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Roundtable Responses
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1. Will consolidation continue to take place in the life sciences sector? Why?

Yes, consolidation, which has been a continuing trend in the biotech and pharmaceutical industries for several decades, will continue. This includes consolidations, particularly acquisitions and mergers, involving large companies. For example in recent years, Roche has fully acquired and integrated Genentech; Merck & Co. acquired Serono and Schering-Plough; Pfizer acquired King Pharmaceuticals; Genzyme is resisting acquisition by Sanofi; Bristol-Myers Squibb (BMS) acquired ZymoGenetic

Many of these consolidations were efforts by ailing large established pharmaceutical companies wanting to improve their product pipeline and portfolios, with the many companies experiencing or projecting loss of revenue as patents on many profitable products expire and these products go the generic or biosimilar route. In other cases, companies acquired manufacturing facilities and platform technologies, e.g., Merck KGaA acquired Millipore; and Merck & Co. acquired Avecia, a major contract manufacturer, Insmed with its biosmilar products and manufacturing facility, and paid over $400 million for GlycoFi, with its primary asset being its proprietary yeast glycosylation technology.

Consolidation today often makes good business sense. With low interest rates and companies of all sizes experiencing problems raising funds from venture capital sources and stock sales, corporate acquisitions can make sense for both parties, especially over next 1-2 years as economic conditions improve.

2. Which relatively unknown companies are the ones to watch in 2011?

Virtually all companies supplying the biomanufacturing industry attempt to offer improved products and technologies, and our Annual Report of Biopharmaceutical Manufacturing has indicated consistently strong growth for the past 7 years—between 11 and 22%--for materials, as well as for services, and instrumentation. Despite the economic downturn, this is likely to continue through 2011. From a *manufacturing* perspective, unknown companies tend to have a difficult time entering the biomanufacturing space, due to the regulated nature of the industry. There's a need for a new supplier to show a track record before they are considered a primary supplier. So the question, in my mind, is not so much which unknown companies to watch, as which emerging technologies are going to radically change the way biopharmaceuticals are manufactured globally. Our Annual Study indicates that the big areas to watch are downstream purification, especially alternatives to chromatography. Filtration, and novel disposable applications are also critical to the industry's focus on cost containment. Tracking and monitoring manufacturing costs will require new ways to monitor manufacturing processes. So expect companies with new assay and process monitoring technologies to emerge dominant over the next few years.

3. What do you think will be the next big leap in technology or innovation in the life science industry?

Major advances in the near-term are likely to involve bioprocessing, in particular, expression systems and related genetic engineering technologies, and downstream purification. Besides making product manufacture cheaper, new technologies, especially single-use equipment, are making manufacturing simpler and more adaptable. This, alone, could open vast biomanufacturing opportunities in developing countries for products such as vaccines, where in-country production is desirable from a public health policy perspective. Further, because the use of disposables in biomanufacturing can lower requirements for process validation, and certain quality operations, production will become more viable in regions that at present have lower quality management expertise. Thus, the next big leap in technology will possibly be an 'enabling' leap, making manufacturing simpler, lower-cost, with more contained quality. The impact on global health could be enormous.

As bioprocessing technology advances, the industry is experiencing significant expansion, particularly with new companies and manufacturing facilities coming online in Asia and other developing countries. With biosimilars expanding the market in developed countries, many more companies will be manufacturing biopharmaceuticals, and costs of manufacture will become even more important as more products compete on the basis of price.

We can expect significant improvements in both expression systems, including even higher yields, and downstream purification in coming years. Expression system companies to watch include those working with plant systems, with these potentially offering cost and safety benefits, even compared to other next-generation mammalian and microbial systems. For example, iBio and Fraunhofer have developed a low-cost cultivated plant-based expression system and are building a plant to manufacture over 1 billion doses/year of recombinant influenza vaccine; and interferon alfa and other products manufactured using cultured single-cell algae are likely to enter the market. Other companies with "hot" plant-based expression systems include SemBiosys Genetics, expressing proteins in field crop seeds, Medicago using tobacco plants, and Sapphire Energy, affiliated with Scripps Research Inst. Such plant expression systems have the capability of producing recombinant proteins at costs of <$1/dose or less than 10% of current costs. Recent advances are even indicating that some plant expression systems can be modified to form human-like glycosylation.

4. What are some of the major regulatory challenges facing the FDA this upcoming year? What impact, if any, will FDA's recent announcement that it will aggressively prosecute executives at companies that violate its regulations have on the life sciences industry?

