Docket No. APHIS-2006-0140
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Comments to USDA/APHIS on a Petition to Deregulate Bayer Rice LL601 – Docket No. APHIS-2006-0140

USDA/APHIS is evaluating a petition to deregulate herbicide tolerant (Liberty Link) rice containing, inter alia, *bar* gene that confers tolerance to glufosinate-based herbicides, designated Event LL601, and has issued an environmental assessment (EA). Pursuant the USDA's September 8, 2006, Federal Register notice, 71 Fed. Reg. 53076, the Center for Food Safety (CFS) submits the following comments concerning the inadequacy of the agency's Environmental Assessment (EA) accompanying the Bayer CropScience petition for deregulation. The petition for deregulation raises a number of issues concerning possible environmental impact that are not adequately addressed by the EA or the petition.

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. CFS represents members throughout the country that support organic agriculture and regularly purchase organic products. See generally http://www.centerforfoodsafety.org

CFS believes that the current U.S. regulatory structure does not provide adequate risk assessment of either human or environmental safety of genetically engineered (GE) crops, and therefore no GE crops should be commercialized until U.S. regulations can assure that all GE crops are safe. Short of such blanket prohibition on GE crop commercialization and given the potential adoption rates and acreage to be affected by LL601 rice, CFS finds that the significant unanswered or inadequately answered safety questions that our analysis has discovered warrant a full environmental impact statement (EIS) under the National Environmental Protection Act (NEPA).

Status of CFS' Petition to Regulate Liberty Link Rice as a Plant Pest

On September 14, 2006, CFS filed a legal petition with USDA/APHIS entitled "Petition to Regulate Liberty Link Rice as a Plant Pest." The petition requests that the Secretary take the following actions:

1. Determine that LibertyLink rice is a plant pest under the Plant Protection Act § 7711.

2. Add LibertyLink rice to the list of organisms that are plant pests.

3. Determine that LibertyLink rice is a regulated article and restrict its introduction, dissemination, interstate movement, and conveyance under 7 C.F.R. §340.0.

These requests encompass both the antecedent organisms LLRice 62 and LLRice 06 and the event LLRice 601 that is subject of the current deregulation. As CFS specifically discussed in the petition, there are a variety of reasons Liberty Link rice varieties, including LLRice 601, should not be deregulated. While the legal petition was filed and is pending with regards to all Liberty Link rice varieties, as it pertains to current LLRice 601 deregulation CFS incorporates by reference all of the arguments (and supporting material filed with the petition) herein as comments to the agency's determination to deregulate LLRice 601 and the adequacy of the accompanying EA. A copy of the legal petition and an index to the reference material supporting the petition are attached. Multiple copies of the reference material are already on file with the agency as part of the filed legal petition. These documents should also be made part of the docket pertaining to the LLRice 601 deregulation. In interest of efficiency, CFS has not provided another copy of this material to accompany its comments, however, should agency require another set of such material CFS will provide them upon request.

APHIS Should Not Evaluate the Deregulation Petition for LL601

The Center for Food Safety objects to USDA's consideration of a petition to deregulate a crop that is not intended for commercialization. Bayer stopped development of LL601 in 2001 for unknown reasons, and has said that it has no plans to market the rice.[a] Deregulation (or determination of non-regulated status) is a process intended specifically to clear a crop for unregulated commercial cultivation and sale.

> *"After several years of field testing and data collection, a company or researcher may choose to begin preparing for commercialization. At this*

[a] USDA Release No. 0306.06, "Genetically Engineered Rice," August 2006, http://www.usda.gov/wps/portal/!ut/p/_s.7_0_A/7_0_1RD?printable=true&contentidonly=true&contentid=2006/08/0306.xml

point, an applicant typically files a petition for the determination of nonregulated status with USDA..."[b]

Absent plans to commercialize LL601, Bayer's intent with this deregulation can be seen only as an attempt to relieve itself of liability for the adverse financial consequences of allowing the illegal entry of a regulated article (LL601 rice) into the environment and food supply. This is an improper use of the deregulation process for which we find no sanction or precedent. It is also a waste and misuse of staff resources, tantamount to aiding and abetting Bayer CropScience in its efforts to evade liability for illegal activity. Center for Food Safety believes such staff resources would be better spent on elucidating how the contamination episode occurred, and preventing the future occurrence of similar episodes. It should be noted that USDA has yet to produce any explanation of the LL601 contamination episode, and apparently will not do so for at least two months.[c]

While the most proper course would be for USDA to reject this petition, we recognize that this is unlikely. If the petition is not rejected outright, however, it must be subjected to a thorough and stringent review process. USDA must not cut corners based on representations by Bayer officials that the company does not intend to market LL601, for two reasons: 1) The petition itself contains no statement that Bayer will not market LL601; and 2) Deregulation is absolute, permanently removing a regulated crop variety and its progeny from USDA oversight. Therefore, if USDA were to deregulate LL601, there would be nothing to stop Bayer from changing its plans and intentionally introducing LL601 to the market in the future.

Unfortunately, there is abundant evidence that USDA has cut corners in this deregulation process. The deficiencies in USDA's review process are of three sorts: 1) Errors in its preliminary environmental assessment (EA); 2) Inadequacy of the data upon which the USDA's EA is based; and 3) USDA's failure to publicly release data that are essential for meaningful public review of Bayer's petition, but have been illegitimately claimed as "confidential business information" by Bayer. We will address the latter problem first.

Information Illegitimately Claimed as "Confidential Business Information" (CBI)

Nearly 40% of the petition consists of full pages denoted "CBI deleted page" (see Table 1). As discussed further below, the deleted material includes crucial information required for a critical evaluation of Bayer's claims and USDA's environmental assessment.

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[b] "USDA's Biotechnology Deregulation Process," USDA Biotechnology Regulatory Service Fact Sheet, February 2006, http://www.aphis.usda.gov/publications/biotechnology/content/printable_version/BRS_FS_biodereg_02-06.pdf.

