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Docket No. APHIS-2008-0023
Regulatory Analysis and Development
PPD, APHIS
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Submitted via the Federal eRulemaking Portal

**RESPONSE TO DOCKET NUMBER APHIS-2008-0023**

The Animal and Plant Health Inspection Service of the USDA has requested comments relative to a proposed rule for aligning regulations for the import, interstate transportation, and environmental release of certain genetically engineered organisms with provisions of the Plant Protection Act. I am submitting comments regarding the proposed rule on behalf of the Biosafety Institute for Genetically Modified Agricultural Products (BIGMAP) at Iowa State University. BIGMAP is dedicated to providing an objective voice for assessing and communicating risks for sound public policy and regulatory decision-making as it pertains to the products of agricultural biotechnology. The goals of BIGMAP are to support expert analysis of risk/benefit assessments and mitigation alternatives, to encourage science-based public debate regarding genetically modified agricultural products, and to communicate the results of these activities to key regulatory and public policy stakeholders. We encourage APHIS to continue to pursue a careful, transparent approach toward the adoption of regulatory standards and processes for genetically engineered organisms. We support a regulatory process that assures public trust through responsible consideration of risks balanced against benefits, and that assures progress through a flexible, adaptive, case-by-case assessment of each new emerging technology. Only such an open, adaptive regulatory planning and implementation process can assure the well-being of society and the environment.

*We support rulemaking which aligns APHIS regulations for genetically engineered organisms with provisions of the Plant Protection Act.*

In view of the provisions of the Plant Protection Act it is appropriate that regulation 7 CFR part 340 is revised to appropriately address risks of genetically engineered organisms associated with plant pests and noxious weeds. The process undertaken by APHIS has been thorough, transparent, and will result in a revised rule that reflects best understanding of the rapidly changing nature and extent of genetically engineered organisms that need consideration under § 340.
We support a science-based framework for regulation.

We support a revised scope of regulation in § 340 that allows for clear decisions under a regulatory standard that is science-based. APHIS has a critical challenge of providing a science-based framework for future regulation that is sufficiently dynamic to accommodate a rapidly evolving base of knowledge. We agree with APHIS that “the mere act of genetic engineering does not trigger regulatory oversight,” (III.A.1, p. 60012). As a society, we cannot afford to close doors on future innovations that may pose significant benefits to humankind and the environment. Therefore, we support a dynamic, flexible approach to regulation of genetically engineered organisms.

Our support for the proposed rule is conditioned on our concern that the matrix for assignments to administrative permit categories (Table 3) will likely prove unwieldy for the case-by-case considerations necessary for dealing with rapidly evolving scientific advances and product trends in biotechnology. APHIS is aware of the need for flexibility in the application of the matrix; as for instance, in recognizing that lack of knowledge of the phenotype or lack of familiarity with the species could change a release category. And that “it should be emphasized that the categories are intended only for initial sorting, and other factors are taken into account in the APHIS evaluation when determining specific permit conditions” (III.B.3, p. 60019). Our concern is that the need to shift permit categories may well be commonplace. If indeed this is the norm rather than the exception, APHIS will have a continual need to justify to interested and affected parties their rationale for departing from the matrix assignment in arriving at permit conditions. While we encourage further consideration of the weaknesses inherent in the matrix approach (see discussion of “risk matrices” below), we realize that APHIS has largely committed to this approach at this stage of rule making. Thus, we recommend further elaboration and emphasis in the proposed rule to recognize that deviation from the initial matrix assignment may be commonplace. Further specifics as to how deviations will be determined and documented are needed for clarity and transparency of the proposed process.

The weakness of the administrative matrix for permit categories is well-evidenced by the determination of APHIS to make an a priori assignment of plants making pharmaceutical and industrial (PMPI) compounds to Category C (p. 60020). Current scientific knowledge and uncertainties cannot support such an broad assignment; that is, there are many instances of specific PMPI compounds and host crops that could justify a Category B versus Category C assignment; and while extra-scientific concerns (such as economic concerns of some stakeholders) may justify the blanket application of Category C now, it may well prove untenable in the future. Thus, in this one example, APHIS has made a departure from their administrative matrix which is not science-based. This is an understandable and difficult position for APHIS which needs to be addressed in clear language. The current statement regarding PMPIs that “stringent permit conditions can continue to effectively minimize the risks that may be associated with the environmental release of such GE plants,” should instead refer to the perceived risks to emphasize the decision is based on other than scientific rationale.

There is a need to clarify language and approach for permit procedures to appropriately address risk and uncertainty.

APHIS refers throughout the document to “persistence risk” to describe plant growth habit as the “exposure” factor in the administrative matrix for permit categories. Risk as it relates to
environmental release of a GE organism is best described as the combined likelihood of exposure and adverse effects realized as a consequence of the exposure (Annex III of the Cartagena Protocol), or in other words risk is a function of exposure and adverse effect. The only grouping of persistence that can be construed in terms of risk is that for Federally-listed noxious weeds (the Severe group, p. 60018) and for this class there is an a priori understanding of the hazard associated with a specific plant and its aggressiveness; otherwise persistence only describes the nature of the plant growth habit, which in itself is not a risk. Since persistence (plant growth habit) alone does not constitute a risk, persistence risk is a misnomer that skews perceptions of risk when making permit category assignments; we suggest the term persistence risk should be replaced by the term persistence factor.

We further suggest that the term potential hazard as stated for groupings (p. 6018) is better described as potential for harm as subsequently used in the administrative matrix. Harm is a broader word than is hazard (which refers to some intrinsic adverse property of the compound) and is more applicable to GE plants than is hazard, since for GE plants intrinsic adverse properties are often not shown.

