It is stated that "[t]he most consequential result of [the National Academy of Sciences report on proposed policy for regulating recombinant DNA–manipulated plants] will be to promote unwarranted regulatory barriers." The question of whether limbless snakes could re-evolve legs is part of a wider exchange regarding issues of the evolution of snakes, based on the discovery of a Middle Eastern fossil snake with limbs. And an imagined exchange between a newly made immortal and John Harris, the author of a recent Science and Society Essay on immortality, emphasizes the potential pitfalls of such a radical change for human society and leads off a series of exchanges on the matter.

NAS Report Under Scrutiny

In her News of the Week article "Transgenic crops report fuels debate" (14 Apr., p. 245), Jocelyn Kaiser discusses the National Academy of Sciences (NAS) report on the proposed Environmental Protection Agency (EPA) policy for regulating recombinant DNA–manipulated plants with enhanced disease or pest resistance. This report is flawed in several respects.

The report is internally inconsistent and conflicts with previous reports by the NAS (*1, 2*) and by other prominent scientific groups (*3, 4*). Two studies from the Academy itself concluded that recombinant DNA techniques are merely an extension, or refinement, of the kinds of genetic manipulation that have been performed for decades or even centuries. In one of those studies, the committee wrote, "With classical techniques of gene transfer...we cannot always predict the phenotypic expression that will result. With organisms modified by molecular methods, we are in a better, if not perfect, position to predict the phenotypic expression" (*2*, p. 13). That committee also made a policy recommendation relevant to the EPA's proposed policy—namely, that "the nature of the process (of genetic modification) is not a useful criterion for determining whether the product requires less or more oversight."

Nor was it only NAS committees that objected to the EPA approach. Kaiser mentions a 1996 report by 11 scientific societies that excoriated the EPA's approach (*3*), but she did not mention that 2 years later the Council on Agricultural Science and Technology (CAST), an international consortium of 41 scientific and professional groups, reiterated the former report's criticisms. The CAST report characterized the EPA's approach as "scientifically indefensible" and said that treating gene-spliced plants as pesticides would "undermine public confidence in the food supply" (*4*).

However, the committee that produced the present NAS report appears to have ignored the crucial aspects of its charge—namely, to "examine the existing and proposed regulations to qualitatively assess their consequences for research, development, and commercialization," and to "provide recommendations...for the existing and proposed regulation" of recombinant plants with enhanced pest-resistance (*5*). Instead, it seems to have accepted the EPA's fundamentally flawed regulatory approach as "given."

How could the NAS have gone so far wrong in its assessment of the EPA policy? Consider the committee members. Members and invited reviewers were included who had obvious conflicts of interest and bias. Three members of the 12-person committee (Stanley Abramson, Fred Betz, and Morris Levin) are former EPA staff who had helped to craft and defend a variety of process-based regulatory policies while at the agency, and another, Rebecca Goldburg, has produced a succession of antibiotechnology tracts over the past decade. Moreover, during the formal review process, the document was reviewed by another former senior EPA official, Lynn Goldman, who had been instrumental in crafting and defending the policy in question, and by an antibiotechnology activist, Jane Rissler.

The most consequential result of this report will be to promote unwarranted regulatory barriers to the development of much-needed pest control strategies that can reduce reliance on chemical pesticides and enhance productivity. The warnings of the reports by the 11 societies and CAST—including decreased choices available to farmers for defending against disease and pests, increased reliance on chemical pesticides, and competitive disadvantages to U.S. research and development—apply as well to this NAS report.

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Snake Origins

The Perspective about snake origins by Harry W. Greene and David Cundall, "Limbless tetrapods and snakes with legs" (17 Mar., p. 1939), misrepresents the alternative viewpoint. They support the idea that the limbed snakes *Haasiophis* and *Pachyrhachis* are advanced snakes that reacquired legs (Reports, "A fossil snake with limbs," E. Tchernov *et al.*, 17 Mar., p. 2010), rather than our interpretation of them as very primitive snakes bridging the gap between mosasaur marine lizards and modern snakes (*1–3*). They then add that "[t]he fossil evidence supports the notion that *Haasiophis* and *Pachyrhachis* are more closely related to terrestrial Macrostomata [advanced snakes] than to marine mosasaurs." These juxtaposed statements imply that we proposed that *Haasiophis* and *Pachyrhachis* are not true snakes but long-bodied mosasaur relatives convergent with snakes. This is not so; our interpretation of them as primitive snakes still views them as true snakes, and thus as being more closely related to other snakes (including macrostomatans) than to mosasaurs.

Artist's rendition of *Pachyrhachis* on a Cretaceous reef.

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Greene and Cundall also ascribe to us the statement that the extreme feeding adaptations of advanced (macrostomatan) snakes are primitive for snakes, and promptly refute it by noting that basal

snakes lack these features: "the greatly enhanced gape ascribed to 'snakes' by Lee *et al.*...actually characterizes only that last subgroup of Serpentes [macrostomatans]." Again, however, our study (*3*) never asserted that uniquely macrostomatan features are primitive for snakes. Rather, it identified as primitive for snakes only traits present in all snakes and in their nearest lizard relatives (*3, 4*): namely, the hinges in the middle and tip of the lower jaw (the mobile intramandibular and symphysial joints).

Our study emphasized, in agreement with Greene and Cundall, that additional feeding adaptations of macrostomatans, such as the "pterygoid walk" for swallowing huge prey, and the dislocation of the tips of the lower jaws that enhance gape, are not primitive but must have evolved within snakes [figure 1 in (*3*)].

