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June 2, 2005

Docket Nos. 05-006-2 and 05-007-2 (submitted separately to each, in quadruplicate)
Regulatory Analysis and Development, PPD
APHIS Station 3C71
4700 River Rd., Unit 118
Riverdale, MD 20737-1238

Re: Comments on Two Environmental Assessments on Permit Application Number 04-302-01r and 05-117-01r: Ventria Rice Expressing Lactoferrin (Docket 05-006-2), and Permit Application Number 04-309-01r and 05-117-02r: Ventria Rice Expressing Lysozyme (Docket 05-007-2)

Dear Sir/Madam:

The Center for Food Safety (CFS), the Union of Concerned Scientists (UCS), and the Interfaith Center on Corporate Responsibility (ICCR) appreciate the opportunity to comment on the above-referenced APHIS Environmental Assessments (EAs) on Ventria Bioscience's proposal to grow genetically engineered (GE) rice that expresses human lactoferrin and lysozyme, both at the same locations in Missouri and North Carolina. We refer to our previous comments on Ventria's permit applications for Missouri, 04-302-01r and 04-309-01r, docket number 05-006-1, which remain applicable to Ventria's application to grow its rice in Missouri. The comments below pertain to the proposed field trials in North Carolina. We note that the limited 20 day comment period for the North Carolina EA is inadequate given the unique issues raised by this location compared to Missouri, and that these comments should be considered to be preliminary due to the limited time available. USDA should extend the comment period for these EAs. For clarity and simplicity, we address only those issues unique to North Carolina. Many risks that must be assessed for the North Carolina field trials are essentially the same as for Missouri. For example, although commercial food rice is not produced in North Carolina, new experimental varieties

that may ultimately be used for breeding may be grown in North Carolina, and could also provide a means of contaminating the food supply. Similarly, wild weedy red rice is not known to exist in North Carolina, but escaped or feral rice has been reported. Although not a weed problem, if contamination of feral rice occurred, it could act as a reservoir of Ventria's genes. Therefore, most of the concerns about contamination of food rice may have parallels in contamination of foundation or quarantine rice seed, and concerns about gene flow to red rice have parallels in gene flow to feral rice. For example, although feral rice is not considered to be a weed, anti-microbial lactoferrin or lysozyme may still provide a fitness advantage due to possible reduction of seed or seedling diseases, as with red rice. Therefore, with the caveats discussed here, as well as other issues clearly specific to Missouri (such as rice acreage in various Missouri counties), all of the points made in our comments about Ventria's Missouri permit applications also apply to the North Carolina applications and are incorporated by affirmation.

CFS, UCS and ICCR believe that these field tests present potentially significant environmental impacts and associated human health risks that have not been adequately addressed in the two EAs. In general, we agree with the recent National Academy of Sciences report that concludes that food crops are usually not a good choice for the production of pharmaceutical crops due to the difficulty of ensuring that contamination of food will not occur.¹ Similarly, an extensive review by scientists with expertise in relevant disciplines also concludes that the use of food crops to produce pharmaceuticals is ill advised.² The authors of that report conclude that although it would be hypothetically possible to ensure that contamination would not occur, in practice, due to the nature of commodity crop production, the prevention of contamination cannot be guaranteed in today's agricultural environment.

NATIONAL ENVIRONMENTAL POLICY ACT CONCERNS WITH THE LACTOFERRIN AND LYSOZYME EAS

It is remarkable that both EAs address exactly the same applicant, same affected environment, same crop, and same classes of foreseeable impacts. Yet, neither EA **even mentions** the existence of the other proposed field test. Neither EA addresses the cumulative impacts of the two projects at the same site or the possibility of any synergistic effects between the two proposals. Thus, the "Cumulative Environmental Effects" sections of each are facially inadequate. This defect underscores the suitability of submitting this joint comment on both EAs, to urge APHIS to consider the impacts of the two proposals cumulatively.

Both EAs are inadequate in their descriptions of the "Need" for the proposals, that is, the need that Ventria seeks to meet with these field tests. The existing "Purpose" description for both EAs is incorrectly placed in "VII. Description of the Field Test/Affected Environment". It should be moved to the existing "II. Purpose and Need" section where it belongs, and should be expanded on as it is now too sparse to tell the reader what Ventria's aims are. Further, the Proposed Action that requires analysis here is not your agency granting a permit, as the EAs put forth, rather the action is Ventria undertaking the field tests. This conceptual confusion weakens

the analysis in the EAs throughout.

