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Pursuant to the notice found at 72 Fed. Reg. 39021 (July 17, 2007), the Center for Food Safety ("CFS") provides the following comments on the USDA, Animal and Plant Health Inspection Service's ("APHIS") Draft Programmatic Environmental Impact Statement for the Introduction of Genetically Engineered Organisms. CFS is a non-profit, membership organization that works to protect human health and the environment by curbing the proliferation of harmful food production technologies and by promoting organic and other forms of sustainable agriculture. *See* generally http://www.centerforfoodsafety.org. CFS and its True Food Network represent over 50,000 members of the public.

**Introduction**

The United States government's regulatory oversight of genetically engineered crops in the United States has been a dismal failure. Millions of acres of these crops have been planted, yet the environmental and health consequences of this widespread planting have not been studied. After these crops are commercialized, USDA asserts no regulatory authority and conducts no study or analysis of the human health, environmental and economic effects of the large-scale introduction of genetically engineered crops. Moreover, as thousands of genetically engineered crops continue to be tested on open fields, it has become apparent that USDA's regulatory oversight and enforcement have provided inadequate containment of these crops and analysis of their impacts.

Since the widespread commercialization of the first genetically engineered crops began over ten years ago, the face of agriculture has changed dramatically. Organic agricultural production now

ranks as the fastest growing segment of U.S. agriculture.[1] The federal regulations governing such production and processing are complete. *See* 7 C.F.R. Part 205. The consumer recognition and market growth of organic agriculture has occurred in part because it explicitly excludes the method of genetic engineering as an acceptable agriculture practice. *See e.g.* 7 C.F.R. §205.105(e). Despite the rise of organic agriculture and other significant changes in U.S. agriculture, rather remarkably this is the first Environmental Impact Statement (EIS) that a federal agency has ever undertaken on its regulation of genetically engineered crops. Unfortunately, the Draft Programmatic EIS ("PEIS" or "DEIS") produced by APHIS is fatally flawed; it fails to consider or adequately analyze the environmental and health issues raised by the original introduction of genetically engineered crops and the continued use and adoption of these crops. It provides no analysis of the impacts of these crops on U.S. agriculture.

APHIS begins with biased assumptions about the positive benefits of genetically engineered crops that are not based in empirical evidence. APHIS claims that agricultural biotechnology has "the potential to benefit agriculture, the environment, human health, the U.S. economy." (PEIS, p. 1). APHIS also includes a section entitled "Positive Impacts," but fails to provide a corresponding discussion of the adverse impacts that have occurred. (PEIS, p. 129-130). This foundational assumption ignores numerous key impacts that have been associated with widespread planting of genetically engineered crops and colors the agency's unwillingness to create a much stricter regulatory regime.

APHIS is obligated to consider the environmental effects of its action even if there are some benefits. 40 C.F.R. § 1508.8 (environmental "[e]ffects may also include those resulting from actions which may have both beneficial and detrimental effects, even if on balance the agency believes the effects will be beneficial"). For example, as discussed in more detail below, the widespread use of genetically engineered crops has accelerated the evolution of herbicide-resistant weeds that present a great threat to U.S. farmers.

The country's widespread use of genetically engineered crops has also substantially impacted the country's ability to export certain food crops. Market losses have already arisen for growers of genetically engineered crops.[2] Unapproved genetically engineered crops found in US agricultural commodities results in severe losses. When the US corn supply was contaminated with unapproved genetically engineered StarLink corn, exports suffered. For example, US corn

[1] In the 1990's, organic agriculture was one of the fastest growing segments of US agriculture with total organic cropland production doubling between 1992 and 1997 to approximately 850,000 acres. (Catherine Greene & Thomas Dobbs, *Organic Wheat Production in the United States: Expanding Markets and Supplies*, Wheat Yearbook 31 (2001)). It doubled again between 1997 and 2001. (USDA, *Data Organic Production, available* at http://www.ers.usda.gov/Data/Organic/ (last visited Oct. 18, 2005)). Organic product sales through all outlets in the US have increased 20-25 percent annually between 1990 and 2000, and reached $7.8 billion in 2000. (Catherine Greene and Thomas Dobbs, note 85, at 31-32.)

[2] Pew Initiative on Food and Biotechnology, US v. EU: An Examination of the Trade Issues Surrounding Genetically Modified Food 3-5 (August 2003).

sales to Japan decreased up to 44% the following year as Japan turned to other sources.[3] More losses are expected due to the LLRICE601 contamination of long-grain rice supplies.[4] Importantly, losses result even from genetically engineered crops that have been deregulated in the US. The market for US products softens because certain markets have not approved a crop or because it is not accepted by consumers. For example, the European Union's concern about genetically engineered corn has caused U.S. exporters to lose about $300 million per year.[5] And the failure to contain genetically engineered material from crops has sparked concerns over human exposure to novel allergens[6] and proteins designed for controlled use as drugs.[7]

In fact, the USDA Inspector General ("IG") recently found numerous shortcomings in the agency's oversight of biotechnology. The IG audited APHIS's oversight of both the notification and permitting processes for genetically engineered crops and found that "weaknesses in APHIS regulations and internal management controls increase the risk that regulated genetically engineered organisms (GEO) will inadvertently persist in the environment before they are deemed safe to grow without regulation." (Office of the Inspector General, USDA, Audit Report: Animal and Plant Health Inspection Service Controls Over Issuance of Genetically Engineered Organism Release Permits, p. i, (2005) (*available at* http://www.usda.gov/oig/webdocs/50601-08-TE.pdf, last visited September 6, 2007) ("APHIS Audit"). In this audit, the Inspector General found that APHIS's notification and permitting procedures were extremely deficient and did not provide sufficient oversight. For example, planting locations were often unknown (*Id*. at 14); field inspections, necessary to "ensure that planted GE crops do not persist in the environment," were grossly inadequate (*Id*. at 27); and field test progress reports, necessary to track environmental impacts, were inadequate. (*Id*. at 35).

The IG is not alone in its criticism of the USDA's oversight process. In 2002, the National Academy of Sciences ("NAS") found numerous shortcomings with the agency's regulatory oversight of genetically engineered crops. NATIONAL RESEARCH COUNCIL, ENVIRONMENTAL EFFECTS OF TRANSGENIC PLANT, NATIONAL ACADEMY PRESS, 2002 ("NRC 2002"). The NAS found, among other things, that the current regulatory program fails to cover all GE crops. It only covers GE crops that contain genetic material from a designated plant pest. Inadequacies noted by the NAS committee include failure to conduct environmental assessments (EA) prior to

[3] Hur, *US Corn Exports to Japan Hit Hard by StarLink*, Reuters (Aug. 31, 2001).
[4] Estimates suggest that farmers lost about $150 million on Aug. 21 and Aug. 22 alone due to the LLRICE601 contamination. David Bennett, *Questions Abound as Rice Industry Faces GMO Concerns*, Delta Farm Press (Aug. 30, 2006).
[5] Pew Initiative on Food and Biotechnology, US v. EU: An Examination of the Trade Issues Surrounding Genetically Modified Food (2005) at 3-4.
[6] "Assessment of Additional Scientific Information Concerning StarLink Corn," Environmental Protection Agency's Scientific Advisory Panel, SAP Report No. 2001-09, from meeting held July 17-18, 2001. Available at: http://www.epa.gov/scipoly/sap/meetings/2001/july/julyfinal.pdf.
[7] Toner, M. (2002). "Alarms sound over 'biopharming' – tainted crops cast doubt on gene altering," The Atlanta Journal and Constitution, Nov. 17, 2002.

most field trials; deficiencies in those EAs that are conducted; mis-regulation of plants producing potentially toxic compounds under the streamlined notification procedure; lack of transparency and too little public participation in decision-making process; excessive claims of confidential business information by companies, hampering public review and input; lack of external scientific peer review of APHIS decisions; scientific deficiencies in decision documents; lack of adequate enforcement in the field, including failure to inspect neighboring fields for contamination to determine whether gene containment is working; poorly trained personnel; and lack of post-deregulation authority.

Numerous other reviews of the APHIS system have also found shortcomings. Several reports have exposed the failure of the agency to have post-market authority, allowing the growing of commercial quantities of some genetically engineered plants under the notification system, and failing to establish a clear regulatory oversight program for genetically engineered animals. *See* Pew Initiative on Food and Biotechnology, *Post-Market Oversight of Biotech Foods: Is the System Prepared* (2003), *available at* http://pewagbiotech.org/research/postmarket/ (last visited September 6, 2007); Pew Initiative on Food and Biotechnology, *Issues in the Regulation of Genetically Engineered Plants and Animals* (2004), *available at* http://pewagbiotech.org/research/regulation/ (last visited September 6, 2007). Other reports have discussed flaws in USDA's oversight system and how it impacts the quality of the seed supply and exposes our food supply to novel contaminants. *See* Union of Concerned Scientists, *Gone to Seed: Transgenic Contaminants in the Traditional Seed Supply* (2004), *available at* http://www.ucsusa.org/assets/documents/food_and_environment/seedreport_fullreport.pdf (last visited September 6, 2007); Union of Concern Scientists, *A Growing Concern: Protecting the Food Supply in an Era of Pharmaceutical and Industrial Crops* (2004), *available at* http://www.ucsusa.org/assets/documents/food_and_environment/Pharma_fullreport.pdf (last visited September 6, 2007). Still others have pointed out serious shortcomings in USDA's process for assessing the impacts of gene flow from field trials. Center for Food Safety, *Contaminating the Wild? Gene Flow from Experimental Field Trials of Genetically Engineered Crops to Related Wild Plants* (2006), *available at* http://www.centerforfoodsafety.org/pubs/Contaminating_the_Wild_Report.pdf (last visited September 11, 2007). And still others have pointed to the uneven (and most often inadequate) regulatory oversight provided by state officials under the current APHIS system. Pew Initiative on Food and Biotechnology, *Tending the Fields: State and Federal Roles in the Oversight of Genetically Modified Crops* (2004), *available at* http://pewagbiotech.org/research/fields/report.pdf (last visited September 6, 2007).

USDA's statements that its regulations should be revised "to ensure a high level of environmental protection" and "to create regulatory processes that are transparent to stakeholders and the public" are laudable. (PEIS, p. 1). However, many of the agency's preferred proposals will actually deregulate or significantly weaken current regulations that have not served to ensure a high level of environmental protection and have failed to provide the public and stakeholders with a transparent process. For example, the agency now claims that because of its familiarity with certain genetically engineered traits, less regulation is appropriate. However, a Federal District Court in the Northern District of California, just this year held that APHIS improperly

deregulated Roundup Ready alfalfa because it failed to conduct an adequate environmental review. *Geertson Seed Farms, et al. v. Johanns*, 2007 WL 518624 (N.D. Cal. Feb. 13, 2007), appeal docketed, Nos. 07-16458, 07-16492 (9th Cir. 2007). The court required APHIS to conduct an Environmental Impact Statement on a Roundup Ready crop, with which APHIS is familiar. *Id*. Despite APHIS' familiarity with this Roundy Ready crop, the federal court found the necessity for more environmental analysis, not less, as APHIS proposes.

Furthermore, APHIS' stated goal "to ensure that the level of oversight is commensurate with risk" is fundamentally flawed and based on incorrect assumptions concerning the strength of APHIS' regulatory program rather than empirical evidence. (PEIS, p.1). APHIS' system allows the commercialization of genetically engineered crops without any post-commercialization study. As a consequence, the environmental effects of the widespread planting of commercialized crops is in many cases unknown, and has not been systematically studied.

Finally, the Center for Food Safety and the Union of Concerned Scientists, two organizations that have long histories of working on issues related to the regulation of genetically engineered crops, both requested extensions of the sixty-day comment period. These requests were motivated by the large volume of material and the important nature of the proposed changes. Although both groups are intimately familiar with the issues presented, it was readily apparent that more time was needed for comprehensive review and analysis.[8] Despite its claim of wanting to produce a regulatory system that is transparent to the public, APHIS denied the extension request. APHIS would prefer to merely give lip service to transparency that fundamentally involves meaningful public participation. By denying the request for extension, APHIS demonstrates that it is more interested in streamlining its process rather than allowing public interest stakeholders to fully evaluate and meaningfully participate in policy-making.

## APHIS PROGRAMMATIC EIS FAILS TO ADEQUATELY ANALYZE FORESEEABLE ENVIRONMENTAL EFFECTS:

An EIS must discuss 'reasonably foreseeable' impacts. 40 C.F.R. § 1502.22. Section 1502.22(b)(4) provides that "'reasonably foreseeable' includes impacts which have catastrophic consequences, even if their probability of occurrence is low, provided that the analysis of the impacts is supported by credible scientific evidence, is not based on pure conjecture, and is within the rule of reason." *See also No GWEN Alliance of Lane County, Inc. v. Aldridge*, 855 F.2d 1380, 1386 n.1 (9th Cir. 1988).

### APHIS Must Assess HT Crop Systems for Weed Resistance Threat

APHIS has not adequately analyzed the environmental effects of weed resistance resulting from transgenic herbicide-tolerant (HT) crop systems. An herbicide-tolerant crop system comprises an herbicide-tolerant crop and associated use of the herbicide that the crop is specifically

[8] In addition, the comment period ran during the summer months, a typical time for vacations.

engineered to tolerate.[9]

In the DEIS, APHIS inexplicably makes no reference to a single glyphosate-resistant weed population in the U.S. Instead, it cites only decade-old reports of glyphosate-resistant ryegrass populations in Australia (DEIS, p. 120). Rather than analyze up to date information on glyphosate-resistant weeds, APHIS ignores the galloping course of glyphosate-resistant weed development on millions of acres of American cropland that has occurred in the last decade.[10]

While weed scientists universally acknowledge that the Roundup Ready crop system has fostered rapid development of glyphosate-resistant weeds on millions of acres of cropland, APHIS turns a blind eye to these facts and instead cites studies – again, from the mid 1990s – that ***predict*** slow development of glyphosate resistant weeds (DEIS, p. 120). These predictions – in studies published in 1993 and 1997 – were made before Roundup Ready ("RR") crops were (widely) planted, and thus were necessarily made in the absence of the current empirical data that demonstrates that RR crop systems foster rapid development of glyphosate-resistant weeds.

Moreover, the DEIS does not discuss a significant use it could make of its noxious weed authority. This would be to assess, and regulate, transgenic herbicide-tolerant (HT) crop systems as noxious weed risks. An herbicide-tolerant crop system comprises an herbicide-tolerant crop and associated use of the herbicide that the crop is specifically engineered to tolerate. As explained *infra*, APHIS cannot meaningfully address the noxious weed risks posed by HT crops without considering them as part of such a crop system.

While judicious use of HT crop systems may offer benefits to growers and American agriculture, their present excessive and unregulated use poses a serious and growing threat. HT crop systems have two serious and inter-related impacts: they foster more rapid development of herbicide-resistant (HR) weeds, and greater use of detrimental weed control methods to kill them. Increased use of toxic herbicides to control resistant weeds has adverse environmental and public health impacts.

APHIS has previously refused to provide any meaningful assessment of HT crop systems. A recent federal district court ruling vacated APHIS's decision to deregulate (approve for commercial cultivation) Monsanto's herbicide-tolerant, Roundup Ready alfalfa. *Geertson Seed Farm*, 2007 WL 518624 (N.D. Cal.). The court's decision means that APHIS will be required to

[9] The concept of "HT crop system" is borrowed from Monsanto, which describes its latest HT soybean in these terms: "The utilization of Roundup agricultural herbicides plus Roundup Ready soybean, collectively referred to as the Roundup Ready soybean system…" From: "Petition for the Determination of Nonregulated Status for Roundup Ready2Yield™ Soybean MON 89788," submitted to USDA by Monsanto on June 27, 2006 (revised November 3, 2006), APHIS Docket No. APHIS-2006-0195, p. 4).

[10] APHIS is well aware of this issue. CFS and others have repeatedly alerted APHIS to the threat of glyphosate-resistant weeds in detailed formal comments on various APHIS decision documents, and has supplemented the comments with numerous scientific and farm press articles documenting the problem.

prepare an environmental impact statement ("EIS") if Monsanto wishes to re-introduce Roundup Ready alfalfa commercially. The court's decision requires APHIS to consider, in the context of an EIS, the potential harm from transfer of the HT trait from Roundup Ready alfalfa to conventional or organic alfalfa. *Id*. at 9.

"For those farmers who choose to grow non-genetically engineered alfalfa, the possibility that their crops will be infected with the engineered gene is tantamount to the elimination of all alfalfa; they cannot grow their chosen crop." … "A federal action that eliminates a farmer's choice to grow non-genetically engineered crops, or a consumers' choice to eat non-genetically engineered food, is an undesirable consequence." *Id*.

The court's decision also requires APHIS to consider, in the context of the EIS, the impacts of commercial introduction of the Roundup Ready alfalfa system on the development of herbicide-resistant weeds. When confronted with the issue of Roundup resistance in the GE alfalfa context, APHIS "found that such a possible impact nevertheless does not warrant the preparation of an EIS because weed species often develop resistance to herbicides and the agricultural community is addressing the issues." *Id*. The court found APHIS' "cavalier response" to be unconvincing, stating that such rationale "is tantamount to concluding that because this environmental impact has occurred in other contexts it cannot be significant." *Id.* The Court also rejected APHIS' argument that "good stewardship" may be the only defense to herbicide-resistant weeds. *Id*. The court required APHIS to address how to in fact ameliorate this problem in its environmental review so that farmers in the real world can engage in practices to address the issue. *Id*.

Finally, the court held that APHIS must consider cumulative impacts of the Roundup Ready alfalfa system in combination with other Roundup Ready crop systems that have already received commercial approval and are widely planted across the country.

The court noted "that it is unclear from the record whether any federal agency is considering the cumulative impact of the introduction of so many glyphosate resistant crops; one would expect that some federal agency is considering whether there is some risk to engineering all of America's crops to include the gene that confers resistance to glyphosate." *Id*. at 11.

This decision sets a precedent for future APHIS decision-making with respect to HT crop systems. APHIS must assess the impacts of HT crop systems with respect to HT trait transfer, development of HR weeds from increased selection pressure, as well as cumulative impacts in future decisions regarding HT crop systems.

**USDA Has Officially Recognized the Need for Management of Resistant Weeds Fostered by HT Crop Systems, But Failed to Act**

In 2001, USDA and EPA set up an interagency work group to develop management programs to forestall or manage the emergence of herbicide-resistant weeds fostered by HT crop systems. 67 Fed. Reg. 60934 (Sept. 27, 2002). The formation of this work group represents official USDA

recognition of the fact that herbicide-resistant weeds are a serious issue that needs to be addressed in assessments of HT crop systems. Despite the formation of this work group, there is no indication that EPA was ever consulted on these issues. As the Court stated in the recent GE alfalfa case: "one would expect that some federal agency is considering whether there is some risk to engineering all of America's crops to include the gene that confers tolerance to glyphosate." *Geertson Seed Farms*, 2007 WL 518624 at 11. However, there is no evidence to suggest that USDA has made any such assessment, or taken any action, to manage development of HR weeds fostered by any pesticide-promoting HT crop system.

**Prevalence of HT Crop Systems: Present and Future**

APHIS needs to analyze both the current state of use of HT crops systems and the impacts of these regulations on its use. HT crops comprise by far the largest class of GE crops, by several measures. Crops with HT traits comprised 81% of commercial GE crop acreage worldwide in 2006,[11] or 4 of every 5 acres. Four HT crops – soybeans, corn, cotton and canola – are commercially planted in the U.S. In 2006, HT soybeans comprised 89% of all soybeans grown in the U.S.; HT corn 36% of all corn;[12] HT cotton 86% of all cotton;[13] and in 2003, HT canola comprised over 75% of all canola.[14] Some of the HT corn and most of the HT cotton is stacked with one or more insect-resistance traits. Herbicide tolerance and/or insect resistance are virtually the only traits found in commercially-grown GE crops.

The vast majority (roughly 99%) of commercially grown HT plants are Monsanto's Roundup Ready crops, tolerant to the herbicide glyphosate, which were planted on over 114 million acres in 2006,[15] an area larger than the state of California. The remaining 1% are Bayer's LibertyLink crops, tolerant to the herbicide glufosinate.[16] There are virtually no commercially-grown

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[11] ISAAA 2006. "Global Status of Commercialized Biotech/GM Crops," Highlights of ISAAA Brief No. 35, International Service for the Acquisition of Agri-Biotech Applications. http://www.isaaa.org/Resources/Publications/briefs/35/highlights/pdf/Brief%2035%20-%20Highlights.pdf.
Crops with HT alone = 68%, HT stacked with insect-resistance = 13%

[12] "Adoption of Genetically Engineered Crops in the U.S.," USDA Economic Research Service. See: http://www.ers.usda.gov/Data/BiotechCrops/alltables.xls. Last visited Sept. 10, 2007. USDA AMS has more reliable data on HT cotton (see next footnote).

[13] USDA AMS (2006). "Cotton Varieties Planted: 2006 Crop," U.S. Dept. of Agriculture, Agricultural Marketing Service, Cotton Program, August 2006. http://www.ams.usda.gov/cottonrpts/MNXLS/mp_cn833.xls.

[14] Cerdeira, A.L. and S.O. Duke (2006). "The current status and environmental impacts of glyphosate-resistant crops: a review," *J. Environ. Quality* 35:1633-1658.

15 Based on Monsanto's latest figures at: "Monsanto biotechnology trait acreage: fiscal years 1996 to 2006," updated October 11, 2006. http://www.monsanto.com/pdf/pubs/2006/Q42006Acreage.pdf.

[16] See Freese, B. (2007). "Cotton Concentration Report: An Assessment of Monsanto's Proposed Acquisition of Delta and Pine Land," ICTA/CTA, February 2007, Section 3.6.2, footnote 31, available at http://www.centerforfoodsafety.org/pubs/CFS-CTA%20Monsanto-DPL%20Merger%20Report%20Public%20Release%20-%20Final%20_2_.pdf (last visited

transgenic HT crops tolerant to any other herbicide.

HT crop acreage, particularly acres planted to glyphosate-tolerant crops, will expand greatly in the near future. Most importantly, Roundup Ready corn adoption has been increasing dramatically in recent years, more than quadrupling from 7.8 to 32.7 million acres from 2002 to 2006. Sugar beet growers have announced their intention to begin growing glyphosate-tolerant sugar beets next year.[17] In addition, five of 11 GE crops being considered for deregulation (i.e. commercial approval) as of August 2, 2007 were herbicide-tolerant.[18] All five of these crops are tolerant to glyphosate; two of the five each have dual tolerance to glyphosate and one other herbicide.

Field trial permit figures are the best prognosticator of longer-term trends in GE crop development. 36.3% of active field trial permits for GE crops involve an HT trait.[19] We note that this 36.3% figure slightly exceeds the historical proportion of GE crop field tests that involve the HT trait, cited by APHIS as "nearly one-third" (DEIS, p. 119). This indicates continued strong interest in the development of new HT crops.

The 352 active permits for field trials of HT crops encompass 18 different plant species and tolerance to more than eight different herbicides. Glyphosate-tolerance is by far the most common HT trait in field tests, though others, especially crops tolerant to dicamba herbicide, are also being extensively tested.[20]

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[17] "Biotech beets gaining approval," Associated Press, August 22, 2007.

[18] See USDA's website "Petitions of Nonregulated Status Granted or Pending as of August 2, 2007" at http://www.aphis.usda.gov/brs/not_reg.html. Last visited on August 23, 2007.

[19] As of August 23, 2007, 352 of 970 active permits (36.3%) involved an HT trait. Some permits involve multiple traits. Information obtained from USDA's website "Field Test Release Applications in the U.S." at http://www.isb.vt.edu/cfdocs/fieldtests1.cfm. For total number of active permits, select "Date/Range" box. On the next page, select "Field Test Permits Currently in Effect" and "Full Record," then "Create Excel File." To arrive at the total number of active permits, it is necessary to delete entries with "Denied" or "Withdrawn" under the "Status" column. For total number of active permits involving HT, go to the original screen and select "Phenotype Category." On next page, select "Herbicide Tolerance (HT)" and "Field Test Permits Currently in Effect" and "Full Record," then "Create Excel File." Delete "Denied" and "Withdrawn" entries as above. Figures current as of August 23, 2007. Note that figures will change as new field test permit applications are received and as permits lapse and become inactive.

[20] Glyphosate-tolerance represents 62% of HT crop field tests, while tolerance to dicamba, or dicamba and glyphosate, represent another 11%. In 18% of HT crop field tests, the herbicide to which the crop is tolerant is considered "confidential business information," or is simply not reported, so there may well be more than eight different HT traits in development. On dicamba-tolerant crops, see also Behrens et al (2007). "Dicamba Resistance: Enlarging and Preserving Biotechnology-Based Weed Management Strategies," *Science*, 1185-1188, May 25, 2007.

In summary, both the present and future of transgenic agriculture are overwhelmingly dominated by herbicide-tolerant crops, and in particular by crops that tolerate the herbicide glyphosate.

HT crop systems can generate or foster the more rapid development of HR weeds via two major mechanisms:

I. Selection of naturally herbicide-resistant weeds due to the increased selection pressure from greater and more frequent use of the herbicide to which the HT crop is tolerant;

II. Transfer of the HT trait to sexually-compatible relatives, either commercial cultivars or weedy species, via pollen flow or pollen flow in combination with seed dispersal.

We first discuss selection for herbicide-resistant weeds.

## HR Weeds From Increased Selection Pressure on HT Crop Systems

### Factors That Foster Development of Herbicide-Resistant Weeds

Weeds resistant to an herbicide such as glyphosate can emerge via two different mechanisms. First, frequent and extensive use of a particular herbicide tends to select for the rare individual plants of a particular weed species that naturally possess genetic resistance to the herbicide. Given the chance to reproduce, the number of resistant individuals increases as their susceptible brethren are killed off, and over time the genetically resistant plants form a larger and larger percentage of the weed population. Secondly, frequent and extensive use of a particular herbicide can also cause weed shifts. Weed shifts occur when populations of a weed species with greater natural resistance to a particular herbicide gradually supplant populations of other weed species with lesser resistance. In either case, herbicide-resistant weeds are a growing and costly problem for American farmers.

Factors that promote development of herbicide-resistant weeds include:

1) **Frequency of natural resistance:** More frequent occurrence of natural resistance to the herbicide in individuals of a particular weed species, or greater natural resistance in the weed species as a whole;
2) **Selection pressure:** Frequent and extensive use of a particular herbicide, which increases the "selection pressure" for resistant weeds or resistant weed species;
3) **Overreliance:** Excessive reliance on a particular herbicide to the exclusion of other weed control methods, including other herbicides; and
4) **Delayed application:** The longer a weed is allowed to grow, the harder it is to kill, and the more likely it is to reproduce. Delaying application of an herbicide increases the potential for weeds, including resistant individuals, to survive and propagate.

### Facets of the HT Crop System that Foster Rapid Development of HR Weeds

Herbicide tolerance permits the HT plant to survive application of a single herbicide that would otherwise kill the [non-biotech] plant. Herbicide tolerance thus allows "over-the-top" application of the herbicide to more easily kill nearby weeds without killing or severely injuring the plant itself. "Over-the-top" is one form of "post-emergence" herbicide application, or

spraying after the crop seed has "emerged" or sprouted. The alternative herbicide regime more common with conventional, non-HT varieties is called "pre-emergence." That is, an herbicide that retains its activity for weeks is applied to the soil before the crop actually sprouts so as to suppress "weed competition" in the critical early life of the plant. Pre-emergence herbicides are also used, though to a lesser extent, with HT crops. HT crops permit greater flexibility in the timing of herbicide applications, allow for herbicide use over a greater portion of the life of the plant, and in general simplify weed management by reducing the number of different weed killers applied. The chief advantages cited for HT crops are convenience and the ability to cover more acres (i.e. reduced labor inputs per acre),[21] both of which are of particular value to larger farmers.[22]

HT crop systems facilitate more rapid development of HR weeds versus conventional crops in three of the four ways cited above. The HT crop's tolerance to a particular herbicide ensures that that herbicide will be used more frequently than it would be with a corresponding conventional crop. This is because: a) only the herbicide the HT crop is engineered to tolerate can be applied "over-the-top" without fear of damaging the crop itself, leading farmers to apply it in preference to other herbicides; and b) herbicide-tolerance greatly widens the "application window" for that herbicide, facilitating repeated applications of the herbicide through part or all of the crop's life span. The ability to apply the herbicide through part or all of the crop's life span also facilitates delayed application, which allows weeds to grow larger, increasing the chances that resistant weeds will survive to reproduce and propagate. HT crops are specifically engineered to facilitate simplified weed control that relies primarily on the single herbicide to which the crop is tolerant, leading to overreliance on that herbicide (DEIS, p. 119). The substantial price premium (technology fee) a farmer pays for HT crop seed offers a further inducement to make use of its engineered property through increased reliance on the herbicide to which the crop is tolerant. Finally, the growing trend to plant different HT crops tolerant to the same herbicide "in rotation" (e.g. corn following soy) increases selection pressure for resistant weeds over longer time spans.

Below, we present empirical evidence supporting each of these arguments for glyphosate-tolerant crops. It is impossible to make any generalizations regarding frequency of natural resistance, which varies according to the weed species and the herbicide in question.

**The Emergence of Glyphosate-Resistant Weeds with Glyphosate-Tolerant Crop Systems**

Monsanto first introduced glyphosate in the U.S. in 1976,[23] and for two decades it was used primarily to control weeds in orchards. There were no reports of glyphosate-resistant weeds over

[21] Duffy, M. (2001). "Who Benefits from Biotechnology," presentation at the American Seed Trade Association Meeting, Chicago, Ill., Dec. 5-7, 2001. http://www.leopold.iastate.edu/pubs/speech/files/120501-who_benefits_from_biotechnology.pdf

[22] Benbrook, C. (2005). "Rust, resistance, run down soils, and rising costs: problems facing soybean producers in Argentina," AgBioTech InfoNet, Technical Paper No. 8, Jan. 2005. http://www.aidenvironment.org/soy/08_rust_resistance_run_down_soils.pdf

[23] Monsanto (2007). Monsanto History, last accessed 1/31/07. See http://www.monsanto.com/monsanto/layout/about_us/timeline/default.asp

these two decades. The first glyphosate-resistant weed populations in the U.S. (rigid ryegrass) were found in almond orchards. In 1998, glyphosate-resistant rigid ryegrass was reported to infest from 11 to 50 sites covering 1,001 to 10,000 acres in California.[24] Glyphosate use increased dramatically with the introduction of Monsanto's Roundup Ready soybeans in 1995, Roundup Ready cotton and canola in 1997, and Roundup Ready corn in 1998.[25] Serious concern over glyphosate-resistant weeds was reported in 2001:

> "Resistance to glyphosate (Roundup) is emerging all around the world, potentially jeopardizing the 2.5 billion dollar market for genetically modified herbicide tolerant crops"[26]

Scientists who identified the first glyphosate-resistant weed (horseweed) in Delaware in 2000 attributed their evolution to the continuous planting of Roundup Ready crops.[27] Ten prominent weed scientists confirmed this assessment in 2004:

> "It is well known that glyphosate-resistant horseweed (also known as marestail) populations have been selected in Roundup Ready soybean and cotton cropping systems. Resistance was first reported in Delaware in 2000, a mere 5 years after the introduction of Roundup Ready soybean. Since that initial report, glyphosate-resistant horseweed is now reported in 12 states and is estimated to affect 1.5 million acres in Tennessee alone."

It is estimated that glyphosate-resistant weeds now infest over 3,000 sites in 17 states.[28] Multiple populations of 8 different weed species have developed resistance since the year 2000: Palmer amaranth, common waterhemp, common ragweed, giant ragweed, horseweed, Italian ryegrass, rigid ryegrass and hairy fleabane.[29] Other weeds developing resistance to glyphosate

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[24] Weed Science Society of America, see http://www.weedscience.org/Case/Case.asp?ResistID=1034 (last visited Sept. 9, 2007).

[25] Monsanto (2007). Monsanto History, *see supra*, note 23.

[26] Farmers Weekly (2001). "Glyphosate resistance is showing a worldwide rise," *Farmers Weekly*, Nov. 23, 2001. http://www.connectotel.com/gmfood/fw231101.txt, (last visited Sept. 9, 2007).

[27] "Herbicide-resistant Weed Identified in First State," University of Delaware press release, February 22, 2001, online at http://www.rec.udel.edu/weed_sci/weedfacts/marestail_resistance.htm (last visited Sept. 9, 2007).

[28] Compiled from data on glyphosate-resistant weeds at Weed Science Society of America, at: http://www.weedscience.org/Summary/UspeciesMOA.asp?lstMOAID=12&FmHRACGroup=Go (last visited Sept. 9, 2007).

