A PRODUCER PERSPECTIVE ON GENE EDITING

OUTLINE

- Technology:
  - Potential for IGA (Intentional Genetic Alteration)
    - Pigs
    - People
  - Challenges for Implementation in Pigs
- Questions and challenges for the industry:
  - Producers
  - Packers
  - Retailers
  - Consumers

POTENTIAL (FOR PIGS)

- Creating animals resistant to viral pathogens
  - Blocking the pathway a virus would use to prevent infection
- Creating animals resistant to bacterial pathogens
  - E. coli. (F18, K88)…pathogens with known and ‘simple’ infectious pathways
- Leverage genetic variants impacting immune system function
- Eliminating or reducing the impact of a disease or condition with a genetic pre-disposition
  - Inherited abnormalities
  - Nuisance traits (inguinal hernia, cryptorchid)
- Performance…directed creation of desirable variants

POTENTIAL (FOR PEOPLE)

- Alpha-Gal
  - *"FDA Approves First-of-its-Kind Intentional Genomic Alteration in Line of Domestic Pigs for Both Human Food, Potential Therapeutic Uses"*
  - https://www.fda.gov/news-events/press-announcements/fda-approves-first-its-kind-intentional-genomic-alteration-line-domestic-pigs-both-human-food
- Consumer Benefits
  - "What's in it for me"
  - Pit less cherries, seedless berries
    - https://www.pairwise.com/our-products
  - Product quality and eating characteristics
  - Nutritional content
  - Expression of therapeutic proteins
- Which set of traits will drive acceptance of the technology by consumers?

CHALLENGES FOR IMPLEMENTATION IN PIGS

- How do we introduce an edit into an existing breeding program and minimize its *negative* impact?
- An edit with a 'major' effect is akin to single-trait selection
- Supporting technology is not efficient:
  - Cell type to edit
    - Option A: Edit embryos
      - Sow reproductive tract results in 'single-use' of the donor
      - Additional generations to deal with mosaicism
    - Option B…Edit cell lines
      - Preserve the donor
      - Cloning
  - Both require embryo transfer
    - A surgical process in pigs
    - Low or highly variable yield

CHALLENGES FOR IMPLEMENTATION IN PIGS

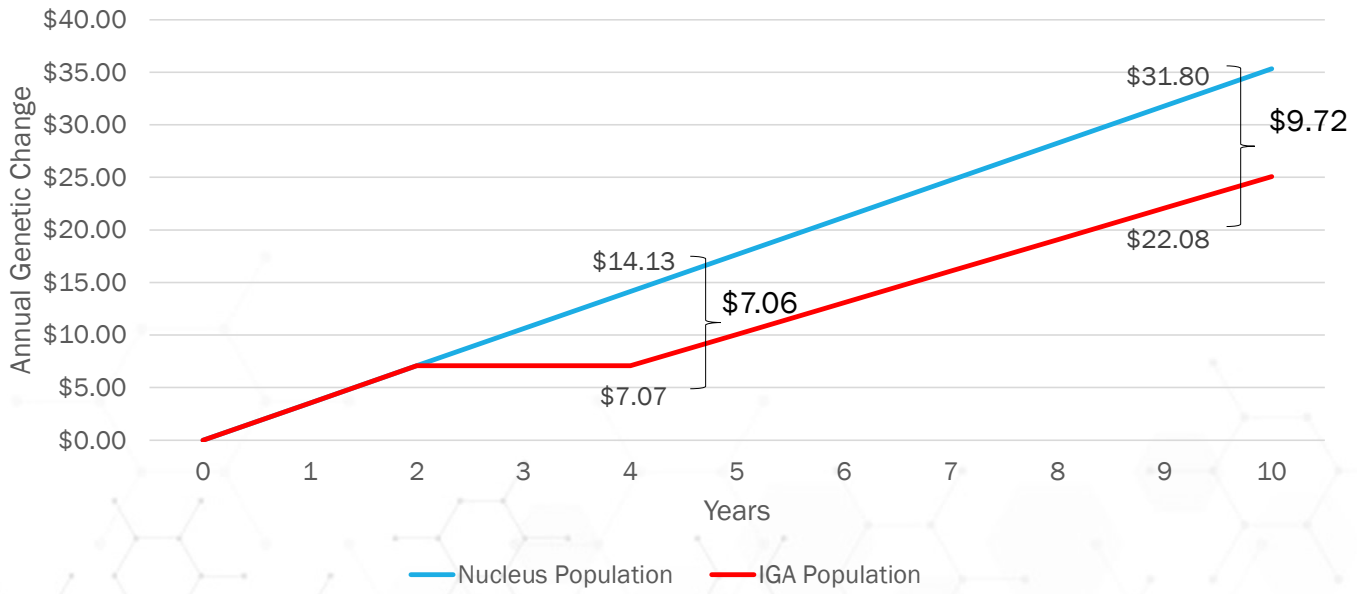
- What are the potential impacts?
  - Founders quickly become 'inferior' animals…*risk of increased genetic lag*
  - Selection for the edit within a nucleus population slows response in other traits
    - The phenotype produced by the edit is 'just another trait'
    - The inclusion of a trait in selection scheme depends on the economic value of the edit and the cost to produce the phenotype/genotype used for selection
    - Does the benefit justify the 'new trait' and create more value?
    - …*Risk to value created or 'balanced value' created*
  - Finally, there is risk to genetic diversity in a nucleus system…*risk to long-term genetic potential*
    - This already exists today, but is easily managed
    - Introduction of IGA could increase this risk, especially if multiple edits are deployed

