

Disclaimer/Publisher's Note: The statements, opinions, and data contained in all publications are solely those of the individual author(s) and contributor(s) and not of MDPI and/or the editor(s). MDPI and/or the editor(s) disclaim responsibility for any injury to people or property resulting from any ideas, methods, instructions, or products referred to in the content.

Article

Design and Manufacture of a Test Device for Small Vacuum Pumps

Victor Amador Diaz ^{1,*}, Scott E. Snyder ² and Amy L. Vavere ¹

¹ Molecular Imaging Core, Department of Diagnostic Imaging, St. Jude Children's Research Hospital, Memphis, TN 38105;

² Molecular Imaging Ligand Development Program, Department of Radiology and Imaging Services, Indiana University School of Medicine, Indianapolis, IN 46202

* Correspondence: victor.amador@stjude.org

Abstract: Vacuum pump wear is the most prevalent failure mode of the IBA Synthera® automated radiochemistry system. Rebuilding or replacing the pump causes equipment downtime and increases the radiation exposure of the service personnel. We built a dedicated test device to assess new or rebuilt pumps prior to installation, thus reducing downtime and radiation exposure during repairs. The Testbed incorporates a microprocessor that actuates the pump, valves, pressure sensor, and communicates with the user through lights, buttons, and an alphanumeric screen. The Testbed increases productivity and safety in the radiochemistry laboratory.

Keywords: Laboratory Automation; Radiochemistry; Synthera; FASTlab; TRACERlab; iPhase; Synthera; Synthesis Module; Radiation Safety; Vacuum; Diaphragm Pump; Laboport; Arduino; LabVIEW

1. Introduction

Vacuum pumps are indispensable components in modern chemistry laboratories. Diaphragm pumps are one type of positive displacement pump that are used for liquid handling, solvent evaporation, distillation, blotting, filtration, solid-phase extraction, and gel drying. Some of these applications expose them to hazardous chemicals that can damage the pump's components. In radiochemistry laboratories, commercial radiosynthesizers rely on diaphragm vacuum pumps to assist in the chemical synthesis of radioactive drugs for positron emission tomography (PET) and single photon emission computed tomography (SPECT) imaging. These synthesizers are automated systems that are housed in lead-shielded fume hoods (or "hot cells") to limit radiation exposure to the chemist[1]. Any downtime of these radiochemistry modules disrupts not only laboratory operations but research and clinical studies.

At St. Jude Children's Research Hospital, we have used IBA Synthera® synthesis modules to produce F-18 labeled radiotracers since 2008. This synthesizer is built to perform chemical reactions using a disposable cassette with a centralized reactor. In simplified terms, the synthesizer comprises a heater, inert gas supply, pneumatics for the cassette valves, and critically, a vacuum pump for evaporating solvents and transferring reagents. This pump (KNF N85.3 KNDC) is essential for achieving a high vacuum to ensure solvent removal as many reactions are sensitive to water.

The working principle of this type of pump is the deformation of a flexible diaphragm disk inside an internal cavity. A con-rod or other reciprocating mechanical linkage mates the diaphragm to the output shaft of a rotating driving mechanism, typically an electric motor. Single acting pumps contain one diaphragm, while double acting models are equipped with two. Each diaphragm head features two directional valves to ensure that fluid is pumped in the correct direction. A pump can be brought back to optimal condition by cleaning the internal surfaces of it heads and replacing the diaphragms, seals, and valves[2] (i.e. rebuilding the pump).

In our use of this equipment, we noticed that over time, the pump would lose its ability to pull high vacuum and fail to pass the pre-synthesis checks. The causes of these pump failures were typically either vacuum leaks or gradual performance drop caused by degradation of the internal diaphragms, valves, and seals. Gradual performance losses were caused by chemical attack by solvents upon the internal rubber components of the pump and by accumulation of condensation in the fluidic cavities, thus reducing the pumped volume on each stroke[3].

There are several reasons that prompted the development of an alternative method or apparatus for the assessment of these pumps was necessary. If the module was used recently, the pump may contain residual radioactive chemicals accumulated during the synthesis. The repair staff would have to wait until it was safe to access the module and remove the pump, potentially causing longer than expected equipment downtime. Damage from aggressive solvents can be minimized by preventative methods such as an enhanced purging the pump after each synthesis (see Supplementary Materials), but the pump had to be replaced or rebuilt, eventually. Radiation safety is paramount in radiochemistry laboratories, notably those producing high volumes for distribution. Once the pump was accessible, it was difficult to troubleshoot in the limited space of the lead-shielded workspace, compounded by the possible presence of low levels of residual radioactivity. When a pump was replaced, testing had to be performed within this same environment using the synthesizer. After the pump is cleaned and all damaged parts replaced, compliance with industry regulations requires that the pump be tested before using it for the production of radiopharmaceuticals[4]. If a pump was rebuilt or a new pump received, the radiosynthesizer had to be used to validate the pumps which prevented use for synthesis during this time and risked damaging the module because of the use of metallic tools and leak finding liquids near the module's electronics[5].

We report here the design, fabrication, and use of a vacuum pump testbed that provides a safe and accessible way to assess the function of a pump away from the radiosynthesizer. It features a clear user interface and an electronic compound pressure gauge in a spill-proof and portable enclosure.