[29] http://www.weedscience.org/Summary/UspeciesMOA.asp?lstMOAID=12&FmHRACGroup=Go (last visited Sept. 9, 2007).

or becoming more prevalent due to glyphosate-induced weed shifts, include velvetleaf,[30] cocklebur and lambsquarters,[31] morning glories,[32] and tropical spiderwort.[33] Johnson grass, as well as annual grasses such as goosegrass (confirmed glyphosate-resistant biotypes in Malaysia), foxtails, crowfootgrass, signal grasses, panicums, and crabgrasses, all have a history of developing resistance to multiple herbicides,[34] making development of glyphosate-resistance more likely in these species.

While glyphosate-resistant weeds are worst in the South and East, they are rapidly spreading throughout the Midwest. Missouri is now home to populations of at least three confirmed glyphosate-resistant weeds – common waterhemp, common ragweed and horseweed – and glyphosate-resistant horseweed was confirmed in Nebraska in 2006. ***A survey of farmers in the Midwest found that 24% of farmers in the northern Midwest and 29% in the south say they have glyphosate-resistant weeds.***[35] Weed experts in the Midwest are predicting further spread of glyphosate-resistant weeds in their states. For instance, Michael Owen, agronomist at Iowa State University, is concerned that with over 90% of soybeans in Iowa planted to Roundup Ready varieties, the rapid adoption of Roundup Ready corn will lead to "an increasing number of crop acres where glyphosate will follow glyphosate" in the popular corn-soybean rotation,[36] vastly increasing selection pressure for glyphosate-resistant weeds (see below). Owen's concerns about the increasing use of RR corn are borne out by the facts. Acreage planted to Roundup Ready corn is growing at an extremely rapid clip, from just 7.8 million acres in 2002 to 24.8 million acres in 2005, to 32.7 million acres in 2006,[37] or more than a four-fold increase in just four years.

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[30] Owen, M.D.K. (1997). North American Developments in Herbicide-Tolerant Crops. Proceedings of the British Crop Protection Conference, Brighton, UK, BCPC: Brighton, UK. 3:955–963.

[31] Roberson, R. (2006). "Pigweed not only threat to glyphosate resistance," Southeast Farm Press, Oct. 19, 2006.

[32] UGA (2004). "Morning glories creeping their way around popular herbicide, new UGA research reports," University of Georgia, August 23, 2004.

[33] USDA ARS (2004). "Little-known weed causing big trouble in Southeast," USDA ARS News Service, August 24, 2004. The spread of tropical spiderwort resistant to glyphosate, particularly in Georgia, is associated with the dramatic increase in Roundup Ready cotton acreage in recent years.

[34] Robinson, E. (2005). "Will weed shifts hurt glyphosate's effectiveness?" Delta Farm Press, Feb. 16, 2005.

[35] Service, R.F. (2007). "A growing threat down on the farm," *Science*, May 25, 2007, pp. 1114-1117.

[36] Owen, M.D.K. (2005). "Update 2005 on Herbicide Resistant Weeds and Weed Population Shifts," 2005 Integrated Crop Management Conference, Iowa State University.

[37] "Monsanto biotechnology trait acreage: fiscal years 1996 to 2006," updated Oct. 11, 2006, available at http://www.monsanto.com/pdf/pubs/2006/Q42006Acreage.pdf (last visited Sept. 9, 2007).

In the DEIS, APHIS inexplicably makes no reference to a single glyphosate-resistant weed population in the U.S. Instead, it cites only decade-old reports of glyphosate-resistant ryegrass populations in Australia (DEIS, p. 120). Rather than analyze up to date information on glyphosate-resistant weeds, APHIS ignores of the galloping course of glyphosate-resistant weed development on millions of acres of American cropland that has occurred in the last decade.

While weed scientists universally acknowledge that the Roundup Ready crop system has fostered rapid development of glyphosate-resistant weeds on millions of acres of cropland, APHIS turns a blind eye to these facts and instead cites studies – again, from the mid 1990s – that ***predict*** slow development of glyphosate resistant weeds (DEIS, p. 120). These predictions – in studies published in 1993 and 1997 – were made before Roundup Ready crops were (widely) planted, and thus were of necessity made in the absence of the empirical data we now have demonstrating that RR crop systems foster rapid development of glyphosate-resistant weeds. The predictions were based on the presumed rarity of natural glyphosate resistance in weed populations. According to a 2005 farm press article quoting leading weed scientists, including Stanley Culpepper of the University of Georgia:

> "The frequency of resistance to glyphosate is unknown but thought to be very low. In that regard, one might assume the potential for resistance to glyphosate is low. And, until recently, that was the prevailing opinion among weed scientists. ***The situation changed, however, with the wide-spread adoption of Roundup Ready technology.*** According to Culpepper, one must also consider the frequency of use. ***"The extensive use of glyphosate on multiple crops certainly increases the risk of resistance evolution.***" (emphasis added)[38]

In other words, no matter how rare natural resistance to glyphosate is among weed populations, that resistance has been amplified due to the tremendous selection pressure exerted by "the extensive use of glyphosate on multiple crops." In fact, the apparent rarity of natural glyphosate resistance in weeds means that greater selection pressure is required to select for (i.e. foster the development of) resistant weeds than would be the case if natural resistance were less prevalent. Thus, the ***fact*** of rapid glyphosate-resistant weed development speaks directly to the tremendous selection pressure exerted by Roundup Ready crop systems, in the form of the increased extent and frequency of glyphosate application, together with overreliance on glyphosate to the exclusion of other weed control methods.

Striking evidence of farmers' overreliance on glyphosate to the exclusion of other weed control methods is provided by a recent survey of 400 farmers in the U.S. Midwest conducted by Syngenta. The researchers found that ***56% of soybean growers in northern states and 42% in southern states use glyphosate as their sole herbicide***. As a result, says USDA plant physiologist Stephen Duke: "the selective pressure for weeds to develop resistance has been

[38] Yancy, C.H. (2005). "Weed scientists develop plan to combat glyphosate resistance," *Southeast Farm Press*, June 1, 2005, available at http://southeastfarmpress.com/mag/farming_weed_scientists_develop/ (last visited Sept. 9, 2007).

huge."[39] The author of a study cited by USDA concurs: "the selection pressure imposed by extensive and exclusive glyphosate use will ***undoubtedly*** result in an increasing frequency of reports of glyphosate-resistant weed biotypes."[40] (emphasis added).

USDA recognizes, but fails to assess this important aspect of HT crop systems. USDA at once states that HT crop systems promote "simpler weed management strategies based on fewer herbicides," but then acknowledges that this "advantage" leads to a serious problem: "overreliance on fewer weed-management strategies will result in the evolution of resistance to the more useful herbicides or population shifts to naturally resistant weed species" (DEIS, p. 119).

USDA's failure to assess and as necessary regulate HT crop systems is no minor lapse. Agronomist Stephen Powles of the Western Australian Herbicide Resistance Initiative states: ***"Glyphosate is as important to world agriculture as penicillin is to human health."***[41] North Carolina weed scientist Alan York has glyphosate-resistant weeds "potentially the worst threat [to cotton] since the boll weevil," the devastating pest that virtually ended cotton-growing in the U.S. until an intensive spraying program eradicated it in some states in the late 1970s and early 1980s.[42] York concedes that: "Resistance is not unique with glyphosate," but goes on to state that: ***"What makes glyphosate resistance so important is our level of dependence on glyphosate***" (emphasis added).[43] Weed scientists report that there are no new herbicides with different "modes of action" on the horizon. Thus, the loss of glyphosate as an effective means of weed control poses serious problems for U.S. agriculture.[44]

**Glyphosate-Tolerant Crop Systems Have Led to Increased Herbicide Use**

**1) Increased Use of Glyphosate**

Glyphosate-tolerant crops have dramatically increased glyphosate use by all measures – number of acres treated, amount applied, as well as frequency and rate of application.

[39] Service, R.F. (2007). "A growing threat down on the farm," *Science*, May 25, 2007, pp. 1114-1117.

[40] Young, B.G. (2006). "Changes in herbicide use patterns and production practices resulting from glyphosate-resistant crops," *Weed Technology* 20: 301-307. Young (2006) is cited at DEIS, p. 119, but APHIS missed this finding.

[41] Service, R.F. (2007). "A growing threat down on the farm," *Science*, May 25, 2007, pp. 1114-1117.

[42] Minor, E. (2006). "Herbicide-resistant weed worries farmers," *Associated Press*, 12/18/06. http://www.enn.com/top_stories/article/5679 (last visited Sept. 9, 2007).

[43] Yancy, C. (2005). "Weed scientists develop plan to combat glyphosate resistance," Southeast Farm Press, June 3, 2005.

[44] Roberson, R. (2006). "Pigweed not only threat to glyphosate resistance," *Southeast Farm Press*, October 19, 2006. http://southeastfarmpress.com/news/101906-herbicide-resistance/

The number of acres treated with glyphosate is reflected in RR crop adoption figures, since glyphosate is invariably applied to RR crops. As noted above, RR crops were planted on over 114 million acres in 2006.

Overall glyphosate use in American agriculture has jumped 10-fold from just 1995 to present,[45] tracking the dramatic rise in RR crop acreage. The amount of glyphosate applied to cotton climbed 753% from 1992 to 2002.[46] The introduction in 2006 of Roundup Ready Flex cotton, which tolerates twice the application rate of original RR cotton and also permits glyphosate application throughout the cotton plant's growing season,[47] promises to lead to continued increases in glyphosate use on cotton. In 2006, 91.886 million lbs of glyphosate were applied to soybeans alone, an astounding 42% increase from the previous year. Glyphosate use on corn has also increased rapidly, rising more than seven-fold from 3.3 million lbs in 2002 to 23.9 million lbs. in 2005, the latest year for which USDA statistics are available.[48]

Both the number and rate of glyphosate applications have also increased. From just 2002 to 2006, annual glyphosate applications to soybeans increased by a substantial 24%, from 1.07 to 1.33 lbs/acre.[49] Glyphosate use on corn has risen even more rapidly, from 0.71 lbs/acre in 2002 to 0.96 lbs/acre in 2005, a 32% rise in just three years.[50]

**2) Increased Use of Other Herbicides**

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[45] Service, R.F. (2007). "A growing threat down on the farm," *Science*, May 25, 2007, pp. 1114-1117.

[46] Steckel, L., S. Culpepper and K. Smith (2006). "The Impact of Glyphosate-Resistant Horseweed and Pigweed on Cotton Weed Management and Costs," Power Point presentation at Cotton Incorporated's "Crop Management Seminar," Memphis, 2006. http://www.cottoninc.com/CropManagementSeminar2006/SeminarProceedings/images/Steckle%20Larry.pdf

[47] Bennett, D. (2005). "A look at Roundup Ready Flex cotton," *Delta Farm Press*, 2/24/05, http://deltafarmpress.com/news/050224-roundup-flex/.

[48] USDA NASS (2007). "Agricultural Chemical Usage: 2006 Field Crops Summary," National Agricultural Statistics Service, U.S. Dept. of Agriculture, May 2007. http://www.nass.usda.gov/Publications/Todays_Reports/reports/agcs0507.pdf; USDA NASS (2006). "Agricultural Chemical Usage: 2005 Field Crops Summary," National Agricultural Statistics Service, U.S. Dept. of Agriculture, May 2006. http://usda.mannlib.cornell.edu/usda/nass/AgriChemUsFC//2000s/2006/AgriChemUsFC-05-17-2006.pdf; USDA NASS (2003). "Agricultural Chemical Usage: 2002 Field Crops Summary," National Agricultural Statistics Service, U.S. Dept. of Agriculture, May 2003. http://usda.mannlib.cornell.edu/usda/nass/AgriChemUsFC//2000s/2003/AgriChemUsFC-05-14-2003.pdf

[49] From an average 1.4 applications of 0.74 lbs. glyphosate per acre in 2002 to an average 1.7 applications of 0.80 lbs./acre in 2006. See USDA NASS reports cited in last footnote.

[50] From an average 1.1 applications of 0.64 pounds per acre in 2002 to 1.3 applications of 0.73 lbs./acre in 2005. See USDA NASS reports cited above.

Since a major feature of HT crop systems is reliance on the single herbicide to which the HT crop is tolerant, one would expect declining use of other weed control methods, including other herbicides. However, the facts do not bear out this expectation. In an exhaustive analysis of USDA data, Charles Benbrook, former head of the Board on Agriculture of the National Academy of Sciences, has demonstrated that the widespread adoption of Roundup Ready crops has increased ***overall herbicide use*** by 138 million lbs. from 1996-2004.[51] Interestingly, Roundup Ready crops slightly reduced herbicide use from 1996-1999, before increased reliance on glyphosate as the near-exclusive weed control method spurred a dramatic rise in glyphosate-resistant weed populations, which in turn has driven accelerating use of both glyphosate and other herbicides since the year 2000.

USDA turns a blind eye to this development, noting merely that "there are methods, such as crop rotation, to minimize the development of herbicide-tolerant weeds…" (DEIS at 120). The Programmatic EIS is defective because it fails to analyze this development. USDA ignores two of the most common methods that extension agents and Monsanto recommend for minimizing resistance: abandoning no-till farming, and the use of an herbicide cocktail, including suggestions for using older herbicides with high environmental toxicity that HT crop systems were supposed to supplant. Examples of such recommendations include:

As early as 2002, Ohio State Extension experts recommended using 2,4-D plus metribuzin plus paraquat as pre-emergence chemicals to control glyphosate-resistant marestail in RR soy.[52] In the same year, Syngenta recommended growers use a number of chemicals, including AAtrex®, Bicep®, DoublePlay®, Dual® MAGNUM, Gramoxone® Max, Princep®, atrazine and metribuzin, with their Roundup Ready soy, cotton and corn crops.[53]

In August 2005, reports of resistant horseweed in California prompted Monsanto to recommend that farmers should "use other chemicals" along with Roundup on their Roundup Ready crops. In addition to adding other herbicides, University of California researchers suggested tillage to control weeds.[54] In September 2005, reports of glyphosate-resistant Palmer amaranth in Georgia cotton fields prompted Monsanto to recommend that farmers use several additional herbicides with Roundup, including Prowl (pendimethalin), metolachlor, diuron and others. The company also suggested that farmers planting any RR crops use pre-emergence residual

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[51] Benbrook, C. (2004). "Genetically Engineered Crops and Pesticide Use in the United States: The First Nine Years," AgBioTech InfoNet, Technical Paper No. 7, Oct. 2004. http://www.biotech-info.net/technicalpaper7.html.

[52] Mark Loux, and Jeff Stachler, "Is There a Marestail Problem in Your Future?" O.S.U. Extension Specialist, Weed Science, 2002.

[53] Syngenta Announces Guidelines To Prevent Weed Resistance To Glyphosate Herbicides, press release,
Greensboro, N.C., February 25, 2002, online at http://www.syngentacropprotection-us.com/media/article.asp?article_id=199

[54] Juliana Barbassa, "Attack of the 12-foot horse weed: Herbicide-resistant strains plague California farmers." Associated Press, August 10, 2005, online at http://lists.ifas.ufl.edu/cgi-bin/wa.exe?A2=ind0508&L=sanet-mg&P=6738

herbicides in addition to Roundup.[55] In the same year, weed scientists in Tennessee noted that Palmer amaranth in the state survived applications of up to 44 ounces per acre of Roundup, and so recommended that farmers use additional herbicides such as Clarity, 2,4-D, Gramoxone Max or Ignite.[56]

In October 2005, reports of glyphosate-resistant weeds in Roundup Ready corn and soybeans prompted Monsanto to recommend using cultivation and additional herbicides, including Harness Extra, Degree Extra, Intrro, Prowl, Valor, and 2,4-D. Weed scientists also suggested using Lasso, Dual, Diuron, Gramoxone, Ignite, Suprend, Direx or MSMA, and noted that weed problems were so severe that herbicides such as Direx, Cotoran and Caporal were in short supply at retailers.[57]

In June 2006, reports of widespread populations of lambsquarters that were not controlled even with application of up to 48 oz per acre of Roundup prompted Iowa State University experts to recommend farmers use additional applications of Roundup and/or other chemicals, including Harmony GT, Ultra Blazer, and/or Phoenix herbicides.[58] Also in 2006, it was reported that farmers would rely increasingly on older herbicides such as paraquat and 2,4-D to control glyphosate-resistant weeds.[59]

In 2007, resistant weeds prompted Monsanto to recommend that farmers use tillage and apply a pre-emergence herbicide in combination with Roundup. Monsanto also noted that it would pay for an additional application of Roundup if growers still experienced weed problems after using a pre-emergence herbicide.[60] By 2007, the American Soybean Association was advocating that farmers return to multiple-herbicide weed control systems on their Roundup Ready soybeans.[61]

Finally, over-reliance on Roundup Ready crops and glyphosate has dampened research into new herbicides, meaning none are on the horizon.[62]

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[55] "Investigation Confirms Case Of Glyphosate-Resistant Palmer Pigweed In Georgia." Monsanto press release, September 13, 2005

[56] "Glyphosate-resistant Palmer Pigweed Found in West Tennessee." Farm Progress, staff report, September 23, 2005.

[57] Andrew Burchett, "Glyphosate Resistant Weeds," Farm Journal, October 4, 2005.

[58] Michael Owen, "Large common lambsquarters is a problem for glyphosate." Iowa State University Extension Agronomy, June 15, 2006, online at http://www.weeds.iastate.edu/mgmt/2006/Largecommonlambsquarters.htm

[59] Roberson (2006), *see supra*, note 31.

[60] Henderson & Wenzel (2007). "War of the Weeds," Agweb.com, Feb. 16, 2007. http://www.agweb.com/Get_Article.aspx?sigcat=farmjournal&pageid=134469.

[61] Tom Sellen, "Herbicide-Resistant Weeds Force Change In Agriculture." Dow Jones, February 7, 2007, online at http://www.cattlenetwork.com/content.asp?contentid=104080

[62] Mueller, T.C., P.D. Mitchell, B.G. Young and A.S. Culpepper (2005). "Proactive versus reactive management of glyphosate-resistant or –tolerant weeds," *Weed Technology* 19:924-933; Yancy, C.H. (2005). "Weed scientists develop plan to combat glyphosate resistance," *Southeast*

USDA statistics on herbicide use demonstrate that farmers are in fact using both more glyphosate (see above) as well as increased amounts of other herbicides. For instance, 2,4-D is the second most-heavily used herbicide on soybeans (after glyphosate). From 2002 to 2006, while glyphosate use on soybeans increased by an astounding 28 million lbs (44% rise), 2,4-D use on soybeans more than doubled from 1.35 to 3.53 million lbs (a 129% increase). Clearly, glyphosate is not displacing 2,4-D.[63]

Atrazine is the most heavily applied herbicide on corn, followed by acetochlor and S-metolachlor/metolachlor. At the same time that glyphosate use on corn climbed seven-fold from 2002 to 2006, atrazine use rose by nearly 22 million lbs. (60% increase), applications of acetochlor increased by over 7 million lbs (32% rise), and the amount of (S-)metolachlor applied rose by nearly 9 million lbs (52% increase).[64] Clearly, glyphosate is not displacing use of the top three corn herbicides, but rather all four herbicides are being applied in substantially increased quantities. Such increased herbicide use constitutes a significant environmental impact that must be addressed in the PEIS.

**HT Crop Systems Can Adversely Impact the Interests of Agriculture**

**1) Increased soil erosion from mechanical tillage to control resistant weeds**

The 1990s saw a huge shift in soybean cultivation practices. From 1990-1996, farmers' use of soil-conserving conservation tillage practices increased from 25% to 60% of soybean acreage.[65] This massive shift largely pre-dated the introduction of Roundup Ready crops.[66] The following three years, from 1997 to 1999, saw a slight decline in conservation tillage acres in soybeans, though it remained near the 60% level.[67] The rise of glyphosate-resistant weeds is beginning to reverse this trend. For instance, weed scientists from California have advised farmers to use tillage with their RR soybeans to control glyphosate-resistant weeds.[68] Press reports also state

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*Farm Press*, June 1, 2005. http://southeastfarmpress.com/mag/farming_weed_scientists_develop/.

[63] See USDA NASS "Agricultural Chemical Usage: Field Crop Summary" reports cited above for the appropriate year.

[64] See USDA NASS "Agricultural Chemical Usage: Field Crop Summary" reports cited above for the appropriate year.

[65] Fernandez-Cornejo, J. and W.D. McBride (2002). "Adoption of Bioengineered Crops," U.S. Dept. of Agriculture, Economic Research Service, Agricultural Economic Report No. 810, May 2002. http://www.ers.usda.gov/publications/aer810/aer810.pdf. See Figure 11 on p. 29 for percentage of soybean acres grown with conservation tillage from 1990-1999.

[66] The first Roundup Ready crop, RR soybeans, was introduced in 1995. In 1996, just 10% of US soy acreage was planted to RR soy.

[67] Fernandez-Cornejo & McBride (2002), *see supra*, note 65.

[68] Juliana Barbassa, "Attack of the 12-foot horse weed: Herbicide-resistant strains plague California farmers." Associated Press, August 10, 2005, online at http://lists.ifas.ufl.edu/cgi-bin/wa.exe?A2=ind0508&L=sanet-mg&P=6738

that Monsanto advises farmers to use tillage with their RR soy.[69] Other experts also recommend that farmers use tillage to control glyphosate-resistant weeds.[70]

Aside from these recommendations, weed scientists have already documented increased use of tillage to control glyphosate-resistant weeds. For instance, acreage under conservation tillage in Tennessee dropped by 18% in 2004, as farmers turned back to the plow to control glyphosate-resistant horseweed; Tennessee counties with the largest cotton acreage experienced the largest decline in conservation tillage, from 80% to just 40%.[71] It is estimated that resistant horseweed has reduced the area under conservation tillage in Arkansas by 15%, with similar trends reported in Missouri and Mississippi. *Id*.

These reductions in conservation tillage due to glyphosate-resistant weeds will increase soil erosion. As glyphosate-resistant weeds continue their rapid spread, the use of tillage to control these weeds will become still more common, increasing soil erosion still more.

**2) Increased production costs from resistant weeds**

As weed resistance increases, costs of weed control will also rise. APHIS must take this economic effect into account. 40 C.F.R. § 1508.8.

a) Increased expenditures on herbicides

An Arkansas weed scientist estimated that Arkansas growers would have to spend as much as $9 million to combat glyphosate-resistant horseweed in 2004.[72] The alternative is even more expensive. Left unchecked, horseweed can reduce cotton yields by 40-70%. Larry Steckel, weed scientist at the University of Tennessee, estimates that on average, glyphosate-resistant pigweed will cost cotton growers in the South an extra $40 or more per acre to control.[73] This represents a substantial burden, as cotton farmers' average expenditure on ***all*** pesticides (insecticides and herbicides) was $61 per acre in 2005.[74]

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[69] Henderson & Wenzel (2007). "War of the Weeds," Agweb.com, Feb. 16, 2007. http://www.agweb.com/Get_Article.aspx?sigcat=farmjournal&pageid=134469.

[70] Andrew Burchett, "Glyphosate Resistant Weeds," Farm Journal, October 4, 2005.

[71] Steckel, L., S. Culpepper and K. Smith (2006). "The Impact of Glyphosate-Resistant Horseweed and Pigweed on Cotton Weed Management and Costs," Power Point presentation at Cotton Incorporated's "Crop Management Seminar," Memphis, 2006. http://www.cottoninc.com/CropManagementSeminar2006/SeminarProceedings/images/Steckle%20Larry.pdf

[72] AP (2003). "Weed could cost farmers millions to fight," *Associated Press*, 6/4/03, http://www.biotech-info.net/millions_to_fight.html

[73] Laws, F. (2006). "Glyphosate-resistant weeds more burden to growers' pocketbooks," *Delta Farm Press*, November 27, 2006, http://deltafarmpress.com/news/061127-glyphosate-weeds/

[74] USDA ERS (2007b). Cost and return data for cotton production: 1997-2005. USDA Economic Research Service, last accessed January 12, 1997. http://www.ers.usda.gov/data/CostsandReturns/data/recent/Cott/R-USCott.xls

b) Other production cost increases

In 2006, Monsanto introduced a "second generation" Roundup Ready cotton known as Roundup Ready (RR) Flex. RR Flex is engineered to withstand application of roughly twice as much Roundup as first generation RR cotton, and to permit application throughout the growing season, rather than only in the early growth stages as with original RR.[75] RR Flex is a clear response to the glyphosate-resistant weed problem, which is driving growers to apply more glyphosate and to apply it more frequently. Producers who adopt RR Flex cotton in the hopes of better controlling resistant weeds will not only pay for more glyphosate, but also spend roughly 40% more for RR Flex.[76]

Since growers of RR crops are spraying Roundup more frequently to control resistant weeds, their fuel expenditures for tractor operation will increase. Those who are driven to use mechanical tillage for control of resistant weeds will likewise expend more on fuel. In particularly bad cases of glyphosate-resistant pigweed in Georgia, the necessity of hand-weeding can cost growers $92 an acre.[77]

c) Potential for decreased yield and other losses

In Georgia, where glyphosate-resistant Palmer amaranth has been confirmed in 48 fields of Roundup Ready cotton, the resistant weed took over some fields, and the cotton had to be cut down, rather than harvested, according to University of Georgia weed scientist Stanley Culpepper.[78] Palmer amaranth can damage cotton pickers, the machines that pluck cotton from the cotton bolls.

Arkansas extension agent Mike Hamilton estimates that an uncontrolled outbreak of glyphosate-resistant horseweed in his state has the potential to cost Arkansas cotton and soybean producers nearly $500 million in losses, based on projected loss in yield of 50% in 900,000 acres of Arkansas cotton and a 25% yield loss in the over 3 million acres of Arkansas soybeans.[79]

**3) Glyphosate Use Linked to Plant Disease, Mineral Deficiencies and Reduced Yield**

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[75] Bennett, D. (2005). "A look at Roundup Ready Flex cotton," *Delta Farm Press*, 2/24/05, http://deltafarmpress.com/news/050224-roundup-flex/.

[76] Jones, M.A. (2006). "Cotton Cultivar Evaluation & Performance in the Southeast," presentation at the 2006 Cotton Inc. Crop Management Seminar, by Michael A. Jones, Ph.D, Cotton Specialist, Clemson University, 2006. http://www.cottoninc.com/CropManagementSeminar2006/SeminarProceedings/images/3_1340_%20Michael%20A.%20Jones.pdf, slide 34.

[77] Laws (2006), op. cit.

[78] Minor, E. (2006). "Herbicide-resistant weed worries farmers," *Associated Press*, 12/18/06. available at http://www.enn.com/top_stories/article/5679 (last visited Sept. 9, 2007).

[79] James, L. (2005). "Resistant weeds could be costly," Delta Farm Press, July 21, 2005.

As documented above, overall glyphosate use in the U.S. has increased ten-fold since 1995,[80] due largely to the widespread introduction of Roundup Ready soybeans and cotton, and more recently the growing adoption of Roundup Ready corn.[81] RR versions of these crops are increasingly grown in rotation, meaning that each year, more prime cropland is sprayed more frequently with glyphosate, with increasing rates applied in many areas to control resistant weeds. While glyphosate is generally regarded as less toxic than many weed killers, a growing body of research suggests that continual use of this chemical may make RR plants more susceptible to disease and prone to mineral deficiencies than conventional crops, as well as reducing their yields. In addition, recent studies suggest that Roundup is much more toxic to amphibians than previously thought.

When Roundup is sprayed on RR crops, much of the herbicide ends up on the surface of the soil, where it is degraded by microorganisms. However, some is absorbed by the plant and distributed throughout its tissues. Small amounts of glyphosate "leak" from the roots of RR plants and spread throughout the surrounding soil.[82] This root zone is home to diverse soil organisms, such as bacteria and fungi, that play critical roles in plant health and disease; and it is also where the roots absorb essential nutrients from the soil, often with the help of microorganisms.

The presence of glyphosate in the root zone of RR crops can have several effects. First, it promotes the growth of certain plant disease organisms that reside in the soil, such as *Fusarium* fungi.[83] Even non-RR crops planted in fields previously treated with glyphosate are more likely to be damaged by fungal diseases such as Fusarium head blight, as has been demonstrated with wheat in Canada.[84] This research suggests that glyphosate has long-term effects that persist even after its use has been discontinued. Second, glyphosate can alter the community of soil microorganisms, interfering with the plant's absorption of important nutrients. For instance, glyphosate's toxicity to nitrogen-fixing bacteria in the soil can depress the absorption of nitrogen

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[80] Service, R.F. (2007). "A growing threat down on the farm," *Science*, May 25, 2007, pp. 1114-1117.

[81] "Monsanto biotechnology trait acreage: fiscal years 1996 to 2006," updated Oct. 11, 2006. http://www.monsanto.com/pdf/pubs/2006/Q42006Acreage.pdf (last visited Sept. 9, 2007).

[82] Motavalli, P.P. et al. (2004). "Impact of genetically modified crops and their management on soil microbially mediated plant nutrient transformations," *J. Environ. Qual.* 33:816-824; Kremer, R.J. et al. (2005). "Glyphosate affects soybean root exudation and rhizosphere microorganisms," *International J. Analytical Environ. Chem.* 85:1165-1174; Neumann, G. et al. (2006). "Relevance of glyphosate transfer to non-target plants via the rhizosphere," *Journal of Plant Diseases and Protection* 20:963-969.

[83] Kremer et al (2005), op. cit.

[84] Fernandez, M.R., F. Selles, D. Gehl, R. M. DePauw and R.P. Zentner (2005). "Crop production factors associated with Fusarium Head Blight in spring wheat in Eastern Saskatchewan," *Crop Science* 45:1908-1916. http://crop.scijournals.org/cgi/content/abstract/45/5/1908.

by RR soybeans under certain conditions, such as water deficiency, and thereby reduce yield.[85] Some scientists believe that this and other nutrient-robbing effects may account for the roughly 6% lower yields of RR versus conventional soybeans.[86]

Other research shows that Roundup Ready crops themselves are less efficient at taking up essential minerals such as manganese through their roots,[87] and that glyphosate inside plant tissues can make such minerals unavailable to the plant.[88] The resultant mineral deficiencies have been implicated in various problems, from increased disease susceptibility to inhibition of photosynthesis.

**Sexual Transmission of Herbicide Tolerance Traits**

Herbicide-tolerant and other GE crops also pose an environmental risk due to the potential for transfer of their traits. This has already been found by the court in *Geertson et al*., "[f]or those farmers who choose to grow non-genetically engineered alfalfa, the possibility that their crops will be infected with the engineered gene is tantamount to the elimination of all alfalfa; they cannot grow their chosen crop . . . A federal action that eliminates a farmer's choice to grow non-genetically engineered crops, or a consumers' choice to eat non-genetically engineered food, is an undesirable consequence." *Geertson et al.*, 2007 WL 518624 at 9.

These are more than theoretical concerns. HT traits have in fact transferred to conventional/organic crops and weedy relatives via cross-pollination, posing the potential for environmental harm, and harming the interests of farmers whose crops become contaminated. As the court held in the GE alfalfa case, "contamination of organic and conventional alfalfa crops with the generically engineered gene has occurred and defendants [APHIS] acknowledge as much." *Id. at* 6. Additionally, gene flow was found in the recent glyphosate-resistant creeping bentgrass case. *Intl. Ctr. for Tech. Assessment v. Johanns*, 473 F. Supp. 2d 9, 15-17 (D.D.C. 2007). From these two cases decided in this year alone, it is clear that biological contamination from gene flow has happened, is a real threat that will happen again, and that APHIS consistently has failed to address the issue through NEPA review or in the real world through effective mitigation measures.

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[85] King, A.C., L.C. Purcell and E.D. Vories (2001). "Plant growth and nitrogenase activity of glyphosate-tolerant soybean in response to foliar glyphosate applications," *Agronomy Journal* 93:179-186.

[86] Benbrook, C. (2001). "Troubled Times Amid Commercial Success for Roundup Ready Soybeans:
Glyphosate Efficacy is Slipping and Unstable Transgene Expression Erodes Plant Defenses and Yields," AgBioTech InfoNet Technical Paper No. 4, May 2001. http://www.biotech-info.net/troubledtimes.html.

[87] Gordon, B. (2006). "Manganese nutrition of glyphosate-resistant and conventional soybeans," in: Great Plains Soil Fertility Conference Proceedings, Denver, CO, March 7-8, p. 224-226.

[88] Bernards, M.L. et al (2005). "Glyphosate interaction with manganese in tank mixtures and its effect on glyphosate absorption and translocation," *Weed Science* 53: 787-794.

