

The National Biomanufacturing Centre®



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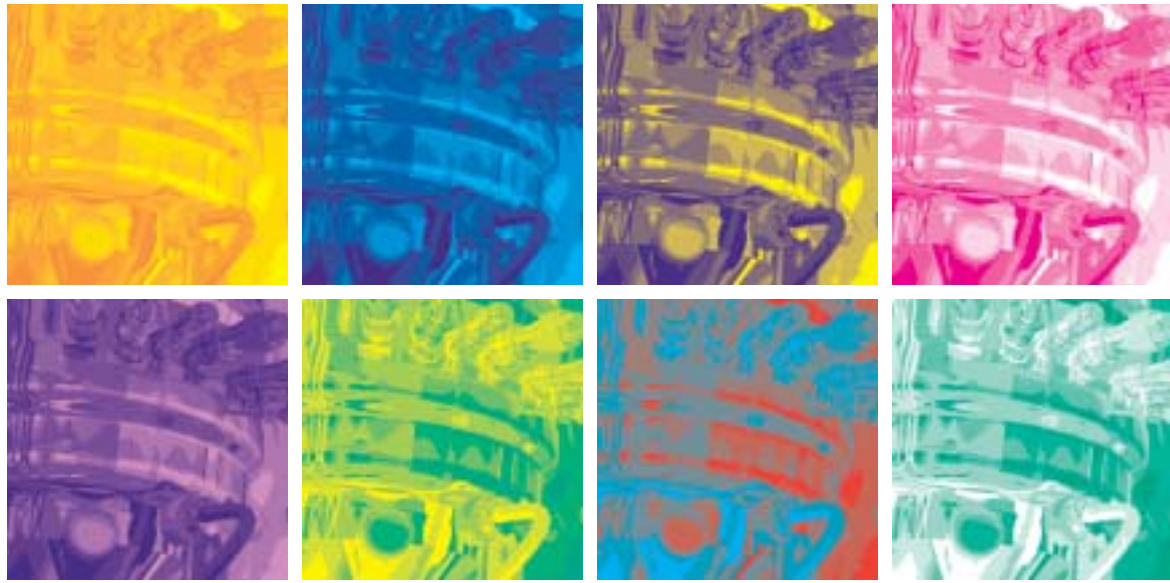


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Accelerating European Biomanufacturing

In an attempt to remedy Europe's sluggish position in the worldwide biopharmaceutical industry, the National Biomanufacturing Centre (NBC) has been established to develop and manufacture biopharmaceutical medicines for clinical trials. This article looks at some of the issues barring the industry's road to success and highlights the aims of the NBC.

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Sceptical investors may see biotech as a “jam tomorrow” industry, but globally biotech is increasingly delivering on its promises. By 2003 there were approximately 120 biopharmaceuticals on the market generating revenues of €33 billion. Biopharmaceuticals have been the fastest growing segment of the global pharmaceutical market during the previous 5 years, recording an impressive 21% compound annual growth. Currently, it is estimated that more than a third of all pharmaceutical products in development are biotech-derived, with revenues potentially rising to €150 billion by the end of the decade.

The biopharm industry: a tale of two continents

Up until now, successful biotech products and companies have, in the main, been developed in the US. Europe is lagging far behind and the gap is growing wider. In 2003, European biotech revenues actually decreased for the first time by 12% compared with 2002, and the sector is yet to see anything approaching the financing recovery in the US. According to Ernst & Young, 77% of global biotech revenues in 2003 were generated in the US and 43% of Europe's publicly traded biotechs have less than 2 years of cash remaining.

One suggested remedy is European industry consolidation, as exemplified by the recent takeover of Celltech, the UK's largest biotech, by UCB, the Belgium pharmaceuticals and chemicals business. Celltech chief executive Goran Ando says the “problem for European biotech is not so much a lack of investment funds, but rather the sector's unstable and fragmented nature.” This is resulting in companies that have some, but not all, of the skills necessary to take projects from early research through to development and approval quickly and efficiently. A small biotech company may have been founded on superb technology, but it won't have the development expertise to deliver a clinically and commercially successful product in a highly regulated market, within tight time and cash constraints.

