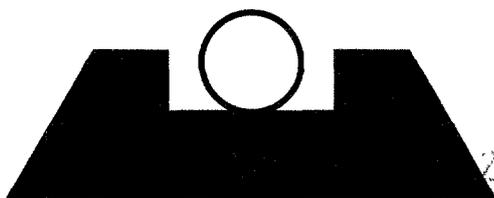


JURIDIC EMBASSY

AMB EURICA CALIFORNIAA
PO BOX 2328
MALIBU, CA 90265-7328
USA



Micro ICU Project

2 12 5 34 MAY 11 11:37 (310) 804-0727
amb @ juridic.org

www.ficu.org

May 7, 2004

Dr. Steven Galson, Acting Director
Center for Drug Evaluation and Research
Food and Drug Administration
C/o Dockets Management Branch (HFA-305)
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Re: NDA 21-045/S-011

Dear Dr. Galson,

I was recently awarded patent for being the first to figure out how to take a test tube baby's temperature correctly. In the past, doctors and scientists confused the baby's endogenous actual body temperature with the environmental temperature created by an incubator oven. I have enclosed a copy of my patent for your convenience and I assume you will recognize that I am a man of some expertise. You may likewise wish to peruse my website for the advancement of fertility intensive care: www.ficu.org.

The reason why I am approaching you is because I am critical of your scientific and medical aptitude regarding the morning-after pill. I am sorry to be so frank about it. However, I am afraid that this is the case.

Presently, you question whether young females can understand the label of the morning-after pill brand Plan B. I question whether you understand it yourself.

Let's do some math here.

It is reported that the pills reduce the chance of pregnancy by 89%. What does this mean? It means per instance of use during a fertile period compared to the chances of pregnancy in the same period using no method. In contrast, it is reported that with perfect use the pills have an annual risk of pregnancy of 19%. What does this mean? It means you can expect 19 annual pregnancies per 100 woman-years of perfect use.

- **Point 1:** If Plan B has an annual risk of 19% with perfect use and the condom has an annual risk of 3% with perfect use, then per instance the chance of pregnancy is reduced more/less by using a condom. The answer is more. *This means that the condom reduces the instant chance of pregnancy by much more than 89%.*
- **Point 2:** Per 100 woman-years of perfect use, how many fewer pregnancies will result from using the condom than Plan B? The answer is 16 pregnancies per year per 100 woman-years of use. Conversely, there will be 16 more pregnancies per year per 100 woman-years of use using Plan B than the condom. (19-3=16)

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- **Point 3:** If studies show that women do not rely on Plan B year-round, does this obviate the observation made in Point 2 above? No, because statistics calculated based on woman-years are not influenced by whether 100 women use Plan B for a year, or 1000 women use Plan B for 1/10th of a year. Thus, each time a man and woman forego a more effective means of family planning in favor of Plan B, the woman-years of use of Plan B will increase. Remember, Plan B reduces the chance of pregnancy per instance only by 89%, whereas as discussed in Point 1 above the condom reduces the chance per instance by much more than this. For this reason, condom use has a much lower annual risk of pregnancy per 100 woman-years of perfect use than Plan B. (3% versus 19%)
- **Point 4:** If a couple foregoes a traditional method once a year thinking that they can rely on Plan B instead, does this increase or decrease unwanted pregnancy? The answer is that unwanted pregnancy will increase, because per 100 woman-years of use the chance of pregnancy is greater with Plan B than with traditional methods like the condom. Thus, statistically, as discussed in Point 3 above, since the overall sum of woman-years does not distinguish between frequent versus infrequent reliance, as more and more woman-years of substituted reliance are racked up, there will be more and more unwanted pregnancies.

Substituted reliance means every so often couples will think they can just rely on the pills rather than using their traditional method. As discussed above, since this will result annually in more unwanted pregnancies (and social hardship) per 100 woman-years of substituted reliance, abortion companies stand to benefit as the public suffers.

