Graver Technologies

E-PAK®

LABORATORY ADSORPTION CARTRIDGE OPERATION MANUAL

E-PAK lab systems are intended for use in a controlled environment and should be set up and operated in accordance with this manual. To promote safety and ensure effective operation Graver strongly recommends reading the entire manual before starting.

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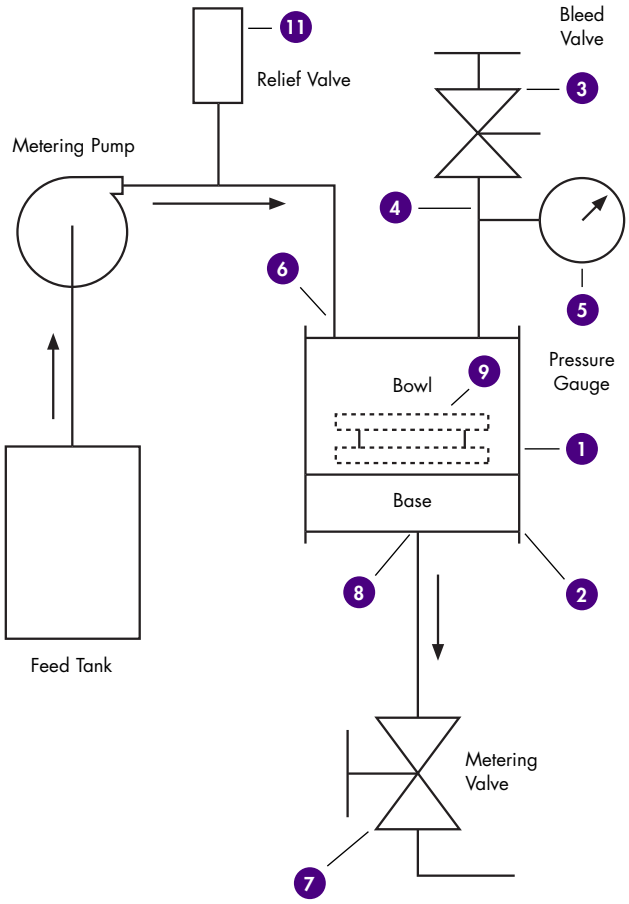
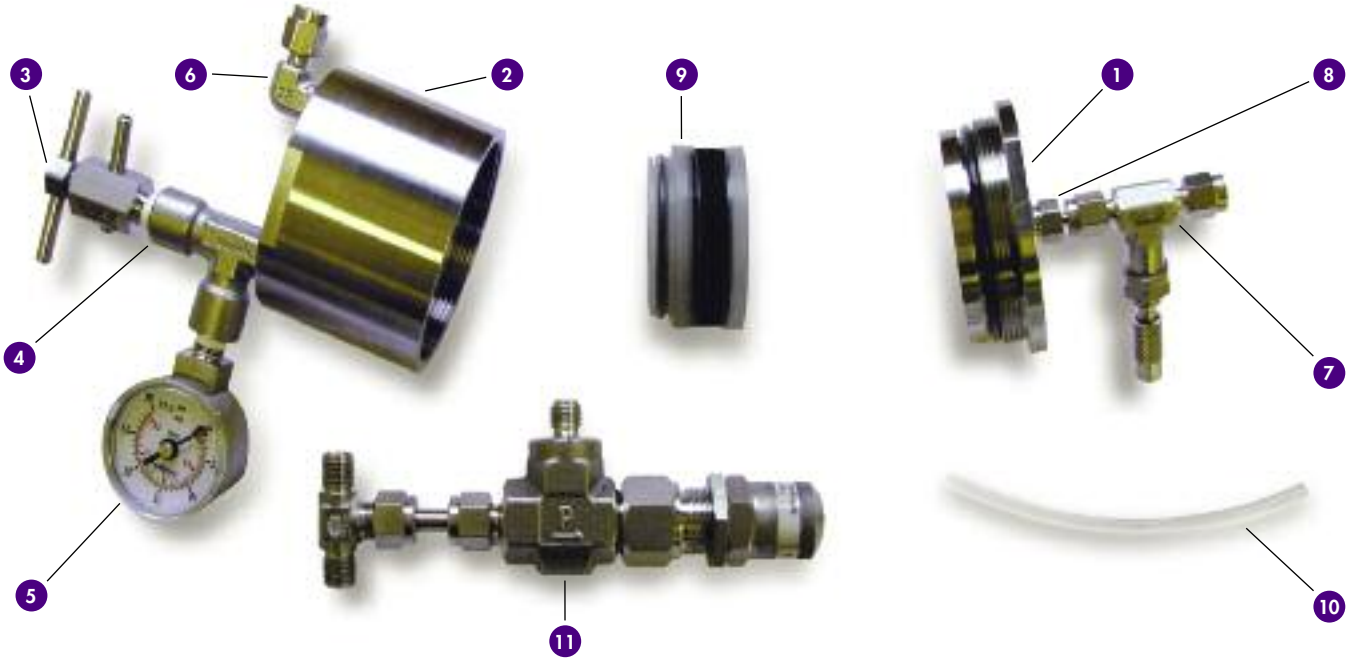
Introduction

