National Student Design Competition
2010

AIChE®

If there are any questions about the Design Competition, student chapter advisors and design course instructors are asked to contact:

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Please read the rules on the following pages carefully before submitting a solution to AIChE.

AIChE

October 2009

Dear Chemical Engineering Department Heads and Student Chapter Advisors,

I am pleased to send you the 2010 AIChE National Student Design Competition statement. Please forward it to those faculty teaching design courses. Following is this year's challenge:

"Manufacturing Facility for a Biopharmaceutical: Monoclonal Antibody"

As always, the names of the sponsoring organization and the authors are being withheld to ensure confidentiality. Both will be announced after the deadline, June 4, 2010.

An entry form – required for each participant -- is available as a separate attachment, and must be submitted along with the completed solution.

We welcome participation by individuals and teams of up to three students. Please indicate the names of all team members on each entry form, and be advised that each team member is required to submit a separate entry form.

Because the National Student Design Competition is a benefit of AIChE student membership, entrants must be AIChE national student members. Any non-member submissions will not be considered. To join, students can download a membership application form at http://www.aiche.org/students/.

Please take time to review the rules, found on the following pages. It is important that all solutions strictly adhere to the Final Report Format.

All submissions must be submitted in an electronic format – and submitted via postal mail on a CD.
Submissions must be no more than two documents --totaling 100 or fewer pages of main text, with an allowable 100 ages of supplementary materials – in one of the following formats: PDF or MS-Word. The requested format is a single PDF file—the Adobe Acrobat program can be used to combine pages from different sources into one document.

Student Chapter Advisors are asked to select the best solution or solutions, not to exceed two from each category (individual and team).

Solutions must be submitted **on a CD** by postal mail or ground delivery -- postmarked no later than Friday, June 4, 2010. Please maintain a copy for your files. To order additional copies of the Student Design Competition statement, email studentchapters@aiche.org or call AIChE at 1-800-AIChemE (242-4363).

If I can be of assistance, please contact me at (646) 495-1333 or via email at studentchapters@aiche.org. Questions relating to the substance of the design problem should be directed to: Professor Richard L. Long, New Mexico State University, at (505) 646-2503 or rilong@nmsu.edu.
Thank you for your support of this important student competition.

Sincerely,
June Lee
AIChE

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AIChE National Student Design Competition
2010

Contest Rules

Solutions will be graded on (a) substantial correctness of results and soundness of conclusions, (b) ingenuity and logic employed, (c) accuracy of computations, and (d) form of presentation.

Accuracy of computations is intended to mean primarily freedom from mistakes; extreme precision is not necessary.

It is to be assumed that the statement of the problem contains all the pertinent data except for those available in handbooks and literature references. The use of textbooks, handbooks, journal articles, and lecture notes is permitted.

Students may use any available commercial or library computer programs in preparing their solutions. Students are warned, however, that physical property data built into such programs may differ from data given in the problem statement. In such cases, as with data from literature sources, values given in the problem statement are most applicable. Students using commercial or library computer programs or other solution aids should so state in their reports and include proper references and documentation. Judging, however, will be based on the overall suitability of the solutions, not on skills in manipulating computer programs.

Departments, including advisors, faculty, or any other instructor, cannot provide technical aid specifically directed at the solution of the national student design competition.

The 2009 National Student Design Competition is designed to be solved either by an individual chemical engineering student working entirely alone, or a group of no more than three students working together. Solutions will be judged in two categories: individual and team. There are, however, other academically sound approaches to using the problem, and it is expected that some Advisors will use the problem as classroom material. The following confidentiality rules therefore apply:

1. For individual students or teams whose solutions may be considered for the contest: The problem may not be discussed with anyone (students, faculty, or others, in or out of class) before or during the period allowed for solutions. Discussion with faculty and students at that college or university is permitted only after complete final reports have been submitted to the Chapter Advisor.

2. For students whose solutions are not intended for the contest: Discussion with faculty and with other students at that college or university who are not participating in the contest is permitted.

