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EPN Comments on EPA'S Proposed Registration of New Active Ingredient, Glycerol Formate, in Ecolab's Product, "DuoGuard RTU"

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The Environmental Protection Network (EPN) harnesses the expertise of more than 650 former Environmental Protection Agency (EPA) career staff and confirmation-level appointees from Democratic and Republican administrations to provide the unique perspective of former regulators and scientists with decades of historical knowledge and subject matter expertise.

EPN appreciates the opportunity to comment on EPA's proposed decision to register an antimicrobial pesticide product containing the new active ingredient, glycerol formate. The new active ingredient is contained in a product named "DuoGuard RTU," and is the subject of an application submitted by Ecolab Inc.

After a review of the decision document and supporting materials, EPN generally supports registration of the products. We do, however, have some concerns about the adequacy of the risk assessment and risk management decisions with respect to the exposures of bystanders. See section I. In addition, as detailed below in sections II - VIII, EPN feels the agency should direct Ecolab to improve its product's labeling in order to receive approval.

EPN has chosen to focus on the proposed end-use product (EP) labeling for the product because labeling is, ultimately, the most important distillation of EPA's regulatory work. As EPA knows, the labeling of a pesticide product is the means whereby the agency communicates to the users of the product how to store, mix, load, apply, and dispose of the product, as well as the other steps the user may need to take to protect themself, others, and the environment. Further, under FIFRA sec. 12(a)(2)(G), it is unlawful for any person to "use a registered pesticide in a manner inconsistent with its labeling." This statutory provision is commonly paraphrased as "the label is the law." All pesticide products' labels must bear a statement immediately beneath the "Directions for Use" heading that reads: "It is a violation of Federal law to use this product in a manner inconsistent with its labeling." In sum, the labeling of a pesticide product is the way that EPA's science-based regulatory decisions about how a product may be used safely and effectively are communicated to and become enforceable for users.

Because pesticide product labeling is such an essential and critical regulatory component in protecting human health and the environment, EPN believes it is vital that the agency make sure that the labeling for a new product, especially one containing a new active ingredient, is well-designed and clearly communicates to users all necessary information about how to use the product. With that in mind, EPN reviewed the proposed labeling for the end-use product, "DuoGuard RTU," and concluded that there are a number of ways in which to improve the draft labeling. These are detailed below. To the extent these comments are

relevant to Ecolab's manufacturing-use products[1], EPN recommends that changes be made to the labeling of those products, as well.

I. Bystander Risk Assessment and Risk Management Determinations

There is the potential for residential exposures (bystanders) including children as the risk assessment states on page 8. However, on page 6 it is stated: "The FQPA Safety Factor (as required by the Food Quality Protection Act of 1996) is intended to provide an additional 10-fold safety factor (10X) to protect for special sensitivity in infants and children to specific pesticide residues in food, drinking water, or residential exposures, or to compensate for an incomplete database." EPA has typically considered application of the FQPA factor where there were residential exposures only, not just when there were dietary exposures. It appears that the 10-fold uncertainty factor (UF) that the assessment includes for an incomplete database would serve this purpose, but the assessment doesn't indicate that to be the reason. Also, there is also no explanation for reducing the UFs for inter- and intra-species extrapolation. **EPN recommends that the agency consider whether, apart from the database UF, there is need for the retention of the FQPA Safety Factor to protect bystanders from residential exposure. EPN also recommends that the agency provide an explanation for its changes to the customary 10X UFs accounting for possible inter-species and intra-species variability.**

Further, in discussing human health incidents in the risk assessment, EPA relies on incident databases for currently registered chemicals (formic acid and hydrogen peroxide) that can produce performic acid (PFA). The discussion adds a caveat, saying that it's unclear how these reported incidents relate to the proposed glycerol formate use patterns and the resulting exposure. The discussion then proceeds to discuss the incidents stating at the end of the hydrogen peroxide discussion: "NIOSH provided recommendations to reduce exposure. These recommendations included calibrating the product dispensers to properly dilute the product to maintain a pH of 2.7 to 4.0 and minimizing the use of the product in non-patient care areas." **Given the inhalation concerns, EPN suggests it would be prudent to say on the labeling not to use in areas where people are receiving in-patient care.**

II. Use and Application Sites:

EPN has two concerns about the labeling for DuoGuard RTU with respect to the sites where it could be used. First, although it appears that the product is intended for use only in healthcare settings, there is no enforceable labeling text that restricts the product to such uses. Second, the agency's human health risk assessment assumes the product will not be used in a manner resulting in residues in food or water. The draft labeling, however, may not contain text necessary to prohibit such use.

