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### 1.0 Purpose

This SOP describes the procedure for chromatography column unpacking and resin reuse and storage. It also describes the cleaning procedure for empty chromatography columns, to include column adaptors, the internal tube, and valve flowpaths (if present).

### 2.0 Scope

This SOP applies to Biopharmaceutical Development Program (BDP) personnel who perform column unpacking and cleaning. The column unpacking procedure described in this SOP applies to packed columns that have already been cleaned per a resin- and product-specific procedure in a Batch Production Record (BPR). The cleaning procedures described in this SOP (both interbatch and interproduct) apply only to empty columns.

### 3.0 Authority and Responsibility

- 3.1 The Manager, Late Process Sciences, Biopharmaceutical Development Program (BDP) has the authority to define this procedure.
- 3.2 BDP personnel are responsible for the implementation of this procedure.
- 3.3 Biopharmaceutical Quality Assurance (BQA) is responsible for quality oversight of this procedure.

### 4.0 Equipment and Material

- 4.1 WFI-quality water.
- 4.2 0.5 N NaOH, BDP PN 46109CL, or BDP approved equivalent.
- 4.3 Clean room wipes, BDP PN 21208, or BDP approved equivalent.

- 4.4 Socket wrench.
- 4.5 Swabs, BDP PN 21674, or BDP approved equivalent.
- 4.6 15 mL polypropylene screw cap centrifuge tube, BDP PN 20006, or BDP approved equivalent.
- 4.7 TOC vials, BDP PN 20442, or BDP approved equivalent.
- 4.8 Peristaltic pump.
- 4.9 Pharmed or silicon tubing.
- 4.10 pH strips, BDP PN 20473, or BDP approved equivalent, or pH meter and standards.
- 4.11 20% ethanol, BDP PN 46202, or BDP approved equivalent.
- 4.12 Paddle for resin re slurring.
- 4.13 Container(s) for resin storage, such as the original container(s), autoclaved carboy(s), or sterile PETG bottle(s).

## 5.0 Post-production Column Unpacking Procedure

- 5.1 Verify the column to be unpacked has been cleaned, post-production according to the BPR.
  - 5.1.1 If the BPR indicates that the product-contact area of the column has been exposed to 0.5 N NaOH for at least 60 minutes or equivalent cleaning agent, this cleaning satisfies the requirements of this SOP, and the column may be rinsed with WFI and sampled according to Section 7.3.
  - 5.1.2 If the cleaning specified in the BPR did not include a 0.5 N NaOH soak of product-contact surfaces for at least 60 minutes, cleaning must be repeated according to Section 7.4 of this SOP before the column may be rinsed and sampled.
- 5.2 Loosen the top adaptor O-ring and remove the top adaptor, being careful not to allow anything on the outer surface of the adaptor to fall into the resin. Rinse the top adaptor support net with 20% ethanol to rinse any residual resin into the column.
- 5.3 Add 20% ethanol to the column for a 50%-70% slurry of the resin. Using a paddle, gently stir the resin until uniform slurry has been achieved.
- 5.4 Pour, or pump, the slurred resin into storage container(s) capable of holding all of the resin.
- 5.5 Label the resin storage container(s) with, at minimum, the following information.
  - Resin Type
  - BDP PN
  - BDP Lot No.
  - Expiration Date
  - Previously Used For/Lot No.
  - Previous Packed Bed Volume
  - MPR No. and Date of Last Cleaning

- Date of Unpacking
- Storage Solution
- Bottle No. (X of Y)
- Initials/Date

5.6 Place the resin container(s) at 2°-8°C for storage.

5.7 Document information on Form 14146-01, Column Unpacking (see Attachment 6).

## 6.0 Rinse Reuse and Storage

6.1 Resin reuse and storage duration is to be determined on a case-by-case basis for different resins being used based on Manufacturer's recommendations, expiration date, next process compliance level (GMP, R&D, etc.) and binding studies performed in-house by the BDP Development staff.

6.2 The following are guidelines for resin reuse:

- The resin must be verified as visually clean
- The resin must be within its expiration date.
- The resin may only be used again for the SAME product or one that is of equal or lesser compliance level (i.e., resin used for an R&D product may not be reused in a GMP campaign).

6.3 Document the information requested on Form 14146-03, Resin Inventory, if resin is to be reused, in order to track resin inventory and usage. Maintain this form in the Resin Inventory Logbook. If the resin is not to be reused dispose of resin appropriately.

