

# South Asia Biosafety Program

NEWSLETTER FOR PRIVATE CIRCULATION ONLY – NOT FOR SALE



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## INDIA

### GM Crops for Animal Feed: Sensitization Workshops

Dr. Vibha Ahuja, Chief General Manager, Biotech Consortium India Limited



Speakers at the workshop on "GM Crops in Animal Nutrition: Science and Safety Aspects" (March 9, 2022).

The livestock sector in India including poultry, cattle, and aquaculture is growing at a rate of 8-10%, resulting in increased demand for animal feed. Availability and high cost of inputs has been a major concern in the recent past, as animal feed is the major input and constitutes 65-70% of the production cost. Globally, maize and soybean, the two important crops for animal feed, have been genetically modified by introgressing various traits and widely adopted, which in turn have led to increased productivity. Products derived from GM soybean and GM maize are widely used for animal feed. In India, the potential feed requirement in the coming years is expected to increase further in view of changing food habits, increase in protein demand, etc. Therefore, technological interventions are urgently needed to ensure availability of enough quantities of quality feed in a cost-effective manner for the survival and growth of the livestock sector. Recently, the Government of India permitted the import of limited quantities of GM soymeal to check against increasing prices and availability. Biotech Consortium India

Limited (BCIL) has collaborated with various agencies, including the Animal Nutrition Society of India (ANSI) and All India Poultry Breeders Association (AIPBA), to organize knowledge sharing workshops about the use of GM crops for animal nutrition.

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#### WORKSHOP ON GM CROPS IN ANIMAL NUTRITION: SCIENCE AND SAFETY ASPECTS

Department of Animal Nutrition, Guru Angad Dev Veterinary & Animal Sciences University (GADVASU), Ludhiana in association with ANSI and BCIL organized a workshop on "GM Crops in Animal Nutrition: Science and Safety Aspects" on March 9, 2022 in Ludhiana. The workshop was attended by more than 100 participants, including animal nutritionists, animal scientists from different universities, Krishi Vigyan Kendras (KVKs), along with dairy and poultry feed millers and farmers.

Dr. Udeybir Singh Chahal, President, ANSI welcomed the delegates and indicated that the objective is to share up-to-date knowledge on

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Speakers and participants at the workshop on “Feed Requirements for the Livestock Sector: Opportunities and Challenges” (April 12, 2022)

GM crops, as products derived from such crops are extensively used for animal feed in several countries. These include maize, soybean meal, cottonseed meal, and canola meal. In India, Bt cotton is already cultivated (>90% area) and Bt cotton seed meal is used. Recently, GM soybean meal has been imported and used. Dr. Vibha Ahuja, CGM, BCIL delivered the keynote address and provided information on the status of GM crops and regulatory and safety aspects. Specific concerns and responses to the use of GM crops for animal feed were also discussed.

In his presidential address, Dr. Inderjeet Singh, Vice Chancellor, GADVASU informed participants that products derived from GM crops are being fed to more than 95% of the animals used for meat and dairy in the USA. He indicated that there is no difference in how GM and non-GM food affect the health and safety of animals and the DNA in such GM products does not transfer to the animals. He emphasized that as the demand for animal products is increasing day by day, new crops with high yield and free from pests, etc., must be developed to sustain production. He emphasized the need to clear the myths related to GM crops regarding cancer, sterility, etc.

Presentations were made by eminent scientists and officials from the Department of Animal Husbandry, Government of India on the status of animal feed requirements in India, as well as an overview of GM crops, particularly maize and soybean. These included Dr. Ani Bency Jacob, Animal Nutritionist from the Department of Animal Husbandry and Dairying, Government of India, Dr. Praveen Chhuneja, Director, School of Agricultural Biotechnology, Punjab Agricultural University, and senior scientists Dr. Dharam Pal Chaudhary from the ICAR-Indian Institute of Maize Research and Dr. Milind Ratnaparkhe from the ICAR-Indian Institute of Soybean Research. Experts from the US Grains Council and US Soybean Export Council spoke about global feed availability, the role of GM crops, and tools for checking feed quality. There were intense discussions regarding the price availability and quality issues related to animal feed, that were moderated by scientists from GADVASU and ANSI.

### WORKSHOP ON FEED REQUIREMENTS FOR THE LIVESTOCK SECTOR: OPPORTUNITIES AND CHALLENGES

The All India Poultry Breeders Association, in association with BCIL and ANSI, organized a knowledge sharing workshop on “Feed Requirements for the Livestock Sector: Opportunities and Challenges” on April 12, 2022 at Hotel Avasa, Hyderabad. More than 80 participants from the poultry industry, seed industry, scientists from research institutions and universities, nutritionists, officials from central and state animal husbandry departments, the media, and other stakeholders participated in the workshop.

