AIV vaccine and YEBIO

Liqiao Zhou
Vice General Manager

Yebio Bioengineering Co., Ltd
China Animal Health & Epizootiology Center

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I. A brief Introduction of Qingdao Yebio Bioengineering Co. Ltd

1. Qingdao Yebio Bioengineering Co. Ltd:
   ----Regulated by the China Animal Health & Epizootiology center (National Animal Quarantine Institute, MOA)
   ----Research, development, production, sales and technical services of veterinary vaccines, diagnostic reagents and relative products.
   ----has 386 staff.
   ----Production capacity is 1.6 billion ml inactivated vaccine annually.
   ----One of largest production capacity, the most advanced production and purification system in China

2. Honors Gained by Yebio
   —MOA Funded Key animal Bioproduct Enterprise
   —One of a group of Avian Influenza Vaccine manufactures appointed by MOA
   — Only State Technology Center in the industry
   —Qingdao New High-Tech Enterprise
   —Standing member of “Bioproduct Branch of China Society of Animal Husbandry and Veterinary Medicine”

3. Location and environment:
   - The plant is located between East and West Dayang Village at Hongdao town, Chengyang District, Qingdao.
   - The site is surrounded by sea on three sides, only 500 m from the nearest coast, with beautiful environment and fresh and clean air, and without any contamination sources nearby.

4. GMP workshop
   The animal Inactivated Vaccine Plant includes inactivated vaccine production workshop, quality test laboratory, experimental animal facility, white oil processing workshop, sewage treatment unit etc. The production workshop was approved by MOA and started to build in 2002 completed in 2003 and passed GMP inspection by MOA. The investment amounted to 52.8 million Yuan with a total building area of 7200 m² including negative pressure clean area of 3200 m².
   ----Production workshop: On the first floor are the finished product store rooms(2-8°C), package material store room, raw material store rooms, label store room, machinery room, pure water preparation room, sewage treatment, fumigation room, pre incubation etc. On the second floor are the finished packaging room and dispensing room with local 100 G cleanness under 10000 G cleanness, emulsification room with 10000 G cleanness; solution preparation room, concentrates inactivating room, waste treatment room and laboratory with 10000 G cleanness; seed virus preparation room with local 100 G cleanness under 10000 G cleanness environment.
   There are 3 separated live virus reproduction and harvest areas under negative pressure. Air
into and out of clean areas will be filtrated continuously through preliminary performance, middle and high performance and high performance filters and discharged air will be filtrated through double high performance filters. At the same time, the air cleaning system of each production operation area is relatively independent so as to prevent cross contamination. Materials are transmitted in the closed tanks and tubes. In the pressure clean areas, there are air tight locks for staff and material movement.

There is change room and buffer room between clean and common areas, there is a second change room at the entrance of clean production area, and There is a shower cubicle in negative pressure area. At each lift there is a buffer room to prevent influences from outside factors.

On the third floor are the sample reception room, quality control file room, routine laboratory, seed virus room, virology laboratory, cell culture and bacteria laboratory

5. Animal facility
Experimental Animal facility is composed of two parts: immunized animal house & virulent (challenged) animal houses that all designed in compliance with GMP requirements . All the experimental chickens are SPF chickens raised in negative pressure isolators and all the animal experiments are conducted in same condition

