

we can head off the possibility that synthesized genes could be used to cause harm. We do not find any value in resorting to science fiction fantasies to foment fear about the process of gene synthesis. In our view, this endangers the very industry that will generate important solutions for our present problems while obscuring the true threats to our security.

#### COMPETING INTERESTS STATEMENT

The authors declare competing financial interests: details accompany the full-text HTML version of the paper at <http://www.nature.com/naturebiotechnology/>.

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1. Nouri, A. & Chyba, C.F. *Nat. Biotechnol.* **27**, 234–236 (2009).
2. Czar, M.J., Anderson, J.C., Bader, J.S. & Peccoud, J. *Trends Biotechnol.* **27**, 63–72 (2009).
3. Hoover, D.M. & Lubkowski, J. *Nucleic Acids Res.* **30**, e43 (2002).
4. Xiong, A.S. *et al.* *Nat. Protoc.* **1**, 791–797 (2006).
5. Reisinger, S.J., Patel, K.G. & Santi, D.V. *Nat. Protoc.* **1**, 2596–2603 (2006).
6. Cello, J., Paul, A.V. & Wimmer, E. *Science* **297**, 1016–1018 (2002).
7. FitzGerald, D. & Pastan, I. *J. Natl. Cancer Inst.* **81**, 1455–1463 (1989).
8. Bügl, H. *et al.* *Nat. Biotechnol.* **25**, 627–629 (2007).
9. Song, L. *et al.* *PLoS One* **3**, e2257 (2008).

#### Chyba and Nouri reply:

Concerns about the possible misuse of gene synthesis in particular and biotech more generally are not “science fiction fantasies,” but rather a legitimate cause for concern. Attempts to address these concerns must be carefully balanced against the extremely important benefits that flow from these technologies, as we emphasize in the first paragraph of our Commentary<sup>1</sup>. The seriousness of the possible misuse of these technologies has been addressed by two National Academy of Sciences committees<sup>2,3</sup>, and in a workshop held by the Royal Society and the International Council for the Life Sciences<sup>4</sup>. (For full disclosure, one of us was a member of one of these Academy committees and a participant in the Royal Society workshop that led to the new report.)

Minshull and Wagner criticize our suggestions on three grounds: first, the “cat is already out of the bag” and “anyone who is sufficiently motivated” can already synthesize genes “or even an entire viral genome”; second, the requirement that legitimate users be able to readily bypass any controls will permit “hackers” to bypass these controls; and third, gene synthesis is “an unlikely tool for anyone considering harm” because there are so many other biological and conventional means to cause harm. We acknowledged these

objections but did not find them sufficient to mean that nothing should be done.

What is striking is that, despite their rhetoric, Minshull and Wagner obviously agree with us on this. They themselves summarize the controls that their companies, and others, have placed on gene synthesis, based on the select agent lists. They require official permits for certain genes to be produced or shipped. Moreover, they call upon governments in the United States and Europe to “require all makers of synthetic genes to screen” synthesis orders. So, in fact, there is no disagreement in principle between their viewpoint and ours; the difference exists in the specifics of its application.

There is no silver bullet that will somehow solve the security challenge of dual-use biotech. Rather, we must implement a web of measures, carefully calibrated so as not to impede legitimate and lifesaving research, that will make it more challenging—not render impossible—the casual or even dedicated misuse of this technology. The hope is that such misuse will be challenging enough that any individual or group contemplating it will choose an altogether different approach to doing harm. But were the technology to become both extremely easy to use and widely available, further steps might be required to help ensure these favorable outcomes.

We do not suggest that gene synthesis companies drop their controls; in fact in our Commentary we applauded the steps that have been taken. Our concern, rather, lies with a possible future—whose trajectory can already be discerned—in which automated DNA synthesis machines diffuse to a large number of users. In this case, additional proposals beyond those applicable to central providers must be considered. Our suggestions, like those implemented by Minshull and Wagner, build on the select agent list and, like theirs, would require some permit structure for the synthesis of especially dangerous sequences which, like theirs, introduces some vulnerability to misuse that must be managed. In effect, we simply recommend extending their practices to a new technology. Given their call for greater government requirements along these lines for their own industry, we are puzzled why they object to our suggestions.

1. Nouri, A. & Chyba, C.F. *Nat. Biotechnol.* **27**, 234–236 (2009).
2. National Research Council. *Biotechnology Research in an Age of Terrorism: Confronting the ‘Dual Use’ Dilemma* (National Academies Press, Washington, DC, 2003).
3. Committee on Advances in Technology and the Prevention of their Application to Next Generation Biowarfare Threats. *Globalization, Biosecurity, and the Future of the Life Sciences* (National Academies Press, Washington, DC, 2006).
4. Science Policy Centre. *New Approaches to Biological Risk Assessment* (The Royal Society, London, 2009).

## Commercialized GM crops and yield

#### To the Editor:

A News article in the July issue<sup>1</sup> brings up some important questions about our report, *Failure to Yield*, which analyzes the contribution of genetic engineering to increased food and feed production in the United States, and its potential for contributing to global food security. I would like to clarify some points by responding to some of the comments made by several researchers interviewed in the article.

We do not recommend that genetic engineering be scrapped in favor of conventional breeding—the main complaint of Jonathan Jones. We note in the executive summary: “Genetic engineers are working on new genes that may raise both intrinsic and operational

yield in the future, but their past track record for bringing new traits to market suggests caution in relying *too heavily* on their success” [emphasis added]<sup>2</sup>. We should favor methods that have been, and continue to be, more successful at increasing productivity, such as conventional and genomics-assisted breeding—this does not mean eliminating genetic engineering.

Our report relied heavily (but not exclusively) on US field trials to derive yield values for genetically engineered traits. Field trials allow the comparison of crop treatments, while holding other variables relatively constant. This allows the testing of the yield contribution of a transgene—which was a goal of our report. Field trials are conducted under ambient