**Herbicide-Tolerant Canola**

Volunteer canola plants tolerant to one, two and even three herbicides are emerging as a serious weed problem in the Prairie Provinces of Canada.[89] These plants are generated by crosses between canola plants tolerant to one of either glyphosate, glufosinate or imidazolinone (the former two generated by rDNA, the latter by mutagenesis). A 1999 study by Agriculture Canada recorded stacking of HT genes in volunteers in all 11 locations studied where Roundup Ready and Liberty Link canola were grown in adjoining fields.[90] According to plant scientist Martin Entz, "The GM canola has, in fact, spread much more rapidly than we thought it could." [91]

HT trait stacking can occur through cross-pollination between crop-crop, crop-volunteer, or even volunteer-volunteer, which occurs at large distances with canola via wind and insect. Canola gene flow is exacerbated by seed dispersal. Seeds are not only left in the field after harvest, they can be accidentally spread on farm machinery, through seed spillage, and perhaps even inside animals that consume them (i.e. undigested seeds excreted in cattle manure. *Id.*

Related weed species provide another avenue for gene flow. In one study, field mustard (*B. rapa* L.) was planted adjacent to three HT canola varieties.[92] Seed from the field mustard plots were collected and planted. After one year, 5.9%, 7.6% and 17.2% of the morphologically identified canola-mustard hybrids were resistant to glufosinate, glyphosate and imazamox, respectively. Fifteen percent of the resistant hybrids were self-compatible. When these single-herbicide-tolerant hybrids were each backcrossed to canola resistant to a different herbicide, 11.9% of the resulting seeds, on average, were tolerant to two herbicides. This demonstrates the potential for related weed species to act as a "genetic bridge" or reservoir for subsequent passage of a transgenic trait back to cultivars, resulting in HT trait stacking.

While canola and related weeds with stacked herbicide tolerance can still be killed with other herbicides, this can mean additional expense for farmers from extra herbicide applications,[93] or the use of more toxic herbicides such as 2,4-D.[94] The spread of canola HT traits has had a substantial negative economic impact on Canadian canola growers. Smyth et al (2002) report that the organic canola industry has been essentially destroyed due to HT trait spread to organic

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[89] "Elements of Precaution: Recommendations for the Regulation of Food Biotechnology in Canada," An Expert Panel Report on the Future of Food Biotechnology, The Royal Society of Canada, p. 122, available at http://www.rsc.ca//files/publications/expert_panels/foodbiotechnology/GMreportEN.pdf (last visited Sept. 9, 2007).

[90] Beckie, H.J., Hall, L.M., Warwick, S.I. (2001). "Impact of herbicide-resistant crops as weeds in Canada," *Proceedings of the Brighton Crop Protection Conference – Weeds*, pp. 135-42.

[91] "Genetically modified canola becoming a weed," CBC News Online, June 22, 2002.

[92] Reddy, S. (2002). "Gene Flow and Accumulation Between Herbicide Resistant Canola (Brassica napus L.) and a Related Weed Species (B. rapa L.), available http://www.ag.uidaho.edu/brassica/thesis-abstract/SR-ABS.pdf (last visited Sept. 9, 2007).

[93] "Regulators worry about volunteer GM crops," by Barry Wilson, The Western Producer, January 2, 2003.

[94] "A new breed of superweed," by Gillian Steward, The Toronto Globe and Mail, June 15, 2000.

cultivars.[95] They estimate conservatively that this lost market was worth $100,000 to $200,000, but acknowledge that the opportunity cost is much greater, given the organic market's great potential for growth, and the 100% premium over conventional canola, before HT trait contamination destroyed it. This example shows the potential for unregulated cultivation of GE crops to adversely impact "the interests of agriculture."

[95] Smyth et al (2002). "Liabilities and economics of transgenic crops," Nature Biotechnology, Vol. 20, June 2002, pp. 537-541.

**Herbicide-Tolerant Rice**

Transgenic gene flow from rice can occur via cross-pollination and through movement of seeds by water, wind, birds and other animals.[96] While mostly a self-pollinator, rice is cited by The Royal Society of Canada as presenting a "moderate to high possibility" of outbreeding.[97] Some reports demonstrate up to 30 percent cross-pollination by wind.[98] The small size and great number of rice grains facilitates seed dispersal. Besides the risk of conventional cultivars becoming contaminated, transgenic treats could enter at least two cross-compatible weed species in the U.S.: wild rice (*Oryza rufipogon*) and annual red rice (*Oryza sativa*). Wild rice is on the list of Federal Noxious Weeds (7 C.F.R. 360) due to its ability to produce rhizomes and shatter (spread seeds) easily. "Annual red rice … causes problems in rice fields because it is carried with cultivated rice and can significantly lower its value by reducing its processing characteristics" *Id*. According to geneticist Dr. Norman Ellstrand, genes from cultivated rice can easily be transferred by hybridization to red rice and other close relatives.[99] Similar to the situation with volunteer canola, the wild rice species could act as a repository and genetic bridge for the spread of GE traits to food-grade rice.

Glufosinate-tolerant rice has already been deregulated, despite USDA's admission that weedy red rice will likely pick up the trait:

> *"It is assumed that the bar gene conferring tolerance to glufosinate will introgress into red rice and could result in a glufosinate-tolerant red rice population. ... However, these hybrid offspring will still be sensitive to other registered herbicides."*[100]

The USDA notes that varieties of rice tolerant to two other herbicides (imidazolinone and glyphosate) are under development. *Id*. Cross-pollination among commercial glufosinate-tolerant rice, other HT rice varieties grown in experimental plots (or commercial plantings, if deregulated), and weedy red rice could lead to doubly- and triply-resistant red or volunteer rice, creating a weed problem analogous to the situation with canola discussed above.

Transfer of the glufosinate-tolerant trait to non-HT commercial cultivars was discovered in 2006, and resulted in considerable harm to the interests of rice farmers and the rice industry. This LibertyLink contamination episode is discussed further in comments under "Issue 7, adventitious presence," *infra*.

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[96] Kinney, W. (2004). "Briefing on the Proposed Protocol for Pharmaceutical Rice," submitted to the AB2622 Advisory Board of the California Rice Commission by Californians for GE-Free Agriculture, March 5, 2004.

[97] See "Elements of Precaution...," op. cit., p. 125.

[98] "Environmental Assessment and Finding of No Significant Impact" for USDA Permit No. 96-355-01 granted to Applied Phytologics, Inc. for a field trial conducted in California in 1997.

[99] Ellstrand et al (1999). "Gene flow and introgression from domesticated plants into their wild relatives," Annu. Rev. Ecol. Syst. 30, p. 545.

[100] USDA FONSI (1998). "Finding of No Significant Impact" for AgrEvo's petition for commercialization of Liberty Link rice, petition number 98-329-01p.

The Center for Food Safety's report, Contaminating the Wild, contains an exhaustive discussion of genetically engineered crop varieties that have the potential to outcross with weedy relatives, and the potential noxious weed and environmental impacts of such trait transfer. Center for Food Safety, Contaminating the Wild? Gene Flow from Experimental Field Trials of Genetically Engineered Crops to Related Wild Plants (2006), available at http://www.centerforfoodsafety.org/pubs/Contaminating_the_Wild_Report.pdf (last visited September 11, 2007).

**Increased Herbicide Use From HT Crop Systems Adversely Impact Public Health and the Environment**

Thorough consideration and evaluation of potential adverse human health effects is essential in any regulatory oversight of genetically engineered organisms ("GEO"). Under NEPA, APHIS must consider human health effects when it evaluates any GEO – it is the "continuing responsibility of the Federal Government to use all practicable means . . . to . . . coordinate Federal plans . . . [in order to] assure for all Americans safe, healthful, productive, and aesthetically and culturally pleasing surroundings; . . . [and] attain the widest range of beneficial uses of the environment without degradation, risk to health or safety, or other undesirable and unintended consequences . . . ." 42 U.S.C. § 4331(b). Where APHIS action poses significant affects public health or safety, it must evaluate such impacts in an EIS. 40 C.F.R. § 1508.27. Courts have recognized that NEPA requires a thorough evaluation of the effects on human health and safety associated with novel food technology. *Stauber v. Shalala*, 895 F. Supp. 1178, 1195 (W.D. Wis. 1995). As the court stated:

> Such incorporation of the health and safety data by reference in the environmental assessment and finding of no significant impact would provide an interested party (or reviewing court) with a complete picture of all analysis bearing on the agency's obligations under the National Environmental Policy Act. *Id*.

APHIS has a poor track record of adequately assessing the human health effects of GMOs. APHIS failure to adequately analyze human health impacts has been a recurrent problem in the deregulation actions of APHIS. For example, The Center for Food Safety commented on APHIS' environmental assessment and preliminary decision to allow SemBioSys Genetics, Inc., to plant genetically engineered proinsulin-producing safflower in Washington, and argued that APHIS failed to analyze significant human health impacts. Docket NO. APHIS-2007-023, available at http://www.centerforfoodsafety.org/pubs/Proinsulin%20Safflower%20Comments%20CFS%20FINAL.pdf (last visited September 7, 2007).

APHIS efforts to strengthen its regulatory authority over the regulation of GEOs is an excellent opportunity to begin conducting thorough human health analyses for all GEOs. To this end, APHIS should regulate the introduction of GEOs under the noxious weed authority contained in the Plant Protection Act ("PPA"). (*See infra*. Issue I). As APHIS stated in the PEIS, utilizing

the noxious weed authority would allow it consider human health effects before deregulating a GEO. (PEIS at 21). By doing so, APHIS will have the authority to regulate any plant that "can directly or indirectly injure or cause damage to . . . the public health." *Id*. Additionally, as APHIS contemplates in the PEIS, APHIS should adopt clear regulations that make human health review mandatory for every plant being considered for deregulation. PEIS at 21. At a minimum, APHIS should base its assessment on the Codex Alimentarius decision Tree.[101]

In order to most effectively assess the human health effects of GEOs, APHIS must adopt a clear set of standards that it will employ on a consistent basis that will afford thorough review of every GEO. APHIS should also refer to a petition submitted to the FDA regarding adequate food safety assessment for further guidelines on what constitutes adequate food safety review. The Center for Food Safety, *Petition seeking the establishment of mandatory pre-market safety testing, pre-market environmental review and labeling for all genetically engineered foods*, March 2000, *available at* http://www.centerforfoodsafety.org/pubs/PetitionGEFoodRegs3.2000.pdf, (last visited September 7, 2007).

Herbicides and other pesticides are known or suspected to have unintended adverse effects on human health and the environment—such as increased risks for cancer, neurological disorders, and endocrine and immune system dysfunction; impaired surface and ground water; and harm to fish and wildlife. Recognizing these adverse impacts, the U.S. Department of Agriculture and the Environmental Protection Agency have long had an official policy in place to reduce the use of agricultural pesticides through promotion of integrated pest management (IPM). The Secretary of Agriculture first announced this policy in 1977. In 1993, the policy was reaffirmed in a commitment by the Deputy Secretary of Agriculture to achieve implementation of IPM practices on 75% of total crop acreage in 2000 to reduce pesticide use and the associated risks.[102]

USDA has thus officially endorsed reduced pesticide use as an overarching policy goal to protect public health and the environment.[103] APHIS too acknowledges that use of pesticides, including herbicides, has significant and predominantly detrimental environmental impacts (DEIS, p. 79). Official USDA policy in favor of IPM practices to reduce chemical pesticide use offers additional support for our recommendation that APHIS regulate pesticide-promoting HT crop systems as noxious weed risks.

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[101] Codex Alimentarius Commission, *Recommended International Code of Practice General Principles of Food Hygiene*, at 30, CAC Doc. CAC/RCP 1-1969 (Adopted 1996, Revised 2004).

[102] "Agricultural Pesticides: Management Improvements Needed to Further Promote Integrated Pest Management," Government Accounting Office, GAO-01-815, August 2001.

[103] Despite these efforts to increase use of IPM, chemical pesticide use in agriculture—which accounts for about three-fourths of all pesticides used in the United States— increased from about 900 million pounds in 1992 to about 940 million pounds in 2000, according to EPA, even as total cropland has decreased. See GAO report cited in last footnote, p. 11.

**1) Potential Health Impacts of Roundup/Glyphosate**

While Roundup is generally considered to be less toxic to human beings than many other herbicides, various researchers have noted adverse impacts on agricultural workers and their children, while laboratory research shows a number of adverse effects on the reproductive system. One common thread in this research is that Roundup brand formulations of glyphosate that contain the "inert ingredient" polyethoxylated tallowamine appear to be more toxic than glyphosate alone.

Roundup use has been associated with increased risk of non-Hodgkin's lymphoma and hairy cell leukemia in pesticide applicators,[104] and increased risk of neurobehavioral disorders in children of Roundup applicators.[105] Roundup/glyphosate has been shown to inhibit steroidogenesis.[106] Both Roundup and glyphosate have been found to inhibit the aromatase enzyme involved in estrogen production, though Roundup was more potent.[107]

Recent studies demonstrate that common versions of the Roundup herbicide that contain a surfactant (i.e. POEA, or polyethoxylated tallowamine) to aid penetration of the active ingredient (glyphosate) into plant tissue are extremely toxic to the tadpoles and juvenile stages of certain species of frogs, killing 96-100% of tadpoles after three weeks exposure and 68-86% of the juveniles after just one day.[108]

**2) Adverse Health Impacts of Other Herbicides**

The rise of glyphosate-tolerant crop systems is associated with the increasing use of other herbicides as well as glyphosate, as demonstrated above with reference to official USDA data on pesticide use. Thus, APHIS should assess associated health impacts from increased use of other herbicides used to control the herbicide-resistant weeds fostered by HT crop systems.

2,4-D is the second-most heavily used herbicide on soybeans (after glyphosate). 2,4-D is a phenoxy herbicide that formed part of the Vietnam War defoliant Agent Orange. Its use has been

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[104] Hardell et al (2002). Exposure to pesticides as risk factor for non-Hodgkin's lymphoma and hairy cell leukemia: pooled analysis of two Swedish case-control studies," *Leuk. Lymphoma*, 43(5):1043-9.

[105] Garry et al (2002). "Birth Defects, Season of Conception, and Sex of Children Born to Pesticide
Applicators Living in the Red River Valley of Minnesota, USA," *Environmental Health Perspectives*, 110, Suppl. 3, 441-449.

[106] Walsh et al (2000). "Roundup inhibits steroidogenesis by disrupting steroidogenic acute regulatory (StAR) protein expression," *Environmental Health Perspectives*, 108(8):769-76.

[107] Richard et al (2005). "Differential Effects of Glyphosate and Roundup on Human Placental Cells and Aromatase," *Environmental Health Perspectives*, 113: 716-720.

[108] Relyea, R.A. (2005a). "The impact of insecticides and herbicides on the biodiversity and productivity of aquatic communities," *Ecological Applications* 15(2): 618-627; Relyea, R.A. (2005b). "The lethal impact of Roundup on aquatic and terrestrial amphibians," *Ecological Applications* 15(4): 1118-1124.

associated with a number of adverse health impacts on agricultural workers who apply the herbicide, including: increased risk of cancer, particularly non-Hodgkin's lymphoma, and increased rate of birth defects in children of men who apply the herbicide. 2,4-D is also a suspected endocrine disruptor.[109] For these reasons, there are various restrictions on residential use of 2,4-D in various countries.[110]

Atrazine is the most heavily used herbicide on corn (not used on soybeans). Atrazine is a triazine herbicide whose use has been linked to endocrine disruption, neuropathy and cancer (particularly breast and prostate cancer). Atrazine is regularly detected in drinking water supplies in the Midwest, and has been associated with low sperm counts in men. Exposure to extremely low levels of atrazine has been linked to sex change and/or deformities in frogs, fish and other organisms. Based on this evidence, and the widespread presence of atrazine in drinking water supplies, the European Union announced a ban on atrazine in 2006. The U.S. EPA re-registered atrazine in 2003 despite objections from scientists and environmental groups.[111]

**Cumulative Impacts Are Not Adequately Analyzed**

APHIS has failed to acknowledge and address significant cumulative impacts associated with the deregulation of genetically modified organisms. APHIS must consider "the impact on the environment which results from the incremental impact of the action when added to past, present, and reasonably foreseeable future actions." 40 C.F.R. § 1508.7; *Muckleshoot Indian Tribe v. U.S. Forest Service*, 177 F.3d 800, 810 (9th Cir. 1999). NEPA requires that the public receive the underlying environmental data from which the agency's experts derived their opinions. *Idaho Sporting Cong. v. Thomas*, 137 F.3d 1146, 1150 (9th Cir.1998).

An EIS that has broad geographic affect must address inter-regional impacts. *Natural Res. Def. Council, Inc. v. Hodel* 865 F.2d 288, 297 (D.C. Cir. 1988). The D.C. Circuit concluded that the agency must sufficiently provide "analysis useful to a decision-maker in deciding whether, or how, to alter the program to lessen cumulative environmental impacts." *Id.* Additionally, "[w]here scientists disagree about possible adverse environmental effects, the EIS must inform decision-makers of 'the full range of responsible opinion on the environmental effects'". An EIS is deficient if it does not present well respected scientists' opinions on the hazards of a proposed action. *Friends of the Earth v. Hall*, 693 F. Supp. 904, 934 (W.D. Wash. 1988) (citing *Citizens Against Toxic Sprays, Inc. v. Bergland*, 428 F. Supp. 908, 922 (Dist. Or. 1977)).

Furthermore, the Supreme Court has stated that where insufficient information on an environmental consequence is unavailable in a particular area of an EIS, the agency is required under CEQ regulations, to "prepare a summary of existing relevant and credible scientific evidence and an evaluation of adverse impacts based on generally accepted scientific approaches

[109] For an overview, see: http://www.beyondpesticides.org/pesticides/factsheets/2,4-D.pdf.
[110] See http://en.wikipedia.org/wiki/2,4-D.
[111] See http://www.beyondpesticides.org/pesticides/factsheets/Atrazine.pdf and http://www.loe.org/shows/segments.htm?programID=06-P13-00016&segmentID=1.

or research methods." *Robertson v. Methow Valley Citizens Council*, 490 U.S. 332, 333-34 (1989).

Here, APHIS has completely abdicated its duty to carefully consider the significant cumulative impacts already found to be associated with its GE deregulation program, and to take a "hard look" at what further cumulative impacts may be associated with this prospective regulatory change. APHIS falsely assumes that there will be no new cumulative impacts. APHIS cannot rely on this assumption. Instead, APHIS must catalogue the potential cumulative environmental impacts that its proposed regulatory changes would have, and provide a summary of the evidence and evaluate these potentially adverse impacts.

APHIS, however, did nothing of the sort in this PEIS. First, APHIS stated that "[t]he only aspects of APHIS' regulatory program with the potential to aggregate with any past, present, or reasonably future actions are the increasing number of GE plants being grown and the increasing number of products on the market derived from the safe introduction of GE plants." (PEIS at 173-74). This statement neglects to address the environmental impacts of increased herbicide use and herbicide-resistant weeds associated with the increases quantity and number of GE plants used as well as any other cumulative impact. *See* 42 U.S.C § 1508.7 ("'Cumulative impact' is the impact on the environment which results from the incremental impact of the action when added to the past, present and reasonably foreseeable future actions . . . . Cumulative impacts can result from individually minor but collectively significant actions taking place over a period of time.")

APHIS' PEIS states, "[t]he cumulative impacts of APHIS' regulatory decisions on individual GE organisms are considered in other NEPA documents prepared on a case-by-case basis as decisions are made." (PEIS at 174). At least one federal court has demonstrated this to be false, that in fact APHIS neglects to consider cumulative impacts in its deregulation decisions. *Geertson Seed Farms et al.*, 2007 WL 518624 at 10. The PEIS also makes the bold statement that "[t]here have been no cumulative impacts resulting from the aggregation of effects from APHIS' current regulations and State actions." As the court held in the *Geertson Seed Farms* case, this simply has not been studied. *Id*.

It is critical that APHIS follows the court's directive and in fact analyzes critical cumulative impacts associated with GE crops. Specifically, the cumulative impacts associated with increased herbicide use and herbicide-resistant weeds must be addressed. Currently, the vast majority of GE plants are modified to confer herbicide tolerance. As demonstrated in the PEIS, APHIS completely neglects to consider the increased use of herbicides, such as Roundup, or the increase in weed resistance to such herbicides. As the U.S. District Court recently held, "APHIS's failure to consider in the context of the development of Roundup resistant weeds that there are already other Roundup Ready crops on the market, and more crops seeking to enter the market, means that it did not take the 'hard look' NEPA requires." *Id.* The court also stated that APHIS "likewise failed to consider how that increased use of Roundup . . . will impact the environment." *Id*.

In addition to increased herbicide use and herbicide-resistant weeds, APHIS must analyze cumulative impacts associated with fertilizer used with GMO crops, impacts on plant and seed diversity, susceptibility to new plant diseases, impacts on non-target organisms, non-GMO seed availability,[112] socio-economics, and other impacts.

APHIS improperly justifies not addressing any substantive environmental impacts by stating, "APHIS has determined that each of the proposed actions to be adopted in the preferred alternative is either as environmentally protective or more protective than the provisions in the current regulations." PEIS at 176. "APHIS has therefore determined that there will be no new significant cumulative impacts as a result of the proposed regulatory changes." *Id.* APHIS' assumption, that its proposed regulatory changes will have no environmental effects, is not based on empirical evidence. Therefore APHIS' conclusion that it need not address any new significant cumulative impacts is similarly inaccurate, and its failure to address cumulative impacts constitutes a NEPA violation.[113]

In evaluating cumulative impacts, APHIS must consider the potential cumulative effects resulting from its proposed regulatory changes. APHIS' proposed risk-based categories for environmental release of regulated GE organisms, discussed *infra*. as Issue 2, could have cumulative impacts such as adverse unintended effects of the transformation process that are overlooked due to the classification system. In addressing possible changes to how APHIS regulates biopharmaceutical crops, APHIS has opted to allow continued field testing. PEIS at 170. This regulatory decision would allow for continued planting of potentially harmful biopharmaceutical crops, with all the risks discussed in this comment.

APHIS has proposed to establish criteria that permit low-level contamination of non-GE crops with regulated GE crops grown in field trials (PEIS at 171.) By allowing low level contamination, APHIS is in essence aiming to permit contamination of crops that one court has determined to trigger NEPA review as a significant environmental effect. *Geertson Seed Farm, et al*, 2007 WL 518624 at 4-9. Thus, at the least, APHIS must acknowledge that permitting low level contamination is a significant NEPA impact, and must acknowledge and analyze the potential cumulative impacts associated with the amplification of the contamination as regulated

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[112] For example, when contamination events take place, contaminated seed stocks may be removed from the market, often causing shortages. This recently occurred with two contamination events in rice, when regulated GE rice LLRICE601 found in the popular conventional Cheniere rice variety, and regulated GE rice LLRICE604 found in Clearfield 131 conventional rice, resulted in the banning of both varieties from Arkansas fields in 2007 and 2008, along with required testing of all other rice seed. Planting prohibitions on Cheniere and Clearfield 131 seed removed 39% of certified commercial rice seed stocks from the Southern market. Bennett, David, "Arkansas' emergency session on CL 131 rice," Delta Farm press, March 1 2007, available at http://deltafarmpress.com/news/070301-cl131-session/ (last visited September 10, 2007).

[113] The PEIS also improperly argues that one potential source of cumulative impacts, namely an "increase in workload to [EPA and/or FDA.]" (PEIS, p. 175). APHIS must look at the environmental effects not agency workload. Agency workload is not a cumulative effect.

GE crops are permitted to cross and/or commingle with non-GE seed stocks, and thereby be propagated.

**Recommendations for Assessment of Cumulative Impacts of HT Crop Systems**

Assessment of cumulative impacts to be expected from the introduction of HT crop systems is necessary. 40 C.F.R. § 1508.7. If pre-existing HT crops tolerant to the same herbicide have already been deregulated, assessment of these pre-existing HT crop systems will provide valuable background information on impacts that have already occurred (e.g. from increased use of the HT crop-associated herbicide and/or other herbicides), and a basis for projecting likely cumulative impacts of the new HT crop system. APHIS should consider the following issues in assessing an HT crop system for possible deregulation:

1) Quantitative assessment of trends in acreage planted to pre-existing HT crop systems, including regional concentration, over at least a decade;
2) Quantitative assessment of trends in use of the HT crop-associated herbicide with pre-existing HT crop systems, if any (amount applied, frequency and rate of application for each crop), over at least a decade;
3) Quantitative assessment of trends in development of weeds resistant to the HT crop-associated herbicide, and weed shifts driven by use of the HT crop-associated herbicide, for pre-existing HT crop systems, including number of weed species and biotypes that have developed resistance or emerged, number and acreage of sites infested, and level of resistance in various weed species and biotypes;
4) Quantitative assessment of trends in the use of herbicides other than the HT crop-associated herbicide, particularly as regards usage to control weeds resistant to the HT crop-associated herbicide, or populations of weeds that have emerged due to weed shifts;
5) Quantitative assessment of trends in the use of conservation tillage for pre-existing HT crop systems, particularly with regard to increased use of tillage to control weeds that have developed resistance to the herbicide associated with the HT crop system, or weed species/biotypes that have emerged due to weed shifts; such analysis should include quantitative assessment of trends in soil erosion associated with these changes in tillage practices;
6) Thorough cumulative assessment of potential adverse impacts to soil biota and crop health associated with increased use of herbicides fostered by pre-existing HT crop systems in combination with the HT crop system under consideration for deregulation;
7) Quantitative assessment of changes in production costs associated with pre-existing HT crop systems, including changes in expenditures on herbicides with respect to resistant weeds, fuel expenditures associated with changes in tillage practices, etc.

In conducting such assessments, APHIS should seek out independent, high quality, up to date information and data. For instance, USDA's National Agricultural Statistics Service collects data on pesticide usage, and the USDA's Economic Research Service develops data on agricultural production costs (see sources cited above). Other sources of high-quality data include university extension agents and farm press articles based on the experiences of extension agents. In past assessments of HT crops for deregulation or environmental release, APHIS has

not referred to official USDA data on agricultural chemical usage, for instance, and fails to do so in the DEIS as well.

**APHIS Failed to Adequately Analyze Socioeconomic and Sociocultural Effects (APPENDIX G)**

APHIS's discussion of socio-economic and socio-cultural effects is inadequate. It mischaracterizes the agency's past performance in this area of oversight, and simply fails to address any real-world effects. NEPA requires the agency to assess socio-economic and socio-cultural impacts that will be associated with USDA's admitted inability to prevent low level presence of GEOs in agriculture, *i.e*. environmental contamination.

As APHIS states in the PEIS, [b]eyond ensuring that GE crop plants pose no plant pest risks, APHIS needs to consider and address, when appropriate, the social, cultural, and economic effects resulting from any significant environmental impact of regulating GE plants and from changing APHIS' regulatory approach. PEIS at 49.

APHIS fails to address the potential socio-economic and socio-cultural impacts due to APHIS recommendations. APHIS provides an improper cursory review of the issues; it failed to analyze the actual socio-economic impacts on farmers and food processors seeking to avoid GE crops and products derived from GE crops and commodities.

APHIS completely neglects to address the effects of GE crops and GE crops regulations on organic farmers, organic food products and the choice to grow, produce, and consume organic foods. For example, no analytical information is present concerning the ability of non-transgenic seed producers to avoid transgenic seed contamination, and the ability of seed sellers to ensure that seed being sold can be guaranteed to be non-transgenic seed. Indeed, current indications are that once transgenic seed is on the commercial market the ability to access non-transgenic seed is significantly hampered.[114] Such results not only have economic impacts on the farmers seeking non-transgenic seed, but also will severely limit the ability of farmers to convert to organic systems and/or expand such acreage. Absent such analysis and information, the agency's EIS is inadequate.

APHIS has failed to address a number of other socio-economic impacts that must addressed as part of the NEPA process. Indeed, the CEQ regulations implementing NEPA state that such impacts must be analyzed.[115] Among the issues that need to be addressed include: (1) impact of

[114] Union of Concerned Scientists, *Gone to Seed: Transgenic Contaminants in the Traditional Seed Supply* (2004), *available at* http://www.ucsusa.org/assets/documents/food_and_environment/seedreport_fullreport.pdf (last visited September 6, 2007)

[115] When an environmental impact statement is prepared and economic or social and natural or physical environmental impacts are related, then the environmental impact statement will discuss all of these effects on the human environment. 40 C.F.R. § 1508.14.

GE crops on U.S. exports and export of U.S. products using material derived from transgenic crops, and (2) the impact of commercial introduction of a GE crop variety that is subject to utility patent protection and likely to displace non-genetically engineered varieties from the market place, and how this decrease in diversity will impact the environment; and (3) the impacts deregulation will have on seed pricing

APHIS has also failed to analyze the impacts of GE contamination on agricultural markets. For example, in September 2000, food products in the US were discovered to be contaminated with StarLink, a variety of GE corn unapproved for human consumption due to concerns that its insecticidal protein could cause allergies. The contamination triggered massive food recalls and lawsuits that in the end cost the biotech and food industries an estimated $1 billion in damages.[116] Also in August 2006, USDA announced widespread contamination of commercial long-grain rice supplies in the South with unapproved LibertyLink Rice 601 (LL601), a variety of rice developed by Bayer CropScience for tolerance to the herbicide Liberty (glufosinate). This episode caused substantial economic damage to U.S. rice exports, significant harm to U.S. rice farmers and the rice industry as a whole, and a loss of faith in the wholesomeness of the U.S. food supply.

USDA also fails to addresses the impact of GE crops on farmers and the community generally with respect to intellectual property rights and the use of those rights by corporations like Monsanto. *See generally*, The Center for Food Safety, Monsanto vs. US Farmers, 2005 available at http://www.centerforfoodsafety.org/pubs/CFSMOnsantovsFarmerReport1.13.05.pdf (last visited September 7, 2007).

In Monsanto v US Farmers, the Center for Food Safety found that Monsanto, the world's leading agricultural biotechnology company, has used heavy-handed investigations and ruthless prosecutions that have fundamentally changed the way many American farmers farm. The result has been nothing less than an assault on the foundations of farming practices and traditions that have endured for centuries in this country and millennia around the world, including one of the oldest, the right to save and replant crop seed. Monsanto v US Farmers highlights the practices of Monsanto specifically, but the issue addressed in this report can arise with any patented GE crop, and must be considered in the socio-economic evaluation of GE crops.

NEPA Requires Climate Change Analysis that AHPIS Failed to Perform

Climate change is an environmental issue of paramount import. The global scientific community's findings on the anthropogenic causes of climate change and climate change's current and future impacts demand that prompt action be taken to integrate climate change analyses into governmental agency planning. The extent to which governments consider climate change impacts in planning governmental actions and take action to mitigate such impacts will strongly affect the extent to which climate change and its consequential dangers are limited or

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[116] "Tests to detect allergens in altered foods fall short," June 12, 2002 *St. Louis Post-Dispatch*, June 12, 2002.

avoided in the coming century. The National Environmental Policy Act ("NEPA"), as our nation's basic environmental charter, is the mechanism incorporating environmental considerations into federal decision-making. The Council on Environmental Quality ("CEQ") is charged with overseeing NEPA and must ensure NEPA's purposes are met by issuing guidance to federal agencies on compliance with the statute. Congress intended federal agencies to consider impacts and mitigation for actions with potential climate change consequences. By enacting NEPA, Congress commanded agencies to consider the environmental impacts of their actions. Recognizing that agency actions contribute to the release and storage of greenhouse gases, there are obvious short and long-term environmental effects related to climate change. Therefore, climate change is within the sphere of environmental effects that Congress intended agencies to consider.

According to CEQ, agencies shall use all practical means to "restore and enhance the quality of the human environment and avoid or minimize any possible adverse effects of their actions upon the quality of the human environment."[117] If a project has potential greenhouse gas effects, in order to allow the public and agency to make an informed decision, disclosure and analysis of climate change impacts is needed.

NEPA and the CEQ implementing regulations require analysis of climate change and its reasonably foreseeable effects because: (1) climate change effects are encompassed by CEQ's definition of "effects;" and (2) because climate change effects are "reasonably foreseeable."

1.Climate Change Effects Are Encompassed By CEQ's Definition of "Effects."

CEQ regulations require that the scope of agency effects analyses encompass direct and indirect, as well as cumulative, effects in agency NEPA documents.[118] Section 1508.8 of the CEQ regulations, defines "effects" to include:

a) Direct effects, which are caused by the action and occur at the same time and place.

(b) Indirect effects, which are caused by the action and are later in time or farther removed in distance, but are still reasonably foreseeable. Indirect effects may include growth inducing effects and other effects related to induced changes in the pattern of land use, population density or growth rate, and related effects on air and water and other natural systems, including ecosystems.

