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Potential of Transgenic Poultry for Biopharming

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CONVENOR : Dr T.K. Bhattacharya, Principal Scientist, ICAR-Directorate of Poultry Research, Rajendranagar, Hyderabad

REVIEWER : Dr Taru Sharma, Director, NIAB, Hyderabad

EDITORS : Dr P.S. Birthal
Dr Malavika Dadlani

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NASC, Dev Prakash Shastry Marg, New Delhi - 110 012
Tel: (011) 25846051-52; Fax: (011) 25846054
Email: naas-mail@naas.org.in; Website: www.naas.org.in

Preface

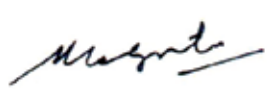
Therapeutic proteins, which have better target specificity, are free from any major side effects, and elicit better responses in chronic patients. These are becoming an integral part of active therapy in the treatment of numerous deadly diseases and for maintaining the well-being of human beings. The global worth of therapeutic proteins in 2021 was estimated at US$ 98.1 billion (www.researchandmarkets.com/reports/5319142/therapeutic-proteins-global-market-report-2021).

However, the production of contamination-free proteins in bulk quantity with desired purity and biological activity poses several challenges. Presently, the medicinal proteins are produced both in prokaryotic systems, such as *E. coli*, and in eukaryotic systems such as fungi, mammalian cells, insect cell lines, cell-free expression systems, and sometimes in transgenic animals. Most of the biopharma products are synthesized under a cell culture-based production system. Mammalian system is preferred over bacteria, plants, and yeast, because of their ability to synthesize proteins of higher order with precision in folding, assembly, and post-translational modifications. The choice of a suitable method of production depends on the structure and molecular complexity of the protein, its intended application, and the cost and quality of proteins thus produced.

Considering the high cost and purity issues in production through cell culture-based methods, transgenic animal platforms, particularly poultry, are being regarded as one of the most efficient to produce therapeutics with cost effectiveness, required volume, and functionality. The transgenic platforms provide a better alternative in spite of some issues of ethical use, and high initial investment. Hence there is a need to bring policy support encouraging investments in the production of therapeutic proteins in the transgenic platforms and creating science-led awareness among the masses emphasizing the overall benefit of such an approach for human wellbeing and animal welfare.

In order to deliberate on these issues, NAAS organized a strategy workshop on “Potential of Transgenic Poultry for Biopharming” on March 15, 2021, in a virtual mode involving stakeholders both from the public and private sectors. The deliberations focussed on identifying actionable points for efficient use of transgenic platform as bioreactor and recommendations to strengthen the pharma sector in the coming years.

On behalf of the Academy, I compliment Dr T. K. Bhattacharya, for convening this workshop, and acknowledge the valuable contributions of eminent panelists, participants, and reviewer in developing this policy paper. I also thank Dr P.S. Birthal and Dr Malavika Dadlani for their editorial support.



(Trilochan Mohapatra)
President

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New Delhi

Potential of Transgenic Poultry for Biopharming

1. BACKGROUND

Cost-effective production of high-quality pharmaceutical proteins is of paramount importance for offering affordable treatment against many deadly diseases and maintaining the good health of human beings and animals. Most of the human and animal proteins are post-translationally modified, which affects their plasma half-life, targeting tissues and/or biological activity. The pharmaceutical proteins have a wide range of products, including monoclonal antibodies (mAbs), vaccines, cytokines, hormones, enzymes, blood products etc.

The primary structure of the proteins is based on the linear combination of amino acids which in higher vertebrates become functional after several post-translational modifications by adding different kinds of molecules to various amino acids or removing certain amino acids, which alter their structure and functions. Out of more than 300 different types of modifications that are known to occur, most common ones are glycosylation, acetylation, phosphorylation, methylation, ubiquitination, halogenation, farnesylation and glycoxidation. (Manzi et al., 2000, Zasloff, 2002; Lane and Beese, 2006, Norregaard, 2004; Van den Steen et al., 1998; Bardor et al., 1999, Mitra et al., 2006). However, more than 50% of all human proteins are glycosylated (Van den Steen et al., 1998). Thus, post-translational modification has medical relevance where same proteins function in different ways during different physiological and pathological stages.