Finally, Greene and Cundall note that some evolutionary transitions are more likely in one direction than in the reverse and conclude that snakes could not have been primitively aquatic (because this would imply a subsequent reversion to terrestriality, an "unlikely" transition).

However, Dollo's sword cuts both ways: None of the more than 50 lineages of limb-reduced reptiles and amphibians have ever re-evolved legs, demonstrating that reacquisition is very unlikely. Yet, interpreting *Haasiophis* and *Pachyrhachis* as advanced snakes implies such an implausible reversal, which is accordingly contemplated in the Perspective and Report. The developmental model cited as support was explicitly designed to explain limb loss (*5*); to assume that the mechanism is fully reversible and can lead easily to limb gain is an extrapolation with neither experimental nor phylogenetic support.

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Response

We agree that the quoted passage erroneously implies that Lee *et al.* (*1*) regarded the controversial Middle Eastern fossils as more closely related to mosasaurs than to snakes. That sentence was written by the *Science* editorial staff. However, our figure accurately portrayed Lee *et al.*'s view that the fossils are more closely related to snakes than to mosasaurs.

We did not attribute to Lee, Scanlon, and Caldwell any such "statement" about advanced snakes, but rather took issue with the comment (*1*) that "the evolutionary transition from the relatively inflexible lizard skull to the highly mobile snake skull remains poorly understood, as they appear to be fundamentally different and *no obvious intermediate stages* have been identified" (emphasis added). They thereby trivialized several well-documented and dramatic shifts in feeding biology within crown-clade snakes [for example, (*2, 3*)] as compared with outgroup lizards; as we noted in our Perspective, within the relevant literature, there is diverse and sometimes imprecise use of the word "snake."

Finally, contrary to Lee, Scanlon, and Caldwell, we carefully avoided absolutes such as "could not have been primitively aquatic" and "can lead easily to limb gain." At this point, published data analyses favor Tchernov *et al.*'s conclusion that *Haasiophis* and *Pachyrhachis* are phylogenetically well within crown-clade snakes. One possible implication is that a well-developed

tetrapod hindlimb evolved in those fossil taxa after having been reduced to a vestige in more basal lineages and their common ancestors. With regard to the purported absence of "experimental and phylogenetic support," we regard recent studies of python limb vestiges and hox genes (*4*) as evidence for morphogenetic regulatory mechanisms that might be conserved in the absence of actual expression of complex features (*5*). And elegantly detailed studies have demonstrated, for example, that mosaic patterns of gains and losses must have occurred in the evolution of pelvic and distal limb elements among various elongate lizards and basal snakes [for example, (*6, 7*)]. Reoccurrences of complex structures might well be improbable, but in the light of comparative and developmental biology, they are not "implausible."

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Immortality, Anyone?

I hope for John Harris's sake (as well as my own) that his predictions of therapeutic immortality (Essay, "Intimations of immortality," *Science*'s Compass, 7 Apr., p. 59) will come true soon. But I fear that his planned ethical controls will not run smoothly. In the not-too-distant future, one of his counseling sessions at "Telomeres R Us" might run something like this:

John Harris: Congratulations, sir! I hear your treatment was successful and that you are now a wealthy immortal.

WI: Thank you.

JH: Before you leave, I would like you to read over this contract and sign it. We call it Option A.

WI [after reading the contract]: Hey! Wait a minute! This says that I consent to "Generational Cleansing" after living "a reasonable number of years, said reasonable number to be determined by the Institute of Medicine, Law, and Bioethics at the University of Manchester."

JH: Isn't that acceptable?

WI [scarlet with rage]: Are you out of your mind? After what I paid for this treatment? This is the biggest load of...

JH: OK! OK! You don't have to sign it. I told you, that's just Option A. Why don't you read this one instead? We call it Option B.

WI [reading out loud]: "I hereby agree to waive all my rights to reproduce; should I do so, I will have all subsequent immortality therapies terminated..."

JH: Yes. Would you prefer to sign that one instead?

WI: Let me ask you a question, doc. What if I tell you to take both of these agreements and stick them in your ear. What would happen to me?

JH: Well, that's difficult to answer at the moment. Potentially, you could face some very serious legal penalties.

WI: Is that so? Well, let me tell you, I'm a very wealthy man, and I can afford the best lawyers. So can my buddies who've also had this treatment. Between us, we can paralyze any planned legislation that might limit our life-spans or our reproductive rights or anything else you can think of. Do you think we're going to sit still and let sanctimonious zealots like you interfere with our hard-won immortality?

JH: That's a very selfish attitude! What about all the people who aren't as rich as you and can't afford the treatment? What about all the people who can't get jobs because immortals like you never retire? What are you going to tell them?

WI: Same as I'm telling you, doc. Get a life!

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The search for immortality has been a long-term endeavor that humankind has pursued since the beginning of time. Philosophers, adventurers, and modern-day scientists have given their best efforts and mental energies to find "the key" or elixir that would allow many (or all) of us to share the "benefits" of this plateau of human existence. To achieve immortality seems to be a goal worthy of a society that sees itself at the pinnacle of development in comparison with its past history.

I believe that this "search for extended life-spans" (immortality) is not necessary at the moment or the foreseeable future. Why so, you might ask? Because the notion of mortality that every one of us carries through life is the engine that propels us to do our best to grow as better individuals. The certainty that life is short and time can't be wasted is and always will be the incentive for all the seekers of truth.

If humankind ever, by its own means, achieves this so-called "immortality," I'm sure that individuals will find that experience boring...even hateful.

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