[c] APHIS's report is not due until late December. See Cole, Nancy. "Gene-altered rice's scope is aired," Arkansas Democrat Gazette, Oct. 6, 2006.

USDA's Animal and Plant Health Inspection Service (APHIS), of which Biotechnology Regulatory Services (BRS) is a part, has developed clear guidelines regarding what constitutes legitimate versus illegitimate claims to protect information as confidential.[d] In order to be deemed confidential business information (CBI), material must be "commercially valuable." Persons desiring CBI protection "must submit a detailed statement containing facts" to support their CBI claims. Finally, the policy requires APHIS to assess the merit of a claim to confidentiality and grant it only "***if review establishes*** that substantial competitive harm would result from disclosure" (emphasis added). We find no evidence in APHIS's environmental assessment or elsewhere that it has reviewed Bayer's CBI claims, much less established that substantial competitive harm would result from the disclosure of this information.

TABLE 1: Information Claimed as CBI in Bayer's LL601 Deregulation Petition

SECTION	TITLE	DELETIONS	PAGES	NO. OF DELETIONS	
				PAGES	FIGURES
Appendix II	Insert Characterization	Full pages deleted	44-52	9	
Appendix III	Vector Backbone Analysis	Full pages deleted	54-58	8	
Appendix IV	Stability of the Insert	Full pages deleted	61-63	3	
Appendix V	Bioinformatics Analysis	Two figures deleted	66, 69		2
Appendix VII	USDA PVP Objective Variety Description for rice	Full pages deleted	76-83	8	
TOTALS				28	2

The petition has 83 numbered pages, though 7 pages are empty except for the title of the appendix which follows. Of the 76 remaining pages that contain information, 28 are completely deleted, while two diagrams containing crucial molecular information have been deleted on two additional pages.

The huge amount of information deleted as CBI in Bayer's petition is primarily molecular in nature, and does not merit protection as confidential for several reasons:

1) Since Bayer officials have stated that the company dropped plans to commercialize LL601 in 2001, it is difficult to understand how molecular information relating to it can be considered commercially valuable, much less how public disclosure of such information could cause "substantial

[d] "Policy Statement on the Protection of Privileged or Confidential Business Information," USDA's Animal and Plant Health Inspection Service, Federal Register, Vol. 50, No. 184, Sept. 23, 1985, pp. 38561-63.

competitive harm" to Bayer. LL601 can have no commercial value if it is not marketed.

2) Much of the molecular information deleted as CBI relates to random events of the genetic engineering process over which Bayer had no control. Because such random events are not subject to control, and are therefore not reproducible, the molecular data that document such events would not give an advantage to any competitor of Bayer, because a competitor could not use such data to replicate the genetic engineering process that resulted in LL601 (assuming, for the sake of argument, that a competitor would want to do this, which seems unlikely).

3) Finally, Bayer itself has stated that the random molecular events documented in the CBI-deleted material have no bearing on the properties of LL601 (an interpretation that we dispute). To take just one example:

> *"The random insertion of an extra 35S promoter or part of it, in the rice genome is unlikely to have any consequence as the effectiveness of the promoter is dependent on its full insertion and inserting close enough to DNA encoding a functional gene."*[e]

In 2002, a National Academy of Sciences (NAS) panel that reviewed USDA's regulatory performance with respect to genetically engineered crops explicitly noted that:

> *"The committee finds that the extent of confidential business information (CBI) in registrant documents sent to APHIS hampers external review and transparency of the decision-making process. Indeed, the committee often found it difficult to gather the information needed to write this report due to inaccessible CBI."*[f]

One explanation offered by the committee is that "the agency is not working to provide as much information as possible to the public."[g] The NAS panel's conclusions apply with force to the present case.

Therefore, we call for postponement of any decision on the deregulation of LL601 until APHIS thoroughly reviews the merit of Bayer's CBI claims in accordance with its policy statement, releases for public review any information not deserving of CBI protection, and grants adequate time for CFS and other public reviewers to offer informed comment on the petition.

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[e] "Application for an Extension of the Determination of Nonregulated Status for Glufosinate-Tolerant Rice (98-329-01p): Transformation Event LLRICE601," Bayer CropScience, p. 15.
[f] "Environmental Effects of Transgenic Plants: The Scope and Adequacy of Regulation," Committee on Environmental Impacts Associated with Commercialization of Transgenic Plants of the National Research Council, an arm of the National Academy of Sciences. National Academy Press 2002, p. 11.
[g] Ibid, p. 177.

One possible explanation for Bayer's illegitimate classification of information as confidential is to prevent independent labs from developing a reliable test for the presence of LL601 in the rice and food supply. Bayer has licensed five labs to develop such a test, which relies on detailed knowledge of the molecular characteristics of LL601 contained in the CBI-deleted portions of Bayer's petition. Without such information, no other lab can develop a reliable test for LL601. The European Union has found that several shipments of rice certified as free of LL601 based on testing done in the U.S. tested positive for LL601 in subsequent counter-tests carried out by the Dutch authorities.[h] As a result, the European Commission will likely require mandatory sampling and counter-testing for LL601 by EC member states of U.S. long-grain rice imports rather than rely on certification by U.S. exporters that their EU-bound rice shipments are LL601-free. This additional testing will impede U.S. rice exports, exacerbating economic harm already experienced by U.S. rice farmers and exporters.

The discrepancy in the results of tests carried out in the U.S. and the EU raises the possibility of flaws – intentional or unintentional – in the test developed and licensed by Bayer. Public disclosure of the molecular information improperly withheld as CBI by Bayer and the USDA would permit independent labs to develop their own tests for LL601 to resolve any potential problems with the existing test. The wider availability of accurate tests for LL601 would benefit U.S. rice farmers and exporters by facilitating shipments of LL601-free rice to the European Union.