2. Materials and Methods

2.1. Design Guidelines

A dedicated test device for Synthera® vacuum pumps was conceived upon realizing that we had accumulated eight malfunctioning pumps in need of repair. Validating the repair of each pump using the Synthera® would not only make it unavailable to scientists, but also risk causing damage to the synthesis module ranging from a broken fluidic connector to a current surge with potential to destroy the module's electronics.

Following the guidelines of the Pharmaceutical Inspection Co-Operation Scheme (PIC/S)[6], we elaborated a list of User Requirement Specifications (URS) that the Testbed would have to satisfy:

- Replicates the fluidic pathway of the Synthera® system.
- Wetted surfaces are resistant to ethanol and acetonitrile, the two most abundant solvents to which the pump is exposed during experiments.
- Fluidic components are tight from 0 to 300 kPa absolute, the operational limits of Synthera®.
- Keeps inert gas supply pressure below 150 kPa, the maximum permissible operating pressure limit set by KNF for the pump.
- Fluidic components are rated to relative gas pressures ranging from -30mm of Hg to 250 kPa.
- A gauge provides the user with constant reading of the gas pressure at the intake of the pump.
- Components surrounding the pump heads can withstand exposure to liquid leak detector solution.
- Compact, portable, and not controlled from a computer.

- Attaching the pump does not require tools.
- Fasteners absorb vibrations from the pump
- Provides easy access to components to simplify maintenance.

Although no limit was set for the materials cost, we aimed to keep it below the price of what we considered the most expensive accidental damage: catastrophic electrical damage requiring a new controller assembly for the module, priced at the time at \$2,200.

2.2. Hardware Overview

Figure 1 shows the components of the testbed's fluidic circuit. The intake manifold features two valves, each of them supplying a different flow of inert gas. Another pair of valves in the exhaust manifold is used to divert gas and liquid waste towards dedicated outlet ports on the rear the of instrument. To ensure that the gas supply does not exceed the operating pressure of the pump, we selected a fixed gas regulator. An electronic pressure sensor provides constant and accurate reading of the pressure upstream of the pump. An earlier version of the instrument featured an analog dial compound gauge for redundancy, but it was eliminated because an electronic gauge proved to be more accurate and readable.

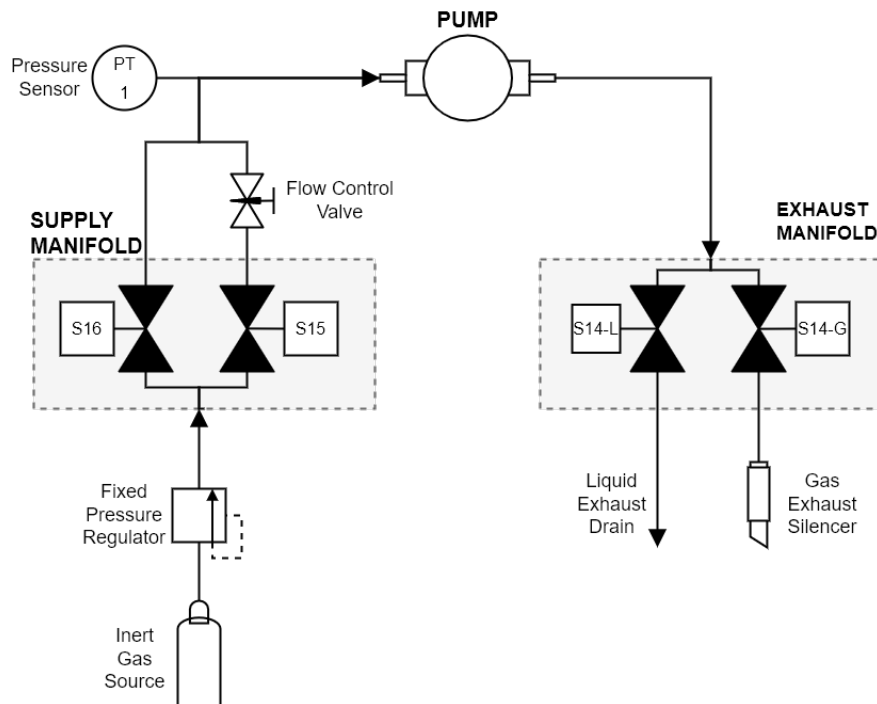


Figure 1. Fluidic diagram of the Testbed

The Testbed uses an Arduino MEGA2560 micro-controller. A custom-built shield acts as a connector interface between the Arduino board and the pressure sensor, LCD, buttons, switches, and a relay board to actuate the valves and vacuum pump. An electronic schematic is shown in Figure 2.

