

Further snag with Stanford patent

Filing error claimed in Cohen-Boyer

Washington

The second Cohen-Boyer patent covering basic processes in genetic engineering may have suffered another setback last week when attorneys for the applicants admitted that there is a serious error in the patent specifications.

The error was one of several potential flaws cited by the US Patent and Trademark Office when, in August, it suddenly reversed its previous decision and decided to reject the patent (see *Nature* 12 August, p.595). Responding just one day before a deadline of 2 November, Stanford University and the University of California concede the error, but argue that the patent is nonetheless valid.

Their response, however, may raise more questions than it answers. Attorney Bertram Rowland, representing the universities, does not explain why he failed to inform the patent office of the error, which, he admits, "was known to the applicants' attorney as early as December 1977". And the two lines of defence he introduces in support of the patent's validity may well be disputed.

Rowland argues that despite the error, the patent office should withdraw its

objections and grant the patent, and he offers two lines of defence for that argument. The first is that even "if applicants had not actually performed any of the experiments described in the experimental section . . . the specification would be enabling (sufficient to allow duplication and thus be patentable), since it teaches how to obtain and clone a functional plasmid containing foreign DNA". In other words, pSC101 is not itself vital, as the instructions provided in the patent explain how to select, isolate and use other suitable plasmids. "Testimonials" from molecular biologists Donald Helinski, Stanley Falkow and Bernard Weisblum are included to buttress the claim that anyone with "ordinary skill" in the field could, since 4 November 1974, have used the patent to prepare a functional plasmid — even without the benefit of a correct recipe for pSC101.

Yet in a submission to the patent office on 24 June 1977, Rowland seemed to take the opposite view — that pSC101 was indeed vital to the patent claims, and that this "new plasmid found by the inventors" was what distinguished their claims from potentially competing work by others.

The second line of defence offered by Rowland is that even if pSC101 is the key, the patent does not need to disclose how to make it since pSC101 was publicly

available at the filing date. A declaration by Cohen, included in the response, states that he made the plasmid available to scientists, subject to two restrictions: "that it would not be passed on; that it should not be used in experiments believed at the time to have the potential to be dangerous". Cohen asserts that "no-one who requested pSC101 was denied pSC101" and that it was thus "widely available".

One patent attorney familiar with the case said that Cohen's restrictions on distribution of the plasmid may defeat this defence; to be safe, he should have deposited the plasmid in a recognized public repository such as the American Type Culture Collection before filing. This was not done until 25 June 1981, six months after the first patent was granted.

Rowland's admission of the error in the second patent application raises a potentially explosive question: should the first patent, which contains the same flaw, be reissued to correct it? Given the problems with the second patent, this is something Stanford would like to avoid. In an interview last week, Rowland tried to avoid the issue, saying, "Given that 99 per cent or more of the people in the field are aware of the situation [the error in the pSC101 recipe], whether I should have to go to the expense of filing for reissuance is an open question". He added, "I don't

UK research councils' budget break

British research councils were told this week how much money they will get next year, but not which council is getting what — surely a formula for a scrap until the detailed allocations are announced in a few weeks' time.

According to Sir Keith Joseph, UK Secretary of State for Education and Science, who made a statement to the House of Commons on Monday, the total to be made available is £509.7 million, a shade above the £507 million requested by the Advisory Board for the Research Councils (ABRC) a few weeks ago (see *Nature* 4 November, p.7) However, the new figure includes a Falklands factor — an extra £4 million for the British Antarctic Survey (BAS), in line with policy announced after the Falklands conflict to increase research in the Antarctic. BAS is a component institute of the Natural Environment Research Council (NERC). NERC would welcome the sum as a gift, a spokesman said this week, but would be worried if it were to be subtracted from its planned budget for other science, or from that of other research councils.

Another unresolved issue is the position of the Agricultural Research Council, which has protested against ABRC's recommendation to hold its budget constant in cash terms for the next three

years at £46 million.

