agreements by expanding the powers of the president in comments released March 8. *Relevant documents are available on InsideEPA.com. See page 2 for details.*

"Administration officials have stated — using a shifting rationale — that Congress is constitutionally prohibited from requiring EPA . . . to do anything that is triggered by the decision of an international body. This theory . . . advocated by a tiny faction of radical legal theorists, contradicts a well-established body of U.S. statutory law that implements important international agreements such as the Montreal Protocol on Ozone Depletion, the North American Free Trade Agreement, [and] the Chemical Weapons Convention . . ."

The groups urge EPA to draft a proposal that would ensure that U.S. regulatory processes run parallel to the international decision-making process for new chemicals. "The administration draft does not require EPA to do anything in response to the various steps of a Stockholm listing decisions, even if the United States is engaged in and fully supports every one of those steps." The groups also oppose language on risk- and cost-benefit analysis in the proposal and say the proposal does not adopt a health-based approach to considering new chemicals for limitations.

A source with pesticide trade group CropLife America favors mandatory public reports by EPA aligned with the different stages of the international process but offered support for EPA's compromise measure.

The American Chemistry Council is broadly supportive of the treaty, especially language incorporating the use of risk and cost-benefit considerations.

An EPA source says administration officials are placing a high priority on the cost-benefit language, but that it will not impede the agency from considering additional chemicals under the treaty that warrant concern. "If we thought it would, we would fight it," the source says.

Agency officials at the March 3 meeting did not provide any written legal analysis of its position, the Democratic staffer says. EPA officials cited previous White House legal counsel opinions and signing statements — including the Clean Diamond Trade Act — but said these documents were confidential under executive privilege, the source says.

Senate environment lawmakers last year approved language that would link the public domestic reporting process under the treaty and the international process, but stopped short of requiring EPA to respond to final international decisions to limit a chemical.

EPA FACES NEW LAYER OF REVIEW AFTER NAS HUMAN SUBJECTS STUDY

EPA science policy officials are grappling with the possibility of adding new layers of review for agency human subjects research after a National Academy of Sciences (NAS) report equalized the ethical standards for both agency and outside research.

The NAS' recommendations could affect research involving intentional dosing of subjects that all of EPA's regulatory programs rely on, making it more difficult for health effects studies to be forwarded in a timely way to EPA program offices, sources say.

"An additional layer of review in an environment of tight budgets and existing difficulties in delivering timely risk assessments . . . sets up another hurdle" to using some data in regulations, according to a science policy official.

And an agriculture committee congressional aide says, "To establish yet another review body is unnecessary and duplicative. The relevant scientific and ethical issues can be handled by existing boards."

In a widely anticipated Feb. report, *Intentional Human Dosing Studies for EPA Regulatory Purposes*, the NAS approved the acceptance of human studies on chemicals whose only goal is to improve risk assessment but says no adverse effects should be tolerated in the research. But for research with broader social benefits, studies that have "transitory" adverse effects are acceptable ethically if they are scientifically robust, according to the NAS. The panel also says human studies should only be conducted when extensive animal research has been done and there is no other way to address a critical scientific uncertainty.

Agency research and other program officials say EPA's Office of Pesticide Programs (OPP), in addressing an issue with unique implications for its regulatory programs, has now entangled the rest of the agency in new and possibly unnecessary requirements.

Citing unresolved ethical issues, OPP declared a moratorium in 1998 on using human pesticide studies in regulations. The ban applied to intentional pesticide dosing studies chemical companies submitted to EPA in an effort to provide the agency with all available data on pesticides and to relax regulatory limits. When basing chemical regulations on test animals, EPA reduces the allowable exposures by a factor of 10 to account for differences between animals and humans. By using human subjects, industry can eliminate the need for the factor of 10.

Pesticide managers sought advice from external advisers at the time about so-called "third-party" research, but EPA's Office of Research & Development (ORD) was concerned the ban could complicate agency research on other industrial chemicals, drinking water contaminants and air pollutants. For example, EPA cited 18 human subjects

studies in its most recent summary of particulate matter (PM) research.

