EMA Update:
A meta-analysis of studies on the association between H1N1 vaccination and pregnancy outcomes was not performed (in at least the studies with the same design) because they all show a RR close to 1 with a CI including 1; it would not be useful to calculate whether this is e.g. 1.2 or 1.1. The EMA therefore considers this report as the final report.

A/H1N1 pandemic vaccines and pregnancy outcomes

Consultancy EMA/2010/29/CN; interim report IV

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Introduction

This is the fourth interim report, which reports on an updated literature review and study progress. Most studies identified in previous reports have now published their results; their study findings are summarised in this document. Given that most authors wanted to publish their results before releasing their study data and most studies have now been published or accepted for publication, we are now able to collect the data from individual studies for inclusion in the meta-analysis. We will report on the meta-analysis in the final report due June 2013.

Literature update

A full literature search has been conducted as an extension and update to the literature search conducted for the previous report, with some duplication of timelines to ensure no papers were missed. The most recent literature review therefore covered the period May 2011 to December 2012. Below is a summary of the searches that have been undertaken up to December 2012.

Conference proceedings

The following conferences were published in: Fundamental & Clinical Pharmacology 2011; 25 (S1): 1-111:

15th Annual Meeting of the French Society of Pharmacology and Therapeutics

78th Annual Meeting of the Society of Physiology

32nd Annual Pharmacovigilance Meeting

12th APNET Seminar

9th CHU CIC Meeting

Other conference proceedings searched were:

27th International Conference on Pharmacoepidemiology & Therapeutic Risk Management, August 2011, Chicago. Pharmacoepidemiolgoy & Drug Safety 2011; 20 (Supp 1)

28th International Conference on Pharmacoepidemiology & Therapeutic Risk Management. August 2012, Barcelona.

3rd North America Congress of Epidemiology, June 2011, Montreal. Am J Epidemiology 2011; 173 (Suppl 11).

45th Annual Society for Epidemiological Research Meeting, 2012 Minneapolis. Am J Epidemiology 2012; 175 (Suppl 11).

Teratology Society 51st Annual Meeting, June 2011. Birth Defects Research (Part A) 2011; 91(5).

Teratology Society 52nd Annual Meeting, June 2012. Birth Defects Research (Part A) 2012; 94(5).

11th Annual Meeting of the International Society of Pharmacovigilance. November 2011. Drug Safety 2011: 34(10): 883-1026

12th Annual Meeting of the International Society for Pharmacovigilance. November 2012. Drug Safety 2012; 35(10): 877-970

14th Annual Conference on Vaccine Research. April 2011.Baltimore.

22nd European Congress of Clinical Microbiology and Infectious Diseases, London 2012. Clinical Microbiology and Infection 2012; 18 (Suppl 3).

5th Global Vaccine Congress. 2011 (published online – no abstracts available)

6th Global Vaccine Congress. 2012 (published online – no abstracts available).

39th Annual Meeting of the European Teratology Society 2011. Reproductive Toxicology 2011; 32(2).

XX FIGO World Conference in Gynecology and Obstetrics October 2012. Int J Gynecol Obstet 2012; 119 (Suppl 3).

Journal Search

The following journals were searched for published studies, letters or conference proceedings using the term 'H1N1'.

International Journal of Gynecology and Obstetrics

Obstetrics and Gynecology

British Journal of Obstetrics and Gynaecology

American Journal of Obstetrics and Gynecology

Obstetrics, Gynecology and Reproductive Medicine

Current Opinion in Obstetrics and Gynecology

European Journal of Obstetrics, Gynecology and Reproductive Biology

International Journal of Epidemiology

American Journal of Epidemiology

Epidemiology

Journal of Epidemiology and Community Health

European Journal of Epidemiology

Journal of Clinical Epidemiology

Pharmacoepidemiology and Drug Safety

Drug Safety

Australian and New Zealand Journal of Public Health

Vaccine

Journal of Vaccines and Vaccination.

Database search

Cochrane Library Issue 12 of 12, December 2012.

('H1N1' OR 'pandemic' OR Exp Influenza A Virus, H1N1 Subtype) AND Exp Influenza Vaccines.