[1] It seems as if there are two manufacturing-use products (MUPs) and a resulting end-use product (EP). Each of the MUPs should have its own label with its own appropriate hazard warnings. The MUPs would have use directions on how to formulate the EP, as well as necessary PPE requirements. The EP should have the actual use directions on how to disinfect/sanitize. This would require a set of acute toxicity studies ("the 6 pack") for the EP (PFA), which doesn't appear to exist. It also appears that there would be one EPA registration number for the EP. The MUPs should each have them as well.

1. The draft end-use product (EP) labeling does not affirmatively restrict use of the product to healthcare settings. The front panel of the product contains the following text: "[This product] [Product name] is for use in healthcare facilities." This wording is consistent with the sites listed in the chart titled: "Table 2 – HARD, NON- POROUS USE SITES AND SURFACES IN HEALTHCARE FACILITIES." EPN notes that there are also several other optional statements referring to hospitals, dental offices, and general healthcare facilities.

   However, these statements do not create an enforceable prohibition against use outside of healthcare facilities. The one standard statement – "[This product] [Product name] is for use in healthcare facilities." – does not restrict use to healthcare locations; it merely allows the use in such facilities. Likewise, the heading on Table 2 does not convey a prohibition or restriction. Moreover, many of the surfaces listed in Table 2 commonly appear in settings other than healthcare facilities, e.g., desktops, mouse pads, and mobile devices. Nearly all of the objects in Table 3 for soft surfaces, e.g., fabrics, chairs, bedding, and curtains, can be found in homes, hotels, dormitories, and other non-healthcare settings. EPN feels it is sensible to confine the use of this product to healthcare facilities. **Therefore, to achieve clarity, EPN recommends that the standard statement be revised to read: "[This product] [Product name] is for use only in healthcare facilities" and that the statement appear immediately below the product name.**

2. EPA's human health risk assessment assumes that use of the product will not result in dietary exposure because it is intended as a "non-food contact" use. The draft EP label contains a chart listing over 150 sites on which the product may be used. While none of the sites appears to specify use on food-contact items or surfaces, the draft labeling does not contain an express prohibition against such use. The proposed label contains three "optional" statements that, if they appeared on the labeling, would prohibit use on objects or sites that could result in residues in food. The first optional statement – "Non-Food Contact" – might appear on the front panel of the label beneath the product name, either by itself or with other product claims. The second optional statement – "Do not use to disinfect dishes, glassware, or utensils." – might appear as the last sentence of a paragraph under a heading describing how to disinfect hard, non-porous surfaces. The third such statement – "This product is not for use on food contact surfaces." – might appear as optional text at the conclusion of a paragraph that, itself, might not appear in the product labeling, as a note to the EPA reviewer indicates the paragraph would appear "on all hospital/healthcare labels."

   EPN considers all of these labeling statements inadequate to prohibit use on food-contact objects and surfaces. The draft labeling designates all of these statements as optional, meaning that the registrant may elect to leave them out of the labeling on the commercially marketed product. In their absence, using the product on food contact objects or surfaces would be legal. Further, even if these statements were on a product labeling, their restrictiveness could be questioned, given Table 2 authorizes use on "hard, nonporous environmental surfaces." Moreover, these statements lack the clarity and prominence that would adequately communicate any intended restriction to potential users. Therefore, **EPN recommends that the agency require Ecolab to revise the text to read: "Do not use this product on dishes, glassware, eating utensils, and surfaces that contact food." This statement should appear immediately below the product name on the front panel of the product.**