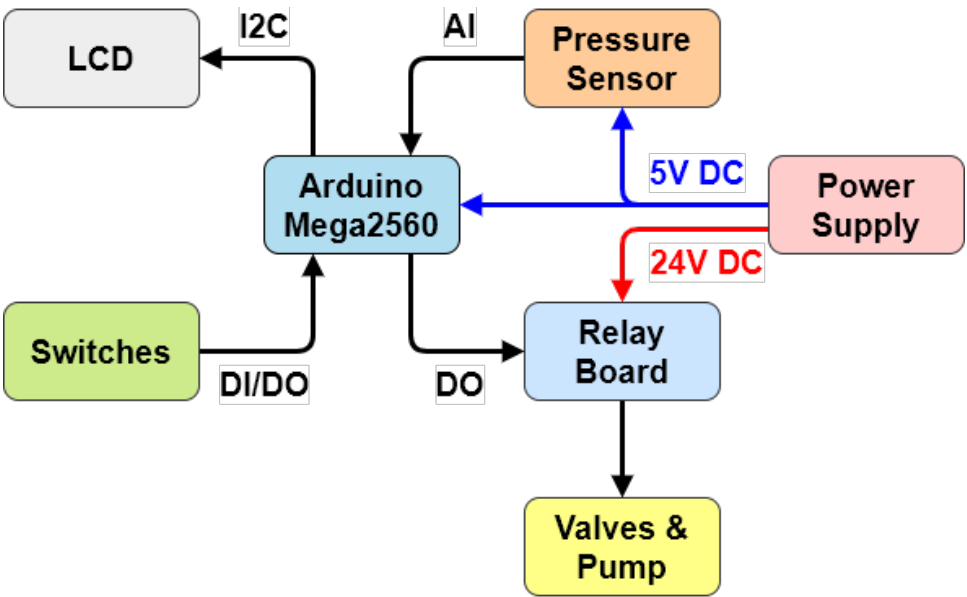


Figure 2. Electronic circuit diagram.

Electronics and valves are mounted to two internal panels. To ease repairs, panels are secured to the enclosure by two 3D printed mounts like the one in Figure 3. They are flexible enough to allow tool-free removal of the panels.

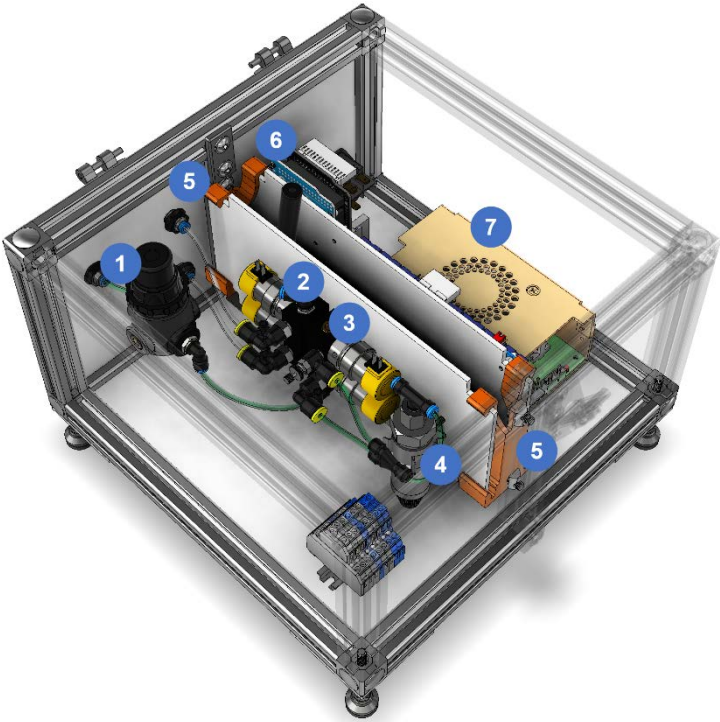


Figure 3: Interior view of the Testbed. The custom-made clamps are highlighted in orange. (1) fixed output pressure regulator; (2) intake manifold; (3) exhaust manifold; (4) electronic pressure/vacuum gauge; (5) custom mounting clamps; (6) microcontroller; (7) Power supply.

A dedicated enclosure was designed in CAD using Autodesk Inventor [Figure 4] and built in-house using polycarbonate panels, t-slotted aluminum extrusion profiles, and connectors. The overall dimensions of the Testbed are 300mm by 300mm 240mm.

