

~~REVISION OF THE~~ CORE SPC FOR TRIVALENT INFLUENZA VACCINES

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Introduction

Requirements affecting the content of SPCs are to be found in a number of EU regulatory documents including Directive 2001/83/EC as amended¹ and in the European Commissions Guideline on the Summary of Product Characteristics. Guidance specific to composing SPCs for human vaccines appears in the Guideline on the Pharmaceutical Aspects of the Product Information for Human Vaccines (EMEA/CPMP/BWP/2758/02). There are also in existence a number of QRD group documents which provide guidance on drafting SPCs.

The function of the present document is to provide additional guidance on the composition of SPCs for inactivated, non-adjuvanted, influenza vaccines prepared using influenza viruses grown in fertilised hens' eggs.

SPCs for live influenza vaccines, and for influenza vaccines produced using cell cultures as virus propagation substrates, fall outside the scope of the document.

In effect, this means that SPCs for vaccines complying with the following PhEur monographs are affected:

- Influenza vaccine (split virion, inactivated) [Monograph 0158]
- Influenza vaccine (surface antigen, inactivated) [Monograph 0869]
- Influenza vaccine (whole virion, inactivated) [Monograph 0159]

Standard text to be used in the SPC is denoted using bold font.

Pieces of text which cannot be specified in the guideline and which therefore need to be generated on a product-specific basis are delimited using the characters < >.

Sometimes no concrete text proposal has been formulated, but instead items of guidance related to specific sections in the SPC are given. These are written in normal font.

On some places a justification (in italic) concerning a proposal has been included.

¹Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use (as amended)

1. NAME OF THE MEDICINAL PRODUCT

The standard requirement is for the invented name of the medicinal product, the strength and the pharmaceutical form to appear.

However, in the case of influenza vaccines, the strength (the haemagglutinin (HA) content for each strain present in the vaccine) should be omitted from the invented name in the SPC.

The common name should be that of the monograph in the *European Pharmacopoeia* with which the vaccine complies.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

<Whole influenza virus (inactivated)> <Influenza virus (inactivated, split)><Influenza virus surface antigens (haemagglutinin and neuraminidase)> of the following strains*:

A/<Official strain> (H1N1) *** like strain (<actual strain>) <n> micrograms HA**

A/<Official strain> (H3N2) *** like strain (<actual strain>) <n> micrograms HA**

B/<Official strain> like strain (<actual strain>) *** <n> micrograms HA**

.....
per <n> ml dose

* propagated in fertilised hens' eggs from healthy chicken flocks

** haemagglutinin

*** When the official strain is directly used: nothing added.

When the strain used is like to the official one: - like strain used <actual strain >.

When the strain used is derived from the official one: - derived strain used <actual strain >.

When the strain used is derived from a strain like to the official one: - like strain used <actual strain> derived from <like strain>.

This vaccine complies with the WHO recommendation (northern hemisphere) and EU decision for the <year/year> season.

For a full list of excipients see section 6.1.

3. PHARMACEUTICAL FORM

The full *European Pharmacopoeia* standard term should be used and a brief description of the product should follow.

4. CLINICAL PARTICULARS

4.1. THERAPEUTIC INDICATIONS

Prophylaxis of influenza, especially in those who run an increased risk of associated complications.

The use of <invented name of vaccine> should be based on official recommendations.

Note: this is standard wording for vaccines.

4.2. POSOLOGY AND METHOD OF ADMINISTRATION

Adults and children from 36 months: 0.5 ml.

Children from 6 months to 35 months: Clinical data are limited. Dosages of 0.25 ml or 0.5 ml have been used. The dose given should be according to the approved dosage for the respective vaccines.

For children, who have not previously been vaccinated, a second dose should be given after an interval of at least 4 weeks.

Justification:

There have been differences in children dosage between Member States and no sound evidence is available to justify a specific dosage.

Immunisation should be carried out by intramuscular or deep subcutaneous injection.

A text like “Immunodeficient patients are recommended to be immunised twice with an interval of at least 4 weeks” should not be included in the SPC.

For instructions for preparation, see section 6.6.

4.3 CONTRA-INDICATIONS

Hypersensitivity to the active substances, to any of the excipients *(if the vaccine contains thiomersal as preservative, the following should be included:)* <product specific: such as thiomersal> and to {residues <product specific: e.g. eggs, chicken proteins, such as ovalbumin >. ~~<Invented name of vaccine> does not contain more than <n> microgram ovalbumin per dose.~~ The vaccine may contain residues of the following substances <product specific>, e.g. antibiotics, thiomersal}.

Immunisation shall be postponed in patients with febrile illness or acute infection

4.4. SPECIAL WARNINGS AND PRECAUTIONS FOR USE

As with all injectable vaccines, appropriate medical treatment and supervision should always be readily available in case of an anaphylactic event following the administration of the vaccine.

<Invented name of the vaccine> should under no circumstances be administered intravascularly.

Antibody response in patients with endogenous or iatrogenic immunosuppression may be insufficient.

~~If thiomersal is used in the manufacturing process which results in levels of thiomersal \geq 40 ng per dose, the vaccine contains residues of thiomersal~~ the following should be mentioned:

Thiomersal (an organomercuric compound) has been used in the manufacturing process of this medicinal product and residues of it are present in the final product. Therefore, sensitisation reactions may occur (see section 4.3).

For levels of thiomersal < 40 ng per dose or undetectable levels, no statements are recommended for inclusion.

4.5. INTERACTION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTION

<Invented name of the vaccine> may be given at the same time as other vaccines. Immunisation should be carried out on separate limbs. It should be noted that the adverse reactions may be intensified.

The immunological response may be diminished if the patient is undergoing immunosuppressant treatment.

Following influenza vaccination, false positive results in serology tests using the ELISA method to detect antibodies against HIV1, Hepatitis C and especially HTLV1 have been observed. The Western Blot technique disproves the false-positive ELISA test results. The transient false positive reactions could be due to the IgM response by the vaccine.

4.6. PREGNANCY AND LACTATION

The limited data from vaccinations in pregnant women do not indicate that adverse fetal and maternal outcomes were attributable to the vaccine. The use of this vaccine may be considered from the second trimester of pregnancy. For pregnant women with medical conditions that increase their risk of complications from influenza, administration of the vaccine is recommended, irrespective of their stage of pregnancy.

<Invented name of the vaccine> may be used during lactation.

4.7. EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

The vaccine is unlikely to produce an effect on the ability to drive and use machines.

4.8. UNDESIRABLE EFFECTS

ADVERSE REACTIONS OBSERVED FROM CLINICAL TRIALS

The safety of trivalent inactivated influenza vaccines is assessed in open label, uncontrolled clinical trials performed as annual update requirement, including at least 50 adults aged 18 - 60 years of age and at least 50 elderly aged 61 years or older. –Safety evaluation is performed during the first 3 days following vaccination.

The following undesirable effects have been observed during clinical trials with the following frequencies:

very common ($>1/10$); common ($\geq 1/100$, $<1/10$); uncommon ($\geq 1/1000$, $<1/100$); rare ($\geq 1/10000$, $<1/1000$); very rare ($<1/10000$), including isolated reports.

Organ class	Very common $>1/10$	Common $>1/100$, $<1/10$	Uncommon $>1/1,000$, $<1/100$	Rare $> 1/10,000$, $<1/1,000$	Very rare $<1/10,000$
Nervous system disorders		Headache*			
Skin and subcutaneous tissue disorders		Sweating*			
Musculoskeletal and connective tissue disorders		Myalgia, arthralgia*			

Organ class	Very common >1/10	Common >1/100, <1/10	Uncommon >1/1,000, <1/100	Rare > 1/10,000, <1/1,000	Very rare <1/10,000
General disorders and administration site conditions		fever, malaise, shivering, fatigue Local reactions: redness, swelling, pain, ecchymosis induration*			

* ~~these~~These reactions usually disappear within 1-2 days without treatment

ADVERSE REACTIONS REPORTED FROM POST-MARKETING SURVEILLANCE

Adverse reactions reported from post marketing surveillance are, next to the reactions which have also been observed during the clinical trials, the following:

Blood and lymphatic system disorders:

Transient thrombocytopenia, transient lymphadenopathy

Immune system disorders:

Allergic reactions, in rare cases leading to shock, angioedema

Nervous system disorders:

Neuralgia, paraesthesia, febril convulsions, neurological disorders, such as encephalomyelitis, neuritis and Guillain Barré syndrome

Vascular disorders:

Vasculitis associated in very rare cases with transient renal involvement

Skin and subcutaneous tissue disorders:

Generalised skin reactions including pruritus, urticaria or non-specific rash

If the vaccine contains thiomersal as a preservative the following should be mentioned:

This medicinal product contains thiomersal (an organomercuric compound) as a preservative and therefore it is possible that sensitisation reactions may occur (see Section 4.3).

If the vaccine contains thiomersal as a residue from the manufacturing process which results in levels ≥ 40 ng per dose the following should be mentioned:

This medicinal product contains thiomersal (an organomercuric compound) as a residue from the manufacturing process and therefore it is possible that sensitisation reactions may occur (see section 4.4).

4.9 OVERDOSE

Overdosage is unlikely to have any untoward effect.

5. PHARMACOLOGICAL PROPERTIES

5.1. PHARMACODYNAMIC PROPERTIES

Pharmacotherapeutic group: Influenza vaccine, ATC Code: <J07BB01> or <J07BB02>
Seroprotection is generally obtained within 2 to 3 weeks. The duration of postvaccinal immunity to homologous strains or to strains closely related to the vaccine strains varies but is usually 6-12 months.

5.2. PHARMACOKINETIC PROPERTIES

Not applicable

5.3. PRECLINICAL SAFETY DATA

Not applicable

6. PHARMACEUTICAL PARTICULARS

6.1. LIST OF EXCIPIENTS

Product specific

According to the recommendation given by the Guideline on Summary of Product Characteristics, residues of production should not be stated in this Section.

6.2. INCOMPATIBILITIES

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

~~<This medicinal product must not be mixed with other medicinal products except those mentioned in 6.6>~~

See corresponding Section in the current template on SPC.

6.3. SHELF-LIFE

~~<n> <months> or <1 year>~~

The value of n should not ~~normally~~ be greater than eleven.

6.4. SPECIAL PRECAUTIONS FOR STORAGE

Product specific.

6.5. NATURE AND CONTENTS OF THE CONTAINER

Standard guidance on composing the entry under this section should be followed. Examples of entries are given in attachment 3 of the Guideline on pharmaceutical aspects of the product information for human vaccines (EMA/CPMP/BWP/2758/02).

6.6. SPECIAL PRECAUTIONS FOR DISPOSAL <AND OTHER HANDLING>

~~Unused vaccine and other waste material should be disposed of in compliance with local rules for the disposal of products of this nature.~~

The vaccine should be allowed to reach room temperature before use.

Shake before use.

Where a single dose 0.5 ml syringe is to be used for administration of a 0.25 ml dose, specific instructions ~~should be added~~will be required. See also section 4.2.

Any unused product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

8. MARKETING AUTHORISATION NUMBER(S)

9. DATE OF FIRST AUTHORISATION / RENEWAL OF THE AUTHORISATION

10. DATE OF REVISION OF THE TEXT