At present, most of the biopharma products are synthesized under cell culture-based production systems of which mammalian systems are preferred over other hosts, such as bacteria, plants, and yeast, because of their ability to perform required protein folding, assembly, and post-translational modifications. However, the cell culture-based systems have limitations of low yield, high possibility of impurity, and cellular contamination leading to high production cost and hence the high market price of the final product. Thus, one of the biggest challenges being faced by the Pharma sector lies in developing appropriate production methods that can lower the costs of recombinant proteins having desired secondary and tertiary structures. Transgenic platform offers the most viable option addressing these challenges and a production system for high volumes with suitable modifications and without the scope of microbial contamination and impurities.

2. BIOPHARMACEUTICALS

Biopharmaceuticals are, thus, pharmaceutical proteins synthesized by employing a series of molecular biology tools. This group of products is different from the broad category of biologicals having pharmaceutical values and being produced using conventional biological methods (Rader, 2008). Biopharmaceuticals, which have an estimated global market of US $ 401.32 billion in 2021 (www.mordorintelligence.com/industry-reports/global-biopharmaceuticals-market-industry) offer many advantages over conventional drugs in terms of target specificity, causing little or no side effects, showing high specificity and activity, and often effective for the treatment of patients who respond poorly to the traditional synthetic drugs (Mitragotri et al., 2014).

Biopharmaceuticals, thus produced in cellular/animal platform using biotechnological processes, is known as biopharming. When the production uses an animal platform rather cell culture, the

process is called animal biopharming. However, animal biopharming is defined more accurately as the farming of genetically modified transgenic animals to produce “humanised” pharmaceutical substances for use in human beings. The prime examples of animal biopharming include transgenic cows, sheep, and goats to produce the biopharma products in milk, and chickens to produce the products in eggs.

Many therapeutic proteins are produced in genetically modified mammalian cell culture through bioreactors. With such a production system, biotherapeutics occupy a significant portion of global drug production. The first biopharma product produced in a transgenic platform was antithrombin (ATryn) synthesized in the milk of a transgenic goat, which was later approved by the European Medicines Evaluation Agency (EMEA) and the Food and Drug Administration (FDA) of the United States for its clinical use (Vazquez-Salat, et al. 2012). In 2011, the EMEA approved the use of the recombinant C1-esterase inhibitor produced in rabbits for the treatment of hereditary angioedema (Vazquez-Salat, et al. 2012). Subsequently, many therapeutics including E2-CSFV, AtrynÒ-Antithrombin III, MM-093 (AFP), Anti-CD20 mAB, CD137 (4-1BB) mAB, Malaria vaccine etc. produced in transgenic goats were commercialized by multi-national biotech companies for their clinical use (Sanchez et al., 2014; Houdebine, 2009; Echelard et al., 2009; Rehbinder et al., 2009; Echelard et al., 2006) (Table 1).

Table 1. Some of the biopharma products produced in the transgenic animals

Products	Developer/Company	Transgenic Animal
Atryn-Atntithrombin III	GTC/rEVO	Goat
Ruconest- C1-Esterase Inhibitor	Pharming	Rabbit
MM-093 (AFP)	GTC/LFB-USA	Goat
Protexia-butyrylcholinesterase	Pharm Athene	Goat
Lactoferrin	Pharming	Cow
Growth hormone	BioSidus	Cow
Factor VIIIa	LFB/GTC	Rabbit
Fibrinogen	Pharming/GTC/LFB-USA	Rabbit, cow
Collagen	Pharming	Rabbit, cow
Factor IX	ProGenetics	Pig
A-1 antitrypsin (AAT)	rEVO/GTC	Goat
Anti-CD20 mAB	GTC/LFB-USA	Goat
CD137 (4-1BB) mAB	GTC/LFB-USA	Goat
Malaria vaccine	GTC/LFB-USA	Goat
Rotavirus VP2/VP6	BPT	Rabbit
Sebelipase alfa (Kanuma)	Alexion - Avigenics Inc.	Chicken

Products	Developer/Company	Transgenic Animal
Alpha-N-acetyl-glucosaminidase (SBC-103)	Alexion - Avigenics Inc.	Chicken
Epidermal growth factor	Seoul National University, Seoul, South Korea	Chicken
ScFv-Fc miniantibody (miR24)	Roslin Institute	Chicken
hIFNβ1a	Roslin Institute	Chicken
hEPO	Daegu, Republic of Korea	Chicken
hIFNα2b	ICAR-Directorate of Poultry Research, Hyderabad, India	Chicken

