SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name: Ex Vivo Lung Perfusion (EVLP)

Device Trade Name: TorEx Lung Perfusion System

Device Procode: PHO

Applicant's Name/Address: Traferox Technologies Inc.

3505 Laird Rd, Unit 16

Mississauga, ON, Canada, L5L 5Y7

Date of Panel Recommendation: None

Premarket Approval Application Number: P250025

Date of Notice of Approval: July 15, 2026

II. INDICATIONS FOR USE

The TorEx Lung Perfusion System is indicated for use in continuous normothermic machine perfusion of donor lungs, initially deemed unsuitable for transplantation, during which time the ex vivo function of the lungs can be reassessed for transplantation in adults. The TorEx Lung Perfusion System includes a mobile cart with embedded software, single-use sterile Organ Chamber and Cannulae set and is used with TorEx Lung Perfusate solution to perform ex vivo lung perfusion for up to 6 hours.

Note: The TorEx System is used to evaluate the quality of donated lungs, but the final determination of the suitability of the lungs for transplant remains with the transplanting surgeon.

III. CONTRAINDICATIONS

There are no known contraindications.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the TorEx Lung Perfusion System and TorEx Lung Perfusate labeling.

V. DEVICE DESCRIPTION

A. Overview of the Device System

The **TorEx Lung Perfusion System** with TorEx Lung Perfusate is an integrated system designed for clinical use that simplifies the Toronto Technique for ex vivo lung perfusion (EVLP) by combining all the necessary equipment required to perform the procedure and placing its controls within a central location.

The **TorEx Lung Perfusion System** houses the lungs in a sterile environment, while ventilating and perfusing them under normothermic conditions. The TorEx Lung Perfusion System consists of a mobile cart (hardware and software), a single use disposable perfusion kit containing organ chamber, and perfusion cannulae. The TorEx Lung Perfusate is a physiological salt solution containing human serum albumin and Dextran 40. The electrolyte composition, pH and human serum albumin simulate key properties of human blood plasma. Dextran 40 counteracts tissue edema and protects the microvasculature against post-ischemic reperfusion injury. Human serum albumin provides oncotic pressure, preventing edema. The solution is sterile (aseptic processing) and intended for single use only.

B. Device System Component Description

B.1 The TorEx Lung Perfusion Cart Hardware

The front view of the TorEx Lung Perfusion Cart, without a TorEx Lung Perfusion Organ Chamber engaged, is shown in Figure 1.

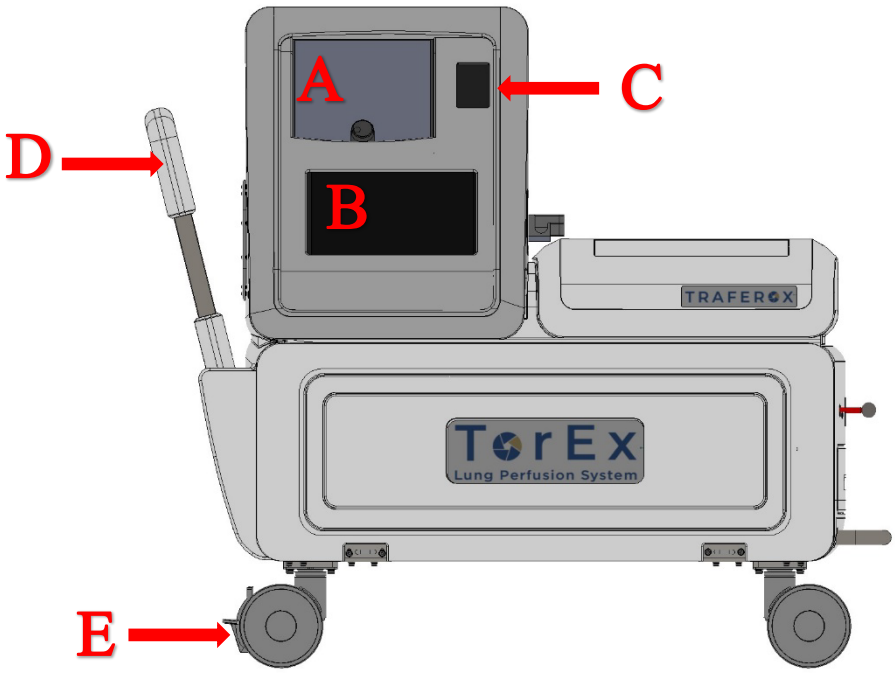

Figure 1: Front view of the TorEx Lung Perfusion Cart without a TorEx Lung Perfusion Organ Chamber attached

The TorEx Lung Perfusion Cart has three touchscreens:

A) Perfusion console
B) BELLAVISTA® 1000 ventilator
C) Cart control screen

Mobility features include:

D) Handlebar
E) Castors with locking mechanism

A) Perfusion Console

The perfusion console is a 510(k) cleared (K973011) perfusion system for respiratory

support. The perfusion console is used to perfuse the lungs during ex vivo lung perfusion. The perfusion system consists of power supply (with battery backup), a centrifugal pump motor, and a main perfusion console that displays controlled parameters and measured variables. The flow rate and pressure are controlled and monitored with the Perfusion Console.

B) The BELLAVISTA® 1000 ventilator

The ventilation in the TorEx Lung Perfusion System is controlled through the BELLAVISTA® 1000 ventilator, which is a 510(k) cleared device (K163127). The ventilator is integrated into the front face of the Cart, as shown in Figure 1. It allows the user to control and measure clinically required ventilation parameters and variables according to the Toronto Technique for EVLP.

C) The TorEx Cart Control Screen and TorEx Lung Perfusion Software

The Cart Control screen, which runs the TorEx Lung Perfusion Software, can be found on the top right of the TorEx Lung Perfusion Cart (Figure 1).

The TorEx Lung Perfusion Software is responsible for the following three main functions:

- Monitors the status of the cart battery
- Control of the waste solenoid valve, to direct perfusate from the reservoir to the waste reservoir
- Implements alarms, error messages, and information messages

The TorEx Cart Control Screen displays the following information:

- the current stage of the perfusion
- the percentage of remaining battery charge and an indication of whether the TorEx Lung perfusion Cart is running on battery power or on mains power
- alarms for hazardous conditions in the system.

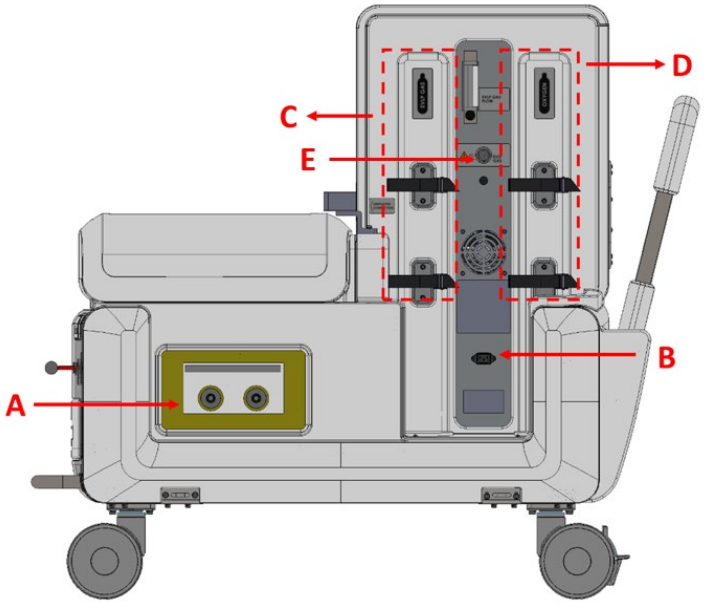

Figure 2: Back view of the TorEx Lung Perfusion Cart without a TorEx Lung Perfusion Organ Chamber attached

A) External heater/cooler connection ports

B) Power cord inlet

C) EVLP gas cylinder holder

D) Oxygen gas cylinder holder

E) EVLP gas inlet (DISS 2220 male connection)

The TorEx Lung Perfusion Cart can house two gas cylinders, one containing medical grade oxygen (100% O2) and the other containing medical grade EVLP gas (86% N2, 8% CO2, 6% O2) for use according to the Toronto Technique for EVLP. The EVLP gas inlet is located on the back of the cart, shown in Figure 2. The oxygen supply inlet is part of the ventilator, located on the left side of the cart.

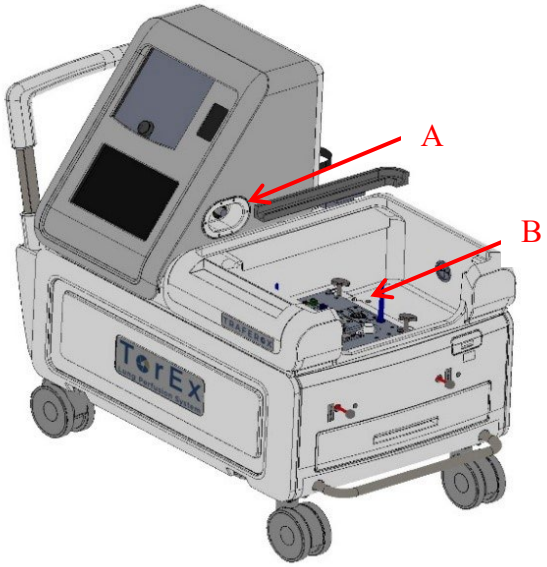

Figure 3: Angled view of the TorEx Lung Perfusion Cart without a TorEx Lung Perfusion Organ Chamber attached

A) Ventilation outlet

B) TorEx Lung Perfusion Organ Chamber holder

The TorEx Lung Perfusion Organ Chamber holder is on the right side of the cart. The organ chamber interface plate is responsible for the connection of perfusion and ventilation circuitry and electrical connections between the TorEx Organ Chamber and the TorEx Cart.

B.2 TorEx Lung Perfusion Kit

The TorEx Lung Perfusion Kit contains single-use disposable components including the organ chamber, cannulas (2 cm PA, LA Rescue, PA rescue), and other disposable accessories. Additional TorEx Lung Perfusion LA Cannula sizes (3 cm, 4 cm and 5 cm) are not included within the standard TorEx Lung Perfusion Kit, but are available to be ordered separately and can be used based on user preference and anatomical considerations.

The TorEx System is designed to operate using an albumin-buffered acellular solution called TorEx Lung Perfusate (TLP). The lungs are flushed and continuously perfused with TorEx Lung Perfusate while remaining at normothermic temperatures. This enables the lung tissue to gradually warm, equilibrate fluid balance, and undergo functional assessment over a period of three to six hours.