Graver Technologies created E-PAK® products to provide a more practical, user-friendly method of using powdered adsorbents like activated carbon and silica in commercial scale pharmaceutical processing. E-PAK laboratory cartridges provide an accurate and convenient means of accessing commercial feasibility for adsorption processes as a result of the close adherence to the form and function of full-size E-PAK cartridges. This manual describes the set up and operation of the E-PAK Laboratory Cartridge system and how to develop and interpret test data.

Flow Schematic



E-PAK Laboratory Cartridge Housing



Parts List

ITEM NUMBER	PICTURE	DESCRIPTION	GRAVER P/N	MANUFACTURER	P/N
1		Base with O-Ring	EPLKH00000 F755572226	Graver Technologies, LLC Parker Hannafin	Q00409 2-226 TEV
2		Bowl	EPLKB00000	Graver Technologies, LLC	JH11012701
3		Bleed Valve	ESBVM4C3SH	Swagelok	SS-BVM2-SH
4		Street T	EM4452K432	Swagelok	SS-2-ST
5		Gauge	EPGM63L100	Swagelok	PGI-40M-PG30-LANX
6		Inlet Elbow	EM4464K360	Swagelok	SS-200-2-2
7		Metering Valve	ESLSS43GF4	Swagelok	SS-SS2
8		1/8" NPT to 1/8" Compression Fitting	Male Tube Adapter	Swagelok	SS-2-TA-1-2
9		E-PAK® 1 cm Lab Cartridge	EPLC941,C944, C947, C948 & C-951	Graver Technologies, LLC	
10		1/8" OD Tubing		McMaster-Carr	51805K41
11		Relief Valve w/t – Fitting 1/4" Compression Tube	ESRV4ARH4A	Parker Hannafin	4A-RH4A-VT-SS-K1

Inspection and Assembly

For convenience Graver has preassembled the E-PAK lab housing and labeled its parts to the extent possible.

1. Inspect the pre-assembled unit for loose fittings or damage. Tighten any fittings that may have loosened during shipment. Contact Graver customer service if any components are damaged or missing.

2. Verify that the pressure gauge indicates 0 psi. If the gauge does not read 0, please contact Graver customer service.

3. Separate the housing base (#1 in the diagrams on page 1 and the parts list on page 2) from the bowl (#2 in the diagrams on page 1 and the parts list on page 2).

4. Select a cartridge (see Cartridge Selection page 6). Insert the cartridge into the base with a slight rotating motion using light pressure. **Tip:** If the test cartridge is difficult to insert, moisten cartridge o-ring with compatible solvent.

5. Reassemble by inserting the housing base into the bowl and rotating clockwise until snug, being careful to avoid cross threading. **Tip:** In most cases, hand tightening will be sufficient to seal the base to the bowl. If leakage occurs, a strap wrench can be used to tighten further. When housing will be used to test an acidic solution, apply a single wrap of Teflon® tape to the base thread to protect against metal gauling of the threads.

6. Secure the housing assembly to a laboratory ring stand. The air bleed value (#3 in the diagrams on page 1 and the parts list on page 2) should be at the top of the assembly. Insert the tubing from the air bleed valve securely into a suitable container that will collect the fluid exiting the valve during air purge operation.

7. Temporarily remove the pre-installed metering valve (#7) from the housing base. Note: The metering valve is removed until the system has been flushed to prevent plugging of its small orifice.

8. Using supplied tubing as shown in diagram on page 1, connect housing inlet to pressure relief valve, pressure relief valve to pump* outlet, pump inlet to feed reservoir and housing outlet to outlet reservoir.

*To achieve satisfactory flow and pressure control, Graver recommends operating the E-PAK system with a laboratory positive displacement pump able to deliver 2.5–10 ml per minute at ≥2 ATM. Graver's laboratory utilizes a Model QG400 pump from Fluid Metering, Inc. with a Q1 or Q2 pump head.