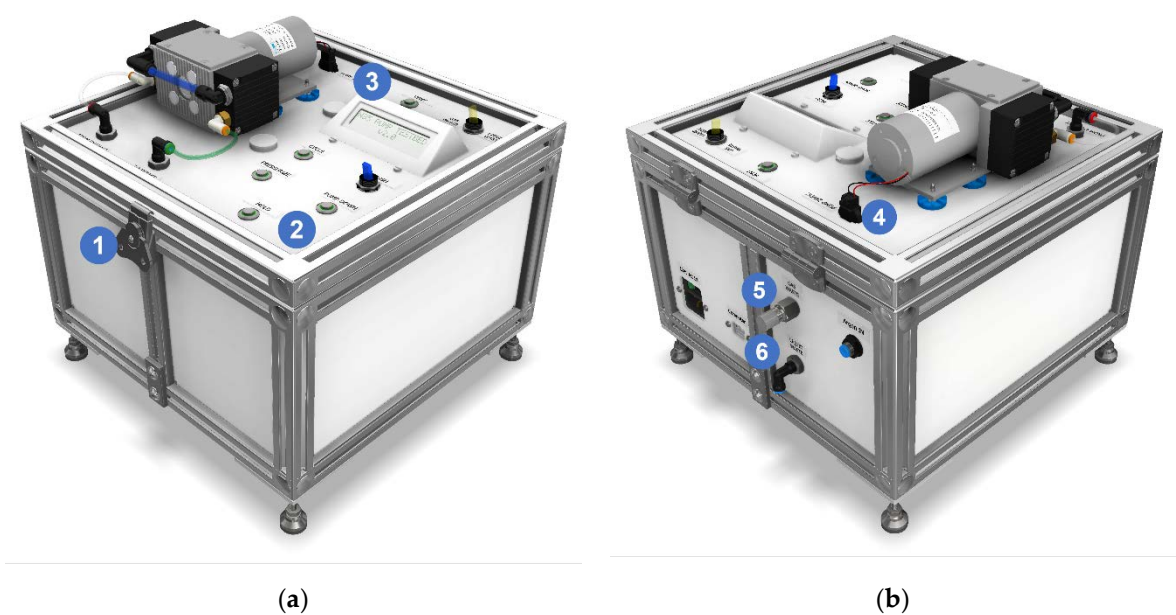


Figure 4: Computer model of the Testbed. (a) Front quarter view shows (1) the quick-turn draw latch, (2) control panel, and (3) custom LCD bezel. (b) Rear quarter view shows (4) the power plug for the pump, (5) muffler for the gas exhaust, (6) and elbow fitting pointing downwards to drain exhaust liquids.

Leak detecting solutions are frequently used in the troubleshooting of faulty pumps. To prevent spills that could damage its internal components, there is a plastic seal between the polycarbonate panels and the aluminum profiles and seals around the controls.

The user interface consists of an alphanumeric LCD screen and illuminated push-buttons and toggle switches [Figure 5]. The current mode of operation is shown in the top row of the screen, while the bottom one is reserved for the pressure reading in the system. The display is mounted to a 3D-printed bezel. The design of this component underwent several iterations, resulting in a shape that makes it easy to assemble, protects the surrounding electronics, and presents the display towards the user.



Figure 5: Lid subassembly featuring (1) captive panel screws and rubber vibration dampening grommets; (2) LCD mounted on the bezel; and (3) illuminated controls.

A green ring around each of the buttons illuminates while the corresponding mode is selected. The paddles of the toggle switches illuminate when the function they each control is active.

Thumb-screw-head captive panels screws secure the pump to the Testbed. Two washers and a spring on each screw keep them attached to the vibration dampers, eliminating the need for tools, tracking loose fasteners.

Users can enter the liquid waste mode with a dedicated toggle switch. A secondary exhaust valve and outputs route the liquid outside the Testbed, where a collection container is placed. The paddle on the gas/liquid waste selector switch illuminates when the liquid waste mode is enabled to alert the user and prevent accidental spills.

A Bill of Materials is available in the Supplementary Materials.

2.3. Operation Modes

Users select from the five available modes of operation by pressing on dedicated buttons on the top of the Testbed:

- **CYCLE:** runs the pump and switches the valves automatically to maintain the negative atmospheric pressure inside the pump. This helps clean the pump head internals. A PID algorithm switches the exhaust valve to maintain 65 kPa absolute in the supply line. The operator can manually increase the flow to force the removal of solvents accumulated inside the pump with the flick of the toggle switch.
- **PRESSURIZE:** increases the internal pressure of the pump. It is used to measure a leak rate or detect leaks.
- **VACUUM:** runs the pump against a closed inlet. Useful to test the quality of the vacuum.
- **HOLD:** closes all valves to measure leak rate or detect leaks.
- **VENT:** the controller opens the exhaust valve to equalize the pressure in the device and the atmosphere. This is recommended before the pump is removed from the instrument.

2.4. Software Interface for Data Logging

Initially, test results were recorded manually in a paper or electronic log. However, after rebuilding and testing several pumps, a data logging application was built using LabVIEW [National Instruments]. Even though LabVIEW could be used to fully control the Testbed, it was decided to limit it to datalogging purposes to shorten development time.

Updates to Arduino code

The source code of the Testbed required little changes to transmit the pressure sensor reading to a computer. The following function was added to the `void.loop()` section to send the reading in kPa whenever it's connected via USB to a computer.

```
if (Serial.available() == 0) {
  Serial.println(pressureKPA);
}
```

Application architecture

The data logger was built using the National Instruments State Diagram Editor toolkit for LabVIEW[7]. This toolkit provides significant benefits over the native implementation of the state machine design pattern. It features a graphical window to arrange states and transitions, as shown in Figure 6. The toolkit translates the diagram dynamically to the wiring block diagram with corresponding case structures, enumerated type variables, and case selectors. Without the toolkit, programmers need to create and maintain the type definition controls for each state.

