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# Are Organs-on-Chips Patentable?

by Douglas J. Bucklin

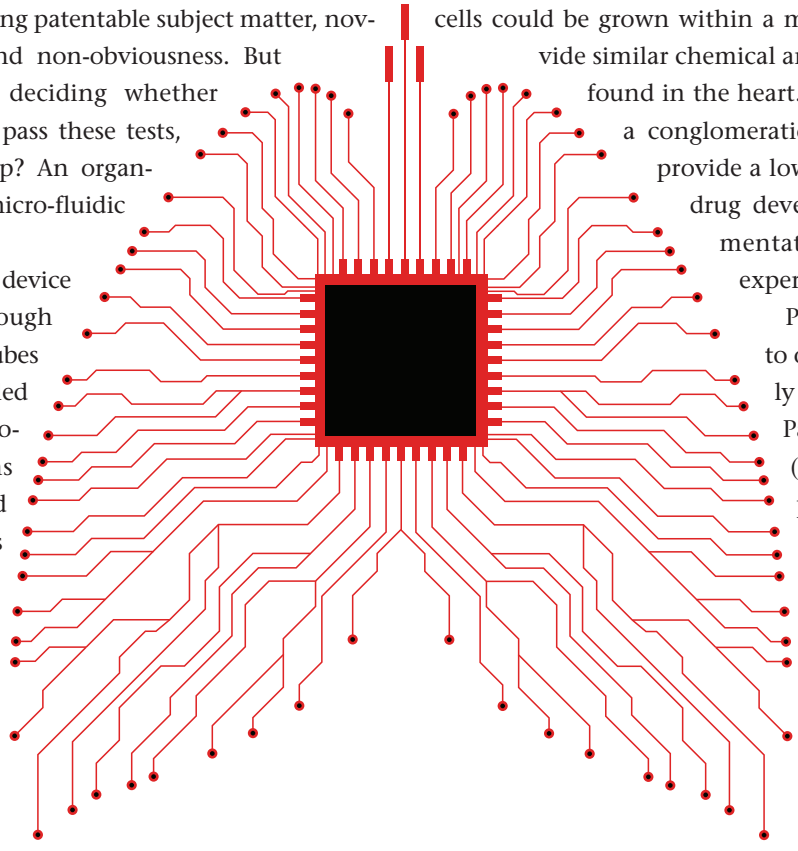
A typical inventor-patent attorney discussion:

***Inventor:*** *"Can I get a patent on an organ-on-a-chip?"*
***Patent Attorney:*** *"It depends."*
***Inventor (annoyed):*** *"That's not helpful, what do you mean?"*

Well, the answer is not simple, but this article provides a brief explanation.

Obtaining a patent on an organ-on-a-chip requires a patent applicant to pass all of the requirements for a patent application, including patentable subject matter, novelty, and non-obviousness. But before deciding whether an organ-on-a-chip might pass these tests, what is an organ-on-a-chip? An organ-on-a-chip is a fusion of micro-fluidic chips and cell cultures.

A micro-fluidic chip is a device that channels fluids through hollow, micrometer-scale tubes on a chip. Techniques called microfabrication of micro-electromechanical systems (MEMS) have been adopted from the microelectronics industry and modified to construct micro-fluidic chips. Refinements using polymers, biomolecules, and self-assembling polymers have been used to create chips that are compatible with biologic chemistry. Various channels and controls can be built into a micro-fluidic chip to achieve precise delivery of chemical reactants and to harvest reaction products. The amount of fluids delivered through the channels is on the range of microliters or less (that is, one millionth of a liter or less). At that scale, a micro-fluidic chip can be a lab-on-a-chip. Reagents can be provided at reduced quantities, the costs of experimentation may be decreased, and results may be obtained quickly. The net effect is that a macro-scale lab in a building can be replaced by a hand-held chip. The addition of cells to a micro-fluidic chip creates an organ-on-a-chip.



## Organ-on-a-Chip

The intent behind making organs-on-a-chip is to mimic entire organs or organ systems in their mechanics, activity, and physiologic responses. For example, a culture of cardiac cells could be grown within a micro-fluidic device and provide similar chemical and physical environments as found in the heart. A practical purpose of such a conglomeration of chips and cells is to provide a lower cost, safer alternative for drug development and toxin experimentation compared to *in vivo* experimentation.