Deficiencies of Bayer Petition and EA for Deregulation for LL601

Impact on Growers

As USDA acknowledges, LLRice 601 is being deregulated because Bayer CropScience "has learned that samples of commercial long grain rice were found to contain low levels of [LL601 Rice]." (EA at 8). The presence of LLRice 601 in the commercial food chain has created new market uncertainty with all U.S. rice. The direct socio-economic impact associated with any agency action deregulating genetically engineered, herbicide tolerant LL601 Rice must be analyzed prior to taking such action. Indeed, the Council on Environmental Quality (CEQ) regulations implementing NEPA state that such impacts must be analyzed.[1] Specifically, the CEQ regulations state:

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[h] Go to http://ec.europa.eu/avservices/ebs/schedule.cfm?date=10/04/2006. Scroll down to GMO Rice: announcement for a broadcast of comments by Philip Tod, spokesperson for the EC's Health and Consumer Protection division.

[1] CEQ issued its regulations implementing NEPA in response to President Carter's Executive Order 11991 (1977). *See*, Andrus v. Sierra Club, 442 U.S. 347, 357 (1979). The Executive Order directed federal agencies to "comply with the regulations issued by the

> 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

Federal courts have also upheld that NEPA requires, where economic analysis forms the basis of choosing among alternatives, that the analysis not be misleading, biased or incomplete. Seattle Audubon Society v. Lyons, 871 F. Supp. 1291, 1324 (W.D. WA 1994). As one court has noted, "In some instances environmental costs may outweigh economic and technical benefits and in other instances they may not. But NEPA mandates a rather finely tuned systematic balancing analysis in each instance." Sierra Club v. Sigler, 695 F.2d 957, 978 (5th Cir. 1983).

In this instance, the USDA has failed to analyze adequately the socio-economic impacts on farmers and food processors seeking to avoid LLRice 601 and products derived from rice containing LL601 rice in their crops and commodities. The agency's EA fails to addresses these impacts on both farmers, users and exporters of both organic and conventional, non-genetically engineered rice. Indeed, given the Plant Protection Act's (PPA) goal of addressing U.S. agricultural product exports and imports, this failure is even more egregious. See generally 7 U.S.C. 7701

The agency has failed to address a number of other socio-economic impacts that must be addressed as part of the NEPA process. Indeed, the CEQ regulations implementing NEPA state that such impacts must be analyzed. Among the issues that need to be addressed include: (1) impact of LLRice 601 on U.S. rice exports and export of U.S. products using rice derived from rice contaminated with LL601; and (2) the impact of allowing LLRice 601 that is subject to utility patent protection will affect farmers;

The EA contains only one conclusory paragraph about the potential impacts of LLRice 601 on raw and processed agricultural commodities. (EA at 12). This oversight is egregious given the discovery of LLRice 601 in food channels has caused significant market disruption. Numerous farmers have elaborated the extent of such socio-economic impacts associated with the rice variety in lawsuits against Bayer CropScience. A sampling of the legal

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Council." *See id.*, *quoting* Executive Order No. 11991. The E.P.A. has adopted the C.E.Q. NEPA regulations. 40 C.F.R. § 6.100, *et seq.*(July 1, 1996); The Supreme Court has held that the regulations are entitled to substantial deference by the courts. Andrus v. Sierra Club at 358; *See, also*, Marsh v. Oregon Natural Resources Council, 490 U.S. 360, 372 (1989).

complaints filed with regard to LLRice 601 is provided as evidence of the impacts that USDA has inadequately addressed. See attached.

Furthermore, the widespread entry of LL601 into rice and processed foods has occasioned 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. LL601 is by some accounts being found in virtually all milled rice samples that have been tested.[i] Japan banned imports of U.S. long-grain rice shortly after USDA's announcement of the contamination episode on August 18, 2006.[j] Though the ban was lifted on September 19th, Japan has announced that it will test all short and medium-grain rice imported from the U.S, which comes chiefly from California.[k] 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…,"[l] underlining the USDA's failure to effectively handle or even monitor this debacle. Japan is the nation's largest export market for rice. Russia recently suspended imports of U.S. rice due to the LL601 contamination episode.[m]

LL601 has been found in 33 of 162 rice samples tested by the EU,[n] and rice supplies and/or food products contaminated with LL601 have been detected in up to nine European countries, including the UK, France, Germany, Greece, Norway, Ireland, Austria, Slovenia and Italy.[o] Supermarket products contaminated with LL601 have been withdrawn in the UK, Germany, France,[p]

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

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

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

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

[m] "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

[n] "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

[o] "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

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

Switzerland, Norway,[q] and perhaps other countries. The UK Rice Industry Association has reportedly stopped importing any U.S. long-grain rice. The world's largest rice processor, Ebro Puleva, has stopped importing U.S. rice since August 2006.[r]

The economic fallout from LL601 is 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.[s] Perhaps most significant is the continued erosion of international confidence in the wholesomeness of the U.S. food supply occasioned by repeated contamination debacles involving unapproved genetically engineered crops. Six years ago, the discovery of massive contamination of U.S. corn products with unapproved, potentially hazardous GE StarLink corn caused massive cutbacks in US corn exports to Asia and other countries as well as numerous product recalls. In 2002, a drug-producing, GE corn variety was discovered in soybean supplies just one step away from incorporation into soy products intended for human consumption. In 2005, Syngenta announced that it had been mistakenly distributing unapproved GE corn Bt10 for over 3 years before the error was detected, or at least reported. The LL601 debacle can only contribute to the growing international consensus that U.S. foodstuffs are to be avoided whenever possible, due to the apparent inability or unwillingness of federal officials to prevent contamination of US crops and foods with unapproved GE varieties.

In a minor attempt to address some of the socio-economic issues, the agency makes cursory statements concerning the impacts on organic farmers. (EA 11-12) In particular, the USDA states the National Organic Program does not require testing of inputs for excluded methods (i.e. genetically engineered products). The agency also claims there will be no impacts on organic farmers because the presence of a detectable residue of a product of excluded methods (i.e. transgenic) does not necessarily constitute a violation of the National Organic Standards. This analysis is incomplete and devoid of any analysis about the current organic marketplace. During the implementation of the Organic Food Production Act the USDA made it clear that the agency views the organic rule as a marketing standard based upon consumer expectations. This approach was stated in its treatment of "excluded methods" (i.e. genetic engineering). The USDA has stated:

> Products created with modern biotechnology techniques have been tested, approved by the appropriate regulatory agencies, and can be used safely in general agricultural production. At the same

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

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

[s] "Gene-altered profit-killer," op. cit.

