FOR THE RECORD

No restrictions for synthetic biology in United States

There's no need to constrain the embryonic field of synthetic biology as there is no evidence that creating biological systems or organisms from inorganic chemicals poses any form of environmental or health risk, according to the United States Presidential Commission for the Study of Bioethical Issues.

"The technical feat of synthesizing a genome from its chemical parts so that it becomes self-replicating when inserted into a bacterial cell of another species, while a significant accomplishment, does not represent the creation of life from inorganic chemicals alone," states the commission, which was asked to review the ethics of synthetic biology in the wake of the May 2010 announcement that researchers at the nonprofit J. Craig Venter Institute in Rockville, Maryland, and San Diego, California, had created the world's first self-replicating, synthetic bacterial cell (www.jcvi.org/cms/press/press-releases/full-text/article/first-self-replicating-synthetic-bacterial-cell-constructed-by-j-craig-venter-institute-researcher/).

"It is an indisputable fact that the human-made genome was inserted into an already living cell. The genome that was synthesized was also a variant of the genome of an already existing species. The feat therefore does not constitute the creation of life, the likelihood of which still remains remote for the foreseeable future. What remains realistic is the expectation that over time research in synthetic biology may lead to new products for clean energy, pollution control, and more affordable agricultural products, vaccines, and other medicines," the commission adds in its report, *New Directions: The Ethics of Synthetic Biology and Emerging Technologies* (www.bioethics.gov/documents/synthetic-biology/PCSBI-Synthetic-Biology-Report-12.16.10.pdf).

Moreover, containment measures could be introduced to prevent any potential risk posed by synthetic organisms, the report states. "For example, 'suicide genes' or other types of self-destruction triggers could be considered in order to place a limit on their life spans. Alternatively, engineered organisms could be made to depend on nutritional components absent outside the laboratory, such as novel amino acids, and thereby controlled in the event of release."

Shutting down synthetic biology research for fear of unanticipated consequences would be irresponsible, the commission argues. "The Commission endorses neither a moratorium on synthetic biology until all risks are identified and mitigated, nor unfettered freedom for scientific exploration. Instead, the Commission believes that the field of synthetic biology can proceed responsibly by embracing a middle ground — an ongoing process of prudent vigilance that carefully monitors, identifies, and mitigates potential and realized harms over time. Responsible stewardship requires clarity, coordination, and accountability across the government. While new agencies, offices, or authorities are not necessary at this time, the Executive Office of the President should lead an interagency process to identify and clarify, if needed, existing oversight authorities and ensure that the government is informed on an ongoing basis about developments, risks, and opportunities as this field grows. This process must be undertaken by an office with sufficient authority to bring together all parts of the government with a stake in synthetic biology and be sufficiently authoritative to effectively engage or oversee engagement with foreign governments."

To that end, the commission recommends that existing federal departments and agencies develop some form of coordinating mechanisms or nonlegislative body to "leverage existing resources by providing ongoing and coordinated review of developments in synthetic biology; ensure that regulatory requirements are consistent and non-contradictory; and periodically and on a timely basis inform the public of its findings."

And given the rapidly-evolving nature of the field, the commission recommends that the US government, and particularly the Federal Bureau of Investigation and the Department of Homeland Security, should "continue to assess the specific security and safety risks of synthetic biology research activities in both institutional and non-institutional settings including, but not limited to, the 'do-it-yourself' community." — Wayne Kondro, *CMAJ*

WHO urges action on antimalarial drug resistance

The world risks losing its most effective treatment for malaria and a decade's advances in controlling the disease, unless swift action is taken to prevent the development and spread of drug-resistant parasites, warns a World Health Organization (WHO) plan released Jan. 12.

More judicious use of artemisinin-based combination therapies (ACTs) — the most potent weapon in the antimalarial arsenal — and increased surveillance for drug resistance are among immediate actions urged in the five-step *Global Plan for Artemisinin Resistance Containment* (www.who.int/malaria/publications/atoz/artemisinin_resistance_containment_2011.pdf). Although ACTs are currently more than 90% effective at treating even the most deadly forms of malaria, resistance to the therapies has already emerged in areas on the Cambodia–Thailand border

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(www.cmaj.ca/cgi/doi/10.1503/cmaj.109-3754).

"The new plan takes advantage of an unprecedented opportunity in the history of malaria control: to stop the emergence of drug resistance at its source and prevent further international spread," said WHO Director-General Dr. Margaret Chan, in a news release (www.who.int/mediacentre/news/releases/2011/malaria_therapies_20110112/en/index.html).

Because unnecessary use of ACTs to treat fevers other than malaria can increase the risk of resistance, the plan recommends diagnostic testing of all suspected malaria cases prior to treatment.

It also calls upon nations to bolster monitoring and surveillance for drug resistance. According to 2010 estimates, only 31 of the 75 countries that should be routinely testing the efficacy of ACTs actually do so.

Moreover, research is needed to develop more rapid techniques for detecting drug-resistant parasites, in addition to new classes of antimalarial medicines.

Until new treatments become available to replace ACTs, the plan recommends a boost in funding to malaria control programs in and around areas where there is evidence of resistant parasites. The plan estimates containment efforts will cost programs up to US$20 more per person in areas of confirmed resistance along the Cambodia–Thailand border, and up to US$10 more per person in at-risk areas in the Great Mekong region.

As a final step, the plan calls for global, national and regional coordination in these efforts.

"We have made tremendous progress over the past decade in the fight against malaria," WHO Global Malaria Programme Director Dr. Robert Newman said in the release. "If we are to sustain these gains … then it is essential that we work together."

The number of malaria cases has dropped by 50% in 43 countries since 2000, according to WHO estimates (www.cmaj.ca/cgi/doi/10.1503/cmaj.109-3765). That accounts for some 730 000 lives saved; nearly three quarters of them since 2006, when the use of ACTs became more widespread. — Lauren Vogel, *CMAJ*

Flu treatment guidelines updated

With the pandemic (H1N1) 2009 virus resurfacing as this year's seasonal influenza, the Association of Medical Microbiology and Infectious Disease Canada has updated flu treatment guidelines to recognize increased drug resistance and a wider range of conditions that up the risk for complications.

Tighter strictures on the use of antiviral drugs among otherwise healthy people and new treatment options for pregnant women, infants and others at risk for complicated influenza are among the changes highlighted in *The Use of Antiviral Drugs for Influenza: Guidance for Practitioners, 2010–11* (www.ammi.ca/pdf/UseOfAntiviralDrugs.pdf).

Under the new guidelines, the once-widely recommended antiviral amantadine is "no longer considered an option" because of widespread resistance. Recommendations are limited to the costlier oseltamivir and zanamivir.

To curb the further spread of drug resistance, the guidelines set a five-day limit on antiviral treatment for uncomplicated influenza and warn against preventative use of oseltamivir among close contacts of flu patients. Except in cases of "defined, significant exposure" and "significant immunosuppression," early treatment for symptomatic infection is preferable.

The guidelines also identify and make special treatment recommendations for groups at high risk of complicated influenza. In addition to people over 65 years old, residents of nursing homes or other chronic care facilities, pregnant women, children under two years old and First Nations, Inuit and Métis Canadians, the list includes individuals with a range of medical conditions, such as morbid obesity, chronic pulmonary diseases, cardiovascular disease, chronic liver disease, metabolic diseases, hemoglobinopathies, immunosuppression and neurologic disease.

Immediate treatment is recommended for all such high-risk individuals, even if more than 48 hours has passed since the onset of their symptoms.

The association has also lifted previous recommendations against the use of oseltamivir among pregnant women because of increased rates of hospitalization and death from complicated influenza during 2009.

New off-label oseltamivir dose regimens for infants less than one year old are also included among the recommendations. For all infants less than two years old, antiviral therapy is now optional based on clinical assessment, even in cases of mild or uncomplicated illness among otherwise healthy babies.

The new recommendations update the association's 2006 guidance on the use of antiviral drugs for influenza (www.cps.ca/english/statements/ID/ID06-04.pdf). — Lauren Vogel, *CMAJ*

Savings sought through colocation of mental health and general hospital

It marks the first time that a specialized mental health hospital and a general, hospital will be housed in the same building in Canada and proponents hope it will result in economies of scale and reduce stigmatization of mental health patients. But others fear the colocation of the North Bay and District Hospital with the Northeast Mental Health Centre in North Bay, Ontario will result in the loss of community treatment operations.

