NEW ENGLAND PDA NEWSLETTER

08 February 2007

Volume 2 Number 1

Connecting People, Science and Regulation

In This Issue

February 15th NEPDA Event
Charles River Laboratories Facility Tour
Chromatography Validation TR14

Presentations by

Stephen Notarnicola, PhD, Biogen Idec
Susan Schniepp, Hospira

Thanks to our Sponsors!

The Chisholm Corp/Pall Corp
www.thechisholmcorp.com
CSSC, Inc.,a Q Pharma Company
www.csscinc.net
Blue Stream Laboratories
www.bluestreamlabs.com

Recent Advances in Bioprocessing Equipment – Membrane Chromatography

By Sourav Kundu, Director, Process Development, Amgen

Current monoclonal antibody production processes include a number of chromatography steps for purification of the expressed protein from the cell culture harvest. These chromatography steps provide separation of the protein of interest from the residual host cell proteins, cell-culture additives and other contaminants. The typical chromatography steps are capture by Protein A resin, followed by a combination of ion exchange and/or hydrophobic interaction chromatography. Typically, the final ion exchange step is intended to be a "polishing" step that removes trace quantities of contaminants. Most commonly, the ion exchange step utilizes an anion exchange resin with a quaternary ammonium (Q) or diethylamine (D) chemistry. In addition to providing purification, the anion exchange step provides virus removal. Greater than 3 logs of virus reduction have been reported from anion exchange resin chromatography steps in the flow-through mode evaluated by scaled-down model and virus-spiking studies (1).

Recent advancements in molecular biology, media development, and bioreactor optimization have led to titers upward of 5 g/L creating a large mass of protein to be processed through the downstream purification steps from a single 10,000 – 15,000 L bioreactor run. As a result, the chromatography columns have grown in size, often reaching 1.4 – 2.0 m in diameter. The magnitude of the chromatography steps have reached their limits in terms of column diameter (equipment design, mobility, flow-distribution concerns), loading (resin capacity concerns), and bed height (resin integrity concerns). These issues are leading to development of novel technologies, such as membrane chromatography.

Membrane chromatography systems employ a disposable filter that contains the appropriate ion exchange chemistry. The protein solution flows through the filter and the contaminants bind to the membrane. In contrast to resin bed chromatography, membrane chromatography provides much greater access to the ligands for binding without depending on long residence time in the column to account for mass transfer limitation resulting from low diffusivity of protein molecules within the resin beads. Membrane chromatography cartridges can be operated at much higher protein loads and much higher flow rates reducing the size of the device and processing time. Loading in excess of 10 kg/L and linear flow rates in excess of 620 cm/h have been reported for polishing of an antibody solution by a Q-membrane operated in a flow-through mode (1). Membrane chromatography offers significant virus reduction capabilities. Virus reduction values of 5-7 logs have been reported with Q-membrane devices at >10.7 kg of MAb/L membrane (1). Another publication reported 4-7 logs of virus reduction using microporous polyethersulfone membrane devices with Q-chemistry (2). Host cell DNA and protein contaminant reduction values comparable to the equivalent column chromatography have been achieved with the membrane devices, notably at much higher protein loads and flow rates. A limitation of these devices appears to be high backpressure generated when working with protein solutions at conditions such as at low temperatures. These disposable devices take up less space on the manufacturing floor, and provide cost advantages as a result of less upfront validation costs, less buffer usage and less processing time despite the expense associated with being a consumable part (3).

As the pressure rises on the biotech industry to reduce cost of goods, reduce cycle time and increase production efficiency, new technologies such as membrane chromatography will emerge as viable and cost-effective options for a routine manufacturing scenario.

References:

Mora J, Sinclair A, Delmdahl N, Gottschalk U. Disposable membrane chromatography – Performance analysis and economic cost model. *Bioprocess International* 2006 (Suppl. 4), 4, 38-43.

Sellick I. Chromatography Advisor #4 - Capturing very large biomolecules with membrane chromatography. *Bioprocess International* 2005, 3, 58-59.

Zhou JX, Tressel T. Basic concepts in Q membrane chromatography for large-scale antibody production. *Biotechnol. Prog.* 2006, 22, 341-349.

FUTURE TOPICS:

Impact of International Outsourcing on Regulatory and Quality Systems

by Mina Gerber and Melissa Smith

Real Life Lessons: HVAC System Validation

By Myron Dittmer

Three Part Series on the New OOS Guidance

By Mina Gerber

NEW ENGLAND PDA PRESIDENT'S MESSAGE

Louis Zaczkiewicz

With the beginning of 2007 comes the biannual change of leadership at the New England PDA. My name is Louis Zaczkiewicz and I am beginning as chapter President. The additional members of this term's board of directors include Jerry Boudreault (President-Elect), Rusty Morrison (Treasurer), Melissa Smith (Secretary), Myron Dittmer (Member At Large) and Bruce Rotker (Member At Large). Each of us will be serving your chapter for a two-year term.

My involvement with the PDA began in the 1980's with a course in sterilization validation in Montreal. A few years later I was involved with the formation of this chapter when Tim Leahey and Bob Pazzano asked for organizing volunteers. Our meetings were at the Millipore Corporation in Bedford and we quickly developed bylaws (committee lead by Mark Staples) and activities (I lead this committee). We elected Bob Pazzano as the first President who continued in this position until Mark Staples took over in 2003. This was the start of our current system where a PDA member is elected to a 2-year President-Elect term followed immediately by a term as President. This system allows for a continuity of leadership and a systematic rotation. Historically the outgoing President has assumed one of the Member-At-Large positions after their term is over.

