Human Genome Project aims to finish 'working draft' next year

[WASHINGTON] For the second time in six months, leaders of the Human Genome Project have brought forward significantly a key deadline for sequencing the three billion bases of the human genetic code.

The National Human Genome Research Institute (NHGRI) announced on Monday (15 March) that scientists in the international sequencing effort are now aiming to complete a 'working draft' by spring next year — 18 months earlier than predicted in a five-year strategic plan released last autumn (see *Nature* **395,** 207; 1998). The working draft will cover at least 90 per cent of the genome, says the institute.

The NHGRI and its British collaborator, the Wellcome Trust, also announced the completion of the genome project's three-year 'pilot' phase and the launch of the full-scale effort to finish sequencing the genome. To this end, they awarded $81.6 million to three academic sequencing centres in the United States, and the Wellcome Trust announced that it is boosting funding of the Sanger Centre in Cambridge, England, by $77 million over the next 12 months (see box).

The three US sequencing centres funded by NHGRI are at the Whitehead/Massachusetts Institute of Technology Center for Genome Research in Cambridge, Massachusetts; the Washington University School of Medicine in St Louis, Missouri; and Baylor College of Medicine in Houston, Texas.

These three centres are expected to produce about 60 per cent of the working draft, with the Sanger Centre producing about 33 per cent. The Joint Genome Institute of the US Department of Energy at Walnut Creek, California, will be responsible for the rest.

The project's leaders said that the efficiency and accuracy of sequencing achieved in the last year of the pilot phase allowed them confidently to bring forward the deadline for completion of the working draft. Meeting the goal will require a 2.5-fold increase in the current rate of sequence production, to 2.5 gigabases per year.

"This is not a blue sky, 'gee we hope we can do it' kind of massive increase in [sequence production]," says Francis Collins, NHGRI director, adding that the new timetable is "eminently doable".

The emphasis on the working draft flows from a hunger among researchers for useful sequence as quickly as they can get it. "It has become clear that the best service to the scientific community is to deliver the draft sequence rapidly, and then to circle back and perform in the course of another year-and-a-half at most the finishing on that sequence,"

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Wellcome boost: the UK Sanger Centre (above) will receive $77m more for its sequencing work.

says Eric Lander, the director of the Whitehead/MIT Center.

"In that way the vast majority of the data will become available rapidly. And by the time that the scientific community needs the precise finished product, it will be ready."

The government-funded researchers deny that the launch of a private effort to sequence the genome by Celera Genomics of Rockville, Maryland, had any influence on their timetable (see *Nature* **393,** 101; 1998). "I would not want people to see this move as reactive to what's going on in the private sector at all," says Collins. "It's part of the plan. It has always been."

Others are less sure. Huntington Willard, chairman of the Department of Genetics at Case Western Reserve University in Cleveland, Ohio, suggests that it might be "kinder to state that the Celera announcement of a year ago woke up NHGRI to what could be done if the resources were made available".

Cross-checking by the centres on each others' work has shown that sequencers are meeting an international accuracy standard of no more than one error in 10,000 bases, with the largest centres achieving rates of fewer than one error in 100,000 bases. Costs have also been cut from $2 per base pair three years ago to an average of 20 to 30 cents per base.

The centres have also shown a better than expected ability to increase their sequencing capacity using economies of scale. The Whitehead Centre, for instance, has increased sequence production 12-fold in the past year without any extra money.

Surmounting one technical hurdle at the end of last year was particularly helpful in allowing the sequencers to advance their timetable. A bottleneck in providing mapped clones to sequencing machines was removed by the fingerprinting of entire libraries of bacterial artificial chromosomes at Washington University.

This will allow the assembly of the whole genome in 400–500 kilobase contiguous stretches, or 'contigs', by June this year, drastically reducing the labour involved in preparing mapped clones for the machines.

Several other sequencing centres involved in the pilot project but not funded in this week's awards may receive funding in another round of awards that NHGRI will announce in May. **Meredith Wadman**

Britain sought to speed-up sequencing efforts

[LONDON] Britain's Wellcome Trust has for some time been urging US funding agencies to bring forward the genome sequencing target date, according to John Sulston, director of the Sanger Centre. The trust has just announced a major increase in funding for the centre's sequencing efforts (see above).

Sulston says that the trust's desire for speed is principally based on concern to meet the desires of researchers and the needs of medical research. He adds that the capability of completing a draft of the genome before schedule has existed for some time, but that US agencies have been keen to proceed with caution.

He denies that the new deadline reflects a desire to beat the 2001 target set by a parallel private-sector initiative to sequence the genome, headed by Craig Venter of Celera Genomics. "The scientific community want this data immediately, and we aim to give it to them," he says.

Sulston acknowledges that the Celera deadline has contributed to "raising the temperature" in the race to obtain a complete sequence.

But he says that, ultimately, medical research has most to gain from the US/UK initiative, which is committed to releasing sequencing data as fast as possible into the public domain, rather than from Celera, whose position on patenting of gene sequences remains unclear.

Michael Morgan, chief executive of the Wellcome Trust's genome campus, says that Celera can still join the US/UK effort. "It would be of huge benefit if they do, as we'd get the job done that much quicker." **Ehsan Masood**