FEB 28 2000

510(k) Summary
Summary of Safety and Effectiveness Information Supporting a Substantially Equivalent Determination
(K991335)

The products:
- **"Medi-Cult Freezing Pack with EFM" Cat.No. 1026**
- **"Medi-Cult Thawing Pack with EFM and IVF" Cat.No 1063**
- **"Medi-Cult Thawing Pack with EFM" Cat.No 1098**

Indication for use:

Medi-Cult Freezing Pack" is for freezing of 1-4 cell stage embryos, & Medi-Cult Thawing Pack" is for thawing of embryos.

Products formulation: All products are based on Embryo Freezing Medium (EFM)

The Freezing Packs contains 3 different solutions reflecting a 3-step procedure and 4 vials:
- **1 x Vial 1: Embryo Freezing Medium (EFM)**
- **1 x Vial 2: EFM and propanediol**
- **2 x Vial 3: EFM, propanediol and Sucrose.**

For thawing the Thawing Packs are used. They are composed as follows:
- **Vial 1: Embryo Freezing Medium (EFM), propanediol and sucrose.**
- **Vial 2: EFM, propanediol and Sucrose.**
- **Vial 3: EFM and Sucrose.**
- **Vial 4: EFM (Cat.No. 1098) or Universal IVF Medium (Cat.No. 1063)**

Product testing control contents:
- **Bioburden, production-test**
- **Integrity filter testing, production-test**
- **Sterility, QC-test**
- **pH, QC-test**
- **Osmolarity, QC-test**
- **Endotoxin, QC-test**

The culture media from Medi-Cult have been used by many European IVF-units since the end of the 1980's. (Produced and distributed by GEA-Biotech 1987 to 1989 and by Medi-Cult a/s from 1989). The Medi-Cult media were at that time introduced as a replacement for in-house prepared culture media. The Medi-Cult products for cryopreservation is in general formulated according to data published in peer reviewed international journals by internationally recognised scientists in the field.

The clinical date shown below comes from clinics using one or several of these products for cryopreservation of zygotes and embryos: The Medi-Cult Embryo freezing medium; The Medi-Cult Embryo freezing pack; The Medi-Cult Embryo thawing pack with EFM and IVF-medium.

We have collected clinical data from clinics that use only products from Medi-Cult. The data from cycles with replacement of cryopreserved embryos are in general not reported as stringent as the data from replacement of fresh IVF/ICSI embryos. Consequently, national data can be difficult to obtain.

A comparison of the clinical performance of clinics using only Medi-Cult media with other IVF-clinics using similar clinical and laboratory routines can give an indicate on the performance of the Medi-Cult culture media. In countries were we have access to both national data and data from individual clinics, clinics using Medi-Cult media generally performs well.

The IVF-units in the Nordic countries use similar clinical and laboratory protocols and their patient populations are comparable. The largest IVF clinics in Norway have been using only Medi-Cult media since the end of the 1980's.

Table1. The outcome after replacement of frozen/thawed IVF-embryos at the IVF-Unit, Dept of Ob. & Gyn. University of Trondheim, Norway in the period 1988-1998.

Number of embryo replacements	Clinical pregnancies	Pregnancy rate per embryo replacement
966	164	17.0

Table 2. The outcome after replacement of frozen/thawed The National Hospital, Oslo, Norway 1994-1996.

Number of embryo replacements	Clinical pregnancies	Pregnancy rate per embryo replacement
465	85	18.3

The national average for Norway is not meaningful since the two other clinics cryopreserving embryos only performed a few cycles (1994 -1996: 37 cycles/ 3 pregnancies 8.1% pregnancy rate)

In Sweden, the Carl von Linne Clinic uses only products from Medi-Cult for culture of gametes and embryos. For the year 1997 their birth rate per frozen embryo replacement was 22% (National data not available).

The Human Fertilisation and Embryology Authority (HFEA) of the UK, collects clinical data from all centres licensed to offer treatment for infertility by assisted reproduction. HFEA publishes these data in a booklet and on the web. The clinical data are presented both unadjusted and adjusted for the demographics of the clinics patient population. In the Table below the clinical data from some UK-clinics that use only Medi-Cult products is shown. These clinics have all given their consent to be presented as clinics using only Medi-Cult products.

Table 3. Live birth rates per embryo replacement in IVF units in the UK April 1, 1996 to March 31, 1997.