When we started this chapter we struggled with our identity as representing New England, since our meetings were generally in the Boston area. We had many discussions about moving the meetings around New England, but in the end settled in at the Cambridge location. Under Myron Dittmer's leadership, we started to mix things up by moving the meetings to the Boston suburbs. The membership responded positively by doubling the attendance at our very first meeting. I feel now is the time to begin the process of going further. We are targeting to have a facility tour in September down in Rhode Island. In May of 2008 we would like to go north to the Baker facility in Sanford, Maine and have a tour and meeting on

isolator systems (this is tentative). Although we haven't received site approvals yet, we are hopeful that NEPDA members will assist in making these tours a reality.

Another item I've been interested in is to get back to having vendor nights. Because we don't have the time or resources to put on a big vendor event, I've set our sites a little lower by having a themed vendor night. Here the vendors would share a common theme and be able to give a short talk about a small aspect of that theme. Our goal is to have a vendor night with the theme: Construction and Validation. We are looking for volunteers interested in planning this event for the beginning of 2008.

Finally we must recognize that we are part of the Global PDA, an organization with a rich heritage of teaching. Over the years the PDA has published 42 technical reports including topics such as steam sterilization practices, CMC controls and Cold Chain Management techniques. We will focus our meeting topics to include a variety of these reports. For example the meeting on February 15 will take place at the Charles River Laboratories and consist of a facility tour and a presentation of the proposed revision to Technical Report 14 on "Industry Perspective on the Validation of Column-Based Separation Processes for the Purification of Proteins". Then on April 11, we will have a tour of the Sypris ship-testing facility in Billerica followed by a dinner meeting on TR-39: "Cold Chain Guidance for Medicinal Products: Maintaining the Quality of Temperature-Sensitive Medicinal Products through the Transportation Environment." We are currently planning meetings on other technical reports such as filtration and steam sterilization. I am sure that these next 2 years will fly by. I hope that the programs that we are planning will encourage you to get more involved in this chapter. If so, here is an open invitation to be part of the planning meetings that we have on the second Wednesday of every other month starting January10. The meetings are held from 6 pm to 7:30 pm at the HCM facility located at 99 South Bedford Street, Suite 2, Burlington, MA. Please RSVP to one of the NEPDA Board members or me so that we can arrange for enough space and refreshments.

Feel free to contact any of the Board members or me with program ideas or to volunteer in the running of this chapter.

Have an idea or question?

Would you like to write an article?

Contact Us

melissa@mjqualitysolutions.com

Links for Training:

http://www.connectlive.com/events/drugdev/

This is a CDER training course complete with on-line quiz! It examines various aspects of the New Drug Application (IND/NDA) processes, including clinical drug testing, the Importance of the Prescription Drug User Fee Act (PDUFA), FDA Modernization Act, Generic drugs and post-marketing surveillance.

http://ocw.mit.edu/OcwWeb/index.htm

This is the MIT OpenCourseWare site-you can see the lectures, review lecture notes, and listen to interviews with instructors in departments like Biological Engineering and Chemistry.

"Reflections of a Past President"

By Myron Dittmer

The New Year brings a change in the NEPDA Board that includes a change in the presidency of our chapter. January began the term of our new chapter president Louis Zaczkiewicz. I look forward, in my new position as Member-at-Large, to working with Louis and other new board members on the planning of chapter events and activities for the next several years. Based on our initial board meeting of 2007, many new and exciting and new events are being planned for our chapter.

I would like to express my sincerest appreciation to the board and planning committee members who worked so hard and helped me over the past several years in planning all the great events we sponsored. It has truly been a group effort. Also, a special thanks to all our many dedicated and committed sponsors who helped support our meetings. Without you it would have been very difficult to put on these events and to maintain the chapter's financial security.

I have, over the past several years, so many wonderful memories and pleasant experiences to reflect upon while president of our chapter. One of the most enjoyable was chairing our monthly board and planning committee meetings and working with such a terrific group of people. The most important thing I did when I became president in January 2005 was to form a planning committee to assist the board in the planning of chapter events. Most of the people who began with me at that time are still part of the committee and some have even moved up to be board members. To all of them I say - thank you! Another enjoyable experience has been in meeting Global PDA staff and especially Henry Kwan, Senior Chapter Liaison. Henry provided us with his valuable advice and insight on matters concerning Global PDA and important information on other chapter happenings. Also, he has taken time from his busy schedule to attend many of our meetings and he continues to be one of our major supporters back at Global PDA. Over the past several years we have seen a dramatic increase in member attendance at our chapter meetings and I attribute this to the extraordinary efforts and good programming by the board and planning committee. Our chapter meeting in May of 2006, on FDA Inspections, drew over 140 people! It was not uncommon for us to have over 70 members attend chapter events. Also, under the energetic direction of Melissa Smith, we implemented our first chapter newsletter including an on-line, electronic version.

I look forward to participating in board activities for the next several years and I know that Louis and his team will continue to provide innovative and creative programming that will continue to generate interest among our members.

Finally, I would like to single out Mark Staples who convinced me to be his President-Elect back in 2003. He became my mentor and someone who I have admired over the years for his counsel and committed efforts in advancing the goals of this organization. Thank you, Mark, for giving me this special opportunity!