COMMENTARY

Your inbox, Mr President

Rejuvenate the Environmental Protection Agency. End the stem-cell ban. Re-engage with the UN on climate change. Six leading voices tell *Nature* what the new US president needs to do to move beyond the Bush legacy.

Christine Todd Whitman
Former administrator of the US Environmental Protection Agency.

Clarify who will speak for the President on environmental matters.

It is clear from everything he has said, that President-elect Barack Obama considers environment and energy issues to be at the top of his agenda. The importance of the commitments he has made cannot be understated and all of them have to be considered in light of the current economic crisis that we are facing.

In terms of key policy matters, the administration must decide how far the Environmental Protection Agency (EPA) should go on meeting the Supreme Court's decision that the EPA has the legal right to regulate carbon dioxide. Although congressional legislation setting a limit on carbon emissions and establishing a trading system or carbon tax would be the best way to move forward, that is unlikely given both the complexity of the issue and the other challenges facing the new Congress.

An early indication of how aggressively the administration will move forwards will be their decision on whether to allow the EPA to grant California a waiver so the state can enforce stricter vehicle-emission standards than those required by the federal government — the state's proposal is a 30% decrease in emissions by 2016. At least 16 other states are anxious to join California, citing the US Clean Air Act, although car-makers in Detroit have fought the regulation vigorously, and successfully, until now.

The Obama administration will also want to look at all the pending regulations moved out in the last few months of the Bush administration, such as those on New Source review — governing when power-plant facilities must install pollution-control technologies — and drilling in wilderness areas. In analyzing these regulations and ensuring both that the work that led to them was complete and that the regulations represent policy supported by the new administration, the incoming appointees would do well to listen carefully to career staff. Such staff are knowledgeable and, for the most part, interested more in a policy agenda than a political one.

Additionally, Obama needs to clarify who will be determining environmental policy — the EPA, the Council on Environmental Quality (CEQ) or the newly created energy tsar Carol Browner. Environment and energy are inextricably linked and, although there is always need for administration-wide coordination, it must be clearly delineated as to who speaks for the president on these issues. Too many voices create confusion and allow issues to fall between the cracks. Although President George W. Bush originally told me that the EPA would be the administration's representative on the environment, subsequent actions by the vice-president and the CEQ proved otherwise. In fact, towards the end of my tenure at the EPA I was told in no uncertain terms that when the CEQ spoke, it was speaking for the president even if on an issue that the EPA felt needed more work. Although I believe that the EPA administrator should be the voice of environmental policy, the president must ultimately decide — and that delineation should be clear and consistent throughout the administration's term.

Finally, the Obama administration needs to be clear on its directives and expectations for the EPA. Morale is low for a host of reasons, not the least of which is because environment was not a priority for the Bush administration. The mood will get worse if staff and appointees feel that they are not part of the crucial discussion and that all decisions are coming from the White House. Incoming administrator Lisa Jackson will find at the EPA many highly talented people whose skills, ideas and extensive institutional knowledge should be cultivated. There are some tremendous public servants there and their contributions should be welcomed and encouraged.

P. FOY/AP PHOTO

2009: the year of climate change?

Timothy E. Wirth
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The United States must lead the way to a new climate deal at Copenhagen.

President-elect Obama has affirmed his intention to lead the United States back into the fight against climate change. His appointments in this area have been nothing short of brilliant, and just two weeks after the election, he told a California climate conference: "Delay is no longer an option. Denial is no longer an acceptable response. The stakes are too high. The consequences, too serious."

The downturn in the economy, far from being an insurmountable obstacle to definitive climate action, is setting the stage for previously unthinkable levels of capital investment that could put the United States on the road to a clean-energy economy, built on rapidly improving technologies and jobs that will remain at home.

Notwithstanding strong climate commitments by the European Union, the rest of the world has been adrift, waiting for the United States to wake from its eight-year sleep. This new American engagement must start with China. The world's two largest emitters have both the capacity and the need to take action, and finding ways to move forwards together would make a broader global agreement achievable.

Such collaboration may be difficult in areas where venture capital is driving innovation and intellectual property is the prize — novel solar technologies, for example. But where the scale of the challenge demands government engagement, such as with technologies for capturing carbon emissions from coal-fired power plants, the two countries could work closely together.

Internationally, some interim steps would be useful en route to a larger deal. Broad-based

commitments to energy efficiency and renewable-energy targets have been torpedoed by American objections in the past but would be constructive building blocks today. A new round of funding to help poorer countries adapt to climate change, delivered (not just pledged) by industrialized countries through the Global Environment Facility, would restore the trust that has been eroded by previously unmet promises. Creating a network of regional technology-innovation centres, as proposed by the United Kingdom's Carbon Trust, would reassure developing countries that they will have access to the technologies they need to respond to climate change.