3. For all students: The problem may not be discussed with students or faculty from other colleges and universities, or with individuals in the same institution who are still working on the problem for the contest, until after June 4, 2010. This is particularly important in cases where neighboring institutions may be using different schedules.

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Submission of a solution for the competition implies strict adherence to the following conditions: **(Failure to comply will result in solutions being returned to the appropriate Faculty Advisor for revision. Revised submissions must meet the original deadline.)**

ELIGIBILITY

- ONLY AIChE NATIONAL STUDENT MEMBERS MAY SUBMIT A SOLUTION. Non-member entries will not be considered. If you would like to become a National Student member, we must receive your membership application prior to submitting your solution. Application forms are found at http://www.aiche.org/students/.
- Entries must be submitted either by individuals or by teams of no more than three students. Each team member must meet all eligibility requirements.
- Each Faculty Advisor should select the best solution or solutions, not to exceed two from each category (individual and team), from his or her chapter and submit them per the instructions below.

TIMELINE FOR COMPLETING THE SOLUTION

- A period of no more than thirty (30) days is allowed for completion of the solution. This period may be selected at the discretion of the individual advisor, but in order to be eligible for an award, a solution must be postmarked no later than midnight June 4, 2010.
- The finished report should be submitted to the faculty advisor within the 30-day period.

REPORT FORMAT

- The body of the report must be suitable for reproduction, that is, computer-generated and in a printable format. Tables, supporting calculations and other appendix material may be handwritten.
- The solution itself must bear no reference to the students' names and institution by which it might be identified. Please expunge all such references to the degree possible.
- **Final submission of solutions to AIChE must be in electronic format (PDF or MSWord).** The main text must be 100 pages or less, and an additional 100 page or less is allowable for supplementary material. The final submission to AIChE must consist of 1 or 2 electronic files.

SENDING THE SOLUTION TO AIChE

- There should not be any variation in form or content between the solution submitted to the Faculty Advisor and that sent to AIChE National. The Student Chapter Advisor, or Faculty Advisor, sponsoring the student(s), is asked to maintain the original manuscript(s).
- **Copy the electronic file (PDF or MS-Word) to a CD, accompanied by its corresponding entry form, and mail the CD to Awards Administrator, AIChE, 3 Park Avenue, 19th Floor, New York, NY 10016**

- **DEADLINE: Entries must be emailed no later than midnight June 4, 2010.**

2010 National Student Design Competition:

Manufacturing Facility for a Biopharmaceutical: Monoclonal Antibody

Overview:
Design a large-scale manufacturing facility that has the flexibility to produce a variety of Monoclonal Antibody (MAb) products. In this design problem you will use a humanized MAb against Vascular Endothelial Growth Factor (VEGF) for design purposes. Your calculations for the amount of MAb needed for design purposes will be based on a similar molecule Avastin™. The first indication that the FDA will probably approve your molecule will be for the treatment of cancer. Another company has a VEGF-A compound approved for colon cancer. Your company has clinical studies currently in the following areas/indications: colon cancer, breast cancer, neovascular glaucoma and macular degeneration.

Introduction:

There are many classes of drugs in development in laboratories today with two of the largest classes being small molecule compounds and biopharmaceuticals. Drugs that are manufactured using biological processes, such as fermentation and extraction as compared to chemical synthesis, are in the biopharmaceutical category. This design problem statement will focus on the biopharmaceutical class of drugs, specifically monoclonal antibodies (MAbs) that are humanized. A humanized antibody is a type of antibody that is made by combining a human antibody and a mouse or a rat antibody together, for instance. The human part of the MAb makes it less likely that the human body's immune system will destroy the MAb. (Please see "Types of Monoclonal Antibodies" below for more information about the different kinds of antibodies) A monoclonal antibody protein consists of two main regions, the Fab (Fragment Antigen Binding) region and the Fc (Fragment crystallizable) region. The Fab region is composed of two identical light chains and portions of two identical heavy chain polypeptides. The complementary region of the antibody that binds to the site on the antigen is the Fab region. The remaining portions of the heavy chains are part of the Fc region which is glycosylated. The structure of the Fc region can be manipulated to customize antibody clearance and interactions of the Fc domains with cellular Fc regions. (Adams 2005). Today monoclonal antibodies are being used to treat a wide variety of illnesses, such as rheumatoid arthritis, Crohn's disease, transplant rejection, and a variety of cancers. The pipelines of biotechnology and pharmaceutical companies are full of the next generation of MAbs. You will be designing a facility that will allow the MAbs of today as well as the MAbs of tomorrow to be manufactured. Our patients are waiting for the next generation of biopharmaceuticals and you in Global Manufacturing will be ensuring that the supply of the next generation of biopharmaceuticals will be available.