Patent applications directed to organs-on-a-chip are currently pending at the United States Patent and Trademark Office (USPTO). For example, U.S. pre-grant Patent Application Publication No. 2015/0004077, which is titled "Integrated Human Organ-on-Chip Microphysiological Systems," describes:

> [0005] In one aspect provided herein is architecture of support structures for micro-physiological representations of living Organs, herein referred to as Organ Chips. Organ Chips are microfluidic devices that comprise living human cells cultured within the microfluidic devices and mimic the three-dimensional tissue-tissue interfaces, mechanically active microenvironments, electrical stimulation, chemical conditions and

complex Organ-level functions of living Organs, such as a breathing lung, beating heart, metabolic liver, flowing kidney, peristalsing gut, reactive airway, contracting skeletal muscle, skin barrier, blood-brain barrier, reproductive/ endocrine testis and self-renewing bone marrow.

This application shows it is entirely possible to file a patent application directed to an organ-on-a-chip. Whether a patent will issue from such a patent application is a more complicated question.

A published example of an organ-on-a-chip is a lung-on-a-chip from the Wyss Institute for Biologically Inspired Engineering at Harvard.[1] The lung-on-a-chip has three, side-by-side, microfluidic channels. The center channel includes a thin, porous membrane across the channel. Human alveolar epithelial cells were grown on one side of the membrane, and human pulmonary microvascular cells were grown on the other. The alveolar epithelial cells and pulmonary microvascular cells are different types of specialized lung cells. A vacuum was connected to the outer channels. By applying or relieving vacuum to the outer channels, the walls separating the outer channels from the middle channel could be deformed—to stretch or contract the membrane. This movement on the membrane approximated the expansion and contraction normally present in lungs, and the lung cells grown on the membrane reacted similarly to the way they would *in vivo*. Efforts are also being made to create a 'human-on-a-chip,' which would aggregate different cell types from different organs in different regions of a multichannel micorofluidic device to mimic multiple organs in the body.[2]

Examples in the discussion below build on a hypothetical lung-on-a-chip roughly patterned on the above lung-on-a-chip example. Whether the actual lung-on-a-chip developed by the Wyss Institute is patentable, or already patented, is not considered.

As mentioned above, the substantive tests for patentability are whether the invention is patentable subject matter, novel, and non-obvious. If an invention passes each of these tests and other formal requirements, an examiner at the USPTO should allow the application, and a patent should issue. To get to this point, an applicant would file a patent application with the USPTO with a description of the invention ending with a series of claims. The claims describe the metes and bounds of the intellectual property that the applicant would like to exclude others from making, using, or selling. The patent examiner will focus on whether the claims recite patentable subject matter and are novel and non-obvious.

## Patentable Subject Matter

The Patent Act states: "[w]hoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title."[3] An invention will satisfy this requirement if: 1) it is directed to a "process," "machine," "manufacture," or "composition of matter," but 2) it is not subject to a judicial exception to these classes of patentable subject matter.

An organ-on-a-chip is clearly a 'manufacture,' since it is a conglomeration of synthetic materials and cells. But cells on an organ-on-a-chip present a possible exception: products of nature are one of the judicial exceptions that are not eligible for patent protection.[4] To avoid the judicial exception, a claim to an organ-on-a-chip must recite something significantly more that limits the use of the cells to a particular inventive concept.[5] The USPTO promulgated guidance to its examiners to use in determining whether claims reciting a natural product fail this test.[6] In short, the USPTO established the following inquiries: (1) is a claim directed to a process, machine, manufacture, or composition of matter; (2A) is the claim directed to a law of nature, a natural phenomenon, or an abstract idea (a judicial exception), and (2B) does the claim recite additional elements that amount to significantly more than the judicial exception?[7]

As stated above, because a claim to an organ-on-a-chip would recite an item of manufacture; it would pass question 1. Because an organ-on-a-chip will have cells, a claim to it will likely be found to include a judicial exception under question 2A. But if the claim includes additional elements—the components of the microfluidic chip—it may be found to be "significantly more" than just cells, and may be patentable subject matter under these tests.

There is an additional test for patentable subject matter termed "streamlined analysis."[8] Under this analysis, questions 1, 2A, and 2B are avoided if it is clear the inventor is not trying to pre-empt others from all uses of the judicial exception. For example, a claim to an artificial hip prosthesis coated with a naturally occurring mineral contains a judicial exception; the mineral is a natural product. But, according to the USPTO, such a claim "clearly does not attempt to tie up the nature-based product," and would be patentable subject matter.[9] Likewise, an organ-on-a-chip may contain cells, but a claim reciting the assembly would not attempt to tie up uses of the cells outside of the microfluidic device. On that basis, a claim to an organ-on-a-chip may also be determined to be patentable subject matter under the streamlined analysis.