Neither the persistence nor potential harm groupings appear to comprehensively consider possible contributing factors to environmental risks. For instance, the persistence groupings as developed by APHIS describe attributes of persistence of the viable host plant with no acknowledgement as to whether residues of the expressed plant product could be problematic and if so how that might reshape the groupings. This is compounded by the additional lack of any stated concern within the harm groupings for potential environmental harms such as non-target exposure (for other than vertebrates or sexually compatible plants) or for adverse effects on ecological services. Explicit statement of how these might be considered or why it is not necessary that they be considered should be made within the proposed rule. In the absence of such an explicit statement of approach, these concerns would default to a NEPA consideration. This may be the desired approach by APHIS and, if so, it should be explicitly stated.

The administrative permit matrix has the attributes and short-comings of risk matrices.

The approach to decision making described in the proposed rule adopts a matrix for describing the administrative permit categories where,

\[
\text{Permit category} = \text{persistence factor} \times \text{potential harm or damage}
\]

Since APHIS describes the two factors “to roughly approximate ‘exposure’ and ‘hazard,’ respectively” (p. 60019), the matrix described is in fact a risk matrix, i.e.,

\[
\text{Risk} = \text{exposure} \times \text{hazard}
\]

The matrix uses groupings (i.e., a qualitative risk ranking system) to describe persistence and harm (ranking proceeds from “low” to “severe” in both instances). Experts in risk analysis have voiced concern regarding the weakness of both risk ranking and risk matrix approaches which can lead to erroneous decision making. We cite specifically here the recent studies of Cox and co-workers (Cox et al., Risk Anal. 25[3], 651-662, 2005 and Cox, Risk Anal. 28[2], 497-512, 2008).
Qualitative systems for rating risks employing ordered categorical labels such as “low,” “medium,” “high,” and “severe” as used in the proposed rule appear to simplify risk assessment input requirements to inform risk management decisions (the administrative permit category in this instance) but do not necessarily improve decisions. Cox et al. (2005) compared the results of qualitative (categorical labels) and quantitative risk assessment systems and found, in general, that risk rating systems generate errors as to:

1. **Reversed rankings**, where higher risk ratings are assigned to situations that have lower risks, and
2. **Uninformative ratings**, which occur due to the inability to discriminate among large and small risks.

According to Cox et al. (2005), despite having appealing properties, the value of information provided from qualitative labels can be zero for risk management decisions; if most risks are small but a few are large. This is because risk ratings may be unable to confidently distinguish the large risks from the small. This would seem to be the common concern for GE organisms.

Furthermore, Cox (2008) found little research to rigorously validate the performance of risk matrices for actually improving risk management decisions. Limitations were identified with respect to:

1. **Poor resolution**. Typical risk matrices can assign identical ratings to quantitatively very different risks (“range compression”);
2. **Errors**. Risk matrices can mistakenly assign higher qualitative ratings to quantitatively smaller risks. For risks with negatively correlated frequencies and severities, they can be “worse than useless,” leading to worse-than-random decisions;
3. **Suboptimal resource allocation**. Effective allocation of resources to risk-reducing countermeasures (i.e., permit conditions in the proposed rule) cannot be based on the categories provided by risk matrices; and
4. **Ambiguous inputs and outputs**. Categorizations of severity cannot be made objectively for uncertain consequences. Inputs to risk matrices (e.g., frequency and severity categorizations) and resulting outputs (i.e., risk ratings) require subjective interpretation, and different users may obtain opposite ratings of the same risks.

These limitations suggest that risk matrices should be used with caution, and only with careful explanations of embedded judgments (Cox, 2008).

In summary, there is a need for caution in using risk matrices. Risk matrices do not necessarily support good (e.g., better-than-random) risk management decisions. Nor do they support effective allocations of limited management attention and resources (Cox, 2008). None-the-less the widespread adoption and convenience of risk matrices make their use an attractive option for setting permit categories. APHIS needs to beware of the potential pitfalls, address that recognition in the proposed rule, and anticipate the need for research to validate the approach they are undertaking.
Food safety considerations.

APHIS states correctly (III.A.1, p. 60014) that is has no direct role in evaluating food safety but will consider available information about toxicity for assessing noxious weed risk. It is not clear what approach APHIS will take when assigning a permit category if toxicity data are lacking, since toxicity is listed as a criterion for each grouping for potential harm (pp. 60018-6019). An explicit statement that mammalian toxicity data are required as a precondition for permitting should be considered.

Low level presence.

With respect to LLP, APHIS states that the proposed criteria to be used in determinations of cause for remedial action are the function of the introduced sequences and key food safety issues (III.E.2, p. 60025). It would seem that for assignment of permit conditions, there would need to also be consideration of the environmental implications of LLP, especially in the event that the gene sequences may integrate into the genome for a wild receptor population. Further clarification of LLP issues versus gene flow issues probably should be considered in this section of the proposed rule.

Future rule-making needs to balance risks and benefits.

Finally, we commend APHIS for the appropriate balancing of benefits and environmental costs within the regulatory process as they have developed the proposed rule. We support the position of APHIS that while economic loss is an appropriate standard for noxious weeds, “economic loss is never simply the result of market preference” (III.A.1, p. 60014) but must relate to physical damage or harm. We encourage a careful, transparent approach toward the adoption of the proposed rule for genetically engineered organisms through responsible consideration of risks balanced against benefits. A flexible, adaptive, case-by-case assessment paradigm must be adhered to so as to assure the ability of APHIS to address future changes in technology.

Respectfully Submitted,

[Signature]

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