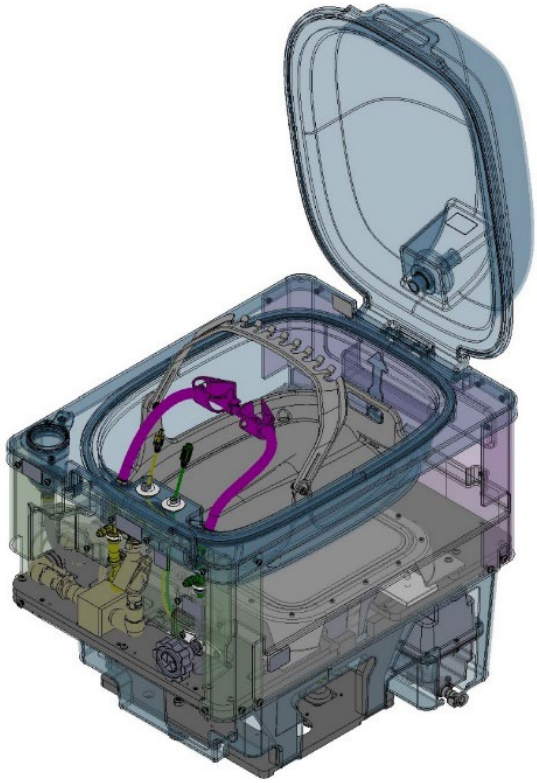

Figure 4: Organ Chamber

Figure 5: TorEx Lung Perfusate

Figure 6: LA cannula (Left-3 cm, Middle Left-4 cm, Middle Right- 5 cm, Right- Rescue)

Figure 7: PA cannula-2 cm and Rescue

VI. ALTERNATIVE PRACTICES AND PROCEDURES

There are several other alternatives for ex vivo perfusion of donor lungs. There are three FDA approved devices (i.e., P160013, P180014, and P240033) on the market for normothermic lung perfusion. On the other hand, standard of care procedures used in the preservation of standard-criteria or ideal donor lungs typically consist of the cold, static storage of the lungs in a hypothermic preservation solution prior to transplantation.

As mentioned above, to date, the FDA has approved three PMAs for EVLP systems with Lung Perfusion Solution: (i) the Organ Care System (OCS™) Lung System (P160013) with OCS Lung Solution (a red blood cell based perfusate) from TransMedics® Inc. (Andover MA, USA); (ii) the XVIVO Perfusion System (XPS™) (P180014) with STEEN Solution™ (an acellular perfusate) from XVIVO Perfusion AB (Göteborg, Sweden); and (iii) the LungFX™ device (P240033) with STEEN Solution from Lung Bioengineering Inc. (Silver Spring, MD, USA).

The OCS Lung Solution along with the OCS Lung System received PMA approval (P160013) in 2018. The OCS Lung Solution is a proprietary solution that is mixed with red blood cells prior to initiating the perfusion. The STEEN Solution, along with XVIVO Perfusion System (XPS) received PMA approval (P180014) in 2019. Finally, the LungFX received PMA approval (P240033) in 2026.

Other alternatives to machine perfusion are cold static preservation, the current standard of care where lungs are simply flushed with cold preservation solution and stored in temperatures typically ranging from 4-10°C prior to transplantation. Finally, an alternative is for the patient to remain on the transplant waiting list. Each alternative has its own advantages and disadvantages. A patient should fully discuss these alternatives with his/her physician to select the method that best meets expectations and lifestyle.

VII. MARKETING HISTORY

Traferox Technologies Inc. (“Traferox”) received a Health Canada Class II Medical Device License 108277 on September 16, 2022 for the TorEx Lung Perfusion System, making it currently commercially available and distributed in Canada. The system has been used commercially since December 2022 in Canada, and over 400 perfusion procedures have been performed at two hospitals in Canada, resulting in over 250 donor lungs available for transplant

that would have otherwise been discarded. TorEx Lung Perfusion System also received approval from Ministry of Health, Israel in February 2025.

TorEx Lung Perfusate (TLP) solution is regulated by Health Canada according to The Interim Policy Position to Address the Safety of Solutions Used to Maintain (perfuse or preserve) Human Organs for Transplantation (Directive) Ref: 12- 110285-345, dated May 31, 2012. This policy is applicable to solutions that are currently sold and used in Canada to maintain human organs for transplantation. The policy defines that organ perfusion and preservation solutions must adhere to the standards of safety with respect to their manufacturing process. The policy does not specify that these solutions are regulated as medical devices in Canada. Traferox received marketing approval for TorEx Lung Perfusate (TLP) on November 12, 2024.

None of these devices have been withdrawn from marketing for any reason related to their safety and effectiveness.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

The TorEx System with TorEx Lung Perfusate (TLP) is indicated for use in continuous normothermic machine perfusion of donor lungs initially deemed unsuitable for transplantation, during which time the ex vivo function of the lungs can be reassessed for transplantation in adults. There is no direct patient contact when this device is used as labeled; however, the device has direct contact with the lungs that are subsequently transplanted into the recipients.

Note: The TorEx System is used to evaluate the quality of donated lungs, but final determination of the suitability of the lungs for transplant remains with the transplanting surgeon.

Patients receiving a lung treated with the TorEx Lung Perfusion System with TLP Solution™ Perfusate may experience adverse events including those experienced with any lung transplant.

Below is a list of the potential adverse effects associated with the use of the device.

- Death
- Respiratory dysfunction or failure
- Respiratory infection
- Sepsis
- Wound dehiscence
- Primary graft dysfunction
- Acute or chronic rejection

IX. SUMMARY OF NONCLINICAL STUDIES

A. Laboratory Studies

Traferox conducted the following bench testing studies to evaluate the performance, safety and reliability of TorEx Lung Perfusion System with TLP.

1. *Biocompatibility*

Biocompatibility testing of the TorEx Lung Perfusion System fluid pathway components and the TorEx Lung Perfusate (TLP)™ was performed in accordance with Biological Evaluation of Medical Devices Guidance - International Standard ISO 10993-1. The specific tests included: cytotoxicity, sensitization, irritation, systemic toxicity, hemocompatibility, and pyrogenicity.

The results showing that all materials are biocompatible are provided in Table 1 below.

Table 1: Biocompatibility Matrix

Experimental Study	**Results**	
	TorEx Lung Perfusate	**TorEx EVLP Kit**
Cytotoxicity study using the MTT, an in vitro assay performed on mammalian cells, mouse fibroblast (L929) and their viability is measured based on the metabolic activity of the cells.	Based on ISO 10993-5 testing, TorEx Lung Perfusate (TLP) is considered moderately cytotoxic in vitro; however, due to its physiological osmolarity and being a hypertonic solution, these results are observed. This does not cause any adverse reaction.	All components that make up a complete device were tested via MEM Elution per ISO 10993-5 and received passing results, with responses classified as mildly or non-cytotoxic; no safety concerns were identified for end users, including for components with mild reactivity.
Intracutaneous reactivity assay, an in vivo assay performed on three rabbits to determine the potential for test article to produce irritation.	Direct injection of TorEx Lung Perfusate (TLP) into rabbits showed no evidence of causing significant irritation and confirms that TLP is non-irritant. The test results conform to relevant sections of ISO 10993-23.	Intradermal testing per ISO 10993-23 showed no visible irritation, and all components are therefore considered non-irritants.

Experimental Study	Results	
	TorEx Lung Perfusate	**TorEx EVLP Kit**
Acute systemic toxicity study following IV injection in mice to determine the potential of test article to produce acute systemic toxicity.	TorEx Lung Perfusate (TLP) showed no signs of gross toxicity, adverse clinical effects, or abnormal behavior and conforms to relevant sections of ISO 10993-11	None of the animals were observed with abnormal clinical signs or significant weight loss. The components are, therefore, considered non-toxic and conform to relevant sections of ISO 10993-11.
The guinea pig maximization sensitization test is conducted with guinea pig to determine the potential for test article to invoke a dermal skin sensitization reaction.	TorEx Lung Perfusate (TLP) showed no signs of dermal irritation and is not considered to be a contact sensitizer. The test results conform to relevant sections of ISO 10993-10.	Test article showed no signs of dermal irritation and is not considered to be a contact sensitizer. The test results conform to relevant sections of ISO 10993-10.
The hemolysis (Direct and Indirect) testing was used to evaluate whether test article stimulates a hemolytic response.	TorEx Lung Perfusate (TLP) was considered non-hemolytic and conforms to relevant sections of ISO 10993-4.	Test article was considered non-hemolytic and conforms to relevant sections of ISO 10993-4.
Material mediated pyrogenicity testing was performed on rabbits to assess febrile response, indicating a pyrogenic response.	TorEx Lung Perfusate (TLP) is non-pyrogenic per ISO 10993-11 and USP <151> requirements.	Test article is non pyrogenic per ISO 10993-11

2. *Sterilization Validation*

a. TorEx Lung Perfusate (TLP)

TorEx Lung Perfusate (TLP) is provided sterile to the user. The device is sterilized via aseptic filtration using a 0.22 µm sterilizing grade filter into sterile PETg bottles with closure. The sterilization method was validated to ensure successful sterilization to a Sterility Assurance Level (SAL) of 10^{-3} in accordance with USP <71> Sterility Tests (method for Membrane Filtration).

b. TorEx Lung Perfusion Kit (Organ chamber, cannulas, and accessories)

These components are also provided sterile to the user. These devices were extracted and tested under GLP conditions in accordance with the ISO 11135 (Medical Devices - Validation and Routine Control of Ethylene Oxide Sterilization). All tests passed, and the products were sterilized by the validated SAL 10^{-6} ethylene oxide sterilization cycle.

3. *Software Verification and Validation*

Software in the TorEx Lung Perfusion Cart was verified and validated in accordance with the FDA Guidance for the Content of Premarket Submissions for Device Software Functions. The device successfully met all predefined requirements and passed all verification and validation activities, and no unacceptable risk is present. Enhanced Documentation, which includes a description of the software (including the architecture), software requirement specifications, software development, management, and maintenance plan, verification and validation protocols/reports, risk management, cybersecurity management, configuration management, software release record, and a list of unresolved anomalies, is available for the device.

4. *Cybersecurity*

TorEx Lung Perfusion System incorporates subsystems that contain software. To address potential cybersecurity risks, Traferox has provided information according to the FDA guidance document entitled, "Cybersecurity in Medical Devices: Quality System Considerations and Content of Premarket Submissions" including a cybersecurity threat model and assessment, validation/verification testing, and a plan for identifying and responding to emerging cybersecurity issues.

