

Does Biotechnology Measure Up?

Facts and feats of a biotechnological nature

JOHN HODGSON
KIRSTY BARLOW

We have attempted to encapsulate the biotechnology of 1993 in answers to questions that have puzzled scholars for years [well, only months, actually, since we first posed them in the June issue of *Bio/Technology* (11:740)]. What follows, therefore, is an idiosyncratic, but, we hope, memorable, compendium for the discerning biotechnophile.

Healthcare

Q. Human growth hormone (rhGH) was the second recombinant protein product (after insulin) to receive regulatory approval. How many miles taller is the human race today as a result of this product?

A. Thirteen kilometers or 8.25 miles taller than it would have been without any growth hormone. We obtained this answer by multiplying patient-years of rhGH by the average growth increase per patient year. According to Howard Firth at Ares-Serono (Geneva, Switzerland), approximately 400,000 patient-years of treatment with recombinant growth hormone have been administered since Genentech's (S. San Francisco, CA) Protropin received FDA (Bethesda, MD) approval in October 1985. Untreated, growth-hormone-deficient patients grow at around 4-5 cm per year; with Ares' rhGH, Saizen, patient growth increases 10 cm over a three-year period, roughly 3.3 cm per year, which tallies with figures from Genentech's Barbara Ross. This global growth spurt is equivalent to an additional 2.3 micrometers per member of the human race—the length of two *E. coli* bacteria laid end to end.

Q. Which nation's regulatory bodies have approved the greatest number of recombinant protein or monoclonal antibody-based drugs?

A. Germany. According to Brigitta Bienz-Tadmor, Becton Dickinson Labware, (Bedford, MA), by mid-1992 German authorities had approved 22 recombinant DNA proteins, monoclonal therapeutics, or recombinant vaccines; Japan was

next with 21; then France (18), Spain and Italy (17), and the U.S. (15).

Q. What is the approximate value of the world wide sales of recombinant protein and monoclonal antibody-based drugs from the launch of human insulin to the present day?

A. This is a tricky one, which requires multiple sourcing and careful definition of scope. Year by year, sales were: in 1992—\$5.9 billion, according to Ernst & Young's *Biotech 93*; 1991—\$4.1 billion (Datamonitor, *World Biotechnology Drugs*); 1990—\$2.75 billion (Datamonitor, *World Biotechnology Drugs*).

Q. Name ten companies that have been or are still involved in the development of sepsis therapies.

A. Choose your own ten favorites from the following list: Centocor (Malvern, PA)—Centoxin (HA-1A anti-endotoxin); Xoma (Berkeley, CA)—E5, BPI; Synergen (Boulder, CO)—Anril (IL-1ra); Chiron (Emeryville, CA)—murine anti-TNF; Bayer/Miles (Leverkusen, Germany/Elkhart, IN)—murine anti-TNF; Ribic-Immunochem Research (Hamilton, MT)—endotoxin fragment (as a vaccine); British Biotechnology (Oxford, U.K.)—BB882 (a platelet activating factor inhibitor); Genentech—BPI; Celltech/Bayer (Slough, U.K.)—humanized anti-TNF; Immunex (Seattle, WA)—soluble TNF receptor, soluble IL-1 inhibitor; Cortech (Denver, CO)—bradykinin antagonist; Incyte Pharmaceuticals (Palo Alto, CA)—BPI.

Q. Name ten companies developing AIDS or HIV vaccines.

A. Bristol Myers Squibb (Syracuse, NY); British Biotechnology; Cellular Products (Buffalo, NY); Connaught (Swiftwater, PA); Hoescht (Frankfurt-am-Main, Germany); IDEC (Mountain View, CA); Merck & Co (Rahway, NJ); Immunotech (Boston, MA); Immune Response (Carlsbad, CA); MicroGeneSys (West Haven, CT); Genentech; Chiron; Repligen (Cambridge, MA); MedImmune (Gaithersburg, MD); Viral Technologies (Washington, DC).

Q. How many miles taller is the human race today as a result of human growth hormone?

John Hodgson is articles editor, and Kirsty Barlow is an editorial assistant, at Bio/Technology.