3. PRODUCTION SYSTEMS

The majority of commercially available biopharmaceuticals contain recombinant proteins as their active ingredients. These proteins are produced in prokaryotes, mainly *Escherichia coli*, or eukaryotes such as fungi (*Saccharomyces cerevisiae* and *Pichia pastoris*), mammalian cells, insect cell lines, cell-free expression systems, and transgenic animals. All these systems employed to produce biopharmaceuticals for human and animal use have their own merits and demerits. When post-translational modifications of the proteins are not required for their biological activity, the prokaryotic system, particularly the bacterial system, is a very good platform to be used for their production. When post-translational modifications of the proteins are required, eukaryotic systems such as yeast, mammalian cell culture, insect cell lines, cell-free expression systems and transgenic animals are the preferred platforms for producing proteins having biological activities. However, out of all eukaryotic systems, transgenic animal platform is considered possibly the best due to production of high quality proteins in bulk. The historical perspective of transgenic research has been delineated in Table 2.

Table 2. Historical milestones of transgenic animal research

(Source:https://www.whatisbiotechnology.org/index.php/science/summary/transgenic/transgenic-animals-have-genes-from-other-species-inserted)

Date/Year	Major events	People involved	Places
1929	Jackson Memorial Laboratories established to develop inbred strains of mice to study the genetics of cancer and other diseases		Jackson Memorial Laboratories, USA
1974	First publication on inserting foreign DNA into mice	Jaenisch & Mintz	Salk Institute, Fox Chase Institute for Cancer Research, USA

Date/Year	Major events	People involved	Places
September 1980	First successful development of transgenic mice	Barbosa, Gordon, Plotkin, Ruddle & Scangos	Yale University, USA
November 1980	Technique published using fine glass micropipettes to inject DNA directly into the nuclei of cultured mammalian cells to generate transgenic mice containing random insertions of exogenous DNA.	Capecchi	University of Utah, USA
November 1981	First successful transmission of foreign DNA into laboratory mice.	Constantini & Lacy	Oxford University, UK, Yale University, USA
December 1982	Giant mice developed by injecting rat growth hormone gene	Brinster & Palmiter	University of Pennsylvania, USA University of Washington Seattle, USA
1985	First transgenic mice created with genes coding for both the heavy and light chain domains in an antibody.	Kohler & Rusconi	Max-Planck Institute, Germany
November 1987	Publication of gene targeting technique for targeting mutations in any gene	Thomas & Capecchi	University of Utah, USA
1988	Patent application filed for a method to create transgenic mice for the production of human antibodies	Bruggeman, Caskey, Neuberger, Surani, Teale, Waldmann & Williams	Laboratory of Molecular Biology, Babraham Institute, Cambridge University, UK
April 1988	Onco-Mouse patent granted	Leder & Stewart	Harvard University, USA
June 1992	First transgenic mouse model created for studying link between DNA methylation and disease	Li, Bestor & Jaenisch	Whitehead Institute for Biomedical Research, USA
1994	First transgenic mice strains reported for producing human monoclonal antibodies	Bruggemann, S.Green, Lonsberg & Neuberger	Cell Genesys, GenPharm, Laboratory of Molecular Biology, UK
July 1996	First cloned mammal, ‘Dolly’ sheep was born.	Wilmut, Campbell	Roslin Institute, UK
July 1997	First sheep cloned with human genes developed	Schnieke, Kind, Ritchie, Mycock, Scott, Wilmut, Colman & Campbell	PPL Therapeutics, Roslin Institute, UK

Date/Year	Major events	People involved	Places
September 2006	First fully human monoclonal antibody drug approved		Agensys, Amgen, USA
2007	Nobel Prize for Physiology and Medicine awarded for discoveries enabling germline gene modification in mice using embryonic stem cells	Capecchi, Evans & Smithies	University of North Carolina, USA University of Utah, USA
September 2015	Beijing Genomics Institute announced the sale of the first micropigs created with the help of the TALENs gene-editing technique		Beijing Genomics Institute, China
October 2015	CRISPR/Cas9 modified 60 genes in pig embryos in first step to create organs suitable for human transplants	Church	Harvard University, USA
April 2017	Diabetes research using transgenic mice shows the protein P2X7R plays important role in inflammation and immune system offering new avenue for treating kidney disease	Menzies	University of Edinburgh, University College London, Imperial College, UK
January 2019	CRISPR-Cas9 used to control genetic inheritance in mice	Grunwald, Gntz, Poplawski, Xu, Bier & Cooper	University of California San Diego, USA

3.1 Bacterial System

Bacterial system dominates the pharma industry facilitating the production of large quantities of pharmaceuticals. In 2010, the total production of pure proteins was 26.4 tons, of which 68% were produced in the bacterial systems and 32% in mammalian systems. The predominant group of proteins produced in bacteria comprised insulins, while most of the products produced in mammalian systems were monoclonal antibodies (Walsh, 2014).