EXAMPLE OF FOUNDER RISK – GENETIC LAG

- (Over) Simplified Scenario:
  - Create founder population – Year 1
  - Intermate Mosaic Founders to produce homozygous animals – Year 2
  - Expand founder population in order to have product for sale – Year 3
  - Minimum of 3 years with limited to no genetic gain, other than the IGA
  - Reduction in non-IGA genetic gain until fixation occurs in the nucleus
- Other Scenarios…Collaboration with KSU/ISU
- Assumptions in example to follow:
  - $3.53 genetic gain per year per market pig
  - Existing index gain reduced by 15% when selection for the IGA is included

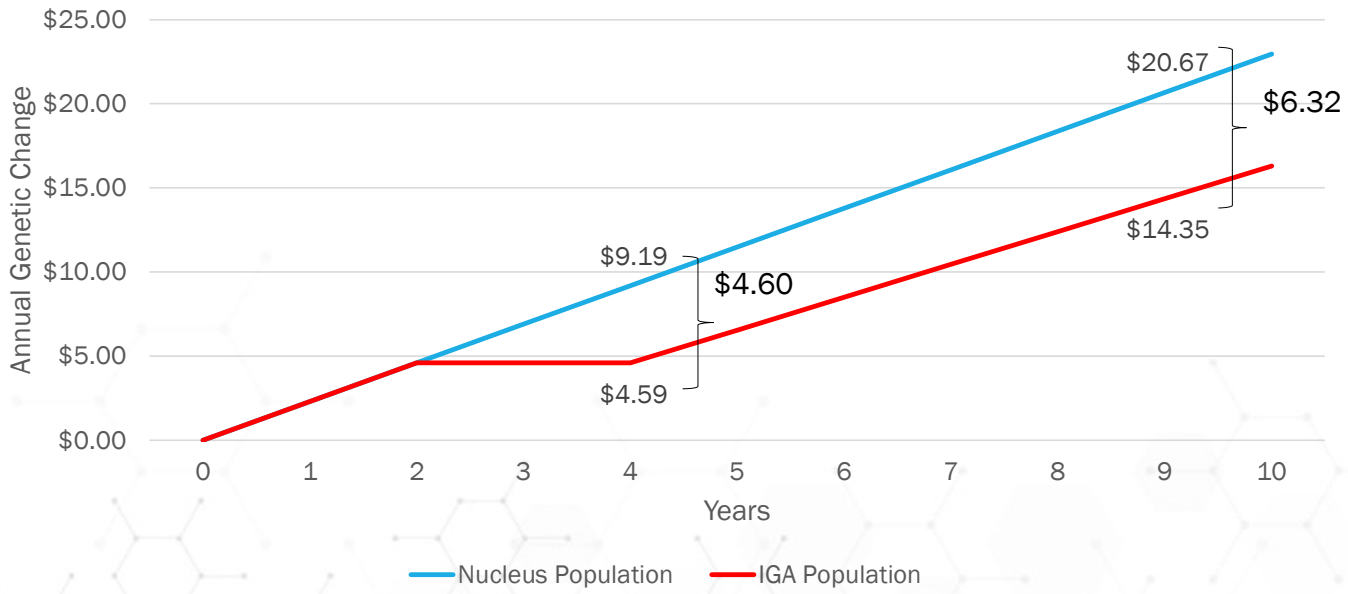
FOUNDER RISK – GENETIC LAG IN THE SIMPLIFIED SCENARIO

Average gain since 2017 = $3.53 per market pig



FOUNDER RISK – GENETIC LAG IN THE SIMPLIFIED SCENARIO

Realized genetic potential is 65% of predicted, $2.30 per market pig



OTHER IMPLEMENTATION SCENARIOS

- Use of techniques to achieve homozygous IGA after 1 year:
  - Today this requires cloning
  - Use of same superior animals as founders
  - Reduce lag by at least 1 year, if not more…this is extremely important
- Taking the 'long' approach:
  - Create an allele frequency in the nucleus system on which to select
  - Repeat process with a new generation of superior animals, adding both index and IGA
  - Target animals with the IGA to commercial flows as allele frequency increases…commercial arrives at IGA status ahead of the nucleus
- Bypass the nucleus altogether, pushing IGA at the commercial level
  - Selection of nucleus animal, followed by a round of cloning and IGA creation
  - Creates a year of lag, but overcome with 'multiple copies' of very Elite sires used at the commercial level