5. *Shelf Life Studies*

Accelerated aging studies were performed in accordance with ASTM F1980. These studies demonstrated that sterility, package integrity, and product functionality could be maintained over the following durations:

- TorEx Lung Perfusate (TLP)™ – 1 year
- TorEx Lung Perfusion Kit™ – 1 year

Real-time aging studies are ongoing to support the accelerated aging results and to extend the shelf life of TorEx Lung Perfusate (TLP) to 2 years.

6. *Electrical Safety Testing*

The TorEx Lung Perfusion System was tested by an independent laboratory to demonstrate that the system meets the requirements for safety and essential performance as outlined in IEC 60601-1 – *Medical electrical equipment – Part 1: General requirements for basic safety and essential performance*. The TorEx System was also evaluated for compliance with the related standards listed in Table 2 below. The test results demonstrated that the System met the applicable requirements of the standards.

Table 2: Electrical Safety Testing Summary

Standards	
IEC 60601-1	Medical electrical equipment – Part 1: General requirements for basic safety and essential performance.
IEC 60601-1-2	Medical electrical equipment - Part 1-2: General requirements for basic safety and essential performance - Collateral Standard: Electromagnetic disturbances - Requirements and tests
IEC 60601-1-6	Medical electrical equipment - Part 1-6: General requirements for basic safety and essential performance - Collateral standard: Usability
IEC 60601-1-8	Medical electrical equipment - Part 1-8: General requirements for basic safety and essential performance - Collateral Standard: General requirements, tests and guidance for alarm systems in medical electrical equipment and medical electrical systems

7. *Electromagnetic Compatibility (EMC) Testing*

The TorEx Lung Perfusion System was tested by an independent laboratory to demonstrate that the system meets the requirements for EMC/EMI as outlined in IEC 60601-1-2 – *General requirements for basic safety and essential performance - Collateral Standard: Electromagnetic disturbances - Requirements and tests.* The test results demonstrated that the System met the applicable requirements of the EMC standard.

B. Animal Studies

The TorEx System was validated in a preclinical study using a porcine lung transplant model comparing the TorEx Lung Perfusion System to the Toronto General Hospital (TGH) Generation 1 EVLP System. The study was conducted under Good Laboratory Practice

standards, adhered to institutional animal protocols, and was performed under controlled conditions. In this study, donor lungs were retrieved from porcine donors (n=5 per group) following standard lung procurement procedures, then flushed with a preservation solution. Lungs were then randomly allocated to either the TorEx group (12h EVLP using TorEx Lung Perfusion System and TorEx Lung Perfusate (TLP)) or the Gen 1 group (12h EVLP using TGH Generation 1 EVLP System and STEEN Solution). The lungs were then cannulated, underwent a 12h EVLP, then the left lung was subsequently transplanted into a recipient pig with a 4 hour reperfusion period.

During the 12 hours of EVLP, standardized hourly assessments were performed to evaluate the performance of the lungs on the device. Results of the analysis showed that the TorEx Lung Perfusion System was successfully able to maintain stable lung physiology during the perfusion period with no significant differences in airway pressures, oxygenation, lung compliances, or hourly perfusate consumption. Lungs perfused on the TorEx Lung Perfusion System also demonstrated excellent post-transplant lung function, demonstrated by high partial pressures of oxygen within the transplanted graft (>300 mmHg). There were no significant differences in post-transplant acute lung injury scores, levels of cell death, or inflammatory profiles between the two groups. A summary of the preclinical data collected in this experiment is summarized in Table 3.

Table 3: Summary of Animal Study

Animal model	Porcine
Sample Size	N=5 per group
Methods	After lung procurement, the lungs were placed either on the TorEx Lung Perfusion System or the TGH Generation 1 EVLP System and were perfused for 12 hours with either STEEN Solution (Gen 1 System) or TorEx Lung Perfusate (TLP, TorEx System). Normothermic ex vivo lung perfusion (EVLP) was performed using detailed methodology, referenced as the Toronto Technique for EVLP. Hourly standardized functional assessments were performed to assess lung function during the procedure. Perfusate samples were taken hourly, and tissue biopsies were also collected throughout the procedure. Following the perfusion, the lungs were transplanted into a recipient animal (pig) following an established porcine left lung

	transplant model[1]. Post-transplant lung function was evaluated for a period of four hours.
Results	Results of the analysis showed that lungs perfused on the TorEx Lung Perfusion System with TLP successfully maintained stable lung function during the perfusion period with no significant differences in airway pressures, oxygenation, lung compliances, or hourly perfusate consumption. Lungs perfused on the TorEx Lung Perfusion System with TLP also demonstrated excellent post-transplant lung function, demonstrated by high partial pressures of oxygen within the transplanted graft (>300 mmHg).
Conclusion	Lungs perfused on the TorEx Lung Perfusion System with TLP were demonstrated to be safe, as evidenced by physiological variables related to perfusion and ventilation monitored during a twelve-hour perfusion period. This, along with physiologic performance during the post-transplant phase, supports the safety and effectiveness of the TorEx Lung Perfusion System and TorEx Lung Perfusate.

C. Additional Studies

A Human Factors study was conducted according to FDA guidance document "*Applying Human Factors and Usability Engineering to Medical Devices*". The study included 30 representative participants who were US residents (15 transplant physicians and 15 organ perfusion specialists), with varying levels of experience in ex vivo lung perfusion (EVLP). Participants represented the intended user population and included individuals with diverse clinical backgrounds and differing levels of familiarity with EVLP procedures.

The study was performed under simulated-use conditions designed to reflect the intended clinical environment and incorporated realistic use scenarios representative of routine clinical practice and all critical tasks associated with the use of the TorEx Lung Perfusion System.

Study results demonstrated that representative users successfully completed the evaluated critical tasks and operated the system as intended under simulated-use conditions using the provided labeling, training materials, and user interface. These findings support that use of the device can be safely generalized to transplant centers with varying levels of

EVLP experience.

X. SUMMARY OF PRIMARY CLINICAL STUDIES

The TorEx Lung Perfusion System has been commercially available in Canada since 2022. This device was developed and commercialized to implement the Toronto EVLP Technique and is equivalent to the Toronto General Hospital (TGH) Generation 1 EVLP System, which has been used clinically since 2008. EVLP procedures performed using these two systems serve as the primary source of clinical evidence for this original PMA.

Traferox provided data from two retrospective analyses to support the TorEx Lung Perfusion System for the safety and effectiveness of continuous normothermic machine perfusion of donor lungs, initially deemed unsuitable for transplantation, during which time the ex vivo function of the lungs can be reassessed for transplantation in adults. Descriptions of these retrospective analyses are presented in Table 4 below.

The device-specific retrospective studies, including the TorEx Study and Gen 1 Study, were conducted at a single institution. Both studies used the Toronto EVLP Technique, a standardized methodology extensively described in the scientific literature and adopted internationally. To complement the device-specific studies, a systematic literature review was conducted to characterize broader clinical use of the Toronto EVLP Technique across multiple transplant centers, patient populations, geographic regions, and levels of institutional EVLP experience. The review used a predefined PICO (Population, Intervention, Comparator, Outcome) framework in which the intervention was EVLP using the Toronto Technique, implemented using different EVLP devices, including technically related systems and non-equivalent platforms such as XPS. The identified literature is not direct device-specific evidence for the TorEx Lung Perfusion System but provides complementary evidence regarding the underlying clinical methodology and its broader implementation. Collectively, this evidence provides context for the clinical experience with EVLP-supported donor-lung assessment and transplantation beyond the single-center TorEx and Gen 1 studies. The clinical evidence should be considered in its totality, including the device-specific studies, and the published literature describing clinical experience with the Toronto Technique.

Table 4: Clinical Evidence

Title of the Analysis	EVLP Group	Control Group
1. TorEx Study: A retrospective study evaluating the outcomes of lungs assessed using the TorEx Lung Perfusion System: A single-center initial experience	n=221 Recipients of lungs perfused on the TorEx Lung Perfusion System	n=379 Recipients of lungs that did not undergo EVLP
2. Gen 1 Study: Retrospective study evaluating the impact of normothermic ex vivo lung perfusion on clinical outcomes at Toronto General Hospital	n=572 Recipients of lungs perfused on the TGH Generation 1 EVLP System (Gen 1 System)	n=1345 Recipients of lungs that did not undergo EVLP
3. Systematic Literature Review (SLR): Summary of published clinical experience with EVLP procedures using the Toronto Technique across multiple EVLP platforms	Recipients of lungs perfused on the: TorEx Lung Perfusion System, TGH Generation 1 EVLP System (Gen 1 System) or non-equivalent devices (e.g., XPS)	Recipients of lungs that did not undergo EVLP; Standard-of-care in lung preservation (static cold storage on ice)

Clinical Context of the Toronto EVLP Technique

The TorEx Lung Perfusion System implements the Toronto EVLP Technique, a standardized method of ex vivo lung perfusion originally developed and clinically validated by the Toronto Lung Transplant Program. The technique utilizes normothermic perfusion and protective mechanical ventilation to maintain donor lungs in a physiologically active state outside the body, enabling functional assessment of donor lungs prior to transplantation.

Since its initial development, the Toronto EVLP Technique has been extensively described in the peer-reviewed literature and has become one of the most widely adopted EVLP methodologies worldwide. The technique has been implemented at numerous transplant centers internationally and has supported thousands of clinical EVLP procedures. The methodology incorporates standardized protocols for donor lung assessment, circuit setup, perfusion management, ventilation strategies, physiologic monitoring, and transplant decision-making, thereby promoting consistent clinical application and reproducible outcomes.

Key characteristics of the Toronto EVLP Technique include the use of an acellular perfusate, maintenance of a closed left atrium, normothermic perfusion conditions, protective ventilation parameters, and comprehensive physiologic assessment of lung function during EVLP. These features were specifically developed to minimize edema formation, preserve pulmonary physiology, and enable reliable evaluation of donor lung suitability for transplantation. The technique has evolved through extensive preclinical and clinical investigation and serves as the foundation for the current clinical use of EVLP.

The TorEx Lung Perfusion System was specifically designed to support implementation of the Toronto EVLP Technique. The clinical studies submitted in support of this PMA were conducted using this established methodology, including the same fundamental perfusion and assessment principles that have been employed throughout the clinical development of EVLP at Toronto General Hospital. Accordingly, the clinical outcomes presented in this PMA reflect the performance of the TorEx Lung Perfusion System when used in accordance with the Toronto EVLP Technique and are representative of the intended clinical use of the device.

