

PERSPECTIVES IN ANIMAL BIOTECHNOLOGY

GENE EDITED PRRS-RESISTANT PIGS

Clint Nesbitt

Global Director, Regulatory & External Affairs

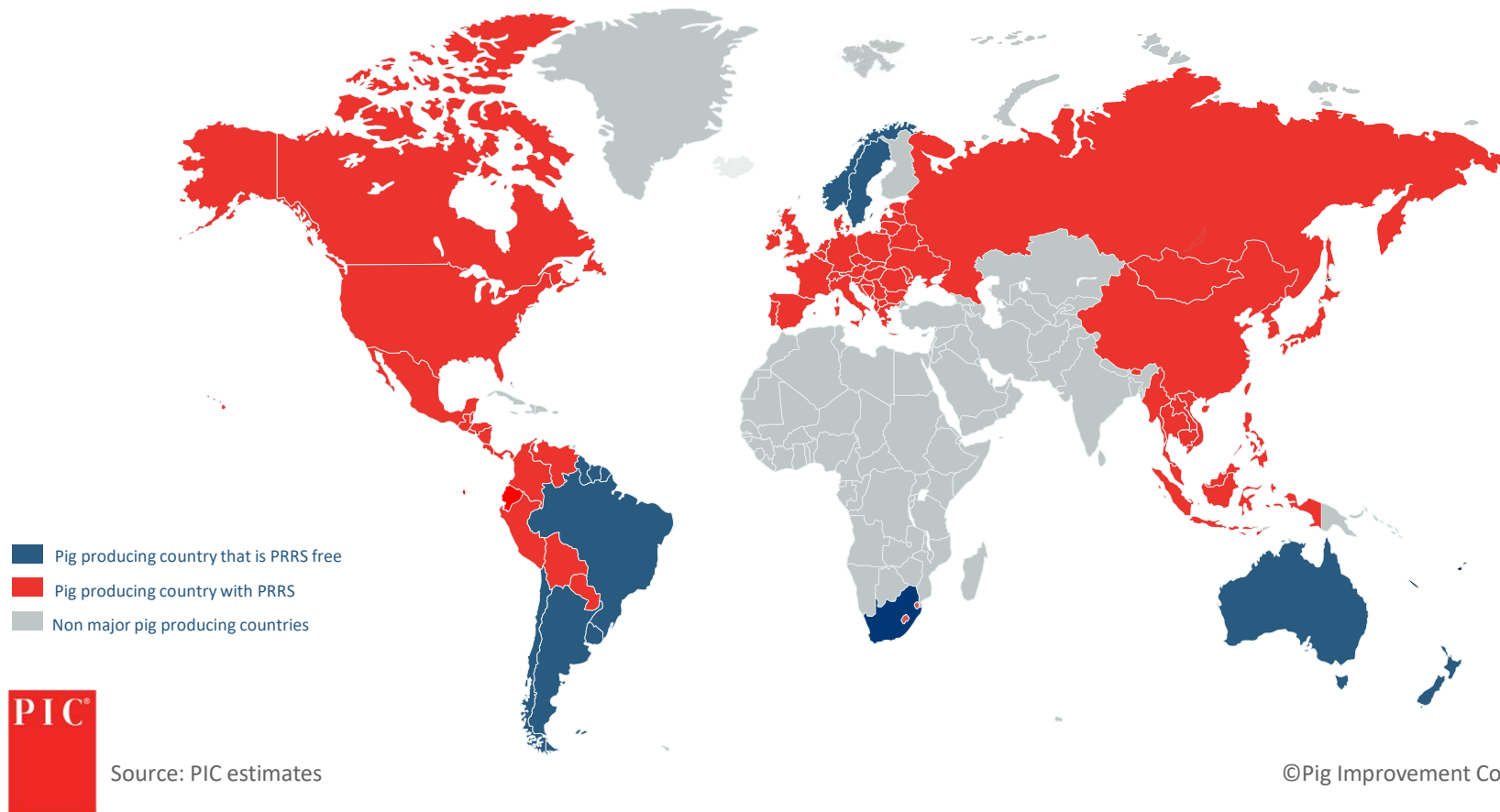
ISBR 2025

November 4, 2025



PRRS is a global problem for pork producers

Endemic in most major pork producing countries



The Impact of PRRS

Throughout the pork value chain



Impact on Growing Pigs

- Fever
- Respiratory challenges
- Impeded growth
- Poor feed conversion rate
- Increased post weaning mortality



“Porcine reproductive and respiratory syndrome caused an estimated \$1.2 billion per year in lost production in the U.S. pork industry from 2016 to 2020, an 80% increase from a decade earlier.”

**National
Hog Farmer**



PRRS prevalence in finishing pigs is amplified due to additional lateral infections of pigs that were PRRS free at the time of weaning

Impact on Breeding Pigs

- Fever
- Decrease in conception
- Increase in sow mortality
- Increase in premature birthing
- Increased post weaning mortality



“It demoralizes our teams at all levels, from the ownership to the newest technicians on the farm”

PORK



PRRS has immunosuppressive characteristics resulting in additional antibiotic use subject to co-infections



Demonstration of PRRS Resistance

nature
biotechnology

 University of Missouri



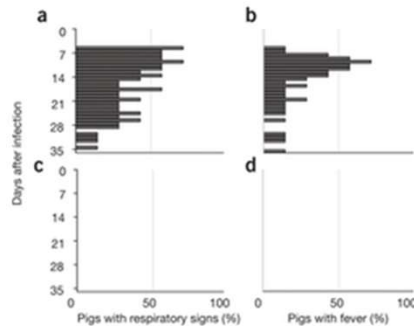
Gene-edited pigs are protected from porcine reproductive and respiratory syndrome virus

To the Editor:

Porcine reproductive and respiratory syndrome (PRRS) is the most economically important disease of swine in North America, Europe and Asia, costing producers in North America more than \$600 million annually¹. The disease syndrome was first recognized in the United States in 1987 and described in 1989 (ref. 2). The causative

disease syndrome and porcine circovirus-associated disease, and can establish a lifelong subclinical infection⁶. In 2006, a more severe form of the disease, called highly pathogenic PRRS, decimated pig populations throughout China⁷. Although genetic selection for natural resistance is an option, success to date has been limited, possibly due to the genetic diversity of the virus⁸.

homologous recombination and somatic cell nuclear transfer) were infected with PRRSV and compared with infected wild-type pigs, no difference in virus replication was found⁹. To test the role of CD163 in infection, we previously created 45 live-born piglets with insertions ranging from 1 bp to 2 kb, deletions from 11 bp to 1.7 kb, as well as a partial domain swap in *CD163* using



 PLOS | PATHOGENS

 ROSLIN

RESEARCH ARTICLE

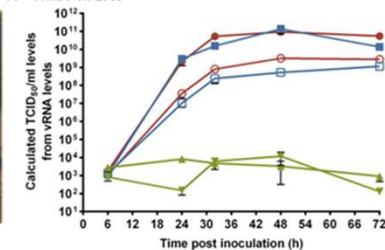
Precision engineering for PRRSV resistance in pigs: Macrophages from genome edited pigs lacking CD163 SRCR5 domain are fully resistant to both PRRSV genotypes while maintaining biological function

Christine Burkard¹, Simon G. Lillico¹, Elizabeth Reid², Ben Jackson², Alan J. Mileham³, Tahar Alt-Alli¹, C. Bruce A. Whitelaw¹, Alan L. Archibald^{1*}

