

TECHNOLOGY

One innovative product technology produced in *E. coli* has already been transferred smoothly from Boehringer Ingelheim Austria GmbH to Biomeva GmbH. The process for this new technology platform was implemented successfully in an extremely short time – the first GMP runs were performed just five weeks after the first technology transfer meeting. Seven weeks later, GMP material was released for clinical trials.

Boehringer Ingelheim's strength and leading position in the large-scale production of biopharmaceuticals, combined with Biomeva's expertise, reliability and flexibility in the technology transfer of



Fig. 3: Chromatography at Biomeva

new processes and the manufacture of clinical trial material using the same technology platform, provides integrated solutions and accelerates the development and production of biopharmaceuticals.

By leveraging the competencies of both organisations, a production alliance was created which reflects unparalleled quality, breadth, and flexibility, allowing clients to achieve an important goal: a reduction of time to market. Host cell expression systems and process formats created at Boehringer Ingelheim facilitate tech transfer for commercial manufacturing without any delay for the customer. This joint effort provides an excellent opportunity to reach a broader audience.

Contact

Dr. Thomas Pultar, CEO
 BIOMEVA GmbH
 Czernyring 22. 69115 Heidelberg
 thomas.pultar@biomeva.com

SEPARATION

Chromatography media scouting

Dr. Jürgen Friedle, Atoll GmbH, Weingarten, Germany

Most suppliers of chromatography products have learned that if they want to sell media to busy process developers, it needs to be in a format that accommodates their normal workflow. As a result, there is now a profusion of scouting cartridges in all shapes and configurations. This approach is a big step forward from having to pack your own columns. However, Atoll GmbH has taken the concept three steps further with a platform to compare all commercially available resins in an identical geometry, either in ready-to-use LC columns or in a 96-array format that can be robotised for automatic operation.

Step Number One: it is now possible to evaluate media from all vendors in the same format, doing away with concerns about different column diameters, varying bed heights, and contributions from diverse frit materials or other housing components. Different results give confidence that they reflect real differences among the media, and not column design artefacts. Atoll can provide any media in MediaScout® MiniChrom columns with logical formats. Various dimensions (diameter (mm) x length (mm)):

- 5x10=0.2 ml
- 5x25=0.5 ml
- 5x50=1 ml
- 8x20=1ml
- 8x 50=2.5ml
- 8x100=5ml
- 11.3x50=5 ml
- 11.3x100=10ml

All support flow rates up to 1500 cm/hr, with a maximum operating pressure of up to 30 bar.

Step Number Two: one of the lessons learned from packing media in large scale columns has been that some degree of axial compression usually needs to be applied to a packed bed in order to obtain its best

Table 1: Prepacked 1 ml-columns of media from different suppliers

Trade Name	Inner Diameter x Length/mm x mm	Column Volume/ml	Vendor
▶ HiTrap™	7.0 x 25.0	1.0	GE Healthcare
▶ AcroSep™	9.4 x 14.8	1.0	Pall
▶ Toyoscreen	6.4 x 31.0	1.0	Tosoh Bioscience
▶ Fractogel® EMD Scout Column	8.1 x 19.4	1.0	Merck KGaA
▶ Econo-Pac®	5.9 x 36.0	1.0	Bio-Rad
▶ MediaScout® MiniChrom	5.0 x 50.0	1.0	Atoll
	8.0 x 20.0	1.0	
	5.0 x 25.0	0.5	
	5.0 x 10.0	0.2	
	5.0 x 5.0	0.1	

