban one can infer that those fibers which were banned:

- were not "medical devices" but "unsuitable materials for implant"
- they were utilized in an unsuitable manner by non-medical organizations
- they had not been notified to FDA before being marketed.

Biofibre® CE 0373/TGA is an implantable medical device (Class IIb according to Directive 93/42/EEC, code 16611, *Prosthesis Hair*, by UMDNS) possessing certificates CE 0373 and TGA (Australian Therapeutic Goods Administration), and is used to cover thinned or bald areas for definitive and/or total alopecia, even of cicatricial nature.

Hereafter we are listing:

- The reasons (reported in bold character) adopted by the FDA, in 1983, to ban fibers in polyester, modacrylic, polyacrylic and processed human hair.
- Medicap Ltd. counter deductions/evidence proving the safety and efficacy of medical device Biofibre® CE 0373/TGA, when implanted in conformity with the *Implant Protocol of Biofibre® CE 0373/TGA for the temporary solution of baldness – User manual* (annex 1).

1. RISKS

1.1 Prosthetic fibers presented substantial risk of illness or injury. The device is dangerous although implanted according to adequate directions.

As emerging from:

- *Risk analysis* (annex 2), carried out in conformity with norms prEN 1441:1994 and Annex I of Directive 93/42/EEC
- pre-clinical tests (annex 3)
- clinical studies (annex 4)

The medical device Biofibre® CE 0373/TGA does not have any unacceptable risks for the safety of the end user since:

a. the device is biocompatible
b. the implant is carried out by respecting a critical protocol which provides for:
   - a physician specialized in this technique
   - the selection of the suitable patient
   - the correct implant technique
   - post-implant periodic medical checks
   - respect of patient's post-implant protocol

c. if necessary, the device can be removed completely.

1.2 Implant of prosthetic fibers may have long-term, as well as short-term risks. Lack of data concerning patient follow-up.

Clinical data shows if there are any adverse events they can be solved by removing the fibers completely which can usually be accomplished without any permanent scarring.
Clinical data on Biofibre® CE 0373/TGA are:

- one prospective clinical study after 2 years on 196 patients; relevant adverse events: 1.02% **(annex 4a)**
- one independent retrospective study after 2 years on 190 patients; relevant adverse events: 1.1% **(annex 4b)**
- one independent retrospective study after 3 years on 503 patients; relevant adverse events: 2.1% **(annex 4c)**
- an accurate monitoring of the feed back information from the market carried out by Medicap Ltd. from 1990 till the present day.

1.3 The human body rejects the implanted fibers because they are not biocompatible. The implants have no protection against the body's immune system. Chronic granulomatous reaction to foreign body in 80% of samples (biopsies).

Pre-clinical tests, clinical and histological data show that device Biofibre® CE 0373/TGA is biocompatible and therefore it is rare to have a negative response from the immune system.
The slight reaction to foreign body is controllable and normal, and is negligible in most typical cases. Biocompatibility studies are included in the annexes.

1.4 Fibers and dyes were mutagenic to Salmonella typhimurium in the Ames Test. Test for acute and chronic toxicity, mutagenicity and allergization were inadequate and irrelevant.

Pre-clinical tests (carried out according to norms ISO 10993, parts 5, 6, 10 and UNI 9582/6) show that medical device Biofibre® CE 0373/TGA is:

- non cytotoxic
- non sensitizing
- non mutagenic (Ames Test)

1.5 Implant of prosthetic fibers produces a heap of cicatricial tissue (fibrosis – cancerogenic stimulus in animals).

Histological studies (annex 5) show that cicatricial tissue (fibrosis) surrounding Biofibre® CE 0373/TGA is negligible.
Both on clinical studies on around 900 patients and in all cases monitored by Medicap Ltd. since 1990 till the present day, no case of cancer deriving from the implant of Biofibre® CE 0373/TGA was ever detected.

1.6 Infection can be caused by contaminated fibers and lack of aseptic implant techniques.

Biofibre® CE 0373/TGA is a medical device which is supplied sterile.
The implant of Biofibre® CE 0373/TGA is a surgical technique which is therefore carried out by doctors who follow asepsis practice and the Biofibre® implant protocol following specialized training.

1.7 Fiber tracts can serve as a portal entry for bacteria from the skin surface.

According to histological studies, this phenomena is very limited with medical device Biofibre® CE 0373/TGA since:

- its chemical nature provokes the formation of a hyperplastic keratinized tissue surrounding the fiber (as protection to the external environment);
- the insertion hole is very small since the diameter of Biofibre® CE 0373/TGA is very thin (0,080 mm ± 0,005);
- flexibility of Biofibre® CE 0373/TGA allows its movement without dilating the insertion hole.

