Potato Leaf Roll Virus Resistance Gene (also known as *orf1/orf2* gene) (006469) Registration Eligibility Document (BRAD)

Issued: 04/00

I. Executive Summary

A. Identity

The New Leaf Plus Potatoes have been genetically engineered to express the Cry III (A) protein from Bacillus thuringiensis subsp. tenebrionis (B.t.t.) and the orf1/orf2 gene from Potato Leaf Roll Luteovirus Virus (PLRV) as the active ingredients. Plant transformation vectors for the two active ingredients were constructed using selectable marker genes. In New Leaf 7Plus Potatoes, the orf1/orf2 gene provides resistance to infection by the Potato Leaf Roll Virus and the Cry III (A) protein controls feeding by the Colorado Potato Beetle . Although this plant-pesticide product contains two active ingredients, this document refers only to the Potato Leaf Roll Virus Resistance Gene (orf1/orf2 gene). The mechanism of resistance provided by the orf1/orf2 gene has not been elucidated at this time. Possible scenarios responsible for inhibition of viral replication include: (1) Protein Driven Inhibition (viral replication inhibited by the three proteins which could be encoded by the orf1/orf2 gene) or (2) RNA Driven Inhibition. Protein driven inhibition as a mechanism of action of the orf1/orf2 gene is questionable due to the lack of conclusive evidence that any of the potential proteins encoded for by the orf1/orf2 gene are expressed. BPPD believes that this lack of evidence is not unexpected as the proteins are difficult to detect even in PLRV infected plants. Although the mode of action of the orf1/orf2 gene remains unclear, there is a long history of consumption of PLRV infected potatoes without any reports of toxicity or other harm caused to the general population from consumption of the plants and food components of these plants such as nucleic acids. Resistance to the Colorado Potato Beetle, as provided by the Cry III (A) protein produced by a gene from B.t.t. , requires ingestion of the protein by susceptible species. Feeding is inhibited with disruption of the midgut epithelium resulting in death of the insect. Detailed information on the mode of action of B.t.t. Cry III(A) is discussed in the B.t.t. Cry III (A) registration eligibility document and will not be addressed in this document.

B. Use / Usage

Planting instructions for growers involves planting the potato seeds on no more than 80% acreage with New Leaf varieties allowing for a minimum of 20% of the potato acreage to be planted in standard varieties to maintain an adequate refuge area. There are no usage data yet since this is the first registration for this active ingredient.

C. **Risk Assessment**

The Agency's human health risk assessment for this plant-pesticide was based primarily on experience with breeding and growing agricultural plants, and preparing and consuming food from such plants. Such food contains nucleic acids, as nucleic acids are ubiquitous in nature and in the food supply. As part of this assessment, the Agency has considered the health risks to the general population, including infants and children. There is a large body of experience with infants and children consuming food containing nucleic acids however, there is no evidence that nucleic acids, as components of food, present a different level of dietary risk for infants and children than they would for the adult population. The risk assessment also included subgroups as part of the general population, (i.e., differences in diet due to the influence of culture), and allowed for consumption pattern differences of such subgroups.

The Agency believes human experience in consuming food containing nucleic acids combined with the knowledge of plant genetics, plant physiology, phytopathology, microbial ecology, ecology, biochemistry and plant breeding are the appropriate considerations in evaluating the potential risks of residues of nucleic acids that are part of a plant-pesticide. These bases of knowledge and experience were integral to the assessment of exposures and hazards associated with residues of nucleic acids that are part of a plant-pesticides

Further, information from the fields of biochemistry, microbial ecology and ecology were also used in evaluating the potential risks of nucleic acids that are part of a plant-pesticide. Nucleic acids produced in living plants are part of the metabolic cycles of plants. They are biotic and thus subject to the processes of degradation and decay that all biotic materials undergo. Biotic materials are broken down to constituent parts through the enzymatic processes of living organisms, and these constituent parts used as the building blocks to make other biotic substances. Because of these characteristics, the potential for exposures to the residues to occur, beyond direct physical exposure to the plant, is limited.

