investment in research," Agilar said. Furthermore, if companies reach the stage of phase I and II clinical trials, the EC will support the generation of 'demonstrative results' to the tune of 35% of the cost of the trials. With help from the EC, Agilar says, the "situation for SMEs is improving dramatically." And it certainly has to if European biotech is to catch up with its counterpart in the USA.

And what of magainin? Not surprisingly, the company has changed its name to Genaera (Plymouth Meeting, USA), but it may be that 'antimicrobial peptides', now precariously near the bottom of Genaera's product list, will be reborn. On 20 November 2002, the company announced an option agreement for "certain antimicrobial peptide intellectual property held by Genaera" with E.I. du Pont de Nemours (Wilmington, USA). Although du Pont sold its pharmaceuticals division to Bristol-Myers Squibb (New York, USA) over a year ago, it still has a sizeable biotechnology interest in agriculture. Whether this will mean the reincarnation of magainins in agriculture is not clear, and Genaera refused to comment on the deal.

...big may not always be beautiful in the pharmaceutical market of the future.

In the meantime, Michael Zasloff is already at the next conceptual stage in the exploitation of antimicrobial peptides. For him, it would merely be logical to see magainins make it to the dispensing chemist; his mind is already busy with the next step. "I think there will be a time when we can stimulate expression of endogenous peptides", he commented. "This is a wonderful area for drug development; we may cure all diseases that are constitutional, but we will always have bugs around us." Although it seems that Zasloff is the victim of powers beyond his control, he may rest assured that one day, when bacterial resistance becomes a larger problem, his magainins will be rediscovered by someone else. As Thomas Edison put it "A good idea is never lost [...] Accordingly, my principal business is giving commercial value to the brilliant but misdirected ideas of others."

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Government rhetoric and their R&D expenditure

A score-card for governments' investments into science and future technologies

If you want to harvest in the autumn, you need to sow in spring. This ancient wisdom holds true not only for agriculture, but for all economic activities. When nations turned their focus from agriculture to industry, the definition of 'sowing' and 'harvesting' changed. The latter is relatively easy to identify: it is the nation's wealth in terms of economic growth, employment level, *per capita* income, exports, and so on. Such achievements point the way not only to re-election of the politicians who ensure a rich harvest, but also to the well-being of all its citizens.

Slightly harder to define is the 'sowing' part—the public and private investments that guarantee economic growth and high employment in the long term. After the industrial revolution took place, governments needed simply to ensure that the social, political and financial structures were in

place to encourage entrepreneurs to start businesses and create new jobs in the emerging industrial sector. Now, at a time of globalization, international corporations move to where they can find the best opportunities in terms of employee salaries and governmental incentives. It follows that robust manufacturing processes are being transferred from their traditional locations in the developed world to areas that offer the best financial projections and the lowest cost structures. As a result, the so-called advanced economies have to find new ways to maintain their privileged status. The common solution is to focus on new discoveries that bring with them ownership of commercially valuable intellectual property and require a phase of development and manufacturing in a highly skilled environment. Thus, the seeds that need to be sown are now investments, from both industry and

Table 1 | Gross domestic product (GDP) and gross domestic expenditure on R&D (GERD) by Japan, the USA and the EU countries

Country	GDP (billion US\$) ¹	GERD as % of GDP ²	GERD estimates (billion US\$)
Austria	220	1.89	4.1
Belgium	267.7	1.97	5.2
Denmark	149.8	2.07	3.1
Finland	133.5	3.67	4.9
France	1,510	2.13	32.1
Germany	2,174	2.52	54.8
Greece	189.7	0.67	1.3
Ireland	104.7	1.21	1.3
Italy	1,402	1.04	14.5
Netherlands	413	2.02	8.3
Portugal	174.1	0.76	1.3
Spain	757	0.97	7.3
Sweden	219	3.78	8.3
UK	1,470	1.86	27.3
EU	9,184	1.90	174.0
USA	10,082	2.70	272.2
Japan	3,450	2.98	102.8

¹Data estimated for 2001. Source: the CIA World Factbook; www.cia.gov/cia/publications/factbook/index.html

²Source: Communication from the European Commission (2002) "More Research for Europe – Towards 3% of GDP" COM 499.

Table 2 | R&D financed by government and industry

Country	R&D financed by industry as % of GERD ¹	R&D financed by industry as % of GDP	R&D financed by government as % of GERD ¹	R&D financed by government as % of GDP	R&D financed by other sources as % of GERD ¹	R&D financed by other sources as % of GDP
Austria	40.1	0.75	40.3	0.75	19.6	0.36
Belgium	66.2	1.30	23.2	0.46	10.6	0.21
Denmark	58.0	1.20	32.6	0.67	9.4	0.19
Finland	70.3	2.60	26.2	0.96	3.5	0.13
France	54.1	1.15	36.9	0.80	9.0	0.19
Germany	66.9	1.70	30.7	0.77	2.4	0.06
Greece	24.2	0.16	48.7	0.33	27.1	0.18
Ireland	64.1	0.78	21.8	0.26	14.1	0.17
Italy	43.0	0.45	50.8	0.53	6.2	0.06
Netherlands	49.7	1.00	35.8	0.72	14.5	0.29
Portugal	21.3	0.16	69.7	0.53	9.0	0.07
Spain	49.7	0.48	38.6	0.37	11.7	0.11
Sweden	67.8	2.56	24.5	0.93	7.7	0.29
UK	49.3	0.92	28.9	0.54	21.8	0.41
EU average	51.8	1.08	36.3	0.62	11.9	0.20
USA	68.2	1.84	27.3	0.74	4.5	0.12
Japan	72.4	2.16	19.6	0.58	8.0	0.24

¹Source: Communication from the Commission of European Communities, 499; 2002. GDP, gross domestic product

government, into science and technology, with the aim of creating well-paid jobs in the high-tech sector and new products for an increasingly demanding global market.

In the context of this article, these investments are referred to as the expenditure on research and development (R&D) as a percentage of the national gross domestic product (GDP; the wealth a whole nation generates by all of its activities). The contenders for the crown of the leading economic zones are now the USA, Japan and Europe. Each watches the others' moves and investments, and tries to gain an advantage. Consequently, the amount spent on R&D has become an important indicator of how a nation is doing in the race to stay ahead or catch up in the global market of high-tech products. Although the R&D figure includes various inadequacies and uncertainties (F. Gannon, *EMBO Rep.* 3, 701; 2002), it certainly allows some important comparisons to be made.

In recent years, we have witnessed a steady increase of R&D investment in the USA, particularly into research in the life sciences. Indeed, the boom in the biotech and information technology industry was driven by US entrepreneurs and academics, with skilful support from the government. Ownership of the technologies and intellectual property resides predominantly in the

USA and will be at the core of future products. It is clear that this investment will be well rewarded and will give the USA a strong advantage in the market for high-tech products.

In Japan the transition has been slower, and based more on innovation designed to add value to existing consumer products rather than on creating new ones. However, this has started to change since the Japanese government announced a few years ago that it is dramatically increasing its investment into basic research. The marriage between the fruits of this research and the well-established connections with industry could thus bring an added advantage to this region.

The situation in Europe is more complex. When speaking jointly, the EU (European Union) member states have a common goal to make Europe the leading knowledge-based economy in the world. The stated means of achieving this is to increase R&D expenditure to approximately 3% of GDP for all EU countries before the year 2010; this is close to the levels of expenditure of the USA (at present standing at 2.70%) and Japan (2.98%). At the moment, the average expenditure of the EU member states is 1.9% of GDP, but with the forthcoming inclusion of central and eastern European countries, this figure is likely to drift a little lower after 2004. Sweden and Finland have already achieved the EU goal, but it remains far off for many

other countries (Table 1). Of course, this is a relative number and when calculated as total spending in dollars, the lead of the USA, because of the sheer size of its economy, becomes even more evident.

Usually, this type of table is used to show the varying gaps between government rhetoric and reality. But the European Commission (EC) recently released a document entitled 'More Research for Europe' (Communication from the CEC, COM 499; 2002)—which is the source of the primary data in this analysis—that gives a more nuanced picture. When the heads of governments met in Barcelona in 2001 to proclaim the 3% target, they immediately softened the challenge for their ministers of finance by deciding that two-thirds of this should come from industry, with the remaining one-third (that is, 1% of GDP) being the government's responsibility. This type of balance between private and public investment is reasonable now that the era of state-supported economies has clearly ended. Indeed, 68.2% of R&D spending in the USA and 72.4% in Japan comes from the private sector.

Table 2, which shows industrial and governmental contributions to R&D spending, shows that there are some dramatic and unexpected variations within Europe. For instance, Finland is obviously doing well in

It is clear that [the investments into R&D by the US government] will be well rewarded and will give the USA a strong advantage in the market for high-tech products.

terms of industry investment as this constitutes 70.3% of the country's R&D spending, whereas in Portugal it is only 21.3%. The direct governmental expenditure on R&D is also listed. Surprisingly, Europe as a whole has a higher proportional public investment in R&D (36.34%) than the USA (27.3%) and Japan (19.6%). But again, the national figures in Europe range from 21.8% in Ireland to 69.7% in Portugal. By using this figure in conjunction with the national R&D expenditure, the government's contribution to R&D as a percentage of the total GDP is derived. Using this figure, the EU, with a governmental contribution of 0.62% of GDP, is closer to both the USA (0.74% of GDP) and Japan (0.58% of GDP). In terms of individual nations, the extremes are Ireland at 0.26% and Finland at 0.96%, and it is interesting to see that the governments of Italy, Portugal and the United Kingdom contribute the same percentage—around 0.5%—of their GDP to support R&D.