6.4 Dispose of resin that is not acceptable for reuse. Contact the Environmental Health and Safety Program (EHS) for proper disposal of resin.

## 7.0 Column Cleaning and Testing Procedure

7.1 New Column Cleaning and Interbatch Cleaning

***Use the following procedure on new columns, and when cleaning is necessary between batches (lots) of the same product. In the latter case, refer to the Master Production Record (MPR) for instructions on when to use this procedure.***

7.1.1 Rinse the empty column thoroughly with WFI and wipe the column with a cleanroom wipe to remove visible particles.

7.1.2 Fill the empty column with 0.5 N NaOH and purge the bottom adaptor mesh screen to remove large air bubbles.

7.1.3 Reattach the top adaptor at its maximum height. Slowly lower the top adaptor until NaOH flows out of the top valve. Adjust the flowpaths of the top and bottom valves to ensure that every flowpath is exposed to the NaOH.

7.1.4 Expose the column and valves to the NaOH for at least 60 minutes.

7.1.5 After the NaOH exposure, remove the top adaptor from the column. rinse with WFI and place on a clean surface.

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- 7.1.6 Thoroughly rinse the column with WFI and allow it to drain through the bottom adaptor valve. Rinse the column until the pH of the effluent collected from the bottom valve is pH 5-7.
- 7.1.7 For columns with disposable mesh screens and support nets, inspect screens and nets for damage. Replace if necessary.
- 7.1.8 Collect and test a rinse sample per **SOP 12169, Rinse Water Sampling for Production Equipment**.
- 7.1.9 CGMP Manufacturing group documents this cleaning on Form 14146-02, Column Cleaning and Testing. Large Scale Production/Late Process Sciences group uses Form 12149-01, Equipment Cleaning, as per **SOP 12149, General Cleaning of Process Equipment**.
- 7.1.10 Use a cleanroom wipe to remove moisture. Replace the top adaptor and label the column per **SOP 14150, Labeling of cGMP Purification Equipment for Cleaning Status**.
- 7.1.11 Move the empty, cleaned column to a controlled area of Class 100,000 or better for storage.
- 7.2 Interproduct Cleaning
- Use the following procedures between production campaigns of different products. This type of cleaning is similar to interbatch cleaning but differs in its sampling requirements. Column cleaning is accomplished by soaking, at a minimum, the product-contact areas of the column tube and associated parts with 0.5 N NaOH for at least 60 minutes. If this is done, the remaining areas of the column may be rinsed with WFI as specified in the following sections. In many cases, the product- and resin-specific cleaning that occurs as part of the MPR includes a 0.5 N NaOH soak for at least 60 minutes, and thus may be used to satisfy the requirements of this SOP.***
- 7.2.1 If acceptable cleaning has occurred as part of the BPR, CGMP Manufacturing group documents this on Form 14146-02, Column Cleaning and Testing, and proceeds to Section 7.3 of this SOP. Large Scale Production/Late Process Sciences group documents this on Form 12149-01, Equipment Cleaning, as per **SOP 12149, Equipment Cleaning of Process Equipment**.
- 7.2.2 If acceptable cleaning has not occurred as part of the BPR, if re-cleaning is necessary due to a test failure, or if cleaning has not been documented, proceed to Section 7.4 of this SOP.
- 7.3 Cleaning Procedure for Columns that had Acceptable Cleaning Documented in a BPR.
- 7.3.1 Rinse the empty column thoroughly with WFI and wipe the column with a cleanroom wipe to remove visible particles.

- 7.3.2 Collect and test samples according to **SOP 21529, *Equipment Interproduct Cleaning and Clearance***.

**NOTE:** Some samples may require disassembly of the column. Disassemble the column, as needed, to obtain those samples using the procedure described below. If rinse samples are necessary on the disassembled column, rinse as many of the column parts with WFI as possible and obtain a representative sample of the rinse water.