Residues of nucleic acids differ from residues of more traditional pesticides. The large body of experience with actual human dietary consumption for nucleic acids coupled

with the different exposure pattern for plant-pesticides (i.e., the living plant itself produces the pesticidal substance, and this substance is used in situ in the plant to protect against pests, rather than the pesticide being applied to the plant) and the biology of the plant are all major characteristics which distinguish plant-pesticides from traditional (and plant-pesticide residues) from traditional pesticides. Additionally, because of their biotic nature, nucleic acids (and their residues) do not resist natural processes of degradation, nor do they bioaccumulate or biomagnify in the tissues of living organisms. Also, humans ingesting them are likely to quickly degrade them and use the parts to fuel their own metabolic processes. Therefore, the potential for exposure is more limited and more circumscribed for residues of nucleic acids than for residues of traditional pesticides.

Based on the information stated above, the Agency believes that there is a reasonable certainty that no harm will result from aggregate exposure to the active ingredient Potato Leaf Roll Virus Resistance Gene. This includes all anticipated exposures for which there is reliable information

1. **Human Health Risk Assessment**

    a. **Toxicological Endpoints**

        No toxicological endpoints were identified.

    b. **Human Exposure**

        Mammalian toxicology data requirements have been satisfied via data waivers and information from the open scientific literature. Data waivers were requested for the following study: Acute Oral Toxicology. Currently, the Agency does not require any further data requirements for plant pesticides other than an In Vitro Digestion Study (required on a case by case basis). The data waivers were granted based on the long history of mammalian consumption of the entire plant virus particles in food, without causing any deleterious human health effects or any evidence of toxicity. Virus-infected plants currently are and have always been a part of both the human and domestic animal food supply and there have been no findings which indicate that plant viruses are unable to replicate in mammals or other vertebrates, thereby eliminating the possibility of human infection. More importantly, however, the tolerance exemption associated with this section 3 registration applies to that portion of

the viral genome coding for the potato leaf roll virus resistance gene and any subcomponent of the resistance gene expressed in the plant and this component alone is incapable of forming infectious particles.

c. **Risk Assessment**

The Environmental Protection Agency believes that the potential for aggregate exposure is minimal to non-existent for this active ingredient. Dietary/oral exposure is not of concern as virus infected food plants have historically been a part of the human and domestic animal food supply with no observed adverse effect to human health and infants and children upon consumption. Non-occupational exposures such as drinking water exposure is minimal to non existent for this active ingredient as the gene is expressed only within the plant tissues.

EPA has not identified any subchronic, chronic, immune, endocrine, or nondietary exposure issues as they may affect children and the general U.S. population. The Agency has considered Potato Leaf Roll Virus Resistance Gene in light of the safety factors in the Food Quality Protection Act (FQPA) of 1996 and has made a determination of reasonable certainty of no harm to the U. S. population in general, and to infants and children in particular.

2. **Ecological Risk Assessment**

a. **Ecological Toxicity Endpoints**

No toxic endpoints were identified.

b. **Ecological Exposure**

Nontarget organism data requirements were waived based on the long history of virus infected food plants as a part of the human and domestic animal food supply with no adverse or insecticidal effects having been observed.

c. **Risk Assessment**

BPPD believes that risks to aquatic organisms will be minimal to non-existent, however mitigating statements will appear on the product label.

D. **Data Gaps / Labeling Restrictions**

There are no data gaps.