The advantages of this system are its well-understood genetics, cell biology, easy handling, ease in culture, high product yield, cost-effectiveness, easy process scale-up, and short turnaround time (Huang et al., 2017; Kesik Brodacka et al., 2012) (Table 3). The limitations of this system include the absence of post-translational modifications of the proteins, the inability to develop correct disulfide bonds, protein solubility issues, and the presence of endotoxins such as lipopolysaccharides (Zeltins, 2013). Of many bacterial systems, *E. coli* has been the choice of expression system in the Biotech industry for large scale production of small recombinant proteins that do not require post-translational modifications (Sanchez-Garcia et al., 2016).

Table 3. Comparison of efficiency of different production systems of recombinant proteins

(Source: Houdebine, 2009)

Feature	Production Platform			
	Bacteria	Yeast	CHO cells	Transgenic Animals
Yield	+++++	+++++	++	+++++
Investment	+++++	+++++	+	+++
Production cost	+++++	+++++	++	++++
Flexibility	+++++	+++++	+	++++
Stability	+++++	+++++	+++	+++++
Scaling up	+++++	+++++	+	++++
Post-translational modification	+	++	+++++	+++++
Purification	+++	+++	++++	+++
Contaminant pathogen	+++++	+++++	++++	++

3.2 Yeast Expression System

The yeast expression system is another microbial system for producing recombinant proteins where two frequently used yeast species are *S. cerevisiae and P. pastoris (*Gupta and Shukla, 2017). Yeasts are capable of producing recombinant proteins with proper foldings and post-translational modifications (Dalton and Barton, 2014). Earlier study revealed that the *P. pastoris system* was much better than the *S. cerevisiae* system as *P. pastoris* can produce complex, terminally sialylated "humanized" glycoproteins and has a better growth rate *(*Gupta and Shukla, 2017). However, the advantages of the yeast expression system are the rapid growth of the organisms in protein-free media and ability to secrete the product extracellularly. But, the major limitation of the system is the production of undesired hyper-mannosylation *(*Gupta and Shukla, 2017), causing altered protein binding activity and immunogenic response in the body, and relatively low yield, which is much prone to proteolytic degradation (Ahmad et al., 2014).

3.3 Mammalian Expression System

The mammalian expression system is generally preferred for manufacturing biopharmaceuticals. In recent years, a steady increase in the use of this expression system has been observed. The major advantages of this system are the production of large, complex molecules requiring specific post-translational modifications, and the lack of requirement of cell lysis to extract proteins (Dumont et al., 2016). For example, myostatin, a growth regulatory protein having medical importance was successfully expressed in chicken myoblast cell culture (Bhattacharya et al., 2014).

The major limitations of this system are potential safety concerns due to the possibility of contamination with animal viruses, complex nutritional requirements of cell culture, slow growth

and fragility of cells, and relatively high production time and cost (Sanchez Garcia et al., 2016). Some of the popular mammalian expression systems include Chinese hamster ovary (CHO) cells, rodent cell lines (NS0, BHK, and Sp2/0), and human cell lines (HEK293, PER.C6, HT1080, and CAP) (Estes and Melville, 2014). Of all cell lines, CHO cell lines are more popular producing seven of the top ten best-selling biopharmaceuticals produced since the year 2016. In general, the number of recombinant proteins produced in mammalian systems that were approved for use as drugs in humans, increased by 60% from the year 2010 to 2014 indicating the importance of the system for producing biopharma products (Sanchez Garcia et al., 2016).

3.4 Insect Cell Line Expression System

Insect cell based recombinant protein production systems fall in between bacterial and mammalian expression systems. Its main advantage over the bacterial system is the incidence of post-translational modifications, and that over mammalian system is the higher growth rate of insect cells than that of mammalian cells. A few biopharmaceutical products such as Cervarix, a vaccine against cancer causing human papillomavirus, is produced using this system.