A

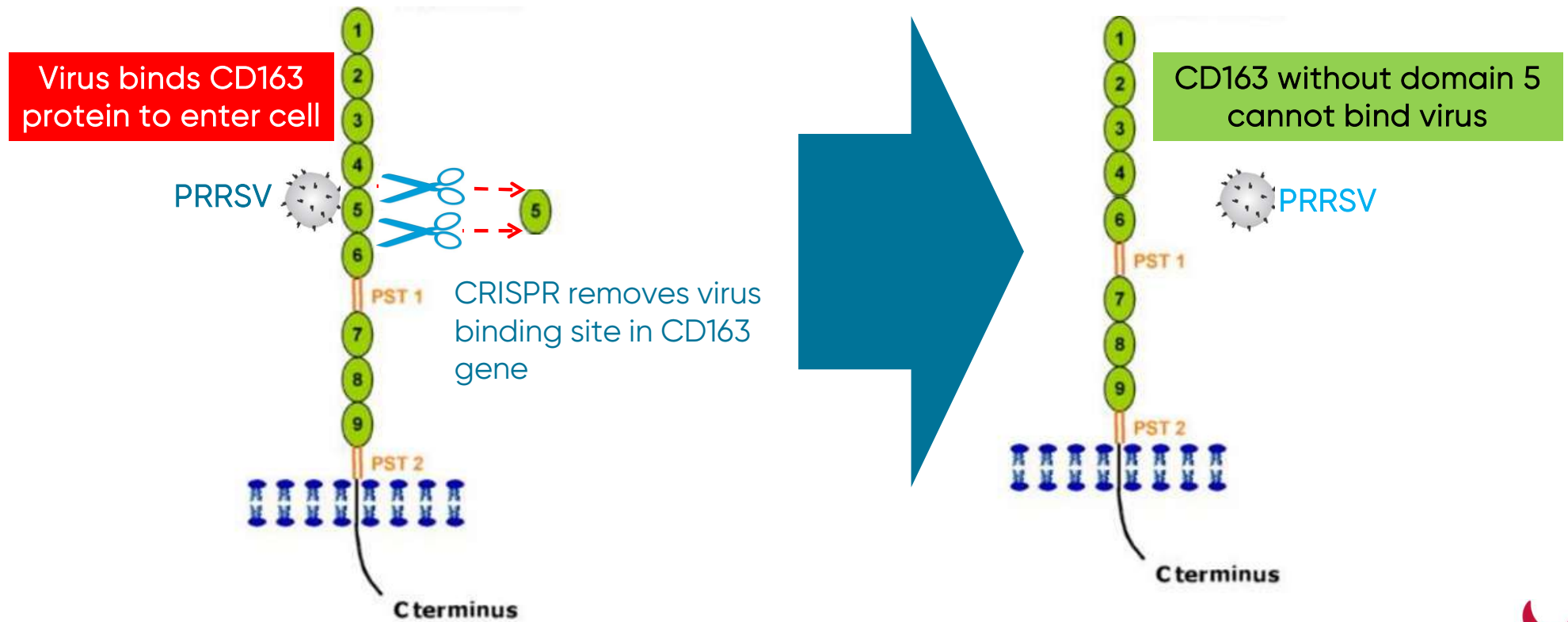


A PRRSV VR-2385



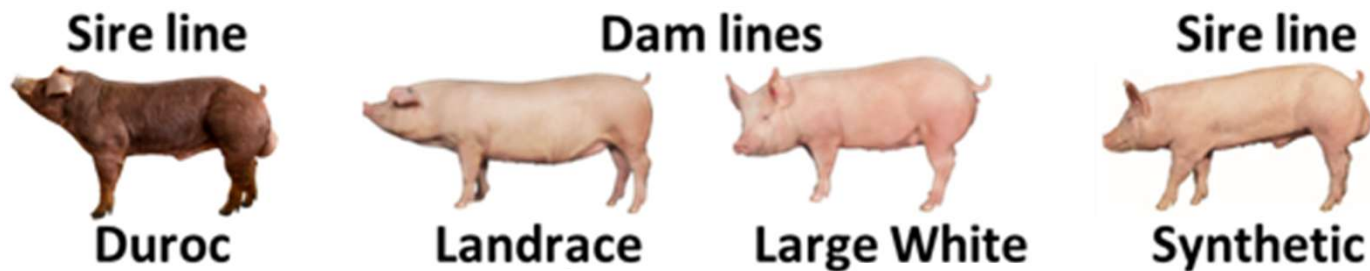
 Genus

Edited Allele Lacks the PRRSV Binding Domain



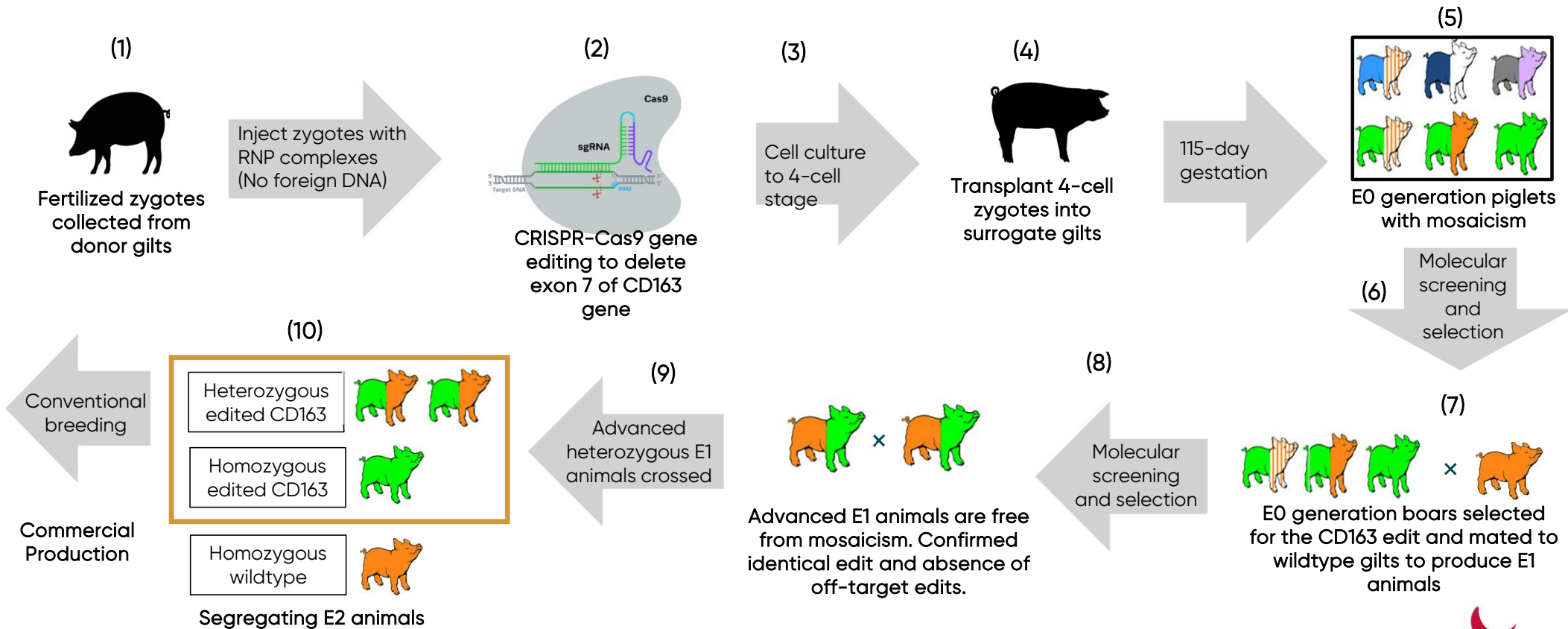
Commercial-Scale Regulatory Strategy

- CD163 PRRSVr edit in four lines (2 dam, 2 sire lines)
- Identical edits in 50–100 individual pigs of each line
 - Not “event by event” approval
 - Representative data from a subset of edited animals



- Seeking full approvals for production and consumption in target markets
- Goal: production as conventional pigs

Creation and Characterization of Edit



Source: Adapted from Cigan and Knap (2022) *CABI Agriculture and Bioscience*, 3:34.