Both EAs fail to adequately describe the features of the Affected Environment for the proposal. A fundamental problem is the excessive claims of Confidential Business Information (CBI) by Ventria and the allowance of these claims by APHIS. Perhaps most important are the withholding of the actual location and acreage of the proposals (p. 4 of both EAs). Knowing the location and size of the field plots is vital for determining where, how, and to whom potential unintended exposures could occur, which are key components in determining risk to the public and the environment.

Further, field test locations are **not** CBI under Federal law. This is the ruling by Federal judges in Hawaii, in a lawsuit involving GE pharmaceutical crop field tests, in the only judicial opinions to date that have considered the question. The attached two Orders, in the case of CFS et al. v. Veneman et al., in which the defendants are the Secretary of Agriculture, the Under Secretary for Marketing and Regulatory Programs, the Administrator of APHIS, and the Deputy Administrator in charge of BRS, bind your agency. (Order of U.S. Magistrate Judge Barry M. Kurren dated June 29, 2004, Denying Defendants' Consolidated Motions for a Protective Order, affirmed by Order of U.S. District Court Judge David A. Ezra dated Aug. 3, 2004, Affirming Magistrate Judge's Order for Discovery etc., U.S. District Court, District of Hawaii, civil case no. 03-00621.) At page 3 of Magistrate Judge Kurren's Order, he unambiguously states: "Field test site locations do not constitute confidential commercial or trade secret information." Those orders directed the USDA defendants to provide the claimed-CBI locations in Hawaii to CFS and others, which they have since done.

To bring your policies into alignment with the law, we urge you to now end your past practice of treating locations as CBI, not just for these two EAs, but for all public documents related to all GE crop field tests. Until then our comments are provisional because any final conclusions about safety or lack thereof depend on the location of the proposed planting. Ventria should not be allowed to grow commercial quantities of GE pharmaceutical compounds for a multi-year span - as it asserts it intends to do - on hundreds or even thousands of acres under APHIS's field test regime, without revealing where. The EAs are inadequate on that basis alone.

Although the permit applications evaluated in these EAs are for a single year, Ventria is proposing to grow rice containing lactoferrin and lysozyme in southeastern Missouri or North Carolina for an indefinite period of time as it seeks to commercialize these products. APHIS cannot reasonably rely solely on the current EAs in assessing the risks from future field tests of Ventria's pharmaceutical rice, as is strongly suggested by statements in the EAs, despite the fact that food rice production has been dramatically increasing in the county where the field tests are proposed in Missouri and the possibility of quarantined or foundation rice in North Carolina.³

MIGRATORY BIRD TREATY ACT CONCERNS WITH THE LACTOFERRIN AND LYSOZYME EAS

Migratory birds are of great ecological and economic value to this country and to others.⁴ They contribute to biological diversity and bring tremendous enjoyment to millions of Americans who study, watch, feed or hunt these birds throughout the United States and other countries.⁵ Recognizing this natural resource, in 1918, Congress passed the Migratory Bird Treaty Act (“MBTA”) to implement the “International Convention for the Protection of Migratory Birds” between the United States and Great Britain (acting for Canada), 16 U.S.C. §701, et seq., with the goal of protecting all migratory birds within the jurisdiction of the United States.⁶ In general, section 703 of the Act prohibits the taking and killing of any migratory bird “at any time, by any means or in any manner . . . to kill . . . any migratory bird . . .”⁷ The MBTA prohibits the USDA from taking actions that kill or take migratory birds without a permit from the Department of the Interior.⁸

The use of genetically engineered pharmaceutical rice may impact the habitat of many migratory birds, such as migrating waterfowl and seed-eating birds that may use Ventria’s rice fields. The effects of the high concentrations of human-derived lactoferrin or lysozyme have not been determined, for example by adequate feeding studies using Ventria’s biopharm rice varieties or with lactoferrin or lysozyme extracted from that rice. Ventria cites a chick feeding study by Humphrey et al. as support for the safety of its rice to birds (EA, page 45). This study was not designed to be a complete toxicology study, but rather was intended to determine effects of lactoferrin and lysozyme rice on growth and on parameters related to intestinal bacteria. The tests were apparently only for about 17 and 19 days (although this is not entirely clear from the reported methodology) and only contained 10% or 5% of either or both types of rice. Several useful parameters were examined, including intestinal tissue properties and leukocyte levels. However, this study falls short of an adequate toxicological study for several reasons. It was too short to determine many potential toxic effects, and the percentage of rice in the diet was too low. It also did not examine many possible toxicological endpoints that would have been examined in a study designed for that purpose. It would also be useful to include at least one other species of bird, especially a species of waterfowl, which may be exposed in Ventria’s rice fields. In addition, issues raised in our discussion of potential human health effects from these proteins as produced in rice may also pertain to birds.

