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## Research article

# Avian influenza vaccine supply chain in Quang Ninh province, Vietnam, 2021

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## Abstract

Highly pathogenic avian influenza (HPAI) is a zoonotic disease that can affect both poultry and humans. Since 2005, the Vietnam government has implemented a national vaccination campaign to prevent the spread of avian influenza (AI). In 2021, the first outbreak of HPAI H5N8 was reported in a chicken farm in Quang Ninh province. To gain a comprehensive understanding of the chain and its relevance to HPAI vaccination in various aspects, and to identify and comprehend the stakeholders involved in the AI campaign and their roles within the vaccine supply chain. A cross-sectional study was conducted from Nov-2021 to Jan- 2022. We purposively selected 114 participants, including 71 poultry farmers using HPAI vaccines, 16 veterinary drug store owners, 18 commune animal health workers (CAHWs), 8 staff from the Centers for Agricultural Services (ATSCs), and one vaccine distributor who were interviewed face-to-face using a structured questionnaire. Three HPAI vaccines (H5N1 clade 1 & 2.3.2.1, H5N1 clade 2.3.4, and H5N1 clade 2.3.2.1b) were used. Distributors stored vaccines at the required temperature and transported them in appropriate vehicles. Vaccines remained in the supply chain for 3–5 months within their 12-month shelf-life period. The free government vaccination campaign, implemented by CAHWs, and administered by the ATSCs, reached 61% of small-scale poultry farms with a 1.19% vaccine wastage rate. Large-scale poultry farms followed the national campaign but paid a fee for the vaccines. We recommend expanding the support for AI vaccination to increase the vaccination rate among large-scale poultry farms, selecting higher efficacy seed vaccines, and that smaller dose vaccine vials are available for cost-effective vaccination.

**Keywords**: Highly pathogenic avian influenza, Quang Ninh province, Vaccination campaign, Vaccine supply chain, Vietnam

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# INTRODUCTION

Highly pathogenic avian influenza (HPAI) is a transmissible disease from birds to humans (Pfeiffer et al., 2007). During 2003 to 2011, Highly pathogenic Influenza A virus subtype H5N1 (A/H5N1) outbreaks were reported in 63 countries and territories. (FAO, 2011). In Vietnam, the first HPAI outbreak by A/H5N1 subtype occurred in December 2003, with more than 5,000 outbreaks detected by 2015, destroying approximately 60 million poultry (DAH, 2013), and infecting 127 people, including 64 fatal cases (WHO, 2021).

In 2014, the HPAI A/H5N6 virus was introduced in the country causing severe clinical disease in pheasants and chickens, and asymptomatic infection in ducks (FAO, 2014). In April 2021, the HPAI A/H5N8 virus was recorded in the country, and the first A/H5N8 virus outbreak occurred on a chicken farm in Quang Ninh province in June 2021 (DAH, 2021a).

Quang Ninh province is in the Red River delta region. The province borders with China to the north. Hills and mountains cover 80% of the mainland area, but the province also has over 2,000 islands (Figure 1). From 2010 to 2021, 136 poultry farms in 43 communes in 15 districts of Quang Ninh province reported outbreaks of HPAI A/H5N6 and H5N8 with 136,459 poultry destroyed. During 2020 to 2021, HPAI outbreaks were found in some vaccinated flocks.


**Figure 1** Geographic location of Quang Ninh province, Vietnam (red colour area).

To control HPAI, the government of Vietnam has applied several measures such as active and passive surveillance, movement control, culling of infected poultry flocks and vaccination. Vaccination is considered as a protective factor for poultry against HPAI (Phuong et al., 2018).

In Quang Ninh province small-scale poultry farms (flocks of < 1000) are supported with the provision of AI vaccines and vaccination services through an annual AI vaccination campaign financially supported by the national government. The campaign takes place in two phases each year and includes identifying and recording the poultry eligible for vaccination, raising awareness about AI disease and the benefits of AI vaccination, and carrying out the vaccination process.

The supply chain has been utilized to understand the production or use of antibiotics in livestock farming. The study in Thailand in 2020 conducted by Aniroot (Aniroot et al., 2020) used the supply chain to investigate the use of antibiotics in pig and poultry farms. The research identified relevant stakeholders involved in the appropriate use of antibiotics in these farms, specifically provincial and regional livestock officers, farm veterinary consultants, cooperative management, contract farmers, cooperative farmers, and independent farmers. Another study in Thailand in 2021 conducted by Banthita (Banthita et al., 2021) examined pet fish stores as a link in the fish supply chain. The study provided detailed information such as the species of fish sold and disease management practices. However, the study did not address other links in the supply chain, such as fish farms or buyers, and therefore did not provide a comprehensive overview of the entire fish supply chain.

Vaccination against HPAI depends on many factors: an efficient supply chain with proper vaccine storage, correct dosage during administration, vaccine matching for circulating strains, and vaccine technology (live vaccine or inactivated vaccine). However, there are few studies on the HPAI vaccine supply chain and its capacity to maintain vaccine quality in Vietnam. Identifying and understanding HPAI supply chain factors could improve the effectiveness of the vaccine supply chain and increase AI vaccinations in Quang Ninh province. We conducted this study to gain a comprehensive understanding of the chain and its relevance to HPAI vaccination in various aspects, and to identify and comprehend the stakeholders involved in the AI campaign and their roles within the vaccine supply chain. By achieving these objectives, we aim to enhance the efficiency of the vaccine supply chain and promote increased AI vaccinations in Quang Ninh province.

## MATERIALS AND METHODS

We conducted a cross-sectional study in Quang Ninh province from November 2021 to January 2022 and AI vaccine usage from January 2021 to December 2021 were reviewed and collected for this research. Based on knowledge of supply chain collected from previous studies, and consulting with the veterinaries of the Quang Ninh Sub DAH about the AI vaccine supply chain in Quang Ninh. There were three steps of the study: identify stakeholders involved in the supply chain of HPAI vaccines; conduct face-to-face interviews with identified stakeholders using a structured questionnaire; and develop HPAI vaccine supply chain diagrams for both small- and large-scale poultry farms. We defined small-scale poultry farms as those with flocks of < 1000 birds, and large-scale poultry farms as those with flocks of ≥ 1000 birds.

From a list of poultry farms using HPAI vaccines provided by Quang Ninh Sub-Department Animal Health (Sub-DAH). By convenient method sampling, we selected poultry farms with a history of HPAI outbreaks and poultry farms without outbreaks. These selected poultry farms were located in 9 communes spanning 6 out of the 13 districts of Quang Ninh province. Furthermore, by convenient method sampling following suggestions from veterinarians of the Quang Ninh Sub DAH, we enlisted veterinary drug stores in 11 communes across 7 districts, commune animal health workers (CAHWs)

from 18 communes in 9 districts, and Animal Health and Technical Service Centers (ATSCs) from 8 out of the 13 districts. We also identified three HPAI vaccine distributors in Quang Ninh.

A structured questionnaire was developed with both closed-ended and open-ended questions. The questionnaire focused on the HPAI vaccine supply chain stakeholders, types of HPAI vaccines, storage and distribution, and loss of AI vaccines in the vaccine supply chain. All interviews were conducted by trained staff from Regional Animal Health Offices 2 (RAHO2) and the Quang Ninh Sub-DAH. We transferred the data to Microsoft Excel 2007 and analyzed it descriptively. To identify the poultry population of Quang Ninh province in 2021 and the AI vaccination rate, we transferred secondary data from the Quang Ninh Sub-DAH to Microsoft Excel 2007 and analyzed it descriptively.

### Ethical considerations

Participants in this study were informed about the study's research topic and objectives. Each participant signed a voluntary consent form. The study protocol was accepted by the Medical Ethics Committee of Hai Phong University of Medicine and Pharmacy, Decision number 02/HDDD, November 24, 2021.

## RESULTS

### Stakeholders of the HPAI vaccine supply chain

There were six key stakeholders involved in the HPAI vaccine supply chain in Quang Ninh province: the Government of Vietnam, vaccine distributors, ATSCs, veterinary drug stores, CAHWs, and poultry farms using the vaccines.

#### The Government of Vietnam

The Vietnamese government implemented a national AI vaccination campaign focused on AI prevention and control starting in 2005. Each year, the government monitors and evaluates the strains of AI circulating in Vietnam, and then assesses the effectiveness of the vaccines available and grants licenses for their importation or production and distribution. Each province then develops a vaccination plan based on the number and type of poultry farms and HPAI outbreaks. Following the national AI vaccination campaign objectives, Quang Ninh province supported small-scale poultry farms to obtain AI vaccines and vaccination services. Large-scale poultry farms in Quang Ninh province were required to purchase AI vaccines and vaccinate their own poultry.

#### Vaccine distributors

In 2021, there were three distributors of HPAI vaccines in Quang Ninh province: Two distributors imported H5N1 clade 2.3.4 and H5N1 clade 2.3.2.1b vaccines from China; the third distributor was a domestic manufacturer for H5N1 clade 1 & 2.3.2.1 vaccines. All three distributors had marketing staff to distribute the vaccines to the Sub-DAH, ATSCs and veterinary drug stores. However, the cold storage facilities of all three HPAI vaccine distributors were in Hanoi, and they would only dispatch the vaccines to Quang Ninh province on demand. Only the domestic manufacturer agreed to participate in the study.

**Agricultural Technical Service Centers (ATSCs)**

An ATSC in each of the 13 districts in Quang Ninh province was established in 2016 through a merger process between the Veterinary Station and the Plant Protection Station in each district. We interviewed 8 of 13 ATSCs in Quang Ninh. The ATSCs were responsible for animal disease prevention and control in their respective districts, including implementing the AI vaccination campaign. Income from vaccine sales made up less than 25% of the total revenue of the ATSCs, and the budget to maintain operations primarily came from the government. ATSCs purchased vaccines twice a year according to the instructions and recommendations of the DAH and included H5N1 clade 1 and 2.3.2.1 vaccines from a domestic manufacturer. Records of importing and exporting vaccines and discarded damaged or expired vaccines were available. During the AI vaccination campaign carried out twice during 2021 the proportion of vaccinated poultry was 60.94% (1,664,658/2,731,444), (Table 1).

**Veterinary drug stores**

Out of the veterinary drug stores in Quang Ninh province, we selected 16 for our study. Interviews were conducted with one veterinary officer from each of these licensed drug stores. The results revealed that the veterinary officers had an average age of 41 (SD 10) and possessed vocational school or higher education. Veterinary officers were trained by the Quang Ninh Veterinary Department or the vaccine distributors. On average, the stores had been in business for approximately 9.2 years (SD 6.2) with 2 to 5 employees each. In these stores, three different types of vaccines were sold, including H5N1 clade 1 & 2.3.2.1, H5N1 clade 2.3.4, and H5N1 clade 2.3.2.1b, following the recommendations of the DAH or distributors. Records of buying and selling vaccines were available.

**Commune Animal Health Workers (CAHWs)**

Our study involved interviews with 18 out of the 130 Commune Animal Health Workers (CAHWs) in Quang Ninh province. The average age of the CAHWs was 41 (SD 8), with 11 being male and 7 females. Their educational backgrounds varied from secondary school to university, and on average, they had 7 years of experience in veterinary work (SD 3). Each commune had an average of 1–2 CAHWs responsible for preventing and controlling animal diseases. The CAHWs were directly involved in administering vaccines to small-scale poultry farmers.

**Poultry farms**

Small scale poultry farms: In our study, we conducted interviews with a total of 63 farmers from small-scale poultry farms. Among them, 11 farms had a history of HPAI A/H5N6 outbreaks after using the H5N1 clade 1 & 2.3.2.1 vaccine, while the remaining 52 farms did not have any history of HPAI outbreaks. We found that these small-scale poultry farmers lacked skills in animal husbandry and had limited knowledge about disease prevention and AI vaccines. The CAHWs injected two doses of AI vaccine to poultry per year: dose 1 from March to May; and dose 2 from September to October.

### Large-scale poultry farms

Our interviews also included 8 large-scale poultry farmers. Among them, three farms had a history of HPAI A/H5N6 outbreaks. One farm had used the H5N1 clade 1 & 2.3.2.1 vaccine, another farm had used the clade 2.3.4 vaccine, and the third farm had used the clade 2.3.1b vaccine. One farm had a history of A/H5N8 outbreaks that used H5N1 clade 1 & 2.3.2.1 vaccine. Four farms had no history of HPAI outbreaks. These large-scale poultry farmers had good knowledge of animal husbandry, vaccination, and poultry diseases. These farms had good hygiene and biosafety practices. The type of AI vaccine was chosen based on the advice of the ATSCs or veterinary drug stores. Farm owners regularly contacted the ATSCs to receive information on diseases, livestock knowledge, and vaccination activities. They also reported livestock data and data on AI prevention to the ATSCs for monitoring and management purposes. These farmers paid for the vaccines for their broilers (one dose per year) and layers (two doses per year) and vaccinated their own poultry.

## Supply chain diagram

### Types of HPAI vaccines in the vaccine supply chain

Three types of HPAI vaccines (H5N1 clade 2.3.4, H5N1 clade 2.3.2.1b and H5N1 clade 1 & 2.3.2.1 vaccines) were distributed in Quang Ninh province. At the ATSCs, only vaccine H5N1 clade 1 & 2.3.2.1 was stored and distributed. We identified that 3,329,316 doses of H5N1 clade 1 & 2.3.2.1 vaccines were used during the study period that accounted for 60.94% of the total poultry flocks. (Figure 2, Table 1). At the sixteen veterinary drug stores we explored, we found three different types of vaccines were available for sell. Large-scale poultry farms purchased 470,000 doses per year including H5N1 clade 1 & 2.3.2.1 (39.4%), H5N1 clade 2.3.4 (20.2%), and H5N1 clade 2.3.2.1b (40.4%). (Figure 3).

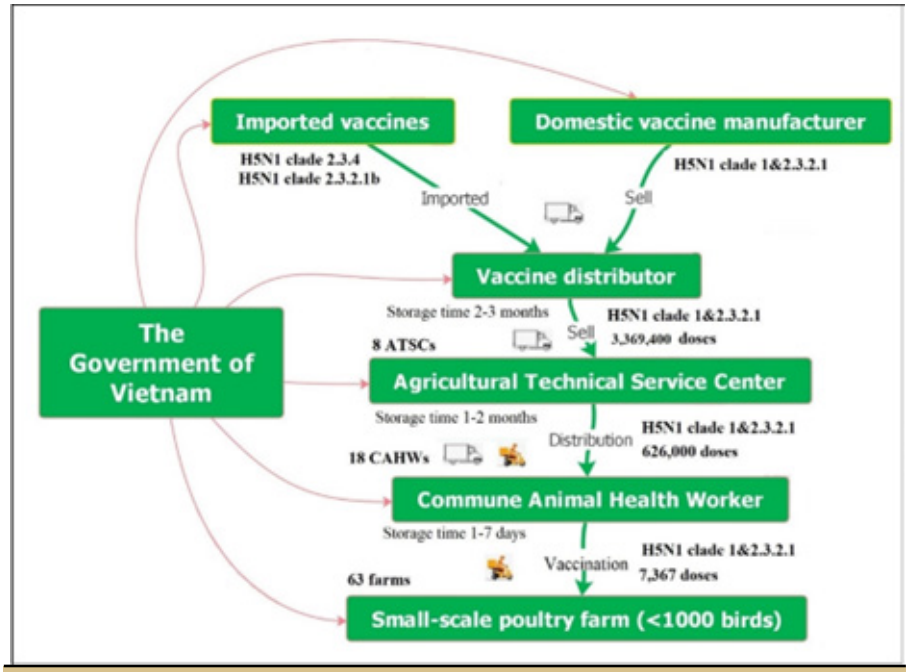


**Figure 2** Avian Influenza vaccine supply chain from distributors to poultry farms with <1000 birds in Quang Ninh province, Vietnam, 2021

* The loss of HPAI vaccines occurs during the administration of vaccines to small-scale poultry farmers by CAHWs. The vaccine waste rate was 1.19 %.

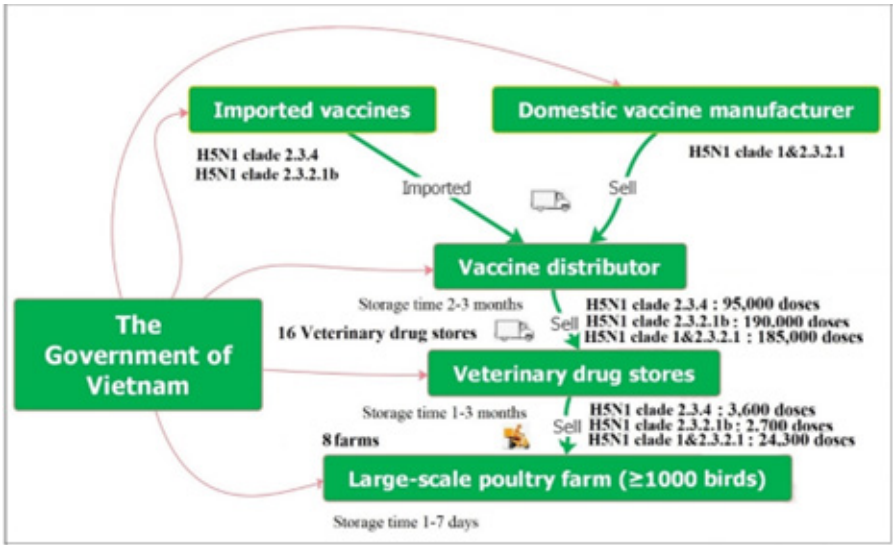


**Figure 3** Avian Influenza vaccine supply chain from distributors to poultry farms with ≥1000 birds in Quang Ninh province, Vietnam, 2021.

**Table 1** Animal Health and Technical Service Centers (ATSCs) in the vaccine supply chain in Quang Ninh province, 2021

| ID | District | Total delivered doses per year | Injected doses for one dose (2 doses/year) | Poultry population (% AI vaccine cover*) | Storage time | Storage equipment | Loss of vaccine per year (%) |
|---|---|---|---|---|---|---|---|
| 1 | Binh Lieu | 154,400 | 75,658 (151,316) | 95,100 (79.56) | 2 months | Refrigerator | 3,084 (2.00) |
| 2 | Dam Ha | 505,000 | 250,000 (500,000) | 339,000 (73.75) | 1 months | Refrigerator | 5,000 (0.99) |
| 3 | Dong Trieu | 1,005,000 | 500,000 (1,000,000) | 1,027,300 (48.67) | 1 months | Refrigerator | 5,000 (0.50) |
| 4 | Ha Long | 256,200 | 125,000 (250,000) | 190,868 (65.49) | 2 months | Refrigerator | 6,200 (2.42) |
| 5 | Hai Ha | 525,200 | 260,000 (520,000) | 308,050 (84.40) | 2 months | Refrigerator | 5,200 (0.99) |
| 6 | Mong Cai | 252,600 | 125,000 (250,000) | 176,016 (71.02) | 1 months | Refrigerator | 2,600 (1.03) |
| 7 | Tien Yen | 422,200 | 207,000 (414,000) | 399,810 (51.77) | 2 months | Cool room | 8,200 (1.94) |
| 8 | Uong Bi | 248,800 | 122,000 (244,000) | 195,300 (62.47) | 1 months | Refrigerator | 4,800 (1.93) |
| | Total | 3,369,400 | 1,664,658 (3,329,316) | 2,731,444 (60.94) | 1-2 months | | 40,084 (1.19) |

Note:

* % AI vaccine cover = Injected doses for one doses/ Poultry population *100

** Loss of vaccine per year (%) = (Total delivered doses per year - Injected doses for two doses)/ Total delivered doses per year*100

**The storage and distribution of HPAI vaccines**

For small-scale poultry farms: Vaccines were usually stored in vaccine manufacturers' warehouses or the vaccine distributors' cool storage for approximately 2-3 months from the production date. After that vaccines were sold and transported in cool vans from distributors to ATSCs within 3–4 hours at controlled temperatures. ATSCs stored and distributed the HPAI vaccines to small-scale poultry farms within 1-2 months of receiving the vaccine and were temperature-controlled daily. There were plans to prevent power outages by having backup generators or uninterruptible power supplies. CAHWs usually spent 10 minutes to 1 hour using a motorcycle with a cooling box to transport the AI vaccine to small-scale poultry farms. The poultry were usually vaccinated on the day of delivery; if not, the vaccines could be stored in the farm's refrigerator for up to 7 days (Figure 2).

**For large-scale poultry farms**

Vaccines were imported from abroad or purchased from domestic manufacturers by vaccine distributors. Then the vaccines were usually stored in vaccine manufacturers' warehouses or the vaccine distributors' cool storage for approximately 2-3 months from the production date. When the vaccines were sold, they were transported to veterinary drug stores within 3–4 hours at controlled temperatures. The vaccines were then stored for approximately 1–3 months in a temperature-controlled environment. Each facility prevented power outages by having backup generators or uninterruptible power supplies. Large-scale poultry farmers came to the veterinary drug stores to buy the recommended AI vaccines. The vaccines were then transported by motorcycle in refrigerated containers for approximately 10-60 minutes to the farms (Figure 3).

**The vaccine wastage in the vaccine supply chain**

In the vaccine supply chain, the loss of HPAI vaccines occurred during the administration of vaccines to small-scale poultry farmers by CAHWs. The AI vaccines were delivered were to the communes through CAHWs for vaccination purposes. The AI vaccine wastage per year was calculated by subtracting the total number of delivered vaccine doses per year from the number of injected doses to poultry during that year. In 2021, the vaccine waste rate was 1.19 % (40,084/3,369,400), (Table 1).

## DISCUSSION

Our study identified the links involved in the HPAI vaccine supply chain for Quang Ninh province, Vietnam. We gained a better understanding of the stakeholders, types of HPAI vaccines available, the storage and distribution processes and vaccine wastage within the chain. We identified that the ATSCs were an important link in the supply chain, especially for small-scale poultry farms.

During our research, we observed the roles of six key stakeholders in the HPAI supply chain. The ATSCs received, stored and distributed HPAI vaccines, the majority to small-scale poultry farms, while the vaccination of poultry was carried out by CAHWs under supervision of the ATSCs. The AI vaccination rate in Quang Ninh province accounted for almost two-thirds of

the total poultry in the province. The report on vaccination rates in Quang Ninh province in 2020 indicated a vaccination rate for poultry of approximately 93% (Van.T, 2020). Therefore, approximately 32% of poultry were vaccinated from other sources, including large-scale poultry farmers who purchased vaccines from vaccine distributors and veterinary drug stores.

In Quang Ninh province in 2021 there were three avian flu vaccines distributed, including H5N1 clade 2.3.4, H5N1 clade 2.3.2.1b and H5N1 clade 1 & 2.3.2.1 vaccines. Of these, H5N1 clade 1 & 2.3.2.1 accounted for the largest quantity, compared to the other two vaccines.

The selection of HPAI vaccine types in each province depends on the circulating strain of HPAI viruses in that province. Every year, the Department of Animal Health (DAH) issues a notice on the strains circulating in each locality, as well as the effectiveness of AI vaccines available in Vietnam against the circulating strains (DAH, 2022b). The DAH also tested HPAI vaccine by challenging the virulence of the virus (DAH, 2022a), (DAH, 2021b). In addition, the results of our study identified that three types of AI vaccines were sold in Quang Ninh province. The H5N1 clade 1 & 2.3.2.1 vaccine was more suitable than the other two AI vaccines with an effectiveness ranging from 70 to 100% against the H5N6 clade 2.3.4.4h strain and achieving 100% protection against the H5N8 clade 2.3.4.4b strain (DAH, 2022a).

However, due to the rapid mutation of AI viruses, there were still cases of vaccinated poultry farm experiencing outbreaks in 2021. This study revealed that 15 poultry farms, including both large- and small-scale farms, that had previously used any of the three available AI vaccines in Quang Ninh province, still experienced outbreaks of HPAI. Several factors in Quang Ninh supply chain could have contributed to this, but continued attention should be given to selecting newer and more effective vaccines to achieve high effectiveness in the prevention and control of AI outbreaks. In the vaccine effectiveness evaluation conducted by the DAH, there were still some vaccines that had very good efficacy against the H5N6 clade 2.3.4.4h and H5N8 clade 2.3.4.4b strains that were circulating in Quang Ninh, such as seed viruses NIBRG-14/ A/ Hubei/1/2010(H5N1)-PR8-IDCDC-RG30 or H5 D7/rD8, both of two vaccines have effectiveness ranging from 90 to 100% against the H5N6 clade 2.3.4.4h strain and achieving 100% protection against the H5N8 clade 2.3.4.4b strain.
We found that the distribution and storage of AI vaccines in Quang Ninh met the technical requirements for cold storage and transportation. The vaccine distributors, ATSCs, and veterinary drug stores had adequate storage equipment and suitable monitoring systems. Their transportation processes complied with the technical requirements for AI vaccine storage during transportation, contributing to minimal vaccine wastage. In the vaccine supply chain, at the vaccine distribution company or the veterinary drugstores, there was no loss of vaccines. The main cause of vaccine loss occurred during the vaccination process carried out by the CAHWs. The HPAI vaccine was in liquid form in a vial. The smallest vial contained 200 doses. One vial was sufficient for several small-scale poultry farms but had to be used within 24 hours after opening. Therefore, some of the vaccine was wasted due to scheduling and transportation routes.

## ACKNOWLEDGEMENTS

We identified the HPAI supply chain stakeholders and their roles and found that the ATSCs played a key role in the government's support of AI vaccination in Quang Ninh province. We recommend that expanding the support for AI vaccination to large-scale poultry farms would be key to increase vaccination rates in the province and prevent and control this disease. Although the AI vaccines distributed in Quang Ninh province in 2021 were still effective against the circulating local virus strains, selecting newer vaccines with higher efficacy, such as selecting vaccine with seed viruses NIBRG-14/A/Hubei/1/2010(H5N1)-PR8-IDCDC-RG30 or H5 D7/rD8, is recommended. We also recommended that vaccine manufacturers and distributors provide smaller dose vaccine vials (e.g., 50 dose vials) to allow cost-effective vaccination for small-scale poultry farms to avoid vaccine wastage.

## AUTHOR CONTRIBUTIONS

This research was conducted with the contributions of all the authors. The authors all participated in the study design, analyzing the results, interpreting the results, and preparing the manuscript. All authors read and approved the final manuscript.

## CONFLICT OF INTEREST

All authors declare that there is no conflict of interest

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