Pandemic influenza vaccines centrally authorised in the EU

http://www.emea.europa.eu/htms/human/pandemicinfluenza/vaccines.htm

(*Web page last updated: 29 April, 2009*)

EMEA pandemic influenza preparedness ~ Influenza vaccines

In the event of an outbreak of pandemic influenza, vaccines would be essential to protect the public against the disease. Normal flu vaccines, which are designed to protect against seasonal flu, are not intended to be used during a flu pandemic. Instead, special pandemic flu vaccines are developed to build up some protection against the pandemic virus in people who have not yet been exposed to it.
Until the pandemic starts, however, the strain of flu virus that will be involved is not known. Therefore, pandemic flu vaccines can only be prepared once a pandemic has started and the strain of flu virus responsible is identified.

Two types of vaccine have been developed to deal with possible future pandemics: mock-up vaccines and pre-pandemic vaccines.

- **Mock-up vaccines** contain a strain of the influenza virus that has been specifically chosen because the population has never been exposed to it. During a pandemic, the World Health Organization formally identifies the virus strain causing the pandemic, and makes it available for vaccines to be developed. Companies are then able to use this official strain to prepare a strain suitable for fighting the pandemic that can replace the original strain in the 'mock-up' vaccine. Because the company has already carried out studies on the mock-up vaccine, it can predict how people will react to the vaccine when the strain causing the pandemic is included. This will shorten the time for a new vaccine to be made available to prevent the spread of the pandemic.

- **Pre-pandemic vaccines** are intended for use before a pandemic to protect against a strain of flu that is expected to cause a future pandemic. The pre-pandemic vaccines currently available contain the influenza virus type A/H5N1 (‘bird flu’) because health experts expect this strain to cause the next influenza pandemic.

In contrast, seasonal vaccines contain virus strains that cause seasonal influenza and not pandemic influenza. Each year, the World Health Organization (WHO) makes recommendations on which flu strains should be included in vaccines for the upcoming flu season.

Vaccines developed for pandemic influenza

Mock-up vaccines

1 Daronrix
2 Focetria
3 Pandemrix
4 Celvapan

Pre-pandemic vaccines

5 Prepandrix
6 Prepandemic influenza vaccine (H5N1) (split virion, inactivated, adjuvanted) GlaxoSmithKline Biologicals

http://www.who.int/csr/disease/swineflu/notes/h1n1_safety_vaccines_20090805/en/index.html

WHO, Pandemic (H1N1) 2009 briefing note 6

August 6, 2009

"Time constraints mean that clinical data at the time
when pandemic vaccines are first administered
will inevitably be limited.
Further testing of safety and effectiveness will need to take place
after administration of the vaccine has begun."

"In some cases, pandemic vaccines are not regarded by regulatory authorities as entirely "new" vaccines,
as they build on the technology used to produce vaccines for seasonal influenza,
established procedures for testing and regulatory control, and an extensive body of safety data."

"In the European Union, the European Medicines Agency uses
a rolling review procedure whereby manufacturers can submit sets of data
for regulatory review as they become available,
without having to wait until all data can be submitted together in a single formal application."

"Also in Europe, some manufacturers have conducted
advance studies using a so-called "mock-up" vaccine."

"Mock-up vaccines contain an active ingredient for an influenza virus
that has not circulated recently in human populations
and thus mimics the novelty of a pandemic virus."

"International sharing of data from such post-marketing surveillance will be vital
in guiding risk-benefit assessments and determining
whether changes in vaccination policies are needed."

http://www.emea.europa.eu/humandocs/PDFs/EPAR/daronrix/H-706-en1.pdf

EUROPEAN PUBLIC ASSESSMENT REPORT (EPAR)

DARONRIX
EPAR summary for the public

How does Daronrix [and the other 'mock-ups'] **work?**

Daronrix is a 'mock-up' vaccine.