II. Overview

A. **Pesticide Overview**

The following active ingredient is covered by this registration decision:

- **Common name:** Potato Leaf Roll Virus Resistance Gene (also known as orf1/orf2 gene)
- **OPP Chemical code:** 006469
- **Trade and other names:** New Leaf Plus Potatoes
- **Registrant:**

  Monsanto Company
  700 Chesterfield Parkway North
  St. Louis, Missouri 63198

B. **Use Profile**

- **Type of pesticide:** Plant - Pesticide.
- **Use Site:**N/A (potato tubers to be planted)
- **Target pests:** Potato Leaf Roll Virus, Colorado Potato Beetle
- **Formulation type:** Seed/Potato Plant.
- **Method and Rates of Application:** New Leaf 7 Plus Potato plants should be planted on no more than 80% acreage with New Leaf varieties allowing for a minimum of 20% of the potato acreage to be planted in standard varieties to maintain an adequate refuge area.
- **Insect Resistance Management:** Resistance management techniques are recommended to be employed for use of this product. The product labeling contains language which instructs the user to plant and manage refuges for susceptible insects.

C. **Estimated Usage**

None used yet since this will be the first registered product.

D. **Data Requirements**

For Potato Leaf Roll Virus Resistance Gene, the mammalian toxicology and ecological effects data requirements have been satisfied via data waivers. Product analysis data requirements are adequately satisfied. The data requirements for granting this registration under Section 3(c)(5) of the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA) have been reviewed by EPA. Based on submitted information, the Agency foresees no unreasonable adverse effects to human health and the environment from the use of this microbial pesticide and recommends an unconditional registration of this new active ingredient for the proposed uses.

E. **Regulatory History**

In May 1997, the Agency received an application from Monsanto Company to register a transformed potato plant genetically engineered to contain a gene which provides resistance from infection by the Potato Leaf Roll Virus and a protein for the control of feeding by the Colorado Potato Beetle respectively. This action involves an end-use product only. There is no technical product.

This action registers the first end-use product using the Potato Leaf Roll Virus Resistance Gene as the active ingredient.

A notice of receipt of the application for registration of Potato Leaf Roll Virus Resistance Gene (also known as orf1/orf2 gene) as a new active ingredient was published in the Federal Register on 12/9/97 (62FR64831), with a 30-day comment period. An announcement of the filing of a pesticide petition requesting an exemption from the requirement of a tolerance was published in the Federal Register on 6/25/97 (62 FR34283-34286)(FRL-5723-2). The final rule was accepted under an experimental use permit (524-EUP-87) and was published on 8/15/97 with a 60 day comment period (62FR43650-43653)(FRL-5738-3). There were no comments to any of the three publications. These notices were published under the active ingredient name Replicase Protein of Potato Leaf Roll Virus and the Genetic material necessary for its' production. An amendment for a name change was submitted to the Agency by Monsanto Company. This amendment was published on 3/17/99 under the revised name of Potato Leaf Roll Virus Resistance Gene (also known as orf1/orf2 gene). This name change does not affect the data already submitted and reviewed. The end-use product was registered on 11/18/98 and announced in the Federal Register on 3/31/99.

F. **Classification**

Potato Leaf Roll Virus Resistance Gene (also known as orf1/orf2 gene) has been classified as a plant-pesticide.

G. Food Clearances / Tolerances

A final rule was published establishing an exemption from the requirement of a tolerance for residues of the Potato Leaf Roll Virus Resistance Gene (also known as orf1/orf2 gene) in or on all food commodities when used as a transformed potato plant.

Safety factors from FQPA were evaluated. EPA has considered, among other factors, available information concerning the aggregate exposure levels of consumers (and major identifiable subgroups of consumers) to the pesticide chemical residue and to other related substances. A large portion of the potato crop produced every year is infected with the Potato Leaf Roll Virus and presumably with the PLRV genes introduced to give New Leaf 7 Plus Potatoes. Therefore, given the lack of toxicity reported with Potato Leaf Roll Virus Resistance Gene in the current food supply, a determination of reasonable certainty of no harm for the general population, as well as subgroups including infants and children, was made.

III. Science Assessment

A. Physical / Chemical Properties Assessment

All product chemistry data requirements for Potato Leaf Roll Virus Resistance Gene technical grade active ingredient are satisfied.

0. Product Identity and Mode of Action

Product Identity

Potato Leaf Roll Virus Resistance Gene (also known as orf1/orf2 gene) is the active ingredient to which this document pertains. The transformed potato contains 0.03% Potato Leaf Roll Virus Resistance gene and 0.2% B.t. CryIII(A) delta-endotoxin (section 3 registered and exempted from the requirement of a tolerance) as the active ingredients.

Mode of Action

Induction of resistance to PLRV infection by the orf1/orf2 gene is not clearly understood at present. The orf1/orf2 gene does, however, induce virus resistance by a non-toxic mode of action. These modes of action could be driven via Protein Inhibition or RNA Inhibition.

1. **Physical And Chemical Properties Assessment**

The data requirements for physical and chemical characteristics that support the registration of New Leaf Plus Potato as the end-use product of Potato Leaf Roll Virus are summarized in Table 1.

Table 1 Product chemistry data requirements

Guideline	Study	Results	MRID
151-20	Product identity;		
151-20	Manufacturing process;	Submitted data satisfy the data requirements for product identity, manufacturing process, and discussion of formation of impurities	44293801
151-22	Discussion of formulation of unintentional ingredients		
151-23	Analysis of samples	Submitted data satisfy the data requirements for analysis of samples	44293801
151-25	Certification of limits	Limits listed in the CSF are adequate	CSF
151-27	Submittal of Samples	Submitted data satisfy the data requirements for analysis of samples	44293801

B. **Human Health Assessment**

Mammalian toxicology data waivers have been submitted and adequately satisfy the requirements set forth in 40 CFR 158.740 for microbial and plant-pesticides for agricultural uses. There is a reasonable certainty that no harm will result from exposure to potato leaf roll virus resistance gene. This includes all anticipated dietary exposures and all other exposures for which there is reliable information.

0. **Toxicology Assessment**

The long history of consumption of virus-infected plants without any reports in the scientific literature of toxicity or other harm caused to the general population are sufficient to support the registration of the active ingredient potato leaf roll virus resistance gene (also known as orf1/orf2 gene).

a. **Acute Toxicity**

The acute mammalian toxicology studies that are normally seen for plant-pesticides [acute oral toxicity and in vitro digestion (not required here)] have been waived as no evidence exists to suggest that virus- infected potatoes would have a negative impact on human health upon consumption. The lack of toxicity associated with virus-infected plants to humans and other vertebrates supports the Agency's decision to grant data waivers for these studies. Plant viruses are unable to replicate in mammals or other vertebrates, thereby eliminating the possibility of human infection. Both PLRV Resistance gene and B.t.t. CryIII(A) delta-endotoxin have been exempt from the requirement of a tolerance when used in accordance with good agricultural practices as active ingredients in a plant-pesticide

Table 2 Product chemistry data requirements

Guideline	Study	Results	MRID
TIER I			
152-30	Acute Oral Toxicity	Waived	

b. **Mutagenicity and Developmental Toxicity**

Mutagenicity and immune response studies are required to support registration of a food-feed use pesticide. Developmental toxicity data are conditionally required if repeated oral exposure or long-term exposure to human females is expected. These data were waived based on the lack of mammalian toxicity of the active ingredient and the fact that potato leaf roll virus resistance gene is exempt from the requirement of a tolerance when used in accordance with good agricultural practice as a plant-pesticide.

Mammalian toxicity data submitted for New Leaf Plus Potatoes is summarized in Table 2.

c. **Subchronic Toxicity**

These data were waived based on the fact that potato leaf roll virus resistance gene is not expected to change the exposure to nucleic acids in foods and nucleic acids in foods are not known to be a source of toxicity. Additionally, potato leaf roll virus resistance gene

is exempt from the requirement of a tolerance when expressed in Russet Burbank potato plants as a result of genetic modification for the purposes of inhibition of viral replication; no residues are expected in treated crops since the entire infectious particles of potato leaf roll virus including the orf1/orf2 gene are found in the fruit, leaves and stems of most plants.

d. **Chronic Exposure and Oncogenicity Assessment**

Chronic exposure studies are conditionally required to support food or non-food uses only if the potential for adverse chronic effects are indicated based on 1) the subchronic effect levels established in tier 1 subchronic oral, inhalation, or dermal studies, 2) the pesticide use pattern, or 3) the frequency and level of repeated human exposure that expected. Oncogenicity studies are required to support non-food uses only if the active ingredient or any of its metabolites, degradation products, or impurities produce, in Tier I subchronic studies, a morphologic effect in any organ that potentially could lead to neoplastic changes. The triggers for chronic exposure and oncogenicity studies were not met.

1. **Effects on Immune and Endocrine Systems**

The Agency has no information to suggest that potato leaf roll virus resistance gene will have an effect on the immune and endocrine systems. Congress has allowed 3 years after August 3, 1996, for the Agency to implement a screening program with respect to endocrine effects.

2. **Dose Response Assessment**

No toxicological endpoints are identified.

3. **Dietary Exposure and Risk Characterization**

The use of orf1/orf2 gene mediated resistance will not result in any new dietary exposure to plant viruses. Entire infectious particles of potato leaf roll virus are found in the fruit, leaves and stems of many plants. Viruses are ubiquitous in the agricultural environment at levels higher than will be present in transgenic plants. Virus infected food plants have historically been a part of the human and domestic animal food supply with no observed

adverse effects to human health and infants and children upon consumption. EPA has considered this information and concludes that the use of this active ingredient as expressed in potato plants will not pose a dietary risk of concern under normal conditions. Moreover, there is no evidence which indicates that adverse effects due to aggregate exposure of the potato leaf roll virus resistance gene (with substances outside the food supply) through dietary, non-food oral, dermal and inhalation occurs

4. **Occupational, Residential, School and Day Care Exposure and Risk Characterization**

   a. **Occupational Exposure and Risk Characterization**

      Due to the nature of the potato leaf roll virus resistance gene produced in plants as part of a plant-pesticide, exposure through any route (i.e., dermal, inhalation) other than dietary is unlikely to occur. Physical contact with the plant or raw agricultural food from the plant may present some limited opportunity for dermal exposure. However, on a per person basis, the potential amounts involved in this exposure is negligible in comparison to exposure through the dietary route. Likewise, the occurrence of inhalation exposure of the active ingredient is negligible in comparison to potential exposure through the dietary route. In some cases, potato leaf roll resistance gene may be present in pollen, thus affording exposure to those individuals in areas exposed to wind blown pollen. However, it is unlikely that exposure to the pollen is equivalent to exposure to potato leaf roll virus resistance gene.

   b. **Residential, School and Day Care Exposure and Risk Characterization**

      No indoor residential, school or day care uses currently appear on the label. Therefore, an assumption of no risk due to lack of exposure has been made.

5. **Drinking Water Exposure and Risk Characterization**

Potential non-occupational exposures in drinking water is negligible. The potato leaf roll virus resistance gene produced in plants as part of a plan-pesticide is an integral part of the living tissue of the plant. As such, these components are subject to degradation and decay, a process which occurs fairly rapidly. The potato leaf roll virus resistance gene does not persist in the environment or bioaccumulate. The rapid turnover of these substances

(genes) in the environment limits their ability to present anything other than a very negligible exposure in drinking water drawn from either surface or groundwater sources.

6. **Acute and Chronic Dietary Risks for Sensitive Subpopulations Particularly Infants and Children**

Dietary risk from potato leaf roll virus resistance gene will be minimal to non-existent due to the nature of the active ingredient. In the absence of any toxicological endpoints, risk from the consumption of residues is not expected for both the general population and infants and children from the use of potato leaf roll virus resistance gene. The lack of toxicity associated with PLRV resistance gene adds further weight to the lack of risk from exposure

FFDCA section 408 provides that EPA shall apply an additional ten-fold margin of exposure (safety) for infants and children in the case of threshold effects to account for pre- and post-natal toxicity and a completeness of the database, unless EPA determines that a different margin of exposure (safety) will be appropriate for infants and children. Margins of exposure (safety) are often referred to as uncertainty (safety) factors. In this instance, the Agency believes there is reliable data to support the conclusion that potato leaf roll virus resistance gene is non-toxic to mammals, including infants and children, and, thus, there are no threshold effects; therefore, EPA has not used a margin of exposure (safety) approach to assess the safety of potato leaf roll virus resistance gene. As a result, the provision requiring an additional margin of safety does not apply.

7. **Aggregate Exposure from Multiple Routes Including Dermal, Oral, and Inhalation**

Aggregate exposure would primarily occur via the oral route, however the use of potato leaf roll virus resistance gene will not result in any new dietary exposure to plant viruses or nucleic acids. Entire infectious particles of potato leaf roll virus are found in the potato tuber, leaves and stems of most infected potato plants and viruses in the agricultural environment are present at higher levels than those in transgenic plants. Risks associated with dermal and inhalation exposure will be negligible in comparison to those likely to arise from dietary exposure. Therefore, based on the lack of toxicity of this active ingredient and the long documented history of safe consumption with no observed effects to human health, infants and children,

the risks (if any) anticipated from aggregate exposure are considered to be minimal.

8. **Cumulative Effects**

Potato leaf roll virus resistance gene (also known as orf1/orf2 gene) does not share any common mechanisms of toxicity with other pesticide active ingredients. There are no reported adverse effects from these use of this plant-pesticide. Further, data from the open scientific literature support a lack of mammalian toxicity/pathogenicity associated with this active ingredient. Therefore, the potential for cumulative effects with other pesticides and substances will be non-existent.

C. **Environmental Assessment**

0. **Ecological Effects Hazard Assessment**

Data waivers for ecological effects studies were requested and supported based on the use of this plant-pesticide and the long history of virus-infected food plants as part of the domestic animal food supply without any reports of adverse effects. The lack of toxicity associated with this plant pesticide supports the fact that risks to non-target species are minimal to non-existent. However, appropriate precautionary label statements under "Environmental Hazards" are presented on the product label.

Nontarget toxicity data requirements for New Leaf 7 Plus Potatoes are summarized in Table 3.

TABLE 3. Non-Target Toxicity Studies - Tier I Guideline Requirements

Guideline	Study	Results	MRID
154-16	avian acute oral	waived	
154-17	avian dietary	waived	
154-18	wild mammal testing	waived	
154-19	fish testing	waived	
154-20	freshwater aquatic testing	waived	

154-21	estuarine & marine animal testing	waived
154-22	nontarget plant studies	waived
154-23	nontarget insect studies	waived
154-24	honey bee testing	waived

1. **Environmental Fate and Ground Water Data**

The need for environmental fate and groundwater data (Tier II) was not triggered under current requirements (40 CFR Section 158.740(d)(2)(vi through xv) because of the lack of toxicity/pathogenicity associated with the active ingredient.

2. **Ecological Exposure and Risk Characterization**

A potential for exposure to nontarget insects, fish, and other wildlife is minimal to non-existent. Data from the open scientific literature indicate a lack of mammalian toxicity associated with this plant pesticide. EPA believes that the lack of toxicity/pathogenicity and mitigating label language for aquatic exposure result in minimal to non-existent risk to wildlife.

IV.

V. RISK MANAGEMENT/REGISTRATION ELIGIBILITY

A. Determination of Eligibility for Registration

Section 3(c)(5) of FIFRA provides for the registration of new active ingredients if it is determined that (A) its composition is such as to warrant the proposed claims for it; (B) its labeling and other materials required to be submitted comply with the requirements of FIFRA; (C) it will perform its intended function without unreasonable adverse effects on the environment; and (D) when used in accordance with widespread and commonly recognized practice it will not generally cause unreasonable adverse effects on the environment.

To satisfy criteria "A" above, potato leaf roll virus resistance gene (also known as orf1/orf2 gene) is not expected to cause unreasonable adverse effects when used according to label instructions. Criteria "B" is satisfied by the current label and by the data presented in this document. It is believed that this new pesticidal active ingredient will not cause any unreasonable adverse effects, is an effective plant-

pesticide for protection from infection by the potato leaf roll virus and for control of feeding by the Colorado Potato Beetle, and does provide protection as claimed satisfying Criteria "C". Criteria "D" is satisfied in that the toxicological properties (if any) of this product are far less toxic than any other conventional pesticide product currently in use.

Therefore, New Leaf Plus Potato is eligible for registration. The only use for this product is as a transgenic potato plant for planting. See use/acreage and refugee plan listed in Table 4, Appendix A.

B. Regulatory Position

0. Conditional / Unconditional Registration

All data requirements are fulfilled and EPA has unconditionally registered New Leaf Plus Potato.

1. Tolerance

Potato Leaf Roll Virus Resistance Gene (also known as *orf1/orf2* gene) is exempted from the requirement of a tolerance for residues in or on all food commodities when used as a transformed potato plant to provide protection from infection by the Potato Leaf Roll Virus (food/feed use). The final rule was signed on August 7, 1997 and published in the Federal Register on 8/15/97. This rule was published under the name Replicase Protein of Potato Leaf Roll Virus and the Genetic Material Necessary for its' production. An amendment to this rule to include a change in the name of the active ingredient to read Potato Leaf Roll Virus Resistance Gene (also known as *orf1/orf2* gene) was published on 3/17/99.

2. CODEX Harmonization

There are no Codex harmonization nor a known international tolerance exemption for potato leaf roll virus resistance gene at this time.

3. Non-food Re / Registrations

There are no non-food uses.

4. Risk Mitigation

Since there are no risk issues, risk mitigation measures are not required at this time for dietary risk, occupational and residential risk, risks to nontarget

organisms (plants and wildlife), or ground and surface water contamination for this product. The product label will, however, bear Environmental Hazards text to mitigate any potential risk to aquatic species.

5. **Endangered Species Statement**

Currently, the Agency is developing a program (The Endangered Species Protection Program) to identify all pesticides whose use may cause potential adverse impacts on endangered and threatened species and their habitats. To aid in the identification of threatened and endangered species and their habitats, several companies have formed an Endangered Species Task Force (EST) under the direction of the American Crop Protection Association (ACPA). Moreover, the EST will assist in providing species location information at the subcounty level, and particularly if an endangered species occurs in areas where pesticides would be used. This information will be useful once the Endangered Species Protection Program has been implemented.

Prior to the implementation of the Endangered Species Protection Program, the Agency will not impose specific labeling on those pesticides that pose risks to threatened and endangered species and their habitats but will defer imposing specific labeling language until implementation of the Program.

c.

D. **Labeling Rationale**

The labeling for products containing the potato leaf roll virus resistance gene (also known as orf1/orf2 gene) complies with the current pesticide labeling requirements.

0. **Human Health Hazard**

a. Worker Protection Standard

Any product whose labeling reasonably permits use in the production of an agricultural plant on any farm, forest, nursery, or greenhouse must comply with the labeling requirements of PR Notice 93-7, "Labeling Revisions required by the Worker Protection Standard (WPS), and PR Notice 93-11, "Supplemental Guidance for PR Notice 93-7, which reflect the requirements of EPA"s labeling regulations for worker protection statements (40 CFR part 156, subpart K). these labeling revisions are necessary to implement the Worker Protection Standard for Agricultural Pesticides (40 CFR part 170) and must be

completed in accordance with, and within the deadlines specified in PR Notices 93-7 and 93-11. Unless otherwise specifically directed, all statements required by PR Notices 93-7 and 93-11 are to be on the product label exactly as instructed in those Notices.

