

NOTICE

Synthetic Porcine GHRH-encoding Plasmid

in the product:

LIFETIDE SW 5 INJECTABLE PLASMID ENCODING PORCINE GHRH

The Australian Pesticides and Veterinary Medicines Authority (APVMA) has before it an application from VGX Animal Health Inc for registration of a new product containing the new active constituent *Synthetic Porcine Growth Hormone Releasing Hormone (GHRH)-encoding Plasmid* ('the active constituent'). The product is LIFETIDE SW 5 INJECTABLE PLASMID ENCODING PORCINE GHRH ('the product'). The product is for use in sows.

In accordance with sections 12 and 13 of the Agvet Code, the APVMA invites any person to submit a relevant written submission as to whether the APVMA should grant the application for approval of the active constituent and registration of the product. Submissions should state the grounds on which they are based. Such grounds should relate only to matters outlined below that the APVMA is required to take into account in deciding whether to grant the application. The APVMA must receive comments within 28 days of the date of this notice.

Particulars of the Application

Proposed product name:	LIFETIDE SW 5 INJECTABLE PLASMID ENCODING PORCINE GHRH
Applicant company:	VGX Animal Health Inc
Name of active constituent:	<i>Synthetic Porcine GHRH-encoding Plasmid</i>
Signal heading:	Schedule 4 Prescription Animal Remedy
Statement of claims:	For use in sows to increase the number of piglets weaned
Pack sizes:	2mL uniject syringe; 10, 20, 50, 100mL glass ; and 10, 20mL PETG; multi-dose vials
Withholding period:	Nil

Summary of the APVMA's evaluation of *Synthetic Porcine GHRH-encoding Plasmid* in LIFETIDE SW 5 INJECTABLE PLASMID ENCODING PORCINE GHRH in accordance with Section 14(3)(e) and (f) of the Agricultural and Veterinary Chemicals Code (the 'Agvet Code'), scheduled to the Agricultural and Veterinary Chemicals Code Act 1994

The APVMA has evaluated the application and in its assessment in relation to human and environmental safety under section 14(3)(e) of the Agvet Code, proposes to determine that:

- (i) The APVMA is satisfied that the proposed use of the active constituent in the product would not be an undue hazard to the safety of people exposed to it during its handling and use.

The Office of Chemical Safety (OCS) in the Commonwealth Department of Health and Aging assessed the human toxicological aspects of this application. There are no objections on toxicological grounds to the approval of the active, a synthetic DNA

expression cassette encoding for porcine growth hormone-releasing hormone (GHRH), manufactured by VGX Animal Health Inc., 2700 Research Forest Drive, Suite 180, The Woodlands TX 77381 USA..

There are no OHS or toxicological objections to the registration of the product containing 2.5mg/mL of the active.. The product will be formulated by VGX Animal Health Inc., 2700 Research Forest Drive, Suite 180, The Woodlands TX 77381 USA..

OCS advised the APVMA that use of the product would not be an undue hazard to the safety of people due to the end use of the product and therefore no safety directions were recommended. OCS advised that no warning or general safety precautionary statements are required.

The OCS advised that with respect to public health standards no ADI or ARfD has been established. Based on the absence of likely residues, no ADI or ARfD is required. Based on the level of hazard and intended use of synthetic DNA expression cassette encoding for porcine growth hormone-releasing hormone (GHRH), the NDPSC at its 49th meeting on 20-22 February 2007 confirmed the schedule 4 prescription animal remedy status noting the need for veterinary supervision of the use of the product

The APVMA accepts the findings and recommendations of OCS on this criterion.

- (ii) The APVMA is satisfied that the proposed use of the active constituent in the product will not be an undue hazard to the safety of people using anything containing its residues.

The product is used as a once in a lifetime treatment for sows of breeding age. No ADI or ARfD has been established and is not required. The Veterinary Residues Section advises that GHRH is a naturally occurring compound which would not be detectable in tissues. An entry in the MRL Standard Table 5 is therefore appropriate. The APVMA accepts the findings and recommendations of OCS on this criterion.

- (iii) The APVMA is satisfied that the proposed use of the active constituent in the product is not likely to be harmful to human beings if used according to the product label directions.

The product is injected intramuscularly and following electroporation, enters skeletal muscle cells at the injection site and resides within the muscle cell. Treated muscle cells produce GHRH at physiological concentrations. The GHRH in turn induces the sow to produce and secrete endogenous growth hormone under the control of normal physiological feedback mechanisms

The National Drugs and Poisons Scheduling Committee (NDPSC) has examined the active constituent and placed it in Schedule 4 Prescription Animal Remedy of the Standard for the Uniform Scheduling of Drugs and Poisons (SUSDP). The appropriate Signal Heading is on the product label.

The OCS has not recommended First Aid and Safety Directions for the product. The product is to be presented in a 2mL single dose Uniject disposable injection device made of polypropylene with a polyethylene inner lining supplied by Becton Dickinson. It will also be presented in a borosilicate glass multi-dose vial with a Teflon-coated butyl stopper and a polyethylene terephthalate G copolymer (PETG) multidose vial with a Teflon-coated butyl stopper.

The APVMA accepts the findings and recommendations of OCS on this criterion.

- (iv) The APVMA is satisfied that the proposed use of the active constituent in the product in pigs is not likely to have an unintended effect that is harmful to animals, plants or the environment. The active constituent is a synthetic porcine GHRH-encoding plasmid which causes the production of a naturally occurring hormone. When used as directed on the label, the Department of the Environment and Water Resources (DEW) noted the lack of adverse effects and low risk to the environment associated with the pattern of use.

The DEW recommended that an MSDS should be provided for the product, the label should include disposal instructions, and that Kanamycin C or related antibiotics for which the kanamycin resistance gene confers resistance should not be administered to animals treated with the product within 7 days of treatment. The Department concluded that providing these conditions are included, the proposal is acceptable and recommended that the APVMA be satisfied that the proposed release will not lead to an unintended effect that is harmful to animals, plants or things, or to the environment.

The APVMA accepts the findings and recommendations of the DEW on this criterion

- (v) The APVMA is satisfied that the proposed use of the active constituent in the product would not adversely affect trade between Australia and places outside Australia. The peak industry body, Australian Pork Limited (APL) advised that it sees no trade risk associated with the registration and use of the product as proposed. The APVMA accepts the advice provided by APL.

In relation to its assessment of efficacy under section 14(3)(f), the APVMA proposes to determine that:

The APVMA is satisfied the data from trials support the efficacy of the product and adequately demonstrate that under local conditions this product is effective for the proposed use. It is clear that intercurrent disease and farrowing house procedures may confound the effectiveness of the product and so it is important that the product be used under veterinary direction so that only appropriate healthy sows under best practice husbandry conditions are treated. Appropriate label amendments have been made.

Written submissions on the APVMA's proposal to grant the application for registration should be addressed to:

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