Types of Monoclonal Antibodies

Paul Ehrlich hypothesized over a century ago that a "magic bullet" could be developed that would allow a substance to directly target a disease but it was not until 1975 that this became a practical vision. Kohler and Milstein reported in 1975 that they successfully fused B-cells and myeloma cells together, thus creating hybridomas and the original method for the production of MAbs. The hybridoma process was never patented. The first MAb product on the market was OKT3 and was approved in the US in 1986 for organ transplant rejection and was a Murine (mouse) IgG2aκ (Kohler and Milstein process). The quest to make MAbs more humanized began in the hope to decrease the human immune response to the mouse immunoglobulin which made the current antibody ineffective upon repeated antibody treatments. (Nicolaides 2006). Chimeric MAbs were developed in which 70% of the sequence is human. It is constructed from variable regions derived from murine sources and the constant regions are derived from a human source. The MAb that you will be producing will be humanized and 95% of the sequence will be human so that the only part of the MAb that is mouse is the antigen binding regions. Biogen Idec has a trademarked MAb which is called Primatized MAb and the variable regions are constructed from cynomolgus macaques and the constant regions are human. There are also human MAbs which are 100% human but the cell lines generate only a small amount of MAb and are typically unstable (Reichert, 2005; Adams 2005).

As one can see Paul Ehrlich's dream of a "magic bullet" is no longer just a dream. There are many different types of MAbs in development and in 2006 alone there were 418 biopharmaceuticals in clinical and non-clinical development with 130 classified as MAbs and 9 already in late stage development (Lubiniecki, obtained 2008).

Design Considerations and Specifications:

You are part of the manufacturing branch of a large pharmaceutical company that has already obtained FDA approval for at least one monoclonal antibody product manufactured using Chimeric or humanized MAbs. The Research and Development Scientists as well as the Trial Clinicians inform you that the company's pipeline is rich with humanized MAbs and early clinical data suggests that the MAbs in development will have more than one indication. An indication as defined here is a condition which makes a particular treatment or procedure warranted. A biopharmaceutical may be approved by a regulatory agency for more than one indication for example metastatic colorectal cancer and metastatic nonsquamous cancer for example. Each indication will increase the amount of product you will need to produce but the amount that is dosed to the patient will not only vary between indications but also within indications. You will not be designing the final formulation but you will need to design a "flexible" manufacturing facility that will allow you to make enough product to meet the quantity demands of a commercial launch. You do not know exactly which products will come

out of the pipeline first and how many indications will meet the efficacy criteria so you must plan accordingly. Your task is to design a facility that will allow you to produce your product at current reported titers of 1 to 2 g/L as well as at projected future titers of 5 to 10 g/L. (Citigroup Report. Lonza AG). As the titers increase one will have to run fewer batches per year which may allow time for production of another product in your facility.. One needs to keep in mind that as titers increase, the burden increases on the downstream purification trains, which will need to be addressed in the design of your downstream units. If at some point your facility has excess capacity (change in titers or a delay in product launches), the company may decide to become a contract manufacturer. If your company later selects to enter into contract manufacturing the following piece of information will be useful: two-thirds of biopharmaceuticals are coming out of companies that have revenues of less than 1 billion dollars. These companies have a need for a Contract Manufacturing Organization (CMO) as they typically do not have the cash reserves to build a manufacturing facility outright.

The production site will be built adjacent to the company's already existing 'Research and Development' site, and small scale pilot plant for Biopharmaceuticals. This site was selected to maximize synergies between: (i) the groups that developed the MAbs and the processes to produce them, (ii) R & D, and (iii) the group that will produce them, namely Global Manufacturing. Since the site has a preexisting facility, utilities and infrastructure such as roads are already present; therefore costs associated with preparing the site to build on will be minimized. The production facility will be designed to meet GMP (good manufacturing practice) regulations as well as European regulations due to the potential that the MAb that will be produced and will be sold internationally. Federal regulation 21 CFR Part 11 (Food and Drug) is the federal guideline you will be following and they can be found on the FDA's website.

When you design your facility, you will need to account for operations beyond just the Seed Train, Upstream, Downstream, Packaging and Storage. For each unit operation time and resources must be allotted for CIP (Clean In Place) and SIP (Steam In Place) and for validation of the vessels. One benefit of using disposables for some unit operations is that they arrive on site sterile and ready to be used, and are disposed of after use eliminating the need for CIP/SIP protocol or revalidation. You will need to develop a protocol for CIP and SIP and schedule it into your process. The following paper is suggested to help you with this task, Stewart, J.M Seiberling, D., "The Secret's Out: Clean in Place" *Chemical Engineering*, 1996. Also all water used in your production facility should be WFI (Water for Injection) and all transfers must be done under sterile conditions.

General Process Description:

A conceptual block flow diagram is shown in the attached figure, to accompany this process description. The block flow diagram shown here is a high level diagram and the designer is encouraged to innovate.

Upstream Processes

MEDIA PREP:

You will need to determine whether you will use a proprietary media formulation that is specific to your company or whether you will use an off the shelf media provided by a company such as Gibco or Lonza. Your facility is considered to be an animal free facility so you will be using a Chemically Defined Medium in your process. The large quantities of medium that will be needed for your process will be made onsite from powdered components. Please design the Media Preparation Area and select whether to use steam in place vessels, disposable vessels or both.

SEED TRAIN:

You will obtain one vial of CHO (Chinese Hamster Ovary Cells) cells for each batch of product that will be produced in your facility. You will be using CHO cells because the current platform for making biologicals is often CHO in the mammalian realm. The first MAbs were made using hybridomas but the yields tended to be low and for this and other unnamed reasons your company decided many years ago to proceed with a CHO platform. The vial size can range from 1 mL to x mL (Genentech recently presented work at ACS where they used bags instead of vials that contained 125 mL of culture in them.) based on the company's method of banking their master cell banks. In order to account for both old and new cell line banking procedures, set the vial volume size to be 1 mL and each vial should contain $1x\ 10^6$ viable cells/mL. The cells will need to be expanded by passaging into larger and larger volumes and after the final scale up in the seed train, the culture will be placed in the production reactor(s). Note the seed train will be a batch process i.e., there will be no addition of feeds including glucose. The doubling time for the CHO cells that you will be using will be 36 hours. Please note that doubling time will vary based on cell line so one may obtain another cell line and it may double in 24 hours or perhaps 48 hours, while ours is 36 hours for this design problem.

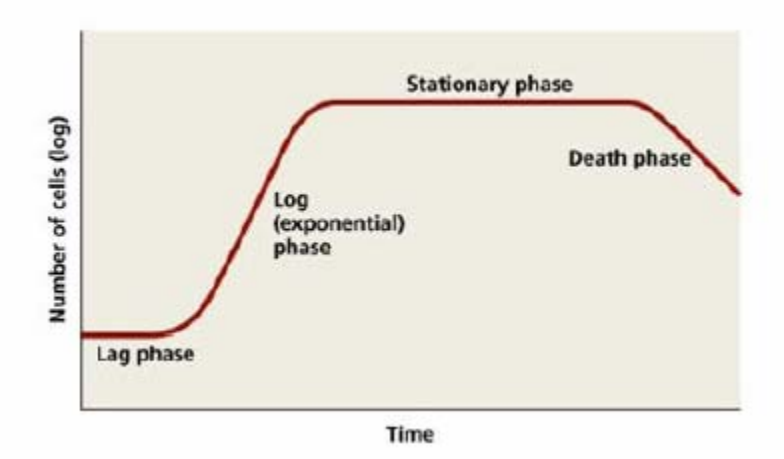
PRODUCTION REACTORS:

Once your cells/cultures leave the seed train they will enter the production reactors. Currently there are a number of types of reactors used to culture cells. A very common reactor used in industry is a stirred tank reactor. You may decide to use a stirred tank reactor or another type of reactor such as a perfusion reactor, a packed bed reactor, or an air lift reactor. Please note that you will need to design your production reactors to meet the requirements of a process that yields 1 to 2 g/L and 5 to 10 g/L (future cell line and process). You will need to base your production bioreactors on worst case scenario ie 1 to 2 g/L of product but if titers improve as suspected, your facility should be able to account for this. (Hint: Use multiple smaller production bioreactors instead of one very large production bioreactor.) For design purposes you may assume that your cell line

produces your product at a rate of 25 pg/(cell*day). For design purposes you must be able to produce a minimum of 1,000 kg of product a year which is approximately the estimated quantity produced for both Enbrel™ and Remicade™ in 2007 (Jagschies, 2009).

Your new production facility will need to have the capability to run both batch and fed batch processes. In this design project you will be designing a process where the cultures are fed. You will need to feed at a minimum glucose to your production bioreactors. The glucose level in your reactors should not go below 2 g/L.

The cell line you are using follows a typical growth curve with the following phases: Lag phase, Log (exponential) phase, stationary phase, and a death phase. Below is an example of a typical growth curve. You will have to decide and explain what is appropriate to use in your design.



DOWNSTREAM PURIFICATION

General Information: 30 to 40% of the costs to manufacture a therapeutic are incurred during purification. (Shukla, 2007)

PRIMARY RECOVERY/HARVEST

After the production reactor protocol is complete, the contents/product needs to be recovered/harvested. The bioreactors are harvested by removing the contents in the reactor and then the broth undergoes centrifugation and filtration to remove biomass, etc. You will need to design your centrifuge and filtration steps and you may need tanks to hold the contents of the reactor(s) while downstream is processing the broth..

Density of Chinese Hamster Ovary Cell Culture Broth: 1.06 g/cm^3. (Kubitschek, H Critical Reviews in Microbiology 1987; 14: 73-97.)

PURIFICATION: PROTEIN A CHROMATOGRAPHY

Protein A chromatography has become an industry standard for both direct capture and purification of monoclonal antibodies. Protein A has a high resolution and in one step it is possible to remove more than 99.5% of the product impurities, thus fewer purification steps need to be utilized when Protein A is used.

Protein A resin is quite expensive and one will need to factor in a regeneration step that meets GMP requirements. The manufacturers of the resins will have a suggested protocol typically to use for regenerating the columns.

You will also need to design storage for the buffers that will need to be used for the purification column(s).

Productivity of the column may be calculated using the following formula

Productivity (P) = (Mass of product/column volume)/time

$$P = \frac{1}{\left(L\left(1/C_0 u_L\right) + \left(N/Q_d u_N\right)\right)}$$ (Equation rearranged and reduced)

Where L is the column length, Q_d is the binding capacity taken as a surrogate for column loading; C_0 is the load concentration; u_L is the velocity for the load step; u_N is the velocity of the non-load steps; N is the number of column volumes for the non-load steps.

VIRUS INACTIVATION:

Virus Filtration/Inactivation is a safety step in the manufacturing process. There are a number of methods that one may utilize such as filtering, solvent/detergent treatment, low pH activation, heat treatment, and chromatography to name a few. You will need to decide what method to use in your production facility. Heat treatment of your MAb product should not be done as a rule of thumb.