Furthermore the patient minimizes and controls bacterial contamination by daily cleansing the implanted area with suitable substances following the physician's instructions.

1.8 Often the treatment of the infection was not effective until the fibers were surgically removed from the scalp.
Several of the injures to users required substantial corrective medical or surgical treatments (e.g.: surgical removal of portions of the scalp and skin grafts).
Possible ulceration and formation of irreversible and permanent scars.

Clinical data and case reports available from 1990 until the present day show that the well-timed and correct diagnosis followed by suitable treatment prevent and solve, most all possible post-implant complications. Patients are required to have post implant evaluations by their physician.
In case of non adequately treated complications a cicatricial fibrotic retraction of the skin around the fibers may take place.
In event of an inadequate response to therapeutic treatments, performed by the physician, complete extraction of Biofibre® CE 0373/TGA, which takes place without surgical intervention, along with suitable therapy, allows complete healing of the scalp.

1.9 Patients treated may never be suitable candidates for autogenous hair transplants because of permanent scarring and repeated episodes of infection from retained implants (permanence of fiber fragment into the scalp).

Clinical data shows that, if needed, the nylon tenacity of Biofibre® CE 0373/TGA allows it to be removed completely, with the knot, without trauma or lasting scars (annex 4b, pages 51-52, pictures). After Biofibre® CE 0373/TGA is completely explanted it is therefore possible to carry out autologous hair transplants if desired.

1.10 Complications and hypothesis of "important" complications: endocarditis, phlebitis, serum hepatitis, benign fatty tumor, heart murmur, visual, auditory, urinary and respiratory problems, possible progressive sclerosis of the scalp and malignant degeneration of the tissue of the scalp, purulent and hemorragic fistulas, numbness up to 6 months after implant, risk of death, induced osteomyelitis, meningitis and encephalitis, hemorrhages, septicemia, cardiac arrest, persistent cephalea, etc.

None of the above mentioned complications emerged both from clinical data on 900 patients and in all cases monitored by Medicap Ltd. since 1990 till the present day.

1.11 Violation of Education Law, section 6512: illegal performance of medical procedures including the surgical implant of synthetic prosthetic hair fibers, administration of anesthetics and the dispensing of drugs.

Biofibre® CE 0373/TGA is a medical device in conformity with European Directive 93/42/EEC, acknowledged with Law Decree no. 46 of February 24, 1997. It is exclusively supplied to doctors qualified to this practice and to implant, preferably specialized in dermatology and plastic surgery (annex 6).

1.12 Surgical techniques performed in the past: traumatic instruments, implant up to 10 fibers contemporaneously, etc.

Since efficacy and safety of implant depend upon different factors, Medicap Ltd. medical division prepared an implant protocol which foresees:

- the suitable patient with healthy scalp
- the use of biocompatible fibers with reversible knot (extractable)
- the use of a very thin hooked needle (trauma free)
- the doctor expert in this method
- an aseptic operating environment
- minimum quantity of anesthetic
- implant of 1 fiber at a time on the galea capitis
- minimum distance between each fiber shall be of around 2 mm
- limiting the implant trauma implanting no more than 800 fibers per session
- post-implant checks shall be carried out by doctors who are expert in skin pathologies.

2. FRAUD

2.1 Deceptive and false publicity (labels and promotional material stated that implant was safe, effective, permanent, painless, approved by the FDA, that fibers used were done with materials scientifically and clinically tested, etc.). Patients were not informed over the most severe risks and complications deriving from the implant of fibers.

Before implanting Biofibre® CE 0373/TGA the patient is correctly informed by doctor on the temporariness of implant, the risk for possible complications, the necessary periodic medical checks, maintenance treatments, etc. This information is listed in 2 documents which are signed by the patient for acceptance before the implant is carried out: the *Informed consent* (annex 1, page 11) and the *Patient's post-implant protocol* (annex 1, page 23).

2.2 Break and fragility of banned fibers (polyester, modacrylic, polyacrylic and processed human hair).

Physical, chemical and mechanical characteristics of Biofibre® CE 0373/TGA (nylon) are much higher than those of banned materials. Therefore, as a rule, if treated according to the post-implant protocol they do not break but will fall naturally according to tractions they will undergo.