> time, consumers have made clear their opposition to use of these techniques in organic food production. This rule is a marketing standard, not a safety standard. Since use of genetic engineering in the production of organic foods runs counter to consumer expectations, foods produced through excluded methods will not be permitted to carry the organic label. 65 Fed. Reg. 13534-35 (March 13, 2000) (emphasis added).

Because of this commitment to consumer preference many food processors, importers, exporters and others now test organic products for the presence of genetically engineered varieties. Indeed, regardless of the National Organic Standards organic products commodities found to be contaminated with genetically engineered varieties (such as LL601) will be returned to the exporter or farmer and will be denied organic market access. USDA's analysis ignores this reality. If the USDA is going to make such an assertion of "no significant impact on organic farming," it needs to analyze whether the marketplace and market-based standards will actually tolerate "adventitious presence" and the impact that such a tolerance will have on organic agricultural producers, processors, and consumers.

Further, APHIS has also provided no evidence that it has taken a "hard look" at the status of the rice seed market. No analytical information is present concerning: (1) the ability of non-transgenic seed producers to avoid transgenic contamination of their foundation rice seed; (2) the ability of seed sellers to ensure that seed being sold can be guaranteed to be non-transgenic rice seed; and (3) the willingness of corporations such as Bayer CropScience to produce and sell non-transgenic varieties that are currently under their patent control. Indeed, current indications are that once transgenic seed is on the commercial market the ability to access non-transgenic seed is significantly hampered. 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 using rice and/or expand such acreage. Absent such analysis and information, the agency's EA cannot support its finding of no significant impact.

Environmental Impacts of Deregulating LLRICE601 Due to Changes in US Rice Growing Practices

If LL601 is deregulated, it will absolve Bayer of domestic legal responsibility for continuing financial impacts on US rice farmers. As long as Bayer is legally responsible for the contamination of US rice supplies, it may be forced to pay for the removal of the contaminated rice from commerce, and to compensate farmers for losses that they were unable to avoid. This responsibility could be lifted if APHIS deregulates LL601.

However, if Bayer's responsibility for LL601 contamination is removed, that will not alleviate the economic harm to U.S. rice growers, but may eliminate their recourse to Bayer. This is because major trading partners, especially Europe and Japan, will likely continue to reject LL601. Currently, those markets will not accept US rice shipments containing LL601 rice contamination. Even regulatory approval in those regions is unlikely to change this, because food retailers in those areas will not accept genetically engineered foods. Producers of genetically engineered seed have recognized this, for example having forgone the commercialization of genetically engineered herbicide tolerant wheat, even though it has been deregulated.

Loss of export markets could have significant environmental implications. For example, loss of markets or price reductions may result in changes in acreage planted to rice. This in turn would substantially affect agricultural practices in rice growing regions. Although it is difficult to predict the results of such changes, because there are different environmental effects from different crops, it can be expected that such changes would have significant environmental consequences.

Therefore, APHIS must carefully evaluate these implications of deregulating LL601 due to the likely effect on exports of rice. So far, APHIS, in its EA, has not conducted such a review. Deregulating LL601 would be an abdication of APHIS responsibility, and would send a clear message of capitulation by APHIS to the interests of Bayer over those of US rice farmers.

Justification of the Extension Petition, and Analysis of the LL601 Deregulation Petition and APHIS Environmental Assessment

APHIS is considering the deregulation of LL601 as an extension of previously deregulated glufosinate-resistant rice events. However, this does not absolve APHIS from performing a thorough safety evaluation under the National Environmental Protection Act (NEPA) or the Plant Protection Act. We believe that APHIS has not satisfied its requirements to perform these thorough assessments.

First, part of the justification for extension is that the gene and protein of the extended event has been evaluated for safety during the deregulation of the previous event(s) – i.e., it is the same gene and protein. For several reasons discussed below, this condition has not been satisfied.

Such an extension also cannot be used to avoid thorough evaluation of possibly harmful "unintended effects" of genetic engineering, because these effects, if present, may be independent of the transgene. In other words, such effects are often transformation-event dependant, and therefore each

transformation event, even of the same gene(s) can have different harmful unintended effects. The Bayer petition is inadequate in its assessment of possible unintended effects, as reviewed below.

Finally, because of inherent differences in the way rice contaminated with LL601 is likely to be grown, compared to currently deregulated LL06 and LL62, the threat of gene flow from the *bar* gene to weedy red rice differs from (and may exceed) the threat from the currently deregulated varieties. Weedy red rice containing the *bar* gene would be a plant pest, as we argue in the attached CFS "Petition to Regulate Liberty Link Rice as a Plant Pest." APHIS tacitly acknowledged the importance of preventing gene flow of the *bar* gene to red rice in its discussion and endorsement of a voluntary resistance management plan in its EA for LL06 and LL62. However, such a plan is not proposed, and cannot be conducted for LL601, as we show below. APHIS did not even discuss resistance management of LL601

Therefore, for all of these reasons, LL601 must not be evaluated as an extension petition and should not be deregulated. Instead APHIS should conduct a thorough EIS of LL601 to fulfill its regulatory responsibilities.

Setting a Precedent for Incomplete Safety Approval of Genetically Engineered Crops

As we demonstrate below, the Bayer petition for deregulation is incomplete in several aspects of safety assessment that APHIS did not adequately consider in its EA. To allow deregulation on this basis would set a bad precedent for US safety assessments, put the environment at risk, and erode international confidence in the US approval process for genetically engineered crops.

Furthermore, although the purpose of the deregulation petition appears to be to resolve the current illegal status of LL601 as a contaminant, APHIS must consider the possibility that Bayer could, after deregulation, commercialize this rice. There may be reasons why Bayer would continue to be uninterested in this option, but there would be nothing preventing Bayer from doing so. Of particular concern is the lack of public disclosure by Bayer for the reasons that it discontinued its commercial pursuit of LL601 in the first place, after several years of field trials. Without knowing the reasons for its dropping LL601 in the past, it is impossible to know whether conditions may have changed that would rekindle Bayer's interest in commercializing LL601 now or in the future. Therefore, APHIS must evaluate the deregulation petition for LL601 as if Bayer would commercialize this rice variety.

Excessive CBI Prevents Adequate Evaluation by the Public of the Bayer Petition

About 40% of the petition is deleted as confidential business information. Although the CBI data are disclosed in summarized form by Bayer, the inability of the public to evaluate the actual data makes it impossible to adequately assess the safety of LL601.

For example, Bayer mentions (Petition, p. 15, last paragraph) that there is a faint band on the blots probing for the vector backbone (which includes an antibiotic gene), which they suggest could be "non-specific binding". Although Bayer's explanation is a possibility, the band may also indicate detection of the vector backbone. One way to confirm this, or determine whether more data is needed for proof of Bayer's contention, is to compare the blot of the non-*bar* rice parent (negative control) to that of the LL601. But Bayer does not mention whether such a control was used, and if used, what the result was. We don't know the answer because the blots are CBI. Neither does APHIS address this issue in its EA.

This use of CBI greatly compromises the public review process, because it makes the public reliant on the interpretation of the data by Bayer, which is not a disinterested or unbiased party. Clearly APHIS also has evaluated the data in its EA, but this is not a substitute for the public review process, which is mandated by statute. In particular, APHIS has allowed Bayer to claim safety data as CBI, and it is questionable that such data should be eligible for such status. Data claimed as CBI by Bayer include:

- The entire section examining the DNA in the rice chromosome near the junction with the *bar* gene insertion;
- Analysis of the possible insertion of the vector "backbone" into the rice genome. This is the part of the vector that is not supposed to insert in this type of transformation process (i.e, when using *Agrobacterium* to deliver the gene), but we now know that this can happen..[t] The backbone includes an antibiotic resistance gene for streptomycin/spectinomycin
- Stability of the insert. One concern here is that Bayer found all or part of an extra CaMV 35S promoter in LL601. Multiple copies can increase the possibility of gene silencing, or turn on other (rice) genes. For example, gene silencing due to CaMV viral infection of transgenic canola that contained a CaMV 35 S promoter has been reported.[u] Silencing of the *bar* gene could result in herbicide damage. Although Bayer performed some tests, such as composition analysis and *bar* gene expression/stability analyses, to address whether unintended

[t] Wilson, A et al., "Genome Scrambling :Myth or Reality?," 2004, EcoNexus

[u] Al-Kaff NS et al., 1998, Transcriptional and post-transcriptional plant gene silencing in response to a pathogen, Science 279: 2113-2115

effects such as gene silencing may have occurred, these tests were inadequate. For example, gene silencing may preferentially occur when the plant is under stress, such as high or low growth temperatures.[v] There is no indication that Bayer performed any such tests, or whether such conditions occurred during field trials.

- One page of bioinformatics analysis
- One page of protein equivalency testing (comparison of the *bar* from LL601 with the one produced in bacteria and used for testing).

Gene Characterization is Inadequate

Although Bayer did some analysis of the junction between the inserted genes and the rice genome (as recommended by Codex Alimentarius), much of the detail is claimed as CBI. Also unfortunately, they did not obtain the sequence of the transgene (or did not report it) to see if it had changed compared to the original gene (as also recommended by Codex).

Changes can occur in the sequence of a protein during the transformation process.[w] The only way to be sure that this has not occurred is to sequence the gene or resulting protein from the genetically engineered plant. Without procession of this sequence, it is inaccurate to assume that the gene and protein in LL601 is the same as those in other glufosinate resistant varieties that have been deregulated. Without that assurance, an essential piece of the justification for the petition extension process is undermined.

This is not merely a theoretical exercise, since even single nucleotide changes can significantly change the structure or function of a protein. For example, a single (intentional) sequence change in the StarLink gene and protein (Cry9C) made it resistant to degradation by the digestive enzyme trypsin. Although changes in sequence may be more likely to cause no noticeable change in the protein, or a change that hampers the function of the protein, changes that may cause harm to people or the environment can only be ruled out by acquiring the sequence from LL601.

Protein Characterization and Equivalency Tests are Inadequate

Bayer implies that the PAT enzyme in LLRICE601 is “the same protein” that is found in other PAT-containing GE crops developed by the company (LLCotton25, LLRICE62, LLRICE06, OSR MS8Rf3 (p. 19, petition). The absence of Appendix II, which contains the DNA sequence of the PAT gene inserted into LLRICE601, prevents us from evaluating this claim. Yet in its environmental assessment,

[v] Meza TJ et al., 2001, The frequency of silencing in Arabidopsis thaliana varies highly between progeny of siblings and can be influenced by environmental factors, Transgenic Res. 10(1): 53-67

[w] Wilson A et al, 2004, op. cit.

USDA states that the sequence of the PAT enzyme produced in LLRICE601 differs by one amino acid from that produced in LLRICE06 and LLRICE62. Even a single amino acid alteration can transform a safe protein into a harmful one (see below). The discrepancy between Bayer's and USDA's account of this basic property of the PAT enzyme in LL601 can only be resolved by public disclosure of the insert (i.e. the information contained in Appendix II).

Bacterially-produced versions of the Bar protein are used in many safety tests, and bacterial proteins may differ in structure and properties compared to plant produced proteins. It is therefore important to show that the bacterial proteins are the same as the plant-produced version. In addition, differences in post-translational modification between the source of the gene and the transgenic plant may lead to potential safety hazards, and therefore must be identified. For example, differences in glycosylation appear to be responsible for increased immunogencity of transgenic bean alpha amylase inhibitor in transgenic peas, leading to the cancellation of the project developing those peas.[x] Bacterially-produced proteins are not glycosylated while plant proteins often are, and the Bar protein comes from bacteria.