MAB purification: Polishing

After Protein A and Viral inactivation, the product needs to be further purified before formulation and packaging. There are multiple ways this last purification step may be conducted such as Anion and Cation Exchange Chromotography, Ceramic Hydroxyapatite, and Hydrophobic interaction. Please note that one's purification train is based on the needs of the process.

You will need to design the polishing step of your process. Some processes use both Anion Exchange and Cation Exchange Chromotography but you will need to decide if this is the right method for your process and explain why you selected your particular polishing step(s).

STORAGE AND SHIPMENT TO AN OFF-SITE FORMULATION FACILITY

Please design a section of your facility to package and store the Monoclonal Antibody until it can be shipped to your formulation group within global manufacturing for final formulation and packaging for one's patients.

The method to store the MAb product at the production site must ensure that the product is stable for a minimum of 1 year before final formulation.

PRODUCTION WASTE:

The manufacturing facility will be built on an existing site. You will be able to utilize the sewer systems that are already on-site but will have to design the pretreatment, "kill tanks," that will feed into the county/city sewage facility.

COST DATA:

Electricity: $0.05/kWhr

Sewer= $5.00/thousand gallons

Water: $0.543 per 1000 liters (Note that this water cannot be used in your process unless you convert it to Water for Injection)

Water for Injection: $1000 per 1000 liters

All prices are delivered to your site and are in current year's dollars.

Production quantity for selected MAbs (Jagschies, 2009)
BDS=bulk drug substance,total quantity < 10 tons/year

Product	Marketing companies	2007 revenue (US$ million)	Estimated quantity (annual kg BDS)
Enbrel*	Amgen/Wyeth	5,275	1,020
Remicade	J&J Centocor/ Schering Plough	4,975	1,098
Rituxan/MabTherma	Genentech/Roche	4,600	1,175
Herceptin	Genentech/Roche	4,046	1,015
Avastin	Genentech/Roche	3,424	873
Humira	Abbott	3,000	121
Xolair	Genentech/Novartis	613	246
Tysabri	Biogen Idec/Elan	343	51
Vectibix	Amgen	170	28

Production levels and sales for principle competition.
* Enbrel is a Fc fusion protein. Dose requirements, treatment cost, and production process are very similar to monoclonal antibodies.

REPORT REQUIREMENTS:

The report should follow the outline suggested in Seider Seader and Lewin. Further details on what should be included in the design report can be found in that text. Write the document from the point of view of the organization's engineer making a report and recommendation to the organization's management.

1. Letter of Transmittal
2. Cover Page
3. Table of Contents
4. Abstract
5. Introduction
6. Process Flow Diagram and Material Balances
7. Process Description
8. Energy Balance and Utility Requirements
9. Equipment List and Unit Descriptions
10. Equipment Specification Sheets
11. Equipment Cost Summary
12. Fixed Capital Investment Summary
13. Safety, Health, and Environmental Considerations
14. Other Important Considerations
15. Operating Cost and Economic Analysis
16. Conclusions and Recommendations
17. Acknowledgements
18. Bibliography
19. Appendix

HELPFUL/INTERESTING INFORMATION

Avastin™ is an example of a MAb that is targeted against VEGF. Information about this molecule maybe found at http://www.gene.com/gene/products/information/oncology/avastin/.

You may find that the Biopharmaceutical SUPERPRO Designer model example on Intelligen's website www.intelligen.com is helpful as you create your design project. Please note that the model works using their evaluation version which is downloadable on their website. The evaluation version of the software does not allow the user to print or save files.

The FDA has given suggested guidelines for the internal layout of a biopharmaceutical facility so you may wish to refer to their website for guidance. www.fda.gov

Industrial trade publications: BioPharm International, BioProcess International, Pharmaceutical Manufacturing, Genetic and Engineering News (GEN), and many more.