III. Precautionary Statements and First Aid Statements

EPN has questions and concerns regarding the Precautionary Statements and First Aid Statements on the draft EP label. As noted in the text setting out the ingredients in the product, DuoGuard RTU is sold in a container with two parts. Part A contains the active ingredient glycerol formate, and Part B contains the active ingredient hydrogen peroxide. According to the Directions for Use (DFUs), the user is instructed to combine two parts to produce a use solution identified by EPA as PFA, the active biocide. Specifically, EPN questions whether the First Aid statements are adequate for exposure to the materials in Part A and Part B and the use solution. According to EPA policy, a product's labeling must include Precautionary Statements and First Aid Statements that are appropriate given the composition of the product as marketed, even though an aqueous use dilution which is made from the product may be less toxic and would trigger different, less stringent Precautionary Statements and First Aid Statements. See section V in Chapter 7 of EPA's Label Review Manual[2]. While not exactly on point, this policy suggests that the DuoGuard RTU label should bear the most protective Signal Word, Precautionary Statements, and First Aid Statements needed for Part A material, Part B material, or the PFA use solution. EPA's Human Health risk assessment indicates that Part A is more toxic than Part B material and the PFA use solution. Accordingly, if EPA has not already done so, **EPN recommends that the agency require that the label contain the Signal Word, Precautionary Statements, and First Aid Statements that are appropriate for exposures to Part A. EPA should also consider whether to permit the addition of different statements regarding exposure to Part B material and/or the PFA use solution. In any case, all such statements should clearly identify to which material they apply.**

IV. Container Design and Mixing Directions

EPN infers from the DFU that the product packaging will have separate compartments for the Part A and Part B materials. It also appears that the packaging of the products is designed so that the user is not exposed to either Part A or Part B when combining them to create the PFA solution. This seems like a prudent measure to protect users from potentially hazardous exposures. However, EPN is concerned, about the possibility that accidental breakage of the product containers may lead users to be exposed to Part A and/or Part B materials. (EPN notes that the Physical and Chemical Hazards warnings caution "Never bring the concentrate in contact with other sanitizers, cleaners, or organic substances." EPN infers that this language anticipates environmental release of the Part A mixture.) Has EPA evaluated the container integrity and the potential for accidental exposure to the product materials other than the PFA solution?

Finally, EPA's registration of DuoGuard RTU needs to address two aspects of the container design: 1) whether the product will be distributed only in a container with a pre-attached dosing cap and separate compartments for the Part A and Part B materials and 2) the upper limit on container contents. EPN finds both aspects unclear. The draft labeling indicates that language reading "Bottle with Pre-attached Dosing Cap" is optional. Further, the Note to Reviewer introducing the Environmental Hazards language states that the paragraph will appear on containers of 5 gallons or more.

Together, this language raises practical concerns. EPN does not understand how a five-gallon container with a pre-attached dosing cap could be designed to permit the users to prepare the PFA solution. A container holding a combined five gallons (or more) of Part A and Part B would weigh over 40 lbs., and EPN believes

[2] https://www.epa.gov/sites/default/files/2018-04/documents/chap-07-mar-2018.pdf

it would be very difficult for many users to shake it "vigorously for 30 seconds," as the DFUs require. **Therefore, EPN requests clarification of the maximum size of the container with a pre-attached dosing cap; EPN recommends a maximum of one gallon. In addition, EPN requests clarification of whether all containers of the product will be sold with a pre-attached dosing cap. If so, the DFUs for preparing the PFA use solution should not be optional. If not, the agency should require additional instructions about how to prepare the PFA solution.**

