

Expanding Vaccine Manufacturing Capacity and Potential: Broad Evolutions in Technology

In advance of the June 2011 Pacific Health Summit on vaccines, NBR is conducting a series of interviews on the latest developments and current issues facing the global vaccines and immunization field. This week, we spoke with Dr. Nigel Darby (GE Healthcare), a key leader in the global healthcare and pharmaceutical industry. This interview was published on the NBR website: <u>http://www.nbr.org</u>.

Nigel Darby is Vice President of BioTechnologies and Chief Technology Officer for GE Life Sciences at GE Healthcare. Prior to joining GE Healthcare, Dr. Darby held a number of positions with AstraZeneca, including Vice President for Chemistry Technology. He has also worked at the UK National Institute for Medical Research, UK M.R.C Laboratory of Molecular Biology, and the European Molecular Biology Laboratory.

By Claire Topal and Karuna Luthra May 16, 2011

An Interview with Nigel Darby

From your perspective as a global life sciences leader, what are the most exciting breakthroughs in science and technology vis-à-vis vaccines manufacturing? What are the broader, international implications of these breakthroughs?

It's an exciting time for vaccine development, with renewed interest and investment, as well as new types of vaccines reaching the market. With increasing understanding of the immune system, new strategies are being developed to increase vaccine effectiveness by using powerful stimulants—adjuvants—to boost the required immune response. While they make vaccines more effective and expand the scope of vaccination, such technologies can also be controversial: in rare cases they could lead to an unwanted immune response, for example to a vaccine impurity. This places a great burden on manufacturing processes to provide vaccines of ever better quality. From an international regulatory perspective, views are mixed on implementing adjuvant technology.

Vaccine developers also have a greater range of choices in terms of the types of molecules used. Traditional vaccines, which are often made through inactivation or crude fractionation of an infectious agent, are now being supplemented by vaccines based on pure proteins, engineered virus particles, DNA, or even cells. These more defined vaccines may have significant advantages in terms of safety and ability to generate the required immune response, thus creating opportunities to develop vaccines against diseases that have previously been intractable to vaccination, such as AIDS and malaria. These more defined technologies could also provide a path to therapeutic vaccines, as recently demonstrated prostate cancer. The challenge with

implementing such technologies is that they require more sophisticated and expensive manufacturing technology, which could limit their broad availability.

What are the greatest scientific and technological challenges you see for global vaccine manufacturing now, and ten years from now?

Many vaccines that are on the market today were developed a long time ago based on empiric research and development, and they have served us well in eradicating important diseases, such as smallpox. Notwithstanding this success, there are increasing demands to develop new manufacturing approaches that will allow us to deliver vaccines more quickly, in larger volumes with greater quality – and to do all this more cost-effectively.

The challenge of delivering a timely response to unpredictable threats, such as pandemic flu, emerging diseases, and bioterrorism, has stimulated significant progress. Ongoing efforts are moving flu vaccine manufacturing to cell-based methods, which can reduce lead times by months compared to traditional egg-based manufacturing. These efforts also significantly increase flexibility of manufacturing by reducing dependence on a limited supply of pathogen-free eggs. Future flu vaccine technologies claim to be able to further lead time reductions, potentially allowing vaccines to be manufactured with a lead time of three months.

Uncertainty in demand and the need to respond to unpredictable threats are also leading to a need for greater flexibility in vaccine manufacturing infrastructure. Traditional models of creating manufacturing facilities for single vaccines based on expensive, fixed infrastructure are being reevaluated as disposable manufacturing technology becomes a reality. These technologies allow facilities to be built that can deal with manufacturing of multiple vaccines in a safe and effective manner with reduced investment in capital infrastructure.

How do you see vaccine manufacturing capacity evolving in emerging economies around the world? In your opinion, is in-country manufacturing capacity important for every country?

Interest from emerging economies in vaccine manufacturing is huge, driven by the costeffectiveness of vaccines in healthcare programs and, in many cases, the desire for selfsufficiency in critical vaccines and medicines. The choice of in-country manufacturing versus import is complex, and it is dependent on the capabilities and infrastructure available. Clearly, manufacturing vaccines domestically can be more cost-effective than importing, and, in some cases, such as pandemic flu, it avoids the risk of global shortages and limited availability of vaccine on the open market. Country-specific requirements, such as a focus on particular disease subtypes, can also be most effectively met locally. Experience suggests that development of indigenous vaccine manufacturing is also a good first step in building the biotech capability that countries require for manufacture of other critical biological drugs, such as insulin and blood products.

