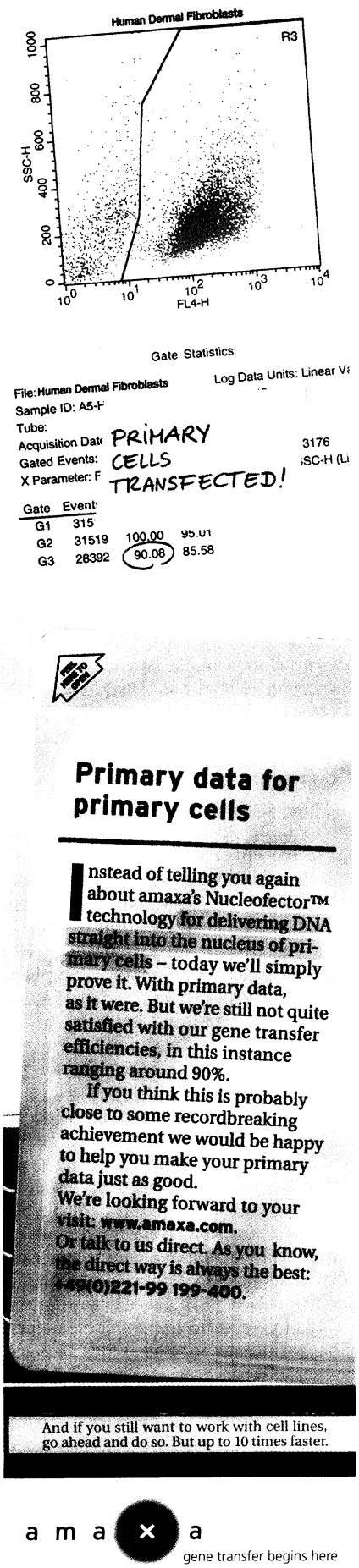

permitted levels of air pollution also increase DNA damage from volatile organic compounds, decrease renal function, and reduce testes volume in adolescents (*2*). A fuller accounting of the potential health and ecological impacts of GHG mitigation that would include such benefits, as well as those noted by Seip *et al.*, would further strengthen the conclusions in our Policy Forum (*3*).

Seip *et al.*'s criticism about the "unreasonable" U.S. GHG position is perhaps best addressed by Donald Kennedy's recommendation in his Editorial "Going it alone" (17 Aug., p. 1221), that "As a lone player, the United States can restore some credibility with its friends and trading partners by demonstrating a serious commitment to mitigating the global warming problem." We agree with Kennedy that there is a need for U.S. action on this issue. As we have recently seen, if we don't all cooperate to address the world's problems, then they will end up on our own doorsteps. That is true with terrorism, and it's also the case with other global threats, like climate change.

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Short-Term Trials and Long-Term Effects

IN THEIR POLICY FORUM "PLACEBO-CONTROLS in short-term clinical trials of hypertension," S. M. Al-Khatib and co-authors demonstrate with meta-analysis that the use of such controls is not associated with an increased risk of serious adverse events for participants in these studies (*Science*'s Compass, 15 Jun., p. 2013). They say that this supports the use of such trials from an ethical standpoint.

There is an important caution not emphasized by the authors. They were only able to focus on short-term outcomes in their analysis. They indicated that there is ample evidence to demonstrate that the use of placebo in long-term studies is not safe. What remains unknown is whether there might be longer term consequences of participation in a short-term, placebo-controlled trial. Most short-term studies do not follow the participants for long-term outcomes. There are, however, some studies that have suggested the possibility of longer term effects. One such study by Geleijnse and colleagues showed long-term effects of restricting dietary sodium during the first 6 months of life (*1*). Children in the lower sodium group still had significantly lower systolic blood pressure than those in the control group after 15 years of followup, despite being on an unrestricted diet except for the first 6 months of life during the clinical trial. Similarly, the Diabetes Control and Complications Trial/Epidemiology of Diabetes Intervention and Complications Research Group showed that HbA1c levels between the former intensive therapy and control groups were similar for 4 years after the study was completed (*2*). Despite similar HbA1c levels during the first 4 years after the intervention trial, the reduction of risk in the progression of retinopathy and nephropathy resulting from the previous 6.5 years of intensive therapy persisted.

"What remains unknown is whether there might be longer term consequences of participation in a short-term, placebo-controlled trial."

These findings suggest that long-term followup of individuals who participate in short-term clinical trials of antihypertensive medication is warranted in order to be sure that the conclusions presented by Al-Khatib and colleagues are valid.

