

GALSAFE- ppl657 rdna construct in domestic pigs not applicable Revivacor Inc.

pPL657 rDNA construct in the GGTA1 gene in domestic pigs

1. PRODUCT IDENTIFICATION

pPL657 rDNA construct in the glycoprotein galactosyltransferase alpha-1,3 gene (GGTA1) in the hemizygous and homozygous GalSafe®¹ lineage of domestic pigs (*Sus scrofa domesticus*) resulting in undetectable endogenous galactose-alpha-1,3-galactose sugar residues on biological derivatives of the homozygous GalSafe® lineage that are intended to be used as sources of food or human therapeutics including excipients, devices, drugs, or biological products.

1 GalSafe® is the registered tradename for Revivacor's lineage of pigs and is not itself subject to FDA approval. Rather, the regulated article subject to FDA approval is the intentional genomic alteration (pPL657 rDNA construct), which is contained in the GalSafe® lineage of pigs.

2. WARNINGS AND PRECAUTIONS

2. Food Safety Warnings:

a. To mitigate the potential development of bacterial resistance to aminoglycoside antimicrobial drugs, GalSafe® pigs should not be treated with an aminoglycoside.

b. Other Warnings:

The GalSafe® lineage must only be housed in physically contained facilities specified in the approved application.

To report suspected adverse events or request other technical assistance, please contact Customer Support at 540-961-5559 or www.revivacor.com. For additional information about adverse drug experience reporting, contact FDA at 1.888.FDA.VETS or www.fda.gov/reportanimalae.

3. TARGET ANIMAL SAFETY

Data from the GalSafe® lineage demonstrated a lack of adverse effects for the pPL657 rDNA construct in the GalSafe® pigs vs. comparator pigs without an intentional genomic alteration (IGA).

With respect to reproductive outcomes, litter characteristics of GalSafe® pigs were evaluated on a quarterly basis using data collected during 2012-2018. Quarterly means, with standard deviations, and ranges are provided in Table 1 below:

Table 1. Summary statistics for litter characteristics of pigs in the GalSafe® herd based on the summary of quarterly values during 2012-2018 (101 litters and 656 piglets born).

Observation	Mean	Standard Deviation	Minimum	Maximum
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Total Piglets Born/Litter (n)	8.1	2.8	3.0	16.0
Live Piglets at Birth/Litter (n)	7.4	2.9	2.0	16.0
Mortality at Birth/Litter (n)	0.8	0.7	0.0	3.0
Pre-Weaning Mortality/Litter (n)	1.9	1.1	0.0	4.0
Weaned Piglets/Litter (n)	5.4	2.8	2.0	13.0
Birth Weight/Piglet (lb.)	2.5	0.4	1.9	3.6
Mortality at Birth (%)	10.0	10.0	0.0	35.0
Pre-Weaning Mortality (%)	25.0	14.0	0.0	56.0

Overall morbidity and mortality for post-weaned (growing and breeding populations) GalSafe® pigs were evaluated on a quarterly basis using data collected during 2012-2018. Quarterly means, with standard deviations, and ranges are provided in Table 2 below:

Table 2. Summary statistics for overall morbidity and mortality of post-weaned (growing and breeding populations) GalSafe® pigs based on the summary of quarterly values (2012-2018).

	Observation	Mean	Standard Deviation	Minimum	Maximum
Mortality	Number of pigs/Quarter (n)	0.7	1.1	0.0	4.0
	%	1.4	2.0	0.0	6.7
	Number of pigs/Quarter (n)	6.6	4.1	1.0	19.0
Morbidity ^a	%	15.3	9.8	2.6	42.9

^aoverall morbidity based on recorded therapy (Rx) events for health observations in systems/categories such as the following: reproductive, lameness (hoof, limbs), respiratory, gastrointestinal, skin/integument, or central nervous system

In a study to compare physiological endpoints in GalSafe® pigs vs. comparator pigs (comparators) without an intentional genomic alteration (IGA), blood samples were collected for evaluations. No differences between GalSafe® and comparators were evident based on the following evaluations: serology, CBC (complete blood count) and comprehensive blood chemistry. Values were within expected physiological ranges.

4. EFFECTIVENESS

Multiple generations of the GalSafe® line have demonstrated genetic consistency as established through genetic tests for the presence of the pPL657 rDNA construct, pPL657 rDNA sequence fidelity and pPL657 rDNA construct integration site consistency. For multiple consecutive generations, phenotypic consistency has been established based on the undetectable levels of galactose-alpha-1,3-galactose sugar residues on biological derivatives of homozygous GalSafe® pigs.

Produced by:
Revivacor, Inc., wholly owned subsidiary of
United Therapeutics
1700 Kraft Dr, Suite 2400

Blacksburg, VA 24060 USA

Customer Support: 540-961-5559 www.revivicor.com

Approved by FDA under NADA #141-542

***pPL657* rDNA CONSTRUCT IN DOMESTIC PIGS**
Revivicor, Inc., wholly owned subsidiary of United Therapeutics

Intentional genomic alteration (heritable *pPL657* rDNA construct) in domestic pigs.

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GALSAFE

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Product Information

Product Type		Item Code (Source)	NDC:86134-001
Route of Administration	NOT APPLICABLE		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
pPL657 rDNA construct in the GGTA1 gene in domestic pigs (UNII: JUB9QR42SC) (pPL657 rDNA construct in the GGTA1 gene in domestic pigs - UNII:JUB9QR42SC)	pPL657 rDNA construct in the GGTA1 gene in domestic pigs	1 [arb'U] in 1 [arb'U]

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:86134-001-01	1 [arb'U] in 1 NOT APPLICABLE		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NADA	NADA141542	01/04/2021	