Table 3 | Difference between actual levels of R&D expenditure and the EU 1% goal, and the increase in R&D expenditure needed to reach this goal. Figures are shown as percentages of gross expenditure on R&D (GERD) or of gross domestic product (GDP)

Country	R&D expenditure by government and other sources (%GERD)	R&D expenditure by government and other sources (%GDP)	Difference from goal (% GDP)	R&D expenditure increase needed to reach goal (%)	Increase needed to reach goal (million US\$) ¹
Austria	59.9	1.11	0.11	–	–
Belgium	33.8	0.67	–0.33	72	880
Denmark	42	0.87	–0.13	19	195
Finland	29.7	1.09	0.09	–	–
France	45.9	0.98	–0.02	2.5	300
Germany	33.1	0.83	–0.17	22	3,695
Greece	75.8	0.51	–0.49	150	930
Ireland	35.9	0.43	–0.57	216	595
Italy	57	0.59	–0.41	77	5,748
The Netherlands	50.3	1.02	0.02	–	–
Portugal	78.7	0.6	–0.4	75	690
Spain	50.3	0.49	–0.51	136	3,860
Sweden	32.2	1.22	0.22	–	–
UK	50.7	0.94	–0.06	11	880
EU average	48.24	0.81	–0.19	31	17,450
USA	31.8	0.86	–0.14	19	14,115
Japan	27.6	0.82	–0.18	30	6,210

¹Based on the 2001 estimate of GDPs as given in Table 1.

Data are also available for payments from 'other sources', that is non-governmental, non-industry sources, which are presumably foundations, external grants and so on. Again there is a wide range from 2.4% in Germany to 27.1% in Greece (the last two columns of Table 2). It is perhaps correct to include this figure, which is equal to GERD minus business expenditure on R&D, as a component of the 1% goal of government expenditure. The combined 'non-industry' spend obtained by adding these two figures appears in the first two columns of Table 3. Again, the ranking of investment by different governments changes. Europe is now at 0.81%, compared with the USA at 0.86% and Japan at 0.82%. The EU country ranking lowest is again Ireland at 0.43%, whereas Sweden has the highest non-industry spend at 1.32% of its GDP.

These are informative figures, but what do they actually mean for various governments? One way to determine the challenges for individual EU countries is to calculate how much they need to increase their public expenditure to reach the target of spending 1% of their GDP on R&D. Assuming that the external sources of non-industry funding remain constant, the remaining input to reach the 1% goal must come solely

from the governments. The amounts needed to reach these goals are shown in Table 3 as a percentage increase of current expenditure. These figures provide a score-card for each of the EU countries. For some, such as Sweden, Austria, Finland, the Netherlands, France and the United Kingdom, the goal of 1% public investment has either been achieved or is within close reach (Fig. 1). For others, including Ireland, Spain, Greece, Italy and

On average, the EU needs to increase its non-industry expenditure by 31% if it wants to reach the target set in Barcelona.

Portugal, it shows that these governments need to dramatically change their funding policies if they are to contribute equitably to the overall EU goal. As the plan is to achieve the overall level of 3% by 2010, some of these countries need to double their governmental expenditure within the next eight years. On average, the EU needs to increase its non-industry expenditure by 31% if it wants to reach the target set in Barcelona. The last column of Table 3 gives some estimates, based on the 2001 GDP figures of how much extra these governments would have to spend to reach the 1% goal—for some, such as Italy, Spain and Germany, this adds up to several billion Euros.

These calculations, of course, rely on some key presumptions—most importantly, that industry will maintain its current level of expenditure in each country. This is not assured in the present economic climate, and countries where the industrial spend balances lower governmental expenditure, such as Ireland and Belgium, could be particularly vulnerable in this context. Being optimistic, one would expect industry to increase its investments, but this requires stimulation from the government in the first instance. Indeed, this chicken-and-egg phenomenon could lead to a need for governments to put their investment in R&D upfront if the necessary industry component is to be attracted. Related to this point is the fact that if the local situation is not conducive to industries that depend on a vibrant scientific environment—that is, those that will be needed for future knowledge-based economies—then these industries may not wait around for the government to imple-

Fig. 1 | Score-card for governments. The difference from the 1% goal of R&D expenditure by government and other sources expressed as a percentage of gross domestic product (GDP).

ment its plans. Some countries, most notably Sweden and Finland, are already at a high level of R&D expenditure, and used wisely, this will give them a further advantage over their neighbours. If this is so, then one could envisage an EU in which some countries perform well in the high-tech sector whereas others compete with emerging economies and developing countries elsewhere in the world for less lucrative jobs in manufacturing. It will also be interesting to see if the long-term economic benefit will be greater

in countries such as Finland, Sweden and Germany where industry investment is now relatively high.

Overall, these numbers convey a variety of messages for European governments. Some can be satisfied that they have reached the 3% goal with a 'correct' input from industry, and any further changes may lead to even more investment and consequently greater long-term benefits. Other member states, however, face a challenge of some magnitude and may need some

encouragement to spend more money on science. Some additional measures to support further spending on R&D have been suggested. One would be to exclude these investments from the criteria that are defined in the so-called Euro stability pact. This would, supporters hope, encourage governments to invest in the future at a time when it is most needed.

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