- 7.3.3 Disassemble the column glass tube from the top and bottom column adaptors.
- 7.3.4 Place all parts of the disassembled column on a clean surface, and place the glass tube on cleanroom wipes as a cushion for the glass.
- 7.3.5 For columns with disposable mesh screens and support nets, remove the old screens and nets from the bottom and top adaptors and discard.
- 7.3.6 Use a cleanroom wipe to remove moisture from the column. Reassemble the column without mesh screens and support nets, if possible. For columns that do not have disposable screens and nets, they will remain intact.
- 7.3.7 Label the column per **SOP 14150, *Labeling of cGMP Purification Equipment for Cleaning Status***.
- 7.3.8 Move the empty, cleaned column to a controlled area of Class 100,000 or better for storage.
- 7.3.9 CGMP Manufacturing group documents this cleaning on Form 14146-02, Column Cleaning and Testing. Large Scale Production/Late Process Sciences group uses Form 21529-03, Interproduct Cleaning Worksheet, as per **SOP 21529, *Equipment Interproduct Cleaning and Clearance***.

- 7.4 Cleaning Procedure for Columns Whose Product- and Resin-Specific Cleaning was not sufficient according to Section 7.2.

- 7.4.1 Rinse the empty column thoroughly with WFI, and wipe the column with a cleanroom wipe to remove visible particles.
- 7.4.2 Fill the empty column with 0.5 N NaOH and purge the bottom adaptor mesh screen to remove large air bubbles.
- 7.4.3 Reattach the top adaptor at its maximum height. Slowly lower the top adaptor until NaOH flows out of the top valve. Adjust the flowpaths of the top and bottom valves to ensure that every flowpath is exposed to the NaOH.
- 7.4.4 Expose the column and valves to the NaOH for at least 60 minutes.
- 7.4.5 After the NaOH exposure, remove the top adaptor from the column, rinse with WFI, and place on a clean surface.
- 7.4.6 Thoroughly rinse the column with WFI and allow it to drain through the bottom adaptor valve. Rinse the column until the pH of the effluent collected from the bottom valve is pH 5-7.

7.4.7 For columns with disposable mesh screens and support nets, remove the old screens and nets from the bottom and top adaptors and discard.

7.4.8 Collect and test samples according to **SOP 21529, Equipment Interproduct Cleaning and Clearance**.

**NOTE:** Some samples may require disassembly of the column. Disassemble column, as needed, to obtain those samples using the procedure described below. If rinse samples are necessary on the disassembled column, rinse as many of the column parts as possible, with WFI, and obtain a representative sample of the rinse water.

7.4.9 Disassemble the column glass tube from the top and bottom column adaptors.

7.4.10 Place all parts of the disassembled column on a clean surface and place the glass tube on cleanroom wipes as a cushion for the glass.

7.4.11 For columns with disposable mesh screens and support nets, remove the old screens and nets from the bottom and top adaptors and discard.

7.4.12 Use a cleanroom wipes to remove moisture from the column. Reassemble the column without mesh screens and support nets, if possible. For columns that do not have disposable screens and nets, they will remain intact.

7.4.13 Label the column **SOP 14150, Labeling of cGMP Purification Equipment for Cleaning Status**.

7.4.14 Move the empty, cleaned column to a controlled area of Class 100,000 or better for storage.

7.4.15 CGMP Manufacturing Group documents this cleaning on Form 14146-02, Column Cleaning and Testing. Large Scale Production/Late Process Sciences Group uses Form 21529-03, Interproduct Cleaning Worksheet, as per **SOP 21529, Equipment Interproduct Cleaning and Clearance**.

7.5 If the column does not meet release specifications, the column must be re-cleaned according to either section 7.1 or 7.4 and re-sampled according to **SOP 21529, Equipment Interproduct Cleaning and Clearance**.

**NOTE:** After columns are cleaned, released, and stored empty, they fall under the purview of their corresponding column packing SOP (see **SOP 14100, Packing Instructions for the BPG Series Columns**, and **SOP 14121, Packing Instructions for FineLine Columns**). In these SOPs, parts such as mesh screens, support nets, and O-rings are replaced. The empty column (with new parts intact) is then exposed again to NaOH before being packed.