Under Executive Order 13816, all federal agencies are also required to take into consideration the impacts of action on migratory birds prior to undertaking federal actions and other activities.⁹ Specifically, federal agencies must prevent or abate the detrimental alteration of the environment for the benefit of migratory birds.¹⁰ 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 concern.¹¹ 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.¹² Accordingly, in considering the issuance of any permit, the USDA must analyze the impacts on migratory birds associated with the growing of Ventria’s biopharmaceutical rice.

In undertaking its assessment, USDA should pay particular attention to migratory bird species

that may inhabit rice fields and/or consume rice seeds. Although rice has not been grown commercially in North Carolina for some time, USDA should reference studies of birds in rice fields in the central and pacific flyways that also migrate along the east coast of the U.S.

Pursuant to E.O. 13186, the USDA should work in collaboration with the Fish and Wildlife Service to ensure that all environmental analyses concerning the introduction of Ventria's pharmaceutical rice, including but not limited to those required under the National Environmental Policy Act, evaluate the effects of the use of genetically engineered rice varieties on migratory bird populations.

SCIENTIFIC CONCERNS WITH THE LACTOFERRIN AND LYSOZYME EAS

In sum, the EAs for lactoferrin and lysozyme rice are inadequate for the following reasons:

- APHIS sets an inadequate 1/4 mile isolation distance to separate Ventria rice from other rice such as food rice, rice grown at field stations, feral rice, or the serious weedy relative, red rice (red rice is not reported to be found in North Carolina, and we refer here to the requirements provisionally accepted in the EA by APHIS, and because red rice may occur in North Carolina in the future). APHIS has underestimated gene flow from rice in the past (based on recently published research) and has seriously underestimated the ability of genetically engineered creeping bentgrass to contaminate surrounding wild relatives.¹³ These and other cases are symptomatic of inadequate data on the ability for gene flow to occur from crops. The 1/4 mile isolation distance accepted by APHIS is unlikely to ensure that gene flow will not occur.
- APHIS allows farm equipment used with Ventria's rice to be used with food rice after cleaning, despite the inability to ensure that such cleaning can remove all of Ventria's rice, which could then be transferred to food rice or contaminate fields containing red rice. A recent report by experts on farm practices confirms that complete cleaning cannot be ensured.¹⁴ Also, there is no requirement to clean farm machinery that was previously used on conventional rice farms prior to use on Ventria's rice, which could allow the contamination of Ventria fields by weedy red rice from a conventional farm. Because of its long seed dormancy, once in Ventria's fields, red rice could be very difficult to eradicate and would likely hybridize with Ventria's rice. Because commercial food rice is not grown in North Carolina, the source of farm equipment to be used with Ventria's rice is unclear, but may involve transport of such equipment from a rice growing region, from which red rice may be transported.
- The EA must not consider isolation distance alone unless prevention of gene flow can be ensured. However, APHIS admits that minimal amounts of gene flow may occur with Ventria's rice. In conjunction with the amount of gene flow, such as by cross pollination, the ability of the transgenes to confer a competitive advantage to rice must be carefully considered because enhanced competitive ability can facilitate permanent escape and spread

of transgenes even when very low levels of gene flow occur. Feral rice is reported to occur in North Carolina, and its fitness may be enhanced by Ventria's genes. However, APHIS does not consider the substantial possibility that lactoferrin or lysozyme could confer a competitive advantage by reducing disease of feral rice grain, despite the fact that these proteins have been used in transgenic crops in previous field tests for the expressed purpose of reducing disease in those plants.

- APHIS does not consider important recent data, and thereby may seriously underestimate the possibility of horizontal gene transfer to bacteria, and possible risk should that occur.
- APHIS as an agency is not qualified to determine the potential human safety risks from lactoferrin or lysozyme rice; further, it has not adequately evaluated those risks in the EA.¹⁵ APHIS has not considered the possible immunological (such as allergy) implications of differences between lactoferrin produced in humans, the source of the gene, and lactoferrin produced in rice, which is chemically different than the human version.
- APHIS apparently accepts evidence that lactoferrin is degraded in the stomach, which would reduce its risk, contrary to evidence presented by Ventria that intact lactoferrin can be found in infant stool.
- APHIS accepts that lactoferrin and lysozyme are denatured by cooking despite questionable testing methods. More importantly, denaturation does not assure that a protein will not be an allergen, although APHIS is apparently reassured by these data.