As for the Social Science Research Council, "a small portion" of the £6 million cut threatened recently by Sir Keith Joseph will fall this year, with more to come in the next two years. It will contribute to a £14 million fund to provide "the first instalment of a programme for new technologies, including the recruitment of young researchers". Of this, £4 million will go to establish courses in information technology in technical colleges and polytechnics. The remaining £10 million is for new blood as well as for the provision of courses in new technologies "primarily to improve the supply of manpower in information technology". Moreover, part of the sum will be allocated not by the University Grants Committee and the universities, but by the research councils, said Sir Keith. So it is impossible to determine exactly how many jobs this £10 million will make available. A separate announcement will give details.

As for the universities themselves, they will enjoy a small increase in their grant for the present academic year (1982-83) from £1,137 million to £1,150 million, and the recurrent grant for 1983-84 will be set at £1,213 million. These figures are fixed in cash terms, and assume a salary increase of only 3.5 per cent.

Robert Walgate

Rowland's concession concerns an article published in November 1977 by co-inventor Stanley Cohen and a co-worker (Cohen, S.N. & Chang, A.C.Y. *J. Bact.* 132, 734; 1977) which contradicts the recipe set out in the patent for making pSC101, the key plasmid used for inserting foreign DNA into *Escherichia coli*. "pSC101 could not be prepared in accordance with the working example", Rowland writes.

The *Journal of Bacteriology* article came to the attention of the patent office only this summer, apparently through an article by an Exxon patent attorney, Albert Halluin. In several footnotes to a chapter he contributed to *The Patenting of Life Forms*, a book published in August by Cold Spring Harbor Laboratory, Halluin cites that article and other potential flaws in the patent. Rowland, after admitting that he knew of the existence of Cohen's article five years ago, writes that "I have no recollection as to why it was not brought to the Examiner's attention in the written record". The patent application was filed on 4 November 1974; it was later split into two parts, and the first patent was granted on 2 December 1980.

know any law that says I have to'.

One old question that has resurfaced in the latest exchange between Stanford and the patent office, and that may bear on the first patent, is whether Cohen and Boyer are the sole inventors, as Stanford and the University of California claim. In its notice of rejection on 2 August, the patent office cites a statement by Dr Robert Helling — a co-author of the 1973 paper in the *Proceedings of the National Academy of Sciences* that is the basis of the patents that appeared in a news story in the 3 April 1980 issue of *Nature* (p.388). Helling, now at the University of Michigan, is quoted as refusing to sign a disclaimer of inventorship as requested by Rowland.

Helling has not, however, pressed any claims to date. And Rowland, in his response to the patent office, asserts that Cohen and Boyer are the sole inventors, having conceived the idea at "a now famous delicatessen in Hawaii" during a scientific meeting in November 1972. This, Rowland writes, rebuts "any implication that the refusal to sign a disclaimer might be equated with an allegation of co-inventorship".

But Helling told me last week "I certainly am a co-inventor. The three of us were equal partners. I went out there to

develop new cloning procedures; Herb (Boyer) was the one who suggested using plasmids, and asked me if Stan (Cohen) could join us". Helling worked with Boyer at the University of California at San Francisco during his 1972-73 sabbatical.

Helling has been discussing the matter with the University of Michigan's attorney and said "we may do something now", but declined to give any details. A call to the attorney was not returned.

Although a recent court decision overturns the patent office's policy of considering co-authorship *prima facie* evidence of co-inventorship, Helling's statement in the 1980 *Nature* story complicates the matter.

Rene Tegtmeyer, the assistant commissioner for patents, said his office will act "promptly" on the case, perhaps reaching a decision within "two or four weeks". If the patent office stands by its rejection on 2 August, Stanford will then have three months to file a request for reconsideration or a notice of appeal to the Patent Office Board of Appeals. A decision might not be reached before the summer of 1984 — and the case could go on still longer if the board's decision were to be referred to the Court of Appeals for the Federal Circuit. **Stephen Budiansky**

Science and Engineering Research Council

Big money for big science?