The single most critical challenge facing FDA is the development of rational regulations for biosimilars. Congress passed a biosimilars approvals-enable law, but it is vague in many respects, leaving many major decisions to FDA, which could well take years to establish a predictable approval path. For example, something as basic as the debate over nomenclature, the types of names, to be used for biosimilars, e.g., whether generic or unique names, may become a

flash-point, more vehemently fought than data exclusivity issues. This is because the names of products reflect and determine how they will be marketed and perceived (as being low-end generics vs. their being unique innovative biopharmaceuticals).

Another major challenge for FDA is foreign manufacturing facilities. Many of these have never been inspected or are inspected infrequently, which may not assure proper compliance with cGMP. This primarily affects drugs, but an ever-increasing number of biopharmaceuticals are being manufactured overseas, in Europe in the short-term, but in China, India and other countries in the longer term.

Regarding prosecutions, the FDA (and DOJ and SEC) are more aggressive in its prosecution of pharmaceutical company executives. However, despite recent fines, some of which have been the largest civil fines in history, it would seem that those prone to acts such as encouraging off-label sales, insider trading, misstating of earnings, will continue to do so.

5. What are some of the highly anticipated products that will launch in 2011?

In terms of biophamaceuticals in the pipeline, applications pending at FDA include a new adenovirus vaccine (for use by the U.S. and other militaries) from Barr Labs./Teva; a new version of Orcel, using the patient's own cultured skin for skin grafts; Replagal (alpha-galactosidase) from Shire Pharma/TKT, expected to provide competition with a similar product from Genzyme; Riquent, involving a double stranded B-cell epitopes oligonucleotide (dsDNA) for treatment of lupus/SLE; RIGSCAN CC49 from Neoprobe, one of the few non-recombiant monoclonal antibody-based products in development; Voraxaze (carboxypeptidase G2) from Protherics for treatment of methotrexate toxicity; recombinant anthrax vaccines from Emergent Biosciences and Pharmathene; Ipilimumab from Medarex and BMS, a CTLA-4 monoclonal antibody for cancer treatment; Benlysta from Human Genome Sciences and GSK, a B-cell-activating factor monoclonal antibody expected to be a blockbuster for treatment of systemic lupus erythematosus (SLE); NuMax, a second-generation respiratory syncytial virus (RSV) monoclonal antibody from MedImmune/AstraZeneca expected to replace its 1st-generation blockbuster, Synagis; Rhucin from Pharming, a recombinant human C1 inhibitor expressed by transgenic rabbits; Elonva, a modified version of follicle stimulating hormone (FSH), from Merck; and TevaGrastim from Teva, a follow-on (now off-patent) version of G-CSF (Leukine) but filed for full, not biosimilar, approval.

6. Will social media play a more prominent role in the life sciences industry in 2011?

You know that something is a trend, when even inherently conservative and tight budget government organizations, such as the FDA, get involved. FDA recently implemented Twitter feeds for its MedWatch program to facilitate the public reporting adverse events and drug/biologic safety hazards. [See "FDA MedWatch Opens Twitter Feed"]

Social media, however, can become a nightmare for pharmaceutical marketing executives who must now consider how their actions, overt, or inadvertent, may result in unapproved marketing activities, promotion of off-label indications, etc. Clearly, social marketing will continue to

grow, and play a part in treatment of virtually all diseases from Tourette's syndrome to ADHD. Still to be addressed is if and how the FDA and other regulatory bodies will expect drug companies to manage their role in social marketing. Most pharmaceutical companies are currently engaged in the use of social media for marketing at some level, and a number of websites such as Pharma and Healthcare Social Media Wiki, are cropping up to track activities, blogs, and trends. But with health-related apps appearing virtually daily, can regulators keep up? The potential for abuse and harm in this largely unregulated field is enormous, and only now being considered.

7. The recent economic downturn has taken its toll on CROs and other companies that support the life sciences industry? What will 2011 bring for these companies?

While the economic downturn has beat-up biomanufacturers badly, their vendors and suppliers have continued to do relatively well, despite the recession. From our Annual Report and Survey of Biopharmaceutical Manufacturing, we find that, supplier sales to this industry have declined from their 16% CAGR in 2007, to a more modest 13% growth in 2009. However, any industry segment with 10% annual growth in the current climate should consider itself fortunate. Those companies with technologies offering cost savings, such as improved expression systems and purification equipment, can expect increased sales.

In terms of markets and revenue, bioprocessing equipment, reagent and services vendors tend to be somewhat insulated from much of the ongoing economic difficulties. Private sector R&D has increased slightly or is remaining steady, and at least for the moment, NIH and other federal life sciences R&D budgets have not been significantly hit with cutbacks. CMOs, technology sources/licensors and vendors should expect the market to remain relatively unchanged, and may even see an increase in revenue as many companies worldwide gear up for biosimilars and biogenerics manufacture.

