Wellcome sets sequencing project in motion

London. Britain's Wellcome Trust has become the first funding agency on either side of the Atlantic to commit firm support for a plan to produce a full-length 'low-pass' sequence of the complete human genome by the year 2002.

As government funding agencies in the United States and the United Kingdom struggle to find the money they hope to raise for such a project, Wellcome announced last week that it had agreed to provide sufficient financial support to the Sanger Centre, at Hinxton Hall near Cambridge, to sequence one-sixth of the genome.

No precise figure has been given. But in a statement, Wellcome says that the money should be sufficient to enable the Sanger Centre to identify at least 500 million of the 3 billion base-pairs in the genome at an eventual estimated cost of less than £0.10 a base pair, giving a minimum figure of £50 million (US$80 million).

Wellcome is by far the largest biomedical charity in Britain, with a £200-million annual budget close to that of the Medical Research Council (MRC), and the money will be additional to funds originally committed to setting up the centre — named after Frederick Sanger, who has twice won the Nobel prize for chemistry — jointly with the MRC.

The total plan aims to cover about 95 per cent of the complete genome sequence with an accuracy of more than 99.9 per cent. It was hatched last year by John Sulston, head of the Sanger Centre, and Bob Waterston, of Washington University in St Louis, Missouri, with whom Sulston has worked on the sequencing — now nearing completion — of the genome of the nematode worm *Caenorhabditis elegans*.

After some initial scepticism, a consensus appears to have emerged among molecular biologists that recent mapping achievements — as well as indications that no major advances in sequencing technology can be expected in the near future — suggest that the time has come for an attack on the complete human genome.

Sulston says he is keen that the project should be truly international, with strategy determined by the participating groups rather than by their funding agencies. "This is not a race; we are open to any type of cooperation [with other laboratories] or splitting up of the genome," he says.

Reflecting this approach, Sulston and Waterston felt the optimal division of labour was for one-third of the sequence to be determined by the Sanger Centre, one-third perhaps in Waterston's laboratory, and one-third by other participating laboratories.

Interested US laboratories are now awaiting the result of reviews of more than 20 applications received in response to a request for proposals sent out earlier this year by the National Center for Human Genome Research (NCHGR) of the National Institutes of Health (NIH).

Final decisions are expected early next year. But there is still some uncertainty about how much money will be available. Although additional funds for mega-sequencing projects have been sought by the Clinton administration in its NIH budget request for the fiscal year which started on 1 October — and have been given priority by Congress during lengthy budget negotiations — final details have yet to be agreed.

NCHGR officials say they are optimistic that the money will be found one way or another. Indeed, they claim that enough progress has been made on mapping projects to make possible the reallocation of sufficient funding within its $114-million annual budget to meet the sequencing requests, even if no new budget figure is agreed and the NIH remains funded on the basis of a continuing resolution.

In Britain, there is similar uncertainty over the money promised, at least informally, by the MRC. Earlier this year, in releasing the science budget for the financial year 1995–96, the government announced that this would include a special item of £9.6 million for genome research and immunology. But beyond a commitment of £2 million to complete the *C. elegans* work, no announcement has yet been made of what type of long-term commitment the MRC may make to human genome sequencing.

The Wellcome Trust hopes that last week's announcement, which it says will allow the Sanger Centre to "spearhead" the international sequencing programme, will help to catalyse efforts elsewhere, and is keen that the resulting sequence should be in the public domain.

According to Sulston, the precise division of labour will be determined by the interests of the laboratories that eventually agree — and are funded — to participate, but is likely to be based on different institutions taking responsibility for different chromosomes.

Sulston says that Wellcome is planning to organize a meeting next year of the major laboratories involved in the area to discuss questions of strategy. "We want to share the leadership," he says. **David Dickson**

Genetic testing 'needs more checks'

San Francisco. US academic and commercial laboratories are rushing to offer genetic testing with a minimum of external review, according to a new survey that reinforces concern among geneticists about the quality of laboratory testing in the United States, as well as the interpretation of results.

The results of the survey led to demands from scientists at the annual meeting of the American Society of Human Geneticists in Minneapolis, Minnesota, last week for a system to evaluate the accuracy and interpretation of tests, as well as turn-around times.

One academic geneticist cited a commercial laboratory that had taken a year to provide test results — and even then had missed two mutations that she had already identified. Others claimed that federal regulations on laboratory quality fail to address the specific technology involved in genetic testing. Furthermore, institutional review boards, which tend to be responsible for evaluating the quality of tests offered as part of a research project, may not have any background in genetics.

Rebecca Anderson, chair of the genetic services committee of the National Society of Genetic Counsellors, said she has great confidence in most laboratories, but would like to see proficiency tests in place. More difficult, she said, may be problems of interpretation of the tests, especially by primary care physicians.

Other geneticists warned of a particular danger in the tendency to use information about high-risk families to make predictions about the general population. Launching population screening for diseases such as cancer or Alzheimer's without more quantitative data about the prevalence of certain mutations would produce only "garbage" information. "It doesn't mean we stop. We just have to be very careful," said Michael Watson, a medical geneticist at Washington University School of Medicine in St Louis, Missouri, and head of the laboratory practices committee for the American College of Medical Genetics.

Another specific concern is the use of genetic tests on children. In general, geneticists have agreed not to carry out such tests on minors unless they are likely to benefit directly. But a group of researchers led by Dorothy Wertz at the Shriver Center in Massachusetts surveyed 186 laboratories listed in Helix, a national directory of DNA diagnostic laboratories, and found a high proportion that tested healthy children.

Results of a survey of academic and commercial laboratories that are developing or offering genetic tests on an experimental basis were presented by Neil Holtzman of Johns Hopkins Medical Institutions in Baltimore, Maryland. The study is intended to inform the work of the Task Force on Genetic Testing for the Human Genome Project, which is developing guidelines for the scientific validation of genetic tests, the assurance of laboratory quality and general education and counselling.

Out of 54 biotechnology companies in the survey that said they were developing genet-