3.5 Cell-Free Protein Synthesis

Cell free protein synthesis (CFPS), also called *in vitro* expression is an alternative to the cellular expression of recombinant proteins. This system uses translation machinery extracted from cells; the enzymes, cofactors and substrates required for the transcription and translation processes are present in the cell extract for facilitating gene expression. In comparison to bacterial or tissue culture cells, CFPS is considerably faster because it does not require gene transfection, cell culture, or protein purification. In this system, PCR amplified coding templates are directly used instead of cloned genes in a typical expression vector for expressing the gene. However, the major limitations of this system have been low production rate, high reagent costs, small reaction scales, and limited ability to protein folding. Sutro Biopharma developed STRO001, an antibody–drug conjugate in this system to treat non-Hodgkin lymphoma and multiple myeloma (https://www.lls.org/research/sutro-biopharma).

3.6 Transgenic Animals

With the advancement of biotechnological research, production of transgenic animals has opened a new vista for efficient production of functional recombinant proteins (Table 1). This system has become popular due to low overall cost of producing complex proteins in large volume and involvement of suitable post-translational modification very close to human proteins (Rohricht, 1999a; 1999b). The production cost of an animal platform is around one tenth of the cost of a bioreactor for a cell platform (Dove 2002). It is also possible to produce double or triple-transgenic animals that have two, three or more transgenes that can synthesize multiple biopharmaceuticals in a single animal. Technique in this regard was perfected to develop triple transgenic chicken for three growth regulatory genes viz. myostatin, activin receptor type 2A and activin receptor type 2B (Bhattacharya et al., 2019). However, the major limitation of this system is very low efficiency of production of transgenic animals. It may be noted that transgenic animals as bioreactors are not advocated for consumption, but they would be used as production machine where biopharmaceuticals are produced. Attempts are underway to improve the efficiency of transgenic procedures for the development of transgenic founders so that they can be multiplied to increase the population size.

4. STATUS OF THE TRANSGENIC POULTRY FOR PRODUCTION OF THERAPEUTICS

The choice of a suitable method for expressing a desired protein depends on its features and intended application. In this context, chicken magnum of transgenic birds has been the major bioreactor for recombinant protein production in eggs, although other relevant alternative systems, such as milk, blood, urine, seminal plasma etc. are also available (Lillico et al. 2007; Brondyk, 2009; Murray et al. 2010; Pinkert, 2014). There is a classical example of cost rationalization in transgenic platform where Dyck et al. (2003) calculated the cost of production of a recombinant protein as around US$ 6 per gram in transgenic platform and US$ 48 per gram in cell culture-based system. Under such circumstances, development of alternative platforms for production of recombinant proteins in transgenic animal bioreactor, specifically in egg, is of paramount importance for pharmaceutical industry. This method is hugely beneficial over cell culture-based methods as chicken lay eggs every day and the proteins can be purified from eggs in bulk volume leading to low cost of production. Chicken as bioreactor has certain advantages over other livestock species for transgenesis such as a shorter generation interval and life cycle than other animals; cost of rearing is lesser than others and multiplication rate of birds is also very high as compared to other animals. One hen lays around 300 eggs annually and accordingly, maintaining a poultry flock of thousand birds may produce thousand eggs every day. Quantitatively, it can accumulate kilograms of eggs laid every day. One egg is around 50g in weight and its ovalbumin protein content is around 5-6g per egg. Thus, on every day we may get kilograms of albumin or egg white. Accordingly, we may produce few kilograms of pharmaceuticals every day from a poultry flock. Hence, transgenic poultry may provide an excellent opportunity as a bioreactor for yielding enormous quantities of pharmaceuticals to meet the world-wide demand. Transgenic birds, thus, provide triple advantages of low cost of production, high productivity and good quality of the synthesized proteins (Park et al., 2015), which combine the best attributes related to the success of any biopharmaceutical production platform. A schematic diagram for development, production and commercialization of therapeutics to be produced in the transgenic animals in India has been depicted in Figure 1.