Apparently no specific tests were done on the LL601 Bar protein for glycosylation (the tests were CBI, only the description was reported, so we can't be absolutely certain). Protein immunoblots (Western blots) were done, but these only determine the size of the protein to about +/- about 5-10%. Glycosylation may contribute only a few percent to the weight of the protein, and therefore is not reliably detected by standard Western blots. No carbohydrate staining was done, as is typical to test for glycosylation, and certainly nothing as sophisticated as the MALDI-TOF MS tests done in the transgenic pea study that detected changes in glycosylation in that plant.

It is possible that Bayer looked for so-called N-glycosylation consensus sequences in the *bar* gene (consensus sequences are similar sequences that are associated with a particular property – in this case one type of glycosylation), because they mention that the *bar* gene:

> "…has no glycosylation sites, which can often be present on food allergens." [thus also admitting that glycosylation is relevant to food allergenicity]. (Bayer petition p. 18)

However, since they are not explicit as to what they mean by this sentence (e.g. they do not specifically mention the consensus sequence), it is not possible to tell exactly what they intend.

The problem with Bayer's analysis is that there is another type of glycosylation in plants (and other higher organisms) called O-glycosylation.

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[x] Prescott VE et al., 2005, Transgenic expression of bean alpha-amylase inhibitor in peas results in altered structure and immunogenicity, J. Agric. Food Chem. 53: 9023-9030

There is no clear consensus sequence for O-glycosylation (no typical "sites"), and the N-glycosylation consensus sequence does not identify it. As with other glycosylation, O-glycosylation can be associated with allergy.[y] Bacteria do not glycosylate, but may incidentally have glycosylation sites that may be recognized by plants, allowing them to glycosylate. For example, the Scientific Advisory Committee for StarLink suspected glycosylation of the bacterial Cry9C in corn (and that was part of their concern about the protein). In summary, Bayer did not conduct sufficient tests for glycosylation, or if they did, did not mention them (for example, if they are CBI), and APHIS did not evaluate this shortcoming.

Unintended Effects

As noted above, unintended effects must be thoroughly evaluated for each separate transformation event, and cannot be skipped because the same gene or protein was used in previous genetically engineered varieties of the crop. The following sections consider inadequate evaluation of several possible unintended effects in LL601 rice.

As a general point, Bayer evaluated several different lines of LL601 in its field trials, but it seems clear that Bayer intends deregulation to apply to LL601 line 5201 (see petition, bottom p. 20). It is unclear how line 5201 may differ from other LL601 lines, but we note that several tests of properties that compared LL601 to Cocodrie either used other lines (e.g. for some disease susceptibility data), or did not specify which lines may have been used (such as for some yield tests or shattering). Unless these other lines are the same as LL601 line 5201, these tests should be considered deficient.

Unintended Effects: Yields

There may be a difference in yield between the parent non-GE variety (Cocodrie) and LL601, especially when treatments are the same (same herbicide), as they should be when comparing varieties. As presented by Bayer, these differences are not quite statistically significant. But the data are not presented clearly, for example, data from different locations are sometimes improperly combined. On the other hand, a meta-analysis of the statistics across all locations and tests was not done (and such an analysis may have shown the differences in yield to be statistically significant).

[y] Himly M et al., 2002, Art v 1, the major allergen of mugwort pollen, is a modular glycoprotein with a defensin-like and a hydroxyproline-rich domain, FASEB J. 10.1096/fj.02-0472fje.

Especially troubling is that most of the data Bayer presents compares LL601 treated with glufosinate to the non-GE rice with conventional herbicide treatment. The different herbicide treatments appear to reduce the differences in yield between LL601 and Cocodrie, and is not a proper comparison for the purpose of seeing if there are any real differences in the ***rice varieties*** (as opposed to the herbicides!). For example, in the only case where they present data on LL601 treated with the same herbicides as conventional Cocodrie, the yields are 6389 lb/acre lb/acre for Cocodrie and 6021 lb/acre for LL601 treated with the same herbicides as Cocodrie, but 6219 lb/acre when LL601 was treated with glufosinate. The proper comparison yield difference is 6389/6021 = 6%. But when LL601 (glufosinate treated) is compared to Cocodrie (conventional herbicides) the ratio is: 6321/6219 = only 1.6% yield difference. The latter seems to be the kind of comparison used in all other tests. So by using the wrong comparator herbicide treatment, Bayer may reduce the apparent differences in yield of Cocodrie compared to LL601.

An example of this applied to the data for Arkansas; average LL601(glufosinate treated) yield = 8694 lb/acre, conventional yield = 9720 lb/acre, or about 12% more. But LL601 treated with conventional herbicides rather than glufosinate (using a correction factor derived from the experiment mentioned above) may be approximately 8694 - 278 = 8416 lb/acre, and the yield difference becomes about 15% rather than 12%. This approaches statistical significance.

The yields of LL601 are consistently less than for Cocodrie, even with improper comparisons, for ALL of the five locations and years of trials reported. When each are considered individually, these differences are not statistically significant. The differences in yield range from about 1% to 12% more for Cocodrie for the five sets of measurements. Consistent trends like this suggests that if more testing was done (which may bring down the variability), a statistically significant (real) yield difference may be revealed. Similarly, if all the tests were done using the proper comparator, bigger yield difference, and possibly statistical significance, may have been observed. At the very least, Bayer should have performed an analysis of the statistical power provided by these tests to allow determination by APHIS and the public of whether they were acceptably sensitive for the purposes of risk assessment. Furthermore, APHIS should not have accepted tests using a clearly inappropriate comparator.

