James Walker

Piston seal and material design
EBA chromatography column - client Biotechflow Ltd

A case study presented by
James Walker

High Performance Sealing Technology

Introduction

Chromatography columns are extensively employed in the biopharmaceutical industry to separate drugs and APIs from the starting materials and any by-products. Accurate separation of the product is essential as many of the resultant materials are directly injected into the bloodstream. This requires effective, and efficient, operation of the chromatography process, as well as extreme levels of cleanliness and biocompatible materials of construction.

Optimising the extraction of proteins from feedstock through the chromatography process, is a delicate balancing act aiming to reduce process time, minimise product loss, maximise yield per batch and the number of batches processed with the minimum labour requirements. In addition, especially for contract manufacturing operations, process flexibility plays an important role in optimising overall operational costs.

Expanded bed adsorption (EBA) chromatography offers a significant opportunity in this optimisation process, providing a single pass operation for the extraction of proteins from crude, particulate containing feed-stock. Unlike traditional chromatography processes, EBA removes the need for separate clarification, concentration and purification. This immediately improves the speed of batch processing and in turn, minimises losses through product degradation that occurs in the traditional multi-stage process.

Background

The challenge facing chromatography column manufacturer Biotechflow, was to design a scalable column that was economic to produce, providing an adjustable bed with a 1m range within an overall maximum height of 2050mm and a $1m^2$ footprint.

Further design detail challenges centred around a range of elements including disposable inlet and outlets, ultrasound receivers and piston geometry. It was in relation to the piston operation that James Walker became involved in the design stage of the new EBA column.

To overcome the 2050mm height restriction, the Biotechflow piston was designed so that no studding, bars or piston body extended outside the column.

This was achieved by designing a ‘balanced dynamic piston’, completely isolated inside the column tube. The piston is moved by either pressure from the liquid below or by increasing air pressure above the piston, rather than necessitating the bulky hydraulic power pack generally associated with chromatography columns.

The brief
The new Biotechflow column design, which incorporates many beneficial new features, placed unique demands on the piston seals in the column. The seal must be designed to allow;

- Lock the piston in place when required.
- Allow an adjustable bed height when the seal is engaged.
- Be able to be cleaned in place between the piston and the column cylinder.
- The seal must move the piston smoothly against the column (no juddering).
- Zero dead space to prevent possible cross contamination.

Couple these requirements with the biocompatibility constraints of USP <87> and <88> and cleanliness requirements of USP <643> and <381>, additionally the material must also be resistant to the cleaning chemicals employed. All of which made the seal design a tough challenge.

Material Engineering
Elast-O-Pure® EP75 Black is a peroxide cured EPDM based compound specifically formulated for bioprocessing applications, particularly in static seals. As the piston seals in the column act as both static and dynamic it was thought that this material, at a hardness of 76 IRHD would be a good fit. Elast-O-Pure® EP75 Black meets all the criteria required including:

Biocompatibility : USP <87> and <88>
Low extractables : USP <643> and <381>
FDA *21 CFR 177.2600* compliant

Additionally, extensive long term testing in typical cleaning solutions, such as caustic and phosphoric acid have shown Elast-O-Pure® EP75 Black to be resistant in both hot and cold solutions even after 150 days.

The materials compounded by James Walker for use in the manufacture of products for biopharmaceutical applications are specifically formulated by the company's materials science department to minimise leachables and extractables without affecting performance.

The company controls every stage of the manufacturing process in-house, from testing of raw ingredients to final inspection of the finished product and is able to offer total traceability for every ingredient and process.

James Walker also ensures that no mould release agents are used in the manufacturing process as many of these are cytotoxic, and increase extractables levels. All additives used to make the compound are totally ADI free (free of all animal derived ingredients).

Seal Design

Biotechflow approached James Walker with a proposed inflatable seal design. This was further developed by the James Walker pharmaceutical applications engineering team into the format adopted in the final column design, which in conjunction with the properties of Elast-O-Pure® EP75 Black, fully addressed the criteria set by Biotechflow.

The seal design consisted of two components; a stainless steel seal carrier and a C-profile elastomeric seal (Figure 1.).

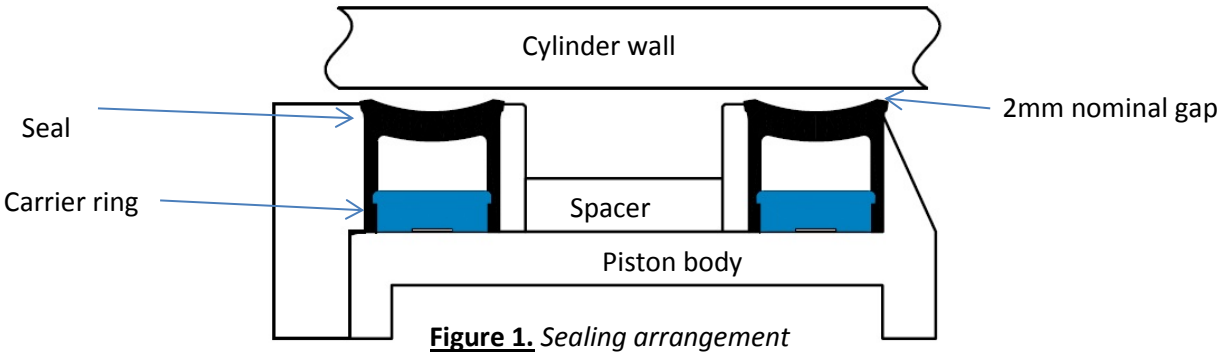
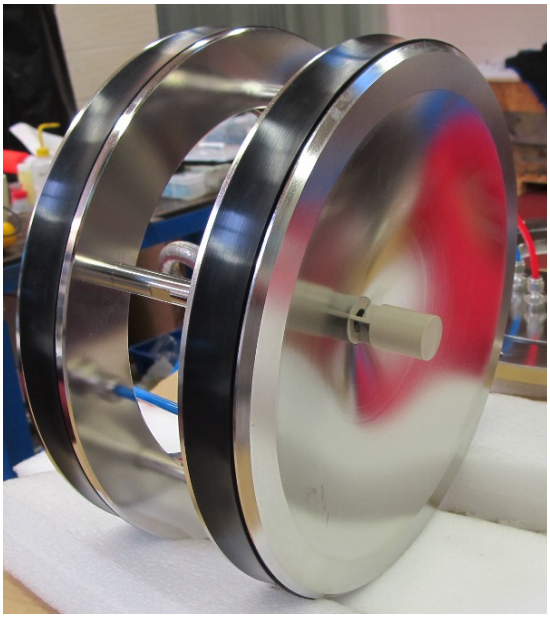


Figure 1. *Sealing arrangement*

The detail shows how this arrangement works in the column. The sealing ring is first placed on the piston diameter, sealing to this surface achieved by the use of two O-rings. Next the seal is placed over the ring and locked in place, over the sealing beads on the carrier ring and held in place with a sealing plate in the arrangement shown.

Figure 2.

This seal arrangement is shown here, fitted in the un-inflated state.



To achieve zero dead-space (effectively leaving no voids or corners that are not able to be cleaned and flushed, where material could build up and potentially cause contamination) the seal was required to fit snugly into the groove width. A moulded profile provided the precise seal profile and tolerances needed.

A moulded seal also allowed us to create a seal with thin flexible side walls but a more rigid outer wall. Such variation in thickness in an extruded profile is difficult to achieve but our moulding techniques were more than capable of meeting the requirement.

Performance

There are three main performance criteria for the seal.

Firstly, it has to be able to lock the piston in place. This occurs at 3 bar when the upper and lower edges of the seal engage. Subsequent trials, at 6 bar inflation, showed the central band of the seal material pushed against the tube wall (see Figure 3) holding the piston securely in place during process.

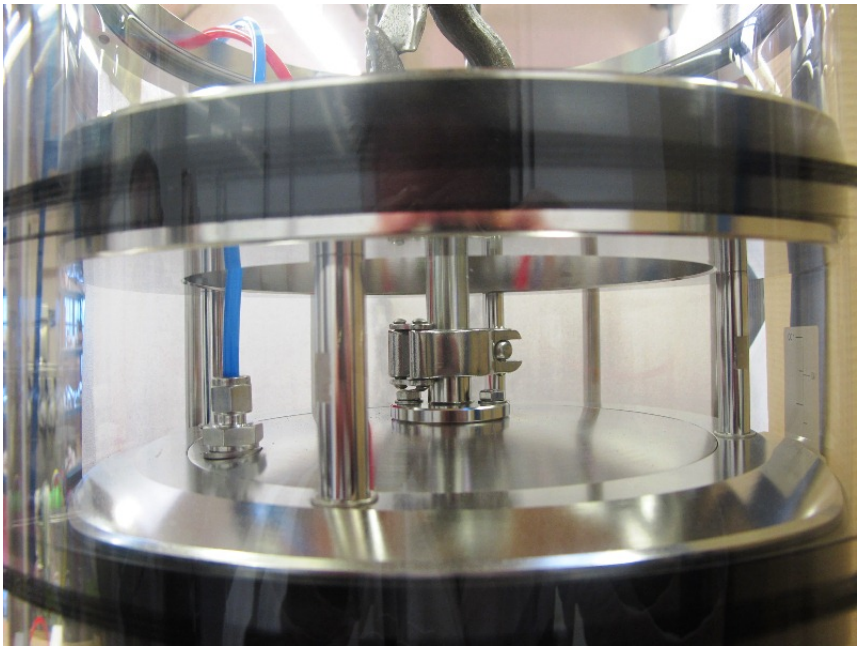


Figure 3.

