

Joint WHO/OIE/FAO consultation on the feasibility of producing human vaccines in veterinary vaccine facilities

Objective

The purpose of the Consultation was to discuss and review issues on the technical and regulatory feasibility of using veterinary production facilities to produce human influenza pandemic vaccines.

The expected outcomes were as follows:

- a. Preliminary assessment of the feasibility of using veterinary vaccine production facilities to produce pandemic influenza vaccine in order to reduce the expected supply shortage;
- b. Explore interest from the veterinary vaccine industry and current vaccine manufacturers to be involved in such development;
- c. Preliminary assessment on differences of regulatory requirements between human and veterinary influenza vaccines;
- d. Contribute to build a relationship between veterinary and human vaccine manufacturers, NRA responsible for human medicines and international organization WHO/OIE/FAO.

Questions for discussion

- Could veterinary manufacturers produce and license human vaccines? If it is possible discuss on costs versus benefits;
- Could veterinary manufacturers produce some raw materials such as allantoic fluids or concentrated antigen, or could they be responsible for the whole production process?
- Do veterinary vaccine manufacturers currently have extra capacity which could be used for the manufacture of human influenza vaccines?
- What could be WHO's role?

Identification of the Challenges

National Regulatory Authorities (EMEA-EU, FDA-USA, SFDA-China, TGA-Australia, ANVISA-Brazil and Ministry of agricultures of these countries) and vaccine manufacturers (EU, USA, Mexico and China), made presentations trying to identify gaps, potential obstacles on vaccine production and regulations; and also veterinary companies and regulators proposed alternative solutions to overcome those issues. Below is a list of issues which have come out from the discussion.

- Lack of information on production capacity for veterinary vaccines as HA content is different. What is the veterinary manufacturers' capacity to process eggs?
- So far there is no product profile available for a pandemic vaccine; there are several clinical trials ongoing to define antigen content, strain, with or without adjuvant, whole versus split virus, live attenuated vaccines, etc.

- Potency test standardization, this assay needs to be standardized with reference materials among labs and vaccine manufacturers to compare vaccine efficacy;
- Veterinary industry does not measure the antigen content for potency test as a release criteria;
- Some regulatory requirements between veterinary and human products need to harmonize. OIE/WHO, FDA/EMA/others should work on this subject;
- During a pandemic, will there be sufficient batch release capacity at National Control Labs in NRAs to assure the quality of the vaccine? This issue should be addressed by the NRAs and WHO to develop standard procedures;
- Would new clinical trials for human vaccines produced in veterinary facilities be needed? In principle, if the whole process, technology and equipment are the same, it might not be necessary. This is something that must be analysed in case by case bases and balanced in the context of an emergency;
- Regulatory pathways to speed the licensing process for human vaccines produced in veterinary plants needs to be developed;
- Liability: there is a need to decide in advance who will take liability for a joint production undertaken by human or veterinary vaccine manufacturers
- Egg supply might not be enough, and alternatives to increase production capacity need to be addressed;
- There are differences between human and veterinary vaccines production process and quality control tests; e.g. downstream process such as purification and inactivation, in quality control, adventitious agents test as part process control in veterinary vaccines is not currently implemented. There will be a need of investments in downstream facilities in veterinary facilities;
- One of the bottlenecks in increasing production capacity is the purification process. Currently, the purification yield for human vaccine is around 65 %; in veterinary vaccines the purification process is very simple;
- Biosafety containment in manufacturing plants: some veterinary vaccine manufacturers will need to upgrade their facilities to produce pandemic human vaccines.

Potential solutions

Production capacity:

- Explore interest in production agreements between human and veterinary vaccine producers. From antigen bulk to finish product as part of the strategy to increase production capacity;
- Explore technology transfer agreements between human vaccine manufacturers to veterinary vaccines manufacturers. Analyse also potential IP rights;
- Public/Private funds available to invest in downstream capacity, cell culture technology, upgrade of biosafety levels. (This option could be part of the Global Action Plan to increase pandemic influenza supply);
- Direct public investment to production and stockpile in non-formulated bulk of vaccine antigen corresponding to currently circulating avian strains will permit a quicker response to the pandemic.

Regulatory issues:

- Public funds available for clinical trials to show immunogenicity and safety. In some cases if it is a technology transfer and production process, equipment and vaccine specification are the same than the product produced in human vaccine facilities, additional clinical data might not be needed. Regulator should further discuss this issue;
- NRAs should discuss various alternatives for egg supplies in a potential emergency situation;
- Explore different scenarios with countries, for governments to waive liability in an emergency situation.

Conclusions

- In principle, the option of producing vaccine for human use in veterinary vaccine manufacturing plants is technically feasible. However, large investments might be needed, e.g. for purification facilities. A cost versus benefit analysis should be done to further assess this as an option and later to justify investments.
- There is low market forces for influenza vaccines, so public funds will be needed to move this option forward, e.g. financing of clinical trials, investing in upgrade veterinary facilities.
- WHO should define the targeted product profile of an influenza vaccine needed in case of a pandemic. This is one of the expected outcome from WHO consultation on the development of a global action plan to increase pandemic vaccine supply.
- The veterinary vaccine industry showed variable interest for this option.
 - IFAH is willing to contribute to a global action plan to increase pandemic vaccine supply, provided some obstacles are overcome e.g. required investments.
 - China and Mexico showed interest to explore this as an option.
 - In the USA and Brazil the veterinary industry has not discussed this issue yet.
- FDA and USDA do not have particular concerns on regulatory issues for emergency use of vaccine produced entirely or partially (in US, EU, respectively) veterinary vaccine manufacturing facilities. EU has already procedures in place for licensing veterinary and human products produced in the same facilities. In some other countries this issue has not been discussed yet.
- Regarding GMP, some veterinary facilities already have the same GMP standards than human vaccine production facilities. A technology transfer would still be needed as the production processes are different
- Using veterinary facilities just for antigen bulk production will not be a solution if they do not take the full process. If veterinary plants increase their antigen production capacity, there will still be a bottleneck for purification processing in human vaccine manufacturing plants.
- Intellectual Property Rights issues need to be addressed in the technology transfer agreements between veterinary and human vaccines.

- The size of the increased capacity and their impact on pandemic vaccine supply potentially provided by this option needs to be thoroughly evaluated.