JUN 2 0 2000

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

(K991334)

The product:

- **"Medi-Cult Hyaluronidase" Cat.No. 1011**

Indications for use:
"Medi-Cult Hyaluronidase" is used in assisted reproduction techniques, (ART), such as IVF, GIFT or similar In Vitro procedure to aid in facilitating pregnancy.
"Medi-Cult Hyaluronidase" is for the removal of cumulus and corona radiatacells which must be removed in order to facilitate access to the oocytes and minimize contamination of the injected needle before ICSI.

Product formulation:
Sperm Preparation Medium supplemented with Hyaluronidase.
It is a HEPES buffered salt solution supplemented with Hyaluronidase. It is ready-to-use and contains Synthetic Serum Replacement (SSR) and Human Serum Albumin (HSA).
The Hyaluronidase raw material is derived from Bovine testes in the USA.
It contains antibiotics – Penicillin and Streptomycin.

A number of trials have shown that the products performs well, (see Clinical Testing section). A number of publications in peer-reviewed books or journals have presented data using Medi-Cult media. Often more than one procent from Medi-Cult has been used in the studies listed.

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 first Medi-Cult products for use in conjunction with Intra Cytoplasmic Sperm Injection (ICSI) were introduced in 1993. These products were designed in accordance with the specification of the clinic that developed ICSI (Palermo et al. Lancet 1992 340 8810 17-18).

A number of publications in peer- reviewed books or journals have presented data using Medi-Cult products for ICSI. Often more than one product from Medi-Cult has been used in the studies.

The clinical result of a given IVF-clinic will depend on the patient population treated, the clinical procedures, the laboratory routines and on the various culture media used. A comparison of the clinical performance of clinics using only Medi-Cult products for ICSI with other IVF-clinics using similar clinical and laboratory routines will 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 products generally performs well.

The IVF-units in the Nordic countries use similar clinical and laboratory protocols and their patient populations are comparable. The clinical data from most Nordic countries are available. In some countries the performance of individual IVF-clinics are available.

The largest IVF clinics in Norway have been using only Medi-Cult media since the end of the 1980'ties and products from Medi-Cult for ICSI. The data collected since the introduction of ICSI in Norway in 1996 are shown below as live birth rates per started cycle. Since all clinics (except one) are using products from Medi-Cult, a meaningful comparison to the national average success rate is not meaningful.

Table. Live birth rates per embryo replacement obtained with ICSI in Norway

Clinic	1996	1997
Dept of Ob & Gyn, Univ. of Trondheim	18,4	22,4
The National Hospital, Oslo	15,9	18,4
Haugesund Hospital	28,6	27,1

In Sweden, the Carl von Linne Clinic uses only products from Medi-Cult for ICSI and for culture of gametes and embryos. It is the only Swedish clinic using Medi-Cult products. For the year 1997 their birth rate per embryo replacement was 32% their clinical results were the best in Sweden and well above the national average of 25%.

There have been no registered complaints for the product and no evidence in the last 1.5 year 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:

12/14/99

Ronald G. Leonardi, Ph. D. Date
President
R & R Registrations
P.O. Box 262069
San Diego CA 92196
1-619-586-0751

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20850

JUN 2 0 2000

Medi-Cult A/S
c/o Ronald G. Leonardi, Ph.D.
President
R & R Registrations
P.O. Box 262069
San Diego, CA 92196-2069

Re: K991334
Medi-Cult Hyaluronidase
Dated: May 22, 2000
Received: May 23, 2000
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
Director, Division of Reproductive,
Abdominal, and Radiological Devices
Office of Device Evaluation
Center for Devices and
Radiological Health

Enclosure(s)

B4. Indication for Use Statement

510(k) Number (if know) K991334

Device Name: **Medi-Cult Hyaluronidase**

Indications for use:

For use in assisted reproduction techniques, (ART), such as IVF, GIFT or similar in vitro procedure to aid in facilitating pregnancy.

Medi-Cult Hyaluronidase is for the removal of cumulus and corona radiatacells which must be removed in order to facilitate access to the oocyte and minimize contamination of the injected needle before ICSI.

PLEASE DO NOT 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 K991334