## 8.0 References and Related Documents

Form 14146-01 *Column Unpacking and Resin Storage*

Form 14146-02 *Column Cleaning and Testing*

Form 14146-03 *Resin Inventory*

SOP 12149 *General Cleaning of Process Equipment*



- SOP 12169**      *Rinse Water Sampling for Production Equipment*
- SOP 14100**      *Packing Instructions for the BPG Series Columns*
- SOP 14121**      *Packing Instructions for the FineLine Columns*
- SOP 14150**      *Labeling of cGMP Purification Equipment for Cleaning Status*
- SOP 21529**      *Equipment Interproduct Cleaning and Clearance*

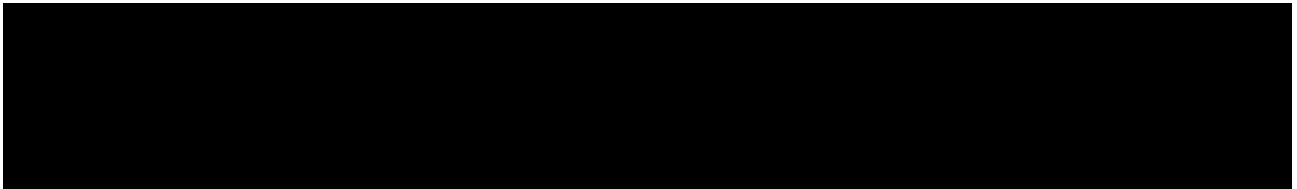
GE BPG Column Instruction Manual, PN 18-1115-22, Edition AE

GE Fineline Column Instruction Manual

## **9.0 Attachments**

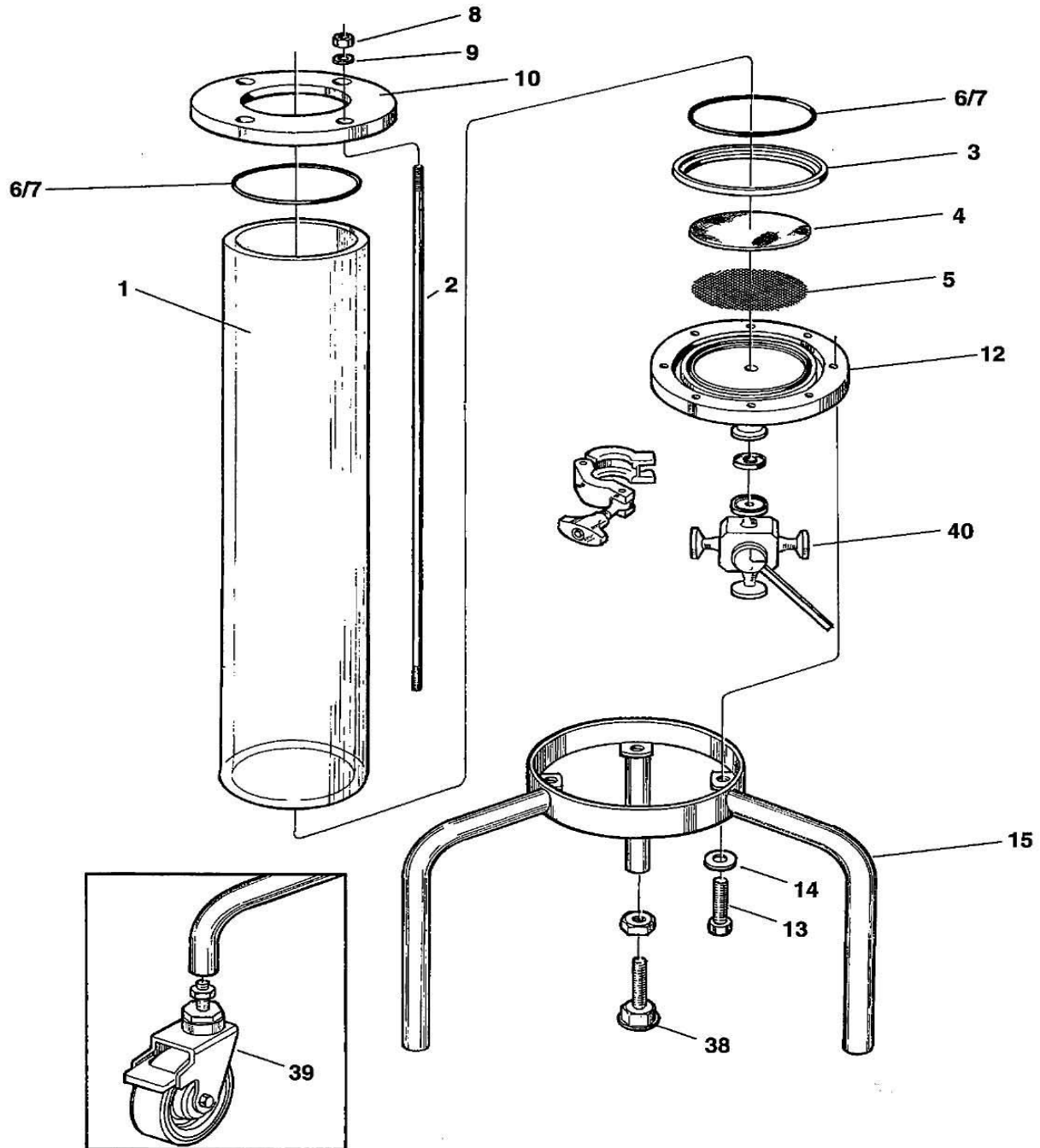
- 9.1 **Attachment 1**    BPG 100, 140, 200 Column Tube Schematic
- 9.2 **Attachment 2**    BPG 100, 140, 200 Column Adapter Schematic
- 9.3 **Attachment 3**    BPG 300 Column Tube Schematic
- 9.4 **Attachment 4**    BPG 300 Column Adaptor Schematic
- 9.5 **Attachment 5**    Fineline Column Schematic

