Traces of the emerald ash borer on the trunk of a dead ash tree in Michigan, USA. This non-native invasive insect from Asia threatens to kill most North American ash trees.

BIOTECHNOLOGY

Genetically engineered trees: Paralysis from good intentions

Forest crises demand regulation and certification reform

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Intensive genetic modification is a long-standing practice in agriculture, and, for some species, in woody plant horticulture and forestry (*1*). Current regulatory systems for genetically engineered crops, in which recombinant DNA is used to asexually insert or modify DNA, were created decades ago with good intentions for caution and forethought. Likewise, forest certification systems were created to promote responsible forest management and sustainable practices. However, both systems are at odds with the need for rapid and innovative biotechnologies to help forests cope with growing pest epidemics and mounting abiotic stresses as a result of global travel and climate change. As the U.S. government recently initiated an update of the Coordinated Framework for the Regulation of Biotechnology (*2*), now is an opportune time to consider foundational changes.

POLICY

Difficulties of conventional tree breeding make genetic engineering (GE) methods relatively more advantageous for forest trees than for annual crops (*3*). Obstacles include multiyear delays until onset of flowering, intolerance of inbreeding, and, as a consequence, introgression of genes from other species or populations is usually not possible in an acceptable time frame. GE methods improve on conventional breeding by enabling rapid modifications without shuffling the genotype during meiosis and without the maladaptation of early hybrids from wide crosses. GE could help in refining wood characteristics for specific products, responding to emerging pest problems (see the photo), adding high-value coproduct traits, improving growth, or accelerating adaptation to changing climates. It can also provide a means for strong containment of tree species when spread beyond plantations is problematic (*4*).

Although only a few forest tree species might be subject to GE in the foreseeable future, regulatory and market obstacles prevent most of these from even being subjects of translational laboratory research. There is also little commercial activity: Only two types of pest-resistant poplars are authorized for commercial use in small areas in China and two types of eucalypts, one approved in Brazil and another under lengthy review in the USA (*5*).

METHOD-FOCUSED AND MISGUIDED. Many high-level science reports state that the GE method is no more risky than conventional breeding, but regulations around the world essentially presume that GE is hazardous and requires strict containment during research and breeding (*6*). Regulatory systems in the EU and most other countries are focused almost exclusively on GE as a method. In the United States and Canada, regulations try to focus on trait novelty or use existing trait-associated authorities. In practice, however, the regulatory triggers have become predominantly method-based and have drifted far from the intent of their authorizing statutes. The U.S. Environmental Protection Agency (EPA) regulates pest-resistant genetically engineered plants as pesticide-producers even if they produce no novel or broadly toxic pesticides (and may regulate genetically engineered plants with genes that are simply growth regulators) (*7*). The U.S. Department of Agriculture uses plant pest sequences that, on their own, are of no conse-

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quence to plant pest risk or that use a former plant pathogen as a vector (now disarmed), as triggers for regulation. No GE regulatory system adequately accounts for the costs of not using a genetically engineered technology or product.

Most genetically engineered trees are scrutinized as any other genetically engineered crop would be by the regulatory system, and subject to strict, zero-tolerance isolation requirements: Regardless of genomic familiarity, trees are placed very far from wild, feral, or planted populations of interfertile species; a large area nearby is monitored for possible spread (e.g., many km^2); and trial trees generally must be cut down before flowering. To develop trees that can actually be used, long-term trials are needed in a variety of environments and genotypes (*7*), where trees will be grown normally—beyond onset of flowering and to a size that will make absolute containment of experimental populations infeasible.

GE can modify complex abiotic stress-tolerance traits in crops—in some cases, where conventional breeding has shown limited success (*8*). This is likely to require multiple gene modifications and extensive phenotypic screening for high levels of resistance without unacceptable pleiotropy—for which the regulatory focus on single insertion events, mostly studied in artificial, contained environments, is a barrier. Many gene combinations and events will need to be studied and tested in conjunction with conventional breeding, so that adding genetically engineered modifications does not unacceptably slow breeding progress. Containment of every event and gene combination over many years during breeding, followed by years of regulatory review before approval of every event of interest, is restrictive, costly, and opens developers to legal liabilities (*7*).