Effects and impacts as used in these regulations are synonymous. Effects include: ecological (such as the effects on natural resources and on the components, structures, and functioning of affected ecosystems), aesthetic, historic, cultural, economic, social, or health, whether direct, indirect, or cumulative. Effects may also include those resulting from actions which may have both beneficial and detrimental effects, even if on balance the agency believes that the effect will

[117] 40 C.F.R. § 1500.2(f).
[118] See 40 C.F.R. §§ 1508.08 & 1508.25.

be beneficial.[119]

Climate change effects clearly fall within the ambit of ecological, aesthetic, historical, cultural, economic, social, or health, among others. This conclusion is further buttressed by CEQ's proactive, anticipatory definition of "affecting," as including those things that "may have an effect on" the environment.[120]

NEPA also requires agencies to consider the cumulative impacts of their proposed actions.[121] By definition, cumulative effects must be evaluated along with direct and indirect effects of a project and its alternatives. "'Cumulative impact' is the impact on the environment which results from the incremental impact of the action when added to other past, present, and reasonably foreseeable future actions regardless of what agency or person undertakes such other actions."[122] Individually minor, but collectively significant actions, taking place over time, can generate cumulative impacts.[123] Accordingly, the climate change effects of a proposed action should be discussed in any cumulative effects analysis to determine if the project will add to the ongoing problem of climate change. In fact, CEQ has previously cited climate change effects as a component of cumulative atmospheric effects to be addressed by agencies in describing the affected environment of a proposed action:

While describing the affected environment, the analyst should pay special attention to common natural resource and socioeconomic issues that arise as a result of cumulative effects. The following list describes many issues but is by no means exhaustive:

Regional and global atmospheric alterations from cumulative additions of pollutants that contribute to global warming, acidic precipitation, and reduced ultraviolet radiation absorption following stratospheric ozone depletion.[124]

2. Climate Change Impacts Are "Reasonably Foreseeable."

NEPA and the CEQ implementing regulations include requiring analysis of "reasonably foreseeable" effects.[125] An environmental effect is "reasonably foreseeable" if it is "sufficiently likely to occur that a person of ordinary prudence would take it into account in reaching a decision."[126] It is well-established that some "reasonable forecasting" by the agency is implicit

[119] 40 C.F.R. § 1508.25.
[120] 40 C.F.R. § 1508.3.
[121] 40 C.F.R. § 1508.25(c); Utahns for Better Transp. v. United States Dep't of Transp., 305 F.3d 1152, 1172 (10th Cir.2002); Kern v. United States Bureau of Land Mgmt., 284 F.3d 1062, 1076 (9th Cir.2002); Vill. of Grand View v. Skinner, 947 F.2d 651, 659 (2d Cir.1991).
[122] 40 C.F.R. § 1508.7.
[123] Id.
[124] Council on Environmental Quality, *Considering Cumulative Effects Under the National Environmental Policy Act*, 24 (January 1997) (emphasis added).
[125] See 40 C.F.R. §§ 1502.4, 1508.8, 1508.18, & 1508.25.
[126] See, e.g., City of Shoreacres v. Waterworth, 420 F.3d 440, 453 (5th Cir. 2005); Dubois v.

in the NEPA process, and that it is the responsibility of federal agencies to predict the environmental effects of proposed actions before they are fully known.[127]

The "reasonably foreseeable" standard is easily met by climate change effects. The overwhelming consensus of national and international scientific evidence supports the conclusion that climate change is resulting from global warming, i.e., the build-up of greenhouse gases in the atmosphere, and that the subsequent changes are adversely affect our global environment. Stated differently, climate change is "reasonably foreseeable," as that phrase is understood in the context of NEPA and the CEQ regulations.[128] The International Panel on Climate Change (IPCC) and the National Academy of Sciences both have concluded that climate change is being caused by the build-up of greenhouse gases in the atmosphere, a result of human activities.[129] The 2002 Climate Action Report provided a long list of widespread and regional impacts on the United States that were likely or very likely to occur as a result of climate change.[130] The National Academies of Science of eleven major nations—including the U.S.—recently issued a joint statement unequivocally declaring that the scientific understanding of climate change is sufficiently certain to justify prompt governmental action.[131] Accordingly, climate change impacts clearly qualify as reasonably foreseeable effects that must be addressed in environmental compliance documents to properly comply with NEPA and CEQ regulations. Unfortunately, the draft EIS does not contain the "reasonable forecasting" of climate change that

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U.S. Dept. of Agriculture, 102 F.3d 1273, 1286 (1st Cir. 1996); Mid States Coalition for Progress v. Surface Transp. Bd., 345 F.3d 520, 549 (8th Cir. 2003) (quoting Sierra Club v. Marsh, 976 F.2d 763, 767 (1st Cir. 1992)) (internal quotation marks omitted).

[127] Scientists' Inst. for Pub. Info. v. Atomic Energy Comm'n, 481 F.2d 1079, 1092 (D.C. Cir. 1973).

[128] CEQ expounded on what is a "reasonably foreseeable" effect in its "Forty Most Asked Questions Concerning CEQ's NEPA Regulations:"

> [I]n the ordinary course of business, people do make judgments based upon reasonably foreseeable occurrences. . . . The agency has the responsibility to make an informed judgment, and to estimate future impacts on that basis, especially if trends are ascertainable . . . . The agency cannot ignore these uncertain but probable, effects of its decisions.

46 Fed. Reg. at 18031.

[129] *See generally* The Intergovernmental Panel on Climate Change (IPCC), Fourth Assessment Report (2007) available at http://www.ipcc.ch; IPCC, Third Assessment Report (2001), *available at* http://www.grida.no/climate/ipcc_tar/ ; National Research Council, Climate Change Science: An Analysis of Some Key Questions vii, 3 (2001) (hereafter "NAS report"), available at http://www.nap.edu/catalog/10139.html?onpi_webextra6

[130] U.S. Department of State, U.S. Climate Action Report 2002, Third National Communication of the United States of America Under the United Nations Framework Convention on Climate Change (May 2002) (hereafter "Climate Action Report"), available at http://www.gcrio.org/CAR2002/.

[131] National Academies of Science, Joint Science Academies' Statement: Global Response to Climate Change, available at http://nationalacademies.org/onpi/06072005.pdf

is necessary under NEPA. The draft EIS neither considers the proposed regulatory changes within the context of climate change nor analyzes the impacts on climate change caused by the continued and widespread commercialization of genetically engineered plants.

The Draft EIS fails to analyze how the environmental changes associated with forecasted climate change will affect the attributes of genetically engineered crops. Instead, the draft EIS views the environment into which future genetically engineered crops will be field tested or commercialized as static. The IPCC's Fourth Assessment Report found that global average surface temperatures will rise over the next century between 1.8 degrees C and 6.4 degrees C.[132] This change in climate will have a profound impact on agriculture and the draft EIS should analyze its review of GMOs within this context.

Without question the temperature changes and atmospheric carbon dioxide levels associated with climate change over the next several decades will affect how genetically engineered crops and crop system will be managed when field tested or commercially released. For instance, it is known that elevated temperature changes caused by climate change can alter the composition of crop seed. Studies have shown that this can impact gene expression in soybeans.[133] Studies have also shown that elevated levels of carbon dioxide in the atmosphere may increase plant tolerance to glyphosate. As described previously, such a result may directly exacerbate the development of weed resistance associated with Roundup Ready crop systems.[134] Other studies have shown that elevated levels of carbon dioxide significantly increase pollen production - an impact of climate change that may influence the ability of APHIS to maintain gene containment.[135] Many studies also speak to the changes in insect pests and plant disease changes that will be associated with climate change.[136] Despite all these (and other) reasonably foreseeable predicted changes in the U.S. agricultural context, the draft EIS fails to even discuss how its future regulatory system will account for changes necessitated by climate change.

Additionally, the draft EIS fails to analyze the climate change benefits of promoting organic systems over continued use of genetically engineered crops. Studies have shown that organic systems have an overwhelming climate benefit compared to conventional systems by significantly increasing soils retention of carbon and nitrogen.[137] As explained earlier in these

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[132] Intergovernmental Panel on Climate Change, Climate Change 2007: The Physical Science Basis, Summary for Policymakers (2007) at 10.

[133] See e.g. Thomas, J.M.G., et al, "Elevated Temperature and Carbon Dioxide Effects on Soybean Seed Composition and transcript Abundance." Crop Science 43:548-1557 (2003)

[134] Ziska, et al, "Future Atmospheric Carbon Dioxide May Increase Tolerance to Glyphosate," Weed Science 47:608-615 (1999).

[135] See e.g. Ziska, et al, "Rising CO2 and Pollen Production of Common Ragweed (*Ambrosia artemisiifolia*), a known allergy-inducing species: implication for public health,: Aust. J. Plant Physiol. 27:893-898 (2000).

[136] Intergovernmental Panel on Climate Change, Report of Working Group II, Chapter 5 (2007) at 283.

[137] See e.g. Drinkwater, et al., "Legume-based cropping systems Have Reduced Carbon and Nitrogen Losses," Nature 396: 262-265 (1998).

comments, the continued development of glyphosate resistant weeds has led to increased management of agriculture land through tillage practices. Conventional tillage systems reduce the ability of soil to conserve carbon. Combined with the dependence of genetically engineered cropping systems on nitrogen-based fertilizers, organic alternatives will yield climate benefits through reducing emissions and better carbon sequestration.

Lest the agency think that climate issues are beyond the scope of the draft EIS, courts have held several instances that climate change impacts must be adequately considered in order to comply with NEPA. In Border Power Plant Working Group v. DOE, a coalition of citizen organizations challenged the Department of Energy's issuance of a FONSI for permits to build electric lines between new power plants in Mexico and southern California. The district court held that the NEPA analysis was inadequate and that the EA failed to disclose and analyze effects of carbon dioxide as a greenhouse gas.[138] In Mid States Coalition for Progress v. Surface Transp. Bd., the Eighth Circuit reviewed a challenge to an EIS for approval of a railroad that would reach coal mines in Wyoming's Powder River Basin.[139] The Court of Appeals held that it would be irresponsible for the Board to approve a project of this scope without first examining the effects, such as global warming, that may occur as a result of the reasonably foreseeable increase in coal consumption.[140] Both cases illustrate that federal courts have interpreted the provisions of NEPA to require that agencies adequately consider the climate change environmental impacts if it is foreseeable that a project will have greenhouse gas effects. Other Courts have similarly grappled with the issues surrounding agency climate change analyses in various forms.[141]

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[138] Border Power Plant Working Group v. DOE, 260 F. Supp. 2d 997, 1029 (S.D. Cal. 2003).
[139] Mid States Coalition for Progress v. Surface Transp. Bd., 345 F.3d 520, 550 (8th Cir. 2003).
[140] Id.
[141] See, e.g., Mid-States Coalition for Progress v. Surface Transp. Bd., 345 F.3d 520, 548-50 (8th Cir. 2003) (addressing a challenge to the approval by the Surface Transportation Board of a railroad to coal mines in Wyoming's Powder River Basin and holding that the EIS was inadequate because, inter alia, it failed to examine the reasonably foreseeable effect on global warming of the subsequent increase in coal consumption); Assoc. Of Pub. Agency Customers v. Bonneville Power Admin., 126 F.3d 1158, 1187-88 (9th Cir. 1997) (addressing a challenge to BPA's EIS for a new business plan on power sales and transmission contracts and holding that the EIS adequately considered climate change effects); Friends of the Earth v. Watson, 2005 WL 2035596, *2-6 (N.D. Cal. 2005) (denying the defendant's motion for summary judgment for lack of standing in a challenge to the Overseas Private Investment Corporation ("OPIC") for its failure to conduct an environmental assessment under NEPA when providing assistance to specific projects that contribute to climate change and finding that the plaintiffs evidence of global warming and its potential impacts were sufficient to demonstrate a reasonable probability that the projects funded by the defendants would harm the plaintiffs' interests); Senville v. Peters, 327 F. Supp. 2d 335, 57-58 (D. Vt. 2004) (addressing a challenge to the Federal Highway Administration's ("FHWA") approval of highway segments because the EIS failed to properly analyze the cumulative and secondary effects of the highway project–including air quality impacts like $CO_2$ emissions impacting global warming–and holding that the plaintiffs had not established a substantial likelihood of significant new air quality impacts stemming from the challenged approval of a highway segment); Border Power Plant Working Group v. Dep't of

Energy, 260 F. Supp. 2d 997, 1028-29 (S.D. Cal. 2003) (addressing a challenge to a FONSI issued for California-Mexico border power plants permits and concluding that the agency had failed to provide adequate environmental analysis, in part because the EA failed to disclose and analyze the effects of carbon dioxide emissions as a greenhouse gas contributing to global warming); Seattle Audubon Soc'y v. Lyons, 871 F. Supp. 1291, 1324 (W.D. Wash. 1994) (addressing a challenge to a forest management plan that included a charge of failing to disclose the impacts of timber harvest on air quality and climate and concluding that the EIS adequately discussed these impacts); see also City of Los Angeles v. Nat'l Highway Traffic Safety, 912 F.2d 478 (D.C. Cir. 1990) per curiam (addressing a challenge to the decision by the National Highway Traffic Safety Administration not to prepare an EIS on fuel economy standards for 1987-89 and holding that the plaintiffs had standing to challenge the standard on global warming grounds, but the lack of an EIS was not arbitrary and capricious); id. at 499-503 (Wald, C. J., dissenting in part) (concluding that the agency should have prepared a programmatic EIS addressing the global warming consequences of the standards approved); Foundation on Economic Trends v. Watkins, 794 F. Supp. 395, 397-401 (D. D.C. 1992) (holding that plaintiffs challenging the failure of agencies to consider global warming on specific actions lacked standing).

**APHIS Fails to Analyze Impacts on Threatened and Endangered Species**

APHIS' analysis regarding compliance with the Endangered Species Act ("ESA") is inadequate. It merely states that it may consult with the Fish and Wildlife Service ("FWS") and may comply with ESA requirements based on its decision tree. APHIS suggests that it must only consult with FWS when it determines based on its decision tree that consultation is necessary. However, APHIS reliance on its decision tree is improper. APHIS must consult with APHIS for any action that may effect a threatened or endangered species. Also, APHIS decision tree is simply too narrow and fails to reflect sound science in analyzing whether threatened or endangered species are at risk.

Section 7(a)(2) of the ESA requires that APHIS, through consultation with FWS, insure that its actions are not likely to jeopardize threatened or endangered species or cause the destruction or adverse modification of critical habitat. 16 U.S.C. § 1536(a)(2). This is both a procedural and a substantive mandate. *Thomas v. Peterson*, 753 F.2d 754, 763 (9th Cir. 1985). The ESA's consultation requirement is strictly enforced because the "procedural requirements are designed to ensure compliance with the substantive provisions." *Id.* at 764.

Consultation is a three-step process: (1) an agency proposing an action must ask FWS for a list of protected species present in the action area; (2) then the agency prepares a biological assessment to determine whether any species is likely to be affected; and (3) if the proposed action "may affect" listed species then the agency must initiate "formal consultation" with FWS. *Forest Guardians v. Johanns*, 450 F.3d 455, 457-58 (9th Cir. 2006). The alternative is if the action is "not likely to adversely affect" any species. In that case, the agency may attempt "informal consultation" to obtain a written concurrence from FWS. *Id.* Only by following these procedural steps can APHIS comply with the ESA's mandate that agencies prevent jeopardy to listed species and critical habitat.

By relying on the decision tree, APHIS fails to follow the procedures required by the ESA because it does not even take the first step toward discharging its consultation duty by identifying species in the action area. "First, the agency contemplating the action must request information from the appropriate federal wildlife service regarding 'whether any species which is listed or proposed to be listed may be present in the area of such proposed action.'" *Forest Guardians*, 450 F.3d at 457 (quoting 16 U.S.C. § 1536(c)(1)).

In *Center for Food Safety v. Johanns*, for example, the court held that APHIS violated the ESA's consultation duty because APHIS "skipped the initial, mandatory step of obtaining information about listed species and critical habitat from FWS and NMFS." 2006 WL 2568023, *12 (D. Haw. 2006). In that case, the plaintiffs challenged APHIS' failure to consult on the effects on endangered species and their habitats for permits allowing field tests of genetically engineered crops that produce pharmaceuticals. *Id.* at *1. APHIS contended that it was not required to consult because it had determined that the field test permits would not affect or harm listed species or critical habitat. *Id.* at *12. The court rejected APHIS' argument because APHIS failed to follow the ESA's procedures. *Id.* "This initial request for information is a predicate to further agency action and may not be ignored, regardless of whatever other process

the agency follows." *Id.* at *11. APHIS cannot ignore ESA procedures and evade complying with the ESA by merely asserting that its action has no effect or poses no harm to listed species.

APHIS' analysis of endangered species issues is also inadequate because it will employ an overly narrow decision tree, ignoring important considerations. The decision tree APHIS analyzed *only* the effects of the enzyme produced by genetic engineering. The two-page decision tree, a checklist lacking any reasoning, explanation, or analysis supporting its decision, is inadequate for ESA purposes. *See e.g., Native Ecosystems Council*, 304 F.3d at 902. APHIS' checklist fails the ESA requirement that "each agency shall use the best scientific and commercial data available." 16 U.S.C. § 1536(a)(2). Answering six questions without any reasoning fails to articulate the analysis required by the ESA. Moreover, the decision tree is narrowly confined to questions about the genetically engineered trait, and fails to consider other direct, indirect, and cumulative impacts. *See e.g., Native Ecosystems Council*, 304 F.3d at 902 (requiring the agency to consider all relevant factors). The scope of ESA consultation must include direct, indirect, and cumulative effects. *See* 50 C.F.R. § 402.14(g).

**ISSUE 1: Scope of Regulation, Noxious Weed Risks, Biological Control Agents**

APHIS should expand its regulatory jurisdiction over genetically engineered organisms (GEO) through use of the noxious weed authority provided by the Plant Protection Act. 7 U.S.C. 7702(10). APHIS should adopt a modified version of Alternative 2 and expand the scope of what is regulated to include noxious weed risk and GE biological control organisms in addition to evaluating plant pest risks, and use genetic transformation as the trigger for regulation. Event-by-event rather than trait-based regulation should be used, as well as mandatory APHIS regulation of all plants generated by direct introduction of any isolated genetic material (including RNA), whether or not it involves recombinant DNA techniques. APHIS should not exclude any class of GE organism from APHIS regulation.

By expanding this regulatory authority, APHIS will have a greater ability to regulate the introduction of novel crops that currently fall outside the agency's existing regulatory reach. It would also ensure that APHIS has authority to control and/or permanently prohibit the introduction of genetically engineered crops such as glyphosate tolerant creeping bentgrass that are novel noxious weeds. The change would also clarify APHIS's legal authority over novel biological control agents such as genetically engineered insects.

Any amendment of the existing regulations should also recognize that state authorities may prohibit or restrict interstate commerce of a GEO based upon the special need provision found at 7 U.S.C. 7756(b)(2)(B).

In addition, any new regulatory regime will require a mandatory review of the human health and economic impacts associated with a GEO. The purpose of the PPA is summarized in its first finding: "the detection, control, eradication, suppression, prevention, or retardation of the spread of plant pests or noxious weeds is necessary for the protection of the agriculture, environment,

and *economy* of the United States." 7 U.S.C. § 7701(1) (emphasis added).[142] In fact, seven of nine introductory findings of the PPA focus on preventing burdens on commerce and the economy. [143] Additionally, the definition of noxious weed provides authority to the agency to assess a GEO's ability to "directly or indirectly injure or cause damage to crops … other interests of agriculture, . . . the public health, or the environment ."[144] 7 U.S.C. 7702(10). As a result, to properly assess any GEO under its noxious weed authority, APHIS must thoroughly assess how a GEO may "damage" U.S. agricultural interests. *Id*. This should include a mandatory review of how the commercial introduction of a GEO or possible low-level contamination of any commodity with the GEO from a proposed field trial will impact the U.S. agricultural economy. A number of such contamination events – StarLink corn, LL 601 rice, and Bt10 corn – have already caused significant damage to the US agricultural economy. Analysis of this potential impact should be completed before allowing any planting, and should be used as part of the agency's assessment of whether or not to issue a field trial permit for, or deregulate, a GEO.

Moreover, the definition of a noxious weed as any plant that can "injure or cause damage to .... the public health" indicates that for the first time the U.S. should require human health safety testing prior to the introduction of any GEO into the environment or commerce. While FDA would have more expertise in assessing and implementing such a system, the agency has failed to do so and only provides limited voluntary safety oversight. Given this situation, USDA should amend its regulations to also include a mandatory human health safety assessment. This regulation and review process should be no less stringent than the most stringent of the safety assessment procedures for any particular test or procedure established by joint consultations of the Food and Agriculture and World Health Organizations or by Codex Alimentarius.[145]

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[142] The ultimate goal – contained in the second half of the first finding – is the protection of US agriculture and economy. 7 U.S.C. § 7701(1). The means to this goal – contained in the first half of the first finding – is the prevention and spread of plant pests. *Id*.

[143] The findings state, for example: "detection . . . of plant pests . . . is necessary for the protection of the . . . economy," 7 U.S.C. § 7701(1); "decisions affecting imports, exports, and interstate commerce in agricultural products . . . shall be based on sound science," 7 U.S.C. § 7701(4); "the smooth movement of . . . plant products . . . is vital to the United State's economy," 7 U.S.C. § 7701(5); export markets could be severely impacted by the introduction or spread of plant pests or noxious weeds," 7 U.S.C. § 7701(6).

[144] "The term 'noxious weed' means any plant or plant product that can directly or indirectly injure or cause damage to crops (including nursery stock or plant products), livestock, poultry, or other interests of agriculture, irrigation, navigation, the natural resources of the United States, the public health, or the environment" 7 U.S.C 7702(10).

[145] FAO/WHO (2000). "Safety Aspects of Genetically Modified Foods of Plant Origin," Food and Agriculture Organization and World Health Organization, 2000, Geneva, Switzerland; FAO/WHO (2001). "Evaluation of Allergenicity of Genetically Modified Foods," Food and Agriculture Organization and World Health Organization, January 2001, Geneva, Switzerland; "Codex Alimentarius Commission (2003). "Guideline for the Conduct of Food Safety Assessment of Foods Derived from Recombinant-DNA Plants," CAC/GL 45-2003.

Despite the agency's past failure to do so, USDA is obliged to assess potential human health impacts of GEOs under its existing NEPA authority. *See Stauber v. Shalala*, 895 F.Supp. 1178, 1195 (W.D. Wisc. 1995) ("Had plaintiffs been successful on their claim that the FDA did not comply with the [FDCA] they might have a claim the [NEPA] requirements were not met either, because both statutes require a thorough evaluation of Posilac's effects on human and bovine health and safety.") Such an analysis is often lacking in the agency's individual NEPA documents. Moreover, reliance on the voluntary consultation process housed at FDA does not in anyway make up for this ongoing NEPA oversight.

APHIS should broaden its regulatory scope to include GE plants that may pose a noxious weed risk. APHIS gives several examples of types of genetically engineered (GE, also called transgenic) plants that it might regulate under its noxious weed authority: plants with multiple traits, plants producing pharmaceutical and other biologically active compounds, and plants with transgenes of unknown function. APHIS should regulate these. Doing so would clarify APHIS' ability to regulate GE plants that could harm the non-agricultural environment. Many GE plants could pose such broader risks. For example, stress and drought tolerance genes may increase the fitness of GE plants or wild relatives not currently considered to be noxious weeds, thereby allowing spread in natural areas.[146] Increased geographic range of stress-tolerant plants could cause harm by displacing other species or exposing non-target organisms to transgene products that could be harmful. As discussed under Issue 4, APHIS should prohibit the environmental release of pharmaceutical-producing crops, food and non-food.

However, APHIS does not discuss the most important use it could make of its new noxious weed authority – to assess, and regulate as needed, transgenic herbicide-tolerant (HT) crop systems as noxious weed risks. We discuss the noxious weed risks posed by HT crop systems in the section entitled: "APHIS PROGRAMMATIC EIS FAILS TO ADEQUATELY ANALYZE FORESEEABLE ENVIRONMENTAL EFFECTS."

By regulating HT crops only as plants pests, APHIS has narrowed its analysis of the potential effects of HT crops. By expanding its regulatory authority to encompass the noxious weed definition, APHIS will necessarily have to examine a broader range of issues related to HT crop systems, which will in turn make its regulation of HT crops more transparent.

**Event-by-event vs. trait-based regulation**

APHIS should regulate on event-by-event basis because this form of regulation better protects the environment and human health than trait-based regulation. While we applaud APHIS for supporting event-by-event regulation (Alternative 2) over the trait-based Alternative 3, we must note inconsistencies and unclarities in its discussion of this issue.

[146] NAS (2004). "Biological Confinement of Genetically Engineered Organisms," National Research Council, National Academy of Sciences, 2004, p. 49.

APHIS states: "The [trait-based] system should be as protective as the current one, except that it would not account for unanticipated changes relating to the transformation process or other differences that may exist at the biochemical level among plants having the same phenotype." (DEIS, pp. 133-34).

The "unanticipated changes relating to the transformation process" in fact would render a trait-based system "less protective" than event-by-event regulation. This is because such unanticipated changes – invisible to a trait-based system – could have detrimental impacts on human health or the environment.

APHIS's discussion is unclear because it fails to define with sufficient rigor either "trait" or "phenotype." Two examples show the potential for confusion. There are now at least three very different mechanisms for glyphosate-tolerance in plants: the glyphosate-tolerant CP4 EPSPS enzyme; the glyphosate oxidoreductase (GOX) enzyme, which degrades glyphosate; and the glyphosate acetyltransferase (GAT) enzyme, which inactivates glyphosate by attaching an acetyl group to it. Clearly, GE plants incorporating different mechanisms of glyphosate-tolerance should be assessed separately, as they might have very different environmental (e.g. non-target organism) or other impacts. Yet in a trait-based approach (depending on how it is defined), assessment of a GE plant incorporating one mechanism (e.g. CP4 EPSPS) might be construed as obviating the need to assess the others. Likewise, Bt plants expressing different Cry proteins, or differing versions of a particular Cry protein, for resistance to the same or similar range of insect pests might be regarded as possessing the same trait. An example of this is three Bt corn events – MON810, Bt11 and Event176 – which express different versions of the Cry1Ab endotoxin in differing amounts in different tissues. Here too, a trait-based approach might very well lead APHIS to forego any assessment or regulation of events that may pose different risks despite possessing the same "trait." An example is the Cry1Ab-based Bt corn Event176, which due to higher expression of insecticidal protein in anther tissue (and perhaps other unidentified differences) relative to MON810 and Bt11 posed greater risks of non-target organism impacts than the latter two events.

In some contexts, APHIS suggests that Alternative 3 would treat different events separately as possessing different traits. For instance, APHIS discusses the "trait-based approach" as associated "with a particular organism expressing a particular transgene or group of transgenes…" (DEIS, p. 133). Under this definition, the "trait" would be specific not only to a particular transgene(s), but also to that transgene or transgenes in a particular organism.

However, in other contexts, APHIS implies a much broader definition of trait: "…with a trait-based approach, entire classes of GE organisms could be removed from APHIS oversight…" (DEIS, p. 134). The wording of Alternative 3 likewise suggests a broader definition of trait: "Use novelty of the trait in the species as the trigger for regulation" (DEIS, p. 132). Finally, APHIS implies that plants "having the same phenotype" would be considered as having the same trait (DEIS, p. 134). These wordings suggest a definition of trait that could cover a large range of different mechanisms/transgenes that result in a similar outcome, but which may have different properties and hence could pose different risks. The definitions of trait and phenotype

in the glossary (Appendix A) are not precise enough to decide between these alternative interpretations.

Different transformation events that give rise to the same or similar trait could be different in two ways:

1) Differences relating to different transgene(s) and/or recombinant protein products of trangene(s) that give rise to the "same" trait (e.g. the glyphosate-tolerance example above); and
2) Unanticipated changes in GE plants transformed with the same transgene(s) due to transformation-related differences.

Both classes of differences could result in GE plants that pose differing risks despite having the "same" or similar trait or phenotype. A trait-based approach, even with the more restricted definition of trait as associated "with a particular organism expressing a particular transgene or group of transgenes…" (DEIS, p. 133) would not account for unanticipated and potentially hazardous changes in the biochemical make-up of a unique transformation event attributable to the transformation process. Therefore, APHIS should adopt event-by-event regulation over the trait-based approach or other alternatives.

**Exclusion of Certain Organisms Based on Risk**

APHIS should not exclude certain genetically engineered organisms or classes of GE organisms from regulatory oversight based on risk. As discussed further in the comments to Issue 2, there is no adequate scientific basis for APHIS to make such exclusions. APHIS itself provides the justification for rejecting this option in its commentary on "trait-based regulation," which it admits "would not account for unanticipated changes relating to the transformation process or other differences that may exist at the biochemical level among plants having the same phenotype" (DEIS, pp. 133-134). Just as regulation by trait would fail to account for such unanticipated and potentially hazardous changes in GE organisms bearing the same trait, so would exclusion of certain (classes) of GE organisms from regulatory oversight. Further, APHIS also cites the National Research Council ("NRC") report entitled *Environmental Effects of Transgenic Plants" The Scope and Adequacy of Regulation*, and APHIS explains that NRC "argued that USDA should regulate all transgenic plants, as there is no scientific basis on which to forecast which ones might pose a risk." (DEIS, p. 20)..

APHIS has not defined how such an exclusion mechanism would work, but rather consigns the specifics to either an administrative action or a rule-making mechanism (DEIS, pp. 23-24). Thus, there is no clear proposal at issue, which makes it difficult to offer informed comment. APHIS's presentation of this issue is also unclear in places, making comment even more difficult.

APHIS first suggests that "existing scientific data be used to identify GE organisms that require little or no oversight ***based on the plant-trait combination*** (Hancock 2003)" (DEIS, p. 23, emphasis added). Yet on the following page, APHIS implies that ***any plant*** transformed with a

particular transgene (e.g. the *nptII* gene) might be excluded from regulatory oversight: "The agency may wish to use such a mechanism to exclude certain types of organisms that APHIS deems safe based on an extensive history of safe use (e.g., the *nptII* gene)" (DEIS, p. 24). The *nptII* gene is neither an organism, as implied here, nor a "plant-trait combination," as suggested on the previous page. This leaves it completely unclear as to how APHIS would implement such an exclusion mechanism.

Other examples of classes of GE organisms that APHIS suggests might be excluded from regulatory oversight include: 1) any GE plants generated from transformation with DNA from the same or sexually compatible species; 2) such intrageneric GE plants, but only if the transformed species is highly domesticated with no wild or weedy relatives; and 3) any GE plant "in which the only transgene expressed was a particular marker gene" (EIS, p. 24).

Exclusion of any of these classes of GE organisms from regulatory oversight is unacceptable due to potential adverse consequences of the transformation process, as explicitly acknowledged by APHIS in the context of trait-based regulation (DEIS, pp. 133-134, as quoted above), of the transformation process. The nature or source of the DNA (whether derived from the same species as the transformed plant, whether it is a marker gene or otherwise) is irrelevant to the issue of transformation-related changes. In addition, the exclusion categories suggested by APHIS completely ignore the nature of the genetic construct of which the transgene of interest is a part. For instance, even if we assume that GE plants incorporating the *nptII* gene have a history of safe use, a new GE transformation event transformed with a novel genetic construct incorporating the nptII gene (e.g. linked to a novel promoter or other novel regulatory sequence) might result in vastly increased expression levels of the gene's protein product, or an altered pattern of expression of the protein product in different tissues, or other unanticipated changes.

Changes of either or both types (transformation-related or genetic construct-specific) could trigger potentially hazardous changes in the novel GE transformation event not seen with prior transformation events incorporating the very same transgene of interest.

Finally, exclusion of certain classes of GE organisms from regulation would directly contradict a fundamental axiom of the U.S. Coordinated Framework for regulation of GE organisms, case-by-case assessment (DEIS, p. 88). For these reasons, and because APHIS has failed to clearly define how such an exclusion mechanism would work, APHIS should not exclude any GE organism or class of GE organisms from regulatory oversight.

**Biological Control Agents**

APHIS should regulate GE biological control organisms because they may harm the environment. Biological control species typically harm some organisms, in particular their target pests, but also may harm non-target species. The properties that make biological control organisms effective may increase the likelihood that they will also harm some non-target organisms. Some biological control organisms have very narrow host ranges or a small number of target species, and may therefore be less likely to harm non-target organisms. However, there are many cases where organisms have been introduced to control a pest, only to cause substantial

harm to non-target species.[147] Genetic engineering to enhance the virulence, aggressiveness, or survival of biological control organisms may cause harm by unintentionally increasing host or geographic range.[148] Also, many biological control organisms can survive and reproduce in the environment. It is therefore important that biological control organisms are rigorously assessed for environmental safety. For live biological control organisms, this assessment should occur before environmental release.

EPA regulates conventional and GE biological control microbes if they are intended to control or mitigate a pest. APHIS regulates insects that may be plant pests, such as non-domestic biological control arthropods. APHIS should also regulate any other GE biological control organisms not already regulated by EPA or APHIS. GE biological control arthropods should be regulated regardless of origin because genetic enhancement may alter host range or other environmental properties.

Biological control nematodes, whether conventional or GE, are typically not regulated by EPA or APHIS. Although there do not appear to be any commercialized biological control GE nematodes at the present time, it is unclear whether GE nematodes would be regulated.