But other agency sources say the way EPA pesticide officials formulated the charge question to the NAS — when EPA asked for advice on the propriety of using human pesticide research — unnecessarily swept up a broad array of agency research when the focus should have been on pesticides. "When OPP forwarded its study recommendations to the NAS, it was clear they had not thought through some of the distinctions" between pesticide research and other environmental health research, an EPA source says. For example, OPP did not consider how some ozone research exposes medically monitored subjects for short periods to pollutant levels many people are exposed to in everyday life, raising questions about whether such exposures warrant intensive additional review.

"The ethical and scientific issues are fundamentally the same whether a human study is conducted by a third party or by EPA."

After EPA issued its moratorium, industry groups like the Center for Regulatory Effectiveness and pesticide manufacturers contested OPP's ban, saying the policy was inconsistent with allowing EPA research labs to intentionally dose human research subjects when performing health effects research.

And last spring, the pesticide makers won a court challenge that found EPA had issued the policy without following the notice and comment steps necessary to ensure the ban was lawfully developed. EPA sources say they will now draft new rulemakings clarifying the use of human subjects research consistent with the NAS recommendations and the court ruling. The rulemakings will affect the pesticide program and the entire agency now that the NAS has equalized the ethical and scientific standards for internal and external studies, sources say.

In its report the NAS concludes, "The ethical and scientific issues are fundamentally the same whether a human study is conducted by a third party or by EPA and the same basic ethical framework should apply to both categories of studies."

ORD managers in the National Center for Environmental Assessment (NCEA) say they are concerned the NAS' conclusions will force the agency to adopt additional layers of review that could hinder the flow of scientific information into regulatory processes.

"They are recommending we adopt a system similar to the Food & Drug Administration's stage 1 clinical drug trials but with additional review," according to one ORD official. "The problem with this is, ORD has a review system, but OPP's move to ban human research now affects all of us," the source says.

EPA does not have an Institutional Review Board (IRB), which most universities or research contract institutes appoint to oversee the scientific and ethical approval of research proposals on human subjects. ORD currently has an Ethics Review Officer who ensures that an IRB reviews all studies EPA sponsors or conducts.

But the panel is now going beyond its recommendation that an IRB review in-house research. The NAS is also calling for a new Human Studies Review Board to supplement but not replace the IRB that would address scientific and ethical questions before research is conducted, as well as study results when completed. An EPA source doubts whether EPA will accept all of the NAS's recommendations. "I would not be surprised if an alternative to forming a new board is the direction the agency takes," the source says.

Another source says, "The real challenge for the agency will be defending decisions made upfront that a certain study would be worthwhile, as opposed to looking at information that's already been developed." The agency will "now be put in a position of judging the utility of information before we have it, and some of that research may not pan out or provide useful information," the source says.

Although the panel says it would be "optimal" if a pre-review of privately sponsored study proposals were mandatory, it says that because of legal and logistical concerns, EPA should only consider making it mandatory. "Any conclusions reached by the board should be advisory and not binding on the sponsoring companies or reviewing IRBs," according to the NAS.

This recommendation has fueled skepticism in the environmental community about whether industry studies will receive adequate review. According to the Environmental Working Group, "If the EPA begins to accept human experiments, we expect to see companies taking advantage of any and all ambiguities in the guidelines" to ease regulations.

But while industry sources say the NAS report is a clear win, they say their research will be conducted according to the highest ethical and scientific standards the NAS calls for.

An ORD official says, "There is currently a lot of discussion about how we should implement the recommendation to go beyond the IRB and establish a new review body. ORD is a big player in this area because of the number of risk assessors and researchers whose work involves" human subjects studies.

An OPP-ORD led workgroup will be addressing how to implement the NAS' recommendations in the coming weeks, but ORD officials say they are unsure how to adapt the advice in a way that will allow important risk research to proceed in a timely way to feed into the regulatory process.