MassBiologics
The Monthly Dose
UMASS MEDICAL SCHOOL
Medicine for Better Lives

MassBiologics and other University News

January 8, 2013 Volume 2, Issue 1

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January Happenings

- Tuesday January 1st: New Years Day
- Friday January 11th: Leaders In Innovation Seminar: William Blackwelder, PhD
- Monday January 21st: Martin Luther King Jr. Day
- Tuesday January 23rd: Town Hall Meeting
- Friday January 25th: Leaders In Innovation Seminar: TBA

Viral Clearance Studies for Biopharmaceuticals

By Rachel Wollacott, PhD

For the drugs we manufacture, patient safety is our number one priority. One of the potential safety concerns are viruses as CHO cell lines are sometimes capable of supporting viral replication and amplification. Fortunately, to date, biopharmaceuticals produced in recombinant cell lines have had an excellent safety record, which is largely due to strict regulatory guidelines and their implementation by pharmaceutical companies.

Potential sources of viral contamination at MBL could include the contamination of the equipment, production system (cell line), or raw materials (cell culture media and feeds). Strict control over these raw materials, including extensive testing of the cell bank and validation of vendors is required. In addition, critical process areas and equipment are thoroughly cleaned and access controlled to ensure that they remain free from contaminants. Additional safety measures are also required during the protein purification process to inactivate and remove viruses. The first step is a chemical inactivation step which involves incubation of the MAb at low pH, or with a chemical, for a given amount of time. This inactivation step is only effective for enveloped viruses. The second, a filtration step, clears non-enveloped viruses by size exclusion using a nanofilter with a 20nm pore size. In addition, viruses can also be separated from the MAb during the two or three column chromatography steps.

The ICH Q5A regulatory guideline indicates that a manufacturer of biological products for human use should demonstrate the capability of the manufacturing process to remove or inactivate known contaminants. One aspect of assessing the viral safety of a biopharmaceutical is to perform a viral clearance study. In these studies, the Process Development group runs a scale-down model for each process step using a process identical to the manufacturing process to estimate how much virus is removed. These experiments are typically performed during the first clinical manufacturing run using process intermediates as starting material. Once we have determined how much virus is removed during each process step, we can assess the safety factor of our process for viral clearance by taking into account the dose of MAb a patient will receive.

Computer Systems Upgrades for 2013

From Microsoft:

"In 2002 Microsoft introduced its Support Lifecycle policy based on customer feedback to have more transparency and predictability of support for Microsoft products. As per this policy, Microsoft Business and Developer products, including Windows and Office products, receive a minimum of 10 years of support (5 years Mainstream Support and 5 years Extended Support), at the supported service pack level."

This means that after April 8, 2014, Windows XP will no longer be supported by Microsoft. There will be no new security updates, free or paid assisted support options or online technical content updates.

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What to Expect… New Monoclonal Antibody Therapeutics

Deborah C. Molrine, MD

What does 2013 hold in the way of new monoclonal antibodies for patient care? There are 29 monoclonal antibodies (mAbs) approved by the FDA for current use with two mAbs approved in 2012: 1) Pertuxumab, a humanized IgG1 targeting human epidermal growth factor receptor (HER)2 to treat HER2 positive metastatic breast cancer in combination with trastuzumab and docetaxel; and 2) Raxibacumab, a human IgG1 to treat inhalational anthrax. Raxibacumab is the second monoclonal antibody approved for an infectious disease indication, the first one being Palivuzumab, a humanized IgG1 approved in 1998 for respiratory syncytial virus (RSV) prophylaxis of igh-risk infants . Twenty-one of the 29 (72%) mAbs are humanized or human and the majority of currently licensed mAbs are for a cancer or immunological indication.

What is on the horizon for 2013? Clinical studies indicate more diversity in the diseases being targeted by monoclonal antibodies with phase 3 studies ongoing in the areas of high cholesterol, post-menopausal osteoporosis, C. *difficile* infection, non-infectious uveitis, SLE , Alzheimer's disease, multiple sclerosis, and asthma in addition to mAbs to treat rheumatoid arthritis, psoriasis, inflammatory bowel disease, and cancers. These late phase studies indicate that monoclonal antibodies are now being considered as a potential therapeutic modality for a broad range of non-cancer conditions and the next few years will be telling as to their success to improve patient care.

An excellent resource for staying abreast of therapeutic monoclonal antibody development is found at

www.landesbioscience.com (mAbs, Janice M Reichert)

Track and Trace

By Catherine Hay, PhD

We are all aware of the very real potential for counterfeit or adulterated medications to be introduced into the supply chain as illustrated by the counterfeit Avastin in early 2012 and the adulterated Heparin in 2008. In order to mitigate the risk of similar events and the possible introduction of diverted or stolen drugs, the FDA and individual states have been discussing the implementation of a drug pedigree system also known as "Track and Trace" for several years. The pedigree system will enable the movement of prescription only products to be tracked through the distribution system to the final sale to a pharmacy or other entity dispensing the product. The system will also enable drugs to be traced back to their point of origin if issues are discovered.

How will this be done? The current proposal is that smallest unit of sale, in our case, the Td 10 pack carton, will contain a unique serialization number. The number will consist of the NDC number and an alphanumeric code of up to 20 characters; the number must be both human and machine readable. Unique identifiers will also need to be applied to each case and pallet to enable the cartons to be tracked without opening up all of the packaging to read the number on every carton; by reading either the case or pallet identifier, one can "infer" that it contains the stated cartons. An electronic transaction history will be created noting each time the carton changes ownership and the details of that transfer. That is, we sell the cartons to the distributor – this is the first transaction; each subsequent sale by distributors will be recorded on the transaction history until the product makes its way to the pharmacy or Dr.'s office.