American leadership on these confidence-building measures would improve the prospect of success in Copenhagen, where the United Nations climate talks resume in December 2009. UN secretary-general Ban Ki-moon has made this one of his highest priorities and has declared 2009 to be the "year of climate change".

The new US administration will have little time to prepare for Copenhagen, but agreement can be reached on the basic elements of a deal — commitments by industrialized countries to emissions targets, credit for avoided deforestation, financial support for adaptation and technology development, along with commensurate actions by rapidly developing countries. The finer details can be given the required attention in the following months, while still leaving enough time for ratification to avoid a post-2012 lapse when the existing commitments end under the Kyoto protocol.

Addressing climate change will require real political leadership domestically and in global negotiations. The commitment Obama has already made to action is remarkable and gives hope to a suffering planet.

Matthew Meselson
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Vast biosecurity expenditures require better oversight and monitoring.

It is seven years since envelopes containing anthrax spores were mailed to news media offices and to two US Senators, causing 11 cases of identified inhalation anthrax, five of which were fatal. In August 2008, the FBI announced that they had traced the source of the spores to the United States Army Medical Research Institute of Infectious Diseases at Fort Detrick in Maryland, one of the many US facilities conducting biodefence research. Although there has been no repetition of such attacks, the episode underscores the need for better oversight of biodefence activities and of the individuals conducting them.

Federal expenditure for civilian biodefence during 2001–08, conducted mainly by the departments of health and human services, homeland security, and defence is estimated at about US$50 billion, of which roughly one-third was for research[1]. Department of Defense (DoD) outlays for biodefence research, development and testing for strictly military objectives currently run at several hundred million dollars per year[2]. Relevant expenditures by the various intelligence agencies have not been made public.

Oversight of biodefence — to ensure that activities comply with existing laws and international agreements — varies from agency to agency, with perhaps the most advanced being that of the Department of Homeland Security (DHS). In addition to scientific peer-review to assess scientific merit, the DHS has a Compliance Review Group (CRG) that reviews all DHS-sponsored research for compliance with the 1972 Biological Weapons Convention and with US criminal law. It also applies the criteria of the National Science Advisory Board for Biosecurity in assessing proposed projects that have potential for hostile misuse. The CRG meets at least twice a year, and before each meeting there is a call for abstracts of proposed projects to be submitted by their respective principal investigators, who at the same time are reminded of their responsibility to ensure compliance with treaty commitments and applicable US law.

CRG members, therefore, are informed about all projects before they commence and the group continues to oversee them as they evolve. Projects deemed by CRG staff to pose risks of actual or perceived non-compliance, or which are likely to pose a dual-use potential for misapplication, are individually briefed to the group and, in some cases, the CRG members are required to acknowledge personal responsibility by signing their names to decisions regarding approval or denial of support for a project.

The compliance procedures in other departments are not as rigorous and there is no process to ensure consistency across government agencies. The DoD, for example, reviews biodefence projects at a broader 'programme' level rather then reviewing individual projects.

Oversight of biodefence activities is likely to come under examination by the new Congress, which could devise guidelines and procedures applicable throughout government. Topics to be considered should include the authority and composition of compliance review boards, criteria for approval of projects, harmonization of procedures, procedures for ensuring the reliability of personnel engaged in biodefence work, provision for site visits, a requirement for periodic reports, and the inclusion of State and Justice Department observers to promote both independence from parochial influences and familiarity with treaty commitments and applicable US law.

The resulting procedure could then serve as a model for consideration by the state parties of the Biological Weapons Convention at its seventh review conference in Geneva, Switzerland, in 2011. The aim would be to agree on a requirement for detailed periodic submissions from each nation describing the oversight procedures

K. LAMBERT/AP PHOTO

Federal expenditure for civilian biodefence during the Bush years totalled more than $50 billion.

it employs to ensure compliance with the convention. The objective would be to increase awareness of the need for improved oversight and to facilitate the development of international measures for enhanced exchange and transparency regarding implementation of the convention.

1. Franco, C. *Biosecur. Bioterror.* **6,** 131–146 (2008).
2. *Roles and Responsibilities Associated with the Chemical and Biological Defense (CBD) Program (CBDP)*, Department of Defense Directive 5160.05E (2008). Available at: www.dtic.mil/whs/directives/corres/pdf/516005p.pdf

Contaminated heparin led to many adverse events in 2008.

Steven E. Nissen
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An end to secrecy will revive the Food and Drug Administration.

After an unprecedented series of revelations about drug and device safety issues, many observers consider the Food and Drug Administration (FDA) a failed agency. The Obama administration has the opportunity to reinvigorate the FDA, but only through major restructuring and policy changes that are designed to protect the agency from undue influence, and to promote transparency.