Operation

1. **SYSTEM FLUSH** – Ensuring that the selected E-PAK cartridge has been installed, flush the system using a compatible solvent. This will remove loose carbon fines and other particulates from the system that could plug the back pressure control valve. This is best accomplished using solvent delivered at ≥10 ml/min. Use vent valve (#3) to remove trapped air from the housing then close the vent and pump the 50–100 ml of solvent through the system. The solvent should be collected and discarded. Verify that the metering valve (#7) has been removed so that the solvent will not flow through the valve. Following solvent flush use a small adjustable wrench to reconnect the metering valve to the housing base and reconnect outlet tubing.

2. **SOLVENT PURGE** – The solvent used for the cartridge pre-flush can be removed by blowing down the system with pressurized nitrogen or it can be removed by chasing out with the test solution. To judge when the flush solvent has been removed, measure the amount of flush solvent required to fill the tubing, pump and housing and discard that volume at the start of the test solution run. In some cases, observing a color change associated with the test solution displacing the flushing solvent can serve the same purpose.

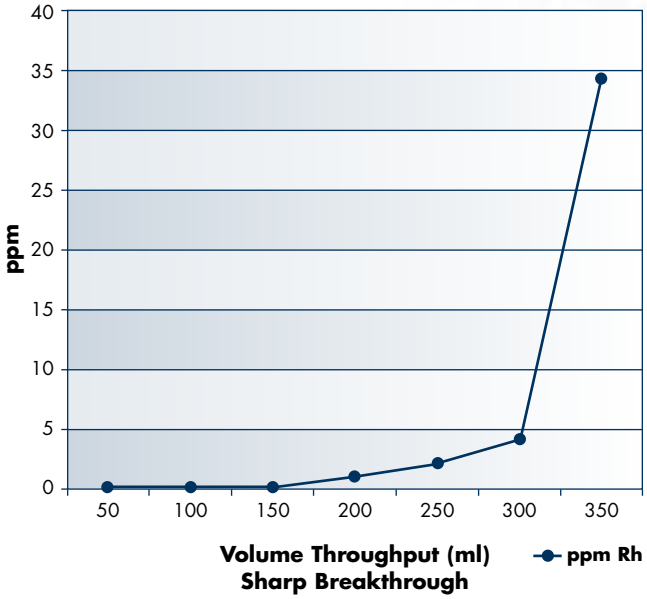
3. **STEP-BY-STEP OPERATION**
   - Verify that all assembly and preparation steps have been completed.

- Fully open the metering valve (#7).
- Set the pump to a low flow setting (i.e. 5ml/min).
- Fully open the air bleed valve (#3) on top of the head.
- Turn the pump on and watch for test fluid exiting from the from the bleed valve. **Tip:** Over the course of the test run, additional gas produced due to degassing from pump action can accumulate in the housing; periodically this gas should be removed through the bleed valve to prevent interference with even flow distribution through the adsorbent cartridge.
- When the bleed valve begins discharging liquid, indicating that all air has been bled from the system, close the bleed valve.
- Closely observe the pressure gauge after closing the bleed valve. Pressure should increase slowly. If pressure increases rapidly, immediately shut the pump off and disassemble the cartridge housing and inspect for blockage. If no blockages are identified, consider feed material characteristics; high viscosity or high solids can create pressure difficulties. **Tip:** Graver recommends that users pre-filter test solutions containing a large amount of insoluble solids.
- If pressure increases slowly it will usually stabilize at between 2 and 6 psi at a pump setting of 5 mls per minute. If pressure and/or flow are not in the target range, slowly adjust metering valve and pump setting as necessary.
- Begin sample collection at intervals according to desired data needs.
- During sample collection, periodically monitor flow and pressure, adjusting metering valve and pump setting as necessary to maintain target range.

Data Collection and Interpretation

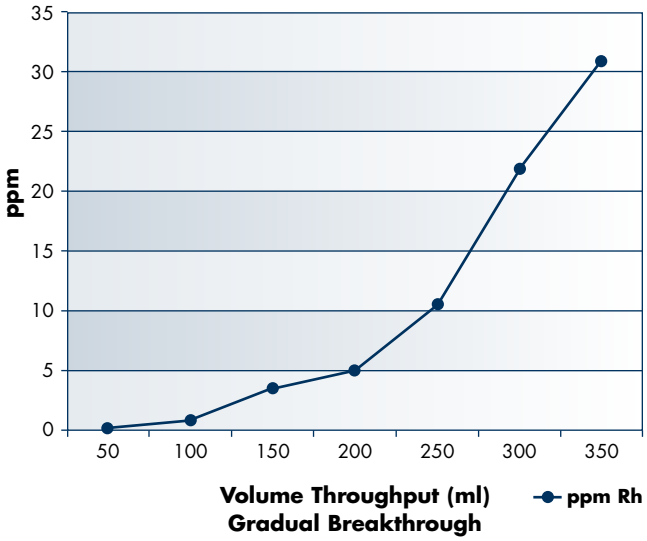
E-Pak cartridges are normally operated using a single pass method carried out at a constant flow rate. Adsorption performance is generally evaluated by constructing a breakthrough curve on an XY plot showing the change in contaminants breakthrough as a function of volume throughput. A breakthrough curve can take one of two typical forms (Sharp or Gradual). Examples are shown below along with some general interpretation and tips for improvement.