This is a special type of vaccine that can be developed to help with the management of a pandemic. Before a pandemic starts, nobody knows which strain of flu virus will be involved, so companies cannot prepare the correct vaccine inadvance. Instead, they can prepare a vaccine that contains a strain of flu virus specifically chosen because nobody has been exposed to it, and to which nobody is immune.

They can test this vaccine to see how people react to it, allowing them to predict how people will react when the flu strain causing a pandemic is included.
Vaccines work by 'teaching' the immune system (the body's natural defences) how to defend itself against a disease. Daronrix contains small amounts of a virus called H5N1.

The virus is whole, but it has been inactivated (killed) so that it does not cause disease. If a pandemic starts, the virus strain in Daronrix will be replaced by the strain causing the pandemic before the vaccine can be used.

When a person is given the vaccine, the immune system recognises the inactivated virus as 'foreign' and makes antibodies against it. The immune system will then be able to produce antibodies more quickly when it is exposed to the virus again. This helps to protect against the disease.
The vaccine also contains an 'adjuvant' (a compound containing aluminium) to stimulate a better response.

http://www.emea.europa.eu/influenza/vaccines/home.htm

Pandemic influenza (H1N1) website

In the European Union, procedures have been put in place to speed up the assessment and authorisation of vaccines that may prove vital in a pandemic situation.Three vaccines that have benefited from these procedures, and which will thus be available for use in the current H1N1 influenza pandemic, are:

- Focetria, which was recommended on 24 September 2009 by the EMEA for an EU-wide marketing authorisation.
- Pandemrix, which was recommended on 24 September 2009 by the EMEA for an EU-wide marketing authorisation.
- Celvapan, which was recommended on 1 October 2009 by the EMEA for an EU-wide marketing authorisation.

Further information on the scientific considerations regarding the licensing of pandemic A(H1N1)v vaccines is available in an Explanatory Note.

One other vaccine, Daronrix, has been authorised as a 'mock up' vaccine for potential use during an influenza pandemic, but has not yet been approved for use in the current H1N1 pandemic.

For further information on how pandemic influenza vaccines are assessed, approved for use and monitored in the EU, see Authorisation procedures.

http://www.emea.europa.eu/pdfs/human/pandemicinfluenza/60825909en.pdf (downloaded 27 October 2009)

Explanatory note on scientific considerations regarding the licensing of pandemic A(H1N1)v vaccines

Experience with pandemic vaccines

For the three pandemic vaccines (Celvapan, Focetria and Pandemrix), **no clinical data are available in pregnant women**.

Clinical trials with the mock-up vaccines and to some extent the A(H1N1)v strain provide immunogenicity results in women of childbearing age. Based on experience from other influenza vaccines, it is assumed that immunogenic responses in non-pregnant women can be extrapolated to pregnant women. *[Not one word about safety!]*

More information:

- Details of the Regulatory process for the authorisation of antiviral medicines and vaccines in the protection against Pandemic Influenza (H1N1) 2009 can be found on: http://ec.europa.eu/health/ph_threats/com/Influenza/docs/flu_staff4_en.pdf
- Detailed information on the vaccines: http://www.emea.europa.eu/influenza/home.htm
- Regularly updated information on the Pandemic H1N1 2009: http://ec.europa.eu/health/ph_threats/com/Influenza/novelflu_en.htm
- European centre of Disease Prevention and Control (ECDC): http://ecdc.europa.eu/en/healthtopics/Pages/Influenza_A(H1N1)_Outbreak.aspx
- World Health Organization (WHO): http://www.who.int/en/
- European Commission, http://ec.europa.eu/health/ph_threats/com/Influenza/novelflu_en.htm

Pandemic influenza vaccines centrally authorised in the EU

EU 666 Biodefense stockpile

information compiled by Désirée L. Röver

from ***European Medicines Agency*** (EMEA, http://www.emea.europa.eu/)

and ***Biopharmaceutical Products in the US and European Markets*** (http://www.biopharma.com)