Piston locked in place at 6 bar inflation with the seal fully engaged at top, middle and bottom.

Secondly, the piston needs to be able to be moved, even when the seal is engaged, automatically maintaining a dynamic pressure on the bed yet adjustable by the operator. Trials at 3.5 bar showed the central section of the sealing face retracts allowing piston movement. The piston is then able to be moved downwards with 0.5 bar ΔP air pressure in the chamber above, or upwards by the liquid pressure below the piston, whilst maintaining column working pressure.

Finally, the system needed to be easy to clean in place. This is simply achieved by deflating the seal. This reduces the seal diameter by 2 mm, giving a circumferential gap for easy cleaning. The column also incorporates an access hatch in the top, giving the operator access for cleaning from above the piston; not something usually achievable in standard column designs.

Operational results

The Biotechflow column design fully met the challenges set out by the user in the requirement specifications to produce a new sanitary column design for expanded bed chromatography which met current Good Manufacturing Practice standards.

Current applications are biopharmaceutical production from crude, high cell density and highly viscous feed streams including cell culture, foods and plasma. This new design Biotechflow EBA column is presently used in Phase II and Phase III production of biopharmaceuticals including monoclonal antibodies (MAbs).

Benefits observed in operation include:

- Suited to clean rooms with restricted ceiling height and floor space
- Production scale runs took 37% time of traditional methods
- Higher yields significantly reduced buffer volume requirement
- Product concentration significantly increased
- Higher throughputs and flow rates and more cell debris removed

This project provides an excellent example of James Walker's competencies and capabilities in applications engineering and material development. From our highly developed precision manufacturing techniques through to bespoke hand-finishing and stringent quality and inspection regimes, James Walker expertise is successfully applied to customer design and engineering projects to help develop new products or adapt existing concepts. We realise customers' ideas even in the toughest of situations.

James Walker

James Walker worldwide sales and customer support

James Walker Asia Pacific
Tel: +65 6267 4788
Fax: +65 6267 4980
Email: sales.sg@jameswalker.biz

James Walker Australia
Tel: +61 (0)2 9721 9500
Fax: +61 (0)2 9721 9580
Email: sales.au@jameswalker.biz

James Walker Benelux
(Belgium)
Tel: +32 3 820 7900
Fax: +32 3 828 5484
Email: sales.be@jameswalker.biz
(Netherlands)
Tel: +31 (0)186 633111
Fax: +31 (0)186 633110
Email: sales.nl@jameswalker.biz

James Walker Brasil
Tel: +55 11 4392 7360
Fax: +55 11 4392 5976
Email: sales.br@jameswalker.biz

James Walker China
Tel: +86 21 6876 9351
Fax: +86 21 6876 9352
Email: sales.cn@jameswalker.biz

James Walker Deutschland
Tel: +49 (0)40 386 0810
Fax: +49 (0)40 389 3230
Email: sales.de@jameswalker.biz

James Walker France
Tel: +33 (0)437 497 480
Fax: +33 (0)437 497 483
Email: sales.fr@jameswalker.biz

James Walker Iberica
Tel: +34 94 447 0099
Fax: +34 94 447 1077
Email: sales.es@jameswalker.biz

James Walker Inmarco (India)
Tel: +91 (0)22 4080 8080
Fax: +91 (0)22 2859 6220
Email: info@jwinmarco.com

James Walker Ireland
Tel: +353 (0)21 432 3626
Fax: +353 (0)21 432 3623
Email: sales.ie@jameswalker.biz

James Walker Italiana
Tel: +39 02 257 8308
Fax: +39 02 263 00487
Email: sales.it@jameswalker.biz

James Walker Mfg (USA)
Tel: +1 708 754 4020
Fax: +1 708 754 4058
Email: sales.jwmfg.us@jameswalker.biz

James Walker New Zealand
Tel: +64 (0)9 272 1599
Fax: +64 (0)9 272 3061
Email: sales.nz@jameswalker.biz

James Walker Norge
Tel: +47 22 706800
Fax: +47 22 706801
Email: sales.no@jameswalker.biz

James Walker Oil & Gas (USA)
Tel: +1 281 875 0002
Fax: +1 281 875 0188
Email: oilandgas@jameswalker.biz

James Walker South Africa
Tel: +27 (0)31 304 0770
Fax: +27 (0)31 304 0791
Email: sales.za@jameswalker.biz

James Walker UK
Tel: +44 (0)1270 536000
Fax: +44 (0)1270 536100
Email: sales.uk@jameswalker.biz

www.jameswalker.biz

BP4538 Registered Office: James Walker Sealing Products and Services Ltd, Lion House, Oriental Road, Woking, Surrey GU22 8AP, United Kingdom. Reg No. 00264191 England