Rh Breakthrough/Sharp



Rapid adsorption kinetics, lower flow rate unlikely to improve capacity.

Rh Breakthrough/Gradual



Limited Kinetics, a lower flow rate may help improve capacity. **Tip:** In general, conditions affecting the solubility of the compound and contaminant, such as time, temperature, and solvent type, will also influence adsorption kinetics, loading capacity and selectivity.

Scale-Up Calculation

Although there are always exceptions, scale-up projections based on a linear extrapolation of adsorbent mass have proven to be quite accurate when test conditions including contact time, temperature, solvent type and contaminant and compound levels are held constant. The following table shows the scale-up/relative change in mass between lab, pilot and commercial size E-PAK cartridges.

DIMENSIONS (DIAMETER x HEIGHT IN CENTIMETERS)	5x1	5x10	16.5x25	16.5x50	16.5x100
CARTRIDGE MASS (GRAMS)	6.5	65	1,842	3,684	7,368
SCALE-UP FACTOR	1	10	283	566	1,132
ABSORBENT MASS (GRAMS)	4.25	42.5	1,197	2,394	4,789
FLOW RATE (ML) @ 2.5 MIN. CONTACT TIME	7	70	2,046	4,092	8,184

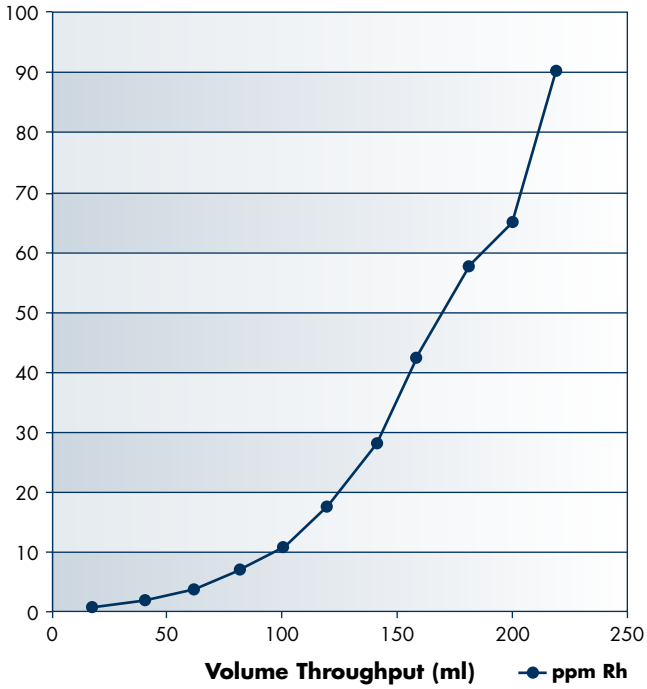
EXAMPLE: A synthetic API reaction mixture containing high levels of Rhodium catalyst and color is evaluated to determine whether adsorption purification can provide a practical means of eliminating re-crystallization done to meet purity requirements.

STARTING CONDITIONS: API concentration – 25g/liter, Rh–350 ppm, Color–0.3 OD @ 470 nm.

Estimated purity level needed to eliminate re-crystallization is Rh ≤ 40 ppm and Color to ≤ 0.15 OD. After testing available E-PAK adsorbents, C-948 is chosen based on capacity and selectivity to remove Rh and color reduction with the least amount of API loss.

Using an E-PAK laboratory system operating at 7ml/min data from the laboratory single pass test is used to construct the following breakthrough curves.