Several entomopathogenic non-GE nematodes are currently used for biological control, especially species in the genera Heterorhabditis and Stinernema.[149] The model nematode C. elegans has been genetically engineered for a number of years, and the sequence of its genome may stimulate genetic engineering of biological control nematodes. Genetic engineering of biological control nematodes is being explored, suggesting that GE nematodes may be introduced into the environment in the future.[150]

Nematodes are extremely abundant and important soil organisms, fulfilling many roles including as saprophytes; insect and plant pathogens; and as fungivores and bacteriovores. Because of their importance ecologically, biological control nematodes should be regulated for safety. It is especially important to regulate GE nematodes, which could have unanticipated harmful effects such as increased host range or altered habitat.

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[147] Louda S.M., Pemberton R.W., Johnson M.T. and Follett P.A. (2003) Nontarget effects – the Achilles' heel of biological control? Retrospective analyses to reduce risk associated with biocontrol introductions. Annu. Rev. Entomol. 48:365-396.

[148] Chet I. and Inbar J. (1994) Biological control of fungal pathogens. Appl Biochem Biotechnol. 48(1):37-43; Maeda S., Volrath S.L., Hanzlik T.N., Harper S.A., Majima K, Maddox D.W., Hammock B.D., and Fowler E. (1991) Insecticidal effects of an insect-specific neurotoxin expressed by a recombinant baculovirus. Virology 184(2):777-80; St. Leger R.J., Lokesh, J., Bidochka M.J., and Roberts D.W. (1996) Construction of an improved mycoinsecticide overexpressing a toxic protease. Proc. Natl. Acad. Sci. U S A. 93:6349-6354.

[149] Liu J., Poinar G.O. Jr., and Berry R.E. (2000) Control of insect pests with entomopathogenic nematodes: the impact of molecular biology and phylogenetic reconstruction. Annu. Rev. Entomol. 45:287-306.

[150] Gaugler R., Wilson M., and Shearer P. (1997) Field release and environmental fate of a transgenic entomopathogenic nematode. Biological Control 9:75-80.

**Issue 2: Risk-Based Categories for Environmental Release of Regulated GE Organisms**

**Summary:**
CFS opposes the development of a tiered risk-based permitting system because each transformation event can have unintended effects that must be assessed on a case-by-case basis. There is no scientific basis for establishing a risk-based system based primarily on past experience with different GE organisms/plants: 1) of the same phenotype category; 2) of the same or similar phenotype; or 3) transformed with the same gene of interest. The preferred, more protective system would include a case-by-case assessment process considerably more stringent than the current notification process, approximating the current deregulation process. If a risk-based system is adopted, APHIS should adopt an enhanced Alternative 4, with across-the-board strengthening of gene containment measures (i.e. for all risk categories) based on the noxious weed risks posed by all regulated GE plants. APHIS should adopt more stringent regulation of all GE plant field trials due to the numerous lapses in gene containment that have occurred with notification field trials.

**Comments:**
APHIS proposes to classify GE organisms "according to risk and familiarity so that oversight and confinement vary by category" (EIS, p. 25). However, GE organisms proposed for environmental release (at least, for the initial field trial of a specific transformation event) are by their very nature novel organisms; APHIS thus has no experience or familiarity with the GE organism on which it can base classification into risk-based categories. The classification proposed by APHIS would only be based on the extremely limited data submitted by the applicant with the field trial permit application, and is thus scientifically indefensible.

Each transformation event is unique due to the inherently imprecise nature of recombinant DNA techniques. rDNA techniques presently used do not allow for control of the number or site of transgene insertion. They often result in fragmentation of the transformation vector, insertion of gene fragments, and consequent generation of novel fusion proteins. Without control over the site of insertion, unintended effects are assured. These may include up-regulation of other genes whose expression products may be toxic or allergenic or pose risks to beneficial insects, or down-regulation of genes expressing nutritional or toxin-suppressing compounds. Disruption of regulatory DNA (e.g. encoding "active RNA") will often have more complex effects, depending on the function of the regulatory DNA and the network of cellular elements or functions subject to its modulation. Due to the still-great ignorance of plant genomes, techniques that permitted site-specific integration, even if they were available, would not be assured of eliminating unintended effects.

For these reasons, each transformation event must be regarded as unique and attended by a peculiar suite of unintended effects. Unintended effects are common in the laboratory. More significantly, a few have been discovered in commercialized GE crops. For instance, there is evidence that several Bt corn events involving differing versions of the bacterial-derived cry1Ab gene (fragment) and its corresponding protein have increased lignin content in stem tissue. This

particular effect may slow degradation of Bt corn residues in the soil versus conventional corn, or have other secondary impacts that have not been investigated.[151] Glyphosate-resistant soybeans treated with glyphosate appear to have lower levels of certain phytoestrogens.[152] These effects were discovered by independent researchers years after commercial introduction of these crops. They were not revealed in supposedly exhaustive studies conducted by the crop developer. Additional research would likely turn up other such effects. Each novel GE crop must be regarded as even more likely to have unintended and undiscovered properties. There is no scientific basis for assigning risk to unique products with undiscovered properties developed with haphazard, imprecise techniques. The unique and non-repeatable nature of each rDNA transformation event makes "case-by-case" assessment absolutely necessary, and invalidates the very concept of "product type," whether for *a priori* risk assignment or any other purpose.

Neither can one rely on a supposed history of safe use of similar products as justification for a particular risk assignment. For instance, say for the sake of argument that all novel GE crops with an herbicide-tolerance trait were to be defined by APHIS as a "low-risk" product type. This would presumably encompass not only glyphosate- and glufosinate- resistance, but also resistance to dicamba, 2,4-D, imidazolinone or any other herbicide as well. But the tolerance mechanisms vary greatly from herbicide to herbicide, as do the toxicities of the HT crop-associated herbicide, and many other factors. There is no scientific justification for considering this heterogeneous group to pose a similar degree of risk (even if we ignore GE-event specific differences).

Take an even narrower "product type" – resistance to glyphosate. There are at least three different mechanisms: CP4 EPSPS, glyphosate oxidoreductase and glyphosate acetyltransferase. One involves an enzyme that is (relatively) insensitive to glyphosate, the second an enzyme that degrades glyphosate, the third an enzyme that acetylates glyphosate (and certain amino acids as well). The fate of glyphosate absorbed by the plant will be different in each case. Different compounds will be generated from the glyphosate absorbed by the plant, and perhaps exuded by the roots, in each case. Effects of the exudates on the rhizosphere will also likely differ in each case. There is no scientific justification for an *a priori* system that classifies these very different GE crops as posing a similar degree of risk.

Assignment of all crops/crop varieties that employ the same mechanism for the same phenotype to a common risk category is also scientifically illegitimate because the unique unintended effects accompanying any transformation event undermine such a risk category, as discussed above. APHIS also implicitly recognizes the potentially adverse consequences of such "unanticipated changes relating to the transformation process…" (DEIS, p. 134). Therefore, there is no scientific justification for assignment of novel GE crops to specific risk categories.

[151] Saxena & Stotzky (2001a). "Bt Corn Has a Higher Lignin Content than Non-Bt Corn," American Journal of Botany 88(9), pp. 1704-06.
[152] Lappe et al (1999). "Alterations in Clinically Important Phytoestrogens in Genetically Modified, Herbicide-Tolerant Soybeans," Journal of Medicinal Food, Vol. 1, No. 4, July 1, 1999.

The only way to at least partially avoid these difficulties would be to collect much fuller data from GE crop field trial applicants prior to the environmental release of any novel GE crop. The data required for notification field trials is far from adequate for meaningful risk assessment of novel GE crops that may be planted year after year on thousands of acres (we note that there is no acreage limit for notification field trials). To our knowledge, crop developers need not provide any data on non-target organism impacts, rhizosphere impacts of the GE crop and any associated cultivation practices (e.g. herbicide use with HT crop systems), compositional data on crop tissues to detect unanticipated changes, molecular data on site and number of transgenes inserted and their site of integration, etc. Such data should be developed by the crop developer from plants grown in tightly controlled greenhouse conditions, and provided to APHIS for assessment, prior to any environmental release.

APHIS should adopt a more stringent assessment of and permit conditions for all GE crops proposed for field trials without *a priori* assignment to risk categories, and only on the basis of such data as described above.

The existing "two-tier" system has not effectively protected the environment nor provided for adequate gene containment, and adding more risk categories will do nothing to redress these deficiencies. APHIS' claim that "[t]he notification option has been an effective regulatory tool" (DEIS, p. 26) is not supported by the facts.

In 2005, the USDA's Office of the Inspector General (OIG) conducted an audit covering GE crop field trials conducted in 2002 and 2003, finding numerous basic deficiencies in APHIS oversight.[153] A few of the more flagrant deficiencies are noted below:

1) In most cases, APHIS doesn't know where or even if many field tests have been planted. In 85% of the permits and 100% of notification field trials that OIG reviewed, only the company's business address, or the state and county of the field trial, was listed as the planting location.

2) APHIS does not require submission of written protocols, and thus does not review them, prior to issuing a notification permit. OIG notes that an APHIS report completed in 2001 concluded that some notification protocols might not be adequate to meet its field test performance standards and identified several major areas in need of improvement. According the USDA's Inspector General, the APHIS study showed that APHIS should in fact review these protocols prior to granting permits. This reality directly contradicts APHIS' claim "APHIS requires effective confinement measures" (DEIS, p. 26).

[153] OIG (2005). "Audit report: Animal and Plant Health Inspection Service controls over issuance of genetically engineered organism release permits," Audit 50601-8-Te, USDA, Office of Inspector General, Southwest Region, December 2005. Online at *www.usda.gov/oig/webdocs/50601-08-TE.pdf*.

3) "APHIS did not maintain a list of planted GE fields." This recalls a similar deficiency in tracking permit information noted by a previous OIG report in 1994, suggesting that APHIS has not corrected this fundamental defect since that time, nearly a decade ago.[154]

4) APHIS failed to conduct scheduled inspections of numerous field trials of both pharmaceutical-producing crops and other experimental GE crops grown under notification. Only 1 of 12 sites inspected by OIG in 2003 had all 5 required inspections; only 18 of the 55 required inspections were performed for the other 11 sites. APHIS claims correctly that "all field releases are subject to inspection" (DEIS, p. 26), but fails to note that it does not conduct most "required" inspections, perhaps because it is unaware of where the field tests are taking place (item 1 above).

5) In two cases, the OIG inspectors discovered that a total of 2 tons of harvested pharma crops had been stored onsite for over 1 year, without APHIS' knowledge, and thus without APHIS inspection of the storage facility, one of many "requirements" of pharmaceutical crop field trial permits.

Given these inadequacies, it is alarming to note that: "Any new system that APHIS considers will incorporate salient aspects of the notification system…." (DEIS, p. 26).

The OIG made 28 recommendations to APHIS to remedy these deficiencies and lapses in its regulatory performance. APHIS rejected 7 of these recommendations, and agreed to only partially comply with two others. Some of the measures APHIS refused to implement include:

1) Development of policies to restrict public access to edible GE crops, especially pharmaceutical-producing crops.
2) Require submission of written protocols prior to approving notification permits
3) Require APHIS review of notification protocols.
4) Distribute written protocols to inspection personnel for notification inspections
5) Impose sanctions for missing or late progress reports from the field trial operators
6) Require applicants to report planned date of disposal of harvests of GE crops producing pharmaceuticals or industrial proteins.
7) Develop and implement written policies and procedures for selecting specific field tests sites for inspection based on risk.
8) Require submission of planting notices, 4-week reports, and harvest/termination reports.

APHIS states that: "The notification option has been an effective regulatory tool: the process features a simplified submission format, expedited agency review, and reduced regulatory burdens for both applicants and the agency while still ensuring safety" (DEIS, p. 26). While notification has been expeditious and had reduced "regulatory burdens," the record is clear that it has not ensured gene containment. APHIS has unduly prioritized efficiency and reducing

[154] Audit Report 33099-9-Hy, dated August 1994, USDA Office of the Inspector General, cited in OIG (2005) (see previous footnote).

regulatory burdens over protecting the environment. This type of regulatory system should not be perpetuated.

Most of the 16 contamination episodes of which we have knowledge have occurred in the US, and involved GE crops grown under notification field trials.[155] Several of these have involved considerable economic damage to U.S. farmers, food companies, as well as the crop developers themselves. Many more contamination episodes have likely occurred, but have either gone undetected or unreported. The many lapses in APHIS regulation of GE crop field trials discussed above increases the likelihood that many contamination episodes have occurred, and will continue to happen without significant strengthening of gene containment standards for ALL GE crop field trials.

Once again, adding more risk categories will do nothing to strengthen APHIS' performance. APHIS should adopt ALL of the OIG's recommendations, and follow up by implementing them.

As discussed in our comments to Issue 7, APHIS should require pharmaceutical crop-level gene containment conditions for all GE crop field trials, regardless of which risk category the crop may be assigned to. If a risk-based system is to be applied, an enhanced Alternative 4 should be adopted. In particular, APHIS is urged to expand its criteria for risk class assignment beyond narrowly construed "risk" and "familiarity."[156] Of particular importance is assessment of the novel GE crop as posing a "noxious weed risk" (EIS, Table 4-2, p. 140). One factor that can make any novel GE crop a "noxious weed risk" is its potential to harm "the interests of agriculture," either directly or indirectly. The presence of unapproved, regulated GE crop material in commercial food supplies can have substantial, adverse economic impacts on American agriculture, as demonstrated with the contamination episodes involving LibertyLink Rice events 601 and 604 and Prodigene's pharmaceutical corn. The common denominator in these episodes was the simple fact that these contaminating GE crops were "regulated articles," and hence unapproved for commercial use, irrespective of the nature of the transgene or its

[155] "Contamination Episodes with Genetically Engineered Crops," Center for Food Safety, August 2006. http://www.centerforfoodsafety.org/pubs/Contamination%20episodes%20fact%20sheet.pdf.

[156] APHIS's criteria for "familiarity" are presented casually, by way of "examples," in a footnote (EIS, Table 4-2, p. 140, footnote 32). Here, we learn that familiarity can mean "Agency experience with the gene product, trait, or similar traits," and that "APHIS has experience with many [unidentified] agronomic and product quality traits." Further, familiarity is established when "key food safety issues of the new substance have been evaluated," and when the gene is derived from a food crop versus another non-food organism. As argued above, experience with "a gene product, trait or similar traits" as found in past GE crop events leaves important unanswered questions concerning the risks posed by a novel GE crop. In addition, food safety evaluations of novel transgenic proteins are notoriously poor, and genes derived from food crops do not necessarily give rise to unproblematic proteins, as evidenced by the example of Brazil nuts transformed with an allergenic soybean protein. In short, APHIS's "familiarity" as defined here forms a poor basis for risk class assignment.

protein product. Therefore, to prevent future harm to the interests of agriculture, all GE crops for environmental release must be subject to much stricter gene containment standards, irrespective of whatever risk category they are assigned. Factors that would tend to place a crop in a higher risk category based on the "noxious weed risk" they pose include the following:

1) Presence of sexually-compatible weedy relatives in the region of the field trial (increases risk);
2) Presence of sexually-compatible commercial cultivars in the region of the field trial (increases risk);
3) Higher potential for cross-pollination between the novel GE crop and
   a) sexually-compatible weedy relatives; and
   b) sexually-compatible commercial cultivars.
4) Higher potential for seed dispersal via animals or other mechanisms to fields of commercial cultivars or the environment;
5) Acreage of the proposed field trial permit (greater acreage increases risk of gene containment lapses; see NAS (2002), p. )
6) Cumulative impacts resulting from other similar GE crops planted commercially or in field trials in the same area.

This issue is discussed in greater detail in the comments to Issue 7.

**Issue 3 – Conditional Deregulation and Regulatory Flexibility**

**Summary:**
USDA should always maintain continuing authority to restrict or otherwise condition the use of any GEO that completes APHIS review. APHIS proposes conditional deregulation of certain GE crops based on "minor unresolved risks." APHIS should not deregulate any GE crop that poses known, unresolved risks, which should be resolved prior to any deregulation decision. However, APHIS should maintain regulatory authority over all GE crops via conditional deregulation to enable it to respond rapidly, effectively and appropriately to risk issues that emerge only after commercialization. In addition, there should be a mandatory deregulation petition process for every stacked GE crop. Finally, multiple crop systems should be used as comparators rather than merely the predominant agricultural system in APHIS's assessment of GE crops for possible deregulation.

**Comments:**

**No deregulation of GE crops presenting known, unresolved risks:**
GE crops should not be commercialized if there are known, unresolved risks, even if they are considered to be minor at the time. Unresolved risk issues clearly point to the need for continued regulation of the pertinent GE crop in field trials until adequate data are collected to resolve it.

The fact that genetically engineered crops have been commercialized and grown on a wide scale does not demonstrate that there is no harm to agriculture or the human environment. Yet, in this PEIS, APHIS states that "[i]n spite of widespread cultivation of GE crops, there have been no

reports of deregulated GE plants causing harm to agriculture or the human environment" (DEIS at 29). In contrast, the National Resource Council came to the opposite conclusion: "claims that the lack of effects from the tens of millions of hectares of transgenic crops that have been planted in the United States during the past three years are nonscientific. There has been no environmental monitoring of these transgenic crops, so any effects might have occurred could not have been detected. The absence of evidence of an effect is not evidence of absence of an effect." NATIONAL RESEARCH COUNCIL, ENVIRONMENTAL EFFECTS OF TRANSGENIC PLANT, NATIONAL ACADEMY PRESS, 2002 ("NRC 2002") at 79.

APHIS' claim that no deregulated crop has caused "harm to agriculture" is patently false, and indicative of the agency's blindness to the many adverse economic impacts GE crops have had on U.S. agriculture.

APHIS deregulated StarLink corn, yet StarLink's illegal infiltration into the seed, grain and food supply resulted in costly recalls of over 300 food products, rejected shipments of contaminated corn, lost income to farmers from lower corn commodity prices, and necessitated destruction of StarLink-contaminated seed lines, among many other "harms to U.S. agriculture."[157] The estimated overall cost of this major contamination debacle to Aventis CropScience, StarLink's developer, as well as farmers and the food industry, has been estimated at $1 billion.[158] The genetic engineering of papaya in Hawaii (no other country in the world grows it) has resulted in huge losses in export income to papaya growers there, and reduced prices, due to rejection of the GE papaya overseas.[159] These are just a few of the many harms to agriculture from the premature introduction of poorly tested, internationally rejected, deregulated GE crops in the United States.

**Continuing regulatory authority required for risk issues that emerge only after commercialization**

Risk assessment at the field trial stage is hampered by the small scale of field trials in comparison to commercial scale plantings, which can be several orders of magnitude larger. Many observers have noted that field trials are inadequate for resolving all environmental issues.[160] Many adverse environmental effects only occur at large field or landscape scales. In

[157] For an overview of press coverage of the StarLink contamination episode of 2000, which continued for at least three years, see http://www.foe.org/camps/comm/safefood/gefood/foodaid/news.html

[158] "Tests to detect allergens in altered foods fall short," June 12, 2002 *St. Louis Post-Dispatch*, June 12, 2002

[159] "The Failure of GE Papaya in Hawaii," Greenpeace International, May 2006. http://www.greenpeace.org/international/press/reports/FailureGEPapayainHawaii

[160] Kareiva P., Parker I.M., and Pascual M. (1996) Can we use experiments and models in predicting the invasiveness of genetically engineered organisms? Ecology 77:1670-1675; National Research Council (2002) "Environmental Effects of Transgenic Plants; The Scope and Adequacy of Regulation," The National Academies Press, Washington, D.C. (see especially Section 6); Snow A.A., Andow D.A., Gepts P, Hallerman E.M., Power A., Tiedje J.M., and

addition, it may take several years for such adverse impacts to become evident.[161] Monitoring of GE plants after commercialization should therefore be the norm rather than the exception, with APHIS retaining authority to impose restrictions, as needed, to ameliorate any problems that develop after commercialization. Post-commercialization monitoring would perform a function similar to that of post-market drug surveillance for adverse effects not detected in clinical trials, whose size is necessarily limited.

Other unanticipated risk issues may emerge based on scientific or agronomic findings not available at the time of the initial deregulation. Such risk issues may or may not be related to the larger scale of commercial plantings vs. field trials. Genetically engineered crops are more likely to pose unanticipated risk issues than crops developed through conventional breeding for several reasons. First, genetic engineering is still a relatively new technology, with commercial GE crops present in the marketplace for barely more than a decade; by contrast, we have a millennia-long history of safe use with crops developed by most traditional breeding methods. Secondly, the science of molecular biology upon which genetic engineering is based is in flux, with new findings regularly upending long-held "truths," for instance the growing awareness that "junk DNA" serves important functions. Third, subtle changes to food crops from the process of genetic engineering may pose longer-term risks to the environment and human health that do not become evident until after decades of exposure. Finally, certain GE crops may be accompanied by substantial changes in agronomic practices causing unanticipated harms after commercialization that require amelioration. For all of these reasons, it would be prudent of APHIS to make ALL deregulation decisions for GE crops conditional, so that rapid, effective and appropriate action can be taken to address emerging risk issues unknown at the time of initial deregulation.

At present, APHIS's only recourse when problems emerge after commercialization of a GE crop is to re-regulate it. Therefore, it would be prudent of APHIS to reserve broad authority to impose restrictions, as needed, on all GE crops the agency deregulates. Conditional deregulations could be accompanied by mandatory monitoring to assess potential risk issues. Such monitoring could be conducted by APHIS, university extension agents, or other independent third parties. The results of monitoring activity would provide the basis for any needed restrictions on cultivation of the pertinent GE crop. This recommendation is in line with the National Research Council, which in 2002 explicitly recommended that APHIS consult independent scientists to aid it in decision-making.[162]

It is worth noting that APHIS' sister agency, the Environmental Protection Agency, grants time-limited registrations to the pesticidal proteins (so-called "plant-incorporated protectants" or PIPs) produced in GE crops under its jurisdictions. These registrations are typically 5-7 years in

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Wolfenbarger L.L. (2004) "Genetically Engineered Organisms and the Environment: Current Status and Recommendations," ESA Position Paper. Ecological Society of America, Washington D.C. http://www.esa.org/pao/esaPositions/Papers/geo_position.htm

[161] Kareiva et al (1996), op. cit.

[162] National Research Council (2002) "Environmental Effects of Transgenic Plants; The Scope and Adequacy of Regulation," The National Academies Press, Washington, D.C.

length. EPA grants time-limited registrations to enable it to consider new data concerning PIPs and the GE crops in which they are produced that emerges after the initial registration. If new scientific research indicates that a PIP has a previously unnoticed human health or environmental effect, EPA can choose not to re-register the PIP, or re-register the PIP and associated GE crop under altered conditions to ameliorate the harm.

APHIS should make use of conditional deregulation for all GE crops to serve similar ends. The next section illustrates how a system of conditional deregulation would have been (and could still be) useful with transgenic HT crop systems.

**Case Study: HT Crop Systems**

Prior to the introduction of transgenic HT crop systems, there was a range of expert opinion on the agronomic and environmental impacts they might have. Some experts believed that HT crop systems might foster greater use of crop rotation, thus slowing the development of weeds resistant to the HT crop-associated herbicide.[163] Many weed scientists held that weed resistance to glyphosate and glufosinate (the herbicides associated with the two major HT crop systems) would develop more slowly than to many other herbicides (Bradshaw et al 1997; Devine et al 1993, as cited by APHIS, DEIS, p. 120). This opinion (with respect to glyphosate) was based at least on part on the presumed rarity of natural resistance to glyphosate in weed populations.[164] Other scientists correctly predicted that HT crop systems would lead to increased reliance on a single herbicide and thereby foster more rapid development of resistant weeds through increased selection pressure.[165]

There is now over a decade of experience with HT crop systems, primarily with glyphosate-tolerant crops planted on over 114 million acres in 2006. Those experts who predicted slow development of weed resistance have been proven decisively wrong. It is now undeniable that glyphosate-resistant weeds pose a substantial threat to the interests of American agriculture, and that this situation was not generally recognized by experts in the field (though it was foreseen by some) when glyphosate-tolerant crops were first introduced.

The lesson of HT crop systems is that APHIS and other informed experts can make faulty judgments in the absence of adequate empirical data. As noted above, data from field trials may not provide a sufficient basis for judging impacts at commercial scale. Access to any data that may exist may be limited by the crop developer for proprietary reasons.

If APHIS had had a conditional deregulation system in place at the time the first HT crop systems were deregulated, it could have taken appropriate steps to address the problem of resistant weeds. First of all, APHIS could have responded to the predictions of some weed

[163] Radosevich, S. R., C. M. Ghersa, and G. Comstock. 1992. Concerns a weed scientist might have about herbicide tolerant crops. Weed Technol. 6: 635–639.

[164] Yancy, C. (2005). "Weed scientists develop plan to combat glyphosate resistance," Southeast Farm Press, June 3, 2005.

[165] See discussion in Martinez-Ghersa et al (2003). Concerns a weed scientist might have about herbicide-tolerant crops: A revisitation," *Weed Technology* 89: 160-167.

scientists that HT crop systems would foster more rapid development of resistant weeds by establishing a monitoring system as a condition of the initial deregulations. The monitoring activity could have been conducted by APHIS itself, or at APHIS's direction by university extension agents or other independent third parties. Such monitoring would have alerted APHIS to the weed resistance problem in a timely manner. Findings from monitoring could have formed the basis for imposition of certain restrictions on HT crop systems to slow development of resistant weeds. Monitoring results would also have been useful to APHIS in assessing the cumulative impacts of deregulating new HT crops tolerant to the same herbicide, imposing conditions on their deregulation, or denying the deregulation petitions, as appropriate.
If properly implemented, conditional deregulation accompanied by monitoring provides flexibility for more appropriate regulatory responses than the current all-or-nothing system.

**Conditional Deregulation vis-à-vis Trait-Stacking**
APHIS should adopt its suggestion of using conditional deregulation to restrict commercialization of certain stacked GE crops resulting from crosses of GE crops that have already been deregulated. However, APHIS should go further and require separate deregulation petitions and review processes for every stacked GE crop.

Currently, APHIS allows two separately deregulated traits to being stacked in crop without any further review. According to experts in the risk assessment process for GE foods, "stacked" crops (crops with two or more GE traits) have a greater potential to exhibit unanticipated and potentially harmful changes due to their more extensive genetic modification. These experts recommend application of more sophisticated testing techniques, such as metabolic profiling, for stacked GE crops than for single-trait GE crops due to the enhanced potential for hazardous unintended effects that accompanies trait-stacking.

> "Present approaches to detecting expected and unexpected changes in the composition of genetically modified food crops are primarily based on measurements of single compounds (targeted approach). … The targeted approach has severe limitations with respect to unknown anti-nutrients and natural toxins, especially in less well known crops. … In order to increase the possibility of detecting secondary effects due to the genetic modification of plants that have been extensively modified, new profiling methods are of interest and should be further developed and validated (non-targeted approach). ***Application of these techniques is of particular interest for genetically modified foods with extensive genetic modification (gene stacking)*** meant to improve agronomical and/or nutritional characteristics of the food plant (emphasis added)." [166]

Another class of concerns is related to stacked GE crops that would be accompanied by altered agronomic practices. To take one example, biotechnology companies are actively developing HT crops with tolerance to two herbicides rather than one, as at present.[167] Such crops would allow "over-the-top" application of two herbicides rather than just one.

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[166] KUIPER, H.A.., KLETER, G.A., NOTEBORN, H..P,J.M., KOK, E.J. (2001). Assessment of the food safety issues related to genetically modified foods. *The Plant Journal* **27**(6), 503-528.
[167] In fact, two dual-HT crops are presently being considered for deregulation by USDA. See petitions 06-271-01p and 07-152-01p at http://www.aphis.usda.gov/brs/not_reg.html

With current generation HT crop systems, companies have often had to petition the U.S. Environmental Protection Agency (EPA) to establish new tolerances (e.g. for glufosinate herbicide on transgenic LibertyLink rice[168]) or increase existing tolerances (e.g. 6 ppm to 20 ppm for glyphosate on Roundup Ready soy[169]) for residues of the associated herbicide in the food and/or feed portions of the pertinent crop. The need for new or increased tolerances is explained by the fact that "over-the-top" application is not practiced with most herbicides on most non-HT crops because it would kill or severely damage the crop, and over-the-top application will likely lead to greater pesticide residues on the food & feed parts of the crop than the pre-emergence application practices common to most non-HT crops. Thus, American consumers are likely already being exposed to higher levels of pesticide residues in their food thanks to the introduction of HT crop systems.

It is generally recognized that some EPA-approved pesticides do have adverse impacts on farmers and agricultural workers; that EPA-approved pesticides include many that are suspected to have adverse impacts such as carcinogenic or endocrine-disruption activity; and that many EPA-approved pesticides have not been adequately tested for long-term adverse effects that they may cause in those who consume residues of these pesticides in food.[170] These concerns – as well as suspected environmental harms of many EPA-approved pesticides – formed the basis for USDA's and EPA's official endorsement of policies to promote integrated pest management practices to reduce the use of agricultural chemicals.[171] Though this program – at least as of 2000 – has not been successful (overall agricultural chemical use increased from 900 to 940 million lbs. from 1992 to 2000, see GAO report in last footnote, p. 11) – the rationale for its implementation speaks directly to the need to reduce agricultural chemical use to better protect human health and the environment.

HT crops that permit "over-the-top" application of two rather than just one herbicide pose several additional concerns above and beyond those of single-herbicide HT crops. First, if biotech companies follow past practice with single-herbicide HT crops and obtain new or increased tolerances for residues of a second herbicide, consumers will likely be exposed to still higher overall levels of pesticide residues in foods. Second, consumers will likely be exposed to higher levels of residues of two herbicides which together may pose risks greater than the sum of the risks posed by each, taken individually. Such interactions leading to enhanced toxicity have been reported in the scientific literature,[172] but have been very little studied. Such interactions

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[168] EPA (2003). Glufosinate-Ammonium; Pesticide Tolerance. *Federal Register*, Vol. 68, No. 188, September 29, 2003, 55833-55849.

[169] EPA RULE (1992). Pesticide Tolerances and Food and Feed Additive Regulations for Glyphosate: Final Rule. *Federal Register*, Vol. 57, 42700.

[170] See discussion, with citations, in the section on herbicide-tolerant crops systems.

[171] "Agricultural Pesticides: Management Improvements Needed to Further Promote Integrated Pest Management," Government Accounting Office, GAO-01-815, August 2001.

[172] For instance, see: "Low Doses of Common Weedkiller Damage Fertility, Pesticide Action Network Update Service, October 11, 2002, at http://www.annieappleseedproject.org/hermixvertox.html.

may involve not only the active ingredients of different herbicides, but also the active ingredient and supposedly "inert" ingredients found in a single pesticide formulation. One example of the latter is the enhanced toxicity of Roundup formulations containing polyethoxylated tallowamine versus glyphosate (the active ingredient) alone.

For these reasons, APHIS should require independent assessments of all stacked GE crops. APHIS should require more complete data from developers of stacked crops, such as metabolic profiling, to better detect potentially adverse unintended effects, which are more likely to occur in stacked crops due to the more extensive genetic modification and insertional mutagenesis to be expected with them. CFS also supports mandatory long-term animal feeding studies for all GE crops, especially those with stacked traits.[173]

In the case of dual-HT crop systems,[174] APHIS should consult with the U.S. Environmental Protection Agency for assessment of the potential for adverse interactive effects on consumers of the pertinent residues to be expected on such crops. While EPA does not normally test for such synergistic effects in the normal course of its pesticide registration process, it would be prudent for it to do so in the special case of dual-HT crops. First, a dual-HT crop system will almost certainly be accompanied by regular over-the-top application of one particular pair of herbicides, leading to increased consumer exposure to residues of both. Second, the number of dual-HT crop systems involving different pairs of herbicides will be limited in number, at least for the foreseeable future. One reason EPA does not examine synergistic adverse impacts of pesticides is surely lack of resources to examine the large number of possible combinations among the many commercially available pesticides. Finally, if dual-HT crop systems are adopted by farmers to even a fraction of the extent of current generation single-HT crop systems, consumer exposure to increased residues of particular pairs of herbicides could increase greatly. Thus, dual-HT crop systems comprise a special case that both deserve EPA's special attention and should be manageable in terms of EPA's staff and financial resources.[175]

**Separate reviews of all stacked GE crops is feasible**

We note that USDA's past practice has been to subject at least some stacked GE crops to a separate review process. Of the 73 GE crops APHIS has deregulated, 12 (16%) are stacked varieties. Of the GE crops currently up for deregulation, 2 of 11 are stacked.[176] Thus, it does not appear infeasible to require a separate deregulation review process for each new stacked crop.

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[173] Freese & Schubert (2004), "Safety Testing and Regulation of Genetically Engineered Foods," *Biotechnology and Genetic Engineering Reviews*, Vol. 21, p. 299-323.