Q. *How much do major corporations currently have invested in the equity of biotechnology companies?*

Sources: BioIndex, Technological Communications (Lafayette, CA) and Bio/Technology (1992) 10:24.

Q. *How much human genome data (in bases) has been deposited?*

A. 27,350,000 bases.
This is the number of bases of human sequence in the public version of the database, which is a collaborative collection between the European Molecular Biology Laboratory (EMBL, Heidelberg, Germany), the National Center for Biotechnology Information (NCBI/GenBank) (Bethesda, MD), and DNA Data Base of Japan (DDBJ) (Shizouka, Japan). According to Catherine Rice at the EMBL Data Library, this figure may be overestimated by as much as 40 percent as a result of duplication, largely stemming from the accession of both genomic sequence and its corresponding cDNA sequence. That would give a figure of as little as 16,410,000 bases or just over 0.5 percent of the human genome.

Finance

Q. *In 1980, Genentech's stock was floated. Including the \$38.5 million raised in that flotation, how much money have biotechnology companies worldwide raised on public markets since then?*

A. \$20 billion.
This estimate comes from Ernst & Young in its annual report of the status of biotechnology, *Biotech 93*. Ernst & Young goes on to estimate that—as a measure of the task facing biotechnology—a further \$40 billion would be required for each of the public biotechnology companies in the U.S. to bring one product to market.

Q. *If you had invested \$100 in Amgen stock at its flotation in 1983, how much would that investment be worth today?*

A. \$1,300.
Lynne Connell at Amgen (Thousand Oaks, CA) used the stock price on July 27, 1993 (\$36 per share) to calculate this figure. Amgen's initial public offering stock price was \$18 per share: the stock split two for one in 1990 and three for one in 1991. The 1983-1993 rise represents an average annual compound increase of 29.2 percent.

Business

Q. *How many biotechnology companies are there (a) worldwide (b) outside the U.S.?*

A. (a) There are 1050-1100 specialist biotechnology companies worldwide and a further 625-

725 corporations with an interest in biotechnology. Mark Dibner at the Institute for Biotechnology Information, North Carolina Biotechnology Institute (Research Triangle Park, NC) provided the data and used the following definition of biotechnology companies: those employing the "new" technologies of genetic engineering, hybridomas, protein engineering and related areas in their research, product development, or manufacturing activities. (b) Only 200-250 of the North Carolina Biotechnology Institute's biotechnology companies, but 450-600 of the corporations, are outside the U.S. There is only one biotechnology company in Japan, according to its definition and data.

Q. *How many biotechnology companies have registered (a) at least one year with an operating profit, (b) more than one year's operating profits, and (c) overall profitability?*

A. (a) There are 12 companies with one year's profit: Dianon Systems (Stratford, CT)—1992; Immucor (Norcross, GA)—1992; Osteotech—1992; Quidel (San Diego, CA)—1992; Vestar—1992; Chiron—1990; Diagnostic Products (Los Angeles, CA)—1990; Somatix Therapy (Alameda, CA)—1990; Genzyme (Cambridge, MA)—1991; MedImmune—1991; Immunex—1991; Agouron Pharmaceuticals (La Jolla, CA)—1991.

(b) There are five companies with more than one year's profits: Amgen—1990/93; Biogen (Cambridge, MA)—1990-93; Elan (Westmeath, Ireland)—1991-92; Genentech—1991-92; Idexx Labs (Westbrook, ME)—1991-92.

(c) There are two companies—Amgen and Idexx Labs—with overall profitability. We feel that it may be worth inserting at this point a major disclaimer directed at litigious souls—more than just these companies may be profitable; we have only surveyed those companies that have been featured in *Bio/Technology's* annual company surveys.

Q. *How much do major corporations currently have invested in the equity of biotechnology companies?*

A. The Institute for Biotechnology Information has recorded 95 equity purchases by large corporations in smaller biotechnology firms in the five-year period between July 1988 and July 1993. Median purchase was about \$5 million and the median amount of equity purchased was 16 percent (this excluded major acquisitions such as Hoffmann-La Roche's (Basel, Switzerland) \$2.1 billion purchase of 60 percent of Genentech). With the Roche investment, Sandoz's \$392 million investment in Systemix/Sandoz and American Home Products' purchase of 60 percent of Genetics Institute for \$666 million, we come to a total investment in biotechnology by major companies of

around \$3.6 billion. The current value of those purchases is unknown but could be viewed in the context of the paper valuation of the entire biotechnology sector.

