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animal research, then who becomes the guinea pig?'

Indeed, it is a significant responsibility for 'society' to make judgements such as these without first knowing all of the facts. And the prevailing fears of what the publication of the human genome actually holds for the future can only be addressed through informed discussions. In this regard, Israel is forging ahead and Izchak Parnas, Director of the Belmonte Science Centre for Youth at the Hebrew University of Jerusalem, described the success of his scheme to address the fear and lack of knowledge in the population. 'The best way is to start in schools. That way you are not being selective; it exposes science to the whole population.' He criticised the education system for the general lack of time and facilities in schools and for not keeping pace with science. 'The

knowledge exists with us, the universities, the research institutions and we have to bring this knowledge to the teachers,' he stressed. Belmonte trains teachers in performing advanced experiments and provides free access to their laboratories to around 160 pupils per day. 'It's a great opportunity to expose students to the spirit of science,' Parnas enthused.

Targeting students so that tomorrow's public is capable of making informed choices was a recurring theme and similar initiatives were presented by Eva-Maria Neher, Director of the 'X-lab' in Göttingen, Germany, and Wilbert Garvin, founder

science. Gauging people's attitudes before and after their visit, she said, 'We actually found an incredible shift from a one-dimensional way of thinking to realising science is something much more complex.'

And, of course, scientists as part of society have their role to play. '91% of scientists thought they had a responsibility to communicate the social and ethical implications of their research to a non-specialist audience. But less than 20% had held any talk or discussion in the last year,' Matterson said. So there appears to be confusion on both sides: the scientists

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member of the European Initiative for Biotechnology Education. Clare Matterson, Director of Medicine Science and History at the UK's Wellcome Trust, also described the many aspects of their 'Medicine in Society' programme to raise awareness and understanding of biomedical science. This is not a simple undertaking as they had found that 'The more people understood, the more questions, the more concerns they had.' Among their more creative ongoing initiatives are the establishment of many interactive centres around the UK to encourage people to think more about science, together with 'Theatre in Education' and 'Sci-Art' to reach the typical high-earner sceptics of

generally do not understand the public's fears and misconceptions, while the public generally do not understand what scientists are doing. There needs to be greater awareness and it is only through bringing the different factions together that the potential of the human genome will be realised. 'Society is not yet prepared for dealing with the new genetics, and therefore a new public dialogue must be established,' Poortman said.

*Susan R. Owens & Holger Breithaupt*

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## Fast tracking drugs to patients

Drug approval agencies are frequently criticised for either being too slow or too fast

**R**egulatory approval of drugs can be an obstacle course and is a process that frequently comes under fire for being too rapid or too lax. Critics often complain that pharmaceuticals are approved too slowly by a process that is too costly and byzantine, which has fatal effects for patients when life-saving anti-cancer and anti-HIV drugs are involved. The US Food and Drug Administration (FDA), the agency responsible for approving new

drugs, has reacted to long standing criticism by streamlining some of its guidelines and procedures, but the bioterrorism crisis in the USA has prompted further scrutiny of the whole drug approval system. The FDA's European counterpart, however, the European Agency for the Evaluation of Medicinal Products (EMA) in London, so far has largely resisted expediting its approval process. But it is unclear whether a faster and slimmed-

down approval process is indeed better for public health. Critics of more rapid approval point to 12 drugs in the past 4 years that were withdrawn from the US market due to serious side-effects and that were, they believe, approved too hastily.

The recent bioterrorism attacks with anthrax spores have again pushed this topic onto the front pages. With frightened Americans hoarding Cipro, the only anti-biotic approved by the FDA to treat

pulmonary anthrax, and Bayer, its German manufacturer, struggling to meet the increasing demand, many started calling on the FDA to quickly approve other

250 million doses of smallpox vaccine. And other efforts threaten to strangle the approval process unless more streamlining takes place: EluSys (Pine Brook, NJ)

human data because testing them by challenging patients with diseases such as inhalation anthrax, bubonic plague, and smallpox "is not feasible and cannot be ethically conducted", Qweder said.