[174] These comments should be taken to encompass multiple-HT crop systems involving tolerance to three or more herbicides, though to our knowledge none are being developed at present.

[175] It is noteworthy that APHIS has invited comment on the EIS from both the FDA and the EPA, and that APHIS has suggested it might engage both agencies in food-safety evaluations (DEIS, pp. 7, 154). It would also be appropriate to engage EPA on this particular issue of dual-HT crop systems.

[176] See http://www.aphis.usda.gov/brs/not_reg.html, as of August 2, 2007. Last visited Sept. 6, 2007.

**Adaptive Management and Multiple Comparators for Deregulation Reviews**

For post-commercial monitoring to be effective, baseline data are needed for comparison with the transgenic crop. Such data should be developed by APHIS or by independent third parties at APHIS's direction. In addition, APHIS should use an adaptive management approach as discussed by the NAS and a recent position paper of the Ecological Society of America (National Research Council, 2002, Snow et al., 2004). Such an approach uses cycles of goal setting and implementation, where each cycle informs the next until adequate data are acquired. APHIS needs to work with the academic and stakeholder communities to determine when and how such an adaptive management system should be implemented. An *ad hoc* approach to this complex issue will not result in efficient or effective experimental design.

Finally, an adaptive management system requires experimental controls to allow comparisons for determining impacts. The predominant agricultural practices often serve as controls, but "no treatment" and viable alternative practices such as organic, biointensive IMP, or other agroecological approaches, should also be included as controls to obtain an accurate and complete picture of relative environmental impact. As with all technologies, agriculture should strive to improve not only productivity, but also to minimize impact on the environment and enhance society. Successful agricultural methods that advance those goals should be included in experimental designs for comparative purposes.

**<u>Issue 4</u> Oversight of Pharmaceutical and Industrial Compounds.**

APHIS should adopt Alternative 3, and prohibit environmental release of GE food and non-food crops that produce pharmaceutical and industrial compounds. CFS has repeatedly petitioned the agency to prohibit open-air field testing of GEOs that produce pharmaceutical or industrial proteins. This was first presented to the agency in 2002 as part of a legal petition by a coalition of organizations called GE Food Alert. Center for Food Safety, Petition on Genetically Engineered Pharmaceutical-Producing Plant Varieties, available at http://www.centerforfoodsafety.org/pubs/PetitionBiopharmPlanting12.16.2002.pdf (last visited September 11, 2007). CFS has commented on past efforts to address these crops.[177] CFS has also repeatedly commented to the agency that food crops should not be allowed to be used to produce pharmaceutical and/or industrial proteins.

A ban should also cover the environmental release of GE plants that contain transgenes of unknown function. Without knowledge of the function of the transgene, APHIS has no scientific

[177] *See* CFS submitted the following comment letters on biopharm crops that are accessible at the CFS website: http://www.centerforfoodsafety.org/pubs/CommentsEIS4.13.2004.pdf, http://www.centerforfoodsafety.org/pubs/CommentsVentriaEA3.24.2005.pdf, http://www.centerforfoodsafety.org/pubs/CommentsVentriaNorthCarolinaEA6.2.2005.pdf, http://www.centerforfoodsafety.org/pubs/SemBioSys-EA%20comments.pdf, http://www.centerforfoodsafety.org/pubs/Biopharm%20Rice%20Kansas%20comments_final.pdf http://www.centerforfoodsafety.org/pubs/Proinsulin%20Safflower%20Comments%20CFS%20FINAL.pdf (all last visited Sept. 9, 2007).

basis for reasonably excluding environmental, public health or other harms from field tests involving a GE crop that contains such a transgene.

APHIS offers no empirical evidence to support its claim that the current system of permit conditions "are sufficiently stringent that the field tests pose no significant risk to the environment, including human health." (DEIS, p. 144) The only way to ensure that experimental pharmaceuticals produced in GE crops pose no risk to public health or the environment is 100% containment, which is not possible. For instance, even the editors of Nature Biotechnology agree that: "Current gene-containment strategies cannot work reliably in the field … Can we reasonably expect farmers to [clean] their agricultural equipment meticulously enough to remove all GM seed?"[178] The National Research Council has also expressed concern: "…it is possible that crops transformed to produce pharmaceutical or other industrial compounds might mate with plantations grown for human consumption, with the unanticipated result of novel chemicals in the human food supply."[179]

APHIS has granted field trial permits to a company producing rice that generates recombinant human lactoferrin and lysozyme, despite the fact that FDA has refused to approve their safety, and the fact that independent medical experts opposing open-air field-testing of lactoferrin rice told USDA that exposure to even trace levels could present health risks.[180] The highly potent nature of some plant-grown experimental drugs makes even low-level contamination of food or feed a particular concern, regardless of what confinement measures are prescribed. For instance, a Canadian company, SemBioSys, has sought USDA approval conduct to field trials of safflower genetically engineered to produce proinsulin, the precursor of insulin, a hormone that is biologically active in the millionths of a gram.[181] No prescribed confinement regime offers adequate security to provide the needed 100% containment for substances of this potency, particularly given the potential for human error, extreme weather events, and the negligence of field trial operators and government regulators. Below, these comments discuss several known contamination episodes involving pharma crops and APHIS' deficient oversight, further reasons to adopt Alternative 3 as the only option that will protect public health and the environment.

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[178] Nature Biotechnology (2002). "Going with the flow," Editorial, Vol. 20, No. 6, June 2002, p. 527.

[179] NRC (2002), op. cit., p. 68.

[180] Freese, B. (2007). "A Grain of Caution: A Critical Assessment of Pharmaceutical Rice," Center for Food Safety, April 2007. http://www.centerforfoodsafety.org/pubs/Pharmaceutical%20Rice-FINAL.pdf. For assessment of health risks by 14 medical experts, see public comments submitted to APHIS by Agennix, Inc., concerning Ventria Bioscience's proposed field trial of lactoferrin rice in Kansas this year (which USDA approved).

[181] See Center for Food Safety's comments on USDA's deficient environmental assessment of this proposed field trial at: http://www.centerforfoodsafety.org/pubs/Proinsulin%20Safflower%20Comments%20CFS%20FINAL.pdf

To our knowledge, there have been three reports of pharmaceutical crop contamination. APHIS itself makes oblique reference to one such incident in which pharmaceutical corn "volunteers" (plants sprouting from unharvested seed that appear in the following season's crop) contaminated 500,000 bushels of soybeans in Nebraska, necessitating their seizure and destruction at an estimated cost of $3 million (DEIS, p. 38).[182] In the same year, 155 acres of conventional corn was destroyed due to concern that it had cross-pollinated with pharmaceutical corn grown in a field trial in Iowa.[183] Another possible contamination episode was suggested by Chris Webster of the drug company Pfizer, who stated at a meeting on pharma crops hosted by the U.S. government, that: "We've seen it on the vaccine side where modified live seeds have wandered off and have appeared in other products."[184]

The potential for further such episodes is enhanced by APHIS' shoddy regulation of pharmaceutical crops. In 2005, the USDA's Inspector General published an audit finding numerous deficiencies in APHIS oversight of pharmaceutical crop field trials. Below, we quote at length from the Inspector General's report to illustrate how far APHIS' performance in this area lags behind its own stated standards:[185]

**APHIS loses sight of two tons of harvested pharma crops**

"We found that two large harvests of GE pharmaceutical crop were stored for over a year by Applicant F cooperators (farmers conducting field tests for Applicant F), even though the permits did not contain information about the storage period so that it could be assessed by APHIS. During our field site reviews, we found that an Applicant F cooperator stored more than half a ton of a GE pharmaceutical crop for 15 months. In another State, 1.4 tons remained in storage at the cooperator's farm for 17 months. The cooperators said that they were waiting for instructions from Applicant F, who eventually instructed them to ship the harvests back to their headquarters. Although the permit applications for the field tests in these two States disclosed that the harvests would be shipped back to Applicant F's headquarters, they did not indicate when the shipments would occur. Thus, the lengthy storage of the pharmaceutical harvests was not approved by APHIS and the safety protocols of the storage facilities could not be assessed. Also, PPQ did not perform inspections during the extended storage to ensure that the GE crops were safely contained in the facilities."[186]

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[182] APHIS fails to note that this episode involved pharmaceutical corn. See Toner, M. (2002). "Alarms sound over 'biopharming' – tainted crops cast doubt on gene altering," The Atlanta Journal and Constitution, Nov. 17, 2002; and "Something Funny Down on the Pharm," Popular Science, April 2003, which later reveals that the contaminated soybeans were destined for veggie burgers and infant formula.

[183] "GM crop mishaps unite friends and foes," New Scientist, Nov. 18, 2002. http://www.newscientist.com/news/news.jsp?id=ns99993073

[184] See "Plant-Derived Biologics Meeting" transcript, April 5 & 6, 2000. www.fda.gov/cber/minutes/plnt2040600.pdf, p. 77.

[185] OIG (2005). "Audit report: Animal and Plant Health Inspection Service controls over issuance of genetically engineered organism release permits," Audit 50601-8-Te, USDA, Office of Inspector General, Southwest Region, December 2005. Online at *www.usda.gov/oig/webdocs/50601-08-TE.pdf*.

[186] *Id*., pp. 41-42

**Locations of pharma crop field trials often not reported**
"Our review of 53 permit field sites included 20 field sites planted under 13 pharmaceutical and industrial permits**.** All 13 permit holders were required to submit planting notices and 12 were required to submit 4-week/28-day reports. However, only 8 of those 12 permit holders were required to provide GPS coordinates on their 4-week/28-day reports; three failed to provide this information. Although not required to do so by APHIS, one permit holder indicated the specific field site location on the planting notice."[187]

**Deficient reviews of applications for pharmaceutical crop field trials**
"During our fieldwork, we obtained copies of the official files for 10 pharmaceutical permits, which APHIS considers high-risk. Our review found that the files did not contain sufficient information to disclose the extent of the biotechnologist's reviews or the criteria they used to arrive at their decisions. Although the files contained letters to State regulatory personnel, we found that other required documentation was not always in the files. For all 10 of the permits, the tracking sheet was not in the file or not initialed. For 7 of 10 permits, the form to identify the plant's genes and other characteristics was also not in the file or not completed. Furthermore, nine of the approved permits had not undergone supervisory review, an essential control over the application approval process.

Even if the required documentation had been present in the files, we concluded that it would not be sufficient to describe the biotechnologists' complete review process. Specifically, the documentation was not sufficient because it did not describe the scope of the biotechnologists' review of risks associated with introducing a particular GE plant and how the applicant planned to mediate those risks. Scientific criteria for approving a field test application might address the likelihood of the unintentional spread of GEOs or the establishment of wild GEO populations, and the effects of regulated GE crops on other species."[188]

**"Required" inspections not conducted**
"Specifically, APHIS announced to the public that pharmaceutical and industrial field sites would be inspected 5 times during the 2003 growing season, but, in fact, we found that only 1 of 12 sampled pharmaceutical field test sites met this requirement."[189]

**Post-harvest permit requirements violated, posing risk that "volunteer" pharma crops will contaminate food supply**
"In September 2003, we visited a field test site where a permit holder had planted a pharmaceutical crop in 2002. PPQ had not inspected the site during the postharvest monitoring period in 2003. When we visited the site, we learned that the permit holder's cooperator had planted soybeans on the field, violating APHIS requirements that restrict the production of food and feed crops at pharmaceutical and industrial GE field test sites in the following season. Those GE field test sites are to be left fallow in the following growing season so that volunteer GE plants are not inadvertently harvested with an unregulated food

[187] *Id*., p. 15
[188] *Id*., p. 25 (footnote omitted)
[189] *Id*., p. 28

crop. Although the cooperator's 2003 monitoring record stated that the 2002 GE field was fallow, the cooperator told us that he had planted unregulated soybeans in the former GE field and cut them down the day before our visit. He left the soybeans standing in the larger field surrounding the former GE field."[190]

A National Academy of Sciences report on biological confinement concludes: "Alternative nonfood host organisms should be sought for genes that code for transgenic products that need to be kept out of the food supply."[191] Pharmaceutical and industrial substances should not be produced in GE food or feed crops in the environment. Growth in contained structures needs to follow methods that do not allow gene flow to occur. For example, typical greenhouse vent systems would allow pollen to escape.

APHIS fails to address the environmental concerns these crops may cause. The analysis in the DEIS with respect to this category is deficient in that respect because there is no analysis about how pharmaceutical and/or industrial crops could effect wildlife in an open environment. Because pharmaceutical compounds are intended to be highly biologically active in higher animals, especially mammals and birds, these animals may be particularly susceptible to harm from exposure in the field:

> "Biopharmaceuticals usually elicit responses at low concentrations, and may be toxic at higher ones. Many have physiochemical properties that might cause them to persist in the environment or bioaccumulate in living organisms, possibly damaging non-target organisms…"[192]

Similarly, industrial compounds are not intended for consumption and therefore may have a higher possibility of harming non-target organisms. Such compounds may generally be more likely to be harmful to non-target organisms, because they are not intended to be consumed, or only to be consumed for medical purposes. For example, the industrial product avidin produced in corn has insecticidal properties (National Research Council, 2002). In addition, aprotinin, a blood-clotting protein, has been grown in corn as a plant-made pharmaceutical; but it was originally classified as a "novel protein" and grown under notification. It has been shown to increase the mortality of honeybees, and may affect other organisms.[193] Also, some industrial enzymes are allergenic, and many pharmaceutical compounds have harmful side effects.

Therefore, APHIS should adopt Alternative 3. As APHIS states, "Alternative 3 would mitigate the consequences of unintended releases to the greatest extent." (EIS, p. 146). This is the only

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[190] *Id*., p. 30 (footnote omitted)

[191] NAS (2004). "Biological Confinement of Genetically Engineered Organisms," National Research Council, National Academy of Sciences, 2004, p. 7.

[192] Giddings, G. et al (2000). "Transgenic plants as factories for biopharmaceuticals," Nature Biotechnology, 18, pp. 1154.

[193] For case studies of avidin and aprotinin as expressed in corn, see appendices 2 and 3 of Freese, B. (2002). "Manufacturing Drugs and Chemicals in Crops: Biopharming Poses New Threats to Consumers, Farmers, Food Companies and the Environment," Friends of the Earth, July 2002. Available at: www.foe.org/biopharm/.

acceptable alternative given the special risks to human health and the environment posed by even low-level contamination of the food supply with bioactive pharmaceuticals.

**Issue 5 Regulation of Non-viable GE Plant Material**

Non-viable GE material may have environmental effects, and therefore all of it should be regulated. APHIS should adopt alternative 3. Depending on how the material is processed, protein or other transgene products are likely to remain present after the material is harvested. For example, drying of plant material may leave much of the transgenic protein and transgenic DNA intact. If incorporated as a soil amendment, proteins may bind to clay but remain active for a considerable period of time.[194] Non-viable plant material can contaminate food and cause problems or be ingested by non-target organisms and wildlife. Regulating all nonviable GE plant material is preferable because it is more protective of the environment, as discussed infra regarding Issue 2, a tiered system based on risk is inappropriate. APHIS provides no justification or evidence supporting its statement that "for most GE, the resulting nonviable material from field testing will not pose a significant risk to the environment." (EIS, p. 170); *see Idaho Sporting Cong. v. Thomas*, 137 F.3d 1146, 1150 (9th Cir.1998) (court requires agency exert opinions to be supported by underlying environmental data).

**Issue 6 Mechanism for Commercial Production of Pharmaceutical Crops Under Governmental Oversight, and Multi-year Permits**

APHIS proposes to establish "a new mechanism involving APHIS, the States, and the producer for commercial production of plants not intended for food or feed in cases where the producer would prefer to develop and extract pharmaceutical and industrial compounds under confinement conditions with governmental oversight, rather than grant nonregulated status" (DEIS, pp. 34, 151).

If Alternative 3 of Issue 4, which would prohibit any environmental release of any GE crop that produces a pharmaceutical or industrial compound, is adopted, this issue would be moot, with a single exception that is discussed further below. In the event that Alternative 3 for Issue 4 is not adopted, APHIS should adopt the No Action alternative, Alternative 1, for Issue 6.

APHIS' proposal for Issue 6 as presented here has nothing to do with the original intent of APHIS' proposal for Issue 6, as presented in its January 2004 scoping document and repeated here in the heading for Issue 6 (DEIS, p. 151). In contrast to the original intent to involve State officials in development of a mechanism for commercial production of pharmaceutical crops under continuing governmental oversight, APHIS here proposes something completely different: to "increase the efficiency of issuing annual permits for repeating field tests" (DEIS, p. 34) by establishing a multiyear permit system. In addition, APHIS proposes to extend this multiyear permitting to non-pharmaceutical as well as pharmaceutical crops ("This mechanism might also

[194] Tapp, H & G. Stotzky (1998). "Persistence of the insecticidal toxin from Bacillus thuringiensis subsp. kurstaki in soil," Soil Biology & Biochemistry 30(4): 471-476.

apply to other types of GE organisms or appropriate activities, such as repetitive research" (DEIS, p. 34)). Neither multiyear permits nor non-pharmaceutical crops were at issue in the original proposal for Issue 6.

These comments first address APHIS' altered proposal for Issue 6, followed by comments on the original proposal.

**Multiyear Permits**

APHIS should not adopt a multiyear permitting system for either pharmaceutical crop permits or notification permits. An annual permitting system, as currently implemented, provides for increased communication between field trial applicants and APHIS, and offers the potential for enhanced oversight. Enhanced oversight is badly needed, and would serve to mitigate potential environmental harms from regulated GE crop plantings. The USDA Inspector General's report makes abundantly clear that APHIS is not performing its regulatory oversight properly even with the current system of annual permits; some of the deficiencies relate to breakdown in communications between APHIS and the petitioner/field trial operator (e.g. failure of companies to file "required" reports, report the planting location of their field trials, or report on the final disposition of regulated materials).[195] Granting multiyear permits would make communications between APHIS and field trial operators still more tenuous, and should be rejected. Multiyear permits would also decrease transparency, giving the public less information. For instance, with multiyear permits the public would be informed that a permit had been issued only in the initial year. The public would not know whether the pertinent field-trial operator was actually planting the regulated GE article under the permit in the later years of the permit period, given the high failure rate in the agricultural biotechnology industry. An annual permitting system would thus provide the public with more up-to-date information about ongoing plantings of regulated GE crops.

Annual permits create an incentive for each field test operator to better comply because of the anticipation of annual regulatory oversight. APHIS wants to trade better environmental protection for the efficiency of a multi-year permit system (DEIS, p.152). Whatever minor increases in efficiency would be achieved are more than offset by the increased potential for environmental harm through a lesser degree of governmental oversight.

**Commercial production of pharmaceutical crops under governmental oversight**

Although the stated purpose of APHIS' proposed regulatory change is to allow for "commercial production" of pharmaceutical crops, APHIS provides absolutely no discussion of how commercial production of a pharmaceutical crop would differ from production of a pharmaceutical crop for research purposes. First, commercial production will involve increased scale, perhaps vastly increased scale, of pharmaceutical crop cultivation. For instance, Ventria Bioscience has proposed commercial cultivation of tens of thousands of acres of pharmaceutical-

[195] APHIS Audit

producing rice,[196] a vast increase in scale (two orders of magnitude) over its current plantings of 100-200 acres in Kansas. Increased scale of planting increases the risks of gene escape, makes gene containment much more difficult, and increases the potential for and scope of harmful adverse effects, such as non-target organisms impacts.[197] APHIS provides no discussion of how it would address this crucial aspect of its proposal, beyond generic references to standard operating procedures and quality management standards (DEIS, p. 35). Increased planting scale also means vastly increased quantities of pharmaceutical crop material whose disposition would have to be monitored. USDA's Office of the Inspector General reported that APHIS lost track of two tons of pharma crop material that were stored in two facilities without its knowledge for over a year, and without prior inspection of the storage facilities. (See discussion in comments to Issue 4). If APHIS is unable to monitor several tons of pharma crop material from research-scale plantings, it will be even less able to track and monitor dozens, hundreds or thousands of tons of pharma crop material that might be generated in the commercial production of multiple pharma crops. The potential adverse environmental or public health impacts of unauthorized use or accidental escape of such harvested pharma crop material would be increased in scope by the increased quantities expected in commercial production.

Secondly, commercial production of pharma crops would likely lessen the incentive of pharma crop companies and contract field trial operators to strictly follow all permit conditions and report adverse impacts (e.g. non-target organism impacts of plant-made pharmaceuticals). This is because a pharma crop company involved in commercial production will have strong financial incentives to meet contract obligations (e.g. for supply of set quantities of pharma crop material to a drug company), and would incur substantial financial losses from any failure to meet such contract obligations, as might well be occasioned by its conflicting duty to report to APHIS any adverse impacts of its pharma crop on the environment. Such financial imperatives are absent, or much less pronounced, for non-commercial, research production of pharmaceutical crops. APHIS provides absolutely no discussion of either of these important issues.

Despite APHIS' original proposal to involve State officials, APHIS does not make a single reference to how States might be involved in the mechanism that it proposes. The description of Alternative 2 that is offered excludes any State involvement. A proper presentation of Alternative 2 would require a discussion of the mechanism by which State officials would be engaged, which State officials would be consulted (in particular, their competence to play a role

[196] Cole, N. "Growers leery of modified rice: Farm group is concerned; don't be hasty, UAMS warns," *Arkansas Democrat-Gazette*, Jan. 29, 2005; Ridnour, H. "Ventria's top officials excited about move to Maryville," *Maryville Daily Forum*, Dec. 9, 2004.

[197] Kareiva P., Parker I.M., and Pascual M. (1996) Can we use experiments and models in predicting the invasiveness of genetically engineered organisms? Ecology 77:1670-1675; National Research Council (2002) "Environmental Effects of Transgenic Plants; The Scope and Adequacy of Regulation," The National Academies Press, Washington, D.C. (see especially Section 6); Snow A.A., Andow D.A., Gepts P, Hallerman E.M., Power A., Tiedje J.M., and Wolfenbarger L.L. (2004) "Genetically Engineered Organisms and the Environment: Current Status and Recommendations," ESA Position Paper. Ecological Society of America, Washington D.C. http://www.esa.org/pao/esaPositions/Papers/geo_position.htm

in the proposed scheme, given the novel nature of plant-made pharmaceuticals and industrial compounds, and the special expertise that would be needed for competent State oversight), the division of responsibilities between State officials and APHIS, whether or not State officials would have veto power over any proposed field trial of pharmaceutical or industrial compounds, availability of competent staff resources among the various States, and many other matters. Absent such a discussion, APHIS has not given an adequate description of Alternative 2, and it must not be adopted for this reason alone.

Finally, APHIS speculates that "it is possible and even likely, that many of these substances do not pose a human-health risk in food and also that they do not pose a risk to agriculture or the environment" (DEIS, p. 34). Such speculation has no value and has no place in this DEIS. APHIS has little or no medical competence to address the potential human health and environmental risks of plant-made pharmaceuticals (see comments to Issue 4).

APHIS' failure to address these issues provides additional support for adoption of a prohibition of all environmental releases of GE crops that produce pharmaceutical or industrial compounds, and even more to prohibit their cultivation for commercial sale of the pertinent pharmaceutical compound.

**Issue 7 – Low-Level Presence of Unapproved GE Crops in Commercial Food Supply**

**Summary:**
APHIS should adopt Alternative 4, or imposition of a strict confinement regime on all field tests of GE crops equivalent to that presently required for pharmaceutical and industrial crops. Unapproved GE crops grown in field trials have on numerous occasions entered the food supply, posing potential hazards to human health and the environment. Such episodes have also caused great harm to American agriculture, in particular economic losses to affected farmers and food companies, and have threatened to undermine confidence in the integrity and wholesomeness of the U.S. food supply, including U.S. food and grain exports. APHIS's noxious weed authority gives it the ability to regulate unapproved GE plants to prevent harm to the interests of agriculture as well as harm to public health and the environment. APHIS should use this authority to impose tighter confinement regimes for all GE crop field trials to prevent, to the greatest extent possible, their entry into the food supply. All instances where "low-levels" of regulated articles are detected in commercial food channels, particularly in seed supplies, should be actionable. That is, APHIS should take action to remove such contaminants from the food, feed and/or seed supply.

**APHIS's rationale for establishing a low-level presence policy**
It is important to understand that APHIS is proposing a "low-level presence" policy at the instigation of the biotechnology and grain industries, in the belief that it will relieve them of liability associated with contamination of the food supply with unapproved GE crops.[198] The

[198] "US Grain Industry, BIO Urge US Government to Expedite 'Trace-Amounts' Policy for Biotech Products," press release, Biotechnology Industry Organization & National Grain & Feed Association, and other trade groups, April 7, 2004,

roots of this policy can be traced back to September 2000, when food products in the US were discovered to be contaminated with StarLink, a variety of GE corn unapproved for human consumption due to concerns that its insecticidal protein could cause allergies. The contamination triggered massive food recalls and lawsuits that in the end cost the biotech and food industries an estimated $1 billion in damages.[199] In July 2001, the EPA rejected a petition from Aventis CropScience (StarLink's developer) to establish a tolerance (i.e. maximum allowable level) for StarLink in the food supply, thereby endorsing a "zero tolerance" policy for unapproved GE traits in food.[200] Aventis had sought this tolerance to avoid liability for recalls and potential health impacts from consumption of StarLink-contaminated products. Years after it was banned, StarLink has continued to show up in US maize as well as food shipments to Bolivia, Japan and South Korea. APHIS describes three other contamination episodes that provided additional impetus to establishment of a low-level presence policy (DEIS, pp. 37-38). APHIS also concedes that establishment of a "low-level presence" policy is "a very high priority for APHIS" due to pressure from "industry associations, crop associations, and commodity trade organizations" (EIS, p. 38).

Like StarLink, experimental GE crops are not intended for human consumption, pose potential health and environmental risks, and could be considered adulterants if even small amounts get into food or grain.

Below, we demonstrate that a low-level presence policy is scientifically indefensible, will lead to greater risks to public health and the environment, and will harm the interests of U.S. agriculture.

**Low-level presence policy scientifically indefensible and unworkable**

Genetically engineered crops grown under permit in field trials are "regulated articles" and by definition have not undergone assessments by the USDA for plant pest or noxious weed risk, by FDA for potential harm to human health, or (in the case of pest-resistant crops) by the U.S. Environmental Protection Agency (EPA) for potential harm to the environment or human health. Absent such assessments, it is prudent to assume that GE crops pose environmental and human health risks, and to impose stringent confinement standards to prevent, to the greatest extent possible, their introduction into the food supply at any level.

APHIS here proposes to sanction the presence of such "regulated articles" in the food, feed and seed supply at unspecified levels, provided certain conditions are met (discussed below). APHIS relies heavily on the term "low-level presence," but fails to explicitly define the term. In practice, the proposal for "low-level presence" presented in the DEIS could essentially allow whatever level of contamination which occurs due to the irresponsibility of the field trial operator, deficient APHIS oversight of compliance with field trial conditions, or other factors. Thus, this proposal could allow undefined levels of regulated articles to contaminate food, feed

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http://www.bio.org/news/newsitem.asp?id=2004_0407_01.

[199] "Tests to detect allergens in altered foods fall short," June 12, 2002 *St. Louis Post-Dispatch*, June 12, 2002.

[200] "EPA Rejects biotech corn as human food; federal tests do not eliminate possibility that it could cause allergic reactions, agency told," *Washington Post*, July 28, 2001.

or seed before the required regulatory reviews have been conducted. Yet these regulatory reviews are the only legitimate basis for determining whether a contamination episode poses human health or environmental concerns. For APHIS, this policy would essentially amount to a "Finding of No Significant Impact" in the absence of the data that is normally demanded as the basis for making such a determination.

Case-by-case assessment of GE crops is a hallmark of the U.S. regulatory process (EIS, p. 88). Just as it is unacceptable to make claims that GE crops as a class are hazardous, so it is scientifically indefensible to claim that, as a class, experimental GE crops that have not undergone the full, relevant reviews by authorities are safe and pose no hazards. The "low-level presence" policy thus stands in direct contradiction to the principle of case-by-case assessment that lies at the heart of US regulatory policy with respect to GE plants.

This situation is not changed by the presumption of "low-level" presence, which as noted above is not defined in any numerical way, for example by granting a blanket tolerance allowing a certain percentage of contamination for any experimental GE crop material. To grant such a blanket tolerance would of course be as scientifically indefensible as allowing an undefined "low-level presence," since such a tolerance would by necessity bear no scientific relationship to the specific properties of the hundreds of possible contaminating GE crops and the transgenic proteins they produce.

**Low-level presence policy will increase risks to public health and the environment**

APHIS should maintain a zero-tolerance policy for unapproved, experimental GE crops in the food, feed and seed supply because anything less compromises food safety, allows for potential amplification of GE traits, and provides a disincentive to practice strict gene containment. Any presence of regulated articles in the food supply must remain "actionable."

*Food Safety*

Experimental GE crops could cause harm even as low-level contaminants in food. For instance, GE StarLink corn was never approved for human consumption due to concerns that its insecticidal protein (Cry9C) might cause allergies. After StarLink contaminated the food supply, expert scientific advisors to the EPA stated that ***there was no minimal level of StarLink's Cry9C insecticidal protein that could be judged safe for human consumption.***[201] Thus, zero tolerance was the only acceptable standard to protect human health.

There are numerous experimental GE crops whose low-level presence in the food supply might pose hazards similar to StarLink. Tomatoes, potatoes, rice, grapes, wheat and barley have been engineered to produce anti-fungal compounds from the class of pathogenesis-related (PR) proteins, which is "widely regarded as a rich source of allergens."[202] An expert in this field

[201] "Assessment of Additional Scientific Information Concerning StarLink Corn," FIFRA Scientific Advisory Panel to the EPA, SAP Report No. 2001-09, from meeting on July 17/18, 2001.

[202] Breiteneder, H. (2004). "Thaumatin-like proteins: a new family of pollen and fruit allergens," editorial, *Allergy* 59(5), p. 479.

warns that such GE plants could cause food allergies.[203] In addition, many crops are being engineered with an insecticidal toxin derived from a soil bacterium (*Bt*) that might also cause food allergies.[204]

Corn and soybeans are being genetically manipulated for radical alterations in oil, protein and starch content for use as animal feed in factory-farm livestock operations. Manipulating plant metabolic pathways could easily have harmful, but difficult to detect, side effects; and it is far from clear whether such animal feed is suitable for human consumption.[205]

Corn, rice, rapeseed (canola) and other crops have been engineered to have sterile pollen or seeds, or "altered fertility." One mechanism for pollen sterility involves generation of barnase, an RNA-degrading enzyme with demonstrated toxicity to rats.[206]

Several pharmaceutical compounds that have been grown in GE plants also have the potential to harm human health, in some cases at extremely low levels. These include aprotinin grown in GE corn and tobacco, which belongs to a family of compounds known to cause pancreatic disease when fed to animals and is also toxic to honeybees; avidin produced by GE corn, which kills insects and causes Vitamin B deficiency in mammals, including humans;[207] and GE rice modified to contain synthetic human milk proteins, which pose a number of potential health issues and have not been approved as safe by the FDA.[208] USDA is presently considering an

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[203] Hoffmann-Sommergruber, K. (2002). "Pathogenesis-related (PR)-proteins identified as allergens," *Biochemical Society Transactions* (2002), Vol. 30, part 6, p. 934. The anti-fungal compounds referred to include chitinases, thaumatin-like proteins, osmotins and glucanases.

[204] Freese & Schubert (2004), "Safety Testing and Regulation of Genetically Engineered Foods," *Biotechnology and Genetic Engineering Reviews*, Vol. 21, p. 299-323., see Case Study of Bt Corn.

[205] Search the USDA database of GE crop field trials at http://www.isb.vt.edu/cfdocs/fieldtests1.cfm for phenotypes "oil profile altered," "fatty acid metabolism altered," "seed composition altered," "protein altered," and "starch metabolism altered," among others.

[206] Search USDA database cited in last footnote for phenotypes "male sterility," "sterility" and "altered fertility." On barnase, see Freese & Schubert (2004), *see supra*, note 172. "Safety Testing and Regulation of Genetically Engineered Foods," *Biotechnology and Genetic Engineering Reviews*, Vol. 21, p. 299-323.

[207] On aprotinin and avidin, see Appendices 2 & 3, Freese, B. (2002). "Manufacturing Drugs and Chemicals in Crops: Biopharming Poses New Threats to Consumers, Farmers, Food Companies and the Environment," July 2002, Friends of the Earth, www.foe.org/biopharm. On pharmaceutical rice, see: Freese et al (2004). "Pharmaceutical Rice in California: Potential Risks to Consumers, the Environment and the California Rice Industry," http://www.centerforfoodsafety.org/pubs/CARiceReport7.2004.pdf. On hormones, search USDA database under "Gene" for "insulin-like growth factor" and "interferon." For aprotinin in tobacco, search on "TMV" under "Organism."