When will the pedigree system be implemented? Ideally the requirement will be implemented under a federal plan so that there is a unified national system rather than having to deal with individual states' requirements. This may not be the case as the state of California is requiring

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Track and Trace… contd.

that, by 2015, fifty percent of a manufacturer's products must comply with the pedigree requirements and the remaining 50% must comply by 2016. In October 2012 Congress drafted a Bill to amend the Federal Food Drug and Cosmetic Act and implement a pedigree system but it is unclear whether this will be in place prior to the CA implementation dates or indeed, whether CA will delay the implementation as a federal requirement is pending. Regardless, the track and trace requirements have implications for Td and it is not too early for us to develop and implement a plan in order to be able to comply with the requirements. Industry standards are already developing in the absence of clear regulatory guidance and we will be looking at these going forward, perhaps jointly with our Td distributor. Whatever system or standard is implemented we can be sure that it will involve installation and qualification of equipment to print and read the unique identifiers, IT systems to handle the data as we create it and to manage the supply chain transactions and, of course, changes to procedures that cover the handling, inspection, rework and distribution of serialized product. While the risk of counterfeit Td product is quite low, it seems that we can look forward to a significant effort to comply with the emerging requirements to establish electronic pedigree or "Track and Trace" capability for our licensed product.

Computer Systems Upgrades for 2013… contd.

Over 95% of our 400 + MassBiologics' computers currently run on Windows XP.

Windows XP is three versions behind Microsoft's currently released operating systems that include:

Windows Vista (released in January 2007)
Windows 7 (released in October 2009)
Windows 8 (released in October 2012)

MassBiologics Information Services Department plans to complete deployment of Windows 7 before the end of 2013.

Windows 7 was chosen in preference to Vista in part because Windows 7 will remain in extended support until 2020, (Three years longer than Vista) and because we have been testing our critical business applications on several computers running on the Windows 7 operating system for over a year and the results have been very positive.

You may ask why not upgrade to Windows 8?

Although Windows 8 is very fast and very powerful, the graphical user interface is a significant departure in appearance from all of the previously released Microsoft operating systems.

More importantly, upgrading to Windows 8 would be very costly for MassBiologics. Many of our computers do not meet the minimum hardware requirements to efficiently run Windows 8 and some of our business applications currently in use will not run at all on a Windows 8 computer.

For example, MasterControl version 5, which was released over seven years ago, is incompatible with the Windows 8 browser (Internet Explorer 10).

We are also taking this opportunity to make two other upgrades to our computers.

Increase computer memory (if needed)

Although not necessarily required for Windows 7, the memory increase will give your computer more room to manage larger programs and larger files.

Upgrade from Microsoft Office 2007 to Office 2010.

Microsoft Office 2010 is not significantly different from Office 2007 and upgrading Office will extend Microsoft support three more years (to 2020).

We are scheduling the system upgrades now and will work with you to ensure that the upgrade is as seamless as possible.

MassBiologics News

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MEDICINE FOR BETTER LIVES

In Our Next Issue……

Department Updates

News from Around Campus

Employee News and Accomplishments

Recap of The Second Town Hall Meeting

And Much More...

MassBiologics HRDI Calendar: January 2013

Wednesday January 9th: Jodie Nosiglia

Wednesday January 16th: Ben Moorghen

Tuesday January 22nd: Jim Mack

Thursday January 31st: Jodie Nosiglia

Note: HRDI staff will be onsite 10am-4pm in Room 2020 of MTP II

For immediate assistance please contact the Human Resources Benefits Service Center Team

PHONE: 508-856-2282 | Monday-Friday, 8:30a.m.-4:30p.m.
EMAIL: Benefits.UMMS@umassmed.edu

ONLINE: www.umassmed.edu/hr/benefits

Towards a Treatment and Diagnostic for Preeclampsia

By: Colby Souders, PhD

At MassBiologics, we strive to tackle unmet medical needs that, while still very serious, may affect only a limited number of individuals. Fortunately, as a result of vastly improved pre- and post-natal care in the US, preeclampsia has become one such medical need. Of the six million pregnancies in the US each year, it is estimated that about 2-6% (120,000-360,000) develop preeclampsia, of which 10% (12,000-36,000) could benefit from a treatment that would alleviate the mother's symptoms in order to safely prolong the pregnancy and avoid delivering the child prematurely.

A plethora of research from both academic and industrial labs has identified a particular protein called sFlt that is secreted in excess by the placenta and is presumed to be the cause of hypertension, proteinuria, renal damage, edema and eventually liver damage and seizures in the mother. In a crude analogy, it is like a foreign intoxication: the placenta secretes a toxic protein causing harmful symptoms. So if preeclampsia looks like a toxin-induced illness, why not try to treat it as such?

That's the goal in the Product Discovery department, where we have developed monoclonal antibodies that bind the sFlt protein. A select number of these antibodies not only show preliminary neutralization of sFlt's effects in a novel mouse model of preeclampsia, but they can also be used as a diagnostic tool. Previous studies have shown that circulating sFlt levels in the mother increase well before symptoms arise. Thus, in an attempt to improve current diagnostics using sFlt as a marker, we developed monoclonal antibodies specific for different forms of the sFlt protein, with the hope that one form will be more indicative of the onset and severity of preeclampsia.