Unintended Effects and Environmental Risks

Data collected from field trials were used to determine whether there were unexpected harmful changes that may have occurred in LL601 due to genetic engineering. A few important diseases were monitored, with one artificial infestation, and the rest naturally occurring. These tests were probably minimally

adequate because infestation levels were moderate to high, which gives a good test.

However, there are a number of other less important diseases that were not mentioned – probably because they did not occur during the years and in those locations where field trials were conducted (which is a fundamental problem with these limited tests). Minor diseases should also be examined. The worst disease epidemic of corn in the US occurred due to an unintended effect from convention breeding, where the previously-minor southern corn leaf blight pathogen caused about a billion dollars damage in a widely planted new corn variety (in 1970 dollars). Therefore, currently minor pests should not be ignored.

Furthermore, Bayer did not even discuss insect susceptibility, although insect pests were reported to be present. Therefore, we do not know whether there were changes in LL601 that altered insect susceptibility. APHIS did nor comment on this oversight.

Seed shattering was evaluated because it is an indicator of possible weediness (there are some reports of feral rice in some states – but not as a significant weed problem). The text of the petition says there are no differences in shattering, but the Table 14 calls Cocodrie a low shattering variety (level 3), and LL601 moderate (level 5). The moderate and low designation can be almost the same (low = 1-5% shattering, moderate = 6-25%), and that may be the explanation for Bayer's contention, but these categories can differ by as much as 24%. At the least, Bayer should have explained the apparent discrepancy between the table and the text, and APHIS should have required an explanation.

An approved Liberty Link rice variety revealed an apparently substantial difference in lectin. Lectin was 400% lower compared to the non-herbicide resistant variety. However, only one experimental replication was conducted, a clearly inadequate protocol for any experimentation, so no statistics could be done to determine the significance of this difference. Unfortunately USDA inappropriately ignored this difference in its EA of LL06 and LL62. Since lectins are involved in plant defense against insects (see discussion and references in CFS petition, "Petition to Regulate Liberty Link Rice as a Plant Pest."),[z] such reductions may mean the plants are more susceptible to some insects (or some insects under some environmental conditions), which could lead to higher insecticide use. **Possible changes in lectins were not even checked for LL601 compared to Cocodrie.** And, in the field trials, there was little discussion about insect infestations (insects were mentioned, but not in any detail).

[z] Peumans WJ et al., 1995, Lectins as plant defense proteins, Plant Physiol. 109: 347-352

Unintended Effects: Potential Health Effects

The LL601 variety is compared with the non-GE variety (Cocodrie) to see if there are any unintended changes that may have health consequences. In general, substances such as toxicants, anti-nutrients, and nutrients are compared as well because they may cause health or environmental harm. These compositional comparisons, at least as reported by USDA, were much less extensive for LL601 than usual (most of this is usually done for FDA, but reported to both agencies). Concentration of anti-nutrients were not reported in Bayer's petition There is no way of knowing whether FDA saw additional data, because such data have not been revealed to the public if they exist, but at least for the other (deregulated) Liberty Link varieties the concentrations of the anti-nutrients lectin, phytate, and trypsin inhibitor were reported in the petition for LL06 and LL62. So by comparison, it seems likely that these anti-nutrients were not examined for LL601. All that was checked for LL601 were several crude values (total protein, carbohydrates, ash, etc.). Also, it is common to have comparison data for each of the 20 amino acids, individual fatty acids, etc., none of which were included for LL601 Data on unintended changes are much less extensive for LL 601 than deregulated LL varieties.

According to USDA, "[n]o significant differences were observed between transgenic rice, transgenic rice sprayed with herbicide, and non-transgenic rice for any of the parameters measured" (EA, page 20). Yet there is a significant problem with this assertion. The cited values for the "fat/oil" and "protein" content of LLRICE601, its parent variety, Cocodrie, and the conventional Bengal variety fall above the corresponding "literature ranges" for these parameters. This suggests that Bayer's measurements were inaccurate, or that it has chosen an inappropriate mix of rice varieties for the literature range values that are cited. Bayer should be required to report the source for its literature ranges for these and other parameters. The measurements should also be repeated.

Overall, unintended effects were not as closely evaluated in LL601 as for LL06 and LL62. APHIS should have requested these data, but ignored these deficiencies in its EA. APHIS may argue that there are sufficient data to determine that no harmful unintended effects have occurred in LL601 without those data, but for the reasons discussed above, and also because potentially harmful unintended effects are impossible to predict because they can originate in so many different ways, more thorough testing is needed.

Potential for Gene Flow to Weedy Red Rice

Transfer of the *bar* gene to weedy red rice by cross pollination is a real possibility from LL601, but was not evaluated by APHIS. APHIS considered gene flow in its environmental assessment of LL06 and LL62, and tacitly admitted the importance of preventing gene flow to this extremely important

weed of rice by positively acknowledging a voluntary resistance management plan proposed by Bayer for those deregulated varieties.

Furthermore, as argued in our "Petition to Regulate Liberty Link Rice as a Plant Pest" (attached, and incorporated by reference), weedy red rice that acquires the *bar* gene would likely be a more serious weed than current red rice, and therefore a plant pest.

Because LL601 continues to be planted as a contaminant of conventional rice, there is continuing opportunity for red rice to be pollinated by LL601, resulting in transfer of the *bar* gene. As glufosinate-resistant red rice spreads, use of LL rice in the future will be compromised.

Even if LL rice is not commercialized for some time, it is likely that the bar gene would remain in hybrid LL601/red rice, or introgressed into red rice, for several reasons. First, we do not know whether the *bar* gene would compromise the fitness of red rice, but no fitness reduction has been reported for this gene. If it does not decrease fitness, it may remain in the red rice population at low levels indefinitely. However, once glufosinate is applied, the rare red rice containing the *bar* gene will rapidly become more common due to elimination of competition from red rice (and other weeds) that are not resistant to glufosinate. Second, the hybrid LL601/red rice seed, and even more so red rice seed containing an introgressed *bar* gene, are likely to have substantial seed dormancy, and may survive many years in the soil. These seeds can germinate years latter, to be selected by glufosinate applications (if, for example LL rice is commercialized).