FAST-TRACK AND REGISTER. A better regulatory approach would give agencies legal authority to fast-track or exempt field research with a genetically modified product intended to provide options for existing or emerging forest health problems, or that have high genomic familiarity. Agencies could rapidly (e.g., in 60 days) perform a categorical assessment when a species, or its ecological function, may be threatened by a spreading pest. This should be a presumptive, categorical exemption when intragenic, homologous, gene-edited, or otherwise functionally familiar genes are used, whose benefits and risks are similar to those of conventional breeding.

In the United States, EPA might take the regulatory lead, with the possible benefit of embedding decisions based on the National Environmental Policy Act in the overall risk assessment of the product rather than having a separate environmental impact statement. This would create stronger authority for future mitigation because of the ongoing registration and renewal process already in place for such products. In contrast to current EPA timing and demands for data, it would need to be more rapid and nimble, with most data generated along the way in an adaptive management framework and opportunities for legal challenges greatly narrowed, especially at the research stage. EPA should categorically exempt plant-incorporated protectants that do not produce broadly toxic pesticides, e.g., genetically engineered plants with genes that induce RNA interference or the various R-genes that trigger natural response pathways.

Environmental risk assessments of forest trees also need reconsideration, given the time required and the constraints to doing ecologically relevant field studies (i.e., complete containment). Such studies often become irrelevant as soon as they are produced owing to ongoing "no-analog" changes to ecosystem structure as a result of climate change (*9*) or introduced insects or diseases. Major changes in the rules and, possibly, new legislation are required.

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We are not suggesting separate regulations for genetically engineered trees. Fundamental regulatory reforms for all crops, discussed for years (*6*, *10*), are needed. In addition to the reforms discussed above, changes should focus on the novelty of functional traits compared with conventional breeding rather than on GE methods. A more realistic and responsive approach would include (i) best management practices rather than strict legal limits for dispersal from most types of research trials; (ii) globally recognized and workable tolerances for adventitious presence during research and commercial use (to avoid costly trade problems due to biologically trivial levels of adventitious presence); and (iii) exemptions for familiar markers and genetic modifications, which are usually more precise and less disruptive than conventional breeding.

A revised system might also require organisms modified using any GE method to be registered before use in the environment—to facilitate detection for trade or market certification and to ensure that they are not missed by regulatory agencies should they pose unanticipated hazards. Registration, however, should not preclude exemptions or accelerated review pathways based on trait and/or genomic familiarity or urgency.

MARKET REFORM. Regulatory processes are not the only obstacles to GE tree research and breeding. All major "sustainable certification" systems prevalent in forestry and forest products preclude use of genetically engineered trees in certified forests (*11*). Although the reason given is often a lack of data, legally authorized research is also not allowed on certified land (*12*). This signals to forest companies that investments in GE are risky and makes GE field research more difficult and costly. A cautious approach was perhaps warranted when GE tree research was nascent. But the Forest Stewardship Council first put in place genetically engineered tree preclusion in 1999; there have since been hundreds of scientific studies, many of them field tests, and none has shown the categorical risks once feared (*13*). A product-not-process approach seems appropriate.

Despite confidence from the majority of scientists, there is public concern over genetically engineered crops and their safety. However, public attitudes vary widely among GE applications (*14*); views toward forest health and genomically familiar applications are likely to be received most favorably. Nonetheless, stakeholder dialogue will be required for change.

It would be prudent and precautionary to ensure that GE tools are available to address urgent forest health and productivity problems. Regulatory agencies and certification systems should reconsider the foundations for their policies, refocusing on trait novelty and need, not method. ■

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