[Student's Name]

'Artificial Lung'

Two stories underground, through a rabbit's warren of grey concrete walled tunnels, the [University of Michigan's Lab] seems a million miles away from the day-lit world. A low lying lab-smell funk pervades the area, reeking of old bath water and the sticky syrupy smell of spilled medium, now growing god-knows-what. The stench of liberally applied industrial strength cleaner wafts down the corridor, mingling with the rest. Underfoot, the sickly grey tile floor is polished, shining like a mirror in the florescent hallway lighting. It makes the Lab-Techs' sneakers squelch as they lead us towards the operating room. Just inside the doors, two large hexagonal operating lamps hover, poised on their stands like insects. The machines around us are silent, a few lights blinking lazily.

"This," the male vet-tech says with a flourish, "is Jennifer Lopez."

A blue nylon sling hangs directly in the center of the operating theater supporting a mass of pink and grey flesh. Her delicately pointed hooves dangle, swaying, and her ears twitch ever so slightly as we crowd around, an unruly mass of students gawping like we've never seen a pig recovering from anesthesia before. J-Lo appears calm and comfortable, her abdomen wrapped securely in a bright blue bandage and decorated with red hearts and stars. Her blonde eyelashes fan up and down as she calmly surveys us with a lovely golden brown eye. On the other side of the room, a clean stainless steel cage lies open, awaiting its next occupant.

Beneath her, a powder blue operating sheet lines the sling she's hanging in that perfectly matches the tech's spotless scrubs. The tech who already spoke smiles warmly, his teeth are smooth and white, and his eyes crinkle at the corners. A few strands of fair hair curl out from under his cap.

In street clothes he could almost be charming. The second tech stands by, her auburn mane curls wildly around her head as she beams at us. Slim as a willow wand, her dark blue scrubs seem to hang on her frame giving her wide blue eyes a hungry look. She is hungry, but for knowledge, rather than food. She's working here in her year off before med school. Her grin grows wider, as if she knows how much of a treat it is for us to see this operating theater.

"Does anyone know what this is?" the male tech asks, holding up a squishy-looking yellowing package.

We don't.

The package is filled with a net of fibers that looks like cotton-wool with protruding plastic tubes. The contraption jiggles, its thick tubing swaying back and forth. The tech explains that it is a prototype of an external artificial lung that the lab is testing. The tubes are connected to the patient's pulmonary artery and vein, allowing oxygen and carbon dioxide to be exchanged through the porous fibers.

"If all goes well," he says, "we're looking at a trial period of about five days."

He goes on to explain that the goal of this "acute" study is to test the amount of oxygen that can diffuse through the fibers' pores and enter the pig's blood stream. The researchers want to test different coatings on the inside of the fibers. They hope to prevent the activation of platelets that cause clotting. If a clot forms, it can break free of the net of fibers and make its way into a patient's blood stream. From there, it could travel to the patient's heart, brain, or other vital organs.

When he mentions the short trial period, the female tech's demeanor changes entirely. She starts to refer to J-Lo as "he," or "it," or "the pig." Her genial smile disappears faster than a rabbit down a hole, and her eyes narrow. Nobody asks what happens "after." We already know.

In the operating theater, I keep waiting for the pig to squeal and struggle, eyes rolling, hooves beating the air savagely in an attempt to get away. But she hangs limply, as docile as a roast that's already been served up. The faces around us appear smooth and detached, accepting this as if it were the most natural thing in the world. I look away, gulping down a wave of nausea. I want to scream or cry and ask the tech how he can live with himself, doing this day in and day out. Instead my face remains impassive, if a little green.

"You've got to remember," he says kindly, "this is for the greater good."

The sentiment is reiterated by [University of Michigan doctor]. "It's really about [improving] quality of life," he says. [University of Michigan doctor] is an intense and professionally brisk man, his hawkish eyebrows perch directly above bright black eyes and a beaky nose. Sitting in a windowless conference room, his shirtsleeves rolled up to his elbows, he patiently explains the development process and testing of the artificial lung. As Lab Coordinator at the [Lab], [University of Michigan doctor] has had a part in nearly every stage of the lung's development. In addition to his regular duties as an investigative researcher he also trains and supervises some of the nearly 100 students and volunteers that work with the lab each semester.

[University of Michigan doctor] explains that the lab's artificial lung is based on the Extracorporeal Membrane Oxygenation (ECMO) technology that Dr. Robert Bartlett pioneered at the University of Michigan more than 30 years ago. ECMO facilitates the transfer of carbon dioxide out of a patient's bloodstream by pumping blood into a membrane system similar to the

artificial lung's fiber network; it then adds oxygen and passes it by a heater before returning the blood to the patient's body.

Although the ECMO technology has saved thousands of lives since its introduction, it also has serious drawbacks. While on ECMO, patients must remain intubated and in an ICU setting, where they can be monitored constantly in case something goes wrong with the machine. Intubation, especially in an ICU, exponentially increases the patients' risk of infection.

In addition to these dangers, the technology has bio-compatibility problems. Each artificial component that the blood comes into contact with increases the chances of clot formation. Heparin, a blood-thinner, is given to minimize clotting problems, but its side effects can include increased chances of internal bleeding. In addition, the pump that pulls blood through the machine can damage red blood cells (known as cell shearing) and activate platelets and white blood cells.