ENVIRONMENTAL SAFETY OF HUMAN-DERIVED LACTOFERRIN AND LYSOZYME PRODUCED IN RICE: GENE FLOW FROM LACTOFERRIN OR LYSOZYME RICE TO FOOD RICE OR FERAL RICE

A critical issue for the environmental safety of pharmaceutical crops is gene flow to rice or feral rice. Cultivated rice can sometimes become weedy, and can grow as a volunteer feral plant in rice growing areas. Feral rice may act as a reservoir for Ventria's pharmaceutical genes if gene flow occurs, and may have environmental impacts.

Appendix V (EA, page 55) cites Radford et al. in noting that escaped rice has been found in South Carolina, Virginia, and several other southeastern states. This appendix also cites Weakley, that this escaped rice is probably not naturalized (the actual quote is: "probably not truly naturalized"), but neglects to mention that Weakley locates this rice in marshes in North Carolina (as well as Georgia and South Carolina).¹⁶ The location of escaped rice populations in North Carolina is not provided. However, although commercial rice production was primarily in southeastern North Carolina, the identification of escaped or feral rice as far north as Virginia, north of North Carolina, suggests that escaped rice may exist in the areas of North Carolina around the proposed Ventria field trials (Washington County, NC). In addition, the single phrase in Weakley, cited by Ventria, that this rice may not be "truly naturalized" may be more a matter of semantics than substantiation that this rice is not capable of survival in the wild. USDA

National Agricultural Statistics Service data does not record rice in North Carolina after 1909 (one thousand acres), or in South Carolina after 1919.¹⁷ Therefore, it is likely that the escaped populations of rice in these states were established early in the twentieth century, and have maintained themselves since that time (there have been limited efforts to grow heirloom east coast rice in South Carolina, but is highly unlikely to be responsible for known and pre-existing feral rice populations). Therefore these wild populations of rice appear to be self-sustaining, and therefore feral. Ventria notes that “Since this location has been farmed for many years with other crops, there has been no opportunity for a weedy rice complex to develop. Therefore, there is no weedy rice present with which the regulated plants could cross.” However, Ventria’s reasoning appears to be incorrect since rice has not been grown anywhere in North or South Carolina for many years, and yet escaped or feral populations have been reported in those states (it may be possible that very small amounts of rice have been grown, but not recorded by USDA, but since this cannot easily be verified, it also cannot be presumed). Ventria’s reliance on this faulty reasoning to determine that escaped or feral rice is not found in proximity to its proposed field site is also likely to be inaccurate. It is therefore important that the proximity of feral rice to Ventria’s proposed field trial sites is determined so that the risk of gene flow can be better established.

Appendix V also notes that there will be a small conventional rice variety trial about a mile from the proposed Ventria site. Ventria claims that this conventional rice trial will not be used for food or further breeding. However, there have been suggestions that other rice variety field trial plots may also be grown in North Carolina. For example, quarantined rice and possibly foundation rice varieties may be grown in North Carolina. It is critically important to determine whether such rice is grown in North Carolina, the locations of such test plots relative to Ventria’s proposed field trials, and the potential for gene flow. Contamination of such plots of quarantined or foundation rice could be even more serious than contamination of food rice in farmers’ fields. Quarantined rice may consist of imported varieties that may ultimately contribute to new rice varieties or rice seed banks. Foundation seeds are often part of the seed variety increase process. Therefore, if foundation rice is produced in North Carolina, it may represent new rice varieties close to commercial deployment. Contamination of either may distribute Ventria’s genes widely into the food supply for an extended period of time.

The potential for gene flow to either conventional rice field plots or feral rice is exacerbated by the potential for hurricanes in North Carolina. Appendix V (page 55) asserts that hurricane force winds would merely lodge Ventria’s rice rather than either uprooting it or stripping seeds from the panicle. This assertion is made without any supporting data, and as such cannot be accepted as valid. Ventria, arguing for this claim, notes that such lodging is a common problem during “high winds.” However, although lodging during conventional storms is not uncommon, to extrapolate to the much stronger winds generated by a hurricane is not valid in the absence of empirical or other adequate support. We are not aware of any studies substantiating Ventria’s claims, and therefore the alternative hypotheses, that either whole rice plants could be uprooted, or that rice grains would be stripped from the plant and carried substantial distances during a hurricane, must be addressed. If some of Ventria’s rice grains were deposited in field plots or near feral rice, they may grow as volunteer plants and cross with or be harvested with (in the

case of the test plots) that rice, and thereby survive in the wild or become part of the seed supply.