## Novelty

The Patent Act uses various formulations to test whether a claim to an invention is 'novel.'[10] In summary, novelty means that no single reference in the public domain discloses all of the elements of the claimed invention prior

to the application's filing date. An examiner at the USPTO will review a claim to an organ-on-a-chip, search the "prior art" to find references similar to the claim, and then compare the claim to each reference found. In the lung-on-a-chip example, the patent examiner would search the relevant literature and patent documents for lung applications and microfluidics. Then the patent examiner would compare a claim to the chip to any prior art references found. The claim would likely recite the microfluidic chip architecture, the components of the chip, the membrane, and the type of cells on each side of the membrane. If none of the prior art references disclose every one of these elements, the patent examiner will conclude that the claim was novel. On the other hand, if one prior art reference disclosed all of the details of the claim, the patent examiner would reject the claim as being anticipated by the prior art. Determining whether any one claim to an organ-on-a-chip is novel would require such a search and examination of the claim.

## Non-obvious

A patent examiner can also reject the claim as being obvious, even when it is novel over the prior art references found where "the differences between the claimed invention and the prior art are such that the claimed invention as a whole would have been obvious...."[11] The fundamental test for obviousness is: "the scope and content of the prior art are to be determined; differences between the prior art and the claims at issue are to be ascertained; and the level of ordinary skill in the pertinent art resolved. Against this background, the obviousness or nonobviousness of the subject matter is determined."[12] That is, would one of ordinary skill in the art consider an invention to be obvious based on the prior art known at the time of the invention? Patent examiners are instructed to follow these steps for any claim—including a claim for an organ-on-a-chip.

Like the novelty test, the obviousness of any one claim to an organ-on-a-chip depends on the specific facts of the case. For example, consider an example of a new lung-on-a-chip that uses different means to stretch or contract the membrane harboring the lung cells. The walls in the new chip where the membrane is anchored may have direct mechanical connections to micro-scale pistons that move inward and outward. A claim to the new lung-on-a-chip would recite these new structures and how to stretch or contract the membrane. On that basis, the claim would be novel over a vacuum-based lung-on-a-chip. But it is an open question whether a patent examiner would conclude that the new features were an obvious modification. It is possible a claim to an organ-on-a-chip would be found to be non-obvious.

## Conclusion

The answer to the inventor's question, "Can I get a patent on an organ-on-a-chip," remains, "it depends." A dusty doctoral dissertation disclosing a microfluidic chip harboring the inventor's cells of interest may be sitting on a shelf in a small college, but virtually unknown since it was deposited. A patent examiner is allowed, encouraged, and even required to search the world of prior art, and may find that dissertation. Whether any one organ-on-a-chip would pass the above tests is unknown at the outset. Experts in the art will likely know what their competitors are doing, and interviews with inventors should probe questions of novelty and non-obviousness. Further, private search firms can be hired to obtain a preliminary view of the prior art. The results of these inquiries can be used to: follow up with the inventors for further information about the invention, determine the differences between what they have invented and what is in the prior art, and construct an application to emphasize those differences.

An organ-on-a-chip may be patentable. And considering the vast effort used to achieve the technology, a patent excluding competitors from making, using, or selling the chip would be useful as a business tool to at least recoup research and development costs. ⚖

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## ENDNOTES

1. *See* D. Huh, *et al*. (2010) Reconstituting organ-level lung functions on a chip, *Science* 328 (5986): 1662–1668.
2. C. Luni, *et al*. (2104) Human-on-chip for therapy development and fundamental science, *Current Opinion in Biotechnology* 25: 45–50.
3. 35 U.S.C. § 101.
4. *Ass'n for Molecular Pathology v. Myriad Genetics, Inc.*, 133 S. Ct. 2107, 2116 (2013).
5. *See Id*. and *Mayo Collaborative Servs. v. Prometheus Labs., Inc.*, 566 U.S. 66, 77, 132 S. Ct. 1289, 1297 (2012).
6. *See* 79 Fed. Reg. 74618 (2014).
7. *Id*.
8. *Id*.
9. *Id*.
10. *See* 35 U.S.C. § 102.
11. 35 U.S.C. § 103.
12. *Graham v. John Deere Co.*, 383 U.S. 1, 17, 86 S. Ct. 684, 694 (1966). *See also KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 127 S. Ct. 1727, 1734 (2007).