## **10.0 Change Summary**



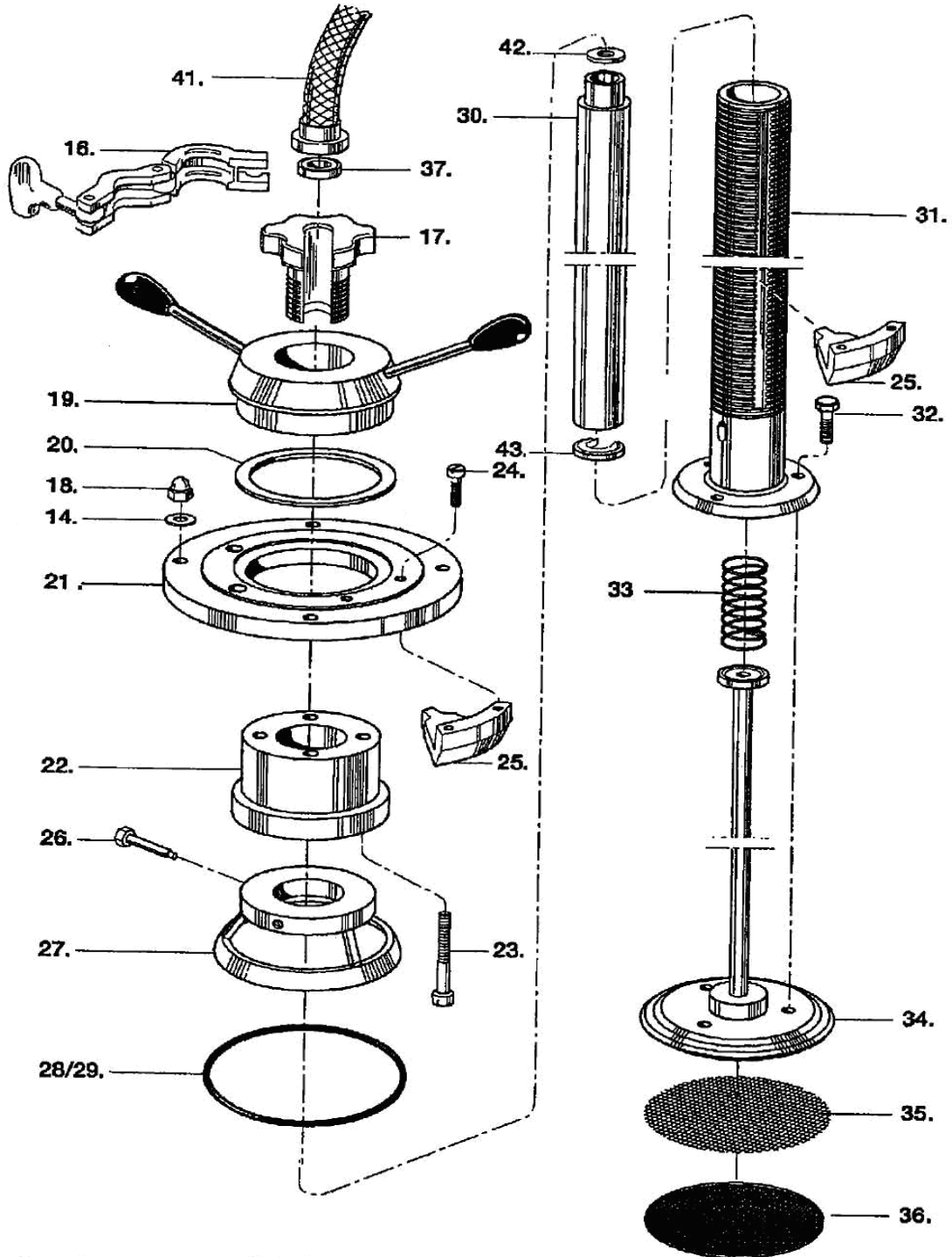
Attachment 1

BPG 100, 140, 200 Column Tube Schematic