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antibiotics to treat anthrax. Similarly, pharmaceutical and biotechnology companies, as well as the average citizen, are wondering whether the industry will be able to manufacture, and the FDA approve, enough smallpox vaccine for the entire country. An editorial in *The Wall Street Journal* (November 15, 2001), entitled 'A Wartime FDA', emphasized that the current exigencies of conducting a war on terrorism require the FDA to streamline the regulatory maze through which vaccine companies must pass to get their products reviewed and approved. 'In previous periods of great urgency—AIDS-related deaths in the 1980s and late-stage cancer patients in the 1990s—only intense public outcry caused the agency to modify its plodding process.'

The journal accuses the regulatory process of being outdated, using vaccine production as an example. As many manufacturers have switched to advanced cell culture techniques since the last smallpox vaccine was produced 20 years ago, the FDA plans to treat the products as 'new drug', with the trials and research that this entails. 'This time-frame is too long, as the average time for a new vaccine to run the FDA's regulatory maze can be six or seven years,' the editorial continued. While the FDA says that such a new vaccine is a 'priority' and that it will take a 'common sense approach', the agency has not elaborated on exactly what that means. 'Rather than viewing the smallpox vaccine as an exception, the FDA should see it as an opportunity to develop a new wartime regulatory model—one that can respond with lightning speed to any innovation in the war on terror,' the editorial urged.

In fact, both drug companies and the FDA are responding to the bioterrorism attacks. Since September 11, at least five drug companies have offered the government free antibiotics to combat anthrax, but some need approval for such a use before they can be prescribed. Three other companies are racing to produce

is working on a monoclonal antibody to give patients rapid immunity against *Escherichia coli*, anthrax or dengue fever. NanoBio (Ann Arbor, MI) has a compound that kills anthrax spores in a few hours and Cepheid (Sunnyvale, CA) is developing a system by which hospitals can rapidly identify infectious diseases. In all, there are approximately two dozen companies working to develop drugs and vaccines against bioweapons. But in addition to a streamlined approval process, these companies also need government financial incentives to aid their research, EluSys's CEO Stephen Sudovar testified to Congress last October.

Also in October, Secretary of Health and Human Services (HHS) Tommy

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## Critics on the opposing side point to drugs that were withdrawn from the market due to serious side-effects

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Thompson testified before Congress that the HHS, the parent agency of the FDA, has increased funding to develop anti-terrorism drugs and vaccines, but he has not stated how the already beleaguered agency plans to review the new drug applications. President George W. Bush has also asked Congress to give Thompson additional FDA funding and manpower in times of public health emergencies to surmount approval hurdles.

Another piece of good news is that the

For most other drugs that do not fall under this rule, the agency was able to reduce the average time required for drug review from 30 to 15 months after the Prescription Drug User Fee Act (PDUFA) was passed in the USA in 1992. The FDA added nearly 700 employees to CDER and CBER (biologics) and in so doing, increased its capability of reviewing more drugs in less time. 'Fast-Track designation, initiated by the FDA Modernization Act (FDMA) of 1997 [...] is designed to facilitate the development and expedite the review of new drugs that are intended to treat serious or life-threatening conditions and that demonstrate the potential to address unmet medical needs,' according to the CDER. 'Actually, Fast-Track designation means that companies can apply at any stage of development to expedite their drugs,' Qweder explained. Between 1998 and March 31, 2001 the FDA approved 10 fast-track designated products with a median response time of 55 days, according to CDER. Of these, eight are for HIV-AIDS and two for cancer.

On the other side of the Atlantic, the whole process is much slower. According to a study published in the *European Journal of Cancer* last year, European cancer patients waited longer than their American counterparts for cancer drugs to be reviewed and approved by the EMEA. 'This means that European cancer patients are deprived of potentially effective treatments which are available for use in other parts of the world,' Kathy Redmond, healthcare consultant and author of the study, said. This is exemplified by the approval times of Hoffmann-LaRoche's (Basel, Switzerland) anti-cancer drug, Gleevec—72 days in the USA compared

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FDA is likely to approve the 'Animal Rule' in the next few weeks to months, said Sandra Qweder, Acting Director of the Office of Review Management at the FDA's Center for Drug Evaluation and Research (CDER). 'This rule, proposed in 1999, would allow drugs and vaccines to be reviewed and approved without

with 8 months in Europe.

Redmond's study examined median EMEA approval times for cancer and anti-HIV drugs between January 1995 and March 2001, which were 471 and 342 days, respectively. 'The EMEA approves anti-HIV drugs faster than cancer drugs and is more likely to approve anti-HIV

drugs under exceptional circumstances,' Redmond said, primarily because the EMEA rarely uses its own fast-track design-

early on, that the EU may not view it as a breakthrough drug and hence not see it as a priority,' she added.

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nation for cancer drugs. In contrast, the FDA's median time for approval of all drugs was 12 months. 'Since 1995, only two of 26 cancer drugs were approved "under exceptional circumstances", whereas in 1999, five of 28 priority drug applications in the US were cancer drugs,' she added.

Some of the obstacles to faster EMEA review, in addition to the lack of staff, are due to conditions particular to Europe. Reviews are performed for 15 member nations in 11 languages and must be ratified by each state. Furthermore, there is not much interaction between the EMEA and the drug manufacturer. 'I believe companies in the US work more closely with the FDA than European nations, which generally have little interaction with its approval agency,' Redmond explained other reasons why the process takes longer in Europe. A company may learn at a late stage that the EMEA is not happy with its data, whereas this is unusual in the USA, she said. And once approved, each national government still must price the drug for market authorisation. Another reason for these discrepancies between the EU and USA is that cancer advocacy is not as mature in Europe, partly due to language barriers. 'The European Commission recognises these problems, and some legislative changes are being considered by the European Parliament for approval,' Redmond said. However, there is still a need to clarify within the EU which drugs can be prioritised. 'My worry is that because Herceptin, for example, was approved in the US

Such dissatisfaction may be an indication that 'the grass is always greener on the other side' because, according to a March 2000 study by the Tufts Center for the Study of Drug Development (Boston, MA), European approval of new biotech drugs overall outpaces US approval. 'Biotechnology product approvals in Europe take 417 days vs. 452 days in the USA for the same products,' the study said. But interestingly, it states that 16 of the 27 drugs that received EMEA approval between 1995 and 1999 were developed by US-based companies, 'where there are fewer legislative constraints'.

Not surprisingly, some critics of the FDA's fast-track system, such as Henry Miller of Stanford University's Hoover Institution, believe that fast-track is not fast enough. "'Underhaul" might be a better word for the purported overhaul they refer to: the aftermath of the misnamed FDA Modernization Act of

gent, standards are excessively high and it ultimately harms consumers. 'The FDA is more adversely affected by approving harmful drugs than by denying approval of beneficial drugs,' he wrote in *Cato Regulation*. One example of this may be the anti-diabetic compound Rezulin, which was approved after a 6-month fast-track review. The drug was withdrawn following the FDA attribution of 63 liver-failure deaths to it. Yet the drug remained on the US market for more than 2 years after the UK had withdrawn it for the same reason.

But speeding up the drug approval process, whether in the USA or in Europe, is largely a red herring; the overall process is 'excruciatingly long and wildly expensive—and both its length and expensiveness have been increasing,' Miller wrote. A new study from the Tufts University's Center for the Study of Drug Development, released in November 2000, shows that the average cost of developing a new drug has nearly quadrupled since 1987—from \$237 million to \$802 million. If the cost had simply risen to match inflation, it would have been only \$318 million in 2000. Most of the increase is related to the rising costs of clinical trials, the study stated. More importantly, the time from laboratory to pharmacy shelf has also increased. 'On

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1997. The act has proved a monumental disappointment,' he wrote a year later in the American Council on Science and Health newsletter. Miller calls the FDA's reporting of median rather than average approval-process times 'statistical legerdemain'.

Michael Ward, staff economist at the US Federal Trade Commission, disagrees, stating that the drug approval process is over-regulated. The process is too strin-

average, drug-development—the time between the synthesis of the molecule and marketing approval—is approximately 14.8 years, more than twice it was in 1964,' Miller wrote. For most cancer patients, 14 years is certainly too long to wait for a new drug.

*Vicki Brower*

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