V. Personal Protective Equipment (PPE)

EPN finds the labeling of the product concerning personal protective equipment (PPE) confusing and apparently in conflict with EPA's assumption in its human health risk assessment. The agency's Proposed Registration Decision states (p. 8): "Occupational workers are required to wear gloves when using/applying the solution." The general directions for use for three broad use patterns – "To Clean Hard Non-Porous Surfaces" and "To Disinfect and Deodorize Hard, Non-Porous Surfaces" and "To Sanitize Soft Surfaces" – do not contain such a requirement. Each simply states to "apply the product via clean cloth to wet . . . surfaces thoroughly." This instruction implicitly conveys that there will be direct skin contact with a wet cloth. The draft EP labeling contains specific "Personal Protection" instructions for PPE when the user is dealing with *Clostridium difficile* and when dealing with "HIV-1, HAB, HBV, and HCV . . . soiled with blood/body fluids." For *C. difficile*, the instruction is to "Wear appropriate barrier protection such as gloves, gowns, masks or eye covering." (Emphasis added.) For the virucidal uses, the instruction reads, " [U]se disposable impervious gloves, gown, masks, and eye coverings." (Emphasis added.) Because the labeling does not have a requirement for users to wear gloves that applies to all uses of the PFA solution, EPA's assessment may have underestimated potential dermal exposure and risk. **EPN therefore recommends that the agency require the labeling to state: "Wear impervious gloves while handling the use solution." This statement should appear with or immediately below the prohibition against use of the product on food contact objects and sites.**

In addition, EPN feels that the two sets of Personal Protection statements that appear in the draft labeling are intended primarily to protect users from exposure to the named pathogens, and only incidentally to reduce exposure to the PFA solution. Both *C. difficile* and the named viruses can be transmitted through the air or via contact with the hands that later result in oral intake, and the various viruses can be transmitted through contact with body fluids. EPN believes that, in situations involving potential exposure to these pathogens, it is prudent for the labeling to recommend PPE to reduce the likelihood that the pathogens will infect the user or be present on the user to transmit to another person. However, EPN, recommends that the labeling distinguish between PPE requirements to protect against exposure to the use solution and recommendations to protect against the transmission of pathogens. **Therefore, EPN recommends revising the Personal Protection statements to read: "To reduce your exposure to these contagious pathogens, you should use disposable impervious gloves, as well as a gown, mask, and eye covering."**

VI. Disposal instructions

EPN found the labeling statements regarding disposal of the product and unused PFA solution to be confusing, vague, and potentially contradictory. The section of the labeling titled Pesticide Disposal reads:

> Pesticide wastes are acutely hazardous. Improper disposal of excess pesticide, spray mixture, or rinsate is a violation of Federal Law. If these wastes cannot be disposed of by use according to label instructions, contact your State Pesticide or Environmental Control Agency or the Hazardous Waste Representative at the nearest EPA Regional Office for guidance.

Elsewhere, the labeling instructs users to "Discard mixed product and prepare a fresh end-use product every 60 min." Finally, the Environmental Hazards language to be included on containers of 5 gallons or more states:

> Do not discharge effluent containing the product into lakes, streams, ponds, estuaries, oceans, or other waters unless in accordance with the requirements of a National Pollution Discharge Elimination System (NPDES) permit and the permitting authority has been notified in writing prior to discharge. Do not discharge effluent containing this product in your sewer systems without previously notifying the local sewage treatment plant authority. For guidance, contact your State Water Board or Regional Office of the EPA.

Some aspects of the disposal instructions are adequate, but others are not. The directions regarding disposal of the empty pesticide container are clear and appropriate. The label also sensibly allows the "disposal" of product via use according to the label(ing). The Pesticide Disposal section, however, does not say what users are to do with the PFA solution that has not been used within the hour after it was prepared. The DFUs simply say to "discard" the solution. If the unused solution is discarded into a protected water body, the Environmental Hazards language that will appear only on some products would make that illegal unless the user both has an NPDES permit and has provided written notice to the permitting authority. This seems unrealistic for a product that could be used in thousands of healthcare facilities in a state. **EPN recommends EPA clarify when an NPDES permit would be required, e.g., always, only when the quantity discharged to a protected water body exceeds a fixed amount, and/or only when the material discharged is the undiluted Part A material. If a trigger for an NPDES permit is based on the amount discharged, EPA should consider how to calculate the volume of discharges – by discharge event, by facility, etc.**

A large discharge directly into protected waters seems unlikely; most users would be more likely to pour the unused PFA solution down a sink or into a toilet. The same Environmental Hazards language requires the user to contact the local sewage treatment plant authority before discharging the unused solution or product.

