

CBDMT® - MARKET AND BUSINESS INTELLIGENCE

WHITE BIOTECHNOLOGY: THE INVISIBLE REVOLUTION

The life science market is generally segmented in four segments: Biotechnology, Pharmaceuticals, Diagnostics and Medical Devices. A common problem is the confusion between the biotechnology and pharmaceutical segments. Let us try to clarify a little bit the 'so trendy' biotechnology market. In fact, there are two kinds of biotechnology: the traditional and the modern biotechnologies. The traditional one is the fermentation mainly used in food and feed applications (Roquette, Danisco, Cargill, ADM...). The modern biotechnology comes from the discovery of recombinant DNA molecules (Stan Cohen and Herb Boyer in 1973), hybridoma technology (Cesar Milstein and Georges Kohler in 1974) and more particularly the development of molecular biology since then.

Let us go from the first biotech company to the invisible revolution – the white or industrial biotechnology.

The first real modern biotechnology company: Genentech Inc.

Genentech Inc. was founded by Herbert Boyer and Robert Swanson in 1976. One year after that, Allan Maxam and Walter Gilbert co-founded Biogen Inc. The same year (1974) Genentech reported the expression of somatostatin, the first human protein produced by a bacterium. In 1980, the first IPO, Genentech went public October 14 at \$35/share, raising \$35 million. Within one day, the stock leaped to \$89/share! The same year Amgen Inc. was founded.

One year later, in 1981 Cal Tech invented an automated gene-sequencing machine that can read 7,000 DNA building blocks a day.

In 1982, Eli Lilly got the FDA approval to sell the first genetically engineered drug, human insulin cloned by Genentech in 1978. Ten years later, Lilly's Humulin had sales of \$702 million.

Then, there was the approval of the first biotech industry product, the recombinant human growth hormone (1985), followed by alpha interferon for cancer treatment and the first genetically engineered vaccine for hepatitis B treatment (1986). In 1994, Calgene received approval to sell its FLAVR SAVER genetically engineered tomato (first GMO food).

Today, the global biotechnology market is still young but currently with a value of more than \$150 billion and an expected growth of about 10 to 15% per annum. In 2007, Genentech announced financial results for the full year with \$11.7 billion total revenue. Genentech is the second most important biotech company behind the leader Amgen with more than \$14.7 billion revenue in 2007.

The biotechnology market is more and more commonly segmented by using colors to segment biotechnology application: -red- for healthcare biotech, -green- for agricultural biotech, -white- for industrial biotech, -blue- for marine biotech, -gold- for bioinformatic- and nanobiotech etc...

The original market and certainly the most well-known is the 'red biotech' segment which includes medicines and diagnostics (Top 10 red biotech companies: Amgen, Genentech, Serono, Biogen, Genzyme, Chiron, Gilead Sciences, CSL, MedImmune, Cephalon). So typically, the red biotech is focused on providing patients with innovative treatments or diagnostics. This segment includes companies working on cells and tissues, stem cells, gene therapy, orphan drugs, proteomics, pharmacogenetics, genetic testing etc...

Red biotechnology: What else? ...White biotech for sure.

When we use the very fashionable "Bioproduction" word, we generally have in mind pharmaceutical recombinant proteins or biopharmaceutical products. This biopharmaceutical market is composed of four segments: therapeutic proteins extracted from biologics, recombinant therapeutic proteins, cell therapy and gene therapy.

This is a huge market estimated to be worth \$40 billion in 2004 and expected to be more than \$100 billion by 2010.

As the red biotech or the pharmaceutical biotechnology 'phagocytes' the biotechnology industry, there is important information to keep in mind: the white biotechnology or the industrial biotechnology or gene-based bioindustry also serves other market segments such as detergent, food, feed, cosmetics, R&D etc.

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White Biotech...

White biotech involves the use of micro-organisms and biological catalysts (enzymes) to produce goods and services. White biotech is a powerful tool to compete with chemical and physical means of reducing energy and material consumption and also minimizing the generation of waste and emissions. White biotech does not simply allow removing pollutants but will prevent pollution at the source. If we just look at the carbon (CO₂) emission market value of \$10,864 million in 2005 (emission of 710 tons of CO₂) compared with \$30,098 million in 2006 (corresponding to the emission of 1,700 tons of CO₂), white biotech will allow emission saving by 'clean' bioprocesses and also to sequester CO₂ emission using photo-synthetic micro-organisms. And this will definitely have a strong impact on the market.

In 2006, the Energy Services business unit of Rhodia sold 1.6 million tons of CER (certified emission reduction, or CO₂ credit) and so generated a €2 million revenue. So if the white biotech allows you to put in place industrial process to sequester the CO₂, you'll be able to sell your emission rights or CER and then to generate significant revenue. So, even if this sounds less 'attractive' than the development of pharmaceutical products, white biotech will bring new treatments or solutions not for us but for our planet. The conclusion is you'll hear more and more about "clean biotech" in the near future.