Science Direct, January 2011 to December 2012

((pandemic or H1N1) AND (influenza or flu)) AND vacc* AND preg*

This search was then limited to the topic of pregnant women

Embase January 2011 to December 2012

(Exp Influenza virus A H1N1 OR Ex Pandemic Influenza OR 2009 H1N1 influenza) AND (Exp Vaccine OR Influenza Vaccine) AND Exp Pregnancy

Pubmed January 2011 to December 2012

(Exp Influenza virus, A H1N1 Subtype OR 'H1N1') AND Exp Influenza vaccines AND Exp Pregnancy

ISI Web of Knowledge January 2011 to December 2012

((pandemic AND (influenza or flu)) OR H1N1) AND vac* AND (pregnant or pregnancy) *searched in the title of the paper.*

Wiley Online Library 2011 to 2012

(H1N1 OR influenza) AND vacc* and pregnan*

Results

Cochrane Library Search

The Cochrane Library Search identified 13 Cochrane Reviews, 6 other reviews, 19 economic evaluations and 296 trials. None of the 13 Cochrane Reviews reported on the safety of the H1N1/A vaccine during pregnancy. Of the 'other reviews' (i.e not Cochrane Reviews), two were potentially useful for the review of their included studies; these were:

Manzoli L, DeVito C, Salantia G, D'Addario M, Villari P, Ionnidis JP. Meta-analysis of the immunogenicity and tolerability of pandemic influenza A 2009 (H1N1) vaccines. Centre for Reviews and Dissemination 2011 e243484

Yin JK, Khandaker G, Rashid H, Heron L, Ridda, Booy R. Immunogenicity and safety of pandemic a (H1N1) 2009 vaccine: systematic review and meta-analysis. Influenza and Other Respiratory Viruses 2011, 5(5): 299-305.

54 of the 296 trials were published between January 2011 and December 2012. There was one trial that investigated the use of the H1N1/A vaccine in pregnant women:

Jackson LA, Patel SM, Swarmy GK, Frey SE et al. Immunogenicity of an inactivated monovalent 2009 H1N1 vaccine in pregnant women. J Infectious Diseases. 2011; 204(6): 854-63.

This study reported on immunogenicity only; not pregnancy outcomes and had also been identified at the previous update. This paper will not be included in the literature review.

ScienceDirect Search

The initial search identified 694 papers. When the limit to the topic of pregnant women was applied this identified 54 papers. These papers were added to a database of searches for January 2011 to December 2012 and reviewed after the removal of duplicate records.

Embase Search

The search identified 151 papers. These were added to a database of searches for January 2011 to December 2012 and reviewed after the removal of duplicate records.

Pubmed Search

The search identified 97 papers. These were added to a database of searches for January 2011 to December 2012 and reviewed after the removal of duplicate records.

ISI Web of Knowledge

The search identified 70 papers. These were added to a database of searches and reviewed after the removal of duplicate records.

Wiley Online Library

The search identified 6 papers. These were added to a database of searches and reviewed after the removal of duplicate records.

There were 377 papers identified from the searches of the electronic databases. After removal of duplicates from the database searches there were 248 papers to be assessed for their inclusion into the review. A final paper was identified manually immediately before release of this report. This resulted in the following shortlist:

PAPERS

Bardage C, Persson I, Örtqvist Å, Bergman U, Ludvigsson JF, Granath F. Neurological and autoimmune disorders after vaccination against pandemic influenza A (H1N1) with a monovalent adjuvanted vaccine: population based cohort study in Stockholm, Sweden. BMJ 2011; 343:d5956 doi: 10.1136/bmj.d5956.

Although pregnancy is listed in the keywords for this paper, no pregnancy-specific outcomes have been reported in this study.

Bednarczyk RA, Adjaye-Gbewonyo D, Omer SB. Safety of influenza immunisation during pregnancy for the fetus and neonate. AJOG Supplement; 2012 (Suppl September); S38-S46

Review summarising all studies of the safety of influenza vaccines in pregnancy including H1N1 /A vaccine. Paper has been checked for citations relevant to the current literature review. One additional study from Japan was identified: Horiya M, Hisano M, Iwasaki Y, et al. Efficacy of double vaccination with the 2009 pandemic influenza A (H1N1) vaccine during pregnancy. Obstet Gynecol 2011;118:887-94. This reported on immunogenicity only; not pregnancy outcomes.