TECHNOLOGY

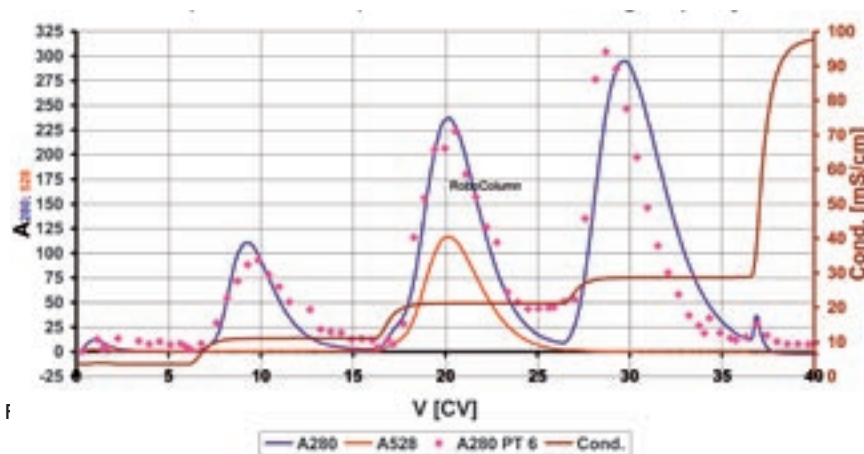
News

■ ES cell cultivation

Jülich/Leipzig – German bioreactor specialist DASGIP AG (Jülich) and the Fraunhofer Institute for Cell Therapy and Immunology (IZI) have received a €1.1 million grant from the German Research Ministry to develop a method for preclinical embryotoxicity testing of drug candidates. DASGIP and stem cell specialists from IZI will establish an *in vitro* test to identify the substance's bone-harming potential, an indicator for embryotoxicity. By adding compounds with known *in vivo* osteotoxic potential, adverse effects on the differentiation of pluripotent stem cells will be monitored in a controlled bioreactor system. Non-human embryonic primate stem cells will be compared to human progenitor cells to study varying molecular reactions compared to mice, the established test organisms. If functional and validated, the system would make 5 million animal tests per year unnecessary.

■ Biotechnica

Hanover – Biomanufacturing will be in the focus of Biotechnica trade fair (7–9 October, 2008), the ultimate European biotech event in Hanover (Germany). With a meeting "Process integration in biopharmaceutical manufacturing" organised by Capgemini Consulting, the Biotechnica will be providing industry professionals with a platform addressing topics such as process integration, tech transfer, new technologies, project management, regulatory aspects and new business models. The meeting is intended to provide an exchange platform for the biopharmaceutical and biomanufacturing industries. Corvay will also be organising a special thematic stand for European biomanufacturing companies.



column HR5/50 (GE Healthcare) vs Robocolumn.

Separation of Ribonuclease A, Cytochrome C, Lysozyme on SP Sepharose XL, sample load 1% of breakthrough capacity. Straight line: Step gradient continuous elution of the 5/50 column with Äkta® system; dotted line: Step gradient elution data of 50→1 fractions with MediaScout Robocolumns on Tecan system. Data: Jürgen Hubbuch, Timm Schröder, Research Institute Jülich, Germany

performance – and to achieve consistent performance. Each type of media has its ideal compression factor. Atoll columns are individually compression packed to provide the correct compression factor for each type of media so that accurate process modelling can be achieved. Dynamic binding capacity data are scaleable for process applications.

Step Number Three: the foundation of a robust purification procedure is a thorough evaluation of qualified media candidates over whatever range of conditions is necessary to characterise their fractionation performance. The amount of time and labour required to conduct scouting of this scope on a column-by-column basis is beyond the

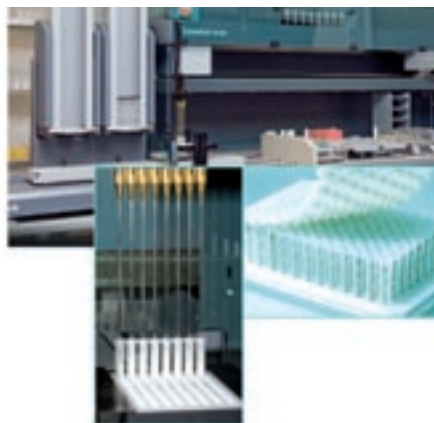


Fig. 2: Workstation for robotic liquid displacement and 96 array format Mini-Columns for centrifugal operation

resources available to many process developers. Atoll offers the means to transcend this compromise. The MediaScout System supports parallel processing with a 96-array plate that accommodates their MiniColumn cartridges. This allows one to evaluate performance on properly packed columns, not just some loose resin in a porous well. Flow can be induced with a centrifuge, positive displacement pipettor, or by fixed tip like that in a TECAN Freedom EVO system. Results obtained by an automated robotic operation show the same performance as experiments with conventional columns (Fig. 1). Whether you want to automate the scouting or just keep it simple, Atoll's system makes high-throughput process development accessible to everyone.

This system also offers tremendous saving potential. Integrating the two technologies entirely removes all of the manual steps for buffer preparation, sample injection and elution, including detection. Depending on the protocol used (Fig. 2), this means 96-array plates can be completely processed in minutes. The integration offers a powerful new tool for high-throughput sample conditioning and process development experts. ▼

Contact

Atoll GmbH
Dr. Jürgen Friedle
Ettishofer Str. 10, D-88250 Weingarten
Tel.: +49-(0)751-56 121 85
j.friedle@atoll-bio.com, www.atoll-bio.com