United States
Environmental Protection Agency
Office of Prevention, Pesticides and Toxic Substances
(7505P)

Pesticide Fact Sheet

Name of Chemical: **Mammalian Gonadotropin Releasing Hormone (GnRH)**

Reason for Issuance: **New Chemical**
Nonfood Use

Date Issued: **September 2009**

1. Description of Chemical

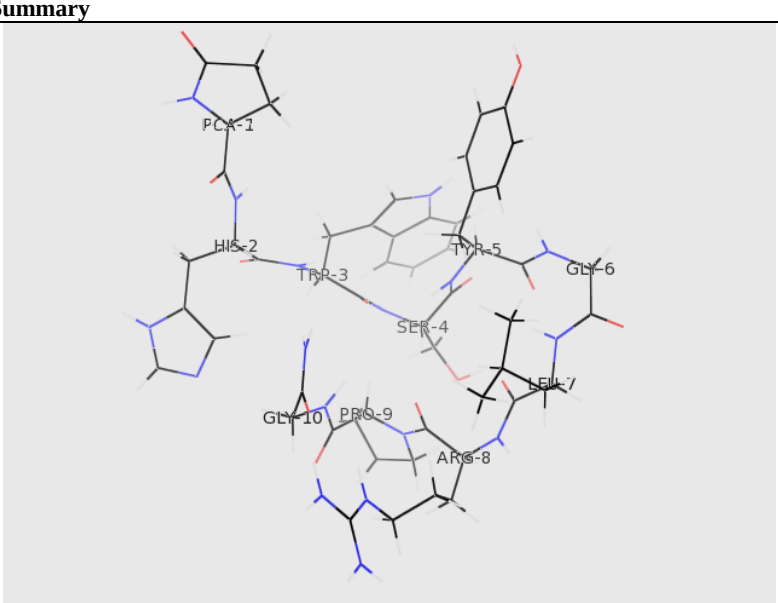
Peptide Chain:	pyroGlu1 -His2-Trp3- Ser4 -Tyr5- Gly6 -Leu7-Arg8-Pro9- G ly10NH2 [GnRH]
Common Name:	Mammalian Gonadotropin Releasing Hormone (GnRH)
EPA PC Code:	116800
Chemical Abstracts Service (CAS) Number:	9034-40-6
Chemical Class:	Sterilant/Hormone
Registration Status:	New Chemical, nonfood use
Pesticide Type:	Mammalian Contraceptive
U.S. Producer:	U.S. Department of Agriculture, APHIS, Pocatello Supply Depot 238 East Dillon Street Pocatello, ID 83201

2. Use Pattern and Formulations

Mode of Action	The active ingredient, Mammalian Gonadotropin Releasing Hormone (GnRH) is conjugated into a large protein that initiates an immune response in the animal with its own GnRH resulting in contraceptive effects for a minimum of one year.
Application Sites	GonaCon will be used to control wild white-tailed deer *Odocoileus virginianus*) populations in areas where they have become a nuisance (e.g, urban and suburban settings).
Methods of Application	The vaccine will be administered to restrained female deer using preloaded syringes with an 18 or 19 gauge stainless steel hypodermic needle intramuscularly into a large muscle mass by hand injection only. GonaCon is classified as a Restricted Use Pesticide. Use is restricted to USDA APHIS Wildlife Services or state wildlife management personnel or persons working under their authority.
Application Rate:	Female deer are injected with a single injection containing 1.0 ml of GonaCon at least two to three months prior to the onset of rut for full contraceptive effect. If multi year contraceptive effects are desired, a second vaccination may be given 30 to 60 days after the first injection or during the following year. Two formulations (basic and alternate) are proposed for registration.

3. Science Findings

Available data supporting the use and registration of Mammalian Gonadotropin Releasing Hormone including product chemistry, toxicology, efficacy, and ecological effects and environmental fate are summarized below.

Table 1. Product Chemistry Summary	
Peptide structure	
Common name	Mammalian Gonadotropin Releasing Hormone (GnRH)
CAS Reg. No.	9034-40-6
Color	white
Physical State	Active: solid: powder EU: liquid: somewhat creamy in appearance
Melting Point	N/A Waiver request
Boiling Point	Waiver request: Solid at room temperature.
Odor	Active: odorless EU: odorless
Stability to Normal and Elevated Temperatures, Metal, and Metal Ions	N/A Waiver request
Oxidation/Reduction Action	N/A Waiver request
pH	Active: NA EU: pH = 6.49
Flammability	N/A Waiver request
Explodability	N/A Waiver request
Vapor pressure	N/A Waiver request
Water Solubility	N/A Waiver request
Storage stability	N/A product's shelf life will be $\leq$ 6 months so not necessary
Corrosion Characteristics	N/A product's shelf life will be $\leq$ 6 months so not necessary

TOXICOLOGY SUMMARY

The Registrant submitted the studies listed in Tables 2, which include a number of toxicity studies. The Registrant submitted waiver requests which were granted for acute inhalation and dermal sensitization.

Acute Toxicity Data GnRH

Table 2. Acute Toxicity			
Guideline No.	**Study Type**	**Results**	**Toxicity Category***
OPPTS 870.1100	Acute Oral Rat	All test animals survived 1 mL exposure.	IV
OPPTS 870.1200	Acute Dermal Rat	All test animals survived 1 mL exposure.	IV
OPPTS 870.1300	Acute Inhalation Rat	WAIVED	IV
OPPTS 870.2400	Primary Eye Irritation Rabbit	No corneal opacity or iritis was observed. 1-hour post-instillation: 3/3 treated eyes exhibited conjunctival redness (score 1-2) and discharge (score 1). No "positive" grade irritation was noted at the 24-hour observation. Treated eyes were free of all eye irritation by 72-hours.	IV
OPPTS 870.2500	Primary Skin Irritation Rabbit	No edema was observed at any treated site. Very slight erythema (score 1) was noted at all 3/3 test sites within 1-hour post-pad removal. Irritation severity decreased thereafter. No irritation was noted at the 72-hour observation. The PDII was 0.5.	IV
OPPTS 870.2600	Dermal sensitization	WAIVED	--

- Toxicity Category IV = No precautions required

Chronic toxicity data requirements were waived. There is no human exposure from use of GonaCon, therefore no toxicity endpoints were selected because of the very limited potential worker and dietary exposure.

ECOLOGICAL EFFECTS

Waivers were submitted to fulfill required ecological effects and environmental fate guideline studies for the registration of GonaCon because of the limited potential for environmental releases. Since the product is labeled only for injection to deer by hand and the substance is expected to be rapidly metabolized in treated animals, the limited

potential risks to non-target organisms resulting from the proposed registration of GonaCon are not expected to exceed the Agency's concern levels.

The proposed registration of GonaCon is expected to have no effect on endangered or threatened species

EFFICACY

GonaCon is intended to render a vaccinated female white-tailed deer infertile for a minimum of one year following vaccination. GonaCon is not expected to affect existing pregnancies but should cause infertility of the vaccinated animal in subsequent years. If multi-year contraceptive effects are desired, a second vaccination may be given 30-60 days after the first injection or during the following year. There is a chance that some vaccinated females will become permanently sterile.

Product performance studies were conducted by APHIS's National Wildlife Research Center (NWRC) both in the field over a two year period and in a laboratory over multiple years to compare two different formulations.

The field test, initiated in 2004 used two sites consisting of fenced federal land near Silver Spring, MD. Female deer in the vaccinated group were dosed with the labeled rate of the vaccine during July and August 2004. All deer were marked with ear tags and radio telemetry collars equipped with mortality sensors. Reproductive status was assessed in the summers of 2005 and 2006 with visual inspection of the udders for signs of lactation.

Results showed 88% efficacy in the summer after vaccination with lactation evident in 3 of the 26 does vaccinated (12%). Of the control group, reproductive status was able to be determined in 13 of the 15 deer and lactation was evident in 11 of those 13 doe (85%).

In the second summer after vaccination lactation was evident in 10 of the remaining 19 vaccinated deer (53%) equating to an efficacy rate of 47%. In the control group, 10 of the 10 remaining deer (100%) had reproductive success.

The lab study results showed the alternate formulation to be more effective than the basic formulation. The alternate formulation had a 100% success rate (5/5 does remained contracepted for two years) compared to the basic formulation with a 60% success rate after two years (3/5 does contracepted). Due to economic and supply reasons however, it is necessary for the product to carry both formulations.

4. Summary of Regulatory Position and Rationale

Available data provide adequate information to support the conditional registration of GnRH as a tool for management of nuisance white-tailed deer.

White-tailed deer have been classified by EPA as a public health pest because they are a host for blacklegged ticks (*Ixodes scapularis*), more commonly known as deer ticks, which are a carrier of Lyme disease.

In many urban and suburban areas white-tailed deer populations have become over abundant and are considered a year-round nuisance causing many human-wildlife conflicts such as destruction on gardens, landscapes and golf courses as well as a cause of numerous vehicle accidents. According to a 2006 study, the National Highway Traffic Safety Administration reported that there are about 1.5 million car accidents with deer resulting in over $1 billion of damage and 150 human fatalities annually.

GonaCon is intended to be used in combination with other management techniques since it cannot alone reduce already over abundant populations.

5. Labeling Restrictions

To mitigate any risks, the following requirements have been imposed:

- Restricted -Use Pesticide classification due to non-target injection hazard.
- Application is restricted to USDA APHIS Wildlife Services or state wildlife management agency personnel or persons working under their authority only.
- Administration of vaccine is only by hand injection to mitigate any non-target or environmental risks that occur with administration with darts.
- Use restricted to only one species: white-tailed deer (*Odocoileus virginianus*).
- PPE requirements include: long sleeved shirt and long pants, gloves and shoes plus socks to mitigate occupational exposure.
- Children are not allowed in areas where product is used
- A warning that pregnant women should not be involved in handling or injecting GonaCon and that all women should be aware that accidental self-injection may cause infertility.

6. Conditional Data Requirements

Because of the unique chemical nature of GnRH additional preliminary analysis and certified limits data are necessary. The registrant must submit this data to the Agency upon completion.

Conditional data required for GonaCon consists of:

- Guideline 830.1700 Validating the method of analysis of the formulation and additional preliminary analysis
- Guideline 830.1750 Certified Limits

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DISCLAIMER: The information in this Pesticide Fact Sheet is for information only and is not to be used to satisfy data requirements for pesticide registration. The information is believed to be accurate as of the date on the document.

APPENDIX I

GLOSSARY OF TERMS AND ABBREVIATIONS

ADNT	Acute delayed neurotoxicity
a.i.	Active Ingredient
aPAD	Acute Population Adjusted Dose
ARI	Aggregate Risk Index
BCF	Bioconcentration Factor
CAS	Chemical Abstracts Service
ChE	Cholinesterase
ChEI	Cholinesterase inhibition
cPAD	Chronic Population Adjusted Dose
%CT	Percent crop treated
DAT	Days after treatment
DEEM-FCID	Dietary Exposure Evaluation Model - Food Consumption Intake Database
DNA	Deoxyribonucleic acid
DNT	Developmental neurotoxicity
DIT	Developmental immunotoxicity
DWLOC	Drinking Water Level of Comparison.
EC	Emulsifiable Concentrate Formulation
EEC	Estimated Environmental Concentration. The estimated pesticide concentration in an environment, such as a terrestrial ecosystem.
EPA	U.S. Environmental Protection Agency
FQPA	Food Quality Protection Act
GLC	Gas Liquid Chromatography
GLN	Guideline Number
LC_{50}	Median Lethal Concentration. A statistically derived concentration of a substance that can be expected to cause death in 50% of test animals. It is usually expressed as the weight of substance per weight or volume of water, air or feed, e.g., mg/l, mg/kg or ppm.
LD_{50}	Median Lethal Dose. A statistically derived single dose that can be expected to cause death in 50% of the test animals when administered by the route indicated (oral, dermal, inhalation). It is expressed as a weight of substance per unit weight of animal, e.g., mg/kg.
LOAEL	Lowest Observed Adverse Effect Level
LOAEC	Lowest Observed Adverse Effect Concentration
LOC	Level of Concern
LOD	Limit of Detection
LOQ	Limit of Quantitation
mg/kg/day	Milligram Per Kilogram Per Day
mg/L	Milligrams Per Liter
MOE	Margin of Exposure

MRID	Master Record Identification (number), EPA's system of recording and tracking studies submitted
MTD	Maximum tolerated dose
NA	Not Applicable
NOEC	No Observable Effect Concentration
NOEL	No Observed Effect Level
NOAEL	No Observed Adverse Effect Level
NOAEC	No Observed Adverse Effect Concentration
NPDES	National Pollutant Discharge Elimination System
OP	Organophosphate
OPP	EPA Office of Pesticide Programs
OPPTS	EPA Office of Prevention, Pesticides and Toxic Substances
PAD	Population Adjusted Dose
PAG	Pesticide Assessment Guideline
PAM	Pesticide Analytical Method
PHED	Pesticide Handler's Exposure Data
PHI	Preharvest Interval
ppb	Parts Per Billion
PPE	Personal Protective Equipment
ppm	Parts Per Million
PRZM/EXAMS	Tier II Surface Water Computer Model
RAC	Raw Agriculture Commodity
RBC	Red Blood Cell
RED	Reregistration Eligibility Decision
REI	Restricted Entry Interval
RfD	Reference Dose
SCI-GROW	Tier I Ground Water Computer Model
SF	Safety Factor
TGAI	Technical Grade Active Ingredient
UF	Uncertainty Factor
µg	micrograms
µg/L	Micrograms Per Liter
µL/g	Microliter per gram
USDA	United States Department of Agriculture
WPS	Worker Protection Standard

APPENDIX II

Citations Considered Part of the Data Base Supporting the Registration of GonaCon.

MRID	Citation	Receipt Date
47649600	United States Department of Agriculture's Animal and Plant Health Inspection Service (USDA APHIS) (2009) Submission of Product Chemistry, Toxicity, Efficacy and Residue Data in Support of the Application for Registration of GonaCon Immunocontraceptive Vaccine. Transmittal of 36 Studies.	22-Jan-2009
47649601	O'Hare, J.; Eisemann, J. (2008) Description of Materials Used to Produce: "GoneCon Immunocontraceptive Vaccine". Project Number: P4417. Unpublished study prepared by US Dept. of Agriculture, APHIS, WS: National Wildlife Research Center. 168 p.	22-Jan-2009
47649602	O'Hare, J.; Eisemann, J. (2008) Description of Formulation Process Used to Manufacture: "GonaCon Immunocontraceptive Vaccine". Project Number: M8546, BT016/02. Unpublished study prepared by US Dept. of Agriculture, APHIS, WS: National Wildlife Research Center. 99 p.	22-Jan-2009
47649603	O'Hare, J.; Pilon, J.; Eisemann, J. (2008) Discussion of the Formation of Impurities "GonaCon Immunocontraceptive Vaccine". Unpublished study prepared by US Dept. of Agriculture, APHIS, WS: National Wildlive Research Center. 56 p.	22-Jan-2009
47649604	O'Hare, J.; Eisemann, J.; Pilon, J. (2008) Preliminary Analysis and Certified Limits "GonaCon Immunocontraceptive Vaccine": Final Report. Unpublished study prepared by US Dept. of Agriculture, APHIS, WS: National Wildlife Research Center. 9 p.	22-Jan-2009
47649605	O'Hare, J.; Eisemann, J. (2008) Enforcement Analytical Method: "GonaCon Immunocontraceptive Vaccine". Unpublished study prepared by US Dept. of Agriculture, APHIS, WS: National Wildlife Research Center. 40 p.	22-Jan-2009
47649606	O'Hare, J.; Eisemann, J. (2007) Product Chemistry: Color, Physical State, Odor, and pH - USDA APHIS GonaCon Immunocontraceptive Vaccine (EPA Reg. No. 56228-xx): Final Report. Project Number: QA/1421. Unpublished study prepared by US Dept. of Agriculture, APHIS, WS: National Wildlife Research Center. 31 p.	22-Jan-2009
47649607	Warren, J.; Stephens, S. (2008) Stability to Normal and Elevated Temperatures, Metal, and Metal Ions: (Gonadotropin Releasing Hormone). Unpublished study prepared by US Dept. of Agriculture, APHIS, WS. 8 p.	22-Jan-2009
47649608	Warren, J.; Stephens, S. (2008) Oxidation/Reduction Chemical Incompatibility: (GonaCon Immunocontraceptive Vaccine). Unpublished study prepared by US Dept. of Agriculture, APHIS, WS. 8 p.	22-Jan-2009
47649609	Warren, J.; Stephens, S. (2008) Flammability: (GonaCon Immunocontraceptive Vaccine). Unpublished study prepared by USDA APHIS. 8 p.	22-Jan-2009

47649610	Warren, J.; Stephens, S. (2008) Explodability: (GonaCon Immunocontraceptive Vaccine). Unpublished study prepared by USDA APHIS. 4 p.	22-Jan-2009
47649611	Warren, J.; Stephens, S. (2008) Miscibility: (GonaCon Immunocontraceptive Vaccine). Unpublished study prepared by USDA APHIS. 8 p.	22-Jan-2009
47649612	Warren, J.; Stephens, S. (2008) Corrosion Characteristics: (GonaCon Immunocontraceptive Vaccine). Unpublished study prepared by USDA APHIS. 8 p.	22-Jan-2009
47649613	Warren, J.; Stephens, S. (2008) Dielectric Breakdown Voltage: (GonaCon Immunocontraceptive Vaccine). Unpublished study prepared by USDA APHIS. 8 p.	22-Jan-2009
47649614	Warren, J.; Stephens, S. (2008) UV/Visible Absorption: (GonaCon Immunocontraceptive). Unpublished study prepared by USDA APHIS. 8 p.	22-Jan-2009
47649615	Warren, J.; Stephens, S. (2008) Viscosity: (GonaCon Immunocontraceptive Vaccine). Unpublished study prepared by USDA APHIS. 8 p.	22-Jan-2009
47649616	Warren, J.; Stephens, S. (2008) Melting Point: (GonaCon Immunocontraceptive Vaccine). Unpublished study prepared by USDA APHIS. 8 p.	22-Jan-2009
47649617	Warren, J.; Stephens, S. (2008) Boiling Point: (GonoCon Immunocontraceptive Vaccine). Unpublished study prepared by USDA APHIS. 4 p.	22-Jan-2009
47649618	Warren, J.; Stephens, S. (2008) Density/Relative Density/Bulk Density: (GonaCon Immunocontraceptive Vaccine). Unpublished study prepared by USDA APHIS. 4 p.	22-Jan-2009
47649619	Warren, J.; Stephens, S. (2008) Dissociation Constant in Water: (GonaCon Immunocontraceptive Vaccine). Unpublished study prepared by USDA APHIS. 8 p.	22-Jan-2009
47649620	Warren, J.; Stephens, S. (2008) Octanol/Water Partition Coefficient: (GonaCon Immunocontraceptive Vaccine). Unpublished study prepared by USDA APHIS. 8 p.	22-Jan-2009
47649621	Warren, J.; Stephens, S. (2008) Water Solubility: (GonaCon Immunocontraceptive Vaccine). Unpublished study prepared by USDA APHIS. 8 p.	22-Jan-2009
47649622	Warren, J.; Stephens, S. (2008) Vapour Pressure: (GonaCon Immunocontraceptive Vaccine). Unpublished study prepared by USDA APHIS. 8 p.	22-Jan-2009
47649623	Eisemann, J.; O'Hare, J. (2008) Chemical Identity: "GonaCon Immunocontraceptive Vaccine". Unpublished study prepared by US Dept. of Agriculture, APHIS, WS: Natiional Wildlife Research Center. 27 p.	22-Jan-2009
47649624	Eisemann, J.; O'Hare, J. (2008) Direction for Use: GonaCon Immunocontraceptive Vaccine. Unpublished study prepared by US Dept. of Agriculture, APHIS, WS: National Research Center. 12 p.	22-Jan-2009
47649625	Lowe, C. (2008) GonaCon Immunocontraceptive Vaccine: Acute Oral	22-Jan-

	Toxicity - Limit Dose Procedure in Rats. Project Number: P320/USDA, 23211. Unpublished study prepared by Product Safety Laboratories. 28 p.	2009
47649626	Lowe, C. (2008) GonaCon Immunocontraceptive Vaccine: Acute Dermal Toxicity - Limit Dose Procedure in Rats. Project Number: 23212, P322/USDA. Unpublished study prepared by Product Safety Laboratories. 28 p.	22-Jan-2009
47649627	O'Hare, J.; Eisemann, J.; Stephens, S. (2008) Acute Inhalation Toxicity: (GonaCon Immunocontraceptive Vaccine). Unpublished study prepared by USDA APHIS. 4 p.	22-Jan-2009
47649628	Lowe, C. (2007) GonaCon Immunocontraceptive Vaccine: Primary Eye Irritation Study in Rabbits. Project Number: P324, 22806. Unpublished study prepared by Product Safety Laboratories. 29 p.	22-Jan-2009
47649629	Lowe, C. (2008) GonaCon Immunocontraceptive Vaccine: Primary Skin Irritation Study in Rabbits. Project Number: P326, 22807. Unpublished study prepared by Product Safety Laboratories. 27 p.	22-Jan-2009
47649630	O'Hare, J.; Eisemann, J.; Stephens, S. (2008) Dermal Sensitization: (GonaCon Immunocontraceptive Vaccine). Unpublished study prepared by USDA APHIS. 4 p.	22-Jan-2009
47649631	O'Hare, J.; Eisemann, J.; Stephens, S. (2008) Chronic Dietary Toxicity: (GonaCon Immunocontraceptive Vaccine). Unpublished study prepared by USDA APHIS. 4 p.	22-Jan-2009
47649632	O'Hare, J.; Eisemann, J.; Stephens, S. (2008) Gene Mutation: (GonaCon Immunocontraceptive Vaccine): (Human). Unpublished study prepared by USDA APHIS. 4 p.	22-Jan-2009
47649633	O'Hare, J.; Eisemann, J.; Stephens, S. (2008) Stuctural Chromosomal Aberration: (GonaCon Immunocontraceptive Vaccine): (Human). Unpublished study prepared by USDA APHIS. 4 p.	22-Jan-2009
47649634	O'Hare, J.; Eisemann, J.; Stephens, S. (2008) Other Genotoxic Effects: (GonaCon Immunocontraceptive Vaccine): (Human). Unpublished study prepared by USDA APHIS. 4 p.	22-Jan-2009
47649635	O'Hare, J.; Eisemann, J.; Stephens, S. (2008) Acute Delayed Neurotoxicity: (GonaCon Immunocontraceptive Vaccine): (Hen). Unpublished study prepared by USDA APHIS. 4 p.	22-Jan-2009
47649636	Gionfriddo, J.; Eisemann, J.; O'Hare, J. (2008) Product Performance: Field Test of a Single-Injection of GonaCon Immunocontraceptive Vaccine In Female White-Tailed Deer. Project Number: QA/1112. Unpublished study prepared by US Dept. of Agriculture, APHIS, WS: National Wildlife Research Center. 31 p.	22-Jan-2009