1. TorEx Study: Retrospective Study Evaluating the Outcomes of Lungs Assessed Using the TorEx Lung Perfusion System: A single-center initial experience

A. Study Design

The TorEx Study is a retrospective, non-randomized, single-center study describing outcomes of patients who received donor lungs that underwent EVLP with the TorEx Lung Perfusion System compared to patients who received donor lungs during the same time frame that did not undergo EVLP prior to transplantation (direct to transplantation). The study group consisted of recipients of lungs perfused on the TorEx Lung Perfusion (TorEx) System who underwent a lung transplant between Dec 6, 2022 and Nov 7, 2025. The control group consisted of patients who received a lung without EVLP according to standard-of-care (SOC) and underwent a lung transplant during the same period of time. The database for the TorEx Study reflected data collected through Jan 12, 2026 and included 600 patients. All patients underwent transplants at Toronto General Hospital and thus, there was one investigational site. The single-center design enhances internal validity by holding institutional practices, surgical technique, and perioperative management protocols constant. This reduces

variability attributable to center-level factors and permits evaluation of device performance under controlled implementation conditions.

This retrospective analysis of data reported from the Toronto Lung Transplant Program compared the outcomes of patients who received donor lungs perfused with the TorEx Lung Perfusion System compared to patients who received donor lungs during the same time frame that did not undergo EVLP prior to transplantation (SOC). In this study, donor lungs were retrieved as per standard protocols. After lung retrieval, the surgical decision to directly transplant the lungs, decline them for use, or place them on EVLP for further evaluation was made. Upon return to Toronto General Hospital, those indicated for ex vivo lung perfusion were perfused using the TorEx Lung Perfusion System. Ex vivo lung perfusion was carried out using standard protocols and assessment criteria. If the lungs were deemed suitable for transplantation, consented recipients were transplanted, and their clinical outcomes were followed.

The TorEx Study was conducted using either STEEN Solution or TLP, providing direct clinical experience with the use of TLP in the intended clinical setting. Specifically, 203 patients (91.9%) were perfused using STEEN Solution and 18 patients (8.1%) were perfused using TLP. STEEN Solution and TLP are identical in composition and key characteristics, so the clinical outcomes generated using STEEN Solution are scientifically relevant to the evaluation of the TorEx Lung Perfusion System when used with TLP.

Clinical Inclusion and Exclusion Criteria

Inclusion of patients in the retrospective TorEx study was limited to those who met the following inclusion criteria:

Donor Inclusion Criteria:

- Ex vivo lung perfusion clinically indicated for donor lungs (for TorEx group)
- Lungs of suitable quality to go directly to transplantation (for control group)

Recipient Inclusion Criteria:

- Actively listed for primary lung transplantation

- Written, informed consent for research provided
- Recipient received a lung transplantation between Dec 6, 2022, to Nov 7, 2025

Patients were not permitted to enroll in the TorEx Study if they met any of the following exclusion criteria:

Donor Exclusion Criteria:

- Donor lungs unsuitable for transplantation

Recipient Exclusion Criteria:

- Refusal of research consent
- Recipient received a lung transplantation before Dec 6, 2022, or after Nov 7, 2025

Follow-up Schedule

All 600 patients were monitored throughout the pre-operative and peri-operative phases, as well as following transplantation. Post-transplant assessments were conducted according to standard-of-care from the time of transplantation until loss to follow-up or the database lock date. For the 12-month survival outcome, 156 patients were lost to follow up or were incomplete at the database lock (Jan 12, 2026), as the lock occurred approximately two months after the most recent transplant included in the analysis.

Preoperatively, donor lungs were evaluated for transplantation, and the following information was gathered:

- Age
- Sex
- BMI
- Race
- Ethnicity
- Donor type
- Last PaO2/FiO2 Ratio Measurement
- Cigarette use
- Cause of Death

Postoperatively, the following data was collected

- Transplant type
- Total lung preservation time
- Grade 3 primary graft dysfunction at 72 h
- Post-operative extracorporeal membrane oxygenation support
- Survival at 30-days, 90-days and 1-year
- Development of chronic lung allograft dysfunction
- Length of post-transplantation hospital stay
- Length of post-transplantation ICU stay
- Duration of post-transplantation ventilation (days)

Clinical Endpoints

The objective of this retrospective analysis was to describe group-specific clinical outcomes among recipients of TorEx EVLP-treated lungs and recipients of lungs transplanted without EVLP from Dec 6, 2022 to Nov 7, 2025.

The primary outcome for the TorEx study was defined as the **incidence of Primary Graft Dysfunction Grade 3 (PGD3) at 72 hours post-transplantation**. Grade 3 primary graft dysfunction was defined by the presence of pulmonary edema on post-operative chest X-ray and a ratio of partial pressure of oxygen in arterial blood to fraction of inspiratory oxygen of less than 200 mmHg (Pa_{O2}/Fi_{O2} ratio).

The following were specified as secondary endpoints:

- Length of post-transplantation mechanical ventilation
- Length of post-transplantation hospital stay
- Length of post-transplantation ICU stay
- Survival analysis (interpreted as all-cause mortality)
- CLAD-Free Survival

B. Accountability of PMA Cohort

At the time of database lock, 600 patients were included in the TorEx study (221 in the

EVLP group and 379 in the SOC control group).

The primary outcome (PGD3) was not available for 17 patients in the EVLP group, and 30 patients in the control group.

For the 90-day survival outcome, 24 patients were lost to follow up or incomplete at database lock (8 in the EVLP group and 16 in the control group). Similarly for 12-month survival, 156 patients were lost to follow up or incomplete at database lock (60 in the EVLP group and 96 in the control group).

C. Study Population Demographics and Baseline Parameters

The study was conducted at a single Canadian transplant center. Nevertheless, selected donor and recipient characteristics were broadly similar to those reported for U.S. lung transplant populations, including major transplant indications, age, sex, body mass index, donor smoking history, and transplant type. Although healthcare delivery and financing differ between Canada and the United States, lung transplant programs in both countries operate within a broadly similar North American clinical context and consider medical urgency, donor–recipient suitability and expected transplant benefit. These demographic and clinical similarities support the relevance of the Canadian experience to U.S. practice but do not independently establish that outcomes will be reproduced across U.S. centers, which may differ in patient selection, EVLP experience, clinical practices, and operator expertise.

The racial distribution in the EVLP donor group was 68.7% White, 1.8% Black, 4.1% Asian, and 25.3% other races. Ethnicity was reported with 0.9% of the EVLP donor group participants who identified as Hispanic/Latino and 21.7% categorized as Unknown/Not Reported. The mean donor age (49.5±15.4 years) and sex distribution (36.7% female) in the EVLP donor group are also reasonably consistent with national trends observed in lung donor populations.

D. Safety and Effectiveness Results

Safety and Effectiveness Results

The incidence of PGD3 at 72 hours post-transplantation was 16/204 (7.8%) in the EVLP group compared to 38/349 (10.9%) in the SOC group, reflecting a reasonably comparable

clinical outcome between the groups – considering the benefit of EVLP. For additional context, a 2023 U.S. review reported PGD3 incidences of 24.9% and 22.3% for portable and static EVLP systems, respectively, even though differences in patient selection, device platforms, clinical practices, and outcome ascertainment limit direct cross-study comparisons.

The secondary endpoints further support the consistency of outcomes between the groups. The 12-month survival rate was 132/161 (82.0%) in the TorEx group and 231/283 (81.6%) in the non-EVLP control group, indicating reasonably comparable long term clinical outcomes – considering the benefit of EVLP. Functional recovery metrics, such as duration of mechanical ventilation (mean 9.5 days versus 5.8 days), ICU stay (mean 12.0 days versus 10.2 days), and hospital length of stay (mean 35.0 days versus 35.1 days) were reasonably comparable between the EVLP and control groups respectively. These findings fall within normal clinical variability and demonstrate no meaningful difference in postoperative recovery or resource utilization compared to conventional transplantation.

The utilization rate of donor lungs assessed on the TorEx Lung Perfusion System during the time period of this study was 66% (221 of 336 lungs assessed were transplanted). These lungs were initially considered not suitable for transplantation based on standard clinical assessment and were subsequently evaluated using the TorEx System, thereby increasing utilization of donor lungs that would otherwise have been declined for transplantation and increasing access to transplantation for patients who otherwise may remain on the waitlist.

Collectively, the TorEx study provides favorable device-specific clinical experience from a high-volume transplant center. However, the study's retrospective, nonrandomized design means that between-group comparisons are descriptive and do not independently establish comparative effectiveness. Further, the single-center study introduces uncertainty regarding the generalizability of the results. Therefore, the observed PGD3, survival, and postoperative recovery outcomes, together with the clinical value of enabling assessment and transplantation of donor lungs that might otherwise be declined, was considered only as part of the totality of evidence supporting a favorable benefit–risk profile for the clinical use of the TorEx Lung Perfusion System.

Subgroup Analyses

Descriptive subgroup analyses provide additional supportive information regarding PGD3 outcomes across racial and ethnic groups. Observed rates of PGD3 at 72 hours were similar between EVLP and SOC across the racial subgroups, including White (10.9% versus 13.1%), Asian (0.0% versus 3.4%) and Black donors (25% versus 0%; noting the small sample size of 4 patients). Observed rates of PGD3 at 72 hours were also similar between EVLP and SOC by ethnicity, including Hispanic or Latino donors (0% versus 0%), not Hispanic or Latino donors (10.3% versus 11.4%), and donors of unknown ethnicity (0% versus 8.6%). The larger subgroup results were generally consistent with the overall study findings and provide supportive context regarding use of TorEx across diverse donor groups. Results from the smallest subgroups should be interpreted cautiously because of limited precision.

Pediatric Extrapolation

In this premarket application, existing clinical data was not leveraged to support approval of a pediatric patient population.

E. Use of Real-World Evidence

Clinical evidence supporting the TorEx Lung Perfusion System includes retrospective analyses derived from routine clinical practice within the Toronto Lung Transplant Program, one of the world's largest and most experienced lung transplant and ex vivo lung perfusion (EVLP) programs. These studies were based on real-world clinical data collected as part of standard patient care and reflected the actual use of EVLP in donor lung assessment, donor lung utilization, and lung transplantation.

The underlying real-world data (RWD) sources included comprehensive donor, recipient, procedural, and post-transplant outcome information maintained within established clinical databases and transplant records. Data were available across the continuum of care, including donor evaluation, EVLP procedures, transplantation, hospitalization, and post-transplant follow-up. These data sources enabled assessment of clinically relevant outcomes including donor lung utilization, primary graft dysfunction, survival, length of stay, and other transplant-related outcomes.