This combination of instructions raises several questions for EPN:

- Why would an NPDES permit and contact with the sewer system authority be required for users of a container holding 5 gallons or more, but not for smaller containers?
- How often and when is a healthcare facility, where users discard unused solution into toilets and sinks, required to notify the sewer system – each release, once a year, only before the initial release?
- Assuming a sewage system prohibits users from discarding the product and/or unused PFA solution into the sewage system, how should users handle any unused solution?
- Has EPA's Office of Pesticide Programs contacted EPA's Regional Office and State Water Boards with guidance about how users must handle unused product and PFA use solution?

EPN recommends that the agency reconsider the portions of the draft DuoGuard RTU labeling that deal with disposal of unused Part A material, unused Part B material, and the unused PFA solution and direct Ecolab to provide clearer, consistent, and more detailed instructions about safe disposal of each.

VII. Application Methods

EPN found the various sections of the DFUs concerning how to apply the PFA solution illogical, and EPN questions whether a FIFRA sec. 2(ee) restriction may be advisable. Specifically, EPN notes the choice of a hand-held matrix that must be used to apply the product seems to depend on the target pathogen, and not the surface or object being treated.

The draft labeling says in several places – the DFUs for cleaning non-porous surfaces, for disinfecting non-porous surfaces, and for sanitizing soft surfaces – to "apply the product via clean cloth." But, curiously, the DFUs for cleaning hard non-porous surfaces also include an optional sentence stating: "For best results, use a dry paper towel or lint-free microfiber cloth." The *C. difficile* instructions for the cleaning prior to disinfection state that the procedure must be performed with a "clean cloth and/or disposable wipe saturated with the disinfectant product [sic; should this read disinfectant solution?]." The DFUs for cleaning and decontamination of surfaces and objects contaminated with blood/body fluids state that the user must "Thoroughly wet the surface with a [cloth] [towelette] [wipe]."

EPN is also concerned about whether the product labeling should include a FIFRA sec.2(ee) restriction. FIFRA sec. 12(a)(2)(G) makes it unlawful for any person "to use any registered pesticide in a manner inconsistent with its labeling." FIFRA sec.2(ee)(3) defines the phrase, "to use any registered pesticide in a manner inconsistent with its labeling," to allow users to make application of a product by any method, "unless the labeling specifically states that the product may be applied only by the methods specified by the labeling." The current draft of the DuoGuard RTU labeling does not contain such a restriction. Consequently, the product could be applied with a mop or as a spray, or poured directly onto a surface, or any other way that a user chooses. In fact, the use of a spray bottle seems quite realistic since the directions for Pesticide Disposal refer to "disposal of excess . . . spray mixture . . ." While this language is not an instruction to apply the product by spraying, it implies that sprays are allowed and anticipated.

Both the matrix used to apply the product and the potential for other application methods are concerns for EPN. EPN is puzzled by the variation in the hand-held matrices – clean cloth, paper towel, lint-free microfiber cloth, disposable wipe, towelette, and wipe – named or required for applying the PFA solution and why the matrix that produces the "best results" for cleaning is named only in an optional sentence. Further, we wonder whether either the user's choice of matrix or the choice to use a method not named on the label, e.g., a spray bottle, could affect the safety or efficacy of the product. EPA's human health risk assessment and efficacy discussions do not address these differences or their potential to affect the risks or antimicrobial efficacy of the product. Although EPN has only anecdotal impressions to support our concerns, we think it likely that there could well be differences in both efficacy and safety depending on which matrix and/or application method are used. **EPN recommends that EPA consider whether to limit the matrices used in hand-held applications and whether to add a FIFRA sec. 2(ee) restriction to the labeling.**

VIII. Other Minor Labeling Comments

In addition to the foregoing comments on the draft DuoGuard RTU labeling, EPN identified several other details of the labeling, some of which are potentially confusing or simply unclear to a user.

- Location of labeling material. EPN has two comments:

    - The draft labeling begins with a "Table of Contents" that lists the major headings and the page on which they can be found when the PDF file is printed. EPN was pleased to note that the Table of Contents is not identified as an optional part of the label. Thus, EPN commends Ecolab for including a Table of Contents for DuoGuard RTU, and, more generally, EPN supports an EPA requirement for inclusion of a Table of Contents for all products whose labeling exceeds five pages. It will give the user a ready guide to the location of information that is important to ensure the product is used safely and effectively.