President and CEO Mark Hurst argues that the colocation will help reduce stigmatization by bringing mental health into the "mainstream of care. … All patients from birth to death and everything in between are going to be cared for in an integrated environment." Hurst also claims it will achieve economies of scale in administrative, information technology and laundry costs.

Skeptics counter that such savings will be offset by higher treatment costs. In the long run, expansion of community-level treatment options would be more cost-effective, says Steve Lurie, chair of the Service Systems Advisory Committee for the Mental Health Commission of Canada and director of the Toronto branch of the Canadian Mental Health Associa-

tion. Treatments offered at the community level, such as assertive community treatment teams, supportive housing, case management and peer support can decrease the need for hospitalization. Lurie adds that hospital stays in Ontario for people who joined a community treatment team are reduced to about 22 days per year from between 25–35 days per year. After five years, that drops to 10 days, while for every assertive community treatment team, about $1.8 million in bed costs are saved, Lurie says. The $8000 to $12 000 cost of supporting a 10–14 day hospitalization for someone with bipolar disorder or schizophrenia could be used to support that person in the community for a full year, he adds.

There's no consensus on whether colocation will actually yield therapeutic benefits to patients, notes Pamela Fralick, president and CEO of the Canadian Healthcare Association. Creating a completely separate institute can be like saying "lets put it out there, let's give it its own face, its own budget, give it profile so that it gets the attention it needs."

But Fralick adds that some believe colocation could be helpful for patients with both addictions and mental health issues, who historically have "fallen through the cracks." Such patients are often told by the general hospital that they can't be treated until their mental issues are resolved, and by the mental health facility that they can't be treated until their addictions are overcome. Fralick adds that integration may prevent one type of care from becoming isolated. — William Burr, Ottawa, Ont.

Canada in "kidney quandary"

While the number of Canadians living with kidney failure has more than tripled over the last two decades, the nation's supply of kidneys available for transplant has not kept pace with the growing demand, according to a report from the Canadian Institute for Health Information.

Some 38 000 Canadians were living with end-stage renal disease in 2009, more than three times the 11 000 people living with the disease in 1990, according to the report, *Treatment of End-Stage Organ Failure in Canada, 2000 to 2009* (http://secure.cihi.ca/cihiweb/products/2011_CORR_Annual_Report_final_e.pdf).

Of those patients in 2009, some 22 300 people (59%) were on dialysis, while roughly 3000 were on the wait-list for a transplant. That's up from 5900 patients (53%) on dialysis and about 1600 on the wait-list in 1990. By comparison, the combined number of patients waiting for liver, heart and lung transplants topped at 932 in 2009.

"Dialysis treatments come at great cost to not only the health care system but also to the patients' quality of life. On average, dialysis patients require treatment in a dialysis centre three times per week, often for four hours per session," Dr. Louise Moist, a nephrologist and associate professor of medicine at the University of Western Ontario in London, said in a news release (www.cihi.ca/CIHI-ext-portal/internet/en/Document/types+of+care/specialized+services/organ+replacements/RELEASE_20JAN11?WT.ac=homepage_banner_kidney_e).

CIHI estimates hemodialysis treatment — the most common form of dialysis — costs some $60 000 per patient, per year of treatment, excluding physician fees or procedures that take place outside a hospital setting. The average cost of a one-time kidney transplant, including hospital stay, is about $23 000 plus $6000 for necessary annual medication to maintain the transplant.

By these estimates, the more than 15 000 patients living with kidney transplants in 2009 saved the health care system roughly $800 million in that year alone. An additional $150 million could be saved annually if all 3000 patients currently on the waitlist were to receive transplants.

But the almost four-year median wait for such transplants means some patients may not receive them in time. Less than a quarter of patients over age 75 — the fastest growing group for kidney failure, accounting for 20% of all cases — will survive five years on dialysis.

The report also found many patients are receiving earlier treatment for end-stage renal disease. Only 31% of patients were "late referrals" in 2009, down from 42% in 2001.

However, "rising obesity rates and an aging population" are putting more people at risk of kidney failure and increased strain on the system, said Moist. "There needs to be a focus on educating Canadians on how to prevent the onset of these diseases that add a heavy burden to our health care system." — Lauren Vogel, *CMAJ*

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