II. Wastes Treatment and Biosafety
1. Waste gas sources, treatment and disposal: Cleaning when moving in and out. Filtration by air conditioning and cleaning system with active carbon, the discharged gas can entirely meet the secondary standard requirements in 《Stinking Contaminant Discharge Combined Standard》 (GB 14554-93). To prevent the live virus spreading into atmosphere, the discharged gas from the 3 production units is treated in the following ways:
   a. The production units are designed in the negative pressure;
   b. Operations of live virus are performed in 100 G cleanliness lamination hooves with separated air-conditioning systems;
   c. The discharged gas is filtrated by double high performance filters, and the quality of gas entirely meets the national GMP standard on air cleanliness requirements;
   d. Specialists are appointed to carry out regular inspections and services, timely change the filtrating membranes and conduct disinfection treatments
   e. Spare power generator set is provided to ensure normal operation of various systems (in case of power off).
2. Waste water sources, treatment and disposal
   a. Waste water containing live microorganism and other without live microorganism are treated separately;
   b. Waste water with live microorganisms is discharged to sewage treatment after heat disinfection, Oil-containing waste water is separated by separator after heat disinfection, the oil part is discharged as garbage and the water part is discharged to the sewage treatment system;
   c. Waste water and mixed wastes from virulent animal house is steam treated;
   d. Public waste water is led to the sewage treatment system after sedimentation in septic tanks.
3. Solid wastes treatment
Solid wastes mainly include animal carcasses, chicken embryos, duck embryos and the used solid media.

a. The challenged animal are directly collected in the heat-resistant plastic bags after death or slaughter and autoclaved and then cinerated;
b. Chicken embryos are autoclaved in special containers and can be used as fertilizer;
c. The used solid medium is autoclaved in special container and sent to garbage station for treatment;
d. The activated sludge from sewage treatment system are collected, packed and dewatered and used as fertilizer for trees and grass in the campus

III. AIV (H5) Inactivated Vaccine Production and Quality Management

1. Seed management
Seed virus (H5) provided by Harbin Veterinary Research Institute is a low pathogenic avian influenza virus strain. It is stored in the Quality Control Laboratory after registration. Seed virus reproduction and identification are conducted using SPF chicken embryos according to 《Stock Virus Reproduction Standards》 by MOA.

Seed virus storage and release: Master seed and production seed virus are stored at –70℃ in Quality Control Laboratory by means of double persons and double locks management. Production seed virus is released strictly on release procedures.

2. Seed Virus Preparation Production Methods
Eggs used in production are from Non AI vaccinated chickens in Yebio’s experimental breeding chicken farm.

3. Process Control
The quality assurance (QA) persons of plant are responsible for the entire process control and each important link who are governed directly by the full time quality control chief (vice general manager), who is responsible both for Yebio’s product quality and to China Control Institute for Veterinary Pharmaceuticals. At the same time, the latter Shandong Provincial Control Institute of Veterinary Medicine dispatch inspectors to the plant to assist supervision and control.

Person in charge of each production inspection line are responsible for the quality and results in his (her) production inspection line.

4. Batch Control
Batch control is strictly conducted in compliance with 《Management Methods of Veterinary Bioproduction》 and 《The Procedure of Production and Detection of AIV Inactivated Vaccine》 .

One final mixing tank is considered as one batch.

5. Finished Products Test
Finished products test includes inspection of physical properties (appearance, formulation, stability, viscosity etc), sterile, safety, efficacy and preserve concentration (formal clehyde, thimerosal)
IV. New branch of Yebio in Hangzhou

As the principal investor, Qingdao Yebio is establishing new biotech company— Zhejiang Yebio. The company was formally registered and founded in April, 2005 in Xiasha Economic Development Area of Hangzhou, the Zhejiang Provincial Capital. Bioproduct GMP workshop with an annual production capacity of 11.8 billion doses will be completed in June, 2006 and will be put into operation in September.

V. Summary

- Yebio has 3 years experience for AIV vaccine production.
- Yebio is the biggest provider for inactivated AIV vaccine in China.
- Yebio has the capacity to produce the high quality and safe AIV vaccine.
- Yebio has a potential and interest to produce pandemic influenza vaccine for human use.

VI. Suggestion

- Establish cooperation with other veterinary vaccine manufactures and human influenza vaccine manufactures.
- Share the information and technique each other.
- Improve and increase the hardware of veterinary vaccine manufacture to meet the requirement of human influenza vaccine manufacturing.
- Adjust and coordinate the international regulations to meet the demand of prevention for pandemic influenza virus.