Recent Publications

➤ Generation, screening, and selection of the edited animals:

Burger et al. (2024) Generation of a commercial-scale founder population of Porcine Reproductive and Respiratory Syndrome virus resistant pigs using CRISPR-Cas. *The CRISPR Journal* 7(1): 12–28.

➤ Phenotypic characterization and meat compositional analysis of the edited animals:

Nesbitt et al. (2024). Pigs lacking the SRCR5 domain of CD163 protein demonstrate heritable resistance to the PRRS virus and no changes in animal performance from birth to maturity. *Frontiers in Genome Editing* 6:1322012.

Global Regulatory Strategy

Approved/Non-GMO Determination:

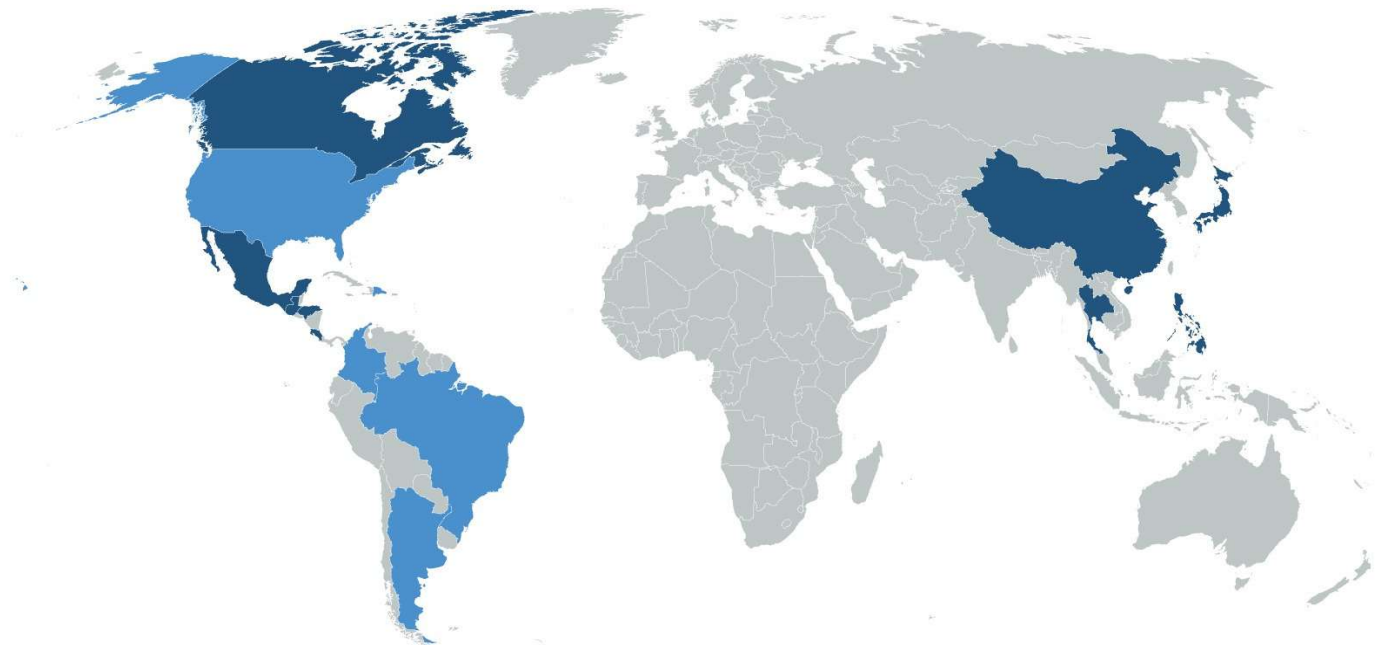
- USA (FDA)
- Colombia
- Brazil
- Dominican Republic
- Argentina

In process:

- Canada
- China
- Costa Rica
- Guatemala
- Honduras
- Japan
- Mexico
- Philippines
- Thailand

