EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Work instructions

Title: EudraVigilance Medicinal Product Dictionary: Population with Approved Substances - type Vaccines		
Applies to: Staff members in the Pharmacovigilance and Risk Management Sector responsible for population of the EVMPD with Approved Substances		
Status: **PUBLIC**		Document no.: WIN/H/3302
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Signature: ON FILE	Signature: ON FILE	Supersedes: WIN/H/3302 (10-JUL-09)
Date: 20-SEP-10	Date: 20-SEP-10	TrackWise record no.: 2910

1. Changes since last revision

Updated to reflect the new organisational names in the Agency.

2. Records

Not Applicable.

3. Instructions

This Working Instruction refers to the SOP/H/3301 – EudraVigilance Medicinal Product Dictionary: Population with Approved Substances.

There is currently no internationally accepted standard terminology available to describe vaccine substances. Vaccine-related substances are classified, entered and maintained in the EVMPD, according to specific conventions.

This WIN is divided in four chapters describing EVMPD population with vaccine-related entries for:

3.1 Parent Organism

3.2 Common Name(s)

3.3. General Vaccine Type

3.4 Antigen(s)

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Each chapter provides definition, steps and examples for the population of the EVMPD with vaccine-related entries according to its type.

3.1. Parent Organism

Definition: A parent organism refers to any micro-organism (bacterium, virus or parasite) used for the elaboration of an 'active substance' in a vaccine (e.g. Influenza virus).

Choice of the preferred language for the Parent Organism 'Approved Substance Name' will depend on the actual language broadly used in the product labelling. Usually English or Latin language is chosen.

The following EVMPD fields should be populated:

- **Substance Name**: enter the English/Latin name
- **CAS number**: not applicable
- **Molecular Formula**: not applicable
- **Chemical/Biological Description**: enter where applicable
- **Source**: enter the Reference Source (e.g EU Ph. or SmPC)
- **Alias(es):** not applicable
- **Translation(s)**: not applicable,
- **Comment:** complete with 'entry cleaned - vaccine' to indicate that the EV code has been updated according to the rules described in this document and to identify the type of the substance in the EVMPD.

Description	Name/Value
Checked	Yes (14/10/2004 12:05.48)
Nullified	No
Type	Approved
EV Code	SUB15397MIG
Substance Name	PARENT ORGANISM X (Latin name)
CAS Number	
Molecular Formula	
Chemical / Biological Descript...	
Comment	entry cleaned - vaccine
	Source
	Substance Translations (-)
	Substance Aliases (-)
	Previous EV Codes (-)
	EVPR Messages (-)

Figure 1. EVMPD example 'Parent Organism' Latin Name as reflected in the EU SmPC

3.2. Common Names

Definition: A common name refers to the title of the relevant European Pharmacopoeia (EU Ph.) monograph (if existing). In cases there is no EU Ph. monograph available, the stylistics and precedents of EU Ph. monograph titles should be observed, including the use of words such as 'live', 'adsorbed', or 'virosome' in parenthesis, if relevant (*reference*: 'Guideline on Pharmaceutical Aspects of the Product Information for Human Vaccines, EMEA/CPMP/BWP/2758/02').

Depending on the availability of the vaccine common name in the EU Ph., the options to populate EVMPD should be as follows:

- Common name available in the EU Ph. (described in 3.2.1)
- Common name not available in the EU Ph. (described in 3.2.2)

3.2.1. Common name available in the EU Ph.

EU Ph. monographs define certain vaccine common names in terms of composition and quality. The EU Ph. monographs are accessible at the EMEA library website:
http://emeaplus/EMEAPlus_Website/Library/Resources/Ebooks.htm

The following EVMPD fields should be populated:

- **Substance Name**: enter the English name
- **CAS number**: not applicable
- **Molecular Formula**: not applicable
- **Chemical/Biological Description**: enter where applicable
- **Source**: enter the Reference Source (i.e. EU Ph.)
- **Alias(es):** enter if available from the Reference Source. Refer to Martindale and/or alternatively to various pharmacopoeias (e.g. British Pharmacopeia or US Pharmacopeia).
- **Translation(s)**: enter as available in the EU Ph. (i.e. Latin, French and Spanish),
- **Comment:** complete with 'entry cleaned - vaccine' to indicate that the EV code has been updated according to the rules described in this document and to identify the type of the substance in the EVMPD.

An example for a EU Ph. monograph is POLIOMYELITIS VACCINE (ORAL), which is defined as follows: *'Oral poliomyelitis vaccine is a preparation of approved strains of live attenuated poliovirus type 1, 2 or 3 grown in vitro cultures of approved cells, containing any one type or any combination of the 3 types of Sabin strains, presented in a form suitable for oral administration'*

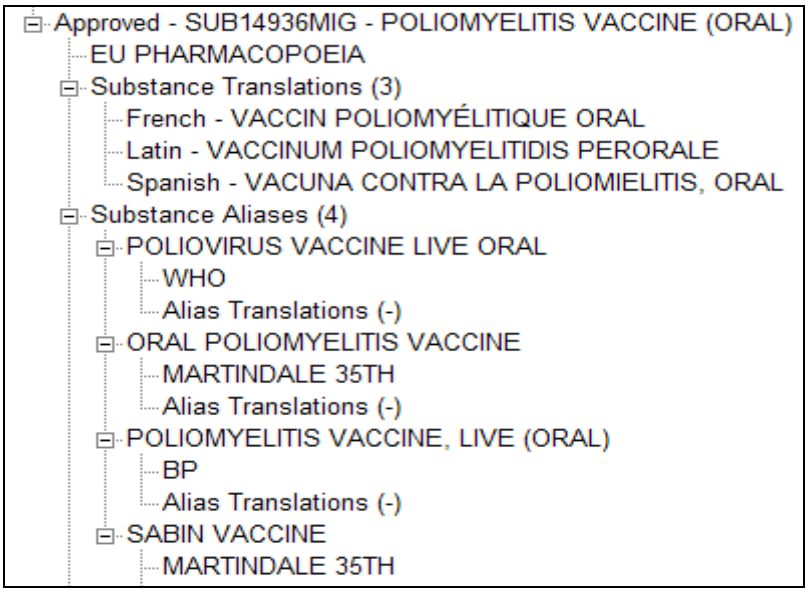


Figure 2. EVMPD example for a common name as defined in the EU Ph.:

3.2.2. Common name not available in the EU Ph.

In certain instances, vaccines are not described in the EU Pharmacopeia (or other pharmacopoeias). It is advised to follow the stylistics and precedents of EU Ph. monographs as defined in the *Guideline on Pharmaceutical Aspects of the Product Information for Human Vaccines*, EMEA/CPMP/BWP/2758/02' for preparing their SmPC.

A fictitious example is the '*Human X Virus'* vaccine. The EU SmPC, section 1 *'Name of Medicinal Product'* provides a common name in line with the aforementioned guideline, which should be used to populate the EVMPD.

<u>The following EVMPD fields should be populated:</u>

- **Substance Name:** enter the **English Name**
- **CAS number**: not applicable
- **Molecular Formula**: not applicable
- **Chemical/Biological Description**: enter where applicable
- **Source**: enter the Reference Source used (i.e. SPC)
- **Alias(es):** where applicable
- **Translation(s)**: where applicable
- **Comment**: complete with 'entry cleaned - vaccine' to indicate that the EV code has been updated according to the rules described in this document and to identify the type of the substance in the EVMPD.

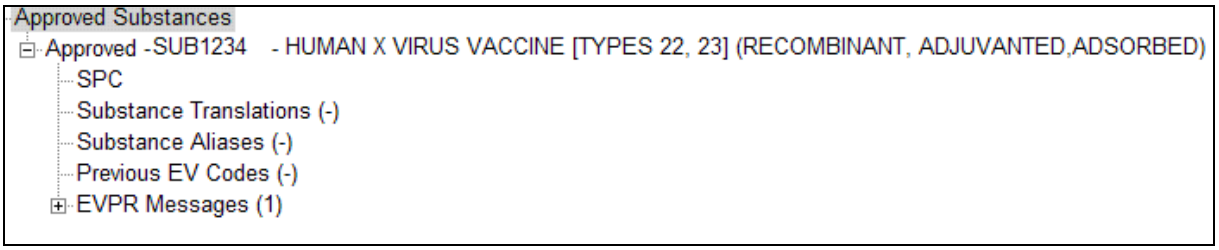


Figure 3. EVMPD example for a common name as defined in an EU SmPC:

3.3. General Vaccine Type

Definition: a general vaccine type relates to the Anatomical Therapeutic Chemical (ATC) classification maintained by WHO Collaborating Centre for Drug Statistics Methodology. The ATC classification is accessible as follows: http://www.whocc.no/

The following EVMPD fields should be populated:

- **Substance Name:** enter the Anatomical Therapeutic Chemical (ATC) classification as applicable for the vaccine
- **CAS number**: not applicable
- **Molecular Formula**: not applicable
- **Chemical/Biological Description**: enter where applicable
- **Source**: enter the Reference Source (i.e. ATC/WHO)
- **Alias(es)**: not applicable
- **Translation(s)**: not applicable
- **Comment**: complete with 'ATC code of the vaccine and entry cleaned' to indicate that the EV code has been updated according to the rules described in this document and to identify the type of the substance in the EVMPD.

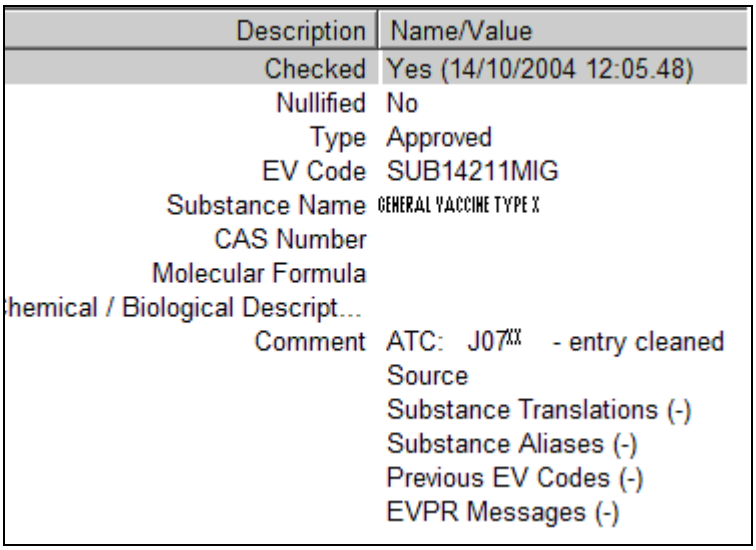


Figure 4. EVMPD example for a general vaccine type in accordance with the WHO/ATC classification

3.4. Antigen(s)

Definition: an antigen refers to a vaccine's active ingredient of microbiological origin prepared to induce protective antibodies.

Antigens are reflected in Section 2 '*Qualitative and Quantitative Composition'* of the Summary of Product Characteristics (SmPC).

This chapter describes:

- Antigens as reflected in the SmPC (see 3.4.1)
- Influenza virus antigens which need to be coded according to specific conventions in SmPC in the EU (see 3.4.2)

3.4.1. Antigens

Antigens reflected in the SmPC Section 2 '*Qualitative and Quantitative Composition'* should be described in the EVMPD on the basis of the following characteristics as applicable (see figure 5):

- Antigen name,
- Serotype,
- Strain description,
- State/modification [e.g. inactivated, live (attenuated)]
- Carrier protein (when antigen is conjugated),
- Adsorbant/adjuvant,
- Host cell (expression system)

The following EVMPD fields should be populated:

- **Substance Name**: English Name
- **CAS number**: not applicable
- **Molecular Formula**: not applicable
- **Chemical/Biological Description**: enter where applicable
- **Source**: enter the Reference Source as applicable (i.e. EU SmPC)
- **Alias(es)**: not applicable
- **Translation(s):** not applicable
- **Comment**: complete with 'entry cleaned - vaccine' to indicate that the EV code has been updated according to the rules described in this document and to identify the type of the substance in the EVMPD.

Example 1: Product A

PRODUCTA suspension for injection
ANTIGEN_XYZ saccharide conjugated vaccine, adsorbed

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 0.5 ml dose contains:

ANTIGEN_XYZ	polysaccharide serotype 1*	2 micrograms
ANTIGEN_XYZ	polysaccharide serotype 2*	4 micrograms
ANTIGEN_XYZ	polysaccharide serotype 3*	2 micrograms
ANTIGEN_XYZ	polysaccharide serotype 4*	2 micrograms
ANTIGEN_XYZ	oligosaccharide serotype 5*	2 micrograms
ANTIGEN_XYZ	polysaccharide serotype 6*	2 micrograms
ANTIGEN_XYZ	polysaccharide serotype 7*	2 micrograms

* Conjugated to the CRM_{197} carrier protein and adsorbed on aluminium phosphate (0.5 mg)

Figure 5. Antigen_XYZ antigens as in EU SmPC Product A

Three EVMPD entries for each of the 7 antigens in Product A need to be created as follows:

- One entry capturing antigen name + serotype
- One entry capturing antigen name + serotype + conjugation with carrier protein
- One entry capturing antigen name + serotype + conjugation with carrier protein + adsorbent.

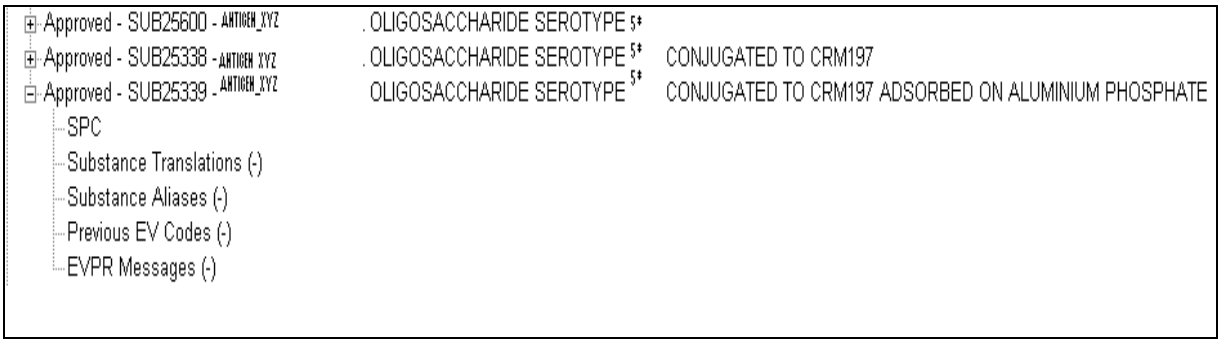


Figure 6. Example of three EV codes with reference to the Product A SmPC and the ANTIGEN_XYZ OLIGOSACCHARIDE SEROTYPE 5* antigen.

General schema for the above example:

Antigen name	Serotype	Conjugated to (e.g. CRM197)	Adsorbed on [e.g. Al(OH)3]

Figure 7

Example 2: Product B

PRODUCT B

Powder and solvent for suspension for injection.

ANTIGEN W , ANTIGEN A , and ANTIGEN F vaccine (live).

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

After reconstitution, one dose (0.5 ml) contains:

ANTIGEN W	virus[1] AAAAA	strain (live, attenuated).....not less than $1x10^3$ $CCID_{50}$*
ANTIGEN A	virus[1] BBBBB	strain (live, attenuated)....not less than $12.5x10^3$ $CCID_{50}$*
ANTIGEN F	virus[2] ccccc	strain (live, attenuated) .....not less than $1x10^3$ $CCID_{50}$*

*50% cell culture infectious dose

[1] produced in chick embryo cells.
[2] produced in WI-38 human diploid lung fibroblasts.

Figure 8. Antigen W, Antigen A and Antigen F in EU SmPC (Product B)

The three antigens of Product B should be presented as follows:

- ANTIGEN W, ANTIGEN A and ANTIGEN F virus as three separate EV codes
- ANTIGEN W, ANTIGEN A and ANTIGEN F virus including descriptor (live, attenuated) with three separate EV codes
- ANTIGEN W, ANTIGEN A and ANTIGEN F virus including descriptor (live, attenuated) and relevant strain description with three separate EV codes
- ANTIGEN W, ANTIGEN A and ANTIGEN F virus including descriptor (live, attenuated), relevant strain names and their host sources (expression system) with three separate EV codes

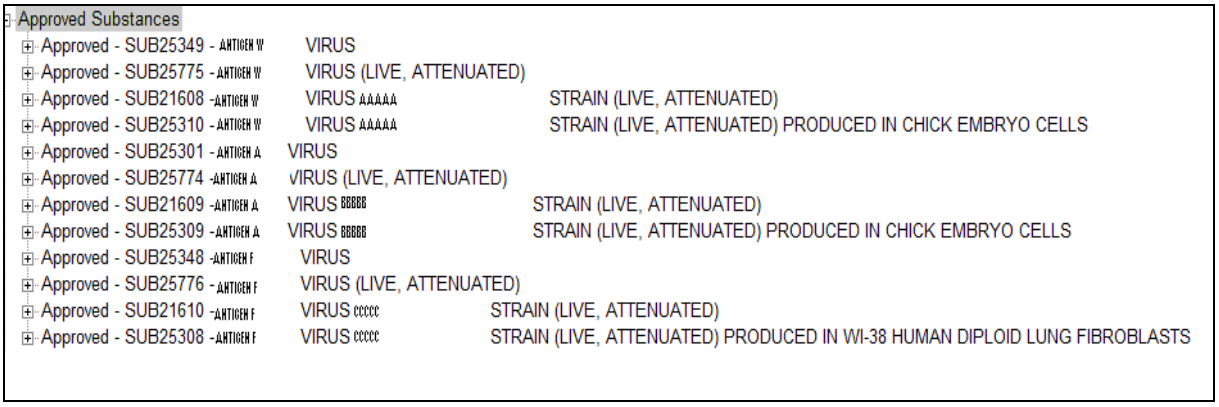


Figure 9. . Example of 12 EV codes with reference to the Product B SmPC.

General schema for the example above:

Antigen name	Strain description	Procedure (inactivated, live attenuated etc.)	Produced on (host cell, e.g. CHO)

Figure 10

3.4.2. Influenza Antigens

Influenza antigens need to be entered in the EVMPD based on the EU recommendations for seasonal and pandemic vaccination plans (in line with WHO proposals), which are published as follows: http://www.emea.europa.eu/htms/human/bwp/bwp.htm

Three steps need to be followed:

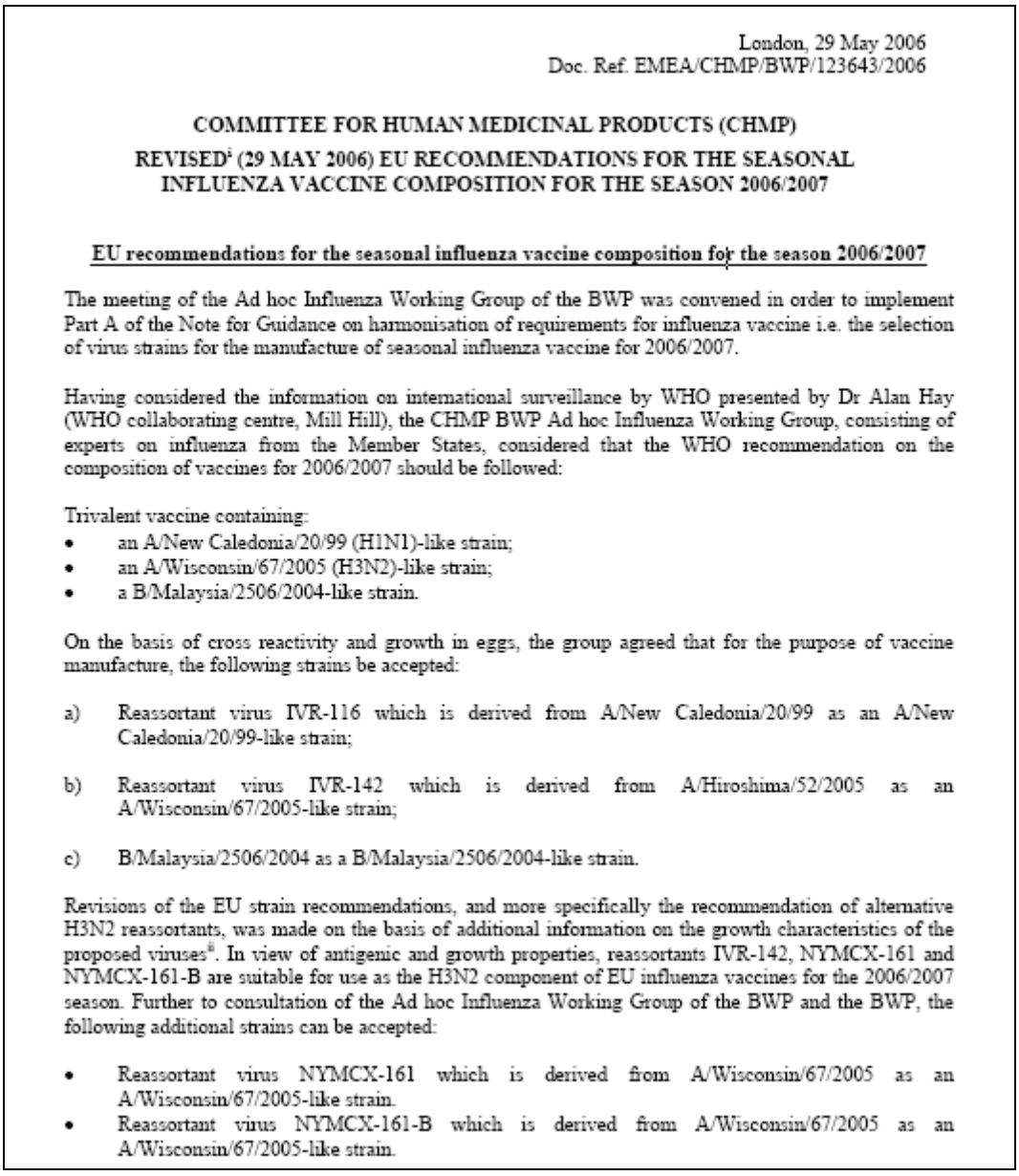
Step 1: Retrieve the relevant seasonal influenza vaccine recommendation

Step 2: Define the number of influenza antigen to be entered in the EVMPD

Step 3: Insert the influenza antigens in the EVMPD

Example: Entry for Influenza antigens for 2006/2007

Step 1: Retrieve the relevant seasonal influenza vaccine recommendation for the season 2006/2007 from the EMEA website.



London, 29 May 2006
Doc. Ref. EMEA/CHMP/BWP/123643/2006

COMMITTEE FOR HUMAN MEDICINAL PRODUCTS (CHMP)

REVISED[i] (29 MAY 2006) EU RECOMMENDATIONS FOR THE SEASONAL INFLUENZA VACCINE COMPOSITION FOR THE SEASON 2006/2007

EU recommendations for the seasonal influenza vaccine composition for the season 2006/2007

The meeting of the Ad hoc Influenza Working Group of the BWP was convened in order to implement Part A of the Note for Guidance on harmonisation of requirements for influenza vaccine i.e. the selection of virus strains for the manufacture of seasonal influenza vaccine for 2006/2007.

Having considered the information on international surveillance by WHO presented by Dr Alan Hay (WHO collaborating centre, Mill Hill), the CHMP BWP Ad hoc Influenza Working Group, consisting of experts on influenza from the Member States, considered that the WHO recommendation on the composition of vaccines for 2006/2007 should be followed:

Trivalent vaccine containing:

- an A/New Caledonia/20/99 (H1N1)-like strain;
- an A/Wisconsin/67/2005 (H3N2)-like strain;
- a B/Malaysia/2506/2004-like strain.

On the basis of cross reactivity and growth in eggs, the group agreed that for the purpose of vaccine manufacture, the following strains be accepted:

a) Reassortant virus IVR-116 which is derived from A/New Caledonia/20/99 as an A/New Caledonia/20/99-like strain;

b) Reassortant virus IVR-142 which is derived from A/Hiroshima/52/2005 as an A/Wisconsin/67/2005-like strain;

c) B/Malaysia/2506/2004 as a B/Malaysia/2506/2004-like strain.

Revisions of the EU strain recommendations, and more specifically the recommendation of alternative H3N2 reassortants, was made on the basis of additional information on the growth characteristics of the proposed viruses[ii]. In view of antigenic and growth properties, reassortants IVR-142, NYMCX-161 and NYMCX-161-B are suitable for use as the H3N2 component of EU influenza vaccines for the 2006/2007 season. Further to consultation of the Ad hoc Influenza Working Group of the BWP and the BWP, the following additional strains can be accepted:

- Reassortant virus NYMCX-161 which is derived from A/Wisconsin/67/2005 as an A/Wisconsin/67/2005-like strain.
- Reassortant virus NYMCX-161-B which is derived from A/Wisconsin/67/2005 as an A/Wisconsin/67/2005-like strain.

Figure 11

Step 2: Define the number of influenza antigen to be entered in the EVMPD

The same influenza strain can be applicable to more than one vaccination seasons. Therefore the EVMPD needs to be checked for existing strains, before a new strain is entered to avoid duplicate entries. According to the reference document (*Figure 11*) the following information needs to be captured:

1. A/NEW CALEDONIA/20/99 (H1N1) - LIKE STRAIN, specified as:
2. A/NEW CALEDONIA/20/99 (H1N1) - LIKE STRAIN (A/NEW CALEDONIA/20/99 REASS. IVR-116)
3. A/WISCONSIN/67/2005 (H3N2) - LIKE STRAINS specified as:
4. A/WISCONSIN/67/2005 (H3N2) - LIKE STRAIN (A/HIROSHIMA/52/2005 REASS. IVR-142)
5. A/WISCONSIN/67/2005 (H3N2) - LIKE STRAIN (A/WISCONSIN/67/2005 REASS. NYMCX-161)
6. A/WISCONSIN/67/2005 (H3N2) - LIKE STRAIN (A/WISCONSIN/67/2005 REASS. NYMCX-161-B)
7. B/MALAYSIA/2506/2004 - LIKE STRAIN, specified as:
8. B/MALAYSIA/2506/2004 - LIKE STRAIN (B/MALAYSIA/2506/2004)

Step 3: Insert the influenza antigens in the EVMPD

Based on the example eight antigens need to be entered in the field 'Substance Name' of the EVMPD with separate EV codes (see figure 12):

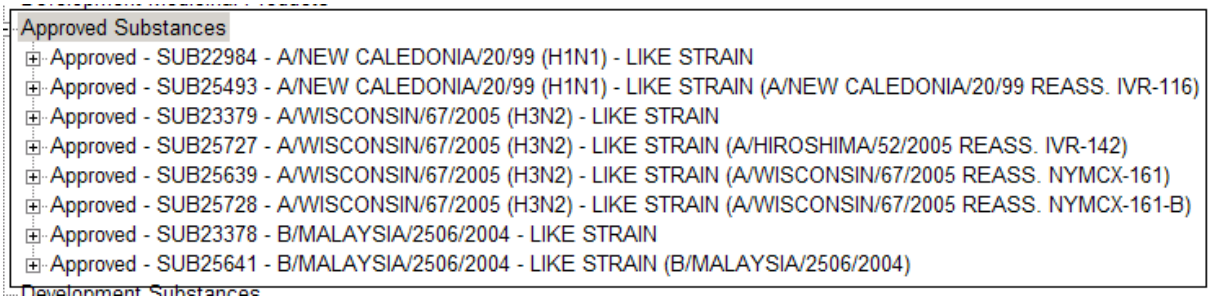


Figure 12

In addition, the following EVMPD fields should be populated in the EVMPD-

- **Substance Name**: enter the antigen
- **CAS number**: not applicable
- **Molecular Formula**: not applicable
- **Chemical/Biological Description**: enter where applicable
- **Alias(es):** where applicable
- **Translation(s):** where applicable
- **Source:** enter the Reference Source used (i.e. INFLUENZA RECOMMENDATIONS)
- **Comment:** complete with 'entry cleaned - vaccine' to indicate that the EV code has been updated according to the rules described in this document and to identify the type of the substance in the EVMPD.