In his opening remarks, Dr. O. P. Chaudhary, Joint Secretary, Department of Animal Husbandry and Dairying, Government of India indicated

that contributions of the livestock sector in agriculture and allied sectors have increased significantly. He indicated that the issue of supply and availability of soybean meal and maize has been brought to the notice of the government, as well as the price volatility. He assured attendees that the government is committed to supporting the livestock industry and several initiatives have been taken, including the permission to import GM soybean meal. He appreciated this initiative and requested that the recommendations be sent to the department.

Dr. Suresh Chitturi, MD, Srinivasa Farms and Vice President, All India Poultry Breeders Association and Mr. D. Raghava Rao, MD, Kohinoor Hatcheries Private Limited shared detailed information on the current feed requirements and potential demand over next decade. It was stressed that the industry holds great potential not only to meet increasing domestic requirements, but it also can lead to exports of animal products. However, this requires consistent

supply of feed to make it competitive in the international market. The opinion was voiced that all options, including the use of GM crops and novel derivatives, should be explored. They also stressed that adoption of GM crops be encouraged so as to increase productivity, which will bring benefit not only to farmers, but also to the livestock farmers and industry.

Dr. Vibha Ahuja, CGM, BCIL spoke about the safety and nutritional aspects of GM crops. She informed participants that state of the art internationally accepted methodologies are available for pre-market safety assessment of GM crops and indicated that there are no confirmed reports of any adverse effect from the use of GM crops in the last 25 years in more than 70 countries. She also clarified various prevalent myths regarding the use GM crops by the feed industry and provided factual information.

Presentations and remarks were made by Dr. S. V. Rama Rao, ICAR-Directorate of Poultry Research, Mr. Ram Kaundinya, Director General, Federation of Seed Industry of India, and Dr. Paresh Verma, Executive Director-Bioseeds Division, DCM Shriram Limited, Hyderabad and senior representatives from the US Grains Council and US Soybean Council.

Participants shared their views and requested the associations to prepare strategic plans and approach the government for timebound decisions so that the industry can benefit from the use of new technologies such as GM crops. The industry participants expressed their desire that imports may be permitted in the short term to meet the current demand and at the same time, policies and investments in research for facilitating the use of GM crops for increasing productivity and tapping future potential could be streamlined.

Both the workshops were well received and recommendations will be forwarded to the Department of Animal Husbandry for their consideration.

## List of Infective Microorganisms Corresponding to Different Risk Groups in India, 2021

The Department of Biotechnology, Ministry of Science and Technology, Government of India revised and updated the “List of Infective Microorganisms Corresponding to Different Risk Groups” in December 2021. The list is a part of the “Regulations and Guidelines for Recombinant DNA Research and Biocontainment, 2017,” notified by DBT pursuant to “Rules for Manufacture, Use/Import/Export and Storage of Hazardous Microorganisms/Genetically Engineered Organisms or Cells, 1989” (Rules, 1989) under the Environment (Protection) Act, 1986 (EPA 1986). These guidelines provide for selection of appropriate biosafety level facilities for working with hazardous microorganisms and genetically engineered organisms.

The list supersedes Annexure I of “Regulations and Guidelines for Recombinant DNA Research and Biocontainment, 2017” and should be read in conjunction with the aforementioned guideline.

The list can be accessed from:

<https://dbtindia.gov.in> | <https://ibkp.dbtindia.gov.in>

### BANGLADESH

## GalSafe Pig: Is It a Possible Solution for Overcoming Certain Allergies?

Nasiha Jahan Muna, Brac University

### STUDENT SHOWCASE

To encourage written discourse on topics related to biosafety and biotechnology among the younger generation, the *SABP Newsletter* dedicates space in select issues to spotlight pieces written by students residing in South Asia. Since articles with the “Student Showcase” tag are meant to reflect the actual views and capabilities of the author(s), they are not revised for content and only lightly edited to conform with the newsletter’s style guide.