From the above four points it is useful to realize that even experts have not completely grasped the contrast between use of a traditional method and even occasional reliance on Plan B as a substitute for a traditional method. Since even experts have not grasped this knowledge from reading the label of Plan B, it is completely obvious that prospective consumers will be unable to grasp the implications of use.

Ironically, it has long been known that regimens of birth control pills used in morning-after pill form are not effective in securing the aim of preventing pregnancy or terminating early pregnancy. It is only in recent times that confused attention has been given to the pills. Obviously, since substituted reliance on the pills will result in more unwanted pregnancies, abortion companies, which back the pills, stand to benefit.

Additionally, one should note that the U.S. Food and Drug Administration is in error when it says an action of the morning-after pill is to prevent the implantation of a fertilized egg, since “eggs” do not implant. Instead, the baby (not the egg) implants only after hatching. Thus, the public must be warned in clear detail that pills such as these are capable of causing death to children capable of complex behaviors like hatching.

In closing, it seems obvious that the brand label itself means to support a culture of substituted reliance for the morning-after pill: Plan B. For example, if “Plan A” was to use a condom, then a couple may decide to rely on “Plan B” instead of waiting to obtain one before sex. The idea of a “Plan B” creates a “play now, deal later” mentality that will be hard for numerous people to resist. Remember, if even big experts have a hard time appreciating the statistical ramifications of use, it is certain that your average couple will be deceived into thinking there is nothing wrong with substituted reliance once in a while and that it is “okay” to do it no matter what the label says. Although figures like a 89%

reduction in risk might seem large or much better than nothing to uninformed couples, compared to other methods like the condom it is very, very bad. Therefore, the problem of even occasional substituted reliance on Plan B is profoundly unacceptable.

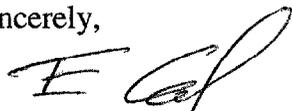
Given the clear problem of Plan B's potential to create a mentality of substituted reliance, there is also the prospect that some couples, though they occasionally intend to make substituted use of Plan B for their traditional method, may in some cases avoid following through and actually using Plan B. Various reasons may factor in such as cost, memory, experiences with illness, or a conscience of real concern for a child who may be aborted trying to hatch or implant. Thus, the "play now, deal later" mentality created by a product that even goes so far as to call itself "Plan B" will obviously introduce instances in which couples anticipate substituted reliance but then do not follow through. This in turn will mean more unwanted pregnancies and yet more profits for abortion companies. Instead, the FDA should advocate sound discipline and respect for life.

Another important point is that statistics on most family planning methods are not available to the public on the basis of reduced pregnancy risk per instance of use as opposed to annually per 100 woman-years of use; risks calculated based on a single instant of use may be called instant rates. For this reason, the public will not be able to compare the statistic on Plan B to other methods. For, although Plan B claims to reduce the instant risk of pregnancy by 89%, couples will not be able to compare this statistic with how much the risk of pregnancy is reduced per instance of use with a condom for example. And, as discussed above, this knowledge is important since one can infer that the instant risk of pregnancy associated with condom use is much less than the instant risk associated with Plan B, as indicated by the lower annual risk associated with perfect condom use (3%) as compared to perfect use of Plan B (19%). Thus, the public has no real way of comparing the meaning of the instant risk statistic for Plan B with other methods, thus making the label realistically unintelligible. Moreover, this serious lack of knowledge will fuel the tendency toward substituted reliance even further.

In summary, it is clear that the investigation has not adequately addressed the problem of occasional substituted reliance regarding use of the morning-after pill Plan B. If it had, the application would have surely been dismissed.

For the above reasons, all support for such pills should be withdrawn.