The next FDA commissioner should serve a fixed six-year term to insulate the agency from political influence. Moreover, the system by which pharmaceutical companies fund a major portion of the FDA's budget through user fees requires re-evaluation.

Secrecy is antithetical to both science and good government, but much of what the FDA knows about drugs, it never publicly discloses. The agency must cease to regard clinical-trial data as proprietary and provide access to all available information on safety and efficacy. This policy should apply to information gathered during approval for drugs, and to post-approval surveillance. The agency needs better harmonization between its Office of Surveillance and Epidemiology, which monitors post-marketing safety, and its Office of New Drugs, which is responsible for post-marketing regulatory decisions.

The current voluntary mechanism for adverse-event reporting is relatively ineffective, because only 1%–10% of events are actually reported. Partnerships with large health-care providers, such as health maintenance organizations that supply care through hospitals, doctors and other providers, are needed to prospectively assess drug safety.

The approaches used to approve drugs need attention. Drug approvals are often based on placebo-controlled clinical trials. However, appropriate use of therapies requires understanding comparative effectiveness. The FDA has increasingly used 'non-inferiority' study designs to support efficacy. In these, a treatment is considered 'approvable' if it retains 50% or more of the effectiveness of a comparable product, which may represent too lenient a standard. The agency has also increasingly used 'surrogate endpoints' (biomarkers or laboratory measures) to support approvals without subsequently requiring more informative clinical-outcome studies.

For medical devices, the agency has authority to clear a product for market if it is deemed 'substantially equivalent' to devices already being sold. This rule has become the principal approach used to approve medical devices. However, even small changes to a device can affect safety, which has resulted in major safety recalls, such as for defective pacemaker leads.

Stronger enforcement capabilities are required throughout the agency. The Division of Drug Marketing, Advertising, and Communications needs the right to restrict direct-to-consumer advertising during the first two years a drug is marketed and to preview advertising to ensure it is not misleading. An FDA policy introduced in 2008 unwisely allows off-label promotion of drugs and devices through distribution of article reprints, an approach that may encourage unsafe use for unapproved indications and discourage appropriate clinical trials to establish new indications.

Currently, about 1,600 facilities in China manufacture drugs or components of drugs marketed in the United States. Recent high-profile cases — such as contaminated heparin — poignantly illustrate the risks inherent in globalization. The FDA must increase inspections and foreign governments must be held accountable for setting regulatory and safety standards for local manufacturing. All of these initiatives require more robust funding of the FDA, which currently has a budget of $2.3 billion with which the Agency must regulate $1 trillion worth of food, drugs, cosmetics and medical devices. The agency's budget is quarter that of the Centers for Disease Control and Prevention, which has a significantly more limited mission. Congress must re-evaluate priorities and recognize that ensuring the safety of food and drugs is a crucial national priority.

NEWSCOM

Calestous Juma
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A smart focus on infrastructure at home means more winners globally.

In the current economic climate, you might think that prospects for US science and technology cooperation with developing countries look grim. An immediate consequence of the recession is that there will be fewer consumers in richer countries for technology exports from the developing world. At the same time, an Obama administration, poised to make historic investments in US jobs and infrastructure, may decide that funding international scientific cooperation is less of a priority as it focuses on fixing problems at home.

Such a view, although understandable, couldn't be more wrong. Far from shutting out the rest of the world, we are about to witness perhaps the most audacious example of the collective insights from world science being applied to policy-making since the US administrations of the early 1960s. Moreover, large-scale investment in infrastructure projects such as transport systems and public housing in the United States is poised to benefit science — and infrastructure — in developing nations.

How? Part of the answer lies in President-elect Barack Obama's choice of science advisers. In choosing John Holdren from the Harvard Kennedy School, as well as the biologists Jane Lubchenco, Harold Varmus and Eric Lander, the president has chosen a quartet of advisers who will think globally and act both globally and locally — perhaps more so than any of their predecessors. The choices indicate that taking action to reduce the rate of biodiversity loss, to tackle climate change and to ensure that the poorest receive the best health care are regarded by the new administration as the right things to do. For each of these advisers and for their wider teams, the national interest and the international interest

will now overlap to a considerable degree.

Such overlapping priorities apply equally to another area of public policy that the Obama team will make their own. In the next few years, US industry and policy-makers will immerse themselves in a task that is usually associated with developing countries: nation-building. The predominant images in the United States for the next few years will be those of men and women in hard-hats upgrading roads, rail networks, schools, hospitals, postal systems, power plants and more.

Some regions of the United States have infrastructure challenges that are similar to those of developing countries. The lessons learned from these regions will offer additional opportunities for global learning. Development needs more than money, it needs skilled and experienced people. Right now, this is what so much international development lacks. Indeed, one reason why genetically modified crops have been slow to take off in Africa is because research and development in richer nations (especially in Europe) isn't happening. All in all, America is set to become a more credible international development partner in the eyes of many poorer countries.