Candela S, Pergolizzi S, Ragni P, Cavuto S et al. An early (3-6 weeks) active surveillance study to assess the safety of pandemic influenza vaccine Focetria® in a providence of Emilia-Romagna region, Italy – Part one. Vaccine published online

This paper reports on an observational cohort study in the La Spezia region in Italy. 370 pregnant women were included in the study population. There was no unexposed comparator group. 359 women responded and reported three preterm births, one of which was in week 1-3 following vaccination, and in three pregnancies early uterine contractions were reported. One AE reported was for a retained placenta, one was for suspected biliary colic, and two women reported hypertension. None of these events were considered to be more frequent than the background rate. At 7.7%, the vaccination rate in this region was a lot lower than had been anticipated by the authorities.

Cherdantsev AP, Kostinov AP, Kuselman AI, Voznesenskaia NV. Vaccination against influenza A (H1N1) in pregnancy.

This paper assessed immunogenicity of MonoGrippol vaccine administered in the second trimester with biochemical markers. It also evaluated the impact on foetal development using human chorionic gonadotropin (HCG), alpha-fetoprotein (AFP) and trophoblastic beta-1-glycoprotein (TBG) level measurements. The paper is in Russian; from the English abstract, the sample size not clear and it is stated HCG, AF, and TBG levels did not differ between the exposed and the comparator group.

Christian LM, Iams JD, Porter K, Glaser R. Inflammatory responses to trivalent influenza virus vaccine among pregnant women. Vaccine 2011; 29(48): 8982-87

This paper was excluded as it reported on seasonal influenza vaccine only

Cristiani C, Tuccori M, Pepe P, Sarteschi A et al. Safety of MF-59 adjuvanted vaccine for pandemic influenza: results of the vaccination campaign in an Italian health district.

This paper also reported on a study in La Spezia, Italy and included 13 pregnant women. No unexposed comparator was present. Vaccinations occurred in weeks 15-36. All pregnancies resulted in a delivery of a healthy baby although one was born prematurely and another had neonatal jaundice. The frequency of these adverse events was not considered to be different from the background rate, although it is difficult to draw conclusions about potential harm with such a small sample size.

Fell DB, Sprague AE, Liu N, Yasseen AS et al. H1N1 influenza vaccination during pregnancy and fetal and neonatal outcomes. American Journal of Public Health 2012; 102:e33-e40

This paper reports on a retrospective cohort study in Ontario (BORN) identified and described in the previous report. It has been included in a fuller review, below.

Folkenberg M, Callreus T, Svanstrom H, Valentiner-Branth P, Hviid A. Spontaneous reporting of adverse events following immunisation against pandemic influenza in Denmark November 2009-March 2010. Vaccine 2011; 29 (6): 1180-84

This is a general report on 1885 spontaneous reports received by the Danish Medicines Agency. Twelve of these involved pregnant women, five of whom had non pregnancy related reactions. Two reports were on uterine contractions, four were for spontaneous abortions and one woman suffered from premature labour that resulted in a stillbirth.

Haberg S, Trogstad L, Gunnes N, et al. Risk of fetal death after pandemic influenza virus infection or vaccination. N Eng J Med 2013;268:333-40

This reports on the Norwegian registry study identified in earlier reports and has been included in a fuller review, below.

Heikkinen T, Young J, van Beek E, Franke H et al. Safety of MF59-adjuvanted A/H1N1 influenza vaccine in pregnancy: a comparative cohort study. Am J Obst Gynecol 2012; 207 (3): 177.e-177.e8

Cohort study conducted in The Netherlands, Italy and Argentina. 4529 pregnant women included who were mostly from the Netherlands. 4385 babies followed up to 3 months of age; of these, 2295 were exposed to Focetria in utero. This is included in a fuller review, below.