The Sponsor evaluated the relevance and reliability of the RWD sources in accordance with principles outlined in the FDA guidance "*Use of Real-World Evidence to Support Regulatory Decision-Making for Medical Devices*" Specifically, the Sponsor assessed whether the underlying data sources contained sufficient detail to address the study objectives, provided longitudinal follow-up across the patient care pathway, captured clinically relevant variables necessary for outcome assessment, and reflected routine clinical practice within the intended use population. Data collection occurred contemporaneously with clinical care, minimizing recall bias and supporting accurate capture of procedural and clinical outcomes.

The Sponsor further evaluated the continuity of patient care represented within the data sources, the availability of follow-up information, the timing of data collection and database updates, and the potential impact of changes in clinical practice patterns over time. Standardized clinical definitions and established transplant program procedures were utilized to support consistency in data collection and outcome assessment. Data quality review procedures were implemented to identify missing data, resolve inconsistencies, and verify key study variables prior to analysis.

Table 5: Use of Real-World Evidence

RWD Relevance Element	Assessment
Sufficient detail to capture study variables and address study objectives	Donor, recipient, procedural, EVLP, and post-transplant outcome data were available to evaluate all predefined study endpoints.
Longitudinality of data source	Data was available from donor evaluation through transplantation and post-transplant follow-up.
Continuity of care	Clinical outcomes were captured within an integrated transplant program with longitudinal patient follow-up.
Timing of data collection and availability	Data was collected during routine clinical care and maintained within established clinical databases.
Changes in clinical practice over time	RWD considered for the studies reflect the current clinical environment. Study design considered temporal changes in donor management, EVLP utilization, and transplant practices. Primary and secondary outcomes were clearly defined, including the use of established diagnostic criteria for PGD3, and were assessed consistently across the study population.

RWD Relevance Element	Assessment
Timing of database updates	Clinical databases were routinely maintained and updated throughout the study period.
Integration of data sources	Relevant donor, recipient, procedural, and outcome information were obtained from established clinical and transplant databases maintained by the institution.
Data linkage methodology	Data was linked using unique patient and transplant identifiers maintained within institutional clinical systems.
Missing data and data consistency	Data review procedures were performed to identify missing information, resolve discrepancies, and verify critical study variables prior to analysis.
Patient privacy protections	Analyses were conducted under institutional ethics oversight using de-identified or appropriately protected patient information.
Representativeness of study population	The study population consisted of donor lungs and consecutive transplant recipients managed according to routine clinical practice and reflected the intended use population for EVLP-based donor lung assessment and transplantation.

The real-world evidence was considered as part of the totality of evidence supporting the safety and effectiveness of the TorEx Lung Perfusion System and was evaluated alongside non-clinical performance testing, biocompatibility testing, software verification and validation, human factors validation, and published clinical literature. Collectively, these data provide evidence regarding the performance of the device when used in routine clinical practice and in accordance with the Toronto EVLP Technique.

2. Gen 1 Study: Retrospective study report evaluating the impact of normothermic ex vivo lung perfusion on clinical outcomes at Toronto General Hospital

A. Study Design

The Gen 1 Study is a retrospective analysis of over 1000 patients and provides a comprehensive review of the clinical EVLP experience at Toronto General Hospital using the TGH Generation 1 System (also referred to as the Gen 1 System). Outcomes of recipients of lungs perfused on the Gen 1 System who underwent a lung transplant between Sep 01, 2008 to Dec 31, 2022 were compared to outcomes of recipients of lungs who were transplanted

without EVLP, according to standard-of-care (SOC) during the same time frame. The database for the Gen 1 Study reflected data collected through October 4, 2024 and included 1917 patients. All patients underwent transplants at Toronto General Hospital and thus there was one investigational site. The single-center design enhances internal validity by holding institutional practices, surgical technique, and perioperative management protocols constant. This reduces variability attributable to center-level factors and permits clearer evaluation of device performance under controlled implementation conditions.

This retrospective analysis of data reported from the Toronto Lung Transplant Program compared outcomes between lung transplant recipients who received ex vivo lung perfusion (EVLP)-treated lungs and those who received conventionally transplanted lungs (without EVLP) according to standard-of-care (SOC), during the period when the Toronto General Hospital (TGH) Gen1 System was in clinical use. The Gen 1 System is functionally and technically equivalent to the TorEx Lung Perfusion System as demonstrated through preclinical testing. Accordingly, the extensive Gen 1 clinical experience provides relevant supportive evidence regarding use of the Toronto EVLP Technique and contributes to the totality of evidence supporting the safety and effectiveness of the TorEx Lung Perfusion System. Because the clinical data were generated using the predecessor Gen 1 System, they are appropriately interpreted as supportive evidence rather than direct TorEx-specific clinical experience.

In this study, donor lungs were retrieved as per standard protocols. After lung retrieval, the surgical decision to directly transplant the lungs (control group), decline them for use, or place them on EVLP for further evaluation was made. Upon return to Toronto General Hospital, those indicated for ex vivo lung perfusion were perfused using the Gen 1 System. Ex vivo lung perfusion was carried out using standard protocols and assessment criteria. The Toronto General Hospital (TGH) Generation 1 EVLP study was conducted exclusively using STEEN Solution. STEEN Solution and TLP are identical in composition and key characteristics, so the clinical outcomes generated using STEEN Solution are scientifically relevant to the evaluation of ex vivo lung perfusion procedures when performed using TLP. If the lungs were deemed suitable for transplantation, consented recipients were transplanted, and their clinical outcomes were followed (EVLP group). The total initial sample size was fixed at the size of the lung transplant database, with a fixed number of patients receiving

lungs that have undergone EVLP.

Clinical Inclusion and Exclusion Criteria

Inclusion of patients in the study was limited to those who met the following inclusion criteria:

Donor Inclusion Criteria:

- Ex vivo lung perfusion clinically indicated for donor lungs and lungs perfused on TGH Generation 1 EVLP System (for EVLP group)
- Lungs of suitable quality to go directly to transplantation (for control group)

Recipient Inclusion Criteria:

- Actively listed for primary lung transplantation
- Written, informed consent for research provided
- Recipient received a lung transplantation between Sep 1 2008 to Dec 31 2022

Patients were not included in the study if they met any of the following exclusion criteria:

Donor Exclusion Criteria:

- Donor lungs unsuitable for transplantation

Recipient Exclusion Criteria:

- Refusal of research consent
- Recipient received a lung transplantation before Sep 1 2008 or after Dec 31 2022

Follow-up Schedule

All patients were monitored throughout the pre-operative and peri-operative phases, as well as following transplantation according to standard-of-care from the time of transplantation until loss to follow-up or the database lock date. Two patients were lost to follow up at 90 days, and 14 patients were lost to follow up at 12 months.

Preoperatively, donor lungs were evaluated for transplantation, and the following information was gathered:

- Age

- Sex
- BMI
- Race
- Ethnicity
- Donor type
- Last PaO2/FiO2 Ratio Measurement
- Cigarette use
- Cause of Death

Postoperatively, the following data was collected

- Transplant type
- Total lung preservation time
- Grade 3 primary graft dysfunction at 72 h
- Post-operative extracorporeal membrane oxygenation support
- Survival at 30-days, 90-days and 1-year
- Development of chronic lung allograft dysfunction
- Length of post-transplantation hospital stay
- Length of post-transplantation ICU stay
- Duration of post-transplantation ventilation (days)

Clinical Endpoints

With regards to safety and effectiveness, the primary objective of this study was to compare outcomes of lung transplants performed from Sep 1 2008 to Dec 31 2022 using lungs perfused on the Gen 1 System with the outcomes of control patients transplanted during the same study period without EVLP.

The primary endpoint for the Gen1 Study was the **incidence of Primary Graft Dysfunction Grade 3 (PGD3) at 72 hours post-transplantation**. Grade 3 primary graft dysfunction was defined by the presence of pulmonary edema on post-operative chest X-ray and a ratio of partial pressure of oxygen in arterial blood to fraction of inspiratory oxygen of less than 200 mmHg (Pa_{O2}/Fi_{O2} ratio).

The following were specified as secondary endpoints:

- Length of post-transplantation mechanical ventilation
- Length of post-transplantation hospital stay
- Length of post-transplantation ICU stay
- Survival analysis (interpreted as all-cause mortality)
- CLAD-Free Survival

B. Accountability of PMA Cohort

At the time of database lock (October 4th, 2024), 1917 patients were included in the Gen 1 Study (572 in the EVLP group and 1345 in the SOC control group). For survival outcomes, two patients were lost to follow up at 90 days, and 14 patients were lost to follow up at 12 months.

C. Study Population Demographics and Baseline Parameters

Donor and recipient demographics in this single-center Canadian cohort were broadly similar to those reported for U.S. lung transplant populations. These similarities support the clinical relevance and applicability of the study findings to U.S. practice, while recognizing that differences among centers in patient selection, EVLP experience, clinical practices, and operator expertise may affect the reproducibility of outcomes.

The racial distribution in the EVLP donor group was 73.8% White, 3.8% Black, 5.1% Asian, and 17.3% other races. Ethnicity was reported with 1.6% of EVLP donor group participants who identified as Hispanic/Latino and 15.6% categorized as Unknown/Not Reported. The mean donor age (44.8±15.6 years) and sex distribution (36.9% female) in the EVLP donor group are also reasonably consistent with national trends observed in lung donor populations.

Donor cigarette use, a known clinical risk factor, was present in approximately 58.6% of EVLP donors, reflecting similar smoking prevalence among U.S. lung donors. Donor BMI values (mean 28.0±6.7) fall within the expected range for the general population. Recipient characteristics also align closely with national lung transplant recipient profiles. The most common underlying diagnoses included interstitial lung disease (51.7%), obstructive lung disease (30.2%), and cystic fibrosis (8.4%), mirroring distributions reported in U.S. transplant centers. Transplant types were predominantly bilateral (75.3%), consistent

with standard of care in North America. Recipient body weights (mean ~70 kg) were also similar to values observed in U.S. registry cohorts.

The demographic similarities support the clinical relevance of the observed cohort to U.S. lung transplant practice and contribute to the external applicability of these findings to clinical settings within the United States.

D. Safety and Effectiveness Results

Safety and Effectiveness Results

The incidence of PGD3 at 72 hours post-transplantation was 76/566 (13.4%) in the EVLP group compared to 166/1340 (12.4%) in the SOC group, reflecting a reasonably comparable clinical outcome between the groups – considering the benefit of EVLP. For additional context, a 2023 U.S. review reported PGD3 incidences of 24.9% and 22.3% in portable and static EVLP systems, respectively[2], even though differences in patient selection, device platforms, clinical practices, and outcome ascertainment limit direct cross-study comparisons.

The 12-month survival outcomes are reasonably comparable between groups, with a rate of 1158/1334 (86.8%) in the EVLP group, and 488/569 (85.8%) in the SOC group. Functional recovery metrics, such as duration of mechanical ventilation (mean 5.0 days versus 7.0 days), ICU stay (mean 9.2 days versus 11.4 days), and hospital length of stay (mean 37.2 days versus 39.9 days), were reasonably comparable between the EVLP and SOC groups respectively. This also showed no clinically meaningful differences, suggesting that EVLP does not lead to increased resource utilization or delayed recovery.

Further, the utilization rate of donor lungs that were assessed using EVLP during the time period of this study was 67% (572 of 851 lungs assessed were transplanted). These lungs were initially considered not suitable for transplantation based on standard clinical assessment and were subsequently evaluated using EVLP, thereby increasing utilization of donor lungs that would otherwise have been declined for transplantation.

The findings demonstrate that patients receiving EVLP-treated lungs experienced clinical outcomes reasonably comparable to those who received conventionally transplanted lungs.

EVLP enables the evaluation and use of donor lungs that would otherwise have been declined under standard criteria, thereby expanding the donor pool. This allows more patients to proceed to transplantation who might otherwise remain on the waitlist, where the risk of morbidity and mortality is significant. The increased transplant rates and reduced waitlist mortality positively contribute towards the overall benefit-risk profile assessment. The observed difference in early risk is outweighed by the meaningful clinical benefit associated with improved access to life-saving transplantation. The observed clinical outcomes, considered together with this meaningful benefit, positively contribute towards the overall benefit–risk profile assessment for the Gen 1 System and provide relevant supportive evidence for TorEx. Between-group comparisons are presented descriptively in recognition of the retrospective study design. Finally, the single-center study introduces uncertainty regarding the generalizability of the results. Therefore, the result of this study was also considered only as part of the totality of evidence supporting a favorable benefit-risk profile for the clinical use of the TorEx Lung Perfusion System.

Subgroup Analyses

Subgroup analyses by race and ethnicity were conducted using descriptive statistics. Rates of PGD3 at 72 hours were similar between EVLP and SOC across donor subgroups, including White (14.1% versus 12.1%), Asian (17.2% versus 12.7%) and Black (4.5% versus 11.4%) donors. By ethnicity, rates were also reasonably comparable: Hispanic or Latino (11.2% versus 19.2%), Not Hispanic or Latino (14.1% versus 11.9%) and Unknown (10.2% versus 10.6%) for EVLP and SOC donor groups respectively. These results provide clinically useful descriptive experience across diverse donor groups and support the relevance of the Gen 1 clinical evidence to a diverse U.S. transplant population. Because the study was not designed to provide definitive subgroup comparisons, results for groups with smaller sample sizes and event counts should be interpreted cautiously.

Pediatric Extrapolation

In this premarket application, existing clinical data was not leveraged to support approval of a pediatric patient population.

3. Systematic Literature Review (SLR)

A. Purpose

The purpose of this literature review is to summarize the published clinical evidence regarding the safety and effectiveness of the Toronto EVLP Technique across multiple EVLP platforms, including the TGH Generation 1 System, the functionally and technically equivalent TorEx Lung Perfusion System, and other platforms implementing the technique, such as XPS. The breadth of this literature provides supportive evidence regarding the established clinical methodology, its implementation across centers and patient populations, and the clinical outcomes reported with EVLP-supported donor-lung assessment and transplantation. Studies using platforms other than TorEx are interpreted as complementary evidence within the totality-of-evidence framework and provide important clinical context alongside the device-specific TorEx and Gen 1 evidence. The device-specific TorEx and Gen 1 evidence are based on a single-center experience, which creates uncertainty regarding the generalizability of the results, and this literature review helps to reduce uncertainty.

B. Literature Search Protocol

A comprehensive literature search was performed to identify relevant primary studies on the use of EVLP for lung transplantation. To achieve this, structured search strategies were performed in the following bibliographic databases including PubMed, EMBASE, and Cochrane Central to identify randomized and non-randomized clinical studies that compared the use of EVLP with the standard of care in lung preservation (static cold storage on ice). The search strategy was established prior to data extraction. The search was executed and last updated on May 29, 2026. The search was performed using a list of pre-defined search terms and Boolean operators with no time restriction: (EVLP OR ex vivo lung perfusion) AND (clinical OR outcome) AND (lung transplant OR lung transplantation). Keyword search was performed in title/abstract. Duplicate articles were removed.

Study screening was performed to include clinical studies that compared the use of EVLP for lung transplantation using the subject device (TorEx Lung Perfusion) or any other equivalent/similar device (i.e., TGH Generation 1 System or XPS system) with a control group (non-EVLP transplants). Methods used to select studies were based on the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines.

Screening was performed by two reviewers first on title/abstract and study eligibility was then confirmed by full-text. Disagreements were resolved through consultation with a third party. A PICO (Population, Intervention, Comparator, Outcome) framework was established to guide the systematic literature review. Specifically, the inclusion criteria were as follows: 1) the population was patients that received single or double lung transplantation using donor lungs of standard criteria or extended criteria; 2) the intervention was EVLP using the Toronto Technique for EVLP, which could be performed by different devices that are equivalent or non-equivalent; 3) the comparator was transplants using donor lungs preserved with standard cold static preservation without EVLP (non-EVLP transplants); 4) the primary outcome was primary graft dysfunction grade 3 (PGD3) at 72 hours post-transplant and secondary outcomes included utilization rate after EVLP, days on mechanical ventilation, intensive care, hospital length of stay, and survival. The PICO framework was developed to identify evidence relevant to the Toronto EVLP Technique and the resulting literature provides information regarding the broader clinical experience, reproducibility, and implementation of this methodology across multiple transplant centers, healthcare systems, and geographic regions.

The resulting literature characterizes the broader clinical experience, implementation, and reported outcomes associated with the Toronto EVLP Technique across multiple transplant centers, healthcare systems, and geographic regions. The PICO framework reflects the intended use of the TorEx Lung Perfusion System and supports evaluation of the clinical evidence concerning the underlying EVLP methodology implemented by the device.

C. Results

Fourteen studies met the inclusion criteria for the literature review. Out of the fourteen comparative studies, four were prospective non-randomized (three single center [3–5]and one multi-center [6]), one was a single-center prospective randomized [7], and nine were single-center retrospective [8–16]. The studies were conducted between 2007 to 2024 in centers across Europe (n=7), Canada (n=5), and US (n=2).

Eleven studies, including one RCT by Slama et al, reported rates of PGD3 at 72 hours as an endpoint (Table 6).

Table 6: Systematic Literature Review: PGD3 at 72 hours

Study	EVLP Recipients	Non-EVLP Recipients	PGD3 at 72h EVLP	PGD3 at 72h Non-EVLP	P
Cypel et al. (2011)	20	116	15%^	30%^	0.11
Cypel et al. (2012)	50	253	2%	8.5%	0.14
Zych et al. (2012)	6	86	NR	NR	NR
Aigner et al. (2012)	9	119	0.0%	NR	NR
Bonffini et al. (2014)	8	28	0.0%	25.0%	0.14
Sage et al. (2014)	31	81	9.5%	8.5%	1.0
Machuca et al. (2015)	28	27	3.0%	18.0%	0.1
Slama et al. (2017)	35	41	2.9%^	2.4%^	1.0
Koch et al. (2018)	9	41	0.0%	0.0%	NS
Zhang et al. (2018)	9	18	0.0%	11.0%	NS
Divithotawela et al. (2019)	230	706	8.0%	11.0%	0.75 (0.44-1.27)*
Noda et al. (2023)	51	99	33.3%	20.2%	0.08
Gouchoe et al. (2024)	110	115	DCD 29% DBD 12%	10.00%	0.026 (all) 0.043 (DCD versus DBD)
Keshavjee et al. (2026)	659	1556	12.8%	10.9%	0.9141

Values are shown in median (range-) or median (IQR,) or mean
^ PGD grade 2 or 3 reported
* Odds ratio for EVLP (95% Confidence Interval)
NR – not reported
NS – not significant

The RCT study by Slama et al compared the use of standard criteria donor lungs in EVLP and non-EVLP transplants, thereby allowing objective evaluation of the safety of this technique. The study reported similar PGD3 at 72 hours (2.9% versus 2.4%, EVLP versus non-EVLP, P=1.0).[7] In the nonrandomized studies, ECD lungs were utilized for the EVLP group. Out of the nonrandomized studies, nine studies that used the TGH Generation 1 System reported PGD3 and found no statistical difference between the EVLP and the non-EVLP group at 72 hours (0-15% versus 0-30% respectively).[3–5,8–12,14,16] Amongst the studies, Machuca et al specifically evaluated the impact of EVLP on donation after circulatory death (DCD) lungs. The study reported a PDG3 rate of 3% in the EVLP group and 18% in the non-EVLP group (P=0.10).[11] Of note, Keshavjee et al reported on the experience of one thousand cases of EVLP, with over 100 cases performed on the TorEx Lung Perfusion System and the remaining using TGH Generation 1 System. No difference was found in the overall PGD3 at

72 hours (12.8% versus 10.9%, EVLP versus non-EVLP, P=0.9141). While this study did not report sub-group analysis on TorEx, the authors cited an earlier abstract[17] that evaluated the initial 100 TorEx transplants. PGD3 at 72 hours in the TorEx cases was 13%, similar to the overall cohort. This is also true for ICU length of stay, hospital length of stay and overall survival.

The study by Zhang et al, which used the Lung Assist device, also reported no significant difference between PGD3 incidence in the EVLP and non-EVLP group (0% versus 11%, P=NS).[13] Noda et al [15] and Gouchoe et al[6] reported single and multi-center experience using the XPS device. The study by Noda et al reported PGD3 at 72 hours of 33.3% in the EVLP group and 20.2% in the non-EVLP group (P=0.08). Gouchoe et al conducted an unplanned post-hoc analysis that compared transplants of DCD lungs after EVLP, donation after brain death (DBD) lungs after EVLP and standard criteria lungs without EVLP. The study found that the use of DCD EVLP lungs was associated with a significantly higher rate of PGD3 (29%) when compared to non-EVLP group (10%, P=0.026) and DBD EVLP (12%, P=0.043).

All fourteen studies compared survival (with different cutoffs) after transplant among the EVLP recipients and non-EVLP recipients and found no statistical difference in any of the survival endpoints (Table 7).

Table 7: Systematic Literature Review: Survival

			30-Day Survival			**90-Day Survival**			**1-Year Survival**		
Study	**EVLP Recipients**	**Non-EVLP Recipients**	**EVLP**	**Non-EVLP**	**P**	**EVLP**	**Non-EVLP**	**P**	**EVLP**	**Non-EVLP**	**P**
Cypel et al. (2011)	20	116	90%	95%	0.33	NR	NR	NR	NR	NR	NR
Cypel et al. (2012)	50	253	96%	96%	1.00	NR	NR	NR	87%	86%	NR
Zych et al. (2012)	6	86	NR	NR	NR	100%	90%	NS	NR	NR	NR
Aigner et al. (2012)	9	119	100 %	96%	0.6	NR	NR	NR	NR	NR	NR
Bonfanti et al. (2014)	8	28	88%	82%	0.64	NR	NR	NR	NR	NR	NR
Sage et al. (2014)	31	81	97%	96%	0.69	NR	NR	NR	93%	92%	0.8

Machuca et al. (2015)	28	27	93%	100%	NS	NR	NR	NR	77%	92%	NS
Slama et al. (2017)	35	41	97%	100%	0.46	NR	NR	NR	NR	NR	NR
Koch et al. (2018)	9	41	91%	100%	NS	NR	NR	NR	NR	NR	NR
Zhang et al. (2018)	9	18	NR	NR	NR	NR	NR	NR	89%	94%	NS
Divithotawela et al. (2019)	230	706	NR	NR	NR	NR	NR	NR	NR	NR	NR
Noda et al. (2023)	51	99	NR	NR	NR	NR	NR	NR	90.2%	89.8%	NS
Gouchee et al. (2024)	110	115	NR	NR	NR	NR	NR	NR	DCD 89% DBD 85%	93.9%	NS
Keshavjee et al. (2026)	659	1556	98%	97%	NS	96%	95%	NS	86%	NR	NS

Nine studies reported 30-day survival, all of which used the TGH Generation 1 device. No statistical significance was observed in any of the studies. Across the studies, 30-day survival ranged from 88% to 100% in the EVLP patients and 82% to 100% in the non-EVLP patients.[3–5,7,8,10–12,16]

Two studies reported 90-day survival and found no difference between the groups (100% versus 90%, EVLP versus non-EVLP, P=NS).[9,16]

Seven studies reported 1-year survival. Of these, four used the TGH Generation 1 system: Cypel et al reported 87% versus 86%, EVLP versus non-EVLP, P=1.00;[9] Sage et al reported 93% versus 92%, P=0.8;[5] Machuca et al reported 77% versus 92%, EVLP versus non-EVLP, P=NS [11], and Keshavjee reported 68% survival in the EVLP group, P=NS[16]. One study used the Lung Assist system: Zhang et al (84% versus 94%, EVLP versus non-EVLP, P=NS). [13] Two studies used the XPS system and reported no difference in the 1-year survival: Noda et al (90.2% versus 89.8%, EVLP versus non-EVLP, P=NS) [15] and Gouchoe et al (89% vs 85% versus 93.9%, DCD EVLP versus DBD EVLP versus non-EVLP respectively, P=NS)[6].

The systematic literature review identified multiple studies evaluating the Toronto EVLP Technique across multiple transplant centers and patient populations. Across 14 included studies, PGD3 at 72 hours and post-transplant survival outcomes were generally similar between EVLP and non-EVLP cohorts. While the literature is not device-specific to the TorEx Lung Perfusion System, the predefined PICO framework, systematic evaluation of the

available evidence, and consistent findings across studies provide complementary evidence that should be considered as part of the totality of clinical evidence.

XI. FINANCIAL DISCLOSURE

The Financial Disclosure by Clinical Investigators regulation (21 CFR 54) requires applicants who submit a marketing application to include certain information concerning the compensation to, and financial interests and arrangement of, any clinical investigator conducting clinical studies covered by the regulation. The two clinical studies supporting this PMA application included two principal investigators. None of the clinical investigators had disclosable financial interests/arrangements as defined in sections 54.2(a), (b), (c), and (f). The information provided does not raise any questions about the reliability of the data.

XII. SUMMARY OF SUPPLEMENTAL CLINICAL INFORMATION

None.

XIII. PANEL MEETING RECOMMENDATION AND FDA'S POST-PANEL ACTION

In accordance with the provisions of section 515(c)(3) of the act as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the Gastroenterology and Urology Advisory Panel, an FDA advisory committee, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this panel.

XIV. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

A. Safety and Effective Conclusions

In the TorEx retrospective study, PGD3 at 72 hours was observed in 16/204 (7.8%) EVLP recipients and 38/349 (10.9%) non-EVLP recipients with available outcome status. Twelve-month survival was observed in 132/161 (82.0%) TorEx recipients and 231/283 (81.6%) non-EVLP recipients. Mean durations of mechanical ventilation were 9.5 and 5.8 days, mean ICU stays were 12.0 and 10.2 days, and mean hospital stays were 35.0 and 35.1 days, respectively. These results provide favorable device-specific clinical experience regarding PGD3, survival, postoperative recovery, and resource utilization following transplantation of TorEx EVLP-treated lungs.

In the Gen 1 retrospective study, PGD3 at 72 hours was observed in 76/566 (13.4%) EVLP recipients and 166/1340 (12.4%) non-EVLP recipients with available outcome status, reflecting a small numerical difference. Twelve-month survival was observed in 488/569 (85.8%) Gen 1 EVLP recipients and 1158/1334 (86.8%) non-EVLP recipients. Mean durations of mechanical ventilation were 5.0 and 7.0 days, mean ICU stays were 9.2 and 11.4 days, and mean hospital stays were 37.2 and 39.9 days, respectively. This large clinical experience provides substantial supportive evidence concerning EVLP-assisted donor-lung assessment and transplantation using a system demonstrated through preclinical testing to be functionally and technically equivalent to TorEx.

For additional context, a 2023 U.S. review reported PGD3 incidences of 24.9% and 22.3% for portable and static EVLP systems, respectively. Selected donor and recipient characteristics in the TorEx and Gen 1 studies were also broadly similar to those reported for U.S. lung transplant populations. These similarities support the clinical relevance of the Canadian experience to U.S. practice.

The systematic literature review used a predefined PICO framework and PRISMA-based study-selection procedures to evaluate published experience with the Toronto EVLP Technique. The 14 included studies documented PGD3, survival, utilization, postoperative recovery, and resource-use outcomes across multiple transplant centers, patient populations, geographic regions, and EVLP platforms. This literature provides complementary support for the established clinical methodology implemented by TorEx and places the device-specific evidence within the broader international EVLP experience.

Collectively, the evidence demonstrates the clinical value of EVLP in enabling assessment and transplantation of donor lungs that might otherwise be declined, thereby potentially expanding the donor pool and increasing access to life-saving transplantation. When considered with the nonclinical testing, device-performance evidence, biocompatibility testing, software verification and validation, human-factors validation, and published literature, the TorEx and Gen 1 clinical experience supports a favorable benefit–risk profile for the TorEx Lung Perfusion System – while also considering that a Post Approval Study (PAS) is required as the Condition of Approval (CoA) to confirm the pre-market data and to provide longer term evidence of safety and effectiveness. Based on FDA’s request, the

labeling should only descriptively present between-group results from the retrospective studies – as opposed to presenting the results as confirmatory comparative conclusions; this is because the two retrospective studies were unplanned and exploratory in nature.

Demographics

The demographic analyses conducted across the two retrospective studies were unplanned and exploratory in nature, performed post hoc to describe donor and recipient characteristics within each study cohort. Descriptive statistics were used to summarize demographic characteristics, and to assess the generalizability of the findings to the U.S. lung donor transplant population. In the retrospective analysis of 572 EVLP and 1345 non-EVLP recipients (Gen 1 Study), racial/ethnic distribution of donors in the EVLP group (73.8% White, 3.8% Black, 5.1% Asian) and primary recipient diagnoses (interstitial lung disease, obstructive disease, cystic fibrosis) were similar to U.S. transplant registry data. Likewise, in the retrospective analysis of 221 EVLP and 379 non-EVLP recipients (TorEx Study), racial/ethnic distribution of donors in the EVLP group (68.7% White, 1.8% Black, 4.1% Asian) and primary recipient diagnoses were similar to U.S. transplant registry data. The mean donor age for the Gen 1 and TorEx studies were (44.8, 49.5 years) and sex distribution (36.9%, 36.7% female) were also reasonably consistent with national trends observed in lung donor populations. Donor smoking history, BMI, and transplant types were also reflective of U.S. practice.

In summary, while demographic comparisons were not pre-specified, the analyses demonstrate that donor and recipient profiles across the TorEx and comparator cohorts are broadly representative of the U.S. donor lung transplant population. This supports the applicability of safety and efficacy findings to the intended U.S. patient population.

B. Benefit-Risk Determination

The benefits of the device are also based on data collected in clinical studies conducted to support PMA approval as described above.

In both studies, recipients of lungs perfused with the TorEx Lung Perfusion System, or the equivalent Gen 1 System, had comparable outcomes to the control groups (recipients of

lungs that went directly to transplantation). Results were comparable for the primary outcome of grade 3 primary graft dysfunction in both studies. There were also no clinically meaningful differences in secondary outcomes (including survival, length of post-transplantation mechanical ventilation, hospital length of stay and ICU length of stay) between the EVLP groups and the control groups in any of the studies.

The risks of the device are also based on data collected in clinical studies conducted to support PMA approval as described above. There were no device-related adverse effects reported in the retrospective studies. There were also no differences in safety outcomes shown in the preclinical study, as evidenced by several parameters, including lung function on EVLP and in recipients and histological analysis.

The alternatives available to lung transplant candidates such as waiting longer for a suitable donor organ without EVLP, undergoing EVLP with the XVIVO XPS system (Gothenberg, SE) or the TransMedics Organ Care System (Andover, MA) or ultimately not receiving a transplant at all, each carry their own limitations and risks. EVLP enables the evaluation and use of donor lungs that would otherwise have been declined under standard criteria, thereby substantially expanding the donor pool. This allows more patients to proceed to transplantation who might otherwise remain on the waitlist, where the risk of morbidity and mortality is significant. Importantly, the patient tolerance for risk in this context is high, as lung transplantation is often a last-resort, life-saving intervention. The TorEx Lung Perfusion System presents minimal added risk to the recipient, as donor lungs are assessed and treated ex-vivo prior to implantation, allowing for safe evaluation of organ viability without direct impact on the recipient during perfusion.

Lastly, while the device incorporates technological advancements, it is not novel in principle. The TorEx System uses the well-established Toronto EVLP Technique, and its safety and performance are strongly supported by extensive experience with the functionally and technically equivalent TGH Generation 1 EVLP System. Descriptive subgroup results across sex/gender, age, race, and ethnicity were generally consistent with the overall clinical experience and did not identify findings that materially altered the favorable benefit–risk assessment.

When considered in the context of increased transplant rates and reduced waitlist mortality,

the overall benefit-risk profile remains favorable. The potential, minimal differences in early risk are compared with the meaningful clinical benefit associated with improved access to life-saving transplantation. Taken together, these considerations positively contribute towards the overall benefit-risk profile assessment for the TorEx Lung Perfusion System.

This submission did not include specific information on patient perspectives for this device.

In conclusion, based on the available information, the data support that the benefits of the TorEx Lung Perfusion System with TorEx Lung Perfusate indicated for the continuous normothermic machine perfusion of donor lungs initially deemed unsuitable for transplantation, outweigh the associated risks – while also considering that a Post Approval Study (PAS) is required as the Condition of Approval (CoA) to confirm the pre-market data and to provide longer term evidence of safety and effectiveness.

C. Overall Conclusions

The data in this application support the reasonable assurance of safety and effectiveness of this device when used in accordance with the indications for use. Two retrospective clinical studies provide favorable and clinically relevant evidence regarding PGD3, mortality, survival, and postoperative recovery with the TorEx System and the functionally and technically equivalent TGH Generation 1 System. The study populations included donor and recipient characteristics broadly similar to those reported for U.S. lung transplant populations. Considered together with the nonclinical testing, device-performance evidence, human-factors validation, and published clinical literature, these findings support a favorable benefit–risk profile for the TorEx Lung Perfusion System – while also considering that a Post Approval Study (PAS) is required as the Condition of Approval (CoA) to confirm the pre-market data and to provide longer term evidence of safety and effectiveness.

D. Limitations of Clinical Evidence

The clinical evidence supporting the TorEx Lung Perfusion System includes retrospective analyses conducted within the Toronto Lung Transplant Program, one of the world's largest and most experienced programs in ex vivo lung perfusion (EVLP) and lung transplantation. These studies provide information regarding the use of the device within routine clinical practice and reflect the implementation of the Toronto EVLP Technique in a high-volume

clinical setting.

The clinical studies submitted in support of this PMA were conducted at a single institution using standardized clinical protocols, established transplant practices, and comprehensive clinical databases. While the studies reflect the experience of a single center, the underlying Toronto EVLP Technique has been extensively described in the peer-reviewed literature and has been adopted by transplant centers internationally. The broader published literature demonstrates successful implementation of this methodology across diverse clinical environments and patient populations.

The retrospective studies utilized real-world clinical data collected as part of routine patient care. These data provide insight into the performance of the TorEx Lung Perfusion System under actual clinical conditions and encompass donor, procedural, transplant, and post-transplant outcomes collected throughout the continuum of care. The Sponsor utilized predefined study protocols, established clinical databases, standardized endpoint definitions, and objective clinical outcome measures to support the relevance and reliability of the evidence.

The systematic literature review identified clinical studies evaluating the Toronto EVLP Technique across multiple institutions, healthcare systems, and geographic regions. While some publications evaluated EVLP systems that differ from the TorEx Lung Perfusion System in certain technological characteristics, these studies provide important context regarding the broader clinical experience, implementation, and adoption of the underlying EVLP methodology implemented by the TorEx Lung Perfusion System.

Accordingly, the assessment of safety and effectiveness for the TorEx Lung Perfusion System is based on the totality of evidence, including TorEx-specific clinical experience and supportive TGH Generation 1 EVLP System evidence, real-world clinical experience, published clinical literature, bench and performance testing, biocompatibility testing, software verification and validation activities, and human factors validation testing. Collectively, these data provide complementary evidence supporting the safety and effectiveness of the TorEx Lung Perfusion System when used in accordance with its intended use and the Toronto EVLP Technique – while also considering that a Post Approval Study (PAS) is required as the Condition of Approval (CoA) to confirm the pre-

market data and to provide longer term evidence of safety and effectiveness.

XV. CDRH DECISION

CDRH issued an approval order on July 15, 2026. The final clinical conditions of approval cited in the approval order are described below.

In addition to the Annual Report requirements, the sponsor must provide the following data in post-approval study (PAS) reports for each PAS listed below.

1. The "*TorEx Study Continuation Long-Term Post-Approval Study*" is an observational, dual-arm, single-center continuation study designed to evaluate the long-term safety and effectiveness of the TorEx Lung Perfusion System in subjects previously enrolled in the premarket TorEx Study submitted in support of the P250025 PMA. The purpose of this study is to obtain long-term post-transplant follow-up data for up to 5 years for all subjects enrolled in the premarket TorEx Study (n = 221 in the TorEx group; n = 379 in the control group). The TorEx group consists of subjects who underwent lung transplantation at Toronto General Hospital and received donor lungs evaluated using the TorEx Lung Perfusion System between December 6, 2022, and November 7, 2025. The control group consists of subjects who underwent lung-only transplantation using conventional cold static preservation (without EVLP) at the same site during the same calendar period. The study is a closed-enrollment retrospective continuation of the premarket study population. The study will follow all enrolled subjects through November 7, 2030 (five years post-transplant for the last enrolled subject). Data completeness will be reviewed at least annually, with particular focus on survival status, chronic lung allograft dysfunction (CLAD), and airway complications. The primary endpoint is patient survival at 1-year post-transplantation. Secondary endpoints include: patient survival at 2, 3, 4, and 5 years post-transplantation; pulmonary function (FEV1) at 1, 2, 3, 4, and 5 years; chronic lung allograft dysfunction (CLAD)-free survival at 1, 2, 3, 4, and 5 years; incidence of Bronchiolitis Obliterans Syndrome (BOS) at 1, 2, 3, 4, and 5 years; and incidence of airway anastomotic complications (including airway ischemia, bronchial anastomotic stricture requiring intervention, bronchial dehiscence, and

bronchial necrosis) within 12 months of transplantation. As the study is a retrospective continuation of the premarket study population, all analysis will be considered descriptive in nature.

PAS Progress Reports must be submitted every six (6) months for the first year and annually thereafter, from the date of the PMA approval letter, unless otherwise specified by FDA. The Final PAS Report should be submitted no later than three (3) months after study completion (i.e., last subject's last follow-up date).

2. The "*TorEx Lung Perfusion System Post-Approval Study*" is a prospective, observational, single-arm, multi-center, all-comers study designed to evaluate the long-term safety and effectiveness of the TorEx Lung Perfusion System under real-world clinical conditions following PMA approval. The purpose of this study is to collect longitudinal outcome data on lung transplant recipients receiving donor lungs evaluated using the TorEx Lung Perfusion System at all United States transplant centers that receive the device. The study will enroll all consecutive, eligible transplant recipients receiving TorEx-evaluated donor lungs at participating centers during a 5-year enrollment period following PMA approval. An external concurrent control cohort of contemporaneous lung transplant recipients receiving donor lungs preserved using conventional cold static preservation (without EVLP) will be derived from the Organ Procurement and Transplantation Network (OPTN) Standard Transplant Analysis and Research (STAR) database for purposes of benchmarking and contextualizing primary endpoint outcomes; this comparator is not intended to establish direct equivalence between populations. The estimated enrollment is approximately 300 transplant recipients in the TorEx cohort over the 5-year enrollment period; the external OPTN STAR control cohort is expected to include more than 1,000 subjects. No specific targets for ensuring diversity with respect to sex, age, race, or ethnicity were established in the protocol; FDA notes this as a gap that should be addressed during PAS protocol finalization. All enrolled subjects will be followed for 5 years post-transplantation (total study duration approximately 10 years). Data completeness will be reviewed at least quarterly, with particular focus on survival

status, CLAD, airway complications, and major adverse events. Post-transplant clinical follow-up assessments of pulmonary function and long-term outcomes will be conducted at 1, 2, 3, 4, and 5 years post-transplantation. The primary endpoint is patient survival at 1 year post-transplantation. Secondary endpoints include: patient survival at 3 and 5 years; pulmonary function (FEV1) at 1, 2, 3, 4, and 5 years; CLAD-free survival at 1, 2, 3, 4, and 5 years; incidence of BOS at 1, 2, 3, 4, and 5 years; incidence of airway anastomotic complications (airway ischemia, bronchial anastomotic stricture requiring intervention, bronchial dehiscence, and bronchial necrosis) within 12 months of transplantation; EVLP-to-transplant conversion rate; duration of mechanical ventilation; ICU length of stay; hospital length of stay; and requirement for extracorporeal membrane oxygenation (ECMO). A safety endpoint of TorEx-related serious adverse events (SAEs) from the time of transplantation through 30 days post-transplantation or initial hospital stay, whichever is longer, will also be assessed. The primary statistical analysis will evaluate 1-year post-transplant patient survival using a non-inferiority framework compared to the OPTN STAR benchmark. Finally, as another example of an issue that will need to be addressed with the draft PAS protocol (i.e., before PAS protocol finalization within a future PMA supplement), FDA notes that the "*TorEx Lung Perfusion System Post-Approval Study*" does not include collection of "grade 3 primary graft dysfunction (PGD3) at 72 hours," and FDA emphasizes that this is important information to include in the PAS protocol to confirm safety as demonstrated by PGD3 rates.

From the date of study protocol approval, the sponsor must meet the following timelines for the "*TorEx Lung Perfusion System Post-Approval Study*:"

- First subject enrolled within 6 months
- 20% of subjects enrolled within 12 months
- 50% of subjects enrolled within 18 months
- 100% of subjects enrolled within 24 months

In addition, the sponsor must submit separate periodic reports on the progress of the "*TorEx Lung Perfusion System Post-Approval Study*" as follows:

- The sponsor must submit PAS Progress Reports every six (6) months until subject enrollment has been completed, and annually thereafter, from the date of the PMA approval letter, unless otherwise specified by FDA.
- If any enrollment milestones are not met, the sponsor must begin submitting quarterly enrollment status reports every 3 months in addition to the periodic (6-month) PAS Progress Reports, until FDA notifies the sponsor otherwise.
- The sponsor must submit the Final PAS Report three (3) months from study completion (i.e., last subject's last follow-up date).

The applicant's manufacturing facility was inspected and found to be in compliance with the device Quality System (QS) regulation (21 CFR 820), which was in effect at the time of the inspection. As of February 2, 2026, the revised part 820, referred to as the Quality Management System Regulation (QMSR), is effective.

XVI. APPROVAL SPECIFICATIONS

Directions for use: See device labeling.

Hazards to Health from Use of the Device: See Indications, Contraindications, Warnings, Precautions, and Adverse Events in the device labeling.

Post-approval Requirements and Restrictions: See approval order.

XVII. REFERENCES

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