2.3 Fall of the fibers soon after implant.

From clinical studies and from case reports available since 1990 to the present day, it emerges that the fall of Biofibre® CE 0373/TGA varies from patient to patient and the yearly average fall being about 10-20%.

2.4 Loss of patient natural hair due to the implant of prosthetic fibers.

As a rule this does not happen if medical post-implant therapies are correct and resolving. As a matter of fact from case reports available since 1990 till the present day it emerges that defluvium of natural hair takes place only in case of neglected or non adequately treated infections.

2.5 Deceptive labeling or without adequate instructions.

Labeling of medical device Biofibre® CE 0373/TGA is in conformity with norm prEN 1041 and therefore carries indications, use, contraindications, directions and side-effects. Furthermore sterility expiration date is indicated and allows materials traceability (annex 7).

3. RISK-BENEFIT RATIO

3.1 Prosthetic hair fibers provide no benefit to the patient's health.

Biofibre® CE 0373/TGA implant is beneficial to the psycho-physical health of all those patients suffering from serious alteration of one's own image, due to definitive and/or total baldness, even of cicatricial origin.

To conclude, based on the favorable risk-benefit ratio demonstrated, in both the *Risk analysis* and from clinical data, it is important to recognize that the implant of Biofibre® CE 0373/TGA does not represent risks for the patient health, therefore it is to be considered as suitable:

- to solve baldness types with no other solution (e.g.: total alopecia, atrophy or cicatricial scalp, insufficient or lack of donor area for autotransplant, refusal from patient for cruel techniques, etc.);
- to integrate other surgical techniques (e.g.: fill in an incomplete hair autotransplant for lack of donor area and/or too thin hair, to cover scars, etc.).

C. **Environmental Impact**

Not Applicable

D. **Economic Impact**

Not Applicable

E. **Certification**

The undersigned certifies, that, to the best knowledge and belief of the undersigned, this petition includes all information and views on which the petition relies, and that it includes representative data and information known which are unfavorable to the petition.

MEDICAP srl
Via A. Lincoln, 15
41012 CARPI (MO) - ITALY -
+39.59.692142 - Fax +39.59.642400
Partita I.V.A. 02037880362

(Signature) _____

(Name of petitioner) *Mrs. Isabella Ruoli, President of Medicap Ltd.*

(Mailing address) *15 Via A. Lincoln, 41012 CARPI (MO), ITALY*

(Telephone number) *+39 059 692142*

(Fax number) *+39 059 642400*

(E-mail) sales@biofibre.com

MEDICAP Ltd. Petition to Revoke the Ban of 21 CFR 895.101
- ANNEXES TO THE FDA PETITION –

1. Implant protocol of Biofibre® CE 0373/TGA for the temporary solution of baldness (user manual).

2. Risk Analysis

3. Pre-clinical tests

   3a Cytotoxicity on extract
   3b Allergic sensitization in Guinea pigs
   3c Under skin implantation in rabbit
   3d Mutagenesis test: Ames Test

4. Clinical studies

   4a PALMIERI B., GRISELLI G., D'UGO A., PALMIERI G., SALTI G., *Evaluation of polyamide synthetic hair. A long-term clinical study,* PANMINERVA MED 2000; 42:49-53.

   4a.1 STUDY PROTOCOL - *Biofibre®: safety and efficacy in androgenetic alopecia. A prospective study.*
   4a.2 FINAL REPORT - *Biofibre®: safety and efficacy in androgenetic alopecia. A prospective stydy.*

   4b SANTIAGO M., MATOZZINHO F., VELONE M., MICHALANY J., *Histological study of the scalp implanted with polyamide artificial fibers,* São Paulo, Brazil.

   4c D'UGO A., *Report on the efficacy and innocuousness of the implant of artificial hair Biofibre®,* Italy.

5. Histological studies

   5a FANTI P.A., PISTORALE T., D'URSO C., MISCIALI C., TOSTI A., *Histological study on 5 cases of patients who underwent artificial hair implantation without complications,* Department of dermatology, University of Bologna and Department of plastic surgery, S. Orsola Hospital, Bologna, Italy.

   5b FANTI P.A., *Comparison between cases with and without clinically evident inflammatory complications in patients subjected to artificial hair implantation,* Department of dermatology, Laboratory of Dermatologic Histopathology, University of Bologna, Italy.

6. Ethical contract

7. Label of Biofibre® CE 0373/TGA

8. Adverse events information for Biofibre® CE 0373/TGA

9. List of certificates and ministerial registrations for Biofibre® CE 0373/TGA

10. Literature on Biofibre® CE 0373/TGA