EPA's Safer Choice Supplemental Considerations for Partnership on Microorganism-based Products

July 2013

Safer Choice's Microorganism Review Checklist (Attachment A) describes the basic information needed to assess the potential hazards of a microorganism, including methods for proper species identification, sources for a thorough human health and ecological effects literature search, and possible exposure patterns based on product use. Assessment of the risk, which is a function of both potential hazards and exposure, evaluates whether the microorganism is a potential pathogen—to any of a broad spectrum of organisms (including humans, other mammals, avian species, aquatic vertebrates and invertebrates, plants and others), and whether there are any other adverse effects and the likelihood of those effects that may result from exposure to this microorganism in the specific use of the product.

- Primary considerations for partnership: The risk assessment concludes that the microorganism is not pathogenic to any species with which it will come into contact and will not cause any other adverse human health or ecological effects (e.g., producing metabolites that are more toxic than the parent) in the specific use of the product. All non-microorganism ingredients must have an acceptable health and environmental profile (as per the Safer Choice Standard).

Please note that Safer Choice typically partners with formulators of end-use products. For microbiological-based products, partnership preference is given to companies who manufacture the microorganism and formulate products for end use, and thereby maintain maximum control over product formulation. Safer Choice may also partner with companies that incorporate a third-party's microorganism into their end-use product, provided that they are able to fully address all partnership elements.

Safer Choice will consider the following additional elements as part of its decision to offer partnership to a manufacturer of a microorganism-based product. These elements may be adapted or modified to fit the specific circumstances of the product review, e.g., microorganism type, intended use, and method of application, with special attention to the potential for human or environmental exposures. (Note: All elements not specifically addressed in the Partnership Agreement will be incorporated by reference.)

I. Consistency in Use of the Strain.

The manufacturer must commit to formulating with only those microorganism strains that were the subject of the risk assessment and Safer Choice review and agreed to in the Partnership Agreement. These strains must be identified through a rigorous taxonomic review (including but not limited to 16S rDNA or rRNA sequencing), which can be provided by a recognized full-service culture collection, whether or not the strain is part of the collection, or by other appropriate means. Such collections may be commercial or governmental (US or foreign) but should be listed with the World Federation of Culture Collections and must offer comprehensive identification services as one of its products. Alternatively, the strains may be identified by an established expert in the systematics of the organism used. The strain must not change without prior Safer Choice notification and review. The manufacturer may not substitute a strain of different species without first securing a third-party risk assessment and Safer Choice review and approval. The manufacturer many substitute another strain of the same species (e.g., a related wild-type or a more productive strain) following a careful evaluation of the taxonomic designation and a determination that a new risk assessment is not needed. Consistency in use of strain helps ensure reproducible, consistent formulations, reliable product performance, and a positive health and environmental profile.

II. Product Purity and Quality Assurance.

(A). Key Elements. Related to consistency of strain is product purity, i.e., measures taken to ensure that the product does not become contaminated with other microorganisms during the manufacturing or formulating process. The manufacturer must have quality assurance/control provisions to ensure product purity both during manufacture and any subsequent processing. An example of useful principles of quality assurance/control measures can be found in the test guidelines for microbial pesticides that the U.S. EPA Office of Pesticide Programs has issued (U.S. EPA Microbial Pesticide Test Guidelines OPPTS 885.1200 and 885.1300). While these guidelines are prescriptive and directed toward the specific needs of regulating microbial pesticides, the elements are informative of the kinds of considerations that can be employed in a quality assurance program for microorganism production. The pesticide guidelines include the following:

- A description of the basic manufacturing process, the starting and intermediate materials, and the steps taken to limit extraneous contamination, both chemical and biological;
- A theoretical discussion on the formation of unintentional components, including microbial contaminants, with a list of procedures to ensure the purity of unformulated products; and
- A demonstration that human or other animal pathogens are not present in the final product.

(B). Testing. The purity testing should occur on a periodic basis; at a minimum, the

testing should occur at the time of product formulation and at a time that approximates the end of shelf life. Records of test results should be available to Safer Choice upon request. Product purity is key to both safety and reliable product performance.

(C). Modifications to Formula. The product must not be modified in any way without providing prior notice to Safer Choice (as specified in the Partnership Agreement, sec. 4). Water may be added by a licensed processor according to the manufacturer's purity specifications, incorporated by reference in the Partnership Agreement. The manufacturer must document its legal relationship with the processor.

(D). Product Containers. Manufacturers, and any downstream processors, must have quality assurance/control provisions to ensure that containers do not contaminate the formulation. The recyclability of containers is a desirable product attribute.

III. Functionality and Product Performance.

(A). Utility of Product Ingredients. The manufacturer must demonstrate that each ingredient contributes to product performance (with evidence of the efficacy of that performance) and would not compromise product purity in any way. Use of certain added fillers or carriers might contaminate the approved microbiological blend (i.e., add foreign bacteria) or otherwise interfere with performance (e.g., impede digestion of organic waste constituents, cause increased clogging of drainfield soils, pass through the system to the receiving environment, etc.).