Transgenic chickens produced human recombinant hIFNb1 in the egg white at an average level of 38 mg/L (Lillico et al., 2007). The human epidermal growth factor was produced in eggs of transgenic chicken (Park et al., 2015). Alexion (formerly known as Avigenics Inc.) developed Sebelipase alfa, a recombinant human lysosomal acid lipase (LAL) for enzyme-replacement therapy to treat LAL deficiency (LAL-D) and SBC-103, a recombinant human alpha-N-acetyl-glucosaminidase designed to treat Mucopolysaccharidosis IIIB, a rare and debilitating infant disease in human being. Thus, the use of transgenic hen eggs as live bioreactors could be of immense importance for production of recombinant proteins in high volume desired by the biotech industries. Successes of recombinant protein production along with the advent of new technologies increase the allure of transgenic animals for the production of therapeutic proteins for human being (Hunter, 2019). However, in India, there is no specific guidelines for producing therapeutic proteins in transgenic platform though guidelines are available for cell culture-based methods.

4.1 Regulatory Support and Care at Handling

Biopharming through transgenic approach offers many benefits by producing the needed pharmaceuticals with proper folding and post-translational modification at an affordable cost. However, it requires necessary policy and regulatory support. The US Food and Drug Administration guidelines in this regard may be an example for preparing regulations of drugs

produced in the transgenic animal platform. The transgenic animals developed for this purpose should be properly tagged with wing/leg bands or RFID tag implanted below the skin for easy identification and be maintained in separate shed surrounded by the boundary walls so that these should not be used for consumption, nor be mixed up with other animals in the farm. Proper care, nutrition and management should be provided to the transgenic animals. Disposal of dead transgenic animals or their tissues used for R&D purpose should be properly done following ethical standards of Institute Animal Ethics Committee and guidelines of Institute Bio-safety Committee and/or RCGM and GEAC, and for clinical trials, Central Drugs Standard Control Organization (CDSCO) guidelines should be followed strictly for further commercial release after due approval from the Drug Controller General of India (DCGI).

5. RECOMMENDATIONS

Keeping in view the present regulatory processes for genetic manipulation and production of high value proteins, the following strategic reforms, scientific and statutory system modifications are suggested for assuring faster, efficient and affordable production of the therapeutics using the transgenic poultry platform.

1. Transgenic animals have tremendous potential for biopharmaceutical production and therefore, there is a need to create awareness among the scientists, stake holders and policy makers to adopt these technologies for production of therapeutics at affordable cost so that the prices of such treatments can be brought down *(Action: ICMR, CSIR, ICAR, DBT, DST, Central Drugs Standard Control Organization)*.

2. Initiating research in Transgenic animals needs approval from the Statutory bodies in place in the country to make the research output well accepted for the benefit of humans as well as animals. Hence, the statutory bodies in the country need to have a relook at the regulatory aspects with human touch and make it hassle free. *(Action: DBT, MoEF, DAHD, ICAR, SAUs, SVUs).*

3. Novel technologies such as 'Knock in' through CRISPR/Cas for precise genetic manipulation should be encouraged to generate transgenic animals for the desired purpose such as production of high value proteins, therapeutics etc. *(Action: DBT, ICAR, DST, CSIR, SAUs, SVUs).*

4. Transgenic poultry system may be given preference for production of bio-pharmaceuticals including biosimilars, immunoglobulins, cytokines etc. The therapeutics already developed through transgenic chicken across the globe will provide guidance to develop and commercialize the products *(Action: ICMR, DBT, CSIR, ICAR)*.

5. Since patenting of animals is not allowed in India, appropriate steps may be initiated to patent the developed transgenic chicken as in other countries where these are permitted so that IPR may be protected *(Action: ICMR, DBT, CSIR, ICAR)*.

6. Biosafety guidelines for the development of transgenic animals as bioreactors may be prepared by the DBT (RCGM) so that the scientific community is able to take up such programs to develop transgenic animals for the production of therapeutics, which would be required to be approved by Central Drugs Standard Control Organization (CDSCO) for their release prior to their use for clinical purposes *(Action: DBT, Ministry of Environment & Forest,*

Central Drugs Standard Control Organization).

7. A regulatory framework may be prepared for regulating the drugs produced using the transgenic animal platform *(Action: DBT, Ministry of Environment & Forest, Central Drugs Standard Control Organization).*

8. There is a need to create sufficient infrastructure in the country for transgenic animal research. Necessary funding and incentives for developing transgenic animal platforms are required to produce low-cost therapeutics *(Action: ICAR, ICMR, CSIR, DBT, DST)*.