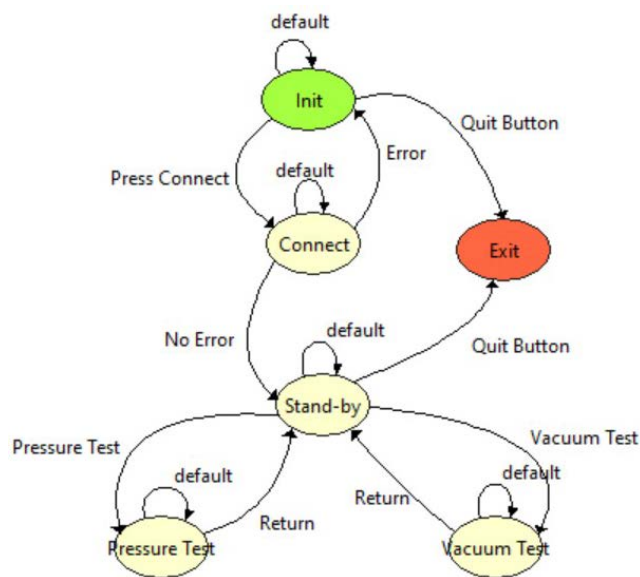


Figure 6: State Machine Diagram of the data-logging application generated with the National Instruments State Diagram Editor toolkit for LabVIEW. Green represents the initial state, yellow is for intermediate, and red is for the terminal state. Arrows represent state transitions.

Application description

The application is organized in purpose-specific pages accessible through tabs. Upon launching the application, users are prompted by the Comms Tab [Figure 7] to select the USB port connected to the Testbed and press Connect. A successful connection will automatically switch to the Main tab.

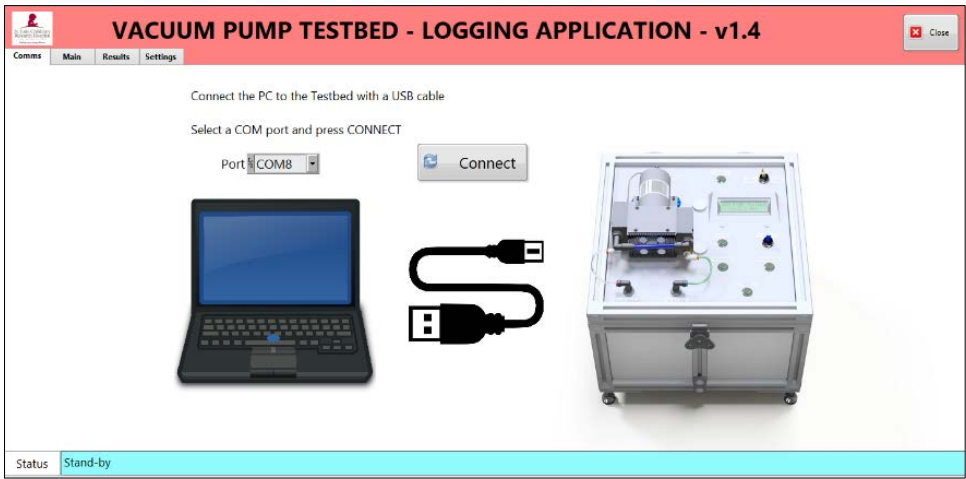


Figure 7. Communications tab.

In the Main Tab, users monitor the reading from the pressure sensor, log pump details, and monitor test results [Figure 8].

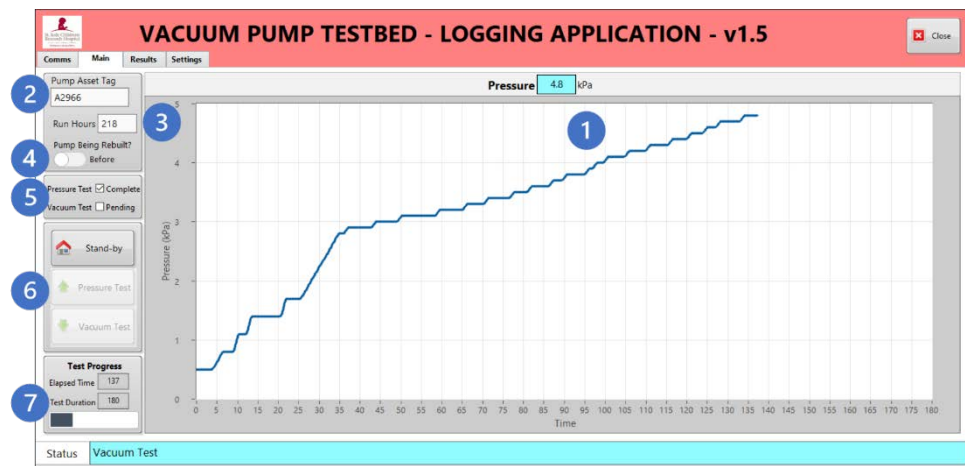


Figure 8. Main Tab. (1) Chart Panel: shows the current pressure value and a historical graph; (2) Pump Asset Tag: the user enters the asset tag value of the pump being tested; (3) Run Hours: the user enters value from the pump’s hour meter (the installation of an hour meter is detailed in the Supplementary Materials); (4) Pump Being Rebuilt?: the user designates if test takes place before or after the pump has been rebuilt; (5) Test Status Panel: automatically checks when the pressure and vacuum tests are complete; (6) Mode Panel: Stand-by: no data is being saved in this mode; Pressure Test: saves readings to the pressurization section of the report; Vacuum Test: saves readings to the vacuum tightness section of the report; (7) Test Progress Panel: Elapsed Time: shows time passed since the start of pressure or vacuum test; Test Duration: shows the duration of the pressure or vacuum test.

The Results Tab is a compilation of all logged data and other pertinent information [Figure 9].