    - The front panel of the container label indicates that additional information may be found elsewhere including in a "fold out," "booklet," "handout," or other "panels" of the label. Then the draft label also includes an optional sentence reading "[Please [refer to] [see] reference sheet for [additional] [directions for use] [information].]" It is unclear whether the additional "reference sheet" and/or "fold out," "booklet," and "handout," will contain text that does not appear in the PDF file in the public docket. If so, EPA should review the material, and the public should have an opportunity to comment on it. Even if not, almost certainly, the location of the major sections of the labeling, as listed in the Table of Contents, will change depending on where the registrant places them. EPA should instruct Ecolab to conform the Table of Contents to reflect the location of major labeling sections.

- First Aid and Emergency Treatment. The First Aid statement for eye exposure says to "Call a poison control center or doctor for treatment advice." And immediately beneath that there is bolded text reading, "FOR EMERGENCY MEDICAL INFORMATION CALL TOLL FREE: 1-800-328-0026" and OUTSIDE NORTH AMERICA, CALL 1-651-222-5352." EPN recommends that the quoted instruction in the first aid statement for eye exposure be deleted, thereby directing all calls to one source for emergency medical information.

- Physical and Chemical Hazards warnings. The warnings advise "Never bring concentrate in contact with other sanitizers, cleaners or organic substances." The warning's reference to "concentrate" is unclear; does it refer to Part A material, Part B material, the PFA solution, or all of these mixtures? In addition, EPN thinks the use of the term "organic substances" is overbroad. Finally, EPN feels the warning should give a reason for directing the user to have no contact between the concentrate and the specified substances.

- Application directions. The DFUs repeatedly say the user must "Apply the product via a clean cloth to wet surfaces thoroughly." This phrasing may be unclear to some users. Although EPN believes the text means that the user is to apply enough of the PFA solution to make the surface wet with the solution, some users may read the instruction to require that the surface must be wet before it is treated with the PFA solution. The latter understanding could lead to the application of water that might spread the pathogens to new objects or surfaces. EPN suggests rephrasing the DFU to read: "Make surfaces thoroughly wet by applying the product via a clean cloth."

- Directions for Fungicidal use. The DFUs indicate that the product is a "one-step 3 fungicide at the specified mixture . . .." Footnote 3 refers to the "Qualifier" that reads "when used according to disinfection directions for all listed pathogens." The DFUs for disinfection include a precleaning step when the surface is visibly soiled. Therefore, EPN feels it is misleading to make an unqualified claim that the product is a one-step fungicide. In addition, the DFUs' reference to a "specified mixture" is unclear.

- Use of the product against *C. difficile.* The DFUs state that the product kills *C. difficile* on hard, non-porous surfaces. EPN is unclear whether this statement means the product is not effective against *C. difficile* on soft surfaces. If so, the DFUs should contain a warning not to use the product on soft surfaces to sanitize *C. difficile*.

- Emerging Viral Pathogens Claims. The draft labeling contains a section with the heading "Emerging Viral Pathogens Claims." Among other things, it follows EPA's policy which allows the registrant to make claims through means other than the label that the product mitigates emerging viral pathogens, provided the users follow label DFUs for other surrogate viruses that appear on the labeling EPA has accepted. In the case of the draft DuoGuard labeling, the Emerging Viral Pathogens Claims table refers to three surrogate viruses: Adenovirus Type 5 strain Adenoid 75 (ATCC VR-5), Norovirus (Feline Calicivirus, strain F-9) (ATCC VR-782) and Poliovirus type 1 Strain Chat, (ATCC VR-1562). Only the Poliovirus is approved for this product; the other two viruses are not listed in Table 1. EPN recommends that the references to the Adenovirus and Norovirus be removed until the registration is amended to add them.

- Bioburden claims. The Bioburden section of the draft labeling titled Optional Marketing Claims contains two initial claims that the product and Formula are "New (and –or Improved) (!)". EPN questions how a product can make a claim to be "Improved!" when it is being marketed for the first time and there has been no change in the formula.

These comments were prepared by William Jordan and Jack Housenger.