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Response

DANIELS OBSERVES CORRECTLY THAT WE ONLY reported short-term outcomes of patients who were enrolled in short-term clinical trials of hypertension. Our study showed that short exposure to placebo in clinical trials of hypertension is not associated with an increased risk of short-term serious adverse events. However, because exposure to placebo in such trials deprives patients from active antihypertensive therapy for the duration of the trial, Daniels raises concerns about the long-term safety of patients enrolled in these trials. Although examination of long-term outcomes of short exposure to placebo in such trials might be important, this was not possible in our review, simply because short-term trials of hypertension do not collect or report data on long-term outcomes.

We agree that data on long-term outcomes would be required to absolutely exclude an adverse effect of short-term placebo use; however, the examples that Daniels provides do not seem to support his argument. First, although the Epidemiology of Diabetes Interventions and Complications study reported persistent benefits from the intensive therapy for diabetes mellitus that was implemented in the Diabetes Control and Complications Trial (DCCT), exposure to this therapy in the DCCT trial was of 6.5-year duration (*1*). Thus, this is an inappropriate example of how "short-term" therapies can significantly affect long-term outcomes.

Second, although the study by Geleijnse and colleagues showed that a low-sodium diet in infancy had a significant effect on blood pressure in adolescence, the authors could not definitively exclude differences in subsequent salt intake as a potential explanation for this finding (*2*). However, even if we assume that this was a real finding, it is conceivable that brief exposures to certain factors during infancy are more likely to result in long-term effects than exposures to such factors during adulthood.

Nonetheless, data regarding the long-term safety of short exposure to placebo would be welcome to ensure the long-term safety of patients who participate in such experiments, provided there is a physiologic mechanism through which withholding active therapy for a short time might be associated with long-term risk. In the case of carefully monitored, short-term exposure to placebo in studies of hypertension, the value of collecting long-term followup data seems questionable. However, given the changing nature of scientific explanations for disease etiology, we support the concept that when possible, short-term studies should collect some longer term safety data.

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Advice for a Better OTA

NOW THAT A SERIOUS EFFORT TO RESTORE THE U. S. Government's Office of Technology Assessment (OTA) has begun, some anomalies in the structure of this much lamented institution need to be addressed (News of the Week, "Memo to Congress: Get better advice" by D. Malakoff, 22 Jun., p. 2229). In the past, the advice from OTA was valuable to Congress, but even more valuable to policy researchers. From their point of view, OTA's location in Congress was a great advantage, because it kept OTA's focus on policy and enforced political neutrality.

This location, however, also led to some problems. OTA never set forth a basic analytic approach to technology assessment. Each study was a unique effort. Its documentation focused on procedures such as how to relate to congressional clientele, how to constitute an advisory committee, and how to present the final results. Consequently, there is no manual from which the aspiring and newly appointed technology assessor can learn the basic intellectual framework underlying the craft: what constitutes an assessment, how one goes about doing one, what techniques are the most useful, and what are the hallmarks of quality. Another problem is that OTA left no direct academic legacy. It drew on the expertise of many individuals, but left behind no institutions that can carry on technology assessments in its mold. Its alumni will soon reach retirement age, leaving a legacy of valuable reports but no students to succeed them. And lastly, the OTA tended to neglect the international dimension of the issues it addressed. This was understandable at the time, but would be a serious anachronism today.

We need a 21st-century OTA, one that retains the laudable features of the previous OTA, but that addresses the institutional issues outlined above. It should have a clear mandate to establish an intellectual methodology and build departments and research teams in universities in different parts of the country. And a new OTA should also place its analyses in an international context by examining the international aspects of the problems it addresses, and by comparing U.S. domestic problems with their counterparts in other countries. In this way, technology assessment could this time become a recognized academic discipline and research activity that could survive any future political vicissitudes.

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Comparing Human Genome Mapping Data

A PRESENTATION GIVEN BY ONE OF US (COLIN Semple) at the joint Cold Spring Harbor Laboratory/Wellcome Trust Conference on Genome Informatics (8 to 12 August, Hinxton, UK) is the topic of a News of the Week

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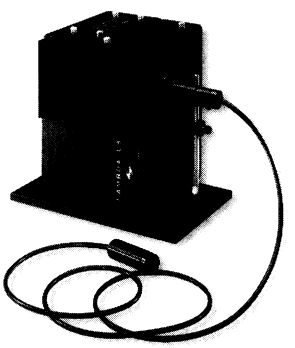

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