Adams, Gregory P and Louis M Weiner, "Monoclonal Antibody Therapy of Cancer," Nature Biotechnology, September 2005, Vol 23, Number 9, pg 1147 -1157.

Blanch, Harvey W, Douglas S. Clark, *BioChemical Engineering*, Florida: CRC Press, 1997.

Datamonitor's Report: Press Release: MAb Sector Growth will Continue to Far Outstrip that of Small Molecules, FierceBiotech, October 12, 2007 www.fiercebiotech.com (obtained 25 September 2008.)

Das, R., and K. J. Morrow, Jr., "Progress in Antibody Therapeutics," American Biotechnology Laboratory, August 2006, pp. 8 and 10.

Gerson, D. F., "Paradigm Change in BioManufacturing: Technology is Transforming Manufacturing Options," *Contract Pharma*, May 2008.

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King, Marita A. "Selection Criteria for WFI Production Equipment, Controlled Environments Magazine, September 2005, http://www.cemag.us/Article_Print.asp?pid=546, Obtained 28 June 2009.

Kubitschek, H. Critical Reviews in Microbiology 1987; 14: 73-97.

Lakshmikanthan, J., *Outsourcing: Biologics Manufacturing: The CMO Advantage*,

BioPharm International, February 2007.

Lubiniecki, A. S., "Presentation: Global Industrial Perspective of Novel Biologicals Development," Centocor R&D/Johnson and Johnson, http://www.pmda.go.jp/english/past/pdf/7-A.LubinieckiPMDA10207.pdf, Obtained 25 September 2008.

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Mallik, A., G. S. Pinkus, and S. Sheffer. "Biopharma's Capacity Crunch," The McKinsey Quarterly: 2002 Special Edition: Risk and Resilience.

Millipore, "Processing Economics of the Millipore Pod System Versus Millistak + HC Lenticular Stacks, http://www.millipore.com/publications.nsf/a73664f9f981af8c852569b9005b4eee/6111b56c265876ca8525733c005daf6e/$FILE/tb1076en00.pdf, Obtained 28 June 2009.

Ozturk, Sadettin, and Wei-Shou Hu, Cell Culture Technology for Pharmaceutical and Call-Based Therapies (Biotechnology and Bioprocessing Series), Florida: CRC Press 2005.

Reichert, Janice M, Clark J Rosensweig, Laura B Faden, and Matthew C Dewitz, "Monoclonal antibody successes in the clinic," Nature Biotechnology, September 2005, Volume 23, Number 9.

Reichert, Janice and Alex Pavlou. "From the Analyst's couch, Monoclonal antibodies market." Nature Reviews: Drug Discovery May 2004, Volume 3.