It would be especially irresponsible to deregulate LL601 without even knowing how widespread the contamination is. Without these data, it is impossible to evaluate the rate of gene flow, and hence the risks. But even at reported frequencies, gene flow is likely to occur. For example, initial reports suggested that the gene was present at a frequency of 0.06% (6 LL601 rice grains per 10,000). Gene flow from rice to red rice at close proximity (as would occur with red rice weeds growing in rice fields) varies greatly, but has been reported as high as several percent.[aa] Furthermore, we do not know how widespread the contamination is, but reports of tests from Europe suggest that about 20% of shipments may be contaminated. With a contamination concentration of 0.06%, gene flow at 1%, and 20% of fields contaminated (as a rough extrapolation from the frequency of contaminated shipments), the frequency of gene flow, when red rice is present, may be around: 0.0006 X 0.01 X 0.2 = 1.2 E-6, or about 1 in a million seeds. Although this seems like a very low number, it must be understood in the contest of the huge number of red rice plants scattered throughout southern rice growing areas, and the large number of seeds produced by each plant. Fields heavily infested with red rice could easily produces a number of hybrid LL601/red rice seeds. When glufosinate herbicide

[aa] E.g. see Langevin SA et al., 1990, The incidence and effects of hybridization between cultivated rice and its related weed red rice *(Oryza sativa* L.), Evolution 44(4): 1000-1008

is later used, these would quickly be selected, providing numerous foci of resistance scattered throughout the south that could then quickly spread.

By comparison, it was recently demonstrated that wild hybrid creeping bentgrass, created by pollination of wild plants by herbicide (glyphosate) resistant creeping bentgrass from a single field trial, became established at a frequency of about 9 plants of 20,400 tested (0.04%). In that case, cross pollination frequencies were as low, or lower, than would be expected for red rice growing in rice fields.[bb]

Furthermore, the resistance management program proposed by Bayer to prevent gene flow to red rice from deregulated LL06 or LL62 could not be applied to LL601. The voluntary resistance management program for LL06 and LL62 relied on the use of glufosinate in LL rice to control red rice and prevent the initial cross pollination from occurring. But because LL601 is only a contaminate in conventional rice, conventional rice fields containing LL601 cannot be sprayed with glufosinate without killing the crop.

Therefore, if LL601 is deregulated, Bayer will not have to pay the expense of removing it from the conventional rice crop, where it will remain, allowing gene flow into red rice.

So far APHIS has not considered this scenario, and it would be irresponsible to deregulate LL601 without careful evaluation.

Migratory Birds

The EA addresses a number of issues required by various Executive Orders, however, the agency ignores Executive Order 13816 that requires all federal agencies to take into consideration the impacts of action on migratory birds prior to undertaking federal actions and other activities.[1] Specifically, federal agencies must prevent or abate the detrimental alteration of the environment for the benefit of migratory birds.[2] Each federal agency is directed to ensure that environmental analysis for Federal agency actions evaluate the effects of that action on migratory birds, with an emphasis on species of

[bb] APHIS may argue that creeping bentgrass is largely an obligate outcrosser, while rice is mainly self fertile. Therefore bentgrass has, intrinsically, very high pollen flow frequencies compared to rice. Although this is true, the actual pollination frequencies are as high or higher in red rice compared to the pollination frequencies cited from the bentgrass field trial because red rice is so much closer to rice when growing as a weed in a rice field. Although red rice is adjacent to rice plants, the wild creeping bentgrass was mostly several kilometers from the genetically engineered creeping bentgrass.

[1] Executive Order 13618, 66 Fed. Reg. 3853 (Jan. 17, 2001).

[2] *Id.* §3(e)(3)

concern.[3] The E.O. also requires agencies to assess whether their actions result in the unintentional taking of migratory birds and to control the establishment of exotic plants that may be harmful to migratory bird resources.[4] Accordingly, in considering the granting of any petition for deregulated status of LLRice 601 the USDA must analyze the impacts on migratory birds associated with such act.

Conclusions

APHIS has prepared and EA evaluating an extension petition evaluation of LL601 for deregulation. Bayer's petition contains substantially less data than other petitions for deregulation. In particular, in comparison to previously deregulated LL06 and LL062 there are a number of deficiencies, especially regarding possible unintended effects. APHIS has ignored or dismissed these deficiencies.

The justification of an extension petition rests on the applicability of data from similar previous deregulation petitions. However, the petition for LL601 falls short of this standard for several reasons discussed above. In particular, unintended effects may differ between each transformation event, and therefore, unintended effects should be as thoroughly examined in an extension petition as in a typical non-extension petition. This was not done for LL601.

Furthermore, deficiencies in the characterization of the LL601 *bar* transgene and transgenic protein mean that the identity of the Bar protein and gene in LL601 has not been shown to be the same as the *bar* gene and protein from previous glufosinate-resistant crops. Therefore, the use of an extension petition is not justified.

Overall, a number of parameters that should have been examined, or more closely examined, were glossed over in this petition and the EA, or the methodology was improper. These included, but are not limited to: lack compositional comparisons, especially of anti-nutrients; inappropriate comparators in yield trials, lack of adequate glycosylation analysis of the Bar protein from LL601; lack any consideration of gene flow to red rice and lack of a resistance management plan. Furthermore, the excessive and unjustified use of CBI by Bayer prevents adequate public review and comment, and thereby subverts the public review process.

APHIS must not cut corners in its safety assessment of LL601 to accommodate the wishes of Bayer to avoid the consequences of actions that

[3] *Id.* §3(e)(6)

[4] *Id.* at §§ 3(e)(9) & (10)

allowed the contamination of US rice. This contamination has already harmed rice farmers through reduced rice exports and falling prices. Letting Bayer off the hook through this hurried risk assessment will allow rice to remain contaminated with LL601, and cause continuing harm to US rice farmers and the environment.

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Attachments

Sent separately as paper copies