

DELETION OF EXON 7 OF CD163 GENE IN DOMESTIC PIGS**Genus plc**

Deletion of exon 7 of *CD163* gene in domestic pigs

A heritable intentional genomic alteration (IGA).

1. DESCRIPTION**1.1 Product Identification**

Deletion of exon 7 of *CD163* gene¹ (abbreviated *CD163*^{ΔE7}) in domestic pigs (*Sus scrofa domestica*). Breeding lines containing one copy (heterozygous) or two copies (homozygous) of *CD163*^{ΔE7} may be identified with the registered tradename “EverThrive™ PRP”. However, only pigs carrying two copies of *CD163*^{ΔE7} (homozygous) are intended to be resistant to Porcine Reproductive and Respiratory Syndrome Virus (PRRSV).

1.2 Product Claim

Deletion of exon 7 of the *CD163* gene in domestic pigs (*Sus scrofa domestica*) is intended to confer resistance to porcine reproductive and respiratory syndrome virus (PRRSV) in homozygous pigs. Pigs carrying one or two copies of *CD163*^{ΔE7}, and their offspring, are intended for breeding or to be used as sources of food.

1.3 Uses

Pigs bearing this label are *CD163*^{ΔE7} heterozygous and are not resistant to PRRSV.

Resistance to PRRSV in the progeny of this pig (and from semen derived from this pig) is affected by the genetic background of the other parent pig it is bred to:

- If the other parent is *CD163*^{ΔE7} homozygous (two copies), approximately one half of the progeny will be resistant to PRRSV.
- If the other parent is *CD163*^{ΔE7} heterozygous (one copy), approximately one in four of the progeny will be resistant to PRRSV.
- If the other parent has no *CD163*^{ΔE7}, none of the progeny will be resistant to PRRSV.

2. WARNINGS AND PRECAUTIONS

Deletion of exon 7 of the *CD163* gene is a recessive genetic trait and only confers resistance to PRRSV in homozygous pigs (two copies). **Pigs bearing this label are *CD163*^{ΔE7} heterozygous and are not resistant to PRRSV. Pigs bearing this label will produce offspring that may or may not be resistant to PRRSV. See 1.3 Uses for additional information.**

3. EFFECTIVENESS

In six live animal viral challenge studies, *CD163*^{ΔE7} homozygous pigs of multiple consecutive generations demonstrated resistance to infection following inoculation with one of seven PRRSV Type II isolates and two PRRSV Type I isolates. In these controlled studies consisting of 101 *CD163*^{ΔE7} homozygous pigs and 108 age-matched controls (*CD163*^{ΔE7} heterozygous pigs and pigs without a *CD163* alteration), resistance to PRRSV infection was determined by demonstrating undetectable PRRSV RNA in serum samples (via PCR) and undetectable PRRSV antibody seroconversion (by ELISA) 21 days following viral inoculation. All *CD163*^{ΔE7} homozygous pigs were resistant to infection following inoculation with one of seven PRRSV Type II isolates and two PRRSV Type I isolates listed in Table 1, whereas no control pigs demonstrated resistance.

¹Chromosome 5, SSC5:63322964-63323378, based upon the Sscrofa11.1 (GCA_000003025.6) genome assembly.

Table 1. Live Animal Viral Challenge Study Results Organized by PRRSV Inoculant

PRRSV Type and Lineage (if applicable)	PRRSV Inoculant and RFLP* (if applicable)	Number of CD163^{ΔE7} Homozygous IGA Animals	Success Rate (%)** in CD163^{ΔE7} Homozygous Animals	Number of Control Animals	Success Rate (%)** in Control Animals
Type II, L8	NVSL97-7895	23	100	26	0
Type II, L1C	UIL21-0712 (RFLP 1-4-4)	21	100	16	0
Type II, L1H	USA/NE/2634-1/2022 (RFLP 1-8-4)	5	100	5	0
Type II, L1A	USA/IN/65239-GA/2014 (RFLP 1-7-4)	5	100	5	0
Type II, L1E	USA/OK/2791-12/2022 (RFLP 1-4-2)	5	100	5	0
Type II, L1D	MLV vaccine (RFLP 1-8-4)	5	100	5	0
Type II, L5	USA/IL/23295-GA-2022 (RFLP 2-5-2)	5	100	5	0
Type I	SD13-15	22	100	27	0
Type I	SD01-08	10	100	14	0

* RFLP = Restriction Fragment Length Polymorphism, a commonly used way of classifying PRRSV strains.