Skin allergy test preparation by doctor on a patient hand. © Arindam Ghosh | Dreamstime.com

In 2009, 12 people were diagnosed with Alpha-gal Syndrome (AGS) in the United States. Over the next 10 years, this number rose to over 34,000<sup>1</sup>. Data suggests that the number of diagnosed patients has been increasing since then. Alpha-gal syndrome significantly impacts human health. Patients may present mild to severe allergic reactions to alpha-gal sugar present in food, including red meat (e.g., pork, beef, and lamb) and other products containing mammalian-based materials (e.g., medicines and cosmetics)<sup>2</sup>. To protect them, on December 14, 2020, the U.S. Food and Drug Administration (FDA) approved a genetically modified animal referred to as “GalSafe pig” for both food and human therapeutic applications because it has no detectable levels of Alpha Gal sugar residues. Following the approval of AquAdvantage salmon in 2015, the GalSafe

**Following the approval of AquAdvantage salmon in 2015, the GalSafe pig became the second GM animal approved for human consumption in the USA.**

pig became the second GM animal approved for human consumption in the USA. This is the first-of-its-kind intentional genomic alteration (IGA) in the line of domestic pigs (*Sus scrofa domesticus*) that can be utilized in food or medicine for humans<sup>3</sup>.

If we look back at the development of the GalSafe pig, a targeting vector was first created containing a vector backbone and a pPL657 rDNA construct (containing the DNA sequences that are homologous to the target region of Glycoprotein Galactosyl Transferase Alpha-1, 3 gene (*GGTA1*) and selectable marker gene neomycin phosphotransferase II gene (*nptII*)<sup>2</sup>. When the intended vector design was confirmed, the Intentional Genomic Alteration (IGA) of the pPL657 rDNA construct was inserted into the *GGTA1* gene derived from porcine fetal fibroblast through rDNA-mediated

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homologous recombination. Next, they were transferred into the enucleated oocytes using Somatic Cell Nuclear Transfer (SCNT). Finally, the resulting embryos were moved to the surrogate dam and from them, 5 hemizygous progenitors were selected for breeding and developing homozygous GalSafe Pigs. Molecular analysis confirmed the successful integration of the construct into the target region, along with no alteration across multiple generations<sup>2</sup>.

The *GGTA1* gene mainly codes for an enzyme responsible for alpha-gal sugar production in cells, tissues, and organs of almost all mammals. The pPL657 rDNA construct disrupts and knocks out the *GGTA1* gene. As a result, the biological derivatives of homozygous GalSafe pigs have undetectable levels of Alpha Gal sugar residues, allowing persons with AGS to use this animal as a source of food and treatments without the risk of developing an allergy to it.

Prior to the approval of GalSafe pigs, the FDA went through a number of risk assessments. They assessed the detailed molecular characterization of the rDNA construct, molecular and phenotypic characterization, human and microbial food safety, and environmental impacts. The FDA also evaluated the concerning issue regarding the presence of the *nptII* selective marker. Additionally, issues related to escape, survival, and reproduction of the GalSafe pigs were also thoroughly evaluated.

Revivicor, a Virginia-based biotechnology company and developer of GalSafe pigs, submitted their environmental assessment (EA) on October 19, 2020. This mainly highlighted two exposure pathways that could cause an environmental risk, namely, escape of GalSafe pigs, and the presence of the *nptII* gene product in the environment.

Various risk management procedures were suggested to address these issues. For example, the facility location was chosen in northern Iowa, which was far away from any activities that might cause any environmental impact. In addition, in the facility, at least three levels of physical containments, such as pens (primary barrier), buildings (secondary barrier), and a perimeter (tertiary barrier) were in place, along with procedural containments, including accidental release management

guidelines, animal tracking, security, etc. at the production facility and slaughterhouse in South Dakota. Even in the case of escape of GalSafe pigs, their long-term survival and dispersal in the ecosystem was found to be low because of the rapid rescue attempts, harsh winter conditions, regulations of hunting, carnivore predation, etc. In addition, the IGA does not provide any selective advantage for survival in the environment. Furthermore, the environmental assessment highlighted that the lack of potential mates lowered the likelihood of reproduction and establishment with IGA containing pigs<sup>4,5</sup>.

Moreover, two issues related to the risk of likelihood of toxicity and increased antimicrobial resistance due to the presence *nptII* gene and NPTII protein were also evaluated in the environmental assessment. It

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was highlighted that though the *nptII* gene and NPTII protein are ubiquitous and widely spread in the environment, the proteases and peptidases present in the soil easily degrade the NPTII protein. Thus, the presence of the *nptII* gene and its protein do not pose any toxic effects in the environment. The concern regarding the possibility

of increasing antimicrobial resistance was also examined. Theoretically, there remains a chance that the *nptII* gene can get transferred to the soil bacteria. Interestingly, this event hasn't been seen yet, though this gene has been in use for more than 3 decades in the transformation of organisms. Though the presence of *nptII* gene and antimicrobial resistance is common in the environment, the possibility of increased microbial resistance is limited. Furthermore, GalSafe pigs are not allowed to get exposed to aminoglycoside, thus no selective advantage. So, in the environmental assessment submitted by Revivicor, different potential impacts associated with the environment were identified and evaluated in detail. Moreover, several precautionary management steps are listed to decrease the risks. Based on this, the FDA concluded that this pPL657 rDNA construct contained in GalSafe pigs does not have any significant environmental impacts, and rather, that they are as safe as the conventional pigs<sup>4,5</sup>.



Piglet (*Sus scrofa domestica*) sleeping in straw. © Jeff Grabert | Dreamstime.com

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Heparin Sodium Injection vial. © Sherry Young | Dreamstime.com

The FDA also evaluated human and microbial food safety as a part of the review to identify whether the GalSafe pigs are safe as food for human consumption or not. For this, possible toxicity, molecular and phenotypical characterization, unintended effects, health status of both IGA and GalSafe pigs, and composition were analyzed. As a transgene product, the NPTII protein is safe as it is found to be heat prone and easily degradable by pepsin and other digestive enzymes. Thus, unlikely a food toxicant or allergen. Furthermore, a nutritional and compositional study showed edible muscle tissues of the homozygous and hemizygous GalSafe pigs were comparable. For the study, they used the standard reference values from the U.S. Department of Agriculture (USDA) National Nutrient Database for Standard Reference (SR). The study concluded that most of the values remained within 20% of the reference value, which indicates no nutritional hazard for the consumers. Therefore, after assessing all the data, the FDA concluded that GalSafe pigs are safe, and that the general population can consume them<sup>2</sup>.

It is clear that GalSafe pigs have a wide range of applications. As GalSafe pigs lack the Alpha-gal sugar, they can be useful for people with AGS. Apart from the potential benefits for human consumption, they also provide some medical usages. They can be used to make medical products for humans, such as heparin (blood thinning drug). GalSafe pigs may also play a vital role in xenotransplantation. They might potentially lessen the immune rejection issues among the patients whose xenotransplantation is expected to be triggered by Alpha-gal sugar. Since the xenotransplantation outputs from the GalSafe pigs have not yet been examined, more research is needed. Similarly, any

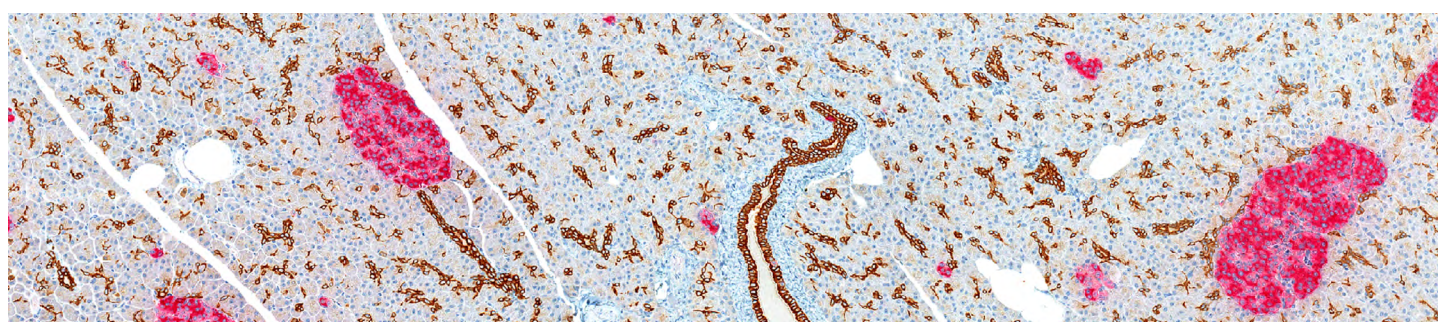
**The FDA concluded that GalSafe pigs are safe, and that the general population can consume them.**

manufacturer willing to develop human medical products from GalSafe pigs first needs to get approval from the FDA. It should be noted that the New Animal Drug Application (NADA) approval was only for the pPL657 rDNA construct, so any such modifications in GalSafe pigs will also need to be approved first<sup>2</sup>.

Alpha-gal Syndrome (AGS) is one of the major public health concerns. Considering this, genetic modification of meat may be a viable solution to the problem while simultaneously assuring human health safety. Consumers have the right to eat food that is both safe and allergen-free. Hence, GalSafe pigs can be considered as a ray of hope for those who are currently unable to eat a bit of red meat without an allergic attack.