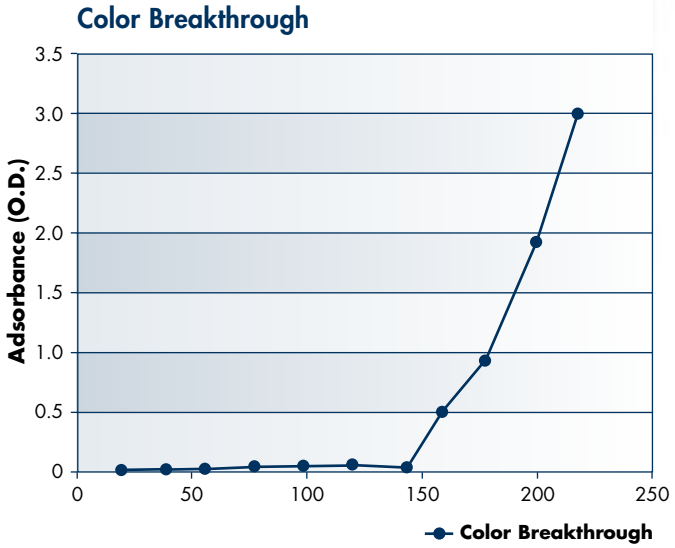
Rh Breakthrough/Curve



INTERPRETATION/SCALE-UP PROJECTION: From the breakthrough curve, the estimated volume of composite sample with a Rh level of ≤ 40 ppm is ~220 ml. The amount of purified API in 220 ml is 5.5 grams. Using linear mass based scale-up projection, the amount of API that can be processed to a satisfactory purity level with the various size cartridges is shown below. The gradual breakthrough suggests that reduced flow rate may help increase capacity.

DIMENSIONS (DIAMETER x HEIGHT IN CENTIMETERS)	5x1	5x10	16.5x25	16.5x50	16.5x100
SCALE-UP X	1	10	283	566	1,132
PROJECTED GRAMS OF PURIFIED API	5.5	55	1,556	3,122	6,224

For larger quantities, multiple cartridges are operated in parallel in a single cartridge housing. See GTX 325 for additional information on available cartridge housings and adapter plates.



INTERPRETATION/SCALE-UP PROJECTION: From the breakthrough curve, the estimated volume of composite sample with a color of ≤ 0.15 adsorbance unit is ~ 240 ml. The amount of purified API in 240 ml is 6 grams. Using linear mass based scale-up projection, the amount of API that can be processed to a satisfactory purity level with the various size cartridges is shown below. The sharp breakthrough suggests that reduced flow rate will not markedly increase capacity.

DIMENSIONS (DIAMETER x HEIGHT IN CENTIMETERS)	5x1	5x10	16.5x25	16.5x50	16.5x100
SCALE-UP FACTOR	1	10	283	566	1,132
PROJECTED GRAMS OF PURIFIED API	6	60	1,698	3,396	6,792

Cartridge and Formula Selection

To aid in the selection of the best E-PAK cartridge, Graver provides a sample kit containing the adsorbents currently available in E-PAK cartridges. In general the best adsorbent for a given application will be the one with the highest capacity and best selectivity. Graver recommends testing each of the powdered adsorbent samples using a stirred batch contact reaction with a starting dosage of 0.5%, a contact time of 30 minutes and temperature similar to that of the full scale process.

POWDERED SAMPLE KIT	E-PAK CARTRIDGE	ECOSORB® PRODUCT W/ SAME ADSORBENT
C-941-PS	C-941	C-941
C-944-PS	C-944	C-944
C-947-PS	C-947	C-947
C-948-PS	C-948	C-948
C-951-PS	C-951	

Note: Custom products available; please call Graver to discuss your application and requirements.

Chemical Compatibility

E-PAK cartridges are manufactured using proprietary technology and materials compatible with commonly used organic solvents. Graver has tested E-PAK cartridges in the following solvents using 48-hour soak tests at ambient temperature and found them to be satisfactory. E-PAK cartridges are suitable for operation at a pH of 1 to 14; C-951 is suitable for pH of 1 to 7.

- Dichloromethane
- Ethyl acetate
- Methanol
- N-ethyl-2-pyrolidone
- Tetrahydrofuran
- Toluene
- Acetic Acid

Scan or click on the links below for additional information on E-PAK® Adsorbent Cartridge Chemical Compatibility.

http://www.gravertech.com/PDF/Product_Sheets/Adsorbents/GTX-336-E-Pak-Chem-Comp.pdf

http://www.gravertech.com/PDF/Product_Sheets/Adsorbents/GTX-323-E-Pak-Brochure.pdf

Contact Graver to discuss use with other solvents.

Safety

E-PAK lab systems are intended for use in a controlled lab environment. It is the operator's responsibility to ensure that the system is set up in strict accordance with this manual and otherwise in a manner that takes into account possible safety hazards of the materials being evaluated.

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