Testing times for UK start-ups

The UK is the clear leader in European biotech in terms of numbers of public companies and quantities of products in clinical development. However, its position is vulnerable. Whilst obtaining funding is still possible, UK investors increasingly insist on a well-developed late-phase product portfolio, or, better still, actual product revenues before committing to funding. Consolidation and rationalization of

product pipelines has reduced the number of companies, employees and products in development. The heady days of 2000, when the sector was ‘awash’ with public and private cash, is a distant memory. Whilst there has been a marked improvement in sentiment in 2004, those companies that have successfully raised funds are increasingly reliant on overseas money. For example, the recent flotation of Ark Therapeutics, the first European initial public offering since 2000, included significant US-sourced funding.

Barriers to success

In addition to the lack of funding and development expertise, successful commercialization of products by UK biotechs requires access to state-of-the-art manufacturing facilities. Manufacture of biopharmaceutical products has always been a challenge because the complexity of active ingredients means the production process can be considered to be part and parcel of the product. Access to high-quality manufacturing facilities has been an even higher priority since the European Union (EU) Clinical Trials Directive came into force in May this year. From this point onwards, products destined for human clinical trials (investigational medical products) must be manufactured to current good manufacturing practice (cGMP) standards. Whilst in theory this does not have to include the manufacture of active pharmaceutical ingredients (APIs), in practice major European regulatory agencies require facilities producing biological APIs to obtain a cGMP manufacturing licence. This effectively cuts off a low-cost, backdoor route for small companies, and academic and charity researchers to obtain human clinical data in the UK through a Doctors and Dentists Exemption (DDX).

The capital outlay required to build, equip and validate manufacturing facilities for cGMP manufacture of clinical trial material is beyond the vast majority of European biotech companies. The facilities available for commercial contract manufacturing vary in quality — and services come at a high cost. So how can small companies or start-ups realize the

Eden Biodesign: the commercial operator.

Having addressed the lack of facilities and funding, NWDA sought a commercial operator with a proven track record in developing biotech products from concept through to successful market approval. Eden Biodesign won the tender for the contract, and with its existing base in the UK’s northwest, is ideally placed to successfully implement such a major project. Eden has successfully raised €7.5m in investment, which will provide the working capital to launch and operate NBC and further expand its international consultancy business. The private placement capital investment was led by US-based Stephens, Inc.

Through the NBC, Eden will operate globally, providing services such as biopharmaceutical design, process development and clinical trial manufacturing, and technical services to fee-paying biotechs and pharma companies. UK SMEs and start-up businesses will be able to gain financial assistance via the access fund to engage those services, following clinical/commercial review by the independent access fund panel.

Prior to the opening of NBC, Eden will provide advice to businesses developing biologics. Once the facility is operational, Eden will deliver a graduate training programme focussed on operational skills development. NBC intends to work closely with the local *Partnership for Learning in Speke*, a unique organization set up by Eli Lilly, GSK, Evans and Jaguar Motors to deliver technical and operator training.

commercialization of fantastic technology and delivery of potential blockbuster products without the necessary funding, expertise and facilities (Figure 1)?

Government vision

The UK government, similar to those of many other countries, recognizes the importance of the biotech industry as key to the economic growth of the country. The Government Pharmaceutical Industry Competitiveness Task Force (2001) included a section on the support of biomanufacture, which identified the development of biopharmaceutical technology as a key focus for the future.

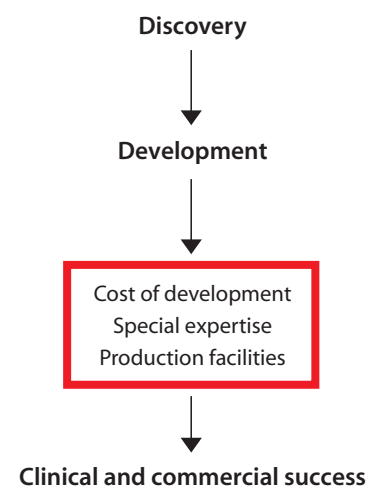
That same year, the government launched a major €39 million support programme called “Harnessing Genomics,” in which biomanufacture was one of four key elements and initiatives to support the innovation to commercialization process. And, in late 2003, the Bioscience 2015 report from the Bioscience Innovation and Growth Team (BIGT), which was set up with a mandate to formulate a strategic approach to the future of the UK bioscience industry, set out six key recommendations, including to “build a strong bioprocessing sub-sector, through the creation of

a network of bioprocessing centres of excellence across the UK.”