7 September 2009

Name	***Company***	***Vaccine***	***Medium***	***Adjuvantia***	***Excipients***
Daronrix *mock-up* H5N1 ***BP#* 393**	*GSK Biologicals*	pandemic influenza vaccine whole virion, inactivated A/Vietnam/1194/2004 15 µg/ 0.5 ml dose	eggs	aluminium phosphate 0.45 mg Al^{3+} aluminium hydroxide, hydrated 0.05 mg Al^{3+} ***BP#* 679**	Sodium chloride Disodium phosphate dodecahydrate Potassium dihydrogen phosphate Potassium chloride Magnesium chloride hexahydrate Thiomersal (50µg) Water for injection
Date of issue: 21 March 2007	http://www.emea.europa.eu/humandocs/PDFs/EPAR/daronrix/H-706-PI-nl.pdf				
Focetria	*Chiron / Novartis*	Influenza virus surface antigens (haemagglutinin and neuraminidase) subm. 12.01.2006 MA 22.02.2007 A/Vietnam/1194/2004 7.5 µg/ 0.5 ml dose	eggs	***MF59C.1***: squalene 9.75 mg polysorbate 80 [1]) 1.175 mg sorbitan triolate 1.175 mg	Sodium chloride Sodium chloride Potassium dihydrogen phosphate Disodium phosphate dihydrate Magnesium chloride hexahydrate Calcium chloride dihydrate Sodium citrate Citric acid Water for injections
H5N1 ***BP#* 395**					
Date of issue: 2 May 2007					

Name	*Company*	*Vaccine*	*Medium*	*Adjuvantia*	*Excipients*
Pandemrix *mock-up* H5N1 ***BP#* 393** *Date of issue*: 20 May 2008	*GSK Biologicals*	clade 2 split virion, inactivated, adjuvanted, suspension and emulsion emulsion for injection A/VietNam/1194/2004 (NIBRG-14)*) 3.75 7.5 µg *BioPharma info:* lab version seed virus (wild type) virus from CDC, created using reversed genetics with reassortment strain combining the H5 and N1 segments with an influenza virus PR 8 strain backbone...	eggs	***AS03***: squalene 10.69 mg DL-α-tocopherol 11.86 mg polysorbate 80 [1]) 4.86 mg	Polysorbate 80 Octoxynol 10 Thiomersal Sodium chloride (NaCl) Disodium hydrogen phosphate (Na_2HPO_4) Potassium dihydrogen phosphate (KH_2PO_4) Potassium chloride (KCl) Magnesium chloride ($MgCl_2$) Water for injections *Emulsion vial:* Sodium chloride (NaCl) Disodium hydrogen phosphate (Na_2HPO_4) Potassium dihydrogen phosphate (KH_2PO_4) Potassium chloride (KCl) Water for injections
EU666 Biodefense Stockpile *) NIBRG is a reassortant strain between A/Vietnam/1194/2004 and A/PuertoRico/8/34					
Celvapan H5N1 ***BP#* ???** *Date of issue*: 4 March 2009	*Baxter AG:* Baxter AG, Austria; Baxter BioScience, Czech Republ.	whole virion influenza vaccine inactivated antigen A/Vietnam/1203/2004 A/Indonesia/05/2005 7.5 µg/ 0.5 ml dose *No studies on genotoxicity and carcinogenicity were conducted* http://www.emea.europa.eu/humandocs/PDFs/EPAR/celvapan/H-982-en6.pdf	vero cells [3])	non-adjuvanted	Tris-buffered saline (TBS) Trometamol Sodium chloride Polysorbate 80 Trypsin Cytodex [2]) Water for injection [2]) surface microcarrier

