Customer Benefits:

- ⇒ **Greater incubation consistency**
- ⇒ **>6x reduction in consumables**
- ⇒ **Elimination of mineral oil**
- ⇒ **Reduced personnel handling**
- ⇒ **Full documentation**
- ⇒ **Small footprint**
- ⇒ **Expandable**

Nanopoint supports the scientific premise that microfluidics, imaging, and effluent sampling can lead to higher quality *in vitro* derived embryos.

Note: Preliminary results from beta customers has shown that the use of dynamic media delivery via Nanopoint's microfluidics system is comparable to static media during mouse embryo development. Beta customers are continuing with their validation of the complete microfluidics and incubation system.

Nanopoint's cellTRAY® Microfluidics System for assisted reproduction applications is intended to help scientists and physicians achieve quality improvements in their *in vitro* embryos, provide time lapse imaging throughout the development of the embryo, easily enable morphology monitoring and metabolic profiling, and foster improvements in cryobiology.

HNU-NANOPOINT
Harnessing the Power of Light

Nanopoint (www.nanopointimaging.com) is a privately-held life sciences company that is advancing the study & treatment of diseases with its extended time-lapse live cell imaging solutions. Nanopoint's patented cellTRAY®, automated microfluidics delivery system, on-stage incubator and imaging software provides solutions to a broad spectrum of applications including drug discovery, assisted reproductive technology and stem cell research.

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cellTRAY®
Microfluidics System
for Assisted Reproduction Applications

Successful outcomes for assisted reproductive technologies have improved over the years but remain below 43% live births. Improvements have been realized with defined nutrient media formulations and timely-added growth factors during the process of oocyte maturation and fertilization. While these early *in vitro* manipulations have resulted in increased embryo development, higher frequencies of successful implantations have not followed possibly due to a low quality status of *in vitro* derived embryos. Up to now, the IVF community has not yet to clearly defined "low quality status embryos" but is recommending thorough morphology monitoring and metabolic profiling for data gathering.

One possibility that may affect embryo quality is the state-of-the-art static culturing of the oocytes and zygotes where these cells are suspended in a drop of media and overlaid with mineral oil. The volume of the media drop provides sufficient nutrients, and waste exchange occurs by simple dilution; the mineral oil acts as a barrier for contaminants. However, solute gradients that result in fluctuating pH can form around the developing embryo which is sensitive to these environmental impacts and as a consequence may affect embryo quality.

Additionally with static culturing, a complete media change step to replenish spent nutrients is necessary at day 3 of embryo development. As can be imagined, a number of variables can be introduced such as changes in temperature, O_2 content, shear forces from the manipulation, and possible contaminants.

A microfluidics platform for culturing eggs would reflect physiologic conditions where nutrients and waste exchange occur rapidly and constantly, and complete media change is eliminated.

Furthermore, reproducing a dynamic culturing environment, as opposed to static, through microfluidics is thought to increase the quality of embryos. In natural conception, the ovum is released from the ovaries and is immediately subjected to waves of fluid that bathe the oviducts. Fertilization and blastocyst development occurs in the oviducts such that the embryo is constantly moving, rolling, and contacting the oviduct walls on its journey prior to implantation.

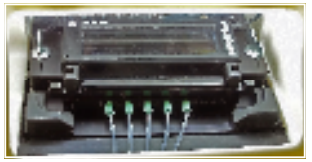
Nanopoint's microfluidics system

- Laminar flow is similar to the *in vivo* condition of the oviduct versus the current static culture method
- Pulse rhythm mimics the *in vivo* condition of the oviduct
- Fluid flow imparts movement and rotation of the oocyte that leads to increased fertilization and provides physiologic benefits such as nutrient media contact on all surfaces of the oocyte/embryo and provides for fresh media without cell manipulations
- Reduced oocyte/embryo stresses due to reduced cell manipulations
- Reduced personnel handling
- Greater consistency of incubation conditions

The cellTRAY® for IVF

- Biocompatible materials—borosilicate glass bottom is bonded to polycarbonate top piece with etched wells and channels
- Well sizes can easily accommodate the loading and unloading of embryos
- Well walls constrain the embryo mimicking the reproductive tract
- Channel dimensions accommodate laminar flow similar to the *in vivo* condition of the oviduct
- Small nutrient media volume (3-5µL) within a well is comparable to the volumes within the lumen of the reproductive tracts
- Lower embryo to media volume ratio within a well promotes increased exchange of nutrients and embryo products

cellTRAY slide is placed into on-stage incubator for duration of embryo development cycle



Microfluidic delivery system and incubator can be used with any microscope with a microtiter plate holder.