There are several wildlife refuges in Washington County, and in particular the Pocosin Lakes refuge has tens of thousands of acres of lakes and wetlands that could serve as possible habitats for feral rice or establishment of feral Ventria rice after a disturbance such as a hurricane.¹⁸ The refuge is also habitat for numerous species of resident and migrating birds which may also disperse Ventria's rice. Although rice has not evolved to pass through the digestive tract of birds or other animals as a means of dispersal, unlike seeds such as in the genera *Rhamnus* or *Rubus*, there are conflicting reports about whether small amounts of rice seed could pass through waterfowl, such as geese, intact. Unless it is conclusively shown not to be the case, this route of dispersal should be considered.

In addition, hurricanes have been noted to create new disturbed sites that could facilitate the establishment of new feral populations of Ventria's rice. For example, the invasion of non-indigenous plants in disturbed sites in Florida was documented after hurricane Andrew.¹⁹ The potential for establishment of feral Ventria rice by such means should be seriously considered by BRS. If this occurred near conventional test plots, contamination of those rice varieties could be facilitated. If the lactoferrin or lysozyme rice genes contaminate feral rice or foundation or quarantine rice it could spread well beyond Ventria's field test sites.

CONCLUSIONS FOR THE LACTOFERRIN AND LYSOZYME EAS

In sum, the lactoferrin and lysozyme rice EAs are inadequate under NEPA and should be revised to address the issues we raise herein and in our previous comments on the EA for the Missouri permit applications. Then APHIS should put them out again for further public comment before any decision is made on the Ventria permit applications. Alternatively, full environmental impact statements should be prepared.

We look forward to your written responses to each of these comments individually and to further participating in the NEPA compliance process. For further information on these comments, please contact either of us listed below.

Sincerely,

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For:

Jane Rissler, Ph.D.
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Margaret Weber, Co-Chair
Water and Food Working Group
Interfaith Center on Corporate Responsibility

Enclosures (incorporated by reference)

Endnotes

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1. National Research Council, 2004, "Biological Confinement of Genetically Engineered Organisms," National Academies Press, Washington, DC
 2. Andow D et al., 2004, "A Growing Concern: Protecting the Food Supply in an Era of Pharmaceutical and Industrial Crops," Union of Concerned Scientists Publications, Cambridge, MA, 02238-9105
 3. APHIS remarks on page 5 of both Missouri EAs: "This EA is prepared because the applicant intends to have plantings of this engineered plant in Scott County, Missouri, for the next several years. The potential for cumulative impacts of repeated plantings in the same area raises new issues that *this* EA addresses. Future plantings are anticipated to increase in size and will be required to meet all the performance and mitigation measures described in *this* EA, standard and supplemental permit conditions, and the permit application." (emphasis added). Similarly, the current EAs note on page 4 referring to North Carolina: "Similar plantings are planned in future

years with an increase in acreage over time.” Therefore, it appears that APHIS intends that the current EAs will be adequate to address both current *and future* cumulative risks. This would contravene NEPA, which requires that an agency’s environmental assessments be based on just the project proposal that is before it at the time. Thus, APHIS should issue a revised EA that corrects this suggestion of prejudgment of expected future permit proposals by Ventria.

4. Exec. Order No. 13,186, 66 Fed. Reg. 3,853 (Jan. 17, 2001).

5. *Id.*

6. See State of Missouri v. Holland, 252 U.S. 416, 435 (“[T]he United States and great Britain agreed to take the necessary measures to insure the preservation of migratory birds.’).

7. 16 U.S.C. § 703.

8. Humane Society of the United States v. Glickman, 217 F.3d 882 (D.C. Cir. 2000).

9. Executive Order 13618, 66 Fed. Reg. 3853 (Jan. 17, 2001).

10. *Id.* §3(e)(3)

11. *Id.* §3(e)(6)

12. *Id.* at §§ 3(e)(9) & (10)

13. Watrud L et al., 2004,

14. Andow D, et al, 2004, “A Growing Concern...” op cit.

15. APHIS has consulted with a representative from FDA to help in its human safety determination, however, FDA has not completed its own human safety assessment, so this assistance is unlikely to be adequate.

16. Weakley’s Flora, www.herbarium.unc.edu/WeakleysFlora.pdf , p. 798

17. USDA/NASS historical crop production data: www.nass.usda.gov:81/ipedb/report.htm

18. Pocosin Wildlife Refuge, <http://www.fws.gov/pocosinlakes/nathist.html>

19. Horvitz CC, et al., 1998, Functional role of invasive non-indigenous plants in hurricane – affected subtropical hardwood forests, *Ecolog. Applications*, 8(4): 947-974