Sincerely,



Mr. Eurica California, Amb.
Juridic Embassy

Attachment: copy of U.S. Patent No. 6,694,175



US006694175B1

(12) **United States Patent**
California

(10) **Patent No.:** **US 6,694,175 B1**
(45) **Date of Patent:** **Feb. 17, 2004**

(54) **METHOD OF MONITORING THE BODY TEMPERATURE OF HUMAN EMBRYOS AND HATCHLINGS**

2002/0068358 A1 * 6/2002 Campbell et al. 435/289.1
2002/0188168 A1 * 12/2002 Koch 600/22

OTHER PUBLICATIONS

(76) **Inventor:** **Eurica California, P.O. Box 2328, Malibu, CA (US) 90265-7328**

OK J., Chu M., and Kim C.-J. "Pneumatically Driven Micro-Objects in Biological Liquid," Proc. IEEE Conf. Micro Electro Mechanical Systems (MEMS'99), Orlando, FL, Jan. 1999, pp. 459-463.*

(*) **Notice:** Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 175 days.

Cone T.E. Jr. History of the care and feeding of the premature infant. Boston: Little, Brown, 1985. pp. 21-22.*

(21) **Appl. No.:** **10/079,955**

Dorland's Illustrated Medical Dictionary. 28th Ed. Philadelphia: W.B. Saunders Co., 1994. pp. 542-543, 1346.*

(22) **Filed:** **Feb. 19, 2002**

Dorland's Illustrated Medical Dictionary. 29th Ed. Philadelphia: W.B. Saunders Co., 2000. pp. 582, 1450.*

(51) **Int. Cl.⁷** **A61B 5/00; A61B 5/01**

Rabin Y. & Podbilewicz B. "Temperature-controlled microscopy for imaging living cells: apparatus, thermal analysis and temperature dependency of embryonic elongation in *Caenorhabditis elegans*." Journal of Microscopy, vol. 199, Sep. (2000), pp. 214-223.*

(52) **U.S. Cl.** **600/474; 600/22; 236/2; 237/3**

* cited by examiner

(58) **Field of Search** 600/473, 474, 600/475, 407, 22, 427, 549, 310; 250/330, 316.1, 338.1, 472.1; 435/289.1, 303.1, 305.2; 209/510, 511; 73/861.95; 236/2-5; 237/3; 607/88, 90-96, 102; 374/100, 120, 121, 132, 133, 141, 145, 163

Primary Examiner—Eleni Mantis Mercader

(57) **ABSTRACT**

(56) **References Cited**

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Infrared microthermography for human embryos and hatchlings. Body temperature is monitored using an infrared camera attached to a microscope. Body temperature is maintained by passing body temperature data through a feedback loop that serves to control body temperature. Keeping the baby's fluid incubation medium lower than an optimum body temperature ensures that cooling can occur if the body becomes overheated. An added source of heat is provided by one or more infrared light emitting diodes focused on the body as tiny heat lamps. The heat lamps are cycled on and off or varied in intensity in accordance with indications (data) from body temperature measurements.

1 Claim, No Drawings

METHOD OF MONITORING THE BODY TEMPERATURE OF HUMAN EMBRYOS AND HATCHLINGS

BACKGROUND OF THE INVENTION

1. Field of the Invention

In general terms, my invention relates to in vitro medical care for the pre-implantation patient. More specifically, my invention relates to a new use for quantum well infrared photodetector (QWIP) technology: monitoring and maintaining the body temperature of human embryos and hatchlings in an engineered environment. The engineered environment is preferably a micro intensive care unit (μ ICU).

A human is an embryo only from conception to hatching. Hatching is an event that takes place when an embryo escapes the shell of the egg that he or she was conceived in. A human is a hatchling only from hatching until implantation (nidation).

2. Prior Art

The quantum well infrared photodetector (QWIP) camera was invented by Sarath Gunapala at NASA's Jet Propulsion Laboratory. (U.S. Pat. No. 6,211,529. Gunapala et al. Infrared radiation-detecting device.) QWIP technology has yielded one of the most sensitive yet affordable handheld long-wavelength infrared cameras. A QWIP camera may have a thermal sensitivity as sharp as 20 mK (twenty thousandths of one Kelvin degree). OmniCorder Technologies (Stony Brook, N.Y.) manufactures its BioScanIR System for imaging and recording thermal data from adult, pediatric, and neonatal patients using a QWIP camera.