[208] Freese, B. "A Grain of Caution: A Critical Assessment of Pharmaceutical Rice," Center for Food Safety, April 2007, at http://www.centerforfoodsafety.org/pubs/Pharmaceutical%20Rice-FINAL.pdf.

application from a Canadian company, SemBioSys, for open-air cultivation of safflower genetically engineered to produce proinsulin, the precursor to insulin, a hormone that can have biological effects at extremely low levels (millionths of gram), and may be active upon ingestion.[209]

Neither consumers nor farmers should be exposed to any level of such potent substances. While some pharmaceutical-producing GE crops would not be covered under the low-level presence policy (i.e. their presence in the food supply would be considered "actionable"), APHIS has proposed that "presence of the [pharmaceutical crop] material may not be cause for agency action" (EIS, p. 39) if abbreviated food safety reviews have been conducted (see "Inadequacy of FDA's Early Food Safety Evaluation" below).

*Possible Amplification of GM Traits*

The transgenes responsible for GE traits are not like inert contaminants. They can spread through cross-pollination with related weeds, and persist over time through the sprouting of unharvested GE seeds in subsequent years. The potential for transgenes to spread and persist is enhanced if the associated GE trait offers a survival advantage, such as resistance to an herbicide or pest.[210] Any related weeds or crop plants that pick up the advantageous trait may have increased survival chances, and even surreptitiously pass it back to the food crop later on. Thus, a trait that is initially present at low levels could amplify over time, with unpredictable consequences.

*Reduced Incentive to Stop Spread of GM Traits*

Eliminating the current "zero tolerance" standard for experimental GE traits in food-grade crops through establishment of a "low-level presence" policy will reduce the threat of liability for such contamination, thereby decreasing the incentive of companies conducting field trials to comply with gene containment protocols. The inevitable result will be more, not less, contamination.

**APHIS Fails to Describe the 'Food-Safety Consultation or Review' That Would Form the Basis for Determinations of Non-Actionable Status**

APHIS's preferred Alternative 3 proposes to exempt from regulation (declare as "non-actionable") the low-level occurrence of regulated articles (i.e. unapproved GE crops) in the food supply on the basis of a 'food-safety consultation or review' (EIS, p. 154). If the transgenic protein expressed by an unapproved GE crop were to pass such a consultation or review, its accidental presence in the food supply would be considered "non-actionable." APHIS defines "non-actionable" as follows:

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[209] See Center for Food Safety's comments on USDA's preliminary environmental assessment of this field trial at See: http://www.centerforfoodsafety.org/pubs/Proinsulin%20Safflower%20Comments%20CFS%20FINAL.pdf.

[210] "Mindful management of genes that produce industrial biochemicals in plants," presentation of Norman C. Ellstrand, geneticist, U of CA Riverside, at the Pew "Pharming the Field" Conference, Washington, DC, July 17 & 18, 2002; see also Gurian Sherman, D. "Contaminating the Wild," Center for Food Safety, see *supra* p. 4.

> "'Non-actionable' in this context means that the commercial commodity containing the low level of otherwise regulated material would not be treated as a regulated article; the commodity could be moved and planted without the need for APHIS biotechnology permits covering the otherwise regulated article" (EIS, p. 155).

In other words, APHIS would treat the contaminated commodity no differently than an uncontaminated one. It would not be removed from commerce: if the commodity is contaminated seed, it could still be planted; if contaminated food or feed, it could be moved in interstate commerce, consumed by human or animal, and/or exported. Hence, this "food-safety consultation or review" effectively functions as a substitute for the regulatory review processes of APHIS and the EPA that are normally required, and in the case of the FDA recommended, before an unapproved GE crop can enter commerce, provided only that the unapproved GE crop has entered commerce by accident rather than intent.[211] It essentially determines whether the general public will be consuming unspecified levels[212] of unapproved GE crops in food derived from contaminated commodities, and whether farmers, unbeknownst to them, will be planting contaminated seeds.

Despite the obvious importance of this "food-safety consultation or review," APHIS tells us next to nothing about it. APHIS's discussion is limited to the following:

> "Both of these agencies [FDA and EPA] either have mechanisms in place or are in the process of establishing mechanisms to provide a food-safety consultation or review of the newly expressed substance early in the field testing process. The PPA explicitly gives APHIS responsibility under the noxious weed provision to consider risks to public health; however, APHIS is not currently using this provision in its regulations" (EIS, p. 154).

Thus, it is not clear which agency (APHIS, FDA or EPA) would perform food-safety reviews, or which agency in which cases. It is not clear that the only agency cited as possessing authority to conduct such reviews (APHIS under the PPA) has the competence to conduct them.[213] Assuming that APHIS were to engage the FDA or EPA (as obliquely suggested here), it is not

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[211] As APHIS makes clear, ***intentional*** introduction of the unapproved GE crop would still be dependent on successful negotiation of the usual regulatory review procedures. We also acknowledge that APHIS reserves authority to take enforcement actions against those parties responsible for the accidental contamination.

[212] As discussed above, APHIS fails to define "low-level presence" in any numerical way (i.e. tolerance); the only operative distinction is whether introduction of the regulated GE crop into commerce occurs accidentally or by intent. In other words, accidental introduction is merely assumed to be "low-level."

[213] See Center for Food Safety's comments on USDA's preliminary environmental assessment of a proposed field trial of proinsulin-producing safflower, which demonstrates clearly that APHIS is not competent to assess the serious medical issues presented by potential exposure to plant-made pharmaceuticals. See: http://www.centerforfoodsafety.org/pubs/Proinsulin%20Safflower%20Comments%20CFS%20FINAL.pdf.

clear how, when, under what circumstances,[214] or by what mechanism this engagement would proceed. ***Either FDA or EPA (we are not told which) does not even have an established mechanism in place to provide a food-safety consultation or review.*** Finally, there is absolutely no specification of criteria or protocols for conducting the food-safety reviews.[215]

The failure to describe the food-safety consultation or review at the heart of APHIS' preferred Alternative 3 is a violation of NEPA. APHIS' analysis of alternatives in the EIS is insufficient because USDA failed to adequately analyze the alternatives it identified in the EIS.[216] EISs must include analysis of the alternatives to the proposed action.[217] NEPA requires that federal agencies consider alternatives to recommended actions whenever those actions "involve[ ] unresolved conflicts concerning alternative uses of available resources."[218] The goal of the statute is to ensure "that federal agencies infuse in project planning a thorough consideration of environmental values."[219] The consideration of alternatives requirement furthers that goal by guaranteeing that agency decision-makers "[have] before [them] and take [ ] into proper account all possible approaches to a particular project (including total abandonment of the project) which would alter the environmental impact and the cost-benefit balance."[220] NEPA's requirement that alternatives be studied, developed, and described both guides the substance of environmental decision-making and provides evidence that the mandated decision-making process has actually

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[214] The only exception to this is that under Alternative 3, APHIS notes that up to 10 cumulative acres of an unapproved GE crop could be grown each year under the "lowest-risk" permit category without the need for a food-safety review; for more than 10 acres/year, either the food safety criterion would have to be met, or the GE plant would have to be field-tested under a more stringent permit type (EIS, p. 158).

[215] APHIS does provide a discussion of GE food safety issues as well as a historical overview of GE food safety-testing protocols (EIS, pp. 86-97). However, its discussion of Issue 7 makes no explicit reference to this section. Moreover, APHIS does not state that it (or the FDA or EPA) would actually apply any of the many studies or protocols it cites for conducting food safety reviews, or if so, which ones. We note that the studies and protocols cited by APHIS exclude many that demand more stringent safety-testing of GE foods. However, even those that are cited represent a range of scientific opinion on the human health risks posed by GE foods and the stringency of testing needed before such GE foods and crops are introduced into the food supply. Thus, this section provides little or no insight into APHIS's proposed policy with respect to the nature of the "food-safety consultation or review" process that would be used to justify deeming "low-level presence" non-actionable.

[216] *See* Bob Marshall Alliance v. Hodel, 852 F.2d 1223, 1228 (9th Cir. 1988).

[217] Id. at 1229 ("consideration of alternatives requirement is both independent of, and broader than, the EIS requirement. In short, any proposed federal action involving unresolved conflicts as to the proper use of resources triggers NEPA's consideration of alternatives requirement, whether or not an EIS is also required.")

[218] 42 U.S.C. § 4332(2)(E).

[219] Conner v. Buford, 836 F.2d 1521, 1532 (9th Cir. 1988).

[220] Calvert Cliffs' Coordinating Committee, Inc. v. United States Atomic Energy Commission, 449 F.2d 1109, 1114 (D.C. Cir. 1971) (emphasis added).

taken place.[221] Informed and meaningful consideration of alternatives-including the no action alternative-is thus an integral part of the statutory scheme[222] that has not been met here in the case of APHIS' proposed food-safety consultation or review.

**Inadequacy of FDA's Early Food Safety Evaluation**

Thus, APHIS's adoption of Alternative 3 would be a violation of NEPA's requirement that alternatives be studied, developed and described. Though APHIS has left completely unclear the nature of this crucial component of its Alternative 3, one possible model that might be employed is a voluntary guidance document developed for industry by the FDA.[223] Like the "food-safety consultation or review" mentioned by APHIS, this voluntary guidance was set up to assist companies in avoiding liability for contamination episodes involving their field-tested GE crops. We summarize some inadequacies of this model below. For a more detailed critique, see Appendix 1.

Most importantly, the FDA's process does not call for any animal feeding tests or advanced analytical techniques to detect unintended effects of the contaminating GE crop, such as unexpected elevations in the levels of native allergen or toxins, or lowered levels of key nutrients. As with APHIS's proposed low-level presence policy, FDA sets no limit on the amount of contaminating GE crop material in the contaminated commodity, merely assuming it will be low. In addition:

1) FDA evaluates only the transgenic protein expressed by the GE crop:
   a) This focus on the transgenic protein ignores the potential for adverse unintended effects of the genetic engineering process on the contaminating GE crop material, and hence the commodity it contaminates.
   b) Potentially adverse unintended effects are also implicitly ignored in the case of those contaminating GE crops with metabolic alterations or other compositional changes that do not involve production of a novel transgenic protein; such crops are excluded from FDA's "early food safety evaluation" guidance.
   c) Potentially adverse unintended effects are also ignored in the context of a GE crop that produces a transgenic protein similar in nature to the protein produced in a GE crop that has already been evaluated.

2) FDA's procedure is inadequate even to rule out harmful impacts of the transgenic protein expressed by the GE crop:
   a) FDA evaluates for only two potential adverse impacts – allergenicity and acute toxicity – and ignores the many other adverse impacts novel transgenic proteins could have on human health, for instance:

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[221] Id.

[222] *See* Bob Marshall Alliance v. Hodel, 852 F.2d 1223, 1228 (9th Cir. 1988).

[223] "Recommendations for the Early Food Safety Evaluation of New Non-Pesticidal Proteins Produced by New Plant Varieties Intended for Food Use," Draft Guidance for Industry, http://www.cfsan.fda.gov/~dms/bioprgui.html.

i) Antinutrient effects
ii) Adverse immune system responses;
iii) Exacerbation of infections;
iv) Adverse impacts from improper folding of a transgenic protein that is otherwise familiar; improperly folded brain proteins – prions – are thought to be responsible for oral transmissible brain-wasting diseases such as bovine spongiform encephalopathy (Mad Cow disease);
v) Teratogenic or other effects from small peptide breakdown products of a transgenic protein
vi) Any subchronic or long-term toxicity of a transgenic protein, since FDA only considers acute toxicity.

b) FDA's procedure is inadequate even to rule out potential allergenicity or acute toxicity of the transgenic protein produced by the contaminating GE crop, as it involves only two inadequate tests:
   i) One test involves determining whether a bacterial surrogate of the novel GE crop protein is degraded in a test tube containing an acidic solution of unspecified pH and undetermined levels of a digestive enzyme (pepsin). Resistance to degradation is regarded as a sign that the protein could cause allergies or have other harmful effects. First, companies nearly always use bacterial surrogate proteins without having established whether they are in fact equivalent to the GE crop protein that should be used in such tests.[224] In addition, experience shows that companies often choose test conditions (low pH and high concentration of digestive enzyme) that foster rapid degradation, and which deviate substantially from the test conditions recommended by international experts,[225] for instance FAO (2001), rendering the results of such a test useless.[226]
   ii) The second test involves comparing the amino acid structure of the novel GE crop protein to the structures of known allergens and toxins contained in certain databases, with similarity in structure indicating potential allergenicity or acute toxicity. The structures of many proteins with adverse effects are not known, or not included in structure databases. In addition, experience shows that companies choose test parameters that reduce the chances of finding matches, test parameters that often deviate substantially from those recommended by international experts, undermining the utility of such tests.[227]

Therefore, application by APHIS of a "food-safety consultation or review" for determination of "non-actionable" status that is modeled on FDA's "early food safety evaluation" would not

[224] Freese & Schubert (2004). "Safety Testing and Regulation of Genetically Engineered Foods," *Biotechnology and Genetic Engineering Reviews*, Vol. 21, November 2004, pp. 305-307.

[225] FAO/WHO (2001). "Evaluation of Allergenicity of Genetically Modified Foods," Food and Agriculture Organization and World Health Organization, January 2001, Geneva, Switzerland

[226] Freese & Schubert (2004), pp. 307-308, 310.

[227] *See supra*, note 144.

provide reasonable scientific assurance of the safety of commodities contaminated with regulated articles that had passed such a review.

As noted above, neither FDA's guidance for "early food safety evaluation" nor the "food-safety consultation or review" proposed here by APHIS is designed to ensure food safety. Former FDA Commissioner Lester Crawford gave the following reasons for the guidance in a speech delivered in 2004 during its development:

> "The development of this guidance is a high priority for the Administration and the industry, to ***enhance public confidence, avoid product recalls, and provide an international model*** to address the presence of low levels of bioengineered plant material in non-bioengineered crop fields."[228] (emphasis added)

APHIS's low-level presence policy is likewise designed to protect biotechnology and food companies from liability for the sloppy practices of field trial operators and deficient oversight that lead to contamination of the food supply with unapproved GE crops in the first place. As APHIS puts it:

> "The desired outcome [of the low-level presence policy] is to assure the public, including domestic and foreign markets, that safety issues have been addressed for regulated materials which, on rare occasions, are detected in commercial products." (EIS, pp. 155-156).

However, history clearly demonstrates that the public, including domestic and foreign markets, have not been assured and should not be assured that the presence of unapproved GE crops in the food supply poses no safety issues, even when U.S. authorities provide *ad hoc* assurances of safety on the basis of abbreviated food-safety evaluations.

**Case Study: LibertyLink Rice 601**

APHIS discusses three past contamination episodes (DEIS, pp. 37-38), but fails to discuss several that have had the greatest adverse impacts on the food industry and the interests of U.S. agriculture. The StarLink contamination episode was discussed above. In August 2006, USDA announced widespread contamination of commercial long-grain rice supplies in the South with unapproved LibertyLink Rice 601 (LL601), a variety of rice developed by Bayer CropScience for tolerance to the herbicide Liberty (glufosinate). This episode caused substantial economic damage to U.S. rice exports, significant harm to U.S. rice farmers and the rice industry as a whole, and a loss of faith in the wholesomeness of the U.S. food supply. Early accounts indicated that LL601 was found in virtually all milled rice samples that had been tested.[229] Japan banned imports of U.S. long-grain rice shortly after USDA's announcement of the contamination

228 Lester M. Crawford, Acting Commissioner of the FDA. Speech before The U.S. Vatican Mission's Conference "Feeding A Hungry World: The Moral Imperative Of Biotechnology," September 2004. http://www.fda.gov/oc/speeches/2004/vatican0924.htmlwww.agbioworld.org.

229 Bennett, D. "Arkansas Secretary of Agriculture addresses GMO rice situation," Delta Farm Press, Aug. 29, 2006. http://deltafarmpress.com/news/060829-arkansas-gmo/

episode on August 18, 2006.[230] Though the ban was lifted on September 19th, Japan then announced that it would test all short and medium-grain rice imported from the U.S, even though they come chiefly from California.[231] Japan's testing of U.S. short- and medium-grain rice is reportedly due to "a lack of information from the U.S. government about how extensive the contamination could be, despite enquiries from Tokyo…,"[232] demonstrating the USDA's failure to effectively handle or even monitor this debacle. Japan is the nation's largest export market for rice. Russia also suspended imports of U.S. rice due to the LL601 contamination episode.[233]

LL601 was found in 33 of 162 rice samples tested by the EU,[234] and rice supplies and/or food products contaminated with LL601 were detected in up to nine European countries, including the UK, France, Germany, Greece, Norway, Ireland, Austria, Slovenia and Italy.[235] Supermarket products contaminated with LL601 were withdrawn in the UK, Germany, France,[236] Switzerland, Norway,[237] and perhaps other countries. The UK Rice Industry Association reportedly stopped importing any U.S. long-grain rice. The world's largest rice processor, Ebro Puleva, stopped importing U.S. rice in August 2006.[238]

The economic fallout from LL601 was huge. Prices on the rice futures market dropped dramatically in the weeks after contamination was first announced. Some in the rice industry predict losses of $150 million.[239] Numerous rice farmers have filed at least 15 class-action lawsuits against Bayer to recover their damages.[240]

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[230] "Japan bans 'contaminated' US rice," BBC NEWS, 8/21/06, http://news.bbc.co.uk/go/pr/fr/-/2/hi/science/nature/5271384.stm

[231] Krauter, Bob. "Japan to test all U.S. rice for GE variety," Capital Press, September 28, 2006, available at http://capitalpress.info/main.asp?SectionID=94&SubSectionID=801&ArticleID=27721&TM=28376.05

[232] "Japan widens testing of U.S. rice for illegal GMO," Reuters, Sept. 28, 2006, http://asia.news.yahoo.com/060928/3/2qjrf.html

[233] "RUSSIA: US rice imports suspended over GMOs," Just-Food.com, Oct. 2, 2006, full article accessible for subscribers only at http://www.just-food.com/article.aspx?id=96181

[234] "EU confirms presence of tainted GMO rice," Reuters, Sept. 11, 2006. http://today.reuters.co.uk/news/articlenews.aspx?type=scienceNews&storyID=2006-09-11T175711Z_01_BRU004904_RTRIDST_0_SCIENCE-FOOD-EU-GMO-RICE-DC.XML

[235] "EU Due to Tighten Import Rules to Keep Out GMO Rice," Reuters, October 3, 2006, http://www.planetark.com/dailynewsstory.cfm/newsid/38340/story.htm

[236] "Gene-altered profit-killer," Washington Post, Sept. 21, 2006, http://www.washingtonpost.com/wp-dyn/content/article/2006/09/20/AR2006092001903.html

[237] "Illegal rice recalled," Aftenposten, Norway, by Randi Johannessen, Sept. 28, 2006, http://www.aftenposten.no/english/local/article1475411.ece

[238] http://www.greenpeace.org/international/press/releases/world-s-largest-rice-company-h

[239] "Gene-altered profit-killer," *see supra*, note 235.

[240] Weiss, R. (2006). "Firm Blames Farmers, 'Act of God' for Rice Contamination," Washington Post, Nov. 22, 2006.

It is important to realize that these serious economic impacts occurred despite official assurances that LL601 posed no health concerns. The FDA issued the following 7-sentence statement on this contamination episode:

> "Bayer CropScience recently notified the U.S. Food and Drug Administration (FDA) and the U.S. Department of Agriculture Animal and Plant Health Inspection Service (APHIS) that trace amounts of a bioengineered variety of rice were detected in samples of commercial rice seed, and may have entered the food and feed supply in the United States. The bioengineered variety of rice, called LLRICE601, expresses the phosphinothricin-N-acetyltransferase (PAT) protein which provides tolerance to glufosinate-ammonium herbicide. This rice variety, not intended for commercialization, was not submitted to FDA for evaluation under the Agency's voluntary biotechnology consultation process. However, crops containing the PAT protein have previously been evaluated for safety by FDA on a number of occasions through the Agency's voluntary biotechnology consultation process. Bayer has informed the Agency that LLRICE601 is present in some samples of commercial rice seed at low levels. In addition, Bayer has provided information about the safety of the PAT protein, molecular characterization, and nutritional composition of grain from LLRICE601. Based on the available data and information, FDA has concluded that the presence of this bioengineered rice variety in the food and feed supply poses no food or feed safety concerns."[241]

The FDA never conducted its usual "voluntary biotechnology consultation process" on LL601. Its evaluation was based solely on information provided by Bayer as to the level of contamination, not on independent analysis, which to our knowledge was never conducted. And FDA's conclusion that LL601 poses no food or feed safety concerns is explicitly based on "available data and information." Appendix 2 compares FDA's casual approach to its "safety assessment" of LL601 to that of the European Food Safety Authority, which provides a much more qualified, nuanced and scientifically grounded assessment.

As noted above, APHIS has not provided adequate information to allow informed comment on the food-safety evaluation that is to be used as the basis for determining whether "low-level presence" of unapproved GE crop material is "actionable" or not. We have discussed the inadequacy of one possible model for APHIS's "food-safety consultation or review" – and further shown that FDA's past practice in such cases (e.g. LL601) has not reassured and should not reassure consumers, domestic or foreign markets that accidental contamination does not pose safety concerns; or prevented economic harm to U.S. farmers or other food industry players.

In view of this evidence, it is clear that APHIS's proposed "low-level presence" policy (its preferred Alternative 3) will not accomplish any of its objectives. It will not ensure the safety of contaminated food supplies, will not provide assurance that such contamination poses no health or environmental concerns, and it will not prevent rejection of contaminated food supplies by domestic or foreign markets, with the associated harm this causes to the interests of U.S. agriculture.

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[241] "U.S. Food and Drug Administration's Statement on Report of Bioengineered Rice in the Food Supply," http://www.cfsan.fda.gov/%7Elrd/biorice.html

**Noxious weed risk requires tighter confinement of all experimental GE crops to protect the interests of agriculture**

The Plant Protection Act gives APHIS the authority to regulate experimental GE crops grown in field trials (regulated articles) as potential noxious weed risks. 7 U.S.C. § 7702(10). APHIS has signaled its intention to utilize this noxious weed authority in its discussion of, and preferred alternative for, Issue 1.

The definition of a noxious weed includes plants or other organisms that have the potential to harm, directly or indirectly, the interests of agriculture. *Id*. The interests of agriculture include economic factors. The presence of experimental GE crops in the food supply has indisputably had adverse economic impacts on U.S. agriculture (as discussed above). Therefore, APHIS has a statutory duty to regulate experimental GE crops to prevent their entry, to the greatest extent possible, into commercial food channels to prevent harm to the economic interests of U.S. agriculture. The best means to do this would be to increase the stringency of gene containment protocols for field tests of all GE crops, and make any presence of such regulated articles "actionable" such that they would be removed from commerce.

Of the alternatives presented for Issue 7, only Alternative 4 would accomplish this objective. Under Alternative 4: "…all permitted field tests would be performed under conditions equivalent to those currently employed for pharmaceutical or industrial GE plants – conditions that have been effective in preventing gene flow"[242] (DEIS, p. 159). APHIS acknowledges that: ***"This alternative would result in the lowest potential for the presence of regulated materials from domestic field tests in commercial commodities and seeds, short of not allowing any field tests at all"*** (EIS, p. 159). In addition, the presence of regulated GE crops in the food, feed and seed supply "would be actionable in the unlikely event that they were detected" (DEIS, p. 159). However, APHIS expresses concern that this alternative "may increase costs and other burdens on the future development of GE plants for general agriculture use," "would increase the time required to review permit applications and to devise appropriate confinement measures for each proposed field test," and would likely reduce the number of permits issued for GE crop field tests (EIS, p. 159). It is important to note that these concerns expressed by APHIS with respect to Alternative 4 are explicitly economic in nature: increased costs to biotechnology companies, and increased demands on APHIS staff resources. The Plant Protection Act does not provide APHIS with the statutory authority to consider any of these concerns.

By APHIS's own admission, Alternative 4 would also lead to fewer contamination episodes, which would mean less associated economic damage to the interests of U.S. agriculture.

[242] While we agree that pharmaceutical crop-level confinement procedures would reduce the likelihood of gene flow, we note that even these tighter confinement conditions can fail. In 2002, pharmaceutical corn grown by Prodigene contaminated soybeans grown the next year on the same site in Nebraska, necessitating seizure and destruction of 500,000 bushels of contaminated soybeans at a cost of roughly $3 million. APHIS discusses this episode without identifying the company involved or the associated costs on p. 38 of the EIS. Thus, while we agree that pharmaceutical crop-level gene containment standards provide greater protection against contamination episodes, they are far from foolproof.

Alternative 4 would result in fewer rejected shipments of contaminated foods by domestic and foreign markets, would prevent economic losses to farmers who bear the brunt of lower commodity prices caused by contamination episodes, and would lower litigation costs for biotechnology companies sued by farmers or food companies for allowing regulated articles into the food supply.

APHIS discusses only three contamination episodes (EIS, pp. 37-38), but inexplicably provides no discussion of the adverse economic impacts these episodes had on U.S. farmers, grain traders and U.S. agriculture as a whole. In the LL601 contamination episode discussed above (which APHIS failed to even mention), damages could run to the hundreds of millions of dollars. Another episode APHIS fails to mention is StarLink corn, which as noted above caused an estimated $1 billion in damages to Aventis CropScience and the food industry. The Prodigene episode involving pharmaceutical corn (discussed in 3 sentences on EIS, p. 38) cost roughly $3 million. Appendix 3 to these comments lists 16 known contamination episodes, most occurring in the U.S. under notification field trial standards. To the best of our knowledge, the economic costs of these episodes has never been calculated, but are likely substantial.

Clearly, APHIS has not provided a thorough economic assessment of Alternative 4. However, the limited discussion it has provided is highly biased by considering only some of the potential costs to biotechnology companies and to itself (in terms of staff resources). It does not even consider the potential cost savings to biotechnology companies like Bayer from reduced litigation expenses. The fuller economic analysis outlined here strongly suggests that Alternative 4 would be best for the economic interests of U.S. farmers and the U.S. food and agriculture system as a whole.

**Conclusion**

APHIS's proposed low-level presence policy (Alternative 3) is scientifically indefensible, will increase risks to human health and the environment, and will damage the economic interests of U.S. agriculture. Alternative 4 would reduce the potential for contamination of food supplies and the environment with unapproved GE crops, and thereby provide greater protection against the potential adverse human health and environmental impacts of such contamination. Although a full economic analysis is lacking, the available evidence strongly suggests that Alternative 4 APHIS would also best protect the economic interests of U.S. farmers as well as the food and agriculture industries.

**Issue 8 Importation of GE Commodities**

APHIS should not allow expedited review of any imported GEO. APHIS should adopt Alternative 3. The USDA should ensure that each imported GEO is scrutinized in the same manner as those produced domestically. Regulatory approvals of GEO commodities in their country of origin should not be accepted by APHIS as a basis for expedited review or exemption from review because foreign regulatory processes and regulations may differ substantially from those employed in the U.S., and therefore such commodities may not meet U.S. standards. For instance, the U.S. has recently had ample experience with extremely poor food-safety oversight systems in China. Earlier this year, melamine-contaminated wheat gluten from China, which

was incorporated into pet food products sold in the U.S., was likely responsible for thousands of pet deaths, and also necessitated a huge recall of contaminated pet food products.[243] Several reports also suggest that organic food production methods in China include prohibited methods, such as use of human manure in fertilizers, and so do not meet the USDA National Organic Program requirements for organic cultivation.[244] Other food-safety threats from foods and other consumer products imported from China include antifreeze in toothpaste, lead in children's toys and banned antibiotics in fish. Oversight of agricultural biotechnology may well be equally deficient in China or other countries seeking to export GEOs to the United States.

In addition, for reasons elaborated in these comments on Issue 2, it cannot be reliably determined whether a given GE crop is low-risk. This is true for GE crops developed outside as well as inside the U.S. Therefore the basic premise for the acceptance of low-risk GE crops from other countries is unsupportable. The comments on Section 7 discuss why the food safety review APHIS proposes prior to exemption of an imported GEO from APHIS review (Alternative 2, DEIS, p. 162) is not adequate to protect public health. Therefore, APHIS should not expedite or exempt any GE crops of nondomestic origin from deregulation review. To the extent this creates any redundancy in oversight of a GEO because of foreign review, it will only provide greater protection of the U.S. public and agriculture.

Any GE crop coming into this country should be subject to a full deregulation review even if it is not for propagation. A basic assumption here is that crops not intended for propagation would in fact not be planted. Recent experience in Mexico with the illicit planting of GE corn suggests that such proscriptions may not be reliably followed. Despite a ban on cultivation of Bt corn, landraces with GE content were discovered there. The source was apparently corn shipments to Mexico that contained Bt corn. Some kernels from these shipments, which were intended only for human and animal consumption, were apparently planted, giving rise to Bt corn that cross-pollinated with native Mexican landraces. This is an example of how a GE commodity "not intended for propagation" can be propagated. Illegally propagated crops that escape confinement may become a permanent part of the landscape.

Even if not intentionally planted, an imported GE plant meant only for food or feed use could be accidentally routed into the food supply, or released into the environment. APHIS' preferred Alternative 2 requires that "the importer certify that the commodity complies with all appropriate criteria and verify that the commodity will be used only for processing, food, or animal feed (DEIS, pp. 162-163).

This verification requirement recalls the "split-approval" given to GE StarLink corn by the Environmental Protection Agency. Under the terms of a stewardship agreement, the EPA charged Aventis CropScience, StarLink's developer, with responsibility for ensuring that StarLink would be used only for animal feed or industrial applications, not for human food.

[243] Barboza & Barrionuevo (2007). "Filler in Animal Feed Is Open Secret in China," New York Times, April 30, 2007.
[244] Lavigne, P. (2006). "Analysis: USDA does not always enforce organic label standards," The Dallas Morning News, July 25, 2006.

Aventis and its seed dealers largely failed to comply with this agreement. They failed to inform many farmers of this "animal-feed only" restriction on sale of StarLink corn harvest,[245] resulting in widespread contamination of the food supply with StarLink, possible harm to public health, numerous food recalls, rejected export shipments, lost income for farmers, and great harm to U.S. agriculture as a whole.

Alternative 2 would set up a similar scenario of "self-certification" in which the importer bears responsibility for ensuring the imported GE crop would not be propagated, either intentionally through planting, or unintentionally through accidental environmental release. Such an honor system is no basis for regulatory policy with respect to GE crops that have not undergone full regulatory review by US authorities. Regulatory provisions that have a good chance of failure should not be adopted.

Only Alternative 3 would avoid these threats by requiring full deregulation review by APHIS of all GEOs proposed for importation into the United States.

APHIS improperly interprets the International Cartagena Protocol on Biosafety, to which the United States is not a party, as asserting relaxed standards for the importation of GEOs that are intended for food, feed, or processing. (DEIS, pp 40-41). While APHIS' assertion may be correct that the process for importing such organisms is less rigorous than that required for other GEOs, APHIS makes an unwarranted leap of reasoning by stating that this disparity in standards is due to the lower level of risk posed by GEOs for food, feed, or processing. For the above reasons, APHIS should not allow expedited review of imported GEOs and should adopt Alternative 3.

**Issue 9 Interstate Movement Exemptions**

APHIS currently exempts just a few GE research organisms such as GE *Arabidopsis* spp. from interstate movement permits or notifications (DEIS, p. 41). APHIS states that is "considering whether to expand the current exemption from interstate movement restrictions to other well-studied, low-risk, GE ***research*** organisms." *Id.* (emphasis added). However, Alternative 2 proposes to exempt not just GE research organisms, but rather the entire class of GEOs qualifying for type 1 designation under the proposed tiered permitting system (Issue 2) from interstate movement permits and notifications. Since the eligibility criteria for a type 1 permit "are very similar to those for notification under the current system," and notification field trials represent over 90% of all field trials, the proposed exemption would cover the vast majority of interstate movements of regulated GEOs, not just research GEOs like *Arabidopsis.* As discussed *infra* in Issue 2, APHIS' proposal to exclude certain "familiar" and "low risk" organisms from regulatory oversight in the context of environmental release is unsupportable. Its similar rationale here is likewise faulty.

[245] Ryberg, W. (2000). "Growers of biotech corn say they weren't warned:
StarLink tags appear to indicate it's suitable for human food products," Des Moines Register, Oct. 25, 2000.

While the potential for inadvertent escape of GEOs during shipment is probably lesser than with environmental release of these GEOs, we note that there have been many unexplained contamination episodes (see Appendix 3). Indeed, APHIS has yet to release its long-awaited report analyzing the causes of the LLRICE601 contamination debacle just last year. This causes of this episode, which involved a GE crop that its developer claims had not been field-tested since 2001, are still unclear. It is possible that lapses resulting in environmental release occurred during shipment of LLRICE601 seed. Other contamination events may have also been caused by shoddy shipping practices, even with the requirement for interstate movement permits/notifications.