After April 21, 1994, except as provided in PR Notices 93-7 and 93-11, all products within the scope of those notices must bear WPS PR Notice complying labeling when they are distributed or sold by the primary registrant or any supplementally registered distributor.

After October 23, 1995, except as provided in PR Notices 93-7 and 93-11, all products within the scope of those notices must bear WPS PR Notice complying labeling when they are distributed or sold by any person.

The labels and labeling of all products must comply with EPA's current regulations and requirements as specified in 40 CFR 156.10 and other applicable notices. Labeling also conforms to Worker Protection Safety standards where re-entry into sprayed fields must not take place until sprays have dried unless protective clothing is employed. Agricultural worker entry is not permitted during the restricted entry interval (REI) of 0 hours for New Leaf Plus Potatoes.

b. **Non-Worker Protection Standard**

There are no non-WPS human health hazard issues.

c. **Precautionary Labeling**

The Agency has examined the toxicological data base for potato leaf roll virus resistance gene and concluded that the proposed precautionary labeling (i.e. Signal Word, Precautionary Statements and other label statements) adequately mitigates the risks associated with the proposed uses.

End-Use product Precautionary Labeling: For New Leaf[7] Plus Potatoes, "CAUTION" is the signal word on the product label.

d. **Spray Drift Advisory:** Not applicable.

1. **Environmental Hazards Labeling**

Provided the following statement is placed into the environmental hazards statement, the risk of potato leaf roll virus resistance gene is minimal to non-existent to nontarget organisms including endangered species.

End-Use Product Environmental Hazards Labeling:

"Do not contaminate water by cleaning of equipment or disposal of wastes."

2. **Application Rate**

It is the Agency's position, that the Instructional Material information attached to the product complies with those instructions provided for current and similar pesticide products. These materials are referred to on the product label and will be accompanied by the product. The Agency has not required a maximum number of applications for the active ingredient. However, instructional information for resistance management techniques using foliar insecticidal sprays are being required as follows:

Foliar application - treat 20% potato acreage (unimproved varieties) with foliar EPA approved insecticides on a as-needed basis.

E. **Labeling**

The label for the end-use product New Leaf 7 Plus Potatoes (EPA Registration Number 524-498) conforms with the labeling requirements for potato leaf roll virus resistance gene (also known as orf1/orf2 gene). Some of the essential label requirements are highlighted below:

- Product name: **New Leaf ^{R} Plus Potatoes**
- Active Ingredient: Potato Leaf Roll Virus Resistance Gene (also known as *orf1/orf2* gene). . . 0.03%
- Signal word is "CAUTION" based on the lack of toxicity of the product New Leaf R Plus Potatoes.
- The product label shall contain the following information:
    - Product Name
    - Ingredient Statement
    - Registration Number
    - "Keep Out of Reach of Children"
    - Signal Word (CAUTION)

- Environmental Hazard Statement
- Seed Storage and Disposal Statement
- Directions for Use

VI. Actions Required by Registrants

Reports of incidences of adverse effects to humans or domestic animals under FIFRA, Section 6(a)2 and incidents of hypersensitivity under 40 CFR Part 158.690(c), guideline reference number 152-16. There are no data requirements, label changes and other responses necessary for the reregistration of the end-use product since the product is being registered after November 1984 and is, therefore, not subject to reregistration. There are also no existing stocks provisions at this time.

VII. Acceptable Use Sites

Table 4. Field Planting of Tubers - Site Registration / Reregistration

New Leaf R Plus Potatoes Tubers should be planted according to variety as indicated on cultural management/instructional material guide which will accompany the tubers as indicated on the product label. Tubers should be planted on no more than 80% acreage with New Leaf varieties allowing for a minimum of 20% of the potato acreage to be planted in standard varieties to maintain an adequate refuge area.	**Official date registered:** 11/18/98