** Success rate is the proportion of animals with undetectable PRRSV RNA in serum samples and undetectable PRRSV antibody seroconversion on study day 21.

In two studies, two out of twenty-six CD163^{ΔE7} homozygous pigs demonstrated resistance following inoculation with a PRRSV Type II – KS06 inoculant (Table 2). The clinical relevance of the reported lack of resistance of CD163^{ΔE7} homozygous pigs to the KS06 isolate is undetermined; this isolate and the lineage to which it is classified were not reported in the commercial swine population of the United States at an appreciable level at the time of evaluation (2022-2023).

Table 2. Live Animal Viral Challenge Study Results Following PRRSV Type II – KS06 Inoculation

PRRSV Type and Lineage	PRRSV Inoculant	Number of CD163^{ΔE7} Homozygous IGA Animals	Success Rate (%)* in CD163^{ΔE7} Homozygous Animals	Number of Control Animals	Success Rate (%)* in Control Animals
Type II, L6	KS06-72109	26	8	22	0

* Success rate is the proportion of animals with undetectable PRRSV RNA in serum samples and undetectable PRRSV antibody seroconversion on study day 21.

4. TARGET ANIMAL SAFETY

In controlled farm studies, pigs containing two copies (homozygous) or one copy (heterozygous) of CD163^{ΔE7} showed no significant differences from unedited (null) pigs for most phenotypic characteristics observed across the lifecycle of the pigs. Differences observed between groups in the studies were not clinically significant and were consistent with

reported ranges for commercial pigs.

Tables 3-4 summarize the results of the observational studies on pigs of Genus PIC elite breeding line L03. Similar data were collected for three additional breeding lines (L02, L65, and L800), demonstrating consistent safety outcomes across all lines studied.

Table 3. Phenotypic Characterization Across Life Stages

Least squares mean (LS Mean) and tests of significance among homozygous ($CD163^{\Delta E7/\Delta E7}$), heterozygous edited ($CD163^{\Delta E7/+}$), and unedited (null, $CD163^{+/+}$) pigs for phenotypic characteristics across the lifecycle of the pigs. N (number of animals observed); BWT (individual piglet birth weight, kg); TEAT (total teat count); WT140 (individual body weight of pig at 140 days of age, kg); LDG (lifetime daily gain, g per day); BF (ultrasound predicted 10th rib backfat depth, mm); LD (ultrasound predicted 10th rib loin depth, mm); *p < 0.05. **p < 0.01.

	$CD163^{\Delta E7/\Delta E7}$		$CD163^{\Delta E7/+}$		$CD163^{+/+}$	
Trait	N	LS Mean	N	LS Mean	N	LS Mean
Early Life Traits						
BWT	121	1.30	298	1.23	138	1.26
TEAT	121	15.91	298	16.16	138	15.97
Finishing Traits						
WT140	55	93.17	58	88.41	55	88.77
LDG	55	636.96	58	614.38	55	611.83
BF	55	8.98	58	10.17**	55	9.99*
LD	55	63.54	58	64.60	55	65.09

Table 4. Female Reproductive Traits

Least squares mean (LS Mean) and tests of significance among homozygous ($CD163^{\Delta E7/\Delta E7}$), heterozygous edited ($CD163^{\Delta E7/+}$), and unedited (null, $CD163^{+/+}$) pigs for female reproductive traits. N (number of litters); GL (gestation length, days); TNB (total number of piglets born); NBA (number of piglets born alive per litter); NBD (number of piglets born dead per litter); MUM (number of mummified piglets per litter). No differences were significant at the p < 0.05 level.

