

California runs stem-cell risk

Hollywood-fuelled enthusiasm – and blue-state contrariness – moved California voters last year to authorise a US\$3 billion handout for the funding of stem-cell research. Unfortunately, it appears that nobody stopped to think through the IP consequences. As a result, the project could now be at risk

In the November general election, Californians thumbed their noses at Bush administration bioethics policies and voted to establish a new state agency to fund human embryonic stem-cell research. Fearing that their states' best researchers would leave to chase the California gold, Connecticut, Illinois, New Jersey, New York and Massachusetts are launching their own stem-cell projects and may well follow California into this costly and uncharted territory.

Stem-cell research had been stalled in the US in the wake of President George Bush's ban on the use of federal funds for studies involving any new cell lines created after 2001. Bush, a pro-life supporter, based his ban on the fact that human embryos have to be destroyed in order to create cell lines.

But scientists claim that these cells hold such a rich potential for human health that further research must continue. They say the ability of stem cells to grow into virtually any kind of bodily tissue could bring replacement parts for diseased hearts and other organs, and the regeneration of damaged spinal cords.

The Bush announcement caused great dismay, with some leading researchers even leaving the country in protest. The University of California lost Roger Pederson, who decamped for Cambridge University in the UK, where he now heads the Centre for Stem-Cell Biology and Medicine.

A potent combination of Hollywood stars, disease-

advocacy groups, labour organisations, the state's medical and academic scientific establishment, and a coalition of biotech business groups persuaded California voters that funding further stem-cell research was a good thing. Silicon Valley real estate developer Robert Klein, a parent whose child has juvenile diabetes, led the effort.

The showbiz angle weighed heavily at election time. Popular actors Michael J Fox and Christopher Reeve urged passage of the bond issue's authorising legislation, Proposition 71. Reeve and Fox enjoyed a special credibility because both suffered from conditions stem-cell research promises to cure. And Reeve's death – related to his spinal-cord injury – right before the November election brought in a sympathy vote that contributed to Proposition 71's 59% pass rate.

The vote authorised the US\$3 billion bond issue, which established and funds a new state agency, to be known as the California Institute for Regenerative Medicine. The institute is to give out US\$300 million per year to stem-cell researchers for the next decade.

Initiative backers promised voters more than cures for the dread conditions that afflicted Reeves and Fox. They also predicted a rich return on the state's investment in the form of patents and licensing revenues derived from the research. A report posted on the pro-Proposition 71 website forecast:

"Royalty revenues of from \$537 million to \$1.1 billion."

The Wisconsin block

However, four months after the campaign, it seems those numbers actually reflect a great deal of optimism and considerable wishful thinking. Robust patents, which appear to cover just about any and all work involving human embryonic stem cells, are in the hands of the Wisconsin Alumni Research Foundation (WARF), the University of Wisconsin's technology transfer agency.

It was at the University of Wisconsin that biologist James Thompson first isolated human embryonic stem cells, with much of his research funded by a California biotech company, Geron Corporation of Menlo Park. Geron has exclusive licences to some of the key Wisconsin stem-cells lines. And last year Geron was issued a patent for a method of stem-cell propagation that will permit commercial-scale production of therapeutic stem cells.

The Geron patent is important because it enables researchers to avoid the use of animal-based media to grow the cell lines. All presently existing embryonic cell lines have had contact with animal media and thus have the potential to bring animal diseases to humans.

Wisconsin has agreed to make its technology available to scientists engaged in non-commercial research. And so has Geron. But the meter starts running the minute anyone develops a viable therapeutic product derived from human embryonic stem cells.

Both Geron and Wisconsin officials say they will seek licensing revenues from any commercial venture. This means that regardless of how much money the state has handed to researchers, California will have to stand in line behind Geron and Wisconsin to receive a royalty return on the state's investment. And barring unprecedented rapid breakthrough

discoveries, other states' projects will be even further down the line from California.

It is true that the strength of the Wisconsin and Geron patents has not been tested through litigation. In fact, very few members of the IP bar in the US have even read the patents through, given that human embryonic stem-cell research is still a relatively rare phenomenon. Until now, there has been so little research in this area that most clients had no need or desire to pay lawyers to review the patents. So it remains to be seen how far Geron and Wisconsin's patents reach. Still, the simple fact of those patents' existence should have given pause to even Proposition 71's most enthusiastic boosters.

No IP expertise

But, surprisingly, thinking through the IP consequences of what they were advocating does not seem to have exercised Proposition 71's backers too greatly. They used two Northern California political law firms to draft the initiative but it is believed that no IP lawyer ever vetted the measure. This was despite the fact that the language of the initiative mentioned intellectual property eight times, patents nine times, royalties six times and licensing twice. Any biotech lawyer with patent expertise could have warned the drafters of the minefield laid by careless use of IP language.

Additionally, although the initiative mandated a number of specific constituencies to be included on the Institute's 29-member Independent Citizens Oversight Committee, intellectual property experts were left out in the cold. The Committee, which is headed up by Robert Klein, has now been formed and it includes, as the initiative required, representatives of various campuses of the University of California system and nationally ranked medical schools and

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research centres within the state. Commercial biotech companies with expertise in life sciences and representatives from certain disease-advocacy groups are also represented. But patent lawyers or other members of the California bar with IP expertise are conspicuous by their absence.

Apparently, there is no way for the state to exert much control over the Institute's activities, even though huge amounts of state money are involved. The drafters bullet proofed the initiative with language that bars any legislative oversight or tinkering for three years. Many committee activities, including those of the working group that is to draft IP policy and licensing agreements, were exempted from the state's open-

meeting laws. Additionally, instead of spelling out just how patent and licensing revenues are to return to the state, the initiative merely says that the Institute must balance the possibilities of revenues against "the need to assure that essential medical research is not unreasonably hindered by intellectual property agreements".

Second thoughts

The buyer's remorse of one California legislator, who was an early and enthusiastic backer of the initiative, provides a cautionary tale. Before the election, State Senator Deborah Ortiz campaigned vigorously for Proposition 71's approval. But afterwards, she introduced legislation to give the state more oversight into the Committee's activities and to guarantee

California a return on its US\$3 billion investment. Given the strength of the initiative's language, it is doubtful that her legislation has much legal weight. But the hearings Ortiz is holding in connection with the proposed legislation are at least bringing her concerns to the public.

And despite the fact that the Institute was supposed to start issuing grants in its first year of existence, it does not look like cheques will be written any time soon. Two lawsuits and one petition under California's Administrative Procedure Act have been filed, seeking greater transparency and control of the Institute's activities. Courts have been asked to review the suits on an expedited basis, but delay seems inevitable.

At present, the California

Institute for Regenerative Medicine bears a frightening resemblance to the Bay Bridge, which connects San Francisco to Berkeley, Oakland and the rest of the East Bay. Badly damaged in the 1989 Loma Prieta earthquake, the bridge has yet to be replaced, even though plans were approved and contracts were signed years ago. The rebuild is stalled because of concerns about fiscal mismanagement by the state agency that oversees road construction. Every day drivers who cross the old bridge can look out their windows and see a row of moored construction cranes, waiting for the go-ahead order so work on the new Bay crossing can get under way. And until concerns about the stem-cell project are cleared up, that too looks like a bridge to nowhere.