

LUNG BIOENGINEERING

LUNGFX™ DEVICE

Patient Brochure (DRAFT)

Version XXMONYY

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GLOSSARY

Acute	Short-term (less than 3 to 6 months)
Blood Gas Analyzer	Medical equipment that tests the fluid samples taken from the lung(s) to provide data on how the lungs are working.
Blood Substitute	Material used instead of real blood.
Bronchostenosis	Narrowing of the small airways in the lungs, making it difficult to breathe.
Burkholderia cepacia	Type of bacteria that causes respiratory (lung) infection.
CLAD	Chronic Lung Allograft Dysfunction. A major decline in lung function that lasts for more than 3 weeks.
CLES	Centralized Lung Evaluation System. This was the previous name for the LungFX device when it was being developed and studied in clinical trials to perform ex vivo lung perfusion. The 2 studies that evaluated the device are named the CLES Pivotal Study and the CLES Traditional Feasibility Study.
Contraindications	Reasons why it is not safe to use a certain treatment or medicine.
Cold Preservation	The cooling down of the lungs to 10°C or 50°F after removal from the donor to allow for transport.
Data	Information collected and used for analysis.
Deoxygenation Gas	Gas that contains 86% nitrogen, 8% carbon dioxide, and 6% oxygen.
Direct to Transplant	Donor lungs(s) that did not go through EVLP using the LungFX device, but were used in a Standard Transplant.
Double Lung Transplant	A surgical procedure in which both of the patient's diseased lungs are replaced with donor lungs.
Dysphagia	Difficulty swallowing
Effectiveness	How well something works.
Electrolytes	Proteins like sodium (salt), potassium, and sugar that help control important bodily functions.
End-Stage Lung Disease	An advanced phase of a lung disease that developed to a point where the lungs are damaged beyond repair and function is failing.
Evaluation	The careful examination of something and judgment of the quality.
EVLP	Ex Vivo Lung Perfusion. A procedure that allows for the evaluation of a donor lung in a controlled environment outside the body (ex vivo).
EVLP Circuit	Tubing set that is designed to provide fluid and move fluid continuously between the LungFX and the lungs. The tubing set also helps to provide deoxygenated gas (gas that contains 86% nitrogen, 8% carbon dioxide, and 6% oxygen), filter the fluid, collect fluid samples, and to collect waste during the EVLP procedure.
Ex vivo	Outside of the body
Function	How something works.
Heater-Cooler Unit	Medical equipment that is used to warm and cool fluid.
Hypoxia	Decrease in oxygen reaching body tissues.
Infection	When harmful germs, like bacteria or viruses, enter the body and cause sickness.
LBE	Lung Bioengineering Inc.

LungFX	The device used to perform ex vivo lung perfusion (EVLP). Previously called the CLES device in clinical studies.
Lung Graft Failure	When transplanted lungs stop working properly.
Lung Transplant	Surgery to remove a diseased or failing lung(s) and replace it with healthier lung(s). The person receiving the lung(s) is referred to as the recipient and the person donating the lung(s) is the donor.
Organ Chamber	Clear dome that holds the donor lungs during the EVLP procedure.
Pneumonia	A bacterial or viral infection in the lungs that causes symptoms such as coughing, fever, and difficulty breathing.
Pressure Monitor	Medical equipment that measures and shows what the pressure is in the lungs during the EVLP procedure.
PGD	Primary Graft Dysfunction. A serious condition where the transplanted lung is injured within the first 72 hours after transplant; it is graded on a scale from 0 to 3 with 3 being the most severe grade.
Pulmonary Embolism	Blood clot in an artery in the lungs, which depending on size can cause difficulty breathing and chest pain.
Pump System	Medical equipment used to move fluid through the lungs and the LungFX device.
Respiratory Failure	A serious condition that makes it difficult to breathe on your own because the lungs do not get enough oxygen into the blood.
Single Lung Transplant	A surgical procedure in which one of the patient's diseased lungs (left or right) is replaced with a donor lung (left or right).
Standard Transplant	Medical procedure where a damaged or diseased organ is replaced with an organ from a donor.
STEEN Solution™	A clear, sterile fluid that contains nutrients, electrolytes (like proteins, salt, and sugar) that is moved through the lungs during the EVLP procedure.
Systemically	Affecting the entire body.
Transplant Rejection	When a recipient's body rejects the transplanted organ.
Ventilator	Medical equipment used to help or replace breathing for the lung by delivering and removing air.