Kallen B, Olausson PO. Vaccination against H1N1 inflenza with Pandemrix ® during pregnancy and delivery outcome: a Swedish registry study. BJOG 2012; 119(13): 1583-1590

18 612 vaccinated women on the Swedish Medical Birth Register, giving birth to 18 844 infants. Vaccination status was obtained from the antenatal medical documents. This is included in a fuller review, below.

Lin T-H, Lin S-Y, Lin C-H, Lin R-I et al. AdminFlu S ® influenza A (H1N1) vaccine during pregnancy: the Taiwanese Pharmacovigilance Survey. Vaccine 2012; 30(16): 2671-2675

A retrospective cohort study in Taiwan different from the one identified previously; it is a comparative cohort study of 198 exposed and 198 unexposed pregnant women. This is included in a fuller review, below.

Mihigo R, Torrealba CV, Coninx K, Nshimirimana D et al. 2009 pandemic influenza virus subtype H1N1 vaccination in Africa – successes and challenges. J Infect Dis 2012; 260 (Suppl 1): S22-S28.

This paper, whilst this gives vaccination coverage in pregnant women, does not report on adverse events in pregnancy. Overview of vaccination in Africa.

Moro PL, Tepper NK, Grohskopf LA, Vellozzi C, Broder K. Safety of seasonal influenza and influenza A (H1N1) 2009 monovalent vaccines in pregnancy. Expert Review of Vaccines 2012; 11 (8): 911-21

This is a review – no further relevant references were identified from its list of references.

Omon E, Damase-Michel C, Hurault-Delarue C, Lacroix I et al. Non-adjuvanted 2009 influenza A (H1N1)v vaccine in pregnant women: the results of a French prospective descriptive study. Vaccine 2011; 29(52): 9649-54

This paper reports on the French study that had been identified in a previous update. It includes an exposed cohort of 569 women and 580 live births and one stillbirth, which was in a high-risk pregnancy with bipartita placenta and previous miscarriages. There was no unvaccinated comparator group. Most vaccinations occurred in the 2nd trimester; 4% occurred in the first trimester. There were no exposed cases amongst the babies who were born with a malformation. The rate of preterm delivery, stillbirth and congenital malformations was not considered to be different in this H1N1 vaccine exposed cohort compared with national statistics in France.

Oppermann M, Fritzsche J, Weber-Schoendorfer C, Keller-Stanislawski B et al. A(H1N1)v 2009: a controlled prospective cohort study on vaccine safety in pregnancy. Vaccine 2012; 30(30): 4445-4452.

German prospective cohort study identified and described in earlier reports. This is included in a fuller review, below.

Pasternak B, Svanstrom H, Molgaard-Nielsen D, Krause D et al. Risk of adverse fetal outcomes following administration of a pandemic influenza A(H1N1) vaccine during pregnancy. JAMA 2012; 308 (2): 165-174

This paper reports on some of the results (birth defects, preterm birth, and small for gestational age) from the database study in Denmark identified in earlier reports. This is included in a fuller review, below.

Pasternak B, Svanstrom H, Molgaard-Nielsen D, Krause TG et al. Vaccination against pandemic A/H1N1 2009 influenza in pregnancy and risk of fetal death: cohort study in Denmark. BMJ 2012; 344: e2794

This paper reports on the association between foetal death and H1N1 vaccine from the same database study in Denmark. This is included in a fuller review, below.

Sammon CJ, Snowball J, McGrogan A, de Vries CS. Evaluating the hazard of foetal death following H1N1 influenza vaccination; a population based cohort study in the UK GPRD. PLoS ONE 2012; 7(12)

This study reports on the association between foetal death and H1N1 vaccine from the General Practice Research Database (GPRD) study identified in earlier reports. This is included in a fuller review, below.

Toback SL, Beigi R, Tennis P, Sifakis F, Calingaert B, Ambrose CS. Maternal outcomes among pregnant women receiving live attenuated influenza vaccine. Influenza and other Respiratory Diseases 2012; 6(1): 44-51

This paper reports on the study period is 2003-2009 and does not include information regarding A/H1N1 vaccine safety in pregnancy. It has been excluded.

Xu R, Luo Y, Chambers C. Assessing the effect of vaccine