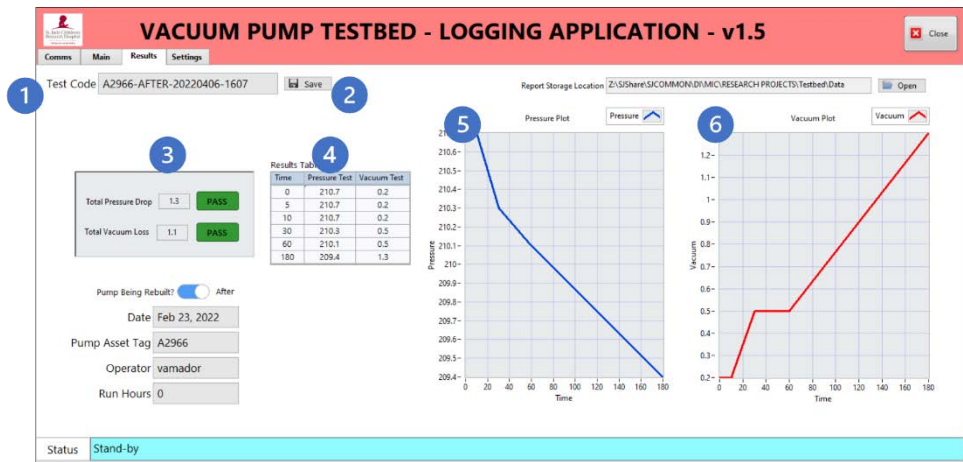


Figure 9. Results Tab. (1) Test Code: a concatenated string automatically generated using the pump asset tag code, rebuild status, date, and time the test was completed; (2) Save button: takes a screenshot of the Results tab and saves it to the chosen destination folder as a JPEG file with the Test Code name; (3) Pass/Fail Panel: reports pressure drop and vacuum loss and compares with acceptance criteria; (4) Results Table: readings at six time points configurable in the Settings tab; (5) Pressure Plot: plots the results of the pressurization test; (6) Vacuum Plot: plots the results of the vacuum tightness test.

The Settings Tab in Figure 10 presents options to change the sampling times, set acceptance criteria, and designate a report destination folder.

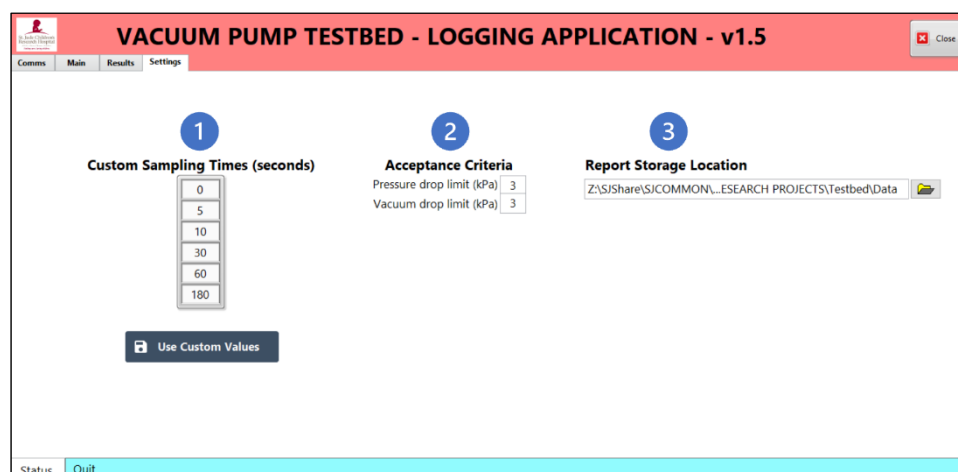


Figure 10. Settings Tab. Allows users to check or change select test parameters. Values are reset to their defaults the next time the application is launched. (1) Custom Sampling Times; (2) Acceptance Criteria; (3) Report Storage Location.

Extended Compatibility

As is, the Testbed is compatible with all Synthra® synthesis modules from IBA, but it can also be used for other pumps with minor modifications. Radiosynthesizers manufactured by GE Healthcare (including all FASTlab and some TRACERlab systems) and the Multisyn from iPHASE Technologies are also equipped with a KNF N85 pump but are fitted with different electrical and fluidic connections.

The general design on the Testbed should allow use with any diaphragm pump with the appropriate connections to ensure fluidic and electrical tightness and communication. In fact, several radiosynthesizers use a KNF Laboport 800 series pump and could benefit from a testbed with minor alterations. These include the ATT Scintomics (GRP), several models from Synthra, Eckert & Ziegler Modular Lab, Elysia – Raytest GAIA systems, and the iPHASE FlexLab. A complete list of compatible radiosynthesizers is available in Appendix A.

3. Results

After assembly of the Testbed, Figure 11, it was leak tested and the absolute pressure sensor was checked against a NIST-certified gauge.