1 INTRODUCTION

Your healthcare provider has determined your end-stage lung disease or failing lung(s) requires you to have a lung transplant and has placed you on the lung transplant waiting list. A lung transplant involves surgery to remove the diseased or failing lungs (either both or just one side) and replace them with healthier lungs. The person receiving the lungs is the recipient and the person donating the lungs is the donor, typically a person who recently died.

Depending on your disease, you may need a single or double lung transplant. It is not known exactly how long you may be on the waiting list since there are more people who need lungs than there are lungs available for transplant. In the United States, many donor lungs are not actually used for transplant. Possible reasons for this include the following:

- The donor lungs were not in good condition.
- There was not enough time to:
  - Complete testing on the lungs,
  - Remove the lungs from the donor and transport them to a recipient, or
  - Find a match between the donor and recipient.
- Healthcare providers offered the donor lungs for a recipient then decided not to use them (test results from the donor lungs may have been unclear and/or there was not enough information available).

In recent years, a procedure was developed to address some of these reasons with the intent of increasing the number of lungs available for transplant. This procedure is called ex vivo lung perfusion or EVLP. In a typical transplant procedure that doesn't use EVLP, an organ is removed from a donor's body and preserved and transported in a sterile, cold solution to the recipient's location. It is critical to minimize the time during which the organ is outside a human body and often when donor lungs become available there is limited time and limited information for the healthcare provider to decide whether the lungs are appropriate for their transplant patient. EVLP is different, because it allows lungs to be preserved outside of the donor (ex vivo) in a controlled environment and lets healthcare providers assess how they are functioning. Your healthcare provider has determined that receiving donor lungs that have been through an EVLP procedure may be an option for you. This document is meant to help you understand the device being used to perform the EVLP procedure. The device is called LungFX and information about it is provided in this brochure.

The LungFX EVLP procedure is performed on donor lungs at a specialized EVLP facility before they are sent to a healthcare provider's hospital for transplant. Transport of the lungs to an EVLP facility will require extra time for preservation both before and after the EVLP. This extra time may introduce some additional risks to the lungs and you that wouldn't occur in a typical transplant organ retrieval process (see 5.1Possible Risks). However, the procedure can allow a healthcare provider more time to collect information on the donor lungs to help make a decision on whether or not to use them for transplant.

Your healthcare provider is your best source of information about lung transplantation and the donor lung waitlist process. The more you know about the process of lung transplantation, the

better you can make informed decisions about your options. This brochure is to help aid you in deciding if donor lungs that have been preserved by EVLP using LungFX (referred to in this brochure as LungFX EVLP-evaluated donor lungs) are right for you. Staying informed will help you communicate with your healthcare provider to choose the best treatment options for your end-stage lung disease.

2 WHAT IS THE PURPOSE OF THE LUNGFX™ DEVICE? (INTENDED USE)

LungFX enables data to be collected about how the donor lungs work in a controlled environment outside the body (ex vivo), to help determine if they will be transplanted into a recipient. The LungFX device is only intended for donor lungs that would not be placed for transplant if LungFX were not used (see *Section* 7*, What Does "Lungs Not Otherwise Used For Transplant" Mean?*).

Patients who may receive LungFX EVLP-evaluated donor lungs must:

- Be 18 years or older
- Have end-stage lung disease (failing lungs)
- Not already have had a lung transplant
- Not be listed for multiple organ transplantation, including lung and any other organ
- Not be listed for live donor lobar lung transplant
- Not be positive for HIV for *Burkholderia cenocepacia* infection

The donor lungs are procured by a healthcare provider and transported (without EVLP) to a Lung Bioengineering Inc. (LBE) facility. LBE is the manufacturer of the LungFX device. The EVLP procedure is then performed by LBE clinical specialists at the facility a with hospital-type operating rooms. These clinical specialists share the data they collect about the donor lungs with your healthcare provider during the EVLP procedure. Your healthcare provider will use this data to help decide whether or not to use the donor lungs for your transplant. If your healthcare provider and you decide to accept the lungs, they will be taken off of LungFX, packaged with preservation solution, and shipped to your hospital.