Even if the recombinant proteins or enzyme or biocatalyst market is a small but significant one estimated at €3.4 billion revenue with an annual growth of about 6.5 to 10%, we also have to stress that in the near future (meaning 2015), more than 10% of the industrial chemical production would actually be produced by industrial bioproduction (more than €300 billion in 2015 against €40 billion 2004 sales volume). It will be a significant market with products or services having a short time to market (no FDA and no EMEA approval...)

Enzyme products such as Insulin were the first biotech products marketed in the 70's. And while enzymes are present everywhere and come in thousands of different forms, there are still only about 25 of them which have actually been industrialized and commercialized. These include Amylase, Proteinase, Lipase, Cellulase, Glycomylase, Glucose Isomerase, Chymosin, Lactase, Pullulanase, Xylanase (paper and pulp industry).

Enzymes are used in textile production (textile finishing, functional textiles), in pulp and paper production (enzymatic treatment of cellulose, enzymatic bleaching and deinking), in food and feed production (nutraceuticals, dietary supplements, functional foods, nutritional beverages), in plastic and chemical production (plastic consumer goods from renewable feedstock), pharmaceutical and vitamin production (antibiotics, vitamin C and B₂) and fuel production (biofuel and hydrogen from renewable feedstock and agricultural residues).

In fact white biotechnology is a real revolution, probably invisible for a lot of people (except biofuel). It seems like a complimentary and an alternative to traditional fossil-based chemistry. All the chemical sectors are and will be drastically impacted by the emergence of white biotechnology industrialization: fine chemicals (chemical product that are made in relatively small quantities and is typically high in cost, vitamin, API), polymers, specialty chemicals (key intermediates) and base chemicals. And so all our consumer products will be made of bioproducts.

Today, there are numerous types of biopolymers based on different raw materials (starch polymers, polylactic acid, polyhydroxyalkanoates, biobased 1,3-propanediol, cellulosic polymers and blends).

One very promising market segment is biocatalysis which is difficult to estimate. But we know that this market segment will affect the market of catalysts estimated by CBDMT at more than \$7 billion with an annual growth of up to 5%.

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The question is why is this revolution invisible?

Because generally innovative white biotech companies are perceived as service-oriented business model companies, and so have been totally misunderstood or have had huge difficulties in showing their real market potential to venture capital companies or investors (VC people normally responsible for “the business of building business”). Generally and this is particularly true in France for instance, those companies are generally ‘science’ oriented versus ‘market’ oriented. I was attending a biotech conference this year, and a VC partner was explaining that they had suffered a setback with ‘white biotech’. Yes of course they had, because they pushed the company they invested in to develop new processes to produce pharmaceutical products also, because venture capital does not exist to fund development of new technology. Instead of that VC exists more particularly to develop new applications of existing technology. And more precisely, venture capitalists are looking for a new application of existing technology that addresses a commercially significant need or problem. And to do so, you do need to know the market to be addressed. Finally, VC’s lack of knowledge and experience about the industrial biotech sector or its end-market (feed, food, cosmetics, chemicals etc...) often leads to a false evaluation of the company value. And that’s why if you look mainly at Europe, only 10 to 20% of industrial biotech start-ups were able to raise money. It is always easier to calculate a NPV (Net Present Value) on a pharmaceutical product than an industrial bioproduction of an essential amino acid (which addresses industrial markets such as food, feed, nutraceuticals, beverages, pharmaceuticals etc...).

Another concern is that mainly in Europe, there’s confusion between bioproduction and GMO. This had a very bad influence on the population and also the investors (GMO crop to produce API)... But a lot of food or feed ingredients are currently produced in huge chemical reactors from terrible chemical raw materials. At the end of the production process, you have a pure product (means no impurity) and it is exactly the same when you use a GMO or naturally modified organism (synthetic biology, directed evolution processes) to produce an ingredient (GMO free, no impurity).

From the first recombinant protein in the 70s, modern biotechnology and more particularly the industrial or white biotechnology is a real alternative technology for the development and the production of goods from renewable resources (in 2015 up to €300 billion in chemical product sales will be bioproduced). It will allow increasing energy and processing efficiency (cost-effectiveness, flexibility, cleanness, sustainability). So please think not only about pharmaceutical products when we are talking about the ‘so trendy’ biotechnology market. The invisible white biotechnology revolution is going on.

Philippe Tramoy, Managing Partner CBDMT.®

For detailed information, feel free to read full article at: <http://www.lifescience-online.com/article.html?a=1005>

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