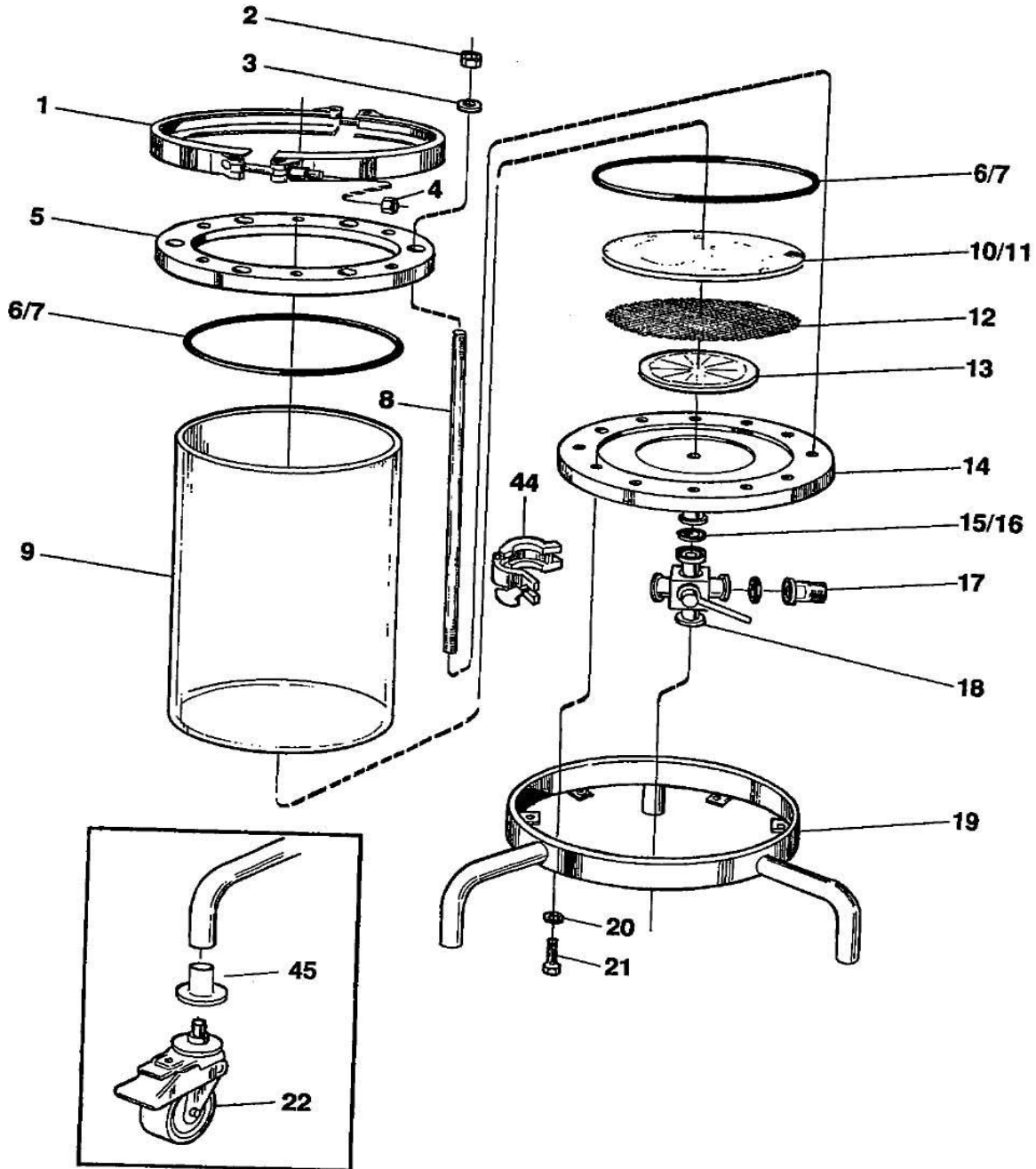




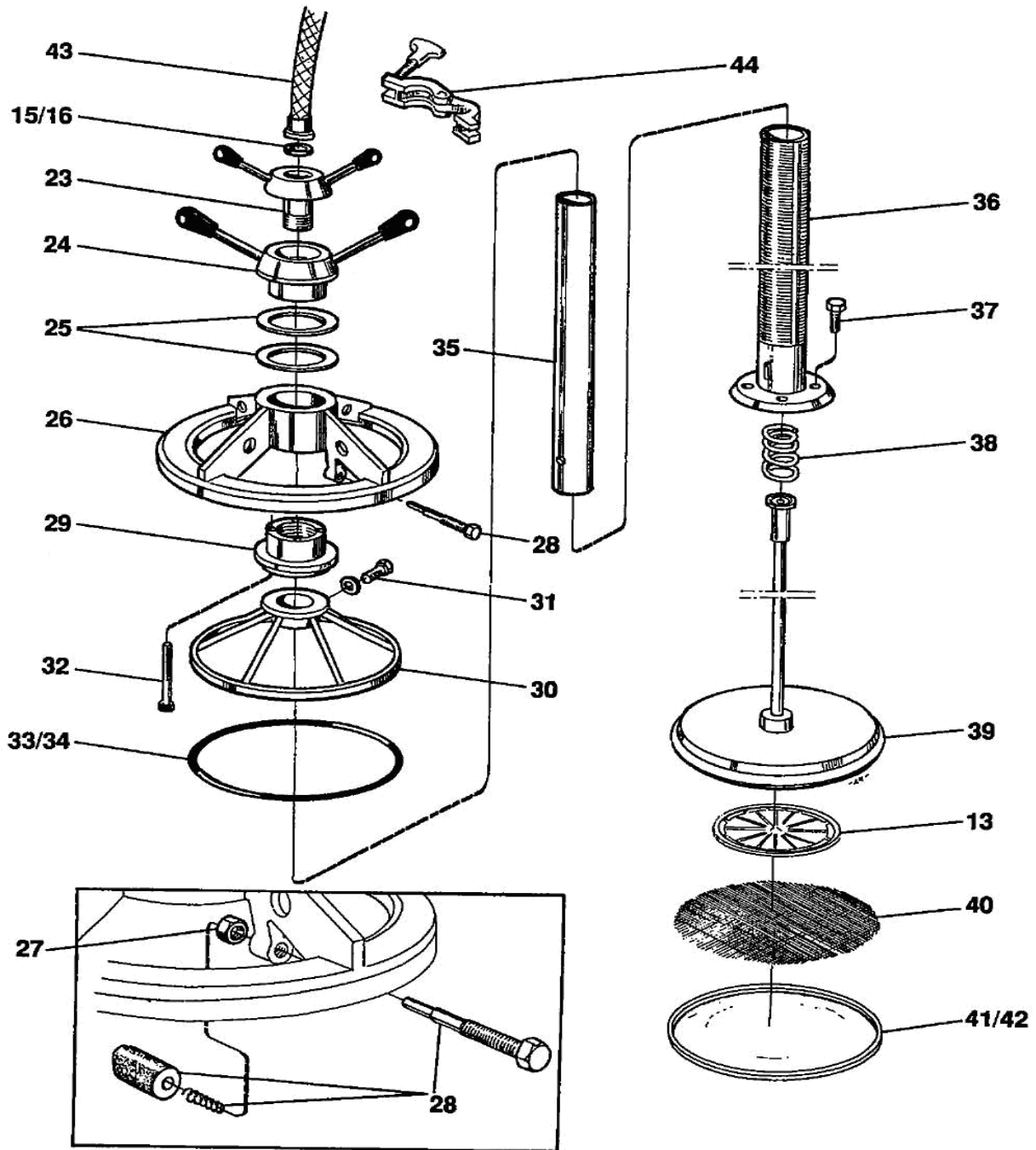
Attachment 2  
BPG 100, 140, 200 Column Adaptor Schematic



Attachment 3  
BPG 300 Column Tube Schematic



Attachment 4  
BPG 300 Column Adaptor Schematic



Attachment 5  
Fineline Column Schematic