(B). Product Performance. The manufacturer must provide performance testing that demonstrates performance that meets its users' needs. In its review criteria of chemical-based products, Safer Choice outlines several ways to demonstrate performance: by comparison testing with a market leading product, by using a standard test method (such as ASTM), or using a non-standard test protocol in cases where standard methods are not available or not applicable.

Given the lack of standardized testing for biological-based products, a manufacturer must provide a literature reference that describes the functionally appropriate use of the relevant microorganism strains (e.g., certain pseudomonads degrade chlorinated solvents); alternatively, if there is not a literature reference, a manufacturer may use a non-standard method. An example of the latter might involve the lab scale application of microorganisms to media or substrates (e.g., sewage sludge), while simulating real-world conditions (temperature, time, oxygen levels).[1] A small-scale test offers several

[1] Performance Testing. A Safer Choice product should perform on a par with industry leading products. Assays should be designed to compare the recognition candidate to a currently recognized product or industry leader and to replicate use directions and, to the extent possible, real-world application conditions. The number and type of substrates tested will be left to the manufacturer's discretion, but test results should support any product performance claims. Degradation of the substrate (e.g., fats, oils, grease (FOG)) should be measured through an appropriate method, for example, respirometry that indicates oxygen consumption or evolved carbon dioxide. Representative photographs would provide helpful documentation to support quantified measurements at various stages of degradation, but are not required. In all cases, protocols should be submitted to and approved by Safer Choice before any testing

advantages: reproducibility, comparability among microorganisms, and affordability. Manufacturers of other products for a similar purpose would be held to a comparable product performance level.

(C). Shelf life. Shelf life should not exceed the period during which microorganisms are efficacious. The manufacturer or formulator must provide evidence that demonstrates product efficacy during the period of potential sale.

IV. Limitations on Product Eligibility

(A). Products for Use in Indoor Environments. Safer Choice is presently reviewing the appropriateness of indoor use of microorganism-based products. Until this review is complete, Safer Choice will not review or consider for partnership microorganism-based products intended for use on carpets, hard surfaces or other indoor environments.[2]

(B). Septic System and Drain Line Applications (including any application where effluent may be released to a septic system or directly to the environment, for example, holding ponds or lagoons; products for bioremediation would be an exception). Microorganism-based products for septic system, drain line, holding pond or similar applications must contain only live or dormant (i.e., capable of germinating) microorganisms and water (limited use of Safer Choice-acceptable nutrients, stabilizers, additives, and colorants would be allowed) and no added emulsifiers (e.g., surfactants or added enzymes) or other ingredients that might interfere with microbial digestion of wastes and the proper functioning of the drainage system. Surfactants are poorly degradable in a tank's anaerobic environment. Many municipalities have prohibited the use of added emulsifiers in septic or drain line maintenance products for industrial or institutional applications (e.g., Corpus Christi, TX and Davidson County, TN).

V. The Partnership Agreement

(A). To obtain Safer Choice recognition for a microorganism-based product, the manufacturer must comply with the above-listed information elements and enter into a partnership agreement with Safer Choice. The partnership agreement governs the relationship between EPA/Safer Choice and its partner, the product manufacturer. It contains, among other elements, provisions covering the following: full ingredient

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is performed.

Note on grease traps: Evidence should be provided that the degradation products would improve drain operations, for example, are of a more fluid consistency (i.e., less sticky) than the subject substrate.

[2] Safer Choice is exploring whether the use of microorganism-based products in these applications raises a concern for hypersensitivity pneumonitis (HP), a group of immunologically mediated lung diseases in which repeated exposures to finely dispersed antigens evoke a hypersensitive reaction resulting in granulomatous inflammations in the distal bronchioles and alveoli. (Note: HP has typically been considered an adult disease because of its association with occupational exposures, but it has been shown to occur in children from exposure to antigens in the home.) Repeated exposure to vegetative *Bacillus subtilis* cells and spores may result in hypersensitivity pneumonitis.

disclosure; notification of changes in formula and the need for prior Safer Choice approval; the manufacturer's commitment to continuous product improvement; limitations and responsibilities regarding use of the Safer Choice recognition and label; and partnership sunset and opportunity for renewal. A sample partnership agreement is available on the Safer Choice web site (at www2.epa.gov/saferchoice/boilerplate-partnership-agreement-formulators-commercial-cleaning).

(B). As a condition for recognition and a provision of the partnership agreement, a manufacturer must agree to include on product labels and literature, the following statement: "Product contains live microorganisms."

(C). Based on the increasing incidence of microbial resistance to antibiotics, the manufacturer must test the microorganism(s) in its labeled product(s) for resistance to a representative set of antibiotics, as specified by Safer Choice.

Attachment A: Microorganism Checklist (see companion file).