#### References

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5. Finding of No Significant Impact (FONSI) (December 14, 2020) In support of an approval of a New Animal Drug Application (NADA). Retrieved from: <https://animaldrugatfda.fda.gov/adafda/app/search/public/document/downloadFonsi/2942>.



Pancreatic islets stained for insulin (red). © Vetpathologist | Dreamstime.com

**CALENDAR OF EVENTS**

EVENT	ORGANIZED BY	DATE	WEBSITE
<b>INDIA</b>			
National Seminar on Horticulture for Sustainable Development, Nutritional & Livelihood Security	National Agricultural Higher Education Project Innovation Grant, Uttar Banga Krishi Viswavidyalaya	May 26-27, 2022 Pundibari (in-person & online)	<a href="https://www.ubkv.ac.in/">https://www.ubkv.ac.in/</a>
Webinar Series for Popularizing Plant Tissue Culture in Asia-Pacific Region and African Countries Towards Realizing its Potential - Webinar 1: Banana, Root and Tuber Crops (Banana & Potato)	Asia-Pacific Association of Agricultural Research Institutions (APAARI)	May 31, 2022 Online	<a href="https://www.apaari.org/">https://www.apaari.org/</a>  <a href="https://zoom.us/webinar/register/WN_P0j9WgzyTKqNgVUCslpxtA">https://zoom.us/webinar/register/WN_P0j9WgzyTKqNgVUCslpxtA</a>
6 <sup>th</sup> International Conference on Current Issues in Agricultural, Biological & Applied Sciences for Sustainable Development (CIABASSD-2022)	Kalimpong Science Centre, Himalayan Scientific Society for Fundamental and Applied Research, ICAR-National Agricultural Higher Education Project (NAHEP)-IG, Directorate of Extension Education, Uttar Banga Krishi Vishwavidyalaya (UBKV), Pondicherry Institute of Agricultural Sciences (PIAS), Agro Environment Development Society (AEDS), and Centre for Environment and Agricultural Development	June 11-13, 2022 Darjeeling	<a href="https://www.ubkv.ac.in/">https://www.ubkv.ac.in/</a>
Webinar Series for Popularizing Plant Tissue Culture in Asia-Pacific Region and African Countries Towards Realizing its Potential - Webinar 2: Perennial Fruits/ Cash Crops (Date Palm, Pomegranate, and Sugarcane)	Asia-Pacific Association of Agricultural Research Institutions (APAARI)	June 30, 2022 Online	<a href="https://www.apaari.org/">https://www.apaari.org/</a>  <a href="https://zoom.us/webinar/register/WN_IMRWAUnDS3i1n6ME1prGQC">https://zoom.us/webinar/register/WN_IMRWAUnDS3i1n6ME1prGQC</a>
Webinar Series for Popularizing Plant Tissue Culture in Asia-Pacific Region and African Countries Towards Realizing its Potential - Webinar 3: Tree/ Woody Plants (Bamboo and Teak)	Asia-Pacific Association of Agricultural Research Institutions (APAARI)	July 29, 2022 Online	<a href="https://www.apaari.org/">https://www.apaari.org/</a>  <a href="https://zoom.us/webinar/register/WN_g5-HqPS-QSGm49HioepD6Q">https://zoom.us/webinar/register/WN_g5-HqPS-QSGm49HioepD6Q</a>
International Conference on Advances in Agriculture and Food System Towards Sustainable Development Goals	All India Agricultural Students Association, Indian Council of Agricultural Research, and University of Agricultural Sciences, Bangalore	August 24-22, 2022 Bengaluru	<a href="https://aafs2022.org.in/">https://aafs2022.org.in/</a>
<b>INTERNATIONAL</b>			
8 <sup>th</sup> Plant Genomics and Gene Editing Congress: Asia	Global Engage Ltd.	October 12-13, 2022 Kuala Lumpur, Malaysia	<a href="https://www.global-engage.com/event/plant-genomics-asia/">https://www.global-engage.com/event/plant-genomics-asia/</a>



**SOUTH ASIA**  
BIOSAFETY PROGRAM

The South Asia Biosafety Program (SABP) is an international development program implemented in India and Bangladesh with support from the United States Agency for International Development (USAID). SABP aims to work with national governmental agencies and other public sector partners to facilitate the implementation of transparent, efficient, and responsive regulatory frameworks for products of modern biotechnology that meet national goals as regards the safety of novel foods and feeds, and environmental protection.


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