Of course, a certain level of infrastructure and expertise will be required for safe, effective manufacturing, and not all countries may be able to achieve that now. However, new approaches, such as manufacturing facilities based on advances in disposable technology, as well as technology partnership programs with emerging economies, are helping to reduce entry barriers

and overall investment needs. Technology is rapidly developing, and even ambitious objectives are in sight, such as setting up modular manufacturing facilities that can easily be relocated and moved around the world to deal with specific in-country needs.

In your opinion, what roles are Asian countries, specifically China and India, playing in terms of innovative approaches to technology and manufacturing – for vaccines and health more broadly?

With their large populations and need for high impact public health programs, Asian countries are strong players in the vaccine market, and their influence is growing. India is already a significant supplier on the global vaccine market, while evolution of the Chinese regulatory framework will likely help it become a major global vaccine supplier within a few years. While both India and China have a strong position in manufacturing more traditional vaccines, a very dynamic industry is evolving with an appetite to try new innovative technologies, in some cases with perhaps more willingness than in Western markets. Given the challenges these nations have in terms of population size and disease burden, I'm confident that they will find ways to drive down the cost of some of today's most expensive vaccines in order to increase general availability.

Unencumbered by the legacies of Western healthcare systems, emerging markets have a tremendous opportunity to redefine the way healthcare is practiced. Dealing as they do with vast populations and the need to deliver rural healthcare within a limited infrastructure, emerging economies will likely be the proving ground for a whole range of new approaches and technologies to delivering healthcare. I'm optimistic that these developments will ultimately also impact the challenges we have in developed countries of delivering affordable, high-quality healthcare.

In the globalized world of the 21st century, why is the term "appropriate technology" so important when we think about the way healthcare is evolving?

There is a vast gap between the developed and developing world in terms of access to technology. For example, two-thirds of the world's population has no access even to reliable X-ray diagnosis. Attempts to simply transfer developed market products often fail due to lack of robustness of the equipment, availability of skilled practitioners, and limited local infrastructure.

The focus on "appropriate technology" reflects the need to provide healthcare technologies that are relevant to the healthcare system and environment within which they need to be used. For example, in countries with a dispersed rural population, more emphasis might be required on developing medical equipment that is portable, rugged, and perhaps battery powered so that it can accompany a travelling healthcare worker. This does not necessarily equate to "low tech" solutions, as continuous innovation, particularly in developing countries, finds ways to incorporate many benefits of sophisticated technologies, such as medical imaging and patient monitoring, into cost effective equipment that can be used in difficult environments with less than optimal infrastructure. Rugged, battery powered ECG¹ and ultrasound equipment are just two examples of the kinds of developments we have seen in recent years.

¹ ECG: electrocardiogram

This is transformational in the sense that it expands affordable access to medical technologies that hitherto have been restricted to highly developed and highly centralized healthcare systems. The great innovation is that the equipment now comes to the patient, no matter how remote, rather than the patient coming to the equipment.

The benefits of diagnostics coupled with information technology have been unevenly distributed throughout the world's population. What innovations do you see on the horizon that might address shifting demographics while matching evolving needs and different budgets? How do you see these trends for "appropriate technologies" developing over the next decade?

The increasing focus on appropriate technology solutions for developing countries will progressively expand access to affordable, quality healthcare. As I noted earlier, sophisticated diagnostic technologies, such as medical imaging and patient monitoring, are increasingly being adapted so that they can be used in the developing world. In addition, there is an increasing trend towards an "in-country, for-country" approach to new technology development. Deep, local knowledge is critical to research, develop, and manufacture any technologies that are designed to meet the specific medical needs and circumstances of developing nations. This trend is accelerating, particularly as R&D within these countries grows to ensure technology development matches local needs.

Advances in IT complement this in a number of ways and are increasingly affordable as the cost of technology continues to fall and mobile data networks proliferate, even in the developing world. Increasingly powerful software solutions can potentially aid doctors in diagnosis, as well as reduce the need for specialist help. This technology is easy to update without the need to purchase new equipment, so physicians and patients can have access to the latest software solutions well into the future, no matter where they are located. Even for more challenging cases, where specialist help is required, remote consultation and evaluation of medical data is increasingly possible, even from rural locations, using high-speed wireless networks.