	$CD163^{\Delta E7/\Delta E7}$		$CD163^{\Delta E7/+}$		$CD163^{+/+}$	
Trait	N	LS Mean	N	LS Mean	N	LS Mean
GL	6	116.2	6	116.5	6	116.8
TNB	6	12.7	6	12.7	6	13.3
NBA	6	11.8	6	11.7	6	13.0
NBD	6	0.8	6	1.0	6	0.3
MUM	6	0.2	6	0.0	6	0.0

In these studies, morbidity and mortality rates were calculated for each group at various life stages (pre-weaning, nursery, finishing, and reproductive). No clinically significant differences were observed between groups. Morbidity and mortality rates for all groups were consistent with reported ranges for commercial pigs.

Separately, larger populations of pigs were evaluated for morbidity and mortality. **Table 5** shows summaries of morbidity and mortality data collected from a larger population of pigs that were homozygous $CD163^{\Delta E7}$ pigs.

Table 5. Mortality and morbidity rates of homozygous CD163^{ΔE7} pigs under normal Genus PIC production practices.

	Percentage (Mean ± SD)
Mortality*	
Adult breeding herd	0.2% ± 0.2%
Piglets, pre-weaning	5.0% ± 1.3%
Piglets, post-weaning	0.7% ± 0.6%
Morbidity**	
Adult breeding herd	0.8% ± 0.3%
Piglets, pre-weaning	12.5% ± 10.8%
Piglets, post-weaning	0.1% ± 0.1%

* Mortality was calculated as the number of mortality events (animals dead or culled for health reasons) in the given sub-population in one week relative to the total number of pigs from the sub-population in the same week, taken from farm-level data across two farms (July to December 2024).

** Morbidity was calculated as the number of morbidity events (animals treated for a morbidity) in the given sub-population in one week relative to the total number of pigs from the sub-population in the same week, taken from farm-level data across two farms (October to December 2024).

5. CONTACT INFORMATION

To report suspected adverse events or for technical assistance, contact Customer Support at 800-325-3398 or www.pic.com.

For additional information about adverse experience reporting, contact FDA at 1.888.FDA.VETS or www.fda.gov/reportanimalae.

6. NAME AND PLACE OF BUSINESS

Produced and distributed by Genus plc and PIC, its wholly owned U.S. subsidiary.

Genus plc
Matrix House Basing View
Basingstoke, Hampshire RG21 4DZ
United Kingdom

PIC
100 Bluegrass Commons Blvd, Suite #2200
Hendersonville, TN 37075

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Deletion of Exon 7 of CD163 Gene in Domestic Pigs				
Deletion of exon 7 of <i>CD163</i> gene (abbreviated CD163 ^{ΔE7}) in domestic pigs (<i>Sus scrofa domesticus</i>).				
Product Information				
Product Type	IGA	Item Code (Source)	NDC not yet assigned	
Route of Administration	NA			
Active Ingredient/Active Moiety				
Ingredient Name		Basis of Strength	Strength	
Deletion of exon 7 of <i>CD163</i> gene in domestic pigs (<i>Sus scrofa domesticus</i>). UNII: G2FPY6HLB3		One copy of CD163 ^{ΔE7} (heterozygous) in domestic pig.	NA	
Packaging				
Item Code	Package Description	Marketing Start Date	Marketing End Date	
NDC not yet assigned	One pig.			
Marketing Information				
Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date	
NADA	N-141-609			
Labeler – Genus plc				
Registrant – Genus plc				
Establishments				
Name		Address	ID/FEI	Business Operations
PIC USA Inc		Adolphus, KY	3010562164	Pig production
PIC USA Inc		Long Prairie, MN	3030563367	Pig production
ABS Global		Waunakee, WI	3015105972	Genomics laboratory

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