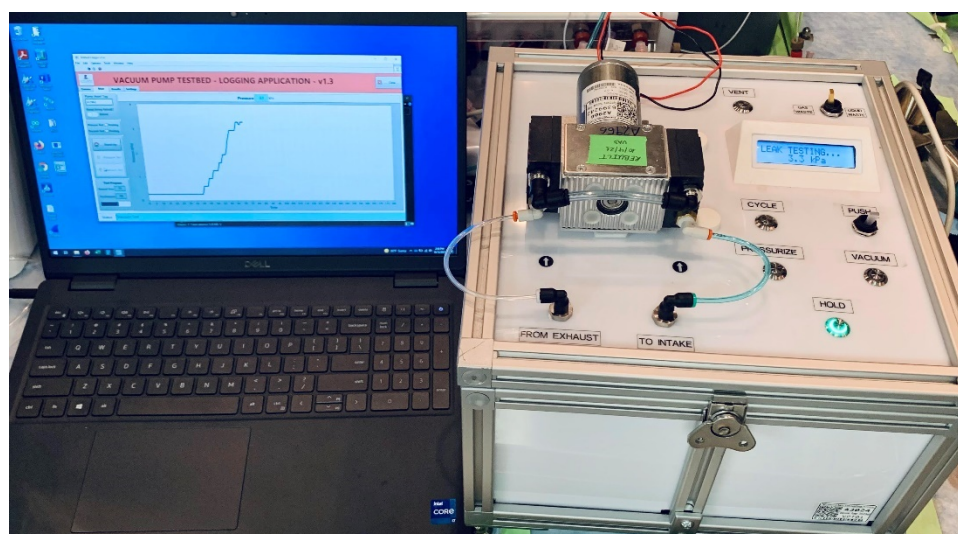


Figure 11. Testbed and LabVIEW application conducting a vacuum tightness test.

3.1 Operation

The installation of the pump and operation of the Testbed are outlined as follows (with the step-by-step procedure listed in the Supplemental Materials). Briefly, the pump is installed by lifting the lid of the Testbed and aligning the four threaded holes with the captive panel fasteners and tightening until the base of the pump touches the blue vibration dampeners. Once the lid is closed and the latch locked, the intake and exhaust of the pump are connected to the Testbed and the pump's electrical connector is attached to the 24V DC socket. The inert gas supply line is attached to the GAS IN port and the Testbed is plugged in.

The power switch is toggled to the ON position (confirmed by a welcome message) and the computer is turned on with the Testbed Logger application loaded. The Testbed is connected to the computer with a male USB-A to male USB-B cable. The communications tab (Comms) on the user interface will require the user to select the correct COM port number followed by pressing CONNECT. Now the Main Tab is visible, and the information fields are populated by the user.

The first test of the pump is performed by pressing CYCLE and allowing the pump to circulate inert gas for at least 5 minutes. During this time, the vacuum valve should open every 2 to 5 seconds, with the pressure reading oscillating around 75kPa. The user should check for condensation forming in the clear tube coming from the exhaust port. During this time, the user should briefly toggle the PUSH switch to increase the pressure (but do not exceed 120 kPa for more than 5 seconds). Larger drops may appear in the exhaust line as solvent is expelled from the pump. Allow the pressure to return to 75 kPa and repeat the PUSH toggle until no condensation is visible.

Next, press VACUUM and verify that the pressure is between 0 and 6 kPa (acceptance criteria for the Synthera system). Once the vacuum stabilizes, press HOLD. Then press VACUUM TEST in the Main tab of the logger application to record the results. When the test is complete, press PRESSURIZE and verify that the pressure is between 200 and 220 kPa. Press HOLD and then PRESSURE TEST in the Main tab of the logger application to record the results. Once the tests are complete, the logger application will show the Results tab. If the leak rate is within limits, press Save to archive the results. Press VENT to equalize pump and atmospheric pressures prior to disconnecting and turning off the Testbed to remove the pump.

If the pump fails the tests, press PRESSURIZE. Once the pressure stabilizes, use your desired leak detection method (electronic gas sensor, bubbling solution, ultrasonic leak detector, etc.) to survey the pump. If the pump is failing to reach the desired vacuum, it may help to flush the pump with ethanol to remove residual water or organic solvents. To flush the pump, press VENT and wait until pressure reaches 100 kPa then toggle the Waste Mode switch to the LIQUID WASTE position. After placing a container under the LIQUID WASTE exhaust port, disconnect the gas supply from the pump's inlet and connect it to a syringe barrel containing 5-10 mL of 100% ethanol. Press VACUUM and allow the pump to suction the solvent, then press HOLD and reconnect the gas supply line to the pump's inlet port. Repeat testing to re-assess the tightness of the pump. At this point, if it fails to meet the acceptance criteria, the pump should be rebuilt.

3.2. Maintenance

After exposure to aggressive solvents during cycling and testing, the Testbed should be purged and dried with inert gas. With no pump on the Testbed, verify that the waste selector is in the GAS WASTE position and use a push-in coupling to join the lines previously connected to the pump. Press CYCLE and let gas flow. Press HOLD and place a container under the liquid waste port on the rear of the Testbed. Move the waste mode selector to the LIQUID WASTE position. Press CYCLE and let gas flow for 5 minutes. Disconnect the main inert gas supply line, move the switch in the power entry module to the OFF position and unplug the Testbed.

Once a year, the Testbed undergoes a series of preventive maintenance tasks:

- Tubing is replaced.

- Fittings and their rubber seals are inspected for wear.
- Valves are disassembled and their internals checked.
- Pressure sensor readings are checked against a NIST-certified gauge. The sensor is not calibrated unless the difference is greater than 10%. (It was not deemed necessary to calibrate yearly because it's not a critical process and the pump will eventually be used on a synthesis module with a calibrated sensor.)

4. Discussion

We believe the Testbed is a valuable tool for the maintenance of laboratory vacuum pumps. Particularly in radiochemistry production facilities, where radiosynthesizer downtime has severe consequences and scheduled downtime is treasured.

It has not only been used to certify rebuilt pumps more than a dozen times, but also for screening of defective new units prior to installation. On one occasion, it revealed a leak from the sealing compound around the fittings of a brand new pump. The pump had been in storage for close to a year. This event also uncovered the fittings mismatch discussed in the Supplementary Materials

Supplementary Materials: The following are available online at www.mdpi.com/xxx/s1, Improvements to fluidic connections, Enhanced pump purge procedure, Reducing Mean Time To Repair (MTTR), Reducing Mean Time To Repair (MTTR), Bill Of Materials.

Author Contributions: Conceptualization, V.A.D.; methodology, V.A.D.; software, V.A.D.; validation, V.A.D.; formal analysis, V.A.D.; investigation, V.A.D.; resources, V.A.D., S.E.S., and A.L.V.; data curation, V.A.D.; writing—original draft preparation, V.A.D. and A.L.V.; writing—review and editing, A.L.V. and S.E.S.; visualization, V.A.D. and A.L.V.; supervision, A.L.V. and S.E.S.; project administration, V.A.D.; funding acquisition, A.L.V. and S.E.S.

Funding: This project was funded by ALSAC-St. Jude Children's Research Hospital.

Conflicts of Interest: The authors declare no conflicts of interest

Appendix A

Table 1. Synthesis modules with natively compatible pumps.

Manufacturer	Radiosynthesizer Model
Ion Beam Applications (IBA)	Synthera
	Synthera V2
	Synthera Plus

Table 2. Modules with readily compatible pumps.

Manufacturer	Radiosynthesizer Model
General Electric Healthcare	FASTlab*
	FASTlab 2*
	TRACERlab FX2 C
	TRACERlab FX2 MeI
	TRACERlab FX C (pro)
	TRACERLAB MX
iPHASE Technologies	TRACERLAB MX FDG
	MultiSyn

* The Testbed testing procedure satisfies the method describe in the maintenance checklist of both models[8,9].

Table 3. Synthesis modules featuring KNF Laboport 800 series pumps.

Manufacturer	Radiosynthesizer Model
ATT Scintomics	GRP
	Hot Box III
Synthra	Gpextent
	HCNplus
	[C-11]Acetate
	RNplus
	RNplus Research
	FDGtwo
	Multitracer
	F-Dopa
	Peptide
Eckert & Ziegler	Ammonia
	Iodine
Eckert & Ziegler	Modular-Lab PharmTracer
	Modular-Lab Standard
Elysia - Raytest	GAIA
	GAIA V2
General Electric Healthcare	TRACERlab FX2 C
	TRACERlab FX2 E
	TRACERlab FX2 N
	TRACERlab FX-FDG
iPHASE Technologies	FlexLab

References

1. Covens P, Berus D, Vanhavere F, Caveliers V. The introduction of automated dispensing and injection during pet procedures: a step in the optimisation of extremity doses and whole-body doses of nuclear medicine staff. Radiat Prot Dosimetry [Internet]. 2010 [cited 2017 Nov 8];140(3):250–8. Available from: <https://academic.oup.com/rpd/article-lookup/doi/10.1093/rpd/ncq110>.
2. Diaphragm Vacuum Pumps N85 and N86. Operating and Installation Instructions. Village-Neuf: KNF Neuberger, Inc.; 2016. p. 40.
3. Pfeiffer Vacuum GmbH. Vacuum Technology Know How. 2009. p. 38.
4. 21 C.F.R. § 212 — Current Good Manufacturing Practice For Positron Emission Tomography Drugs. US FDA US FDA; 2011.
5. Mobley RK. An Introduction to Predictive Maintenance (Second Edition) [Internet]. Second. An Introduction to Predictive Maintenance (Second Edition). Butterworth-Heinemann; 2002. pp. 394–433. Available from: <http://www.sciencedirect.com/science/article/pii/B978075067531450018X>.
6. Pharmaceutical Inspection Co-operation Scheme. PI 011-3 - PIC/S Guidance - Good Practices for Computerised “ Gxp ” Environments. PIC/S Secretariat; 2007. Available from: <https://picscheme.org/docview/3444>.
7. LabVIEW State Diagram Toolkit Download - NI [Internet]. [cited 2022 Feb 23]. Available from: <https://www.ni.com/en-us/support/downloads/tools-network/download.labview-state-diagram-toolkit.html#374363>.
8. GE Healthcare. DOC0839069 - FASTlab Service Manual [Internet]. 3rd ed. 2019 [cited 2022 Jan 21]. Available from: <https://customer-doc.cloud.gehealthcare.com/copyDoc/DOC0839069/3>.
9. GE Healthcare. DOC1615837 - FASTlab 2 Synthesizer Service Manual [Internet]. 11th ed. 2021 [cited 2022 Jan 21]. Available from: <https://customer-doc.cloud.gehealthcare.com/copyDoc/DOC1615837/11>.