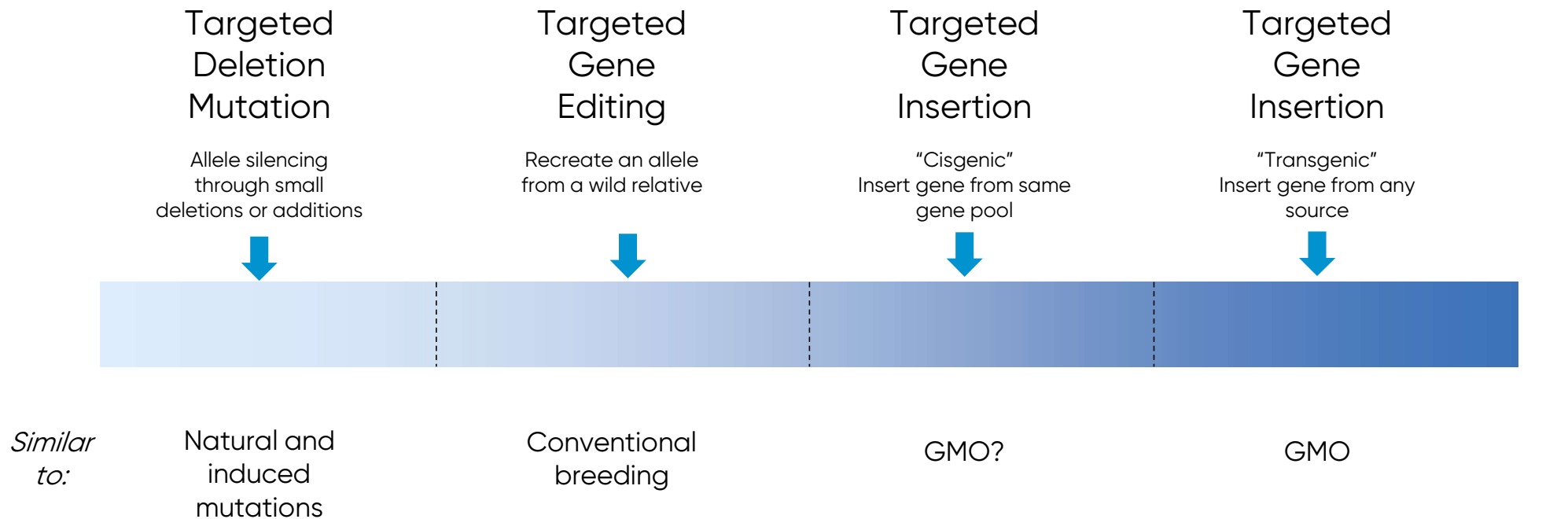
PRRS Resistant Pig Approval

Approved In Process



PRRS Resistant Pig • Updated as of 07/11/2025
This map shows countries where PIC has received regulatory approval or determination, as well as those where approval processes are currently underway. Additional countries will be added as PIC continues to pursue global regulatory clearance.

Gene Editing Continuum



Example Regulatory Systems

➤ US FDA, Canada (three agencies)

- Basically uses same regulatory framework as with GMOs
- US: “intentional genomic alteration”; Canada “novelty”
- Full assessment of food/feed safety, animal health, env. impact

➤ Colombia, Brazil, DR, and others

- Determination that the product is not subject to GMO law/regs

➤ Japan (three agencies)