Infrared cameras are generally better at picking out actual differences in temperature than they are at picking out actual temperatures. A measure of imaging performance, thermal sensitivity validates a numerical difference between two or more temperature measurements on a thermal imaging map. This form of relative measurement is meant to reflect a real temperature difference between points on the map. In contrast, thermal accuracy validates a numerical identity between a temperature measurement and the corresponding real temperature. This form of absolute measurement is meant to establish a number reflecting the real temperature of a point on the map. A point on the map can serve as a reference temperature when it is known with greater thermal accuracy than the thermal accuracy specified for the camera. Depending on the accuracy of the reference, the camera may yield an effective thermal accuracy nearly equal to its thermal sensitivity.

Heat lamps emit infrared radiation to provide a heating source. Heat lamps are often used to warm neonates, especially if they are born premature. An infrared light emitting diode (LED) emits infrared radiation on a very small scale. The shell of a human embryo's egg covers an inner diameter of approximately 100 microns (0.1 millimeters) at fertilization and has a spherical shape. Because human embryos and hatchlings are so small, an infrared LED can generate enough heat to warm the baby.

Miriam Menkin discovered the first reported human in vitro fertilization in 1944, with support from Harvard physician John Rock. (Marsh M. and Ronner W. *The Empty Cradle: Infertility in America from Colonial Times to the Present*. Baltimore, Johns Hopkins University Press, 1996. p. 171-209.) Death of the child introduced the problem of "miscarriage in vitro". Today there is a growing effort to

reduce miscarriage in vitro by engineering better environments. Yet this effort has been impeded by some experts who prefer unimaginative reliance on crude petri dish methods.

We are arriving at the point where as humans we will be able to care for our children from conception with the utmost intelligence and resource. Ironically, the last steps are not technology. They are simply courage.

Although micromanipulation techniques and petri dish practices have been employed since the inception of human in vitro fertilization, the advent of a new branch of engineering called micro electro mechanical systems (MEMS) has sparked interest in improving the technology of in vitro fertilization. To this end, David Beebe et al. have invented a MEMS-based means of providing embryos and hatchlings with fluidic ventilation. (U.S. Pat. No. 6,193,647. Beebe et al. Microfluidic embryo and/or oocyte handling device and method.)

By promoting child health and strength up until the time of being introduced to the maternal body, engineered environments will make pregnancy more survivable for children created and first cared for outside the maternal body. This benefit comes in addition to the benefit of reducing in vitro miscarriage itself.

My institution, Juridic Embassy, has sponsored new progress in fertility care, in an effort to advance diplomatic regard for the rights of children as patients in medicine. As a consequence of my research in this area, I initiated the Micro ICU Project in response to the general lack of care being provided to children created by in vitro fertilization. The synergy of the project was created by the needs of the children in light of impressive new engineering technologies, particularly MEMS. Using integrated micro-fabrication technologies (IMT) such as complementary metal oxide semiconductor technology (CMOS) and MEMS, as well as various large-scale technologies, the goal of the project is to perfect an elaborately engineered environment called a micro intensive care unit, or μ ICU, for human embryos and hatchlings.

One objective of the Micro ICU Project is to provide a means to monitor and maintain body temperature. This objective provides the subject matter of my present invention.

3. Statement of the Necessity

In modern fertility programs, human embryos and hatchlings are incubated outside the maternal body in a fluid incubation medium. Prior art methods of temperature monitoring and maintenance rely exclusively on a measurement of the temperature of the fluid incubation medium. The temperature of the medium is set to 37 degrees Celsius using a temperature-controlled incubator oven or microscope stage warmer.

However, because of endogenous heat production, which is the heat produced by a baby's own body, the baby's body temperature can differ from the ambient temperature of the surrounding environment or medium. Accordingly, the baby can become overheated, leading to exhaustion, dysfunction, and death, when only the temperature of the environment is controlled. (Cone T. E. Jr. *History of the Care and Feeding of the Premature Infant*. Boston: Little, Brown, 1985. p. 21-22.) Thus, a problem with the prior art in the field of in vitro fertilization is its focus on the temperature of the fluid incubation medium, instead of on body temperature itself.

What is needed to modernize the art of in vitro fertilization is a method to monitor and maintain the baby's actual body temperature.

BRIEF DESCRIPTION OF THE INVENTION

To monitor the body temperature of a human embryo or hatchling: attach a quantum well infrared photodetector

(QWIP) camera to a microscope and use appropriate computer technology to thermally image the embryo or hatchling.

To maintain the body temperature of a human embryo or hatchling: keep the fluid incubation medium slightly below optimum body temperature to ensure cooling can occur if the body becomes overheated; provide an added source of heat by focusing tiny heat lamps on the body of the embryo or hatchling; cycle the heat lamps on and off or apply them with varying intensity to maintain optimum body temperature in accordance with body temperature measurements obtained by the above-stated monitoring method.

DETAILED DESCRIPTION OF THE INVENTION

The main thrust of my invention is to employ an infrared camera to monitor the body temperature of a human embryo or hatchling under a microscope. The embryo or hatchling is kept in a fluid incubation medium in an engineered environment.

My invention prefers a quantum well infrared photodetector (QWIP) camera with a high thermal sensitivity (20 mK), such as the ThermoCAM® SC 3000 from FLIR Systems (North Billerica, Mass.), although other infrared technology can be substituted. To effectively enhance the thermal accuracy of the camera, a reference temperature can be obtained (for example, by thermocouple) with respect to the fluid incubation medium or other point in the camera's field of view. Although the camera can be fitted with its own microscope lens, my invention prefers attachment of the camera to the camera port of an inverted microscope—the microscope having a camera port and being suitable for visualizing the body of a human embryo or hatchling; for example, the IX70 Inverted Research Microscope from Olympus America (Melville, N.Y.). By employing means of computer technology to process, store, and display output from the camera, my invention enables medical practitioners to thermally image the body temperature of each embryo or hatchling who is visualized under the microscope.

To maintain optimum body temperature for a human embryo or hatchling, a means of cooling the body must be provided for when the baby's temperature is too high, and a means of warming the body must be provided for when the baby's temperature is too low. A preferred determination of low or high temperature is made by comparing data from the QWIP camera with an established value for optimum body temperature. Although an assortment of means for cooling and heating can be described or anticipated, my invention

prefers heat lamps as the means of heating and further prefers a cool fluid incubation medium as the means of cooling. To provide a means of cooling, the fluid incubation medium is kept slightly cooler than the optimum body temperature. To provide a means of heating, one or more infrared light emitting diodes are employed as tiny heat lamps focused on the body to provide an added source of heat when needed to offset the ambient coolness of the fluid incubation medium. The heat lamps are cycled on and off or varied in intensity to maintain the optimum body temperature, in accordance with body temperature measurements obtained preferably by the above-stated monitoring method.

I claim:

1. A method of monitoring an actual body temperature of a human embryo or hatchling and maintaining an optimum body temperature of the human embryo or hatchling comprising:

- (a). attaching a quantum well infrared photodetector camera to a microscope, the microscope having a camera port and being suitable for visualizing the body of a human embryo or hatchling;
- (b). employing means of computer technology to process, store, and display output from the quantum well infrared photodetector camera, so as to thermally image and measure an actual body temperature of the human embryo or hatchling who is visualized under the microscope and which said actual body temperature can differ from an ambient temperature of a fluid incubation medium;
- (c). maintaining the human embryo or hatchling in the fluid incubation medium, wherein the ambient temperature of said fluid incubation medium is being kept slightly cooler than required for an optimum body temperature of the human embryo or hatchling so as to ensure cooling if the body of the human embryo or hatchling becomes overheated;
- (d). providing an added source of heat by focusing one or more tiny heat lamps on the body of the human embryo or hatchling;
- (e). cycling the tiny heat lamps on and off or varying them in intensity to maintain the optimum body temperature, by comparing the actual body temperature of the human embryo or hatchling obtained in step (a) and step (b) with the optimum body temperature.

* * * * *