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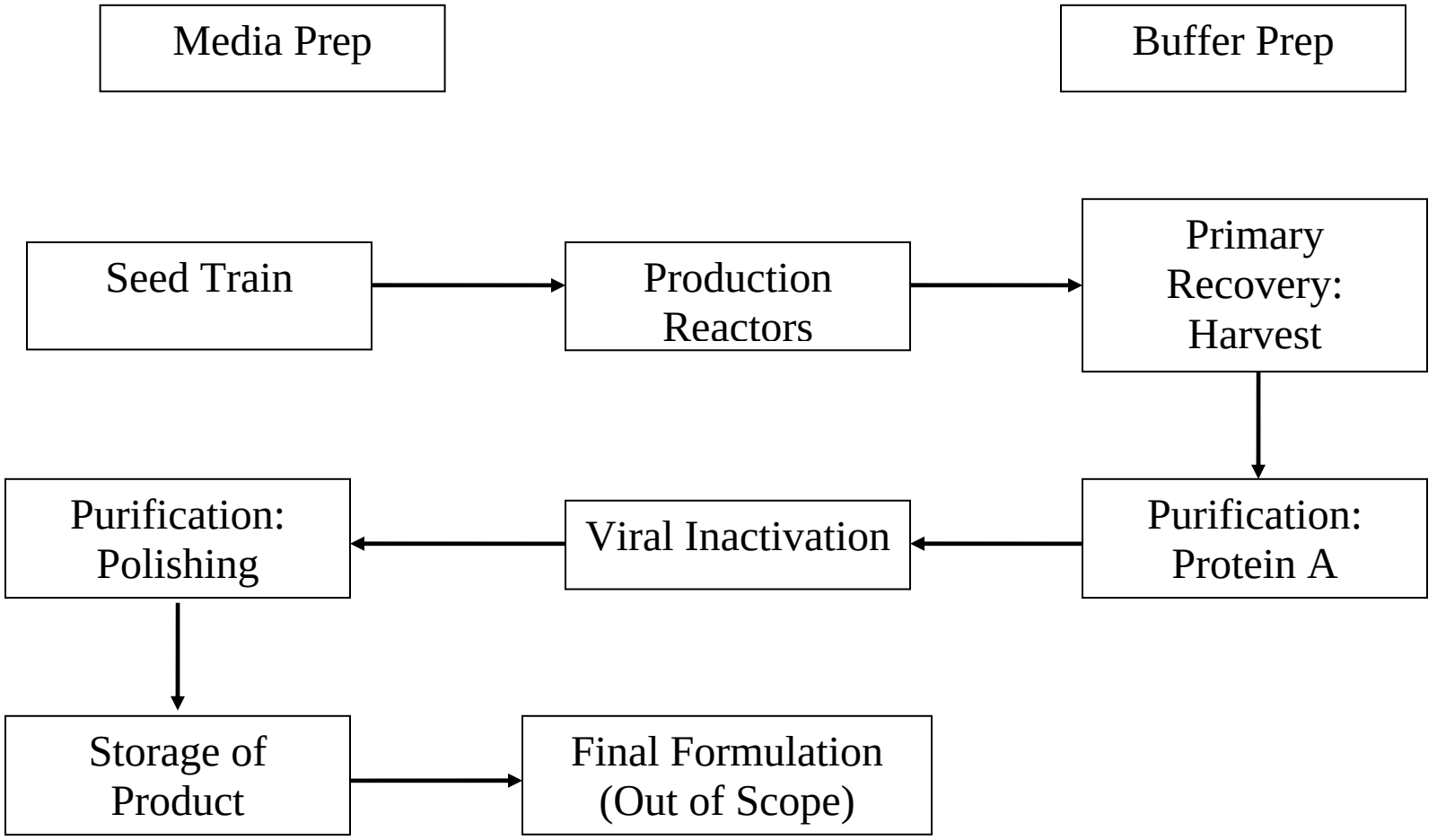
Shukla, Abhinav A., Mark R. Etzel, Shishir Gadam, *Process Scale Bioseparations for the Biopharmaceutical Industry.* Florida: CRC Press, 2007.

Stewart, J.M Seiberling, D., "The Secret's Out: Clean in Place" *Chemical Engineering*, 1996.

Note: This problem statement has some hypothetical data and thus it does not necessarily represent an accurate real case.


Media Prep
Buffer Prep
Seed Train
Production Reactors
Primary Recovery: Harvest
Purification: Protein A
Viral Inactivation
Purification: Polishing
Storage of Product
Final Formulation (Out of Scope)

2010 AIChE NSDC Errata Sheet:

- The productivity equation given in the 2010 NSDC has a typo in it. The "L" and the left most "(" are incorrectly reversed. The correct form of this equation is given below:

$$P = 1/L((1/C0uL) + (N/QduN))$$

- A typo has been noted on p.8: currently the CFR reference reads "21 CFR 11" whereas it should read "21 CFR 111".

- Further correction to #2 above (Effective April 01, 2010) – "21 CFR part 111" was given as the regulatory CFR for the 2010 NSDC. Actually it is "21 CFR 211". This second typo has been noted. Student competitors will not be penalized for relying on 21 CFR 111, but those who have not begun the problem should use "21 CFR 211".