Northwest England: One of Europe’s leading bio clusters

Northwest England harbours major manufacturing facilities for top-tier US biopharmaceutical companies such as Eli Lilly, Chiron and Medimmune. This biomanufacturing cluster has developed out of the region’s historical base of pharmaceutical and chemical manufacturing,

Figure 1 Barriers to a clinically and commercially successful biotech product.



which includes AstraZeneca, GSK, Aventis Pharma and Bristol Myers Squibb.

The region has a strong life sciences research base, with world-class universities in Liverpool and Manchester; the Liverpool School of Tropical Medicine; major UK National Health Service teaching hospitals; and centres of specialist research excellence such as the Christie Hospital. Biotech spin-offs are assisted by the internationally recognized bioscience incubators at MerseyBio and Manchester Innovation.

Bionow, the biotechnology sector group of the North West Development Agency (NWDA), is tasked with driving the growth and development of the biotech cluster in the region, and increasing its already significant international reputation for commercial biomanufacture. A major initiative to achieve these goals is the UK National Biomanufacturing Centre (NBC), which was announced by the NWDA in early 2003, before the BIGT report was published.

The National Biomanufacturing Centre

In 2000, an outline plan for a national biomanufacturing facility near Liverpool was put forward to the UK's Department of Trade and Industry. It received a commitment for initial funding from the Secretary of State for Trade and Industry in 2001.

The €45 million project was then fully developed by Bionow and additional funding was secured from public and private sources during 2002. Following final review by the UK government's Treasury, and with part-financing by the EU's European Regional Development Fund (ERDF), the project is now under way. Work started in June 2004, and the NBC is expected to be operational in late 2005/early 2006, allowing sufficient time for the highly technical and complex construction process to be completed.

The 4000 m² NBC will provide the expertise and facilities to develop and manufacture biopharmaceutical medicines for clinical trials, thus overcoming the barriers to successful product development. Its role is to support new and existing biotechnology companies, providing product

Table I Services available from the NBC.

Technology	Mammalian	Microbial	Virus
Guidance and advice	✓	✓	✓
Process design and development	✓	✓	✓
Preclinical manufacturing	✓	✓	✓
GMP manufacture Phase I	✓	✓	✓
GMP manufacture Phase II	✓	✓	✓
GMP manufacture Phase III	Partner	Partner	Partner
Formulation	✓	✓	✓
Filling	Partner	Partner	Partner
Clinical trial supply logistics	✓	✓	✓

development services designed to fill skill and resource gaps that exist within these organizations.

The operational services of the NBC will be aimed at the production of preclinical and clinical material, including cell banking, active ingredient manufacture (fermentation and purification) and supply to clinical centres. Such technologies will help the NBC to become Europe's leading biopharmaceutical design centre, capable of producing a variety of novel medicines.

The facility has been designed to be as flexible as possible, allowing projects to be undertaken on every major biopharmaceutical product technology. Three carefully designed, segregated cGMP production suites will allow mammalian, bacterial and viral products to be manufactured simultaneously (Table I). The suites are designed to biocontainment (the Health and Safety Executive's 'Advisory Committee on Dangerous Pathogens' and the 'Advisory Committee on Genetic Modification') category 2, and will be fully compliant with the latest EU and US GMP guidelines. The cGMP clinical trial manufacturing facilities are supported by three dedicated non-GMP product development suites and extensive analytical laboratories.

In short, the goal of the NBC is to be an engine for growth, propelling early stage UK biotech companies up the value chain by rapidly moving products into clinical development. By adding clinical and commercial value to products through the application of best product-development practices, biotech companies will be better placed to raise funding in tomorrow's financial environment and achieve

satisfactory out-licensing agreements with major pharma. NBC's investment also includes a €4.5 million access fund that will provide assistance to UK-based small- and medium-sized enterprises (SMEs), particularly in the region, helping them to purchase services from the facility.

Summary

The NBC is an innovative vehicle for the delivery of much needed expertise and manufacturing capability to early stage biotechnology companies and product development programmes. The resulting impact will not only ensure medical evaluation of innovative products that might not otherwise be developed; it will also encourage the growth of the UK biomanufacturing industry, through the development of the regional cluster, thereby ensuring that the area plays a leading role in this new growth market.

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