International development for the United States will become an extension of local development — just as it is for China's current efforts in Africa, and just as it was during the birth of the Green Revolution in agriculture, when US scientists took a lead in developing technologies for high-yielding crop varieties and these invariably spread to help the rest of the world.

Domestic economic policy and the aspirations of developing countries will converge over the next few years. The Obama administration — and the many development cooperation institutions in the United States — cannot afford to miss out on this historic opportunity to do the right thing.

J. SCHYTTE/STILL PICTURES

Nation building could become an important US export.

George Daley
Associate Professor, Children's Hospital Boston, Massachusetts, USA.

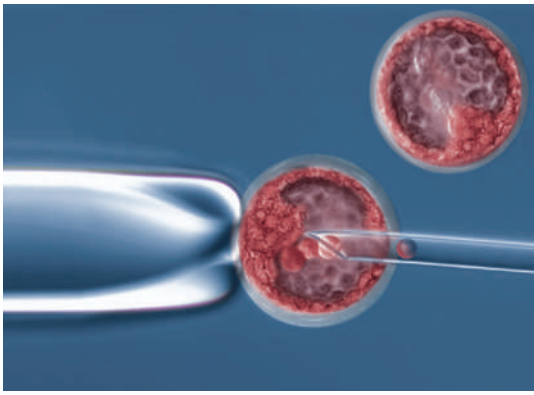
Put the NIH in charge of stem-cell guidance and oversight.

The Obama administration has given every indication that it will swiftly eliminate restrictions on federal funding for research on human embryonic stem cells. This could potentially allow labs to study the nearly 1,000 cell lines that have been derived since August 2001, the arbitrary cut-off date chosen by president George W. Bush's administration. Newer cell lines have important properties that make them valuable for medical research. For example, lines generated from preimplantation genetic diagnosis can be used to model human diseases such as fragile X syndrome, neurofibromatosis and various forms of bone-marrow failure.

Still, significant challenges remain in harmonizing stem-cell research and reasserting the United States's role as a leading force in this field. Under the Bush policy, a number of US states have stepped in to fund embryonic stem-cell research — California, most prominently, but also states including New Jersey, New York, Wisconsin, Connecticut, Illinois, Maryland and, most recently, Massachusetts. That has created a Balkanized set of principles for regulation and protocol, and has obfuscated financial administration in laboratories that must keep these funding streams separate. Moreover, ethical guidelines for deriving and maintaining human stem-cell lines have taken a parochial turn, with subtle but sometimes meaningful discrepancies that could complicate future collaboration across state and international boundaries.

The situation reflects the fact that the National Institutes of Health (NIH) — which should have been the main arbiter in charge of oversight of stem-cell research in the United States — has largely been sidelined during some of the most dramatic and game-changing discoveries and debates of the past eight years.

The best policy outcome would be to return the NIH to its rightful role as arbiter of stem-cell research in the United States, making funding decisions based on scientific merit rather than ideology, and ensuring uniform standards of ethical oversight, most readily by endorsing the Guidelines from the National Academy of Science and the International Society for Stem Cell Research. Because so many countries look to the leadership of the NIH to set principles for how they operate within their own borders, this would have an enormous impact on policies worldwide.



Work with human embryos will remain restricted.

ILLUSTRATION: FOTOFINDER/MEDICALPICTURE

A second issue looms on the horizon. The Dickey amendment, which has been a rider on the Department of Health and Human Services appropriations bill since 1995, precludes using federal money for the creation or destruction of human embryos for research purposes. So although hundreds of cell lines could be approved for federally funded research projects, subject to NIH approval, the amendment bars funding for research such as somatic cell nuclear transfer or work on embryos discarded from *in vitro* fertilization procedures to derive new cell lines.

In my opinion, this legislative barrier represents a blockade to essential forms of embryo research that could aid health care for birth defects, women's infertility and some cancers. The political reality may dictate that the few labs doing this (mine included) will have to continue to rely on state or private funding in the near term for this work. But the new Obama administration would be well advised to commission a comprehensive and thoughtful analysis of the scientific, medical and ethical issues pertinent to human-embryo research, and to act on the recommendations in the best interest of society as a whole.

Beyond the stem-cell issue, there is a pressing need for increased funding for all areas of biomedical research, given the inadequate NIH budgets of the past few years. It would be a Pyrrhic victory to win expanded federal funding of embryonic stem-cell research without seeing a greater overall investment in the NIH. Even in the current financial crisis, funding for biomedical research is a smart investment that is certain to yield handsome returns. ■

See Editorial, page 235, and visit http://tinyurl.com/7ct8h7 to respond to these Commentaries.