[University of Michigan doctor] is hopeful that the artificial lung will help to avoid some of these problems. Because the technology relies on the body's natural heart to pump the blood, the artificial pump and heater are unnecessary. This reduces damage to the cells and minimizes the clotting risks. The artificial lung is intended to be worn in a vest or sling alongside the body, allowing the patient to move freely, and likely even be able to go home while waiting for a transplant organ to become available. "On ECMO…the patient can at least exercise, prepare for their transplant, brush their teeth… with the artificial lung, we're hoping that a patient can go home, [or] be in a non ICU unit at the hospital." [University of Michigan doctor] says.

Although the technology has advanced rapidly in recent years, it still needs improvement before human trials can begin. "Ideally," says [University of Michigan doctor], "you want to be able to

maintain the patient on an artificial lung forever." At the moment, however, high rates of clotting within the fibers leads to the lung's eventual failure. Attempts to slow the rate of clotting have required extensive testing both on the bench-top and in animal models.

[Assistant Professor in the Department of Pediatrics and investigative researcher at the University of Michigan] has been working on this project since its initial design and development stages. Most of his work has been in bench testing the device. Also known as *'in vitro'* testing, bench testing takes place outside of the body. The device's fluid mechanics are tested in a traditional laboratory setting; one of the tests includes pumping glycerol, which mimics blood's viscosity, through its fiber network. Scientists use this information to predict how much pressure the patient's heart will need to produce for the device to work. However, "There are some things that we just can't test on the bench," [Assistant Professor] says "Though, we do everything we can there," he adds quickly.

In 2007 [Assistant Professor]'s team successfully completed the first thirty day trial of the device in a sheep model. Although the gas-exchange function of the device worked, animal trials pose their own challenges. "I don't want to talk about that too much," [Assistant Professor] says, "but I will say a few things." he adds, smiling indulgently, "Sheep are not humans. You can not reason with them about how they should behave with an artificial lung on… They've got this tube in them and they're thinking 'I don't want this thing on me.'" After several seven day trials, his team had developed better protocols to keep the sheep safe and comfortable during the test. In recent years, the lab has conducted acute studies in pigs to fine-tune the device's fluid mechanical functions of the device.

According to the University of Michigan's Animal Research website, over 98% of the animals used for research at the University are rats, mice, fish, and frogs. Although the [Lab]'s use of pigs, sheep, and other large mammals is relatively uncommon, all experiments that require animal testing undergo extensive planning to ensure that the fewest possible number of animals are used without impacting the scientific integrity of the experiment and are subject to stringent regulations to ensure humane treatment of the animals. A regulatory board must approve the protocols before animal use is approved for any project. Both [Assistant Professor] and [University of Michigan doctor] have been directly involved in the animal testing aspect of the device's development. "We give a human kind of care to the animals," [University of Michigan doctor] says, "in that we control pain, we don't abuse them, we follow every single procedure." he pauses for a moment, "And maybe more than in humans," he adds slyly, allowing himself a brief smile. In the next moment, however, his face has shifted, all traces of levity entirely disappearing. "We do this in order to…" he hesitates, searching for the right words, "to… make things easier," he finishes honestly. "The role that animals play here is critical," he adds, conviction shining in his eyes.

In the sunlit atrium of the Biomedical Sciences Research Building, [Assistant Professor] pauses, his fingers smoothing across his short graying beard. When he does answer, his words are slow and measured, his voice dry. "When you're doing animal studies," he says, "you want to aim for two things. One, you want an animal that has similar physiology to humans. And two, you want to go with the least sentient animal you possibly can… Sheep do not have the emotional complexity of dogs, or pigs even." He explains. "It sounds cruel, but they're not very smart, and so they're not as distressed by the testing." It's hard to imagine this poised man with warm brown eyes struggling to come to terms with his difficult work. "These days I'm not very hands

on, if that's what you're asking," he says, leaning forward to survey me from behind his round silver glasses. "It's left to surgical fellows and lab techs to do most of that work, but in the past, I certainly have."

Back in the [Lab], a padded blue nylon sling lies folded on a table in the middle of the office, its rough weave catching the light. A stack of freshly laundered scrubs waits patiently, peeking out from under the table. Nearby, an enormous steel canister marked MEDICAL OXYGEN glimmers under the fierce hallway lighting. In a conference room just down the hall from the operating theater, [University of Michigan doctor] offers to show me one of the earlier incarnations of the artificial lung. "We actually have one here," he says, rummaging through a cardboard box on the other side of the room. Returning, [University of Michigan doctor] places an older model of the artificial lung on the conference table between us. With a surgeon's eye, he scrutinizes me carefully. "So you weigh what…A hundred and fifteen… a hundred and sixteen pounds?" I blink, more than a little taken aback. "A hundred and fifteen, exactly," I manage to say. "That's about sixty kilograms, so this one would work for you." He says, handing me the artificial lung. The cylinder feels heavy and solid in my hand, its outer shell is rigid and roughly textured. It's hard to imagine that someday soon, this could save some of the nearly 1,200 patients who die waiting for a lung transplant each year. Maybe that's enough to make J-Lo's sacrifice worth it in the end.