ANNEX F

PUBLIC INFORMATION SHEET FOR
DIRECT USE AS FOOD AND FEED, OR FOR PROCESSING
(to be accomplished by the Applicant and notarized)

PROPOSAL FOR DIRECT USE AS FOOD
AND FEED, OR FOR PROCESSING
Provitamin A Biofortified GR2E Rice

1. Applicant's Name

Philippines Rice Research Institute (PhilRice)
—and—
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2. Applicant's Address

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4. Name of Responsible Officer/Authorized Representative

Responsible Officers: Dr. Sailila E. Abdula
Executive Director, PhilRice
—and—
Dr. Matthew Morell
Director General, IRRI

Authorized Representatives: Dr. Roel Suralta
Golden Rice Project Leader, PhilRice
—and—
Dr. Donald J. MacKenzie
Regulatory Affairs & Stewardship Leader, Golden Rice, IRRI

5. Description of the Regulated Article for Direct Use (mention the crop, transformation event, new trait conferred, name of the gene transferred, method of transformation, and advantages of the trait conferred)

Rice event GR2E (IR-ØØGR2E-5) was developed using recombinant-DNA techniques to express elevated levels of provitamin A (mainly β-carotene) in the rice endosperm, which is converted in the body to vitamin A. GR2E rice was produced by *Agrobacterium tumefaciens*-mediated transformation of embryogenic rice calli with plasmid pSYN12424 resulting in the introduction of the phytoene synthase (*psy1*) gene from *Zea mays* (*Zmpsy1*), the carotene desaturase I (*crtI*) gene from *Pantoea ananatis*, and the phosphomannose isomerase (*pmi*) gene from *Escherichia coli* as a selectable marker.

GR2E rice is intended to complement existing efforts to mitigate vitamin A deficiency by supplying consumers
in societies whose diet is primarily rice-based with a portion of the estimated average requirement for vitamin A.

6. If to be imported, Country (ies) of Origin of the Regulated Article

The Philippines is the intended country of cultivation of GR2E rice and is the country of origin. Therefore, the use of GR2E rice in food, feed, or for processing will only occur following propagation approval in the Philippines.

7. Brief Summary of Potential Effects on Human and Animal Health and the Environment (summarize human and animal health and environmental assessments done and studies implemented indicating potential effects on human and animal health and the environment)

The safety assessment of GR2E rice evaluated information on the history of safe use of rice as a crop, the source of donor genes introduced into GR2E rice, the molecular characterization of the modified plant, the stability of the inserted genetic elements, characterization of new proteins produced in the modified plant and their expression levels, the potential allergenicity and potential toxicity of the newly expressed proteins, and the nutrient composition of GR2E rice compared to conventional rice.

Molecular characterization of the introduced DNA within event GR2E confirmed the presence at a single insertion site of one copy of the inserted DNA that was stably inherited over multiple generations as a single genetic locus per Mendelian rules of inheritance. Expression of the ZmPSY1 and CRTI proteins was limited to the rice endosperm with maximum concentrations in mature grain of approximately 0.245 ppm and 0.03 ppm, respectively. The PMI protein was expressed in all rice tissues measured and accumulated to maximum concentrations of 1.89 ppm and 0.796 ppm in mature grain and straw, respectively.

A tiered "weight-of-evidence" approach was followed in assessing the safety of the *Zm*PSY1, CRTI, and PMI proteins expressed in GR2E rice. The *Zm*PSY1 and CRTI proteins did not display significant amino acid sequence similarity with known allergens nor were there any primary sequence structural alerts for potential toxicity based on similarity searches against a database of known and putative protein toxins. Both *Zm*PSY1 and CRTI were rapidly and completely digested in the presence of simulated gastric fluid containing pepsin, and the enzymatic activity of both proteins was destroyed following treatment at temperatures well below those used during cooking.

Due to the non-food source of the *crtI* gene, acute oral toxicity testing of CRTI protein in mice was conducted as a further assurance of safety and demonstrated a lack of any observable adverse effects at a dose of 100 mg/kg body weight, which represents at least a 115,000–fold margin of exposure relative to any realistically conceivable human dietary intake from GR2E rice.

Based on its presence in a wide range of food and feedstuffs derived from genetically engineered maize lines, and on the extensive history of prior regulatory reviews in the Philippines, additional characterization of the PMI protein was unnecessary. Previously submitted safety studies reviewed in the context of other genetically engineered plant events are directly applicable to the safety assessment of PMI protein expressed in GR2E rice.

The genetic modification resulting in GR2E rice was only intended to increase levels of provitamin A (primarily β-carotene) in the rice endosperm. To confirm the intended effect and the lack of any meaningful unintended consequences of the genetic modification, compositional parameters were compared between GR2E rice and control, unmodified, rice. Compositional analyses were performed on samples of rice grain and straw obtained from PSB Rc82 rice containing event GR2E and near-isogenic control PSB Rc82 rice that was grown at four separate sites in the Philippines during 2015 and again in 2016. The compositional assessment included analyses for proximates, fibre, and minerals in samples of straw, and analyses for proximates, minerals, vitamins, amino acids, fatty acids, vitamins, and key anti-nutrients in grain samples. Samples of processed bran derived from GR2E and control rice were also analyzed for proximates, fibre, and minerals.

Among the 69 compositional components that were tested for in samples of GR2E and control PSB Rc82 rice grain, and 10 components that were assessed in derived bran and straw samples, the only statistically significant difference observed from the multi-year combined-site analysis was for stearic (C18:0) acid, a minor fatty acid component, measured in grain samples (not including the intended difference in provitamin A levels). Except for β-carotene and related carotenoids, the compositional parameters measured in samples of GR2E rice, including stearic acid, were within or similar to the range of natural variability of those components in conventional rice varieties with a history of safe consumption. Overall, no consistent patterns emerged to suggest that biologically meaningful changes in composition or nutritive value of the grain or straw had occurred as an unexpected, unintended consequence of the genetic modification.

Collectively, the studies performed for GR2E rice have not identified potential health and safety concerns, and support the conclusion that food and/or livestock animal feed derived from provitamin A biofortified GR2E rice is as safe and nutritious as food or feed derived from conventional rice varieties.

8. Brief Summary of Potential Benefits (Describe how the new trait will benefit farming, the farmer, the environment, and society as a whole)

Vitamin A is an essential nutrient required for normal functioning of the visual system and protection from disease and infection. In south and southeast Asian countries, where two-thirds or more of daily calories are obtained from rice, many people are battling against vitamin A deficiency due to an imbalanced diet with limited access to fresh fruit, vegetables, and animal products. Persistent vitamin A deficiency is the leading cause of childhood blindness and increases the risk of death from common childhood infections.

Despite significant progress since 2003, vitamin A deficiency remains a serious public health nutrition problem in the Philippines, particularly among preschool age children where the prevalence ranges from 19.6 percent for 1–5-year olds up to 27.9 percent for children under one year of age.

GR2E rice is intended to complement existing vitamin A deficiency control efforts, such as food fortification, vitamin A supplements, and dietary diversification, by supplying up to 30–50 percent of the estimated average requirement for vitamin A for preschool age children and pregnant or lactating mothers.

9. Countries Where Approvals Have Been Granted (for FFP; for Commercial Propagation)

As of the date of this submission, GR2E rice is not approved for use in food or livestock animal feed or for propagation in any country.

The public is hereby invited to submit their comments to the BPI Director (within 60 days from date of publication) on the proposal for the direct use as food and feed, or for processing of GR2E rice.

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Approved for Publication: _____

Director
Bureau of Plant Industry
Date: