ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Zoonotic Influenza Vaccine Seqirus suspension for injection in pre-filled syringe
Zoonotic influenza vaccine (H5N8) (surface antigen, inactivated, adjuvanted)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Influenza virus surface antigens (haemagglutinin and neuraminidase)* of strain:

A/Astrakhan/3212/2020 (H5N8)-like strain (CBER-RG8A) (clade 2.3.4.4b) 7.5 micrograms**
per 0.5 ml dose

* propagated in fertilised hens' eggs from healthy chicken flocks
** expressed in micrograms haemagglutinin (HA).

Adjuvant MF59C.1 containing per 0.5 ml dose:

squalene (9.75 mg), polysorbate 80 (1.175 mg), sorbitan trioleate (1.175 mg), sodium citrate (0.66 mg) and citric acid (0.04 mg).

Zoonotic Influenza Vaccine Seqirus may contain trace residues of egg and chicken proteins, ovalbumin, kanamycin, neomycin sulphate, formaldehyde, hydrocortisone and cetyltrimethylammonium bromide which are used during the manufacturing process (see section 4.3).

For the full list of excipients see section 6.1.

3. PHARMACEUTICAL FORM

Suspension for injection (injection).

The vaccine is a milky-white liquid.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Zoonotic Influenza Vaccine Seqirus H5N8 is indicated for active immunisation against H5 subtype influenza A viruses in individuals 6 months of age and above.

The use of this vaccine should be in accordance with official recommendations.

4.2 Posology and method of administration

Posology

Individuals 6 months of age and older: administer two doses (0.5 ml each), at least 3 weeks apart.

Data on a third dose (booster) administered 6 months after the first dose are limited (see sections 4.8 and 5.1).

Paediatric population

The safety and efficacy of Zoonotic Influenza Vaccine Seqirus H5N8 in individuals aged less than 6 months have not yet been established.

Elderly population

No dose adjustment is required in elderly individuals ≥65 years of age.

Interchangeability

No data to support interchangeability of Zoonotic Influenza Vaccine Seqirus H5N8 with other H5 monovalent vaccines are available.

Method of administration

Zoonotic influenza vaccine Seqirus H5N8 should be administered by intramuscular injection, preferably in the anterolateral aspect of the thigh in infants or in the deltoid muscle region of the upper arm in older individuals

The vaccine should under no circumstances be administered intravascularly, subcutaneously or intradermally.

The vaccine should not be mixed in the same syringe with any other vaccines or medicinal products.

For precautions to be taken before administering the vaccine, see section 4.4.

4.3 Contraindications

History of an anaphylactic (i.e. life-threatening) reaction to the active substance, to any excipients or to trace residues (egg and chicken proteins, ovalbumin, kanamycin and neomycin sulphate, formaldehyde, hydrocortisone and cetyltrimethylammonium bromide) of this vaccine (see section 6.1).

4.4 Special warnings and precautions for use

Traceability

In order to improve the traceability of biological medicinal products, the name and the batch number of the administered medicinal product should be clearly recorded.

Hypersensitivity and anaphylaxis

Caution is needed when administrating this vaccine to individuals with a known hypersensitivity to the active substance, to any of the excipients listed in section 6.1 and to residues (eggs and chicken proteins, ovalbumin, kanamycin and neomycin sulphate, formaldehyde, hydrocortisone and cetyltrimethylammonium bromide).

As with all injectable vaccines, close observation for 15 min is recommended and appropriate medical treatment should always be readily available in case of a rare anaphylactic event following the administration of the vaccine.

Concurrent illness

Vaccination should be postponed in individuals with acute febrile illness or acute infection. The presence of a minor infection and/or low-grade fever should not delay vaccination.

Anxiety-related reactions

Anxiety-related reactions, including vaso-vagal reactions (syncope) can occur following, or even before, any vaccination as a psychogenic response to the needle injection. This can be accompanied by several neurological signs such as transient visual disturbance, paraesthesia and tonic-clonic limb movements during recovery. It is important that procedures are in place to avoid injury from fainting.

Thrombocytopenia and coagulation disorders

As with other intramuscular injections, the vaccine should be given with caution in individuals receiving anticoagulant therapy or those with thrombocytopenia or any coagulation disorder (such as haemophilia) because bleeding or bruising may occur following an intramuscular administration in these individuals.

Immunocompromised individuals

The antibody responses in immunocompromised individuals may be insufficient to provide protection (see section 5.1).

Duration of protection

The duration of protection following the primary vaccination schedule is unknown.

Limitations of vaccine effectiveness

There is no immune correlate of protection established for influenza A caused by H5 subtypes. Based on humoral immune responses to Zoonotic Influenza Vaccine H5N1, after two doses a protective immune response may not be elicited in all vaccinees.

Cross-reactive immunity

There are no clinical cross reactivity data with the Zoonotic Influenza Vaccine Seqirus H5N8. The degree of immune response that may be elicited to influenza A(H5) viruses of subtypes or clades different to that of the vaccine strain Zoonotic Influenza Vaccine Seqirus H5N8, is unknown (see section 5.1 Information from nonclinical studies).

Excipients

Sodium
This vaccine contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially 'sodium-free'.

Potassium
This vaccine contains potassium, less than 1 mmol (39 mg) per dose, that is to say essentially 'potassium-free'.

4.5 Interaction with other medicinal products and other forms of interaction

There are no data on co-administration of Zoonotic Influenza Vaccine Seqirus H5N8 with other vaccines. If co-administration with another vaccine is considered, immunisation should be carried out on separate limbs. It should be noted that the adverse reactions may be intensified.

4.6 Fertility, pregnancy and lactation

Pregnancy

No data are available regarding the use of Zoonotic Influenza Vaccine Seqirus H5N8 during pregnancy.

Limited data obtained from women who became pregnant during the course of clinical trials with Zoonotic Influenza Vaccine H5N1 or similar pandemic H1N1 vaccines adjuvanted with MF59C.1 were insufficient to inform vaccine-associated risks in pregnancy.

However, it is estimated that during the 2009 H1N1 pandemic more than 90 000 women were vaccinated during pregnancy with an H1N1 pandemic vaccine similar to Zoonotic Influenza Vaccine H5N1 which contains the same amount of adjuvant MF59C.1 as Zoonotic Influenza Vaccine Seqirus H5N8.

Post-marketing spontaneously reported adverse events and an interventional study do not suggest direct or indirect harmful effects of H1N1 vaccine exposure on pregnancy.

In addition, two large observational studies designed to assess the safety of H1N1 vaccine exposure in pregnancy showed no increase in the rates of gestational diabetes, preeclampsia, abortions, stillbirth, low birth weight, prematurity, neonatal deaths, and congenital malformations among almost 10 000 vaccinated pregnant women and their offspring compared with unvaccinated controls.

Since Zoonotic Influenza Vaccine Seqirus H5N8 is expected not to be used in an emergency situation, its administration during pregnancy might be deferred as a precautionary approach.

Healthcare providers need to assess the benefit and potential risks of administering the vaccine to pregnant women taking into consideration official recommendations.

Breast-feeding

No data are available regarding the use of Zoonotic Influenza Vaccine Seqirus H5N8 during breast-feeding.

The potential benefits to the mother and risks to the infant should be considered before administering Zoonotic Influenza Vaccine Seqirus H5N8 during breast-feeding.

Fertility

There are no data concerning human fertility for Zoonotic Influenza Vaccine Seqirus H5N8. A study in rabbits did not indicate reproductive or developmental toxicity of Zoonotic Influenza Vaccine H5N1 (see section 5.3). Male fertility has not been assessed in animals.

4.7 Effects on ability to drive and use machines

Zoonotic Influenza Vaccine Seqirus H5N8 has no or negligible influence on the ability to drive and use machines. However, some of the effects mentioned under section 4.8 may temporarily affect the ability to drive or operate machinery.

4.8 Undesirable effects

Summary of the safety profile

No clinical data exist with Zoonotic Influenza Vaccine Seqirus A/Astrakhan/3212/2020 (H5N8)-like strain (CBER-RG8A) (clade 2.3.4.4b). The safety of Zoonotic Influenza Vaccine Seqirus H5N8 is inferred from safety data of the Zoonotic Influenza Vaccine H5N1 vaccine (at least 7.5 micrograms (mcg) HA, MF59C.1 adjuvanted) containing either the A turkey/Turkey/1/2005 (NIBRG 23) (clade 2.2.1) or the A Vietnam/1194/2004 (NIBRG-14) (clade 1) strains.

Zoonotic Influenza Vaccine H5N1 Seqirus has been evaluated in healthy children (6 months to 17 years of age), healthy adults (18 to 60 years of age) and healthy elderly (over 60 years of age) following a 1, 22 day primary vaccination schedule, and booster vaccination.

The safety of H5N1 vaccine combined with MF59C.1 adjuvant containing either the A/turkey/Turkey/1/2005 or the A/Vietnam/1194/2004 strain has been evaluated in nine clinical trials in healthy subjects involving 5 055 adults and elderly (7.5 or 15 micrograms HA), and children (7.5 micrograms HA). There were 4 041 adults subjects of 18 to 60 years of age, 540 elderly

subjects 61 years of age and above. In the paediatric population, there were 214 subjects 6 to 35 months of age, 167 subjects 3 to 8 years of age and 93 subjects 9 to 17 years of age.

The overall safety profile was similar across the adult, elderly and paediatric populations.

Irrespective of antigen dose, or age group, most local and systemic adverse reactions after administration were of short duration, with onset close to the time of vaccination, and were mild or moderate in severity. Across all trials, there was a general trend towards decreased reports of local adverse reactions after the second vaccination compared with the first.

In adults 18 to 60 years, the most frequently reported (≥10%) adverse reactions were injection site pain (59%), myalgia (34%), headache (26%), injection site redness (24%), fatigue (24%), injection site induration (21%), injection site swelling (15%), chills (13%) and malaise (13%).

In elderly subjects (≥61 years), the most frequently reported (≥10%) adverse reactions were injection site pain (35%), myalgia (24%), injection site redness (17%), headache (16%), chills (12%), fatigue (10%) and malaise (10%).

In children and adolescents 3 to 17 years of age, the most frequently reported (≥10%) adverse reactions were injection site pain (95%), headache (61%), myalgia (60%), fatigue (41%), injection site redness (60%), injection site induration (34%), injection site swelling (34%), malaise (32%), nausea (25%), chills (19%), sweating (18%), diarrhoea (18%) and injection site ecchymosis (16%).

In infants and children 6 to 35 months of age, the most frequently reported (≥10%) adverse reactions were injection site redness (62%), irritability (57%), tenderness (55%), unusual crying (48%), sleepiness (45%), injection site induration (38%), injection site swelling (37%), change in eating habits (36%), diarrhoea (34%), fever (27%), injection site ecchymosis (19%), vomiting (10%), sweating (10%) and unusual sweating (10%).

Tabulated list of adverse reactions

The solicited and unsolicited adverse reactions reported after any vaccination doses (i.e. first, second or booster) across subjects age, are listed according to the following MedDRA frequency convention and system organ class:

Very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1 000 to <1/100); rare (≥1/10 000 to <1/1 000); very rare (<1/10 000).

Table 1. Adverse drug reactions

MedDRA System Organ class	Very common (≥1/10)	Common (≥1/100 to <1/10)	Uncommon (≥1/1 000 to <1/100)	Rare (≥1/10 000 to <1/1 000)
Immune system disorders				Anaphylaxis
Metabolism and nutrition disorders	Change in eating habits[1]	Loss of appetite		
Nervous system disorders	Headache			
Gastrointestinal disorders	Nausea[2], diarrhoea[2], vomiting[2]			
Skin and subcutaneous tissue disorders	Sweating[2], Unusual sweating[1]		Urticaria	
Musculoskeletal and connective tissue disorders	Myalgia	Arthralgia		
General disorders and administration site conditions	Injection site swelling, injection site pain, injection site tenderness[1], injection site induration, injection site redness, injection site ecchymosis[2], fatigue, malaise, chills/shivering, sleepiness[1], irritability[1], unusual crying[1], fever[3]	Injection site haemorrhage		

1 Reported only in paediatric subjects 6-35 months
2 Reported as Common in adults (18-60 years) and elderly (≥ 61 years)
3 Reported as Very common only in paediatric subjects 6 months-8 years. Reported as Common in adolescents and adults 9-60 years of age and Uncommon in eldery (≥ 61 years)

The majority of these side effects usually disappear within 3 days without treatment.

Clinical trials in special populations

Adverse reactions in special populations have been evaluated in two clinical trials, V87_25 and V87_26, involving adult (18-60 years) and elderly (≥ 61 years) subjects with underlying medical conditions (N=294) or immunosuppressive conditions (N=295).

Across studies V87_25 and V87_26, the safety of Zoonotic influenza vaccine H5N1 in healthy adult and elderly subjects was consistent with existing safety data from previous clinical trials. However, in immunocompromised subjects 18 to 60 years of age, slightly higher rates of nausea (13.0%) were reported. In addition, higher rates of arthralgia (up to 23.3%) were reported in both adult and elderly subjects, who were immunocompromised or with underlying medical conditions.

The following solicited adverse reactions were additionally collected in these two studies and reported with the following frequencies across subjects who received Zoonotic Influenza Vaccine H5N1 irrespective of age or health status: diarrhoea (up to 11.9%), loss of appetite (up to 10.9%) and vomiting (up to 1.7%). In both studies, subjects with underlying medical and immunosuppressive conditions reported higher frequencies of diarrhoea, loss of appetite and vomiting compared to healthy subjects (irrespective of age).

Post-marketing surveillance

No postmarketing experience exists for Zoonotic Influenza Vaccine Seqirus H5N8.

In addition to the adverse events listed from clinical studies, the following adverse events were reported from post-marketing surveillance with an H1N1 pandemic vaccine, similar to Zoonotic Influenza Vaccine Seqirus H5N8 (licensed for use from 6 months of age during the 2009 influenza pandemic, and containing the same MF59 adjuvant and manufactured with the same process).

Blood and lymphatic system disorders
Lymphadenopathy.

Immune system disorders
Allergic reactions, anaphylaxis including dyspnoea, bronchospasm, laryngeal oedema, in rare cases leading to shock.

Nervous system disorders
Dizziness, somnolence, syncope, presyncope, neuralgia, paraesthesia, convulsions and neuritis.

Cardiac disorders
Palpitation, tachycardia.

Respiratory, thoracic and mediastinal disorders
Cough.

Gastrointestinal disorders
Abdominal pain.

Skin and subcutaneous tissue disorders
Generalised skin reactions including pruritus, non-specific rash, angioedema.

Muscoskeletal and connective tissue disorders
Muscular weakness, pain in extremities.

General disorders and administration site conditions
Asthenia.

The following additional adverse events were reported from post-marketing surveillance with seasonal non-adjuvanted trivalent vaccines in all age groups and a seasonal trivalent MF59-adjuvanted subunit influenza vaccine approved for use in elderly individuals 65 years of age and older:

Blood and lymphatic system disorders
Thrombocytopenia (in some cases reversible platelet counts less than 5000 mm^3).

Nervous system disorders
Neurological disorders, such as encephalomyelitis and Guillain Barré syndrome.

Vascular disorders
Vasculitis which may be associated with transient renal involvement.

Skin and subcutaneous tissue disorders
Erythema multiforme.

General disorders and administration site conditions
Extensive swelling of injected limb lasting more than one week, injection-site cellulitis-like reaction (some cases of swelling, pain, and redness extending more than 10 cm and lasting more than 1 week).

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V.

4.9 Overdose

No case of overdose has been reported.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Vaccines, influenza vaccines; ATC Code J07BB02.

Mechanism of action

Zoonotic Influenza Vaccine Seqirus H5N8 provides active immunisation against the influenza virus strain contained in the vaccine. Zoonotic Influenza Vaccine Seqirus H5N8 induces humoral antibodies against H5 subtype influenza A viruses haemagglutinins. These antibodies neutralise influenza viruses. Specific levels of haemagglutination inhibition (HI) antibody titres post-vaccination with inactivated influenza vaccine have not been correlated with protection from influenza virus, but the HI antibody titres have been used as a measure of vaccine efficacy. Antibody against one influenza virus type or subtype confers limited or no protection against another. Furthermore, antibody to one antigenic variant of influenza virus might not protect against a new antigenic variant of the same type or subtype. Zoonotic Influenza Vaccine Seqirus H5N8 contains the adjuvant MF59C.1 (MF59), which is designed to increase and broaden the antigen-specific immune response and to extend the duration of the immune response.

Clinical efficacy

No clinical data exist with Zoonotic Influenza Vaccine Seqirus A/Astrakhan/3212/2020 (H5N8)-like strain (CBER-RG8A) (clade 2.3.4.4b). Results from clinical trials carried out with Zoonotic Influenza Vaccine H5N1 containing either the A turkey/Turkey/1/2005 (NIBRG 23) (clade 2.2.1) or the A/Vietnam/1194/2004 (NIBRG-14) (clade 1) strains, are summarised.

Immune response to Zoonotic Influenza Vaccine H5N1 A/Vietnam/1194/2004 and A/turkey/Turkey/1/2005

Adults (18-60 years)

A phase 2 clinical trial (V87P1) was conducted with Zoonotic Influenza Vaccine H5N1 (A/Vietnam/1194/2004) in 312 healthy adults. Two doses of Zoonotic Influenza Vaccine H5N1 were administered three weeks apart to 156 healthy adults. Immunogenicity was assessed in 149 subjects.

In phase 3 clinical trial (V87P13) 2 693 adult subjects were enrolled and 2 566 received two doses of Zoonotic Influenza Vaccine H5N1 (A/Vietnam/1194/2004) administered three weeks apart. Immunogenicity was assessed in a subset (N=197) of subjects.

In a third clinical trial (V87P11) 194 adult subjects were enrolled and received two doses of Zoonotic Influenza Vaccine H5N1 (A/turkey/Turkey/1/2005) administered three weeks apart. Immunogenicity was assessed in 182 subjects.

The seroprotection rate, seroconversion rate and the seroconversion factor for anti-HA antibody to H5N1 A/Vietnam/1194/2004 and to H5N1 A/turkey/Turkey/1/2005 in the adults measured by SRH assay are reported below (Table 2).

Table 2. Immune responses to H5N1 A/Vietnam/1194/2004 and to H5N1 A/turkey/Turkey/1/2005

Anti-HA antibody (SRH)	Study V87P1 A/Vietnam/1194/2004 21 days after 2nd dose N=149	Study V87P13 A/Vietnam/1194/2004 21 days after 2nd dose N=197	Study V87P11 A/turkey/Turkey/1/2005 21 days after 2nd dose N=182
Seroprotection rate (95% CI)*	85% (79-91)	91% (87-95)	91% (85-94)
Seroconversion rate (95% CI)**	85% (78-90)	78% (72-84)	85% (79-90)
Seroconversion factor (95% CI)***	7.74 (6.6-9.07)	4.03 (3.54-4.59)	6 (5.2-6.93)

* Seroprotection: SRH area ≥ 25 mm^2

** Seroconversion was defined as an SRH area ≥25 mm^2 for subjects who were seronegative at baseline (Day 1 SRH area ≤4 mm^2) or a significant (at least 50%) increase in SRH area for subjects who were seropositive at baseline (Day 1 SRH area >4 mm^2)

*** geometric mean ratios (GMRs) of SRH

MicroNeutralisation (MN) results against homologous A/Vietnam/1194/2004) indicate a seroprotection and seroconversion rate ranging from 67% (60-74) to 85% (78-90) and 65% (58-72) to 83% (77-89), respectively. Immune response to vaccination assessed by MN assay is in line with results obtained with SRH.

In Study V87P11 MN results against homologous A/turkey/Turkey/1/2005 indicate a seroprotection and seroconversion rate of 85% (79-90) and 93% (89-96), respectively. Immune response to vaccination assessed by MN assay is in line with results obtained with SRH.

Persistence of antibodies after primary vaccination in this population was assessed by hemagglutination inhibition (HI), SRH, and MN assays. Compared to the antibody levels obtained at day 43 after completion of primary vaccination schedules, antibody levels at day 202 were reduced by 1/5 to 1/2 from their prior levels.

Elderly (≥61 years)

The seroprotection rate, seroconversion rate and the seroconversion factor for anti-HA antibody to H5N1 (A/Vietnam/1194/2004 and to A/ turkey/Turkey/1/2005) in subjects aged 61 years and older (limited number of subjects were above 70 years of age; N=123) measured by SRH assay assessed in three clinical studies are reported below (Table 3).

Table 3. Immune responses to H5N1 (A/Vietnam/1194/2004 and to A/ turkey/Turkey/1/2005) in subjects aged 61 years and older[a] measured by SRH assay

Anti-HA antibody (SRH)	Study V87P1 A/Vietnam/1194/2004 21 days after 2nd dose N=84[a]	Study V87P13 A/Vietnam/1194/2004 21 days after 2nd dose N=210[b]	Study V87P11 A/turkey/Turkey/1/2005 21 days after 2nd dose N=132[c]
Seroprotection rate (95% CI)*	80% (70-88)	82% (76-87)	82% (74-88)
Seroconversion rate (95% CI)**	70% (59-80)	63% (56-69)	70% (61-77)
Seroconversion factor (95% CI)***	4.96 (3.87-6.37)	2.9 (2.53-3.31)	3.97 (3.36-4.69)

[a] Ages 62-88 years; [b] Ages 61-68 years; [c] Ages 61-89 years

* Seroprotection: SRH area ≥ 25 mm^2

** Seroconversion was defined as an SRH area ≥25 mm^2 for subjects who were seronegative at baseline (Day 1 SRH area ≤4 mm^2) or a significant (at least 50%) increase in SRH area for subjects who were seropositive at baseline (Day 1 SRH area >4 mm^2)

*** GMRs of SRH

MN results against homologous A/Vietnam/1194/2004 (Studies V87P1 and V87P13) indicate a seroprotection and seroconversion rate ranging from 57% (50-64) to 79% (68-87) and 55% (48-62) to 58% (47-69), respectively. MN results, similar to SRH results, demonstrated strong immune response after completion of priming vaccination series in a population of elderly subjects.

In Study V87P11, MN results against homologous A/turkey/Turkey/1/2005 indicate a seroprotection and seroconversion rate of 68% (59-75) and 81% (74-87), respectively. Immune response to vaccination assessed by MN assay is similar to SRH results.

Persistence of antibodies after primary vaccination in elderly subjects as assessed by HI, SRH, and MN tests reduced from 1/2 to 1/5th of their post-vaccination level at day 202 as compared to day 43 after completion of primary schedules. Up to 50% (N=33) of the elderly subjects aged 62 to 88 years immunised with Zoonotic Influenza Vaccine H5N1 in trial V87P1 were seroprotected at six months.

A third (booster) dose of Zoonotic Influenza Vaccine H5N1 was administered 6 months onwards after the primary vaccination. Results are shown by SRH.

The seroprotection rate, seroconversion rate and the seroconversion factor for anti-HA antibody to H5N1 A/Vietnam/1194/2004 measured by SRH assays are reported below (Table 4).

Table 4. Immune responses to H5N1 A/Vietnam/1194/2004 measured by SRH assays

	Study V87P1 Adults booster after 2nd dose	Study V87P2 Adults booster after 2nd dose	Study V87P1 Elderly booster after 2nd dose
SRH	N=71	N=13	N=38
Seroprotection rate (95% CI)*	89% (79-95)	85% (55-98)	84% (69-94)
Seroconversion rate (95% CI)**	83% (72-91)	69% (39-91)	63% (46-78)
Seroconversion factor (95% CI)***	5.96 (4.72-7.53)	2.49 (1.56-3.98)	5.15 (3.46-7.66)

* Seroprotection: SRH area ≥ 25 mm^2

** Seroconversion was defined as an SRH area ≥ 25 mm^2 for subjects who were seronegative at baseline (Day 1 SRH area ≤ 4 mm^2) or a significant (at least 50%) increase in SRH area for subjects who were seropositive at baseline (Day 1 SRH area >4 mm^2)

*** GMRs of SRH

Long term booster immune memory

A single vaccination with Zoonotic Influenza Vaccine H5N1 (A/Vietnam/1194/2004) induced high and rapid serological response in subjects primed 6-8 years previously with two doses of a different surrogate H5 vaccine, having same formulation as Zoonotic Influenza Vaccine H5N1 but using the strain H5N3.

In a phase 1 clinical trial (V87P3) adult subjects aged 18-65 years primed 6-8 years previously with 2 doses of MF59-adjuvanted H5N3 vaccine/A/Duck/Singapore/97, were administered 2 booster doses of Zoonotic Influenza Vaccine H5N1 (A/Vietnam/1194/2004). SRH results after the first dose, that mimic prepandemic priming plus single heterologous booster dose, revealed seroprotection and seroconversion rates of 100% (74- 100) and an 18-fold increase in SRH area (GMR).

Alternative vaccination schedules

In a clinical trial evaluating 4 different vaccination schedules in 240 subjects 18 to 60 years of age, where the second dose occurred either 1, 2, 3 or 6 weeks after the first Zoonotic Influenza Vaccine H5N1 (A/Vietnam/1194/2004) dose, all vaccine schedule groups after 3 weeks from the second vaccination achieved high levels of antibodies as evaluated with SRH. SRH seroprotection rates

ranged from 86% to 98%, seroconversion rated from 64% to 90%, and GMR ranged from 2.92 to 4.57. The magnitude of immune response was lower in the group who received the second dose 1 week later and higher in the groups with longer interval schedules.

Subjects with underlying medical or immunosuppressive conditions

Immunogenicity of Zoonotic Influenza Vaccine H5N1 (A/turkey/Turkey/1/2005) in adults (18 to 60 years) and elderly (≥61 years) subjects with underlying medical conditions (Study V87_25) or immunosuppressive conditions (mainly HIV-infected subjects) (Study V87_26) in comparison to healthy adults (18 to 60 years) and elderly (≥61 years), was evaluated in two randomised, phase 3 controlled clinical trials (with a seasonal trivalent inactivated MF59-adjuvanted subunit influenza vaccine approved for use in elderly subjects 65 years of age and older as a comparator). In trial V87_25 and V87_26, 96 and 67 subjects, respectively, were over the age of 70 years. In both trials, immunogenicity of Zoonotic Influenza Vaccine H5N1 was shown by HI, SRH and MN assays following both the first and second dose.

Geometric mean area, seroprotection rate, seroconversion rate and the seroconversion factor for anti-HA antibody to H5N1 A/turkey/Turkey/1/2005 measured by SRH assays 21 days after the second dose are reported below (Table 5).

Table 5. Immune responses to H5N1 A/turkey/Turkey/1/2005 measured by SRH assays 21 days after the 2nd dose

Study V87_25				
	Adults (20- 60 years)[a]	Adults (19- 60 years)[a]	Elderly (61-84 years)[a]	Elderly (61-79 years)[a]
Anti-HA antibody (SRH)	Medical Conditions N=140	Healthy N=57	Medical Conditions N=143	Healthy N=57
Geometric Mean Area (95% CI)*	31.07 (27.43-35.19)	58.02 (48.74-69.06)	29.34 (26.07-33.01)	27.78 (22.57-34.18)
Seroprotection rate (95% CI)*	65.00 (56.5-72.9)	89.47 (78.5-96)	58.74 (50.2-66.9)	57.89 (44.1-70.9)
Seroconversion rate (95% CI)*	72.86 (64.7-80)	98.25 (90.6-99.96)	64.34 (55.9-72.2)	66.67 (52.9-78.6)
Seroconversion factor (95%CI)**	3.33 (2.94-3.77)	6.58 (5.53-7.83)	2.37 (2.10-2.66)	2.96 (2.41-3.64)
Study V87_26				
	Adults (20- 60 years)[a]	Adults (18-59 years)[a]	Elderly (61-84 years)[a]	Elderly (61-91 years)[a]
Anti-HA antibody (SRH)	Immuno-compromised N=143	Healthy N=57	Immuno-compromised N=139	Healthy N=62
Geometric Mean Area (95%CI)*	26.50 (22.49-31.22)	48.58 (40.01-58.99)	26.85 (23.01-31.33)	23.91 (18.89-30.26)
Seroprotection rate (95%CI)*	60.84 (52.3-68.9)	87.72 (76.3-94.9)	58.99 (50.3-67.3)	53.23 (40.1-66)
Seroconversion rate (95%CI)*	61.54 (53-69.5)	89.47 (78.5-96)	64.75 (56.2-72.7)	56.45 (43.3-69
Seroconversion factor (95%CI)**	3.16 (2.69-3.73)	7.10 (5.85-8.62)	3.15 (2.70-3.68)	2.83 (2.24-3.58)

[a] actual age range of population enrolled

* measured by SRH assay seroprotection: SRH area ≥25 mm^2, seroconversion: SRH area ≥25 mm^2 for subjects with a baseline SRH area ≤4 mm^2 or a minimum 50% increase in SRH area for subjects with >4 mm^2.

** geometric mean ratios of SRH

HI results for the two clinical studies revealed lower values than those reported in previous studies. Seroconversion rates against homologous A/turkey/Turkey/1/2005 ranged from 37.50% to 43.10% in healthy adults, and from 19.18% to 26.47% in adults with immunosuppressive or underlying medical conditions, respectively; seroconversion rates ranged from 21.43% to 30.65% in healthy elderly subjects, and from 24.49% to 27.86% in elderly subjects with immunosuppressive or underlying medical conditions. Similar trends were observed for seroprotection rates in both studies.

MN results against homologous A/turkey/Turkey/1/2005 indicate a seroconversion rate of 66.67% in healthy adults, and ranging from 33.57% to 54.14% in adults with immunosuppressive or underlying medical conditions, respectively; seroconversion rates ranged from 24.39% to 29.03% in healthy elderly subjects, and from 31.65% to 39.42% in elderly subjects with immunosuppressive or underlying medical conditions. Similar trends were observed for seroprotection rates in both studies.

In both studies V87_25 and V87_26, the lower levels of antibodies (as measured by HI, SRH and MN assays) and reduced seroprotection rates in adults and elderly (≥ 61 years old) subjects with underlying medical or immunosuppressive conditions, suggest that Zoonotic Influenza Vaccine H5N1 may not elicit the same level of protection against A/H5N1 strain as compared to healthy adults (see section 4.4). These studies provided limited immunogenicity data in subjects with some underlying medical (in particular, renal impairment and peripheral cardiovascular disease) and immunosuppressive conditions (in particular, transplant recipients and patients under cancer treatment). In these trials, lower levels of antibodies and reduced seroprotection rates against homologous H5N1 A/turkey/Turkey/1/2005 were also measured in healthy elderly subjects, as compared to healthy adults, though previous studies showed induction of sufficiently immunogenic responses against H5N1 strains (see above for information on elderly).

Paediatric population

The immunogenicity of aH5N1 in the paediatric population was assessed in studies V87P6 and V87_30.

Study V87P6 was conducted with Zoonotic Influenza Vaccine H5N1 (A/Vietnam/1194/2004) in 471 children from 6 months to 17 years of age. Two doses (7.5 micrograms HA with 100% MF59 adjuvant, 0.5 ml dose each) of Zoonotic Influenza Vaccine H5N1 were administered three weeks apart and a third dose (7.5 micrograms HA with 100% MF59 adjuvant, 0.5 ml) 12 months following the first dose. After 3 weeks from the second vaccination (day 43) all age groups (i.e. 6 to 35 months, 3 to 8 years and 9 to 17 years) achieved high levels of antibodies to (A/Vietnam/1194/2004) as evaluated with SRH and HI assays are reported below (Table 6).

Table 6. Immune responses to H5N1 A/Vietnam/1194/2004 measured by HI and SRH assays 21 days after the 2nd dose in paediatric subjects 6 months to 18 years of age

		Children (6 to 35months)	**Children (3-to 8 years)**	**Adolescents (9 to 17years)**
		N=134	**N=91**	**N=89**
HI	Seroprotection rate (95% CI)* Day 43	97% (92-99)	97% (91-99)	89% (80-94)
	Seroconversion rate (95% CI)** Day 43	97% (92-99)	97% (91-99)	89% (80-94)
	Seroconversion factor*** Day 43 to Day 1	129 (109-151)	117 (97-142)	67 (51-88)
SRH		**N=133**	**N=91**	**N=90**
	Seroprotection rate (95% CI)° Day 43	100% (97-100)	100% (96-100)	100% (96-100)

		Children (6 to 35months)	Children (3-to 8 years)	Adolescents (9 to 17years)
		N=134	N=91	N=89
	Seroconversion rate (95% CI)°° Day 43	98% (95-100)	100% (96-100)	99% (94-100)
	Seroconversion factor (95% CI)°°° Day 43 to Day 1	16 (14-18)	15 (13-17)	14 (12-16)

* Seroprotection defined as HI titre ≥ 1:40

** Seroconversion defined as non-detectable titre to ≥1:40, or 4-fold increase from a detectable Day 1 titre

*** Geometric mean ratios of HI

° Seroprotection: SRH area ≥25 mm2

°° Seroconversion defined as an SRH area ≥25 mm2 for subjects who were seronegative at baseline (Day 1 SRH area ≤4 mm2) or a significant (at least 50%) increase in SRH area for subjects who were seropositive at baseline (Day 1 SRH area >4 mm2)

°°° Geometric mean ratios of SRH

MN results against a A/Vietnam/1194/2004 indicate a seroprotection rate of 99% (95%CI: 94-100), a seroconversion rate ranging from 97% (95%CI: 91-99) to 99% (95%CI: 96-100) and a GMR ranging from 29 (95%CI: 25-35) to 50 (95%CI: 44-58).

Study V87_30 was a randomised, observer-blind, multicentre study to measure the immunogenicity of six formulations in terms of H5N1 A/turkey/Turkey/1/2005 and MF59 adjuvant ratio. In this study, 420 paediatric subjects 6 months to 8 years of age were divided into two age cohorts: 6 to 35 months of age (N=210) and 3 to 8 years of age (N=210).

The vaccine was administered in two separate injections given 3 weeks apart. Antibody levels against A/turkey/Turkey/1/2005 were measured by HI and MN assays three weeks after the second vaccination (Day 43). The immunological response for the the approved formulation (7.5 micrograms HA with 100% MF59 adjuvant, 0.5 ml dose) and the study formulation with half the antigen content (3.75 micrograms HA with 100% MF59 adjvant, 0.5 ml dose), are presented below (Table 7).

Table 7. Immune responses to 7.5 mcg and 3.75 mcg H5N1 A/turkey/Turkey/1/2005 measured by HI and MN assays 21 days after the 2nd dose in paediatric subjects 6 months to 8 years of age

Formulation		7.5 micrograms HA/ 100% MF59 Adjuvant		3.75 micrograms HA/ 100% MF59 Adjuvant	
Age groups		6 to 35 months	3 to 8 years	6 to 35 months	3 to 8 years
		N=31	N=36	N=36	N=33
HI	Seroprotection rate (95% CI) * Day 43	87% (70-96)	86% (71-95)	86% (71-95)	88% (72-97)
	Seroconversion rate (95% CI)** Day 43	87% (70-96)	86% (71-95)	86% (71-95)	88% (72-97)
	Seroconversion factor (95% CI)*** Day 43 to Day 1	24 (14-40)	22 (14-34)	31 (19-51)	20 (13-31)
MN	% with Titre ≥1:40 (95% CI) Day 43	100% (89-100)	100% (90-100)	100% (90-100)	100% (89-100)
	Seroconversion rate (95% CI)** Day 43	100% (89-100)	100% (90-100)	100% (90-100)	100% (89-100)
	Seroconversion factor (95% CI)*** Day 43 to Day 1	165 (117-231)	125 (92-171)	214 (156-294)	132 (95-182)

* Seroprotection defined as HI titre ≥ 1:40
** Seroconversion defined as non-detectable titre to ≥1:40, or 4-fold increase from a detectable Day 1 titre
*** Geometric mean titre ratios

Information from non-clinical studies

Immunogenicity

Immunogenicity of Zoonotic Influenza Vaccine Seqirus H5N8 was evaluated in the ferret model (Study LC-07). The immunogenicity of a single-dose (12.5 micrograms HA) or two-dose vaccination with a 3-week interval, was evaluated using a standard HI assay. Pseudoviruses expressing HA and NA homologous proteins:
A/Astrakhan/3212/2020 (H5N8) clade 2.3.4.4b
and heterologous proteins:
A/turkey/Turkey/1/2005 (H5N1) clade 2.2.1
A/Hubei/1/2010 (H5N1) clade 2.3.2.1a
A/duck/Bangladesh/19097/2013 (H5N1) clade 2.3.2.1a
A/duck/Bangladesh/17D1012/2018 (H5N1) clade 2.3.2.1a
A/American wigeon/South Carolina/22-000345-001/2021 (H5N1) clade 2.3.4.4b
A/Ezo red Fox/Hokkaido/1/2022 (H5N1) clade 2.3.4.4b
A/chicken/Ghana/AVL-76321VIR7050-39/2021 (H5N1) clade 2.3.4.4b
M2 IDCDC-RG78 UC (H5N1) clade 2.3.4.4b
A/duck/Vietnam/NCVD-1584/2012 (H5N1) clade 2.3.2.1c
A/Guangdong/18SF020/2018 (H5N6) clade 2.3.4.4h
to Zoonotic Influenza Vaccine Seqirus H5N8, were utilized as antigens.

Two doses of the vaccine 3 weeks apart induced significant antibody response against homologous strain and heterologous H5N1 strains A/American wigeon/South Carolina/22-000345-001/2021 and A/Ezo red Fox/Hokkaido/1/2022 (H5N1) both within the same clade 2.3.4.4b of the vaccine. A slight decrease in GMTs for all strains was observed when measured 7 weeks after the second dose. A single-dose vaccination induced lower but still significant levels of HI antibodies.
No cross reactivity was detected (GMT < 1:10) for heterologous preudovirus strain A/chicken/Ghana/AVL-76321VIR7050-39/2021 (H5N1) although within the same clade 2.3.4.4b of the vaccine.
No cross-reactivity was observed against pseudovirus H5 strains outside the 2.3.4.4b clade.

Efficacy

Efficacy against challenge with virus homologous and heterologous to vaccine strains was evaluated in the ferret model (Study 765-N106857). Zoonotic Influenza Vaccine H5N1 (A/Vietnam/1194/2004 clade 1) and Zoonotic Influenza Vaccine H5N1 (A/turkey/Turkey/1/2005 clade 2.2.1) were tested. Animals received one or two doses of vaccine containing 3.75 or 7.5 micrograms of antigen, followed by intranasal challenge on Day 42 after the second vaccine dose with a lethal dose of A/Vietnam/1203/04 virus.

All animals receiving 2 doses of Zoonotic Influenza Vaccine H5N1 were protected, and 94% of animals receiving a single dose of Zoonotic Influenza Vaccine H5N1 were protected. 87% of animals challenged with virus heterologous to the vaccine strain after 2 doses of vaccine were protected, and a single dose of heterologous vaccine protected 56% of the animals.

In a similar study, intranasal challenge was delayed until approximately 4 months after the second dose of vaccine was administered (Study 780-N007104). In this study 100% of animals were protected against homologous challenge, and 81% of animals were protected against heterologous challenge. Vaccination protected animals from lethal challenge even when HI antibody titres were low or undetectable.

In Study 673-N106850, Zoonotic Influenza Vaccine H5N1 containing 7.5 micrograms of antigen (A/Vietnam/1194/2004) was immunogenic, able to fully protect against mortality and to reduce virus shedding from nasal washes after a lethal homologous challenge. In Study CBI-PCS-008, Zoonotic Influenza Vaccine H5N1 containing either 7.5 or 15 micrograms of antigen (A/Vietnam/1194/2004) was able to reduce the proportion of animals shedding virus as well as the amount of virus shedding after a non-lethal homologous challenge. Serological testing indicated both doses were immunogenic and induced cross-reactive antibodies against A/turkey/Turkey/1/2005 (Study VIV-PCS-001).

Efficacy against challenge with the heterologous virus A/Indonesia/5/2005 was also tested (Study 2810200). Ferrets received one or two doses of vaccine (A/Vietnam/1194/2004). Two doses of vaccine protected 92% of animals, and a single dose of vaccine protected 50% of animals against challenge with the A/Indonesia/5/2005 virus. Lung damage was reduced in vaccinated groups. Viral shedding and viral titres in lungs were also reduced, suggesting that vaccination may reduce the risk of viral transmission.

5.2 Pharmacokinetic properties

Not applicable.

5.3 Preclinical safety data

No preclinical safety data are available with Zoonotic Influenza Vaccine Seqirus H5N8.

Non-clinical data obtained with Zoonotic Influenza Vaccine H5N1 and with seasonal influenza vaccine containing MF59C.1 adjuvant reveal no special hazard for humans based on conventional studies of repeated dose toxicity, local tolerance, female fertility, and reproductive and developmental toxicity (through the end of the lactation period).

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium chloride
Potassium chloride
Potassium dihydrogen phosphate
Disodium phosphate dihydrate
Magnesium chloride hexahydrate
Calcium chloride dihydrate
Water for injections.

For the adjuvant, see section 2

6.2 Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

6.3 Shelf life

2 years.

6.4 Special precautions for storage

Store in a refrigerator (2 °C – 8 °C).
Do not freeze. Discard if the vaccine has been frozen.
Keep the pre-filled syringe in the outer carton in order to protect from light.

6.5 Nature and contents of container

0.5 ml in pre-filled syringe (type I glass) with plunger-stopper (bromo-butyl rubber).

Packs of 1 or 10 pre-filled syringes. Each pre-filled syringe contains 1 dose of 0.5 mL

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

The vaccine comes ready to use. Gently shake before use.

After shaking, the normal appearance of Zoonotic Influenza Vaccine Seqirus H5N8 is a milky-white suspension.

Visually inspect the suspension prior to administration. In case of any particles and/or abnormal appearance, the vaccine should be discarded.

Any unused vaccine and waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Seqirus S.r.l.
Via del Pozzo 3/A, S. Martino
53035 Monteriggioni (SI)
Italy.

8. MARKETING AUTHORISATION NUMBER(S)

EU/1/23/1761/001
EU/1/23/1761/002

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 09 October 2023

10. DATE OF REVISION OF THE TEXT

Detailed information on this medicinal product is available on the website of the European Medicines Agency http://www.ema.europa.eu/.

ANNEX II

A. MANUFACTURERS OF THE BIOLOGICAL ACTIVE SUBSTANCE AND MANUFACTURER(S) RESPONSIBLE FOR BATCH RELEASE

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

A. MANUFACTURERS OF THE BIOLOGICAL ACTIVE SUBSTANCE AND MANUFACTURER RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturers of the biological active substance

Seqirus Vaccines Ltd
Gaskill Road, Speke, Liverpool
L24 9GR
UK

Name and address of the manufacturer responsible for batch release

Seqirus Netherlands B.V.
Paasheuvelweg 28
1105BJ Amsterdam
Netherlands

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Medicinal product subject to medical prescription.

- **Official batch release**

In accordance with Article 114 of Directive 2001/83/EC, the official batch release will be undertaken by a state laboratory or a laboratory designated for that purpose.

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

- **Periodic safety update reports (PSURs)**

The requirements for submission of PSURs for this medicinal product are set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and any subsequent updates published on the European medicines web-portal.

PSUR submission when Zoonotic Influenza Vaccine Seqirus is used during an influenza pandemic:

During a pandemic situation, the annual frequency of PSUR submission may not be adequate for the safety monitoring of a pandemic vaccine for which high levels of exposure are expected within a short period of time. Such situation requires rapid notification of safety information that may have the greatest implications for benefit-risk balance in a pandemic. Prompt analysis of cumulative safety information, in light of extent of exposure, will be crucial for regulatory decisions and protection of the population to be vaccinated.

In consequence, as soon as the pandemic is declared and the zoonotic vaccine is used, the Marketing Authorisation Holder (MAH) shall submit more frequent simplified PSURs with a periodicity defined in the Risk Management Plan (RMP).

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

- **Risk management plan (RMP)**

The marketing authorization holder (MAH) shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2 of the marketing authorisation and any agreed subsequent updates of the RMP.

An updated RMP should be submitted:

- At the request of the European Medicines Agency;
- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.

If the dates for submission of a PSUR and the update of a RMP coincide, they can be submitted at the same time.

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARDBOARD BOX

1. NAME OF THE MEDICINAL PRODUCT

Zoonotic Influenza Vaccine Seqirus suspension for injection in pre-filled syringe
Zoonotic influenza vaccine (H5N8) (surface antigen, inactivated, adjuvanted)

2. STATEMENT OF ACTIVE SUBSTANCE

One dose of 0.5 ml contains: Influenza virus surface antigens (haemagglutinin and neuraminidase), propagated in fertilised hens' eggs from healthy chicken flocks, of strain:

A/Astrakhan/3212/2020 (H5N8)-like strain (CBER-RG8A) (clade 2.3.4.4b) 7.5 micrograms haemagglutinin

Adjuvant: MF59C.1 oil in water emulsion containing squalene, as the oil phase, stabilised with polysorbate 80, sorbitan trioleate, sodium citrate and citric acid.

3. LIST OF EXCIPIENTS

Sodium chloride
Potassium chloride
Potassium dihydrogen phosphate
Disodium phosphate dihydrate
Magnesium chloride hexahydrate
Calcium chloride dihydrate
Water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Suspension for injection.

1 pre-filled syringe (0.5 ml)
10 pre-filled syringes (0.5 ml)

5. METHOD AND ROUTE OF ADMINISTRATION

To be administered intramuscularly into the deltoid muscle

Read the package leaflet before use.

Gently shake before use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator.
Do not freeze.
Keep the pre-filled syringe in the outer carton in order to protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

Dispose of in accordance with local requirements.

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Seqirus S.r.l.
Via del Pozzo 3/A, S. Martino
53035 Monteriggioni (SI)
Italy.

12. MARKETING AUTHORISATION NUMBER

EU/1/23/1761/001 1 prefilled syringe
EU/1/23/1761/002 10 prefilled syringes

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Justification for not including Braille accepted

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

LABEL FOR SYRINGE

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE OF ADMINISTRATION

Zoonotic Influenza Vaccine Seqirus injection
Zoonotic influenza vaccine (H5N8)
IM

2. METHOD OF ADMINISTRATION

Intramuscular use

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

0.5 ml

6. OTHER

B. PACKAGE LEAFLET

Package leaflet: information for the user

Zoonotic Influenza Vaccine Seqirus suspension for injection in pre-filled syringe
Zoonotic influenza vaccine (H5N8) (surface antigen, inactivated, adjuvanted)

Read all of this leaflet carefully before you receive this vaccine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or nurse.
- If you get any side effects, talk to your doctor or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Zoonotic Influenza Vaccine Seqirus is and what it is used for

Zoonotic Influenza Vaccine Seqirus is a vaccine for use in individuals 6 months of age and older , intended to be given in the context of risk of outbreaks of zoonotic influenza (coming from birds) to prevent flu caused by H5 subtype influenza A viruses.

Zoonotic influenza viruses occasionally infect humans, and can cause disease ranging from mild upper respiratory infection (fever and cough) to rapid progression to severe pneumonia, acute respiratory distress syndrome, shock and even death. Human infections are primarily caused by contact with infected animals, but do not spread easily between people.

Zoonotic Influenza Vaccine Seqirus is intended also to be given when there is anticipation of a possible pandemic due to the same or a similar strain.

When a person is given the vaccine, the immune system (the body's natural defence system) will produce its own protection (antibodies) against the disease. None of the ingredients in the vaccine can cause flu.

2. What you need to know before you are given Zoonotic Influenza Vaccine Seqirus

You should not receive Zoonotic Influenza Vaccine Seqirus:

- if you have previously had a sudden life-threatening allergic reaction to any ingredient of Zoonotic Influenza Vaccine Seqirus (listed in section 6) or to any of the substances that may be present in trace amounts as follows: egg and chicken protein, ovalbumin, formaldehyde, kanamycin and neomycin sulphate (antibiotics), hydrocortisone or cetyltrimethylammonium bromide (CTAB). Signs of an allergic reaction may include itchy skin rash, shortness of breath and swelling of the face or tongue. However, in a pandemic situation, it may be appropriate for you to be vaccinated with Zoonotic Influenza Vaccine Seqirus provided that appropriate medical treatment is immediately available in case of an allergic reaction.

Warnings and precautions
Talk to your doctor or nurse before having this vaccine

- if you have had any allergic reaction to any ingredient contained in the vaccine, to egg and chicken protein, ovalbumin, formaldehyde, kanamycin and neomycin sulphate (antibiotics), hydrocortisone or cetyltrimethylammonium bromide (CTAB) (see section 6. Further information);

- if you have a severe infection with fever (over 38 °C). If this applies to you then your vaccination will usually be postponed until you are feeling better. A minor infection such as a cold should not be a problem, but your doctor or nurse should advise whether you could still be vaccinated with Zoonotic Influenza Vaccine Seqirus;

- if you have a bleeding problem or bruise easily.

Fainting can occur following, or even before, any needle injection. Therefore tell the doctor or nurse if you fainted with a previous injection.

Zoonotic Influenza Vaccine Seqirus may not fully protect everyone who is vaccinated, especially elderly subjects and those with weakened immune systems, such as HIV patients, or those with underlying long term medical problems, such as diabetes, lung disease or heart problems. Tell your doctor if you have a weak immune system or an underlying long term medical problem.

In any of these cases, TELL YOUR DOCTOR OR NURSE, as vaccination may not be recommended, or may need to be delayed.

Children

Children aged less than 6 months of age
Vaccination is currently not recommended in this age group.

Other medicines and Zoonotic Influenza Vaccine Seqirus
Tell your doctor or nurse if you are taking or have recently taken or might take any other medicines, including medicines obtained without a prescription or have recently received any other vaccine.

If administration of Zoonotic Influenza Vaccine Seqirus with other vaccines cannot be avoided, the vaccines should be injected into separate limbs. In such cases, you should be aware that the side effects may be more intense.

Pregnancy and breast-feeding
If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or nurse for advice before receiving this vaccine. Your doctor needs to assess the benefits and potential risks of giving you the vaccine.

Driving and using machines
Some effects mentioned under section 4. “Possible side effects” may affect the ability to drive or use machines.

Zoonotic Influenza Vaccine Seqirus contains sodium and potassium.
This vaccine contains less than 1 mmol sodium (23 mg) per dose, i.e. essentially “sodium free”.
This vaccine contains less than 1 mmol of potassium (39 mg) per 0.5 ml dose, i.e. essentially “potassium free”.

3. How Zoonotic Influenza Vaccine Seqirus is given

Your doctor or nurse will administer the vaccine in accordance with official recommendations.
A dose (0.5 ml) of the vaccine will be injected into the upper arm (deltoid muscle) or upper thigh, depending on the muscle mass.The vaccine should never be given into a vein.

Individuals 6 months of age and older:
One dose of 0.5 ml will be given. A second dose of 0.5 ml should be given after an interval of at least 3 weeks.

There is limited experience in elderly over 70 years of age.

If you have any further questions on the use of this medicinal product, ask your doctor or nurse.

4. Possible side effects

Like all medicines, Zoonotic Influenza Vaccine Seqirus can cause side effects, although not everybody gets them.

Tell your doctor immediately or go to the casualty department at your nearest hospital if you experience the following side effect – you may need urgent medical attention or hospitalisation:

- difficulty in breathing, dizziness, a weak and rapid pulse and skin rash which are symptoms of an anaphylactic reaction (a very severe allergic reaction)

Allergic reactions may occur following vaccination, and these may be severe. Doctors are aware of this possibility and have emergency treatment available for use in such cases. Get urgent medical attention if you experience any of the following signs or symptoms of a severe allergic reaction: difficulty in breathing, swelling, lightheadedness, fast heartbeat, sweating and loss of consciousness.

The side effects listed below have occurred with a vaccine similar to Zoonotic Influenza Vaccine Seqirus based on a similar virus (H5N1) during clinical studies in adults, including the elderly and children. These side effects may occur with Zoonotic Influenza Vaccine Seqirus.

Side effects from clinical studies:

Very common (may affect more than 1 in 10 people):
- Pain/tenderness at the site of injection
- Hardening of the skin at the injection site
- Injection site redness
- Injection site swelling
- Bruising of the skin at the injection site*
- Aching muscles
- Headache
- Fatigue
- Generally feeling unwell
- Shivering
- Sweating*
- Nausea*
- Change in eating habits**
- Diarrhoea
- Vomiting
- Sweating and unusual sweating**
- Sleepiness**
- Iritability**

- Unusual crying**
- Fever***

** Reported as, Common, in adults and elderly*
*** Reported only in infants and young children 6-35 months of age*
****Reported as Very common only in children 6 months-8 years. Reported as Common in adolescents and adults 9-60 years of age and Uncommon in eldery (over 61 years)*

Common (may affect up to 1 in 10 people):
- Aching joints
- Injection site bleeding
- Loss of appetite

Uncommon (may affect up to 1 in 100 people)
- Hives (Urticaria)

These side effects usually disappear within 1-2 days without treatment. If they persist, CONSULT YOUR DOCTOR.

Side effects in persons with underlying long term medical problems such as diabetes, lung disease or heart problems and weakened immune systems (immunocompromised) such as HIV patients
Nausea, aching joints, diarrhoea and loss of appetite were reported very commonly. In addition, vomiting was commonly reported.

Other side effects observed after routine use
The additional side effects listed below have occurred in the days or weeks after vaccination with another vaccine based on a similar virus (H1N1) and with the same adjuvant. These side effects may occur with Zoonotic Influenza Vaccine Seqirus.

- Generalised skin reactions including
  - Itching
  - Rash or swelling of the skin and mucous membranes
  - Angioedema (abnormal swelling of the skin, usually around the eyes, lips, tongue, hands or feet, due to an allergic reaction).

- Disorders of the gut such as
  - Abdominal pain

- Dizziness, drowsiness.

- Neurological disorders such as
  - Severe stabbing or throbbing pain along one or more nerves
  - Tingling
  - Fits
  - Neuritis (inflammation of nerves)
  - Syncope or presyncope (fainting or feeling about to faint)

- Swollen lymph nodes, palpitations (irregular or forceful heart beat), tachycardia (faster than normal heart beat), weakness, pain in the extremities, cough and asthenia (unusual weakness).

- Allergic reactions possibly with shortness of breath, wheezing, swelling of the throat, or leading to a dangerous decrease of blood pressure, which, if untreated, may lead to shock.

In addition, side effects listed below have occurred in the days or weeks after vaccination with adjuvanted and not-adjuvanted vaccines given routinely every year to prevent seasonal flu. These side effects may occur with Zoonotic Influenza Vaccine Seqirus.

- Low blood platelet count which can result in bleeding or bruising.
- Vasculitis (inflammation of the blood vessels which can cause skin rashes, joint pain and kidney problems).
- Erythema multiforme (type of allergic skin reaction that occurs in response to medications, infections, or illness).
- Neurological disorders such as encephalomyelitis (inflammation of the central nervous system), and a type of paralysis known as Guillain-Barré Syndrome.
- Swelling, pain and redness at the injection site extending to more than 10 cm and lasting more than one week (Injection site cellulitis-like reaction).
- Extensive swelling of injected limb lasting more than one week.

Reporting of side effects
If you get any side effects, talk to your doctor or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects, you can help provide more information on the safety of this medicine.

5. How to store Zoonotic Influenza Vaccine Seqirus

Keep this vaccine out of the sight and reach of children.

Do not use Zoonotic Influenza Vaccine Seqirus after the expiry date which is stated on the carton and the label. The expiry date refers to the last day of that month.

Store in a refrigerator (2 °C – 8 °C).
Do not freeze.
Keep the pre-filled syringe in the original outer carton in order to protect from light.

Do not throw any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help to protect the environment.

6. Contents of the pack and other information

What Zoonotic Influenza Vaccine Seqirus contains

- Active substance:
  Influenza virus surface antigens (haemagglutinin and neuraminidase)* of strain:

  A/Astrakhan/3212/2020 (H5N8)-like strain (CBER-RG8A) (clade 2.3.4.4b)7.5 micrograms** per 0.5 ml dose

  * propagated in fertilised hens' eggs from healthy chicken flocks
  ** expressed in microgram haemagglutinin.

- Adjuvant MF59C.1:
  The vaccine contains per 0.5 ml: 9.75 mg squalene, 1.175 mg polysorbate 80, 1.175 mg sorbitan trioleate, 0.66 mg sodium citrate and 0.04 mg citric acid.

- Other ingredients:
  The other ingredients are: sodium chloride, potassium chloride, potassium dihydrogen phosphate, disodium phosphate dihydrate, magnesium chloride hexahydrate, calcium chloride dihydrate and water for injections. See Section 2 - Zoonotic Influenza Vaccine Seqirus contains sodium and potassium.

What Zoonotic Influenza Vaccine Seqirus looks like and contents of the pack

Zoonotic Influenza Vaccine Seqirus is a suspension for injection in a pre-filled syringe.
The suspension is a milky-white liquid.
It is provided in a ready-to-use pre-filled syringe, containing a single dose of 0.5 ml for injection.

Packs of 1 or 10 pre-filled syringes.

Not all pack sizes may be marketed.

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Detailed information on this medicine is available on the European Medicines Agency web site: http://www.ema.europa.eu.