SOME IMPLEMENTATION QUESTIONS TO CONSIDER

- Genetic Lag is a ***real cost*** to the pork producer
- The value of the IGA should at least equal lost genetic gain
- How the genetic supplier implements will impact the value created
- There are risks to genetic variation and long-term genetic gain
- *It is completely infeasible to create a new population for every edit*

GENETIC TAKE-HOMES

- The technology used to create and deploy an IGA must improve:
  - Cost…likely will decrease over time
  - Efficiency…how accurate we can be the ‘first time’, editing technology
  - Scalable…for widespread implementation, the industry lacks the resources
  - Reproductive technologies…embryo transfer in pigs is inefficient and surgical
- The approval process matters
  - 5+ year FDA process slows deployment and adds cost
  - Biology of pigs adds multiple years to the distribution path
  - Patents can literally expire before full realization of value
  - The approval process issue is as big or bigger as the generation interval issue

WHAT ABOUT INDUSTRY IMPACT?

"There are known knowns. These are things we know that we know. There are known unknowns…<these> are things that we know we don't know. But there are also unknown unknowns. There are things that we don't know we don't know. And if one looks through the history of our country and other free countries, it is the latter category that tend to be the difficult ones" – Donald Rumsfeld

QUESTIONS FOR THE INDUSTRY – PRODUCER COST

- Using disease prevention as an example, disease increases cost for a production system:
  - Prevention (Vaccine and Biosecurity)
  - Treatment (Antibiotic use)
  - Death loss and production drag
- What is the cost of the pathogen to a system of production?
- Based on this cost, what is the value of the IGA?
- What return do you want on that investment?
- What would you pay?
- Reciprocally, what level of performance would you give up to obtain the IGA phenotype?

QUESTIONS FOR THE INDUSTRY - CONSUMER

- Optimistically, consumers will understand the benefits
  - Improved animal welfare
  - Contribution to sustainability
  - Improved product attributes…this is ideal
  - Application to human disease should benefit acceptance in food
- Transparency
  - Transparency will be paramount in this process
  - Should the product be clearly labeled? What is, or should be, the industry stance on this question?
  - We cannot afford to focus only on producer benefits
  - We can argue the science all day long, but ultimately, we must deliver what the consumer wants whether we agree with the position or not

QUESTIONS FOR THE INDUSTRY - CONSUMER

- Pork demand is paramount to a successful industry
- Will Gene Edited meat increase or decrease overall demand for our products?
- If two packages sit side by side and one is labeled as ‘containing IGA’ or ‘Gene Edited’…which product commands a higher price?
- Is the fact that pork is/could be ‘first’ (in the barnyard) a risk to the position of pork relative to other proteins?
- Consumers care about:
  - Price, Quality and Safety
  - Welfare, antibiotic use and sustainability are not at the top of the list for most
  - Where does this technology fit?

QUESTIONS FOR THE INDUSTRY - PACKER

- Packers will likely make decisions based on retailers
- Retailers make decisions based on consumers and consumer demand…and likely won't make a decision early in the rollout
  - This is a problem for species with longer generation intervals
  - Once the process begins (permanent genetic change), you cannot roll it back quickly (IGA is not PayLean)
- Will Edited Pigs be worth more or less to a packer?
- Will IGA Pork need to be segregated, and who bears that cost?
- What record-keeping and traceability will be required by producers and packers and who absorbs this cost?

QUESTIONS FOR THE INDUSTRY - MARKETS

- Export Markets:
  - Over 30% of U.S. pork is exported
    - Mexico, Japan, Canada, S. Korea, China…plus others
  - IGA must be approved in all export markets, each with a unique process
  - There is currently no international standard or method of acceptance
  - Trade risk:
    - Traceability will be important…can the U.S. reliably segregate product?
    - Could artificial trade barriers be used against U.S. pork?
- Impact on the hog market:
  - Like all innovations, increased efficiency will have a cost
  - Decrease of a major disease will increase pork supply (10-20%)
    - Will demand keep up with the additional supply or will it pressure prices lower?
    - Will price pressure force further consolidation and reduce producer numbers?
  - What will the industry look like if demand crashes, and we have oversupply?

OUR POSITION

- As a leading supplier of improved genetics, we are supportive and optimistic about the benefits that gene-editing and other approaches to intentional genetic alterations will bring to producers and society
- We have insured we are in position to deliver on these technologies when the time is right to do so
- The industry must acknowledge there are significant questions to be answered prior to deploying these technologies and we must engage in that discussion

OUR POSITION

As a Producer We believe:

- Transparency,
- …Industry and Consumer engagement and education,
- …and a thorough understanding of the impact on domestic and international demand
- …Are all crucial to the successful use of gene-editing in livestock

RUMSFELD APPARENTLY HAD A LOT TO SAY ABOUT THIS…

"Test ideas in the marketplace. You learn from hearing a range of perspectives. Consultation helps engender the support <that> decisions need <in order> to be successfully implemented"


QUESTIONS?