Because of the vast swath of regulated GEOs that would be covered by this exemption (not merely GE research organisms, as originally proposed), and the uncertainty surrounding environmental release of regulated GEOs during shipment even with the current system, APHIS statement that the two alternatives "should each provide protections equal to the present system…" (DEIS, p. 166), is unsupported by the facts. The chief benefit of Alternative 2 is to "reduce regulatory costs and burdens (DEIS, p. 42). Yet the cost of such streamlining may well be increased risk of inadvertent environmental release of regulated GEOs during shipment. Inadvertent contamination episodes have in some instances burdened U.S. farmers and the food industry with huge costs.

USDA admits that the No Action alternative is highly protective of the human environment. (EIS, pp. 165-166). APHIS should therefore adopt the No Action alternative to maintain a higher level of oversight of interstate movement of regulated GEOs not specifically exempt under 7 CFR 340.2.

**<u>Issue 10</u> Container requirements for shipment of regulated GE organisms**

APHIS proposes to change its container requirements for shipment of regulated GE organisms from the current prescriptive system to performance-based standards. The chief reason APHIS gives for this proposed change is to "reduce the burden on applicants as well as increase the efficient use of APHIS resources" (DEIS, p. 43). However, it is unclear why the current system of prescriptive container requirements should necessarily entail such burdens on applicants or APHIS. APHIS' explanation is that applicants often request variances to use a different container not specified in the current prescriptive system, and that APHIS staff spend time reviewing these variance requests (DEIS, p. 42). Yet applicants could avoid these burdens by simply using prescribed containers, and APHIS could reduce demands on its staff resources by refusing to consider variance requests. This is the simplest alternative, but one that APHIS does not consider.

The purpose of prescriptive container requirements is to prevent environmental release of regulated GEOs. Prevention of environmental release must be the prime consideration in weighing any possible changes to the current system, not regulatory burden on applicants or APHIS.

With a performance-based standard, APHIS would merely specify criteria for container design and construction. APHIS acknowledges that with a performance-based standard for containers: "The regulated community would be responsible for the design of appropriate containers that will prevent environmental releases. Each applicant would certify that the proposed transport containers will meet APHIS performance standards" (DEIS, p. 43). However, this shifts the responsibility for determining what specific container design will accomplish the objective of preventing environmental release from APHIS to applicants. A performance-based system could open the door to substandard containers that do not prevent environmental release of regulated GEOs as well as those listed in the prescriptive requirements, for cost-cutting, convenience, or other reasons. A performance-based system without oversight, as proposed here, amounts essentially to "self-certification" by applicants as to the adequacy of their containers.

The USDA Office of the Inspector General criticized USDA for just such "self-certification" of compliance with performance standards in the context of APHIS' notification permit system.

> "Performance-based regulatory standards set objectives and desired outcomes without specifying how they are to be achieved, thus giving approved applicants the flexibility to determine how these objectives/outcomes can be met. ***APHIS is relinquishing its regulatory responsibility in favor of self-certification by the notification applicants—namely the applicants merely certify in their notification applications that they will meet the performance standards. Yet, in 2001, APHIS' own survey of notification protocols found that some protocols may not be adequate to meet the field test performance standards.*** Without documented approved protocols, APHIS has no basis to determine if the applicant's procedures meet the performance standards. To reach management decision, APHIS needs to provide its science-based support for its policy that written protocols will not be required or reviewed prior to approval of field tests."[246]

The situation here is exactly analogous. "Self-certification" is unacceptable, and Alternative 2 should be rejected.

If APHIS knows of newer container designs that perform as well as those in its current prescribed list, it should add those designs to the list. This should reduce the number of variance requests, as APHIS acknowledges (DEIS, p. 43). However, if even this reduced number of variance requests burdens APHIS staff resources, APHIS should simply refuse to consider variance requests. This refusal to consider variances would be all the more justifiable with an expanded list of prescribed containers.

APHIS should therefore adopt Alternative 3, with the proviso that it should simply reject variance requests if they continue to be an excessive burden on its staff resources.

[246] APHIS Audit, p. 22, emphasis added.

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# Appendix 1[247]

**The "Early Food Safety Evaluation" Will Not Ensure Safe Food**

The FDA anticipates increased contamination from the rising number and acreage of experimental GE crop field trials. That is the stated reason for this guidance. Yet due to the factors discussed in Section I – the FDA's failure to quantify or in any way delimit what it means by "intermittent" and "low-level" contamination, the potential for transgenes to persist and amplify in the environment for future transfer to food crops, the likely increase in contamination levels resulting from this guidance, etc. – we must proceed on the assumption that contamination is in principle unlimited. In other words, the food safety evaluation must be based on the worst-case scenario of "100% contamination," or exposure to 100% unmixed experimental GE crop. This is not only the only logical course, it is also consistent with the precedent established in the StarLink case, where Aventis CropScience and the EPA based their estimates of exposure to StarLink's Cry9C insecticidal protein on a variety of corn products made from 100% StarLink corn. If it was proper to follow this course in the case of StarLink, where intensive assessment had already established the magnitude of contamination and the corresponding levels of exposure for various subgroups, then it is still more appropriate in the case of this guidance, which purports to cover ***all manner*** of transgenic GE crop proteins as contaminants in food ***for the indefinite future*** with ***no attempt*** to estimate the extent of contamination in any particular case or in the aggregate.

The StarLink case also demonstrates the potential for low-level presence of a transgenic protein to pose a health risk. According to the EPA's Scientific Advisory Panel on StarLink, which included leading U.S. allergists:

> *"... the Panel concluded that based on reasonable scientific certainty, there is no identifiable maximum level of Cry9C protein that can be suggested that would not provoke an allergic response and thus would not be harmful to the public."*[248] *(p. 35)*

*1) Unintended effects of genetic engineering excluded from evaluation*

The most serious defect of the "early food safety evaluation" is that it proposes to examine only the potential risks from the contaminating transgenic protein, while completely ignoring the unintended and potentially harmful effects of genetic engineering on the contaminating transgenic crop material and the commercial grain, feed or seed it contaminates. Unintended effects are implicitly ignored in two additional contexts: 1) The FDA's decision not to provide for evaluation of experimental GE crops involving metabolic alterations or compositional

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[247] Excerpted from: "Comments to the U.S. Food and Drug Administration re: Guidance for Industry: Recommendations for the Early Food Safety Evaluation of New Non-Pesticidal Proteins Produced by New Plant Varieties Intended for Food Use," FDA Docket No. 2004D-0369, by Bill Freese, Research Analyst, Friends of the Earth, January 24, 2005.

[248] "Assessment of Additional Scientific Information Concerning StarLink Corn," EPA's Scientific Advisory Panel, SAP Report No. 2001-09, p. 35. http://www.epa.gov/oscpmont/sap/2001/july/julyfinal.pdf.

changes rather than novel proteins; and 2) The FDA's decision to not evaluate transformation events expressing similar proteins based on the "same" transgene once the transgenic protein from a single such event has been evaluated. This latter exclusion makes it extremely clear that the FDA neglects the potential for harmful unintended effects.

Yet the plant transformation and tissue culture techniques used in plant genetic engineering generate an extremely high rate of unintended effects relative to traditional selection-based breeding methods for the following reasons: imprecision of techniques, frequent mutagenesis and interspecific incompatibilities.

**Imprecision:** FDA officers[249] and others speak of rDNA techniques as "precise," yet all of the rDNA techniques applied to plants (i.e. chiefly, *Agrobacterium*-mediated gene transfer and particle bombardment via "gene gun") are in fact crude and haphazard. None of these techniques permit control over the genomic site of insertion or the number of transgene copies inserted. All allow for fragmentation of the genetic construct, resulting in incorporation of gene fragments and hence possible generation of fusion proteins. Unbeknownst to the FDA, whose consultation documents are sadly in error on these and other points, Monsanto's Bt corn event MON810 contains an unintentionally fragmented cry1Ab gene, and may well generate an odd-length fusion protein.[250]

**Mutagenesis:** The mechanisms by which plant genomes integrate transgenic DNA in Agrobacterium-mediated transformation and particle bombardment are poorly understood, but are thought to involve a wound response that triggers DNA repair and degradation enzymes.[251] As recently documented in great detail, these techniques and tissue culture invariably cause deletions of plant genomic DNA, random mutations and chromosomal rearrangements.[252] Examples include translocations of up to 40 Kbp,[253] scrambling of transgene and genomic DNA,[254] large scale deletions of over a dozen genes,[255] and frequent random insertions of

[249] Kessler et al (1992). "The safety of foods developed by biotechnology," *Science*, 1747-1832.
[250] Freese, W. & Schubert, D. (2004). "Safety Testing and Regulation of Genetically Engineered Foods," *Biotechnology and Genetic Engineering Reviews,"* Vol. 21, Nov. 2004, see pp. 308-313.
[251] Kohli, A et al (1998). "Transgene organization in rice engineered through direct DNA transfer supports a two-phase integration mechanism mediated by the establishment of integration hot spots," Proc Natl Acad Sci USA 95: 7203-7208.
[252] Wilson, A. et al (2004). "Genome Scrambling – Myth or Reality? Transformation-Induced Mutations in Transgenic Crop Plants," EcoNexus, Technical Report, Oct. 2004, www.econexus.info.
[253] Tax & Vernon (2001). "T-DNA-associated duplication/translocations in *Arabidopsis*: Implications for mutant analysis and functional genomics," Plant Physiol 126: 1527-1538.
[254] Makarevitch et al (2003). "Complete sequence analysis of transgene loci from plants transformed via microprojectile bombardment," Plant Mol Biol 52: 421-432.
[255] Kaya, H et al (2000). "*hosoba toge toge*, a syndrome caused by a large scale chromosomal deletion associated with a T-DNA insertion in *Arabidopsis,"* Plant Cell Physiol 41(9): 1055-1066.

plasmid DNA.[256] Genome-wide mutations are also common. Several studies suggest that 35-58% of Agrobacterium-mediated transgene insertion events disrupt functional plant DNA (Ibid), with a corresponding potential for alterations in native toxins and regulatory proteins, and associated disruptions in cellular metabolism.

**Interspecific incompatibilities:** The components of cells from a particular species/tissue have evolved to work together seamlessly, and cannot be introduced into a foreign genomic context without unpredictable consequences. For instance, DNA polymerases exhibit much elevated error rates when replicating transgenes from other species,[257] while host organisms often do not express unmodified transgenes at appreciable levels. Genetic engineers have learned various tricks to overcome these incompatibilities, such as the use of powerful viral promoters, bacterial enhancers and codon optimization of the transgene to match the host A-T:G-C ratio, but little is known of the mechanisms underlying either the interspecific incompatibility of cellular components or the *ad hoc* fixes.

The factors presented above must be viewed in the context of what little we know of plant functional genomics. Estimates of the number of chemical compounds in the combined plant kingdoms range from 90,000 to 200,000 different molecules, with a single species such as *Arabadopsis* containing roughly 5,000. [258] The production of these compounds at appropriate levels is controlled by exceedingly complex and interactive cellular processes of which we are largely ignorant. Functional genomics studies are only beginning to parse out this complexity. One technique used in such studies is genetic modification. For instance, in a study of just 88 metabolites in potatoes, Roessner et al (see previous reference) found that ***the majority*** exhibited significantly altered levels in one or more of 4 lines transformed for altered sucrose metabolism relative to conventional potatoes. In addition, nine ***novel*** metabolites undetected in conventional potatoes were also found in one or more of the transgenic lines. These effects of genetic modification – significant alterations in the levels of over half the metabolites measured, plus generation of nine novel metabolites – clearly give rise to concern. If we assume for the moment that this example is typical, and scale up from 88 metabolites to a theoretical 5,000 constituents for the typical plant, genetic engineering can be expected to significantly alter the levels of literally thousands of native plant constituents and generate dozens or perhaps hundreds more novel compounds. And while the vast majority of such alterations and novel compounds will likely be unobjectionable, the much larger-than-expected pool of putative changes raises the likelihood that undesirable or harmful alterations will be found among them.

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[256] See Wilson et al (2004), section 1.1.2, p. 9 for references. *See supra*, note 251.

[257] Kunkel, T. (1985). "The mutational specificity of DNA polymerases α and γ during *in vitro* DNA synthesis," Journal of Biol Chem 260(23): 12866-12874.

[258] ROESSNER, U., LUEDEMANN, A., BRUST, D., FIEHN, O., LINKE, T., WILLMITZER, L. AND FERNIE, A.R. (2001). Metabolic profiling allows comprehensive phenotyping of genetically or environmentally modified plant systems. *The Plant Cell* **13**, 11-29.

Compositional changes are common in transgenic food crops. Haslberger and Kuiper et al give a sampling of unintended effects in transgenic plants that have been detected.[259] They include increased or reduced glycoalkaloid content, impaired carbohydrate transport and adverse tuber tissue perturbations in transgenic potatoes; necrotic lesions in GE wheat; and formation of unexpected carotenoid derivatives in rice engineered to express provitamin A. Yeast engineered with multiple copies of a native gene expressed 3-fold higher levels of phosphofructokinase, resulting in an unexpected 40- to 200-fold increase (depending on the transformation event) in methyglyoxal, a toxin and mutagen.[260] Such unintended effects have also been detected in GE plants after their commercialization (see section III).

Given the data presented above, the FDA's arbitrary exclusion of unintended effects from its "early food safety evaluation" is scientifically indefensible, as is its extremely inadequate evaluation of compositional changes during the premarket voluntary consultation process. Currently, testing for unintended compositional changes in GE crops is mostly limited to measurement of overall lipid, carbohydrate and protein levels, together with targeted measurement of amino acids and a few arbitrarily selected nutrients, anti-nutrients and allergens. Obviously, large numbers of potentially harmful alterations, including novel metabolites, will go undetected. As noted by Kuiper et al (2001), with such limited targeted analysis "unexpected changes are merely identified by chance." Since such changes cannot be predicted to be neutral, beneficial or harmful, rigorous testing is required to identify those that have the potential to cause harm. The urgent need for such testing is highlighted by the dozens of deaths and over 1,000 crippling disabilities in people who contracted eosinophilia myalgia syndrome from consuming a tryptophan food supplement produced in genetically modified bacteria.[261] While other mutagenic plant breeding techniques (e.g. irradiation and chemical mutagenesis) are little used today, their products should also be subjected to increased scrutiny.

*2) Hazards related to the novel transgenic protein not properly evaluated*

a) Only two endpoints considered, many others ignored:

[259] HASLBERGER, A.G. (2003). Codex guidelines for GM foods include the analysis of unintended effects. *Nature Biotechnology* **21**(7) , 739-741; KUIPER, H.A.., KLETER, G.A., NOTEBORN, H..P,J.M., KOK, E.J. (2001). Assessment of the food safety issues related to genetically modified foods. *The Plant Journal* **27**(6), 503-528.

[260] Inose, T & Murata, K (1995). "Enhanced accumulation of toxic compound in yeast cells having high glycolytic activity: a case study on the safety of genetically engineered yeast," *International Journal of Food Science and Technology* 30: 141-146.

[261] Though never established beyond doubt due to the manufacturer's destruction of the culpable strains, the increased concentration of tryptophan in the GE bacteria (versus the unmodified strains previously used without incident) is thought to have fostered generation of toxic byproduct. For an excellent weighing of the available evidence, see Fagan, J. "Tryptophan Summary," Nov. 1997, http://www.psrast.org/jftrypt.htm.

The FDA considers only the potential of the novel transgenic protein to be toxic or allergenic. Yet proteins can have numerous other effects that require analysis.[262] For instance, proteins can be antinutrients, like avidin, which binds biotin and thus causes vitamin B deficiency. Proteins like lactoferrin have immunomodulatory activity. Proteins like lysozyme and lactoferrin have bactericidal properties in some situations, while lactoferrin actually promotes the growth of certain pathogenic bacteria by supplying them with needed iron in others.[263] Improperly folded proteins are implicated in brain-wasting prion diseases, and are even thought to be the actual infectious agent. Transgenic proteins that differ in subtle respects from the "same" protein in its native version can elicit destructive immune system responses, as is thought to be the case with recombinant human erythropoietin generated in certain E. coli systems, which is implicated in over 100 cases of red blood cell aplasia.[264] Small peptide breakdown products of proteins have been shown to have teratogenic and other effects, as have unusual amino acid analogs. Clearly, the FDA needs to broaden its range of endpoints beyond toxicity and allergenicity[265].

b) Recommended tests inadequate to address the two endpoints considered:

The tests recommended by the FDA in the guidance are ridiculously inadequate even to judge the two endpoints it does consider – allergenicity and toxicity. Proper evaluation of the toxicity and allergenicity of novel transgenic proteins demands much more than a simple *in vitro* digestibility test and a database search for amino acid homology to known allergens and toxins. Toxicity testing requires animal feeding trials, preferably at least a subchronic 90-day feeding trial in a rodent model, with careful examination for gastrointestinal tract damage as well as the typical signs of toxicity. Such transgenic-protein-specific trials should be supplemented with multigenerational trials of rodents fed the whole GE food to test for harmful unintended compositional alterations. Allergenicity testing should include animal studies to determine whether ingested proteins reaches the bloodstream and otherwise follow the decision-tree protocol specified in FAO-WHO 2001.[266]

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[262] For a general discussion, see "Mammalian Toxicity Assessment Guidelines for Protein Plant Pesticides," FIFRA Scientific Advisory Panel to the EPA, SAP Report No. 2000-03B, September 28, 2000.

[263] Freese et al (2004), op. cit.; Weinberg, E.D. (2001). "Human lactoferrin: a novel therapeutic with broad spectrum potential," *J. Pharmacy & Pharmacology* 53(10), pp. 1303-10. http://munstermom.tripod.com/HumanLactoferrin2001.htm.

[264] Freese, B (2003). "Comments on draft guidance for industry: Drugs, biologics and medical devices derived from bioengineered plants for use in humans and animals," Friends of the Earth, Jan. 2003, pp. 23-25. http://www.foe.org/biopharm/commentsguidance.pdf

[265] See Freese & Schubert (2004), *see supra*, note 172, and Wilson et al (2004), *see supra*, note 251, for recommendations.

[266] FAO-WHO (2001). Evaluation of Allergenicity of Genetically Modified Foods. Report of a Joint FAO/WHO Expert Consultation on Allergenicity of Foods Derived from Biotechnology, Jan. 22-25, 2001. http://www.fao.org/es/ESN/food/pdf/allergygm.pdf

**The "early food safety assessment" is unscientific and fosters "regulatory junk science"**

Section II addressed the inadequacies in the FDA's "early food safety assessment" scheme and the sorts of testing needed in order to detect potentially harmful effects of transgenic proteins or compositional changes in novel genetically engineered foods. In this section, we will address the need to critically evaluate whatever studies are conducted and ensure that they meet accepted standards of scientific practice and integrity. The need for such critical evaluation should be obvious, given the fact that companies with a financial interest in the success of their products normally also conduct the tests to evaluate their safety. If this conflict of interest situation was not clearly perceived before, the recent antidepressant and Vioxx scandals should bring it into sharp focus. As Don Kennedy outlined in a recent Science editorial, some of the major shortfalls in the FDA's drug review process are the dependence upon manufacturers to voluntarily submit information, their disregard of advice from expert FDA scientists and outside advisory committees, and the lack of a robust reporting system once a product is released.267

These inadequacies in the FDA's drug review process are also present in its handling of GE foods. Only the situation is worse. Here, the chief difficulties are: 1) The GE food review process is voluntary rather than mandatory; 2) The FDA does not have an adequate evidentiary basis to conduct a critical evaluation; 3) As discussed in Section II, premarket testing is woefully inadequate; and 4) There is absolutely no post-marketing surveillance system to catch potential health impacts after release of the crop.

Several specific instances of the weakness of this system are:

1) In several instances, biotech companies have refused to respond to FDA requests for additional information beyond that which they initially submitted. Since their participation in a consultation with the FDA was voluntary, they were under no obligation to do so.268 In at least one instance, a company seems to have submitted false information regarding the molecular characterization of its transgenic crop, or FDA badly misinterpreted whatever summary data were submitted.269

2) Companies have neglected to test for levels of toxins and antinutrients in their GE food crops, or at least to submit such data to regulators:
   a) Examples include the failure of companies to submit data on levels of the antinutrient phytate in GE corn and on several toxicant alkaloids in GE tomatoes.270
   b) Company fails to test for the presence of the pollen-sterilizing toxin barnase in the kernels of GE male-sterile corn.271

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267 "Clinical trials and public trust," Science 306: 1649.

268 Gurian-Sherman, D. (2003). "Holes in the Biotech Safety Net: FDA policy does not assure the safety of genetically engineered foods," Center for Science in the Public Interest, Washington, DC.

269 Freese & Schubert (2004), *supra*, note 172, see section with case study on Bt corn.

270 Gurian-Sherman, D. (2003), op. cit.

3) Potentially harmful unintended effects have been completely missed in the consultation process:
   a) Tomatoes genetically engineered with 1-aminocyclopropane-1-carboxylic acid deaminase (ACCase) for delayed ripening were discovered to accumulate higher levels of dangerous heavy metals (e.g. in one event, 5 times more cadmium) than conventional tomato plants; though these particular ACCase tomatoes never underwent FDA's consultation process, very similar ACCase tomatoes passed safety review at the FDA in 1994 without even testing for a similar effect 6 years before academic researchers made this finding;272
   b) Corn hybrids derived from 2 transformation events involving the Bt protein Cry1Ab (MON810 and Bt11) exhibited 33-97% higher lignin levels in stem tissue.273 Lignin is non-digestible, presenting potential animal feed and biodegradation issues, and it is also a product of the shikimic acid pathway in plants, which generates aromatic biomolecules that are constituents of up to 35% of the dry mass of plants, including plant toxins such as rotenone, which has been implicated as a possible cause of Parkinson's disease. This finding was published by academic scientists six years after these two varieties of Bt corn went on the market in 1996 after passing through FDA's voluntary consultation process without detection of this major disruption to normal plant metabolism or any possible related, yet undetected, effects.

4) Potential allergenicity of Bt corn goes undetected by regulators

We will deal in more detail with this example because it involves regulatory breakdown in the very area of allergenicity assessment addressed by this guidance. The Cry1Ab protein present in both MON810 and Bt11 exhibits substantial digestive stability as well as amino acid homology to a known allergen (vitellogenin), both considered suggestive evidence of allergenicity. Yet neither FDA nor EPA acted on these findings.

EPA relied on a Monsanto in vitro digestive stability study on Cry1Ab that seemed to demonstrate rapid degradation. Yet EPA ignored other studies in its files that demonstrated Cry1Ab had substantial digestive stability. Comparison of these studies reveals that Monsanto's experiment was conducted under aberrant conditions – an extremely low pH (1.0) not representative of gut conditions and a huge excess of digestive enzyme (pepsin) relative to Cry1Ab. One or both of these factors likely explain the rapid digestion Monsanto observed, for other tests conducted by academic scientists at pH 2.0 and a smaller excess of pepsin to Cry1Ab revealed up to 60-fold greater digestive stability. Since the latter conditions are closer to (though still harsher than) digestive stability test conditions recommended by international experts (FAO-

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[271] Freese, B. (2003). "Genetically Engineered Crop Health Impacts Evaluation – GAPS Analysis," Friends of the Earth, Washington, DC. http://www.foe.org/safefood/gapseval.pdf

[272] Gurian-Sherman, D. (2004). "A Look at the Unintended Effects of Genetically Engineering Food Plants Re: the National Academy of Sciences Report on Unintended Effects," The Center for Food Safety, Washington, DC.

[273] SAXENA, D. AND STOTZKY, G. (2001). *Bt* Corn Has a Higher Lignin Content than Non-*Bt* Corn. *American Journal of Botany* **88**(9), 1704-1706.

WHO 2001), the tests by academic scientists indicating digestive stability should have carried more weight than the faulty study conducted by the financially-interested GE crop developer.

FDA research scientist Steven Gendel discovered amino acid sequence homology between Cry1Ab and vitellogenin, an egg-white allergen. EPA ignored this finding in its re-registration of Cry1Ab-generating Bt corn in 2001 even though it had no or very little data on file from either Monsanto or Syngenta. Instead, EPA requested that Monsanto submit its own amino acid homology study, largely without specification of search parameters.

By failing to specify test conditions for corporate testing, or at least subjecting corporate tests to critical scrutiny, the EPA missed two pieces of suggestive evidence indicating Cry1Ab could cause allergies. FDA needs to learn from this experience. The guidance does not specify conditions to be followed for digestive stability or amino acid homology tests, but rather only cites possible guidelines. This gives corporate GE crop developers ample leeway to manipulate test conditions to obtain "desired" results, as Monsanto clearly did in the digestive stability study cited above. Since FDA does not demand methodological information on either test, it will not be able to critically evaluate the results and decide whether they are valid or not.

Thus, the FDA's claim to provide "a scientific framework in which to evaluate the safety of new proteins" is simply not true. Instead, the "early food safety assessment" must be labeled an open invitation to "regulatory junk science." Regulatory junk science is a form of pseudoscience in which an assay or other scientific procedure conducted for regulatory purposes is deliberately designed to achieve a preconceived, "desired" result that assures regulatory approval or non-action concerning an identified or potential hazard. It sometimes involves many iterations of the "same" test with arbitrary manipulation of test conditions each time until the "desired" result is achieved. Such junk science is insidious because it fosters a false sense of confidence concerning the safety of a product, in this case a novel transgenic protein.

# Appendix 2

The LL601 contamination debacle should be assessed in the broader context of our regulatory agencies' virtual abandonment of their responsibilities in protecting Americans from the potentially hazardous presence of experimental GE crops in the food supply. The Center for Food Safety believes that untested, unapproved GE crops that enter the food supply unintentionally merit at least the same level of scrutiny as those formally proposed for market introduction. The FDA disagrees, as demonstrated by its casual approach to the LL601 episode. Below, we contrast the differing approaches to LL601 of the FDA and the European Food Safety Authority.

| | **FDA**[274] | **European Food Safety Authority**[275] |
|---|---|---|
| On exposure to LL601 | Relies on Bayer's report alleging "trace amounts," despite independent reports suggesting widespread contamination of commodities and presence in foundation seed | "Exposure levels to LLRICE601 in the EU Member States cannot be estimated accurately from the data provided and little is known with respect to the extent of LLRICE601 in the rice supply." |
| On adequacy of available data | FDA merely relies on data submitted by Bayer, assuming without evaluation or qualification that it is fully adequate to support FDA's "assessment" | "The available data are not sufficient to allow the safety of LLRICE601 to be assessed in accordance with the EFSA guidance for risk assessment." |
| On potentially hazardous, unintended effects of the genetic engineering process used to create LL601 (i.e. unrelated to the PAT protein) | FDA completely dismisses potentially hazardous, unintended effects of genetic engineering in those cases where illegal GE crops enter the food supply through the negligence of the biotech company and USDA. | "The company stated that there were no indications of unintended changes due to the genetic modification. The data package does not include the required raw data to verify this assumption." |
| On potential human health impacts | Despite no independent information on the amount of LL601 in the food supply, no evaluation of the adequacy of Bayer's data, no acknowledgement that LL601's protein differs from that in two approved LibertyLink rice events, and no assessment of unintended effects from the genetic engineering of LL601, FDA says without qualification that LL601 "poses no food or feed safety concerns." | After repeatedly emphasizing the inadequacy of the data supplied to it by Bayer and USDA re: exposure level and unintended effects, EFSA issues a carefully qualified statement that LLRICE601 is "**not likely** to pose an **imminent** safety concern to humans or animals." [emphasis added] This carefully qualified statement leaves open the possibilities of an altered assessment upon submission of full data, and potential impacts from longer-term exposure. |

[274] See http://www.cfsan.fda.gov/%7Elrd/biorice.html.
[275] Quotes from EFSA's statement and press release on LLRICE601:
http://www.efsa.europa.eu/etc/medialib/efsa/press_room/press_release/pr_gmo_llrice601.Par.0001.File.dat/pr_gmo_rice601_en.pdf;
http://www.efsa.europa.eu/etc/medialib/efsa/science/gmo/statements/gmo_llrice601.Par.0001.File.dat/efsa_statement_gmo_LLrice601.pdf

# Appendix 3

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August 2006

# Contamination episodes with genetically engineered crops*

The following are just a few of the dozens of episodes in which pollen or seeds from genetically engineered (GE) crops have contaminated conventional crops, often causing seed or product recalls, and other problems for farmers and consumers.

*August 2006* — Bayer CropScience and Riceland Foods report widespread contamination of commercial long-grain rice supplies, including exports, with Bayer's unapproved, herbicide-tolerant GE rice, LL601. Japan immediately suspends imports of US long-grain rice and orders testing of processed rice products that might contain it. Since Bayer stopped field-testing the rice in 2001, it has likely been in the rice seed supply, the food chain and/or the environment for 5 years or more.

*August 2006* --- EPA scientists announce that golf course grass (i.e. bentgrass) genetically engineered to withstand Monsanto's Roundup herbicide escaped the test plot via pollen flow or seed dispersal to form viable plants up to 2.4 miles away. Bentgrass can cross-pollinate with many different grasses, and 175 permits authorizing cultivation of over 4,400 acres of GE bentgrass have been issued since 1993.

*December 2004* — Biotech giant Syngenta reveals to U.S. authorities that it had mistakenly distributed an unapproved GE corn variety, Bt10, to U.S. farmers from 2001 to 2004. Enough Bt10 to plant 37,000 acres and produce 165,000 tons was distributed. The episode resulted in numerous rejected corn shipments to Japan and the EU. Bt10 remains unapproved by US regulatory authorities.

*September 2004* --- In the longest "gene flow" incident on record, genetically engineered bentgrass (see above) was found by EPA scientists to have cross-pollinated conventional grass up to 13 miles away in Oregon. The Forest Service and Nature Conservancy report that bentgrass can displace natural grass species in forest and native prairie settings. Herbicide-resistant bentgrass weeds created by such cross-pollination could also endanger the grass seed industry.

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* Revised and updated from: BRIEFING ON THE PROPOSED PROTOCOL FOR PHARMACEUTICAL RICE, Attachment 2, Submitted to the AB2622 Advisory Board of the California Rice Commission, March 5, 2004, Prepared by Californians for GE-Free Agriculture

*December 2003* — UC Davis researchers discover that, for seven years, they had been mistakenly distributing for research purposes GE tomato seed in place of a conventional variety.

*July 2003* — Over 100 farmers in Italy discover that the non-GE corn seed they planted was contaminated with an unapproved GE variety.

*May 2003* — Tests show that biotech crops have contaminated wheat grown in the US, even though GE wheat is not approved for marketing. Grain industry experts warn that approving GE wheat could mean the end of US exports to Europe and Asia.

*September 2002* — An experimental corn variety genetically engineered as a "biofactory" for drug-production, produced by ProdiGene, Inc. of Texas, contaminates corn and soybean fields in Iowa and Nebraska. 155 acres of corn is destroyed and 250,000 bushels of contaminated soybeans worth $3 million are quarantined at the elevator and destroyed.

*April 2002* — Corn grown in Argentina and sold as corn flour in Europe is discovered contaminated with a GE variety that is not approved for planting in Argentina or for human consumption in Europe.

*Sept 2001* – Scientists were surprised to discover GE crop material in wild maize in Oaxaca, Mexico despite the country's moratorium on GE crop cultivation, in effect since 1998. It is thought that GE maize seed in food aid shipments from the US was saved and planted.

*July 2001* – Austrian authorities order thousands of acres of corn destroyed when tests show contamination of non-GE seed by two unapproved GE corn varieties.

*April 2001* — Just months after the StarLink fiasco, Monsanto is forced to recall thousands of bags of canola seed contaminated with a GE variety not approved for sale to Canada's major export markets. Incineration is planned for over 10,000 acres of fields already planted with the unapproved crop.

*September 2000* — Over 300 food products were recalled due to contamination by a GE corn (StarLink, produced by Aventis CropScience), not approved for human food due to concerns that it might trigger hazardous food allergies. Experts estimated that half of the state's corn – about 1 billion bushels – could be contaminated. Exports of corn to Japan decreased by 44% in one year. StarLink contamination is still being discovered in US corn shipments three years later.

*May 2000* — Nearly 15,000 acres of farmland in five European countries are contaminated with unapproved GE canola when pollen from the unapproved variety blows into a non-GE seed producers' field. In addition, French authorities reveal that unapproved GE seeds have contaminated nearly 10,000 acres of corn planted there.

*December 1997* — Unapproved GE sugar beet from a Monsanto test field is sent to a sugar refiner, where it contaminates natural sugar sold for animal feed.

*May 1997* — Monsanto is forced to recall 60,000 bags of canola seed when it discovers the seed contains unapproved gene-altered DNA, due to contamination from a planting error by a seed producer.