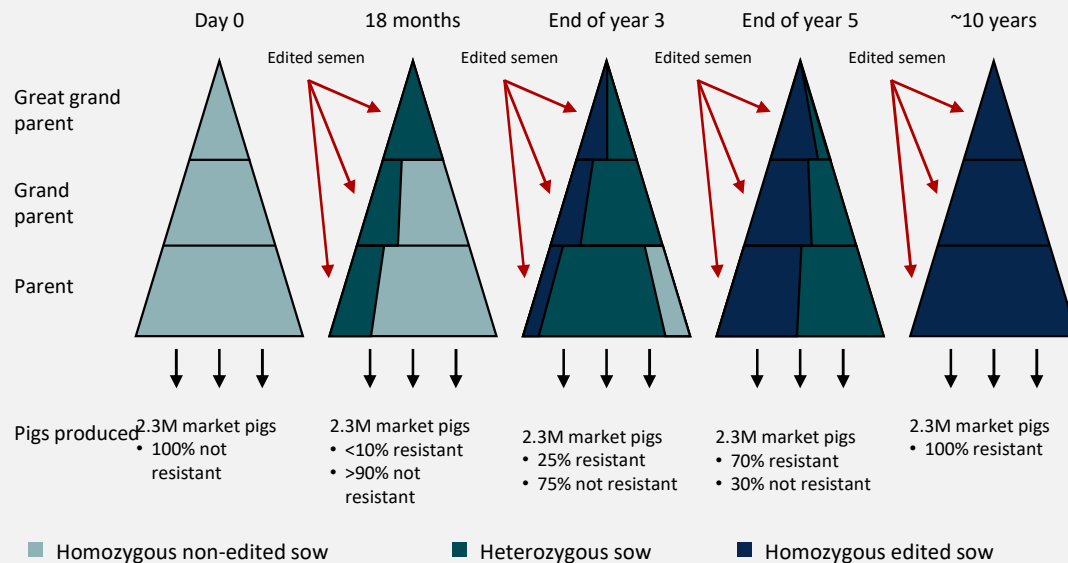
- Hybrid: Nearly GMO-like assessment, but ends with non-GMO determination

FDA Technical Sections

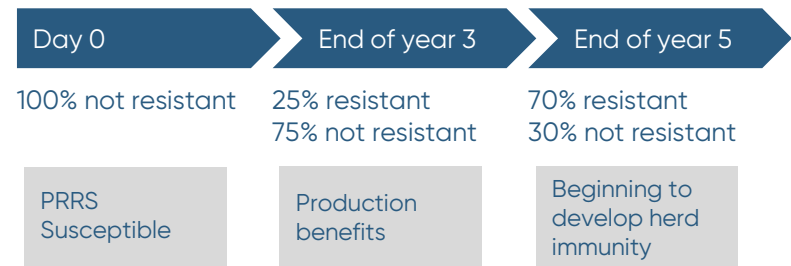
✓	Step 1	Product Definition	The step forms the foundation for FDA's evaluation process; requires a broad statement characterizing the animal and the claim being made
✓	Step 2	Molecular Characterization of Altered DNA	Description of the alteration, purpose, function, components and composition of the alteration, sequence, and how it was achieved
✓	Step 3	Molecular Characterization of Animal Lineage	Description of the methods used for alteration of target site, generation and characterization of the animals (E0, E1, E2), detection methods, off target effects and breeding strategy to produce commercial animals
✓	Step 4	Phenotypic Characterization	Comparative phenotypic characterization and assessment of genome altered animals with controls for animal health including growth rates, reproductive function, behavior, and animal physiology
✓	Step 5	Genotypic & Phenotypic Durability	Demonstration that genome alteration is stably-inherited and the phenotype is consistent and predictable over at least two generations
✓	Step 6	Food Safety and Environment Safety	Assessment of safety of the food derived from genome altered animals for human or animal consumption (compositional analyses), and any potential environment impacts (EA)
✓	Step 7	Effectiveness/Claim Validation	Validation of the claims for the characteristics that the genome altered animals are intended to exhibit, demonstration that the animals are indeed resistant to PRRSv

Incorporation of Trait Into Herds

Introgression of PRRS-resistant trait in 100,000 sow customer herd (base case)



PRP dissemination



Semen and boars will be the primary delivery method

Potential levers to accelerate the rate of genetic dissemination



Faster sow replacement



Alternative insemination techniques



Reduced semen dosage

Constant integration of elite conventional genes to maximize PRP genetic merit

Market Acceptance

Building social license so participants of pork chain comfortable and confident with utilization of PRP