A potentially important difference of emphasis between the British Science and Engineering Research Council (SERC) and the Advisory Board for the Research Councils (ABRC) was apparent at the publication of the research council's report (HMSO, £4) last week. For while the advisory board said in its advice to the Secretary of State for Education and Science that the time had come to halt the retreat from Big Science (see *Nature* 4 November, p.1) SERC chairman Professor John Kingsman refers to "broadening out from the support of 'big science' to a better

spread of science and engineering". Kingsman says that the advisory board's recommendation would be only one element in the council's decision how best to spend its money next year.

SERC's principal area of concern is the dual-support system through which funds for science research are provided jointly through the University Grants Committee (UGC) and the research councils. The SERC report says little about how far SERC is prepared to go to compensate for the dwindling UGC contribution, but also claims that "the quantity and quality of

research grant applications are being maintained".

Professor I. Butterworth, chairman of SERC's Nuclear Physics Board, is more pointed, saying that the board wants SERC to provide a certain number of permanent posts in nuclear physics attached to universities until UGC is once again able to play its part.

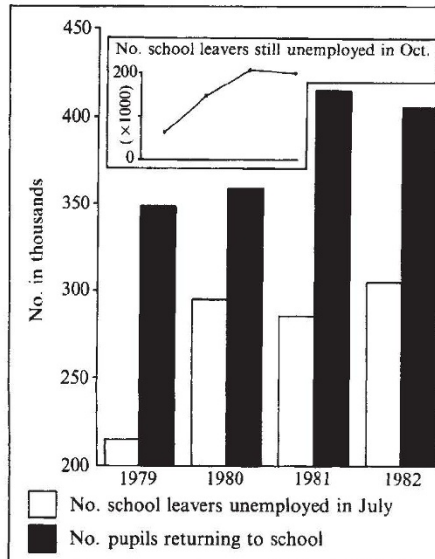
Since 1978, the proportion of support for nuclear physics within SERC's overall budget has dropped from more than 30 per cent to about 20 per cent. The intended opening at Daresbury of the Nuclear Structure Facility (a heavy-ion accelerator) after an extended delay will provide some stimulus but, according to Professor Butterworth, its full utilization will be delayed. There is also a fear that if full support is given to LEP, the electron-positron collider at CERN in Geneva, it may not be possible to fund other particle physics experiments.

To judge from the report, physicists are also concerned that support for such fields as atomic spectroscopy, semiconductor research, superfluidity and superconductivity appeared to be decreasing relative to such fields as biology, chemistry and applied mathematics. Apparently a special committee has been considering criteria to be used in deciding the relative balance of support between different fields, but its conclusions have not been made public. And there is a possibility that the Synchrotron Radiation Source at Daresbury, from which X-ray spectroscopists have derived particular benefit, may be affected by rising costs, which may make necessary a choice by the Science Board between research grants on the one hand and further development and general support of central facilities on the other.

Support for information technology and space science, both recommended by the Advisory Board for the Research Councils, are, however, both booming at SERC. The two fields are beginning to link up, with the recent development of remote control of telescopes via satellite links between the Royal Greenwich Observatory and telescopes in Hawaii. Such developments might pay for themselves in reduced travel budgets for astronomers.

On the more contentious issue of the use of the South African Observatory (see *Nature* 23 September, p.291), the council says it is not in the business of taking political decisions at the expense of the interests of science and that, moreover, it had felt little pressure from the community and none from the government to sever its links with its South African equivalent.

The press conference called by SERC was made all the more bland by the decision not to make the report available in advance. Thus SERC, proud of its autonomy, has followed a government directive resulting from the premature publication in the national press of details of medals awarded for the Falklands fighting. **Philip Campbell**



As the probability of long-term unemployment for the British school leaver has increased (reflected in the October unemployment figures), the number of pupils returning for further education has gone up. There has been no increase in resources made available to schools and extra pupils are being swallowed up by existing classes. However, fears that this would lower the standard at GCE 'O' and 'A' level are not borne out by statistics published by the examining boards, which show no real change in the pass rate during this period. The decline in numbers returning to school in 1982 is at least partly due to the rapid expansion of the Youth Opportunities Programme during 1981-82 from 360,000 to 553,000. **Melanie Kee**