Name	*Company*	*Vaccine*	*Medium*	*Adjuvantia*	*Excipients*
Prepandrix	*GSK Biologicals*	clade 2 split virion, inactivated, adjuvanted	eggs	***AS03***: squalene 10.69 mg DL-α-tocopherol 11.86 mg polysorbate 80 [1]) 4.86 mg	*Suspension vial*: Polysorbate 80 Octoxynol 10 Thiomersal Sodium chloride (NaCl) Disodium hydrogen phosphate (Na_2HPO_4) Potassium dihydrogen phosphate (KH_2PO_4) Potassium chloride (KCl) Magnesium chloride ($MgCl_2$) Water for injections *Emulsion vial*: Sodium chloride (NaCl Disodium hydrogen phosphate (Na_2HPO_4) Potassium dihydrogen phosphate (KH_2PO_4) Potassium chloride (KCl) Water for injections
H5N1		VietNam/1194/2004 (NIBRG-14) *)			
***BP#* 393**		*BioPharma info:* see **Pandemrix**			
date of issue: 14 May 2008					

EU666 Biodefense Stockpile

*) NIBRG is a reassortant strain between A/Vietnam/1194/2004 and A/PuertoRico/8/34

Name	*Company*	*Vaccine*	*Medium*	*Adjuvantia*	*Excipients*
Prepandemic influenza vaccine H5N1 ***BP#* 392** *date of issue*: 26 Sept. 2008	*GSK Biologicals*	prepandemic influenza vaccine split virion, inactivated, adjuvanted A/VietNam/1194/2004 (NIBRG-14) *) 3.75 7.5 µg	eggs	***AS03***: squalene 10.69 mg DL-α-tocopherol 11.86 mg polysorbate 80 [1]) 4.86 mg	*Suspension vial*: Polysorbate 80 Octoxynol 10 Thiomersal Sodium chloride (NaCl) Disodium hydrogen phosphate (Na_2HPO_4) Potassium dihydrogen phosphate (KH_2PO_4) Potassium chloride (KCl) Magnesium chloride ($MgCl_2$) Water for injections *Emulsion vial*: Sodium chloride (NaCl Disodium hydrogen phosphate (Na_2HPO_4) Potassium dihydrogen phosphate (KH_2PO_4) Potassium chloride (KCl) Water for injection

EU666 Biodefense Stockpile

*) NIBRG is a reassortant strain between A/Vietnam/1194/2004 and A/PuertoRico/8/34

Legenda:

Date of issue = Date of issue of Marketing Authorisation valid throughout the European Union (http://www.emea.europa.eu/)
BP# ... = Sample number in database *Biopharmaceutical Products in the US and European Markets* (http://www.biopharma.com)

[1]) **Polysorbate 80** is an infertility inducing agent. '*Fertility Impairing Vaccine And Methods of Use' (*U. S. Provisional Application No. 60/070,375, filed January 2,1998, U. S. Provisional Application No. 60/071,406, filed January 15,1998)
http://www.whale.to/v/tween_80.html , http://www.exploringvaccines.com/?p=455

[2]) Cytodex is a surface microcarrier: dextran beads with a particle size of 131-220 µm,
http://www.gelifesciences.co.jp/catalog/pdf_attach/18106061.pdf

[3]) Vero cells: African green monkey kidney cells
(Dyncorp US patent 5.911.998, Dyncorp US patent 6.025.182, Dyncorp US patent 6.117.667)

[4]) Although adjuvants generally enhance immunogenicity, their effect on the 2009 H1N1 virus is unknown.
Trial of Influenza A (H1N1) 2009 Monovalent MF59-Adjuvanted Vaccine, NEJM 2009;361
http://www2.le.ac.uk/offices/press/pdf-files/articles-on-ebulletin-2009/september-2009/Clark%20DRAFT.pdf/

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Vaccine and Related Biological Products Advisory Committee on November 9, 1998
Dr. Andrew Lewis, head of the CBER DNA Virus Laboratory in the Division of Viral Products confirmed that "**All the egg-based vaccines are contaminated.…** These fertilized chicken eggs are susceptible to a wide variety of viruses." The participants also realized that only a very small fraction of these small contaminants have been identified and there are likely hundreds more to be discovered."
http://www.globalresearch.ca/index.php?context=va&aid=15452

