Regulatory regimes for transgenic crops

To the editor:

In presenting their justifications for reducing the regulatory burden on transgenic food crops (*Nat. Biotechnol.* **23**, 439–444, 2005), we feel that Strauss and colleagues significantly misrepresent the implications and rationale of our report *Genome Scrambling-Myth or Reality? Transformation-Induced Mutations in Transgenic Crop Plants*[1]. Unlike their characterization of our work, we did not specifically "argue for rejection if even a single base pair is changed." In full, our relevant recommendations were that "transgenic lines containing genomic alterations at the site of transgene insertions be rejected" and that "the insertion of superfluous DNA be considered unacceptable."

Leaving aside the fact that a single base pair change may result in serious phenotypic consequences, these recommendations are best viewed in context. As documented in the report, thorough analysis reveals that all particle bombardment transgene insertion events include extensive rearrangements or loss of host DNA as well as insertion of superfluous DNA. Furthermore, a large fraction of even apparently simple *Agrobacterium tumefaciens*–mediated transgene insertion events also result in large-scale host DNA rearrangement or deletion and superfluous DNA insertion[2]. For example, loss of 76 kbp of host DNA[3] and duplication/translocation of up to 40 kbp of host DNA have been reported at T-DNA insertion sites[4].

Widespread use of transgenic crops carrying insertion-site mutations of this magnitude will, in our opinion, lead sooner or later to harmful consequences. Nevertheless, detailed inspection has shown that mutations such as these would almost certainly pass unnoticed through both the molecular and phenotypic characterization stages of the regulatory systems of both the European Union and the United States[5–8].

We do agree with Strauss and colleagues that analysis of the phenotype is the one true measure of safety. However, rigorous assessment only at the phenotypic level is time consuming, expensive and, more importantly, of unproven effectiveness[9]. In this context, our recommendations for the detection and elimination of transformation-induced mutations from commercial crop plants are conceived as a straightforward and effective way to reduce the probability of unexpected deleterious phenotypes arising in transgenic crop plants and of protecting consumers and others from an unnecessary risk.

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To the editor:

In the April issue (*Nat. Biotechnol.* **23**, 439–444, 2005), Strauss and colleagues argue that the methods used to produce food crops should not be the focus of regulatory oversight, only the phenotypic traits of the resultant plants as defined in terms of standard agricultural practice. They propose that any risk and safety assessments of crops produced by genetic engineering (GE) should be based only upon the nature of the introduced genes. They also claim that transgenic crops face a "daunting" array of regulatory requirements. However, safety testing requirements in the United States are largely voluntary and in my view inadequate (for a review of regulations from my perspective, see ref. 1). Safety concerns related to the GE process itself as well as its unintended consequences are set aside by Strauss and colleagues as irrelevant, for they claim that the products of genetic events that occur naturally and with standard plant breeding techniques are fundamentally the same as those that occur with GE. Are these arguments a valid reflection of what is known about the precision and consequences of the GE process compared with naturally occurring genomic variation?

The basic assumption underlying the concept of a one-to-one relationship between the transgene and the resultant phenotype is that the GE process is relatively precise. However, none of the current transgene insertion techniques permits control over the location of the insertion site or the number and orientation of the genes inserted. Indeed, over one-third of all *Agrobacterium tumefaciens*–mediated insertion events disrupt functional DNA[2,3]. These and related transformation and cell culture–induced changes in chromosomal structure have been recently documented in great detail[4]. For example, translocations of up to 40 kb[5], scrambling of transgene and genomic DNA[6], large-scale deletions of over a dozen genes[7] and frequent random insertions of plasmid DNA[8] can all be caused by the procedures used to make transgenic plants. In fact, the most commonly used transformation procedure is sometimes itself