3 WHAT IS THE LUNGFX DEVICE AND WHAT DOES IT DO?

LungFX is a centralized lung evaluation system (CLES) that uses several devices that work together to perform an EVLP procedure. Many of the devices used are what you would typically find in a hospital operating room during open heart surgery (see image of the LungFX device below). Some of the devices are hospital equipment that can be reused for many EVLP procedures and some are single-use only and are thrown away after every EVLP procedure.

The reusable devices include the following:

- A machine called a perfusion system that includes:
  - A pump system (*images B, K, and G*) for moving fluid through the lungs and LungFX
  - A machine (*image H*) that:
    1. Controls the speed of how fluid is moved through the lungs and LungFX.
    2. Measures and shows the speed of the fluid, the temperature of the fluid and the

pressure in the lungs.

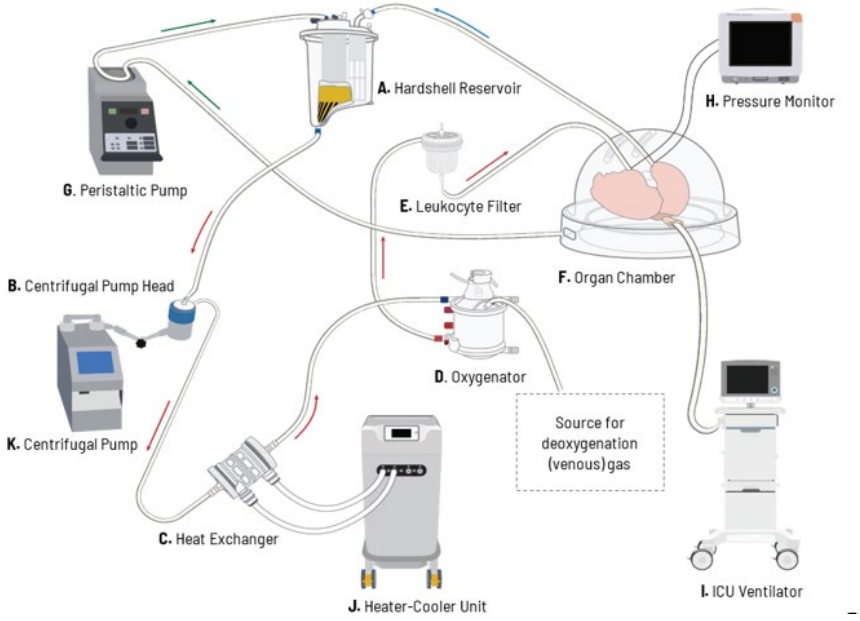
- A machine (*image J*) for warming and cooling the fluid (called a heater-cooler unit)
- A machine (*image I)* to help the lungs breathe (called a ventilator)
- A machine (*not shown*) that tests the fluid samples taken from the lungs to provide data on how the lungs are working (called a blood gas analyzer).

The single-use devices are those that come in direct contact with the donor lung, so they are sterilized before the procedure. These include the following:

- A clear fluid (called STEEN Solution, *not shown*) containing nutrients, electrolytes (proteins, salt, and sugar), and other ingredients that help the lungs function similar to how they would inside the body.
- A clear dome (called an organ chamber, *image F*) that holds the lungs during the EVLP procedure. A tubing set (called an EVLP circuit, *images A, C, D, and E*) that provides and moves STEEN Solution continuously between LungFX and the lungs, controls the amount of carbon dioxide and oxygen in the fluid, filters the fluid, collects fluid samples, and collects waste fluid during the EVLP procedure .

Figure 1 LungFX Device





Before taking the donor lungs out of the donor, a healthcare provider will have already made arrangements to use LungFX; however, your healthcare provider can decide instead to take the lungs directly for your transplant without EVLP if appropriate.

If the decision is to proceed with EVLP, the donor lungs are sent directly from the donor's hospital to the LBE facility, where the clinical specialists who perform the EVLP procedure will bring them into an operating room and put them in the LungFX organ chamber. Once the lungs are in the organ chamber, they are connected to the EVLP circuit. The STEEN Solution fluid is warmed to and then kept at normal body temperature by the heater-cooler unit, and the perfusion system circulates the fluid continuously between LungFX and the lungs. The ventilator maintains the desired pressure in the lungs until completion of the evaluation. During the EVLP procedure, information is collected and shared with your healthcare provider to help them evaluate how well the donor lungs work.