Name of clinic	Number of FER*-cycles	Live birth rate per embryo replacement %
Chelsea and Westminster Hospital	24	20.8
CARE at Park Hospital	95	20.0
The Woking Nuffield Hospital	38	15.8
Leeds General Infirmary	333	14.1
Nurture	104	7.8
Holly House Fertility and IVF	115	17.4
Guy's and St Thomas Assisted Conception Unit	651	27.1
UK national average	4646	12.1

*FER: Frozen embryo replacement

The Medi-Cult Blastocyst Freezing and Thawing pack has recently been introduced for cryopreservation and thawing of human blastocyst. This product is based on the work of Yves Menezo and co workers who has developed a protocol for freezing and thawing of human blastocysts. (Y.Menezo et al., In Proceedings of ASRM, Boston, 1996 & Y.Menezo & A.Veiga. In Proc. of 10th World Congress of IVF & Assisted Reproduction, Vancouver (Canada), May 1997). Since introduction of a commercially available product identical to the formulation of Menezo and co-workers, many clinics have started to use The Medi-Cult Blastocyst Freezing and Thawing pack. Clinical data available indicates that our product has the same performance as indicated by Menezo.

There have been no registered complaints on the product and thus no evidence in the last 1.5 years that the product has been the cause of any serious adverse events in connection with its intended use.

Thus based on the Federal Register Notice (Final Rule, Vol. 63, No. 175, page 48429, September 10, 1998), "Obstetric and Gynecologic Devices; Reclassification and Classification of Medical Devices Used for In-Vitro Fertilization and Related Assisted Reproduction Procedures" effective on October 13, 1998 and the supportive clinical data we feel that the safety and effectiveness of the product for its intended use is shown in the present submission.

Prepared and Submitted by:

Rene Wiberg-Leonardi for February 18, 2000

Ronald G. Leonardi, Ph. D. Date
President
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1-858-586-0751

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20850

FEB 28 2000

Medi-Cult A/S
c/o Ronald G. Leonardi, Ph.D.
President
R & R Registrations
P.O. Box 262069
San Diego, CA 92196

Re: K991335
Medi-Cult Freezing and Thawing Packs
Dated: December 14, 1999
Received: December 15, 1999
Regulatory Class: II
21 CFR 884.6180/Procode: 85 MQL

Dear Dr. Leonardi:

We have reviewed your Section 510(k) notification of intent to market the device referenced above and we have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (Premarket Approval), it may be subject to such additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 895. A substantially equivalent determination assumes compliance with the Current Good Manufacturing Practice requirements, as set forth in the Quality System Regulation (QS) for Medical Devices: General regulation (21 CFR Part 820) and that, through periodic QS inspections, the Food and Drug Administration (FDA) will verify such assumptions. Failure to comply with the GMP regulation may result in regulatory action. In addition, FDA may publish further announcements concerning your device in the Federal Register. Please note: this response to your premarket notification submission does not affect any obligation you might have under sections 531 through 542 of the Act for devices under the Electronic Product Radiation Control provisions, or other Federal laws or regulations.

This letter will allow you to begin marketing your device as described in your 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801 and additionally 809.10 for in vitro diagnostic devices), please contact the Office of Compliance at (301) 594-4591. Additionally, for questions on the promotion and advertising of your device, please contact the Office of Compliance at (301) 594-4639. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR 807.97). Other general information on your responsibilities under the Act may be obtained from the Division of Small Manufacturers Assistance at its toll-free number (800) 638-2041 or (301) 443-6597 or at its internet address "http://www.fda.gov/cdrh/dsma/dsmamain.html".

Sincerely yours,

Daniel G. Schultz, M.D.
Captain, USPHS
Acting Director, Division of Reproductive,
Abdominal, and Radiological Devices
Office of Device Evaluation
Center for Devices and
Radiological Health

Enclosure(s)

510(k) Number (if known) K991335

Device Name: Medi-Cult Freezing Pack and Thawing Pack

Indications for Use:

Freezing Pack is for freezing of 1-4 cell stage embryos.

Thawing Pack is for thawing of embryos.

(PLEASE DO NO WRITE BELOW THIS LINE – CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of Device Evaluation (ODE)

Prescription Use ✓ OR Over-The-Counter Use ___
(Per 21 CFR 801.109)

(Optional Format 1-2-96)

(Division Sign-Off)
Division of Reproductive, Abdominal, ENT,
and Radiological Devices
510(k) Number K991335