8. Which developing markets represent the greatest opportunities for drug makers? Why?

While most companies are looking toward the rapidly growing opportunities in China, India and Brazil, the Middle East offers some attractive mid-term growth opportunities. Based on research from our recent *"Quick Guide to Biotechnology in the Middle East"* the Middle East region, with its 280 million people, spends around US$10.6 billion on pharmaceuticals. As purchasing power in individual countries, and government efforts to reform healthcare grow, companies are finding opportunities for products in almost every therapeutic area. While most headline coverage of the Middle East is limited to politics, dramatic changes in Middle Eastern healthcare have gone mostly unnoticed. The Middle East is experiencing a rising demand for healthcare, which is transforming this part of the world. As a result, there are new opportunities for private companies that did not exist even a few years ago.

- Oman building US$1 billion integrated health care city outside Muscat.
- The United Arab Emirates integrated healthcare city in process for US$3.4 billion. Ownership of three public hospitals are now privatized.

- Bahrain construction of US$1.6 billion health island, Dilmunia, will feature a comprehensive health environment.
  - Pfizer, Amgen and Genzyme setting up their regional headquarters at Dubai Biotechnology and Research Park (DuBiotech)
  - AstraZeneca and Pfizer/Wyeth have regional headquarters at Dubai Health Care City
  - GSK has exceeded 10% market share in Saudi Arabia; Pfizer has just over 6% of market

9. Do you think the US is losing its competitiveness in science and engineering? Why?

The U.S. remains by far the leader in the pure and applied life sciences. Yes, more corporate technology, funding and other resources are increasingly being shipped overseas, but the U.S. will long remain a global leader, able to compete with any other country in the life or pharmaceutical sciences or industry.

In terms of education, although the US continues to output excellent science and engineering graduates, other countries are rapidly closing the gap. China, for example, has seen geometric growth in enrollments at institutions of higher learning since 2000. For the first time, Chinese PhD graduates from excellent institutions are finding it difficult to find domestic jobs. So, it is not be so much that the US is losing ground in science, but that the gap is closing. I'm a believer in competition, and if other countries are establishing themselves on the scientific competitive stage, this will benefit all as competitive pressures result in new products and technologies reaching the markets sooner.

The Bio/pharmaceutical industry has clearly become an international business. 5 or 10 years ago few companies even had a 'China' or 'India' strategy. Today, most are actively investing or researching opportunities for product sales, or for manufacturing, or as CRO or even CMO partners. This internationalization, partnering, offshoring and outsourcing represents an inevitable evolution of this industry as we recognize domestic markets or domestic manufacturing just is no longer enough to remain competitive. The ever increasing populations and global affluence in many developing countries outpace U.S growth. Yet, for the time being, many continue to lack the expertise and talent necessary to research, develop and commercialize new technologies. Managing the process of science is clearly an area where US competitiveness in science and engineering is likely to remain dominant.

Regarding the loss of its R&D and manufacturing base, it is natural for companies to concentrate growth and invest in lower-cost R&D and manufacture regions. So, yes, the U.S. is, on balance, slowly losing valuable R&D and manufacturing investments, expertise and infrastructure to foreign companies. But does that equate to loss of competitiveness? Because competitiveness is based on delivering better products, more efficiently, and less expensively, whether at the company or country level, the U.S. will remain a dominant force in the industry for the foreseeable future.

10. What effect will healthcare reform have on the life sciences industry in 2011?

Health care reform will have little direct effect on the life sciences and biopharmaceutical industries and their technology, reagents and equipment suppliers. If anything, health care reform provides assurance of a long-term, healthy and growing U.S. market for improved pharmaceuticals and other health care innovations. There will be increasing emphasis on the cost-effectiveness of products, but this is nothing new and healthcare reform has not significantly changed the situation in the U.S. (e.g., there are still no mandates for cost-effectiveness considerations in FDA approvals). Other trends in this area will continue, such as increased use of generics, with biosimilars increasing in the market in coming years.

11. What are some of the other major challenges that pharma, bio and med devices companies may face in 2011?

Major challenges facing the private sector include maintaining or finding new sources for needed revenue, particularly funding for R&D-intensive companies and for manufacturing companies, with most needing to make or pay for recent investments in new facilities. Mergers and acquisitions may tend to increase as companies use these both rightly and wrongly to boost their product portfolios/pipelines and balance sheets in the short term. Competition for experienced professionals will likely increase, particularly with the U.S. and other developed countries having aging populations, combined with most becoming more insular and restricting immigration, including even the most talented and accomplished foreign citizens.

Depending on the recovery from the current recession, there may also be reductions the NIH and other federal life sciences R&D budgets. Some of the extraordinary increases in recent years may either be frozen or taken back. This may affect R&D-centric vendors and may result in more Ph.D's on the open job market.