If the information collected shows the lungs are not working as desired, your healthcare provider can decide not to use them. If the information shows the lungs are working as desired, your healthcare provider can accept the lungs for transplant. In that case, at the completion of the evaluation, the lungs are cooled to 10°C (50°F) and prepared or a second transport to your hospital, where the transplant takes place in a standard manner. In addition to the two transport times, the EVLP procedure can last up to 6 hours.

4 WHEN SHOULD THE LUNGFX DEVICE NOT BE USED? (CONTRAINDICATIONS)

There are no known reasons why LungFX cannot be used to evaluate donor lungs. Your healthcare provider and the OPO make the decisions about whether donor lungs should undergo EVLP or can instead be transplanted without EVLP or should not be used for your transplant.

5 WHAT ARE THE RISKS AND BENEFITS?

5.1 POSSIBLE RISKS

- All lung transplant procedures include risks such as death, transplant rejection, lung graft failure, and infection.

The following risks should be discussed with your doctor:

- LBE sponsored a clinical study (the CLES Pivotal Study) that looked at survival after transplant in patients receiving donor lungs after LungFX EVLP. The study also compared these patients' survival to the survival of patients who received donor lungs that didn't have LungFX EVLP. The results of the study suggested that transplantation with donor lungs that had LungFX EVLP assessment could result in a decrease in your life expectancy after transplant as compared to receiving lungs transplanted directly without LungFX EVLP.
    - The percentage of patients in the study who survived to one year after receiving LungFX-evaluated lungs was less than what had been expected from earlier results with EVLP. Of the 94 patients who received EVLP donor lungs, 15 [15.9%] died within one year. This frequency of deaths was also greater than the rate of death reported among patients in the trial who didn't receive EVLP donor lungs (6 deaths out of 80 patients [7.5%])
    - Longer-term survival (out to 5 years after transplant) of LungFX EVLP-evaluated donor lung recipients is not well known, because the CLES Pivotal Study was finished relatively recently. At 2 years, survival of EVLP recipients was 72%, compared to 86.5% for recipients with lungs that had not received EVLP. However, data routinely collected by the U.S. Government for all transplant patients show that in a smaller, earlier study of the LungFX device, the 5-year survival rate for patients in the EVLP group was 50.0% compared to 53.8% of patients in the non-EVLP group.
    - Some of the differences in observed survival may be related to specific characteristics of the transplant procedure, for example: was the transplant single-lung or double-lung; was the overall preservation time of donor lungs relatively long or relatively short (LungFX is not intended for preservation times longer than 20 hours in total); was the procurement of the lungs carried out after brain-death or circulatory (heart)-death of the donor. Your healthcare provider can discuss what can

and cannot be understood from these differences (called subgroup analyses).
  - It is not known if LungFX EVLP might affect a recipient's risk for developing and severity of chronic lung allograft dysfunction (CLAD).

- Your recovery after transplant may be more challenging than if your lungs had not received EVLP. In clinical studies, when compared to patients who received lungs that did not undergo LungFX EVLP, patients who received a lung after LungFX EVLP experienced more difficulty breathing and had longer times on life supportive equipment such as ventilators and use of other machines that provide oxygen to the bloodstream (e.g., an ECMO [extracorporeal membrane oxygenation] machine that acts like an artificial heart and lung when a patient's own heart and lungs don't work).
- Because the following patients were not included in any LungFX clinical study, the risks are generally unknown in these populations:
  - Patients who are younger than 18 years old;
  - Patients who need more than 1 organ transplant;
  - Patients getting a repeat transplant;
  - Patients receiving partial lungs from a living donor;
  - Patients who have human immunodeficiency virus or *Burkholderia cepacia.*

In the CLES Pivotal study, patients reported the following side effects:

- The most common serious side effects (ones that required medical treatment) included: respiratory failure, acute respiratory failure, transplant rejection, and pulmonary embolism. Patients receiving LungFX-evaluated lungs experienced these serious side effects more frequently than did patients receiving donor lungs without LungFX.
- The most common side effects which were reported by more than 1 out of 10 (10%) patients who received LungFX EVLP-evaluated donor lungs (the EVLP group), and they were reported more frequently than in patients who did not receive EVLP lungs. These side effects included:
  - Transplant rejection (when the body reject the transplanted lung) – 25.5%
  - Respiratory failure (when the lungs cannot move enough oxygen to and from the body) – 17%
  - Acute (short-term) respiratory failure – 14.9%
  - Hypoxia (decrease in oxygen reaching body tissues) – 14.9%
  - Pneumonia – 11.7%
  - Bronchostenosis (narrowing of the small airway in the lungs) – 11.7%
  - Dysphagia (difficulty swallowing) – 10.6%
  - Pulmonary embolism (blood clot in lung's blood vessel[s]) – 10.6%
- For patients who did not receive LungFX EVLP-evaluated donor lungs (the non-EVLP group), these side effects were also reported:
  - Transplant rejection – 22.5%
  - Respiratory failure – 11.3%
  - Acute (short-term) respiratory failure – 13.8%
  - Hypoxia – 10.0%

- Pneumonia – 5.0%
- Bronchostenosis – 6.3%
- Dysphagia – 8.8%
- Pulmonary embolism – 8.8%

5.2 POTENTIAL BENEFITS

As noted in the introduction, it is not known exactly how long you may be on the waiting list, since currently there are more people who need lungs than there are lungs available for transplant. A potential benefit of being able to evaluate donor lungs using LungFX is that it may increase the number of lungs available for transplant, and patients like you, who are awaiting transplant, may receive lungs sooner than if you were to wait for a standard transplant. Although it's not possible to fully predict your waiting time in advance, your healthcare provider can provide you with waiting times that are typical for patients like you who have your type of lung disease.

In any organ transplantation, time is critical because the longer it takes to receive an organ transplant after death of the donor, the less acceptable the organ might be for transplant. LungFX was designed to help lungs work like they would if they were inside the body, and the EVLP procedure gives healthcare providers more opportunity to evaluate how well the lungs are working. Potential benefits of this evaluation time include giving the transplant physician more time to make sure the lungs are working properly before you receive them. If your transplant physician decides the donor lungs are not appropriate for you, LungFX provides an opportunity to match the lungs with another person on the waiting list.

6 WHAT CAN YOU EXPECT?

Your lung transplant surgery is performed the same way whether or not you receive lungs that went through EVLP using the LungFX device. The difference between receiving LungFX EVLP-evaluated donor lungs or receiving a standard lung is in how the lungs are preserved and assessed before transplant. In a standard transplant, the donor lungs are assessed while inside of the donor, but with LungFX EVLP-evaluated donor lungs, the lungs are assessed both inside and outside of the body. Your healthcare provider will make the final decision whether the donor lungs are acceptable for you. If the donor lungs are considered acceptable, the lungs will be transported to your healthcare provider's hospital for your transplant surgery.

As a potential recipient of LungFX EVLP-evaluated donor lungs, you do not have to do anything differently. Your healthcare provider and transplant team will describe all the steps before, during, and after your transplant surgery. Your care during and after your transplant surgery will be the same as it would be if you received a standard transplant with donor lungs that were not evaluated by EVLP using the LungFX device.

7 WHAT DOES "LUNGS NOT OTHERWISE USED FOR TRANSPLANT" MEAN?

"Lungs not otherwise used for transplant" refers to a variety of reasons why a donor's lungs would not be chosen for standard transplant. Possible reasons include the following:

- The donor lungs do not meet a healthcare providers' expectations for an ideal transplant based on the information they review at the time of donation.
- There are concerns about the donor's medical history including their age, smoking history, or how they died, and if their history might make the lungs perform poorly.
- Logistical challenges (such as coordinating the time of the procurement with needs of other (non-lung) donated organs) prevent any suitable recipient from being identified..

Speak to your healthcare provider for more information about and examples of what in practice are lungs not otherwise used. Regardless of the reason a donor's lungs were not going to be used for standard transplant, the EVLP procedure using the LungFX device will allow your healthcare provider an opportunity to better determine whether the lungs are acceptable for your transplant requirements.

Speak to your healthcare provider to find out more about the use of LungFX EVLP-evaluated donor lungs so you can make an informed choice for treatment of your end-stage lung disease.