Farmer/Producer



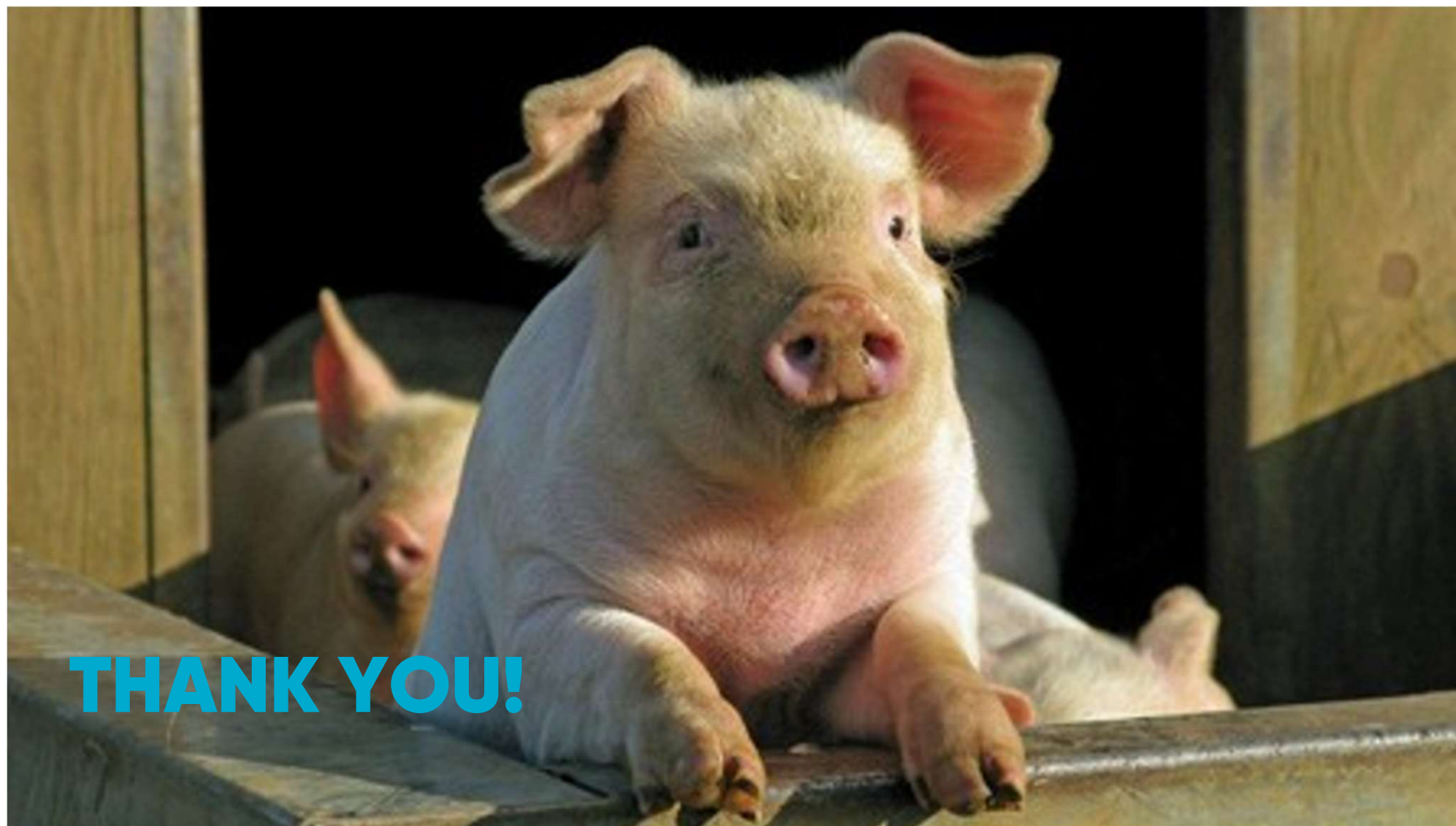
Packer/Processor



Food Service/Retail



Consumer



THANK YOU!