Q. *In 1983, when Bio/Technology was launched, it was certainly the case that the combined sales in companies that supplied research equipment and reagents to the biotechnology community exceeded the combined product sales of the biotechnology companies themselves. Is this still the case?*

A. No. According to data provided by Frost and Sullivan (London, U.K. and Silicon Valley, CA), 1992/1993 world sales of biotechnology equipment and consumables is around \$2.0-2.5 billion. This estimate encompasses actual sales figures and estimates for sales research biochemicals, cell culture consumables and hardware, and "biotechnology instrumentation" such as sequencers, fermentation equipment, high-tech separations apparatus, thermal cyclers, gene transfer hardware, and software. World sales of biotechnology pharmaceuticals, on the other hand, have been estimated by Ernst & Young to be \$5.9 billion (for 1992) and by Datamonitor to be \$4.1 billion (for 1991).

Q. *Are any single companies equivalent to the combined commercial biotechnology sector in terms of (a) sales volume, (b) employees, (c) research and development expenditure, or (d) paper valuation?*

A. (a) Total biotechnology sales volume in 1992 (\$5.9 billion according to Ernst & Young) was roughly equivalent to that of Takeda (Osaka, Japan; \$5.5 billion in 1991), Intel (Hillsboro, OR; \$5.8 billion in 1991), or one-tenth of that of AT&T (New York, NY; \$60 billion in 1991). (b) The biotechnology sector employs 70-80,000 people, a similar number to Lockheed (San Diego, CA), Canon (Tokyo, Japan), or Rhône-Poulenc (Paris, France). (c) Biotechnology R&D expenditure (\$4.9 billion in 1992, according to Ernst & Young) is only just exceeded by the combined total R&D spending in 1991 of the top-spending chemical giants, Bayer (Leverkusen, Germany), Hoechst (Frankfurt, Germany), and CIBA (Basel Switzerland) at \$5.3 billion. In the electronics field, Siemens (Erlangen, Germany; \$5.12 billion in 1991), and IBM (Armonk, NY; \$5.0 billion in 1991) are close to the biotechnology figure. (d) We estimate the biotechnology sector to have a paper valuation of \$20-30 billion, about that of Glaxo (London, U.K.; approximately \$25 billion) but only about a third that of AT&T (New York, NY; approximately \$85 billion). *Sources:* figures on the R&D spending, sales, and employees of nonbiotechnology companies were taken from *The 1993 R&D Scoreboard*, published by Company Reporting

(Edinburgh, U.K.); company valuations were taken from *The Financial Times* (August 5, 1993).

Q. *How much benefit do lawyers gain from the average biotechnology patent dispute?*

A. No one is saying, but the answer is probably somewhere between "Much less than Amgen" and "Much more than Genetics Institute."

Agriculture and environment

Q. *Approved field trials of recombinant plants started in autumn 1986 with the planting of tobacco in the U.S. and Belgium. Since then, 94 percent of approved trials have been conducted in just five countries. Which?*

A. Canada, 35.7 percent; U.S., 37.4 percent; France, 9.1 percent; Belgium, 7.3 percent; U.K., 5.3 percent.

Source: OECD Report to the Group of National Experts on Safety in Biotechnology: Evaluation of Bio-safety Information Gathered During Field Releases of GMOs, December 1992. Survey covers 1986-92 period.

Q. *On which five crops have the greatest number of field trials been conducted?*

A. Rapeseed, 289, potato, 122; tomato, 71; tobacco, 72; corn, 65; flax, 49.

Source: OECD Report to the Group of National Experts on Safety in Biotechnology: Evaluation of Bio-safety Information Gathered During Field Releases of GMOs, December 1992. Survey covers 1986-92 period.

Q. *What is the current sales value of products of biotechnology in the agriculture market?*

A. \$184.5 million, apparently. *Source: Standard and Poors cited in Bio/Technology 11:554, May.*

Q. *How long has bovine growth hormone (bovine somatotropin, or BST) been waiting for regulatory approval as a milk yield-increasing agent?*

A. The FDA authorized the sale of meat and milk from BST-supplemented cows as safe for human consumption in 1985. This means that BST has been awaiting regulatory approval for eight years.

Q. *Most of the major crops species can now be stably transformed with—and express—heterologous DNA. But in what chronological order were the breakthroughs achieved?*

A. Transformed tobacco, 1983 (*Plant Cell Reports 5:81*); tomato, 1986 (*Plant Cell Reports 5:81*); sunflower, 1987 (*Bio/Technology 5:1201*); rape, 1987 (*Plant Cell Reports 6:321*);

Q. *How much benefit do lawyers gain from the average biotechnology patent dispute?*

from DNA to DRUGS

NATURE INTERNATIONAL CONFERENCE IN EUROPE 1993

2 ~ 3 December 1993

Holiday Inn Crowne Inn, Amsterdam

This 2 day interdisciplinary meeting will bring together scientists from around the world to explore the exciting pathway from basic research in molecular biology and genetics to the development of new therapeutic agents.

The programme will consist of the following sessions:

Thursday 2nd December

OPENING ADDRESS:

John Maddox, Editor of Nature

Morning session:

Gene mapping and molecular diagnosis

Afternoon session:

New therapeutic agents

Friday 3rd December

Morning session:

Targeting and delivery of agents

Afternoon session:

New approaches to vaccine development

Top international speakers will include:

**JEAN-LOUIS MANDEL, TOM BLUNDELL,
INDER VERMA, DANIEL COHEN, BARRY BLOOM,
WARNER GREENE, RUTH NUSSENZWEIG**

BOOK BEFORE SEPT 30 & SAVE £50

Before September 30

Standard rates including evening reception: £295 plus £54.57 VAT (total payable £349.57)

Special rates for full time academics and government employees only: £225 plus £41.63 VAT (total payable £266.63)

After September 30

Standard rates including evening reception: £345 plus £63.83 VAT (total payable £408.83)

Special rates for full time academics and government employees only: £275 plus £50.88 VAT (total payable £325.88)

FOR FULL PROGRAMME DETAILS AND A BOOKING FORM,

PLEASE COMPLETE AND RETURN TO:

PIPPA BURNETT, CONFERENCE ADMINISTRATOR, FROM DNA TO DRUGS, 4 LITTLE ESSEX STREET, LONDON WC2R 3LF, UK.

TEL: +44 (0)71 836 6633 EXT 2593 FAX: +44 (0)71 379 5417.

BLOCK CAPITALS PLEASE

SURNAME

FORENAMES

JOB TITLE/POSITION

PLACE OF WORK

ADDRESS

POSTCODE/COUNTRY

A

potato, 1987 (*Theoret. Appl. Genet.* 73:744); rice, 1989 (*Bio/Technology* 6:1072); maize, 1990 (*Plant Mol. Biol.* 7:43); wheat, 1992 (*Bio/Technology* 10:667); and barley, 1993 (unpublished as yet).

People

Q. How many people are involved in biotechnology research worldwide?

A. Pick a number, any number. The one we have chosen is derived by dividing the Ernst & Young's industrial biotechnology R&D spending (\$4.9 billion in 1992) by the cost of an average researcher which we estimate from our own salary and research budget surveys to be around \$240,000. This dubious approach yields the highly accurate answer of 20,417.

Q. Who is the highest paid biotechnology CEO (a) in the U.S., and (b) outside the U.S. (and what do they make)?

(a) The highest-ever U.S. compensation was reported anonymously in *Bio/Technology's* annual compensation survey last year at \$1,000,001, which consisted of a basic \$125,000 salary, \$225,000 in bonuses, \$650,000 in consulting fees, and \$1 from *Bio/Technology* for completing the survey form.

(b) No one is saying at present; but according to press reports, the CEO of a small U.K. biotechnology company is remunerated £500,000 (worth around \$850,000).

To find the best,
use the best.

BIO/TECHNOLOGY

Advertise your
recruitment
opportunities

in
BIO/TECHNOLOGY'S
classified pages.