6. CONCLUSION

The biopharmaceutical market has been developing at a faster rate than the market for other drugs. Biopharma products produced in the transgenic animals have been the major candidate for efficient therapeutic value, voluminous and economical production, and above all accurate post-translational modifications. The demand for biopharma products is increasing on account of the increase in the incidence of chronic diseases, and the growing number of diabetes, cancer, and autoimmune diseases. Insight into the mechanisms underlying various medical conditions has facilitated identification of specific factors and processes triggering the pathological changes, which has transpired continued research on the applicability of biopharmaceuticals in new clinical conditions. The growth of the biopharmaceutical market is significantly influenced by the rapid scientific progress in molecular biology, increases in the knowledge about expression systems, better understanding of the operational processes, and technological know-how related to the scale up of recombinant protein production. Research programs in this area need continued support.

The antibody market, although highly successful, is also becoming very crowded. In some cases, multiple mAbs target the same therapeutic target. The mainstreaming of biosimilar mAbs and potential development of competing products further decreases the competitive pressure and incentive to innovate. To meet the demand for the products, transgenic birds will be the best approach as they can produce a large volume of functional biopharmaceuticals with greater economic efficiency and without sacrificing the animals for further downstream processing. The profile of products through clinical trials suggests that biopharmaceutical approvals over the next few years will continue to be predominantly protein-based rather than nucleic acid- or cell-based.

To realize the potential of transgenic animal platforms in biopharming, a sound regulatory framework, funding for the creation of necessary infrastructure, collaborations in research and creating awareness among all stakeholders will be crucial.

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LIST OF PARTICIPANTS

1. Dr T. Mohapatra, President, NAAS and Secretary, DARE & DG, ICAR, New Delhi
2. Dr A.K. Singh, Vice President, NAAS, New Delhi
3. Dr P. Joshi, Secretary, NAAS, New Delhi
4. Dr R.K. Singh, Former Director, IVRI, Izatnagar, Bareilly, U.P.
5. Dr K.C. Bansal, Secretary, NAAS, Gurugram
6. Dr Subeer S Majumdar, Former Director, NIAB (DBT), Hyderabad
7. Dr A.K. Rawat, Former Advisor, DBT, New Delhi
8. Dr Nitin K Jain, Head, Animal & Livestock Biotechnology Unit, DBT and Member Secretary, RCGM, DBT, New Delhi
9. Dr Arjava Sharma, Former Director, ICAR-NBAGR, Karnal, Haryana
10. Dr V.K. Saxena, ADG (AP&B), ICAR, Krishi Bhawan, New Delhi
11. Dr R.N. Chatterjee, Director, ICAR-DPR, Hyderabad
12. Dr Abhijit Mitra, Director, ICAR-CIRC, Meerut
13. Dr Arun Kumar Tomar, Director, ICAR-CSWRI, Avikanagar, Malpura, Rajasthan
14. Dr T.K. Dutta, Director, ICAR-CIRB, Hisar, Haryana
15. Dr A.K. Tiwari, Director, ICAR-CARI, Izatnagar, Bareilly, U.P.
16. Prof. G Dhinakar Raj, Former Director, DBT Translational Research, TANUVAS, Chennai
17. Dr G. Taru Sharma, Director, DBT- NIAB, Hyderabad
18. Dr P. Kumar, Principal Scientist, Animal Genetics Division, ICAR-IVRI, Izatnagar, Bareilly, U.P.
19. Dr S.V. Rama Rao, Principal Scientist, ICAR-DPR, Hyderabad
20. Dr A.R. Sen, Principal Scientist, ICAR-NRC on Meat, Hyderabad
21. Dr Ajay Mandal, Principal Scientist, ICAR-NDRI ERS, Kalyani, West Bengal
22. Dr Manishi Mukesh, Principal Scientist, ICAR-NBAGR, Karnal, Haryana
23. Dr A.K. Ghosh, Professor, College of Veterinary & Animal Science, GBPUA&T, Pantnagar, Uttarakhand

24. Dr S.K. Bhanja, Principal Scientist, CARI, Izatnagar, Bareilly, U.P.
25. Dr U. Rajkumar, Principal Scientist, DPR, Hyderabad
26. Dr T.K. Bhattacharya, Principal Scientist, DPR, Hyderabad
27. Dr L.L. Prince, Principal Scientist, DPR, Hyderabad
28. Dr V. Vohra, Principal Scientist, NDRI, Karnal, Haryana
29. Dr N. Ganguli, Scientist D, NIAB, Hyderabad

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