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Conflict of interests:

http://royalsociety.org/downloaddoc.asp?id=3521
Summary of oral evidence dr. James Robertson en John Wood,
This document shows how dr. Robertson (NIBSC) virtually controls all viral material to be used for the production of H1N1 and H5N1 vaccines. And how much dr. Robertson stands to gain financially from the ones eventually being used in marketed vaccines.
http://nwoobserver.wordpress.com/2009/10/03/dr-len-horowitz-anglo-american-flu-genocide/

H1H1 PANDEMIC VACCINE ~ FOCETRIA

Name	*Company*	*Vaccine*	*Medium*	*Adjuvantia*	*Excipients*
Focetria (2)	*Chiron / Novartis*	Influenza virus surface antigens (haemagglutinin and neuraminidase) subm. 12.01.2006 MA 22.02.2007	eggs	***MF59C.1*** :[4]) squalene 9.75 mg polysorbate 80 [1]) 1.175 mg sorbitan triolate 1.175 mg	Sodium chloride Potassium chloride Potassium dihydrogen phosphate Disodium phosphate dihydrate Magnesium chloride hexahydrate Calcium chloride dihydrate Sodium citrate Citric acid Thiomersal 0,05 mg Water for injections
H1N1 **BP# ??**		A/California/7/2009 (X-179A) 7.5 µg/ 0.5 ml dose (expressed in microgram haemagglutinin) Two doses, 3 weeks apart			

Date of first issue
2 May 2007
Date of revision of the text
09/2009

http://www.emea.europa.eu/humandocs/PDFs/EPAR/focetria/emea-combined-h710en.pdf

*Recommended by the CHMP on **24 September 2009**.*
It has been sent to the European Commission for the adoption of a formal decision applicable in all European Union Member States.

- This pandemic influenza vaccine H1N1 has been authorised based on data obtained with a version containing H5N1 antigen supplemented with data obtained with the vaccine containing H1N1 antigen.
  The Clinical Particulars section will be updated in accordance with emerging additional data.
- There is currently ***no clinical experience*** with Focetria (H1N1) in adults, including the elderly, children or adolescents.
  The decision to use Focetria (H1N1) in each age group defined below should take into account the extent of the clinical data available with a version of the vaccine containing H5N1 antigen and the disease characteristics of the current influenza pandemic.
- The dose recommendations are based on the safety and immunogenicity data available on the administration of the MF59C.1 adjuvanted vaccine containing 7.5 ug HA derived from A/Vietnam/1194/2004 (H5N1) at 0 and 21 days to adults, including the elderly, and children between 6 months and 17 years of age. See sections 4.8 and 5.1.
- Caution is needed when administrating this vaccine to persons with a known hypersensitivity (other than anaphylactic reaction) to the active substance, to any of the **excipients** and to **residues** (***eggs*** and ***chicken protein***, ***ovalbumin***, ***kanamycin*** and ***neomycin sulphate***, ***formaldehyde*** and ***cetyltrimethylammonium bromide*** (CTAB)).
- Animal reproduction studies have not been conducted with this —[vaccine]. ***It is also not known whether the vaccine can cause fetal harm when administered to a pregnant woman, or can affect reproduction capacity***.
  EMEA Summary of product characteristics: http://www.emea.europa.eu/humandocs/PDFs/EPAR/focetria/spc/emea-spc-h385en.pdf

H1H1 PANDEMIC VACCINE ~ PANDEMRIX

EMEA Press Release H1N1 vaccines: http://www.emea.europa.eu/pdfs/general/direct/pr/60258209en.pdf

Name	*Company*	*Vaccine*	*Medium*	*Adjuvantia*	*Excipients*
Pandemrix	*GSK Biologicals*	clade 2 split virion, inactivated, adjuvanted, suspension and emulsion emulsion for injection	eggs	***AS03***: Squalene 10.69 mg DL-α-tocopherol 11.86 mg polysorbate 80 [1]) 4.86 mg	Polysorbate 80 Octoxynol 10 Thiomersal Sodium chloride (NaCl) Disodium hydrogen phosphate (Na_2HPO_4) Potassium dihydrogen phosphate (KH_2PO_4) Potassium chloride (KCl) Magnesium chloride ($MgCl_2$) Water for injections *Emulsion vial:* Sodium chloride (NaCl) Disodium hydrogen phosphate (Na_2HPO_4) Potassium dihydrogen phosphate (KH_2PO_4) Potassium chloride (KCl) Water for injections
H1N1		A/California/7/2009 (X-179A) 3.75 7.5 µg			
BP# ??					
Date of first authorisation: 20 May 2008					
		This vaccine contains 40 times more squalene than the anthrax vaccine given in the first Gulf War			

This pandemic influenza vaccine has been authorised based on data obtained with a version containing H5N1 antigen supplemented with data obtained with a vaccine containing H1N1 antigen. The Clinical Particulars section will be updated in accordance with emerging additional data. There is currently very limited clinical experience with an investigational formulation of Pandemrix (H1N1) containing a higher amount of antigen (see section 5.1) in healthy adults aged 18-60 years and no clinical experience in the elderly, in children or in adolescents. The decision to use Pandemrix (H1N1) in each age group defined below should take into account the extent of the clinical data available with a version of the vaccine containing H5N1 antigen and the disease characteristics of the current influenza pandemic.

EMEA Summary of product characteristics: http://www.emea.europa.eu/humandocs/PDFs/EPAR/pandemrix/emea-combined-h832en.pdf
EPAR summary for the public: http://www.emea.europa.eu/humandocs/PDFs/EPAR/pandemrix/Pandemrix_summary_strain_update.pdf

Name	*Company*	*Vaccine*	*Medium*	*Adjuvantia*	*Excipients*
Celvapan	*Baxter AG:* Baxter AG, Austria;	whole virion influenza vaccine inactivated antigen	vero cells [3])	non-adjuvanted	Trometamol Sodium chloride Polysorbate 80
H1N1	Baxter BioScience, Czech Republ.	A/California/07/2009 (H1N1)v 7.5 µg/ 0.5 ml dose expressed in mg haemagglutinin			Trypsin Cytodex [2]) Water for injections
BP# ???					[2]) surface microcarrier

Date of first authorisation:
4 March 2009

http://www.emea.europa.eu/humandocs/PDFs/EPAR/celvapan/spc/emea-spc-h982pu17en.pdf

European Medicines Agency recommends authorisation of Celvapan for use against pandemic influenza

Published 02/10/2009

Following the authorisation of Focetria and Pandemrix on 29 September, the Agency has recommended that a third pandemic-influenza vaccine, Celvapan, be authorised by the European Commission for use in protecting EU citizens against 'swine flu'.

A Commission decision is expected shortly.

There is currently no clinical experience with Celvapan (H1N1) in adults, elderly, children or adolescents (updated 9 October 2009)

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http://www.emea.europa.eu/humandocs/PDFs/EPAR/celvapan/H-982-en6.pdf

From: **ASSESSMENT REPORT FOR Celvapan ~ Procedure No. EMEA/H/C/000982**:

- ***Genotoxicity and Carcinogenicity***

  No studies on genotoxicity and carcinogenicity were conducted with the candidate vaccines.

- ***Reproduction Toxicity***

  A reproductive and developmental toxicity study is scheduled but the data are not available for the time being.
  This is acceptable according to the relevant guidelines. A rat study with A/Indonesia/05/2005 candidate vaccine was initiated in March, 2008 and the final study report was available in November, 2008. Another rat study with A/Vietnam/1203/2004 candidate vaccine was initiated in August, 2008 and the final study report will be available in April, 2009. This timetable is considered acceptable, as for a mock-up pandemic vaccine having such data before authorization is not necessary.

  The excipients of animal origin, Trypsin and Cytodex, are used in the production of the Active Substance (p.7/55).

SEASONAL FLU VACCINE ~ VAXIGRIP

https://www.vaccineshoppecanada.com/secure/pdfs/ca/vaxigrip_e.pdf

Name	***Company***	***Vaccine***	***Medium***	***Excipients***	***Clinically relevant nonmedicinal ingredients***:
Vaxigrip	*SanofiPasteur*	Inactivated influenza trivalent Types A and B (split virion) of (0,5 ml dose) 15 µg HA A/Brisbane/59/2007 (H1N1)-like strain [A/Brisbane/59/2007 (IVR-148)] 15 µg HA A/Brisbane/10/2007 (H3N2)-like strain [A/Uruguay/716/2007 (NYMC X-175C)] 15 µg HA B/Brisbane/60/2008-like strain (B/Brisbane/60/2008)	eggs		(0,5 ml dose) 2 µg Thimerosal ≤30 µg Formaldehyde Triton® X-100 Sucrose (trace amount) Neomycin (trace amount)
Date of approval: April 2009					

As each dose may contain traces of ***formaldehyde***, ***Triton® X-100*** and undetectable traces of ***neomycin***, which are used during vaccine production, caution should be exercised when the vaccine is administered to subjects with hypersensitivity to one of these substances or the antibiotic and the antibiotics of the same class.

Known systemic hypersensitivity reactions to egg proteins (egg or egg products), to chicken proteins,
-- Influvac 2009/2010 does not contain more than 1 µg ovalbum per dose --
or any component of VAXIGRIP® or a life-threatening reaction after previous administration of influenza vaccine or a vaccine containing the same substances.

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N.B.: Triton X-100

http://www.roche-applied-science.com/pack-insert/1332481a.pdf

Triton X-100 [Octylphenolpoly(ethyleneglycolether)x]

For life science research only. Not for use in diagnostic procedures. FOR IN VITRO USE ONLY.

Triton X-100 (trademark of Rohm & Haas Company, Philadelphia, PA, USA) is one of the most commonly used non-ionic detergents for solubilizing membrane proteins during isolation of membrane-protein complexes.

SEASONAL FLU VACCINE ~ INFLUVAC

http://www.solvaypharmaceuticalsme.com/images/pil/Influvac2009-2010.pdf

Name	***Company***	***Vaccine***	***Medium***	***Excipients***
Influvac	*Solvay Biologicals BV*	Influenza virus surface antigens (haemagglutinin and neuraminidase) of: 15 µg HA A/Brisbane/59/2007 (H1N1)-like strain [A/Brisbane/59/2007 (IVR-148 reass.)] 15 µg HA A/Brisbane/10/2007 (H3N2)-like strain [A/Uruguay/716/2007 (NYMC X-175C reass.)] 15 µg HA B/Brisbane/60/2008-like strain (B/Brisbane/60/2008)	eggs	Potassium chloride Potassium dihydrogen phosphate Disodium phosphate dihydrate Sodium chloride Calcium chloride Magnesium chloride hexahydrate Water for injections

Date of approval/revision of text:
April 2009

Hypersensitivity to the active substances, to any of the excipients and to ***residues of eggs***, ***chicken protein*** (Influvac 2009/2010 does not contain more than 1 µg ovalbum per dose), ***formaldehyde***, ***cetyltrimethylammonium bromide***, ***polysorbate 80***, or ***gentamicin***

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

http://www.biodiem.com/index.asp?menuid=070.020

LAIV is a novel intranasal live attenuated influenza vaccine being developed to prevent infection from endemic and pandemic influenza

LATEST NEWS - 2 SEPTEMBER 2009

WHO SUB-LICENSES BDM'S LAIV TECHNOLOGY

BioDiem has licensed the majority of the international rights to the live attenuated influenza vaccine to Akzo Nobel's ***Nobilon*** who are responsible for developing a data package for registration in Europe and the rest of the world with access to the data for North America . Nobilon will produce the vaccine for world distribution and undertake marketing in Europe and the rest of the world. BioDiem and Nobilon have shared rights in Japan subject to future agreement and BioDiem retains marketing rights in North America .

Nobilon is developing a live attenuated influenza vaccine for intranasal delivery based on BioDiem's Master Donor Strains (MDS), to be produced in mammalian cell culture. The pre-clinical development is well underway and to date Nobilon have confirmed the cold-adaptation and temperature sensitive properties of our MDS.

The next step for Nobilon is to produce cell-culture grown reassortant virus for vaccine production. They will first establish the genetic purity of MDS virus after cloning the virus grown on a mammalian cell culture substrate. Preparing the vaccine for clinical trial is a complex, multistep, time consuming process and requires the kind of resources and expertise that Nobilon can provide. A strong collaboration has been developed between Nobilon, the Institute of Experimental Medicine (IEM) in St. Petersburg and BioDiem, including staff exchanges designed to accelerate technology transfer and vaccine development.

Comment (Sept. 30, 2009) **by researcher Patrick Jordan on the red highlighted text:**

"What this tells me is that they are gearing up not for environmental factors that might affect a personal application of the vaccine (a mist up the nose of an individual as the product comes out of its Cold Chain - the method by which they keep the vaccine from losing potency and breaking down) but rather a Mass Application such as they do on chicken farms where they spray it as a shower on the chickens. **My take is that they are trying to make this stable enough to spray on mass amounts of people**."

Name	*Company*	*Active substance*	*Excipients*
Tamiflu 30 mg hard capsule	*Roche Registration Limited*	Oseltamivir phosphate is a pro-drug of the active metabolite Oseltamivir (oseltamivir carboxylate).	*Capsule core:* Pregelatinized starch (derived from maize starch) Talc Povidone Croscarmellose sodium Sodium stearyl fumarate *Capsule shell:* Gelatin Yellow iron oxide (E172) Red iron oxide (E172) Titanium dioxide (E171) *Printing ink:* Shellac Titanium dioxide (E171) FD and C Blue 2 (indigo carmine, E132)
Date of first authorisation: 20 June 2002 *Date of last renewal:* 20 June 2007			
Shelf life: 7 years			

http://www.emea.europa.eu/humandocs/PDFs/EPAR/tamiflu/Tamiflu_PI_clean_en.pdf

Further post marketing surveillance data on selected serious adverse drug reactions:

In patients with influenza who were receiving Tamiflu, there have been postmarketing reports of convulsions and delirium (including symptoms such as altered level of consciousness, confusion, abnormal behaviour, delusions, hallucinations, agitation, anxiety, nightmares), in a very few cases resulting in accidental injury or fatal outcomes. These events were reported primarily among pediatric and adolescent patients and often had an abrupt onset and rapid resolution. The contribution of Tamiflu to those events is unknown. Such neuropsychiatric events have also been reported in patients with influenza who were not taking Tamiflu.

http://www.emea.europa.eu/humandocs/PDFs/EPAR/tamiflu/emea-combined-h402en.pdf

The use of oseltamivir during pregnancy and lactation to treat or prevent the novel Influenza A (H1N1) in case of a pandemic

There are no adequate data from the use of oseltamivir in pregnant women.

Name	*Company*	*Active substance*	*Excipients*
Relenza inhalation powder	*GalxoSmithKline*	Zanamivir 5mg/dose, predispensed quantity	Lactose monohydrate ca. 20mg, containing milk protein

Shelf life:
7 years

Date of first authorisation:
02-09-1999/10-02-2008
Date of last renewal:
06-09-2009

http://www.lakemedelsverket.se/SPC_PIL/Pdf/enhumspc/Relenza%20inhalation%20powder%20pre-dispensed%20ENG.pdf
Neuropsychiatric events have been reported during administration of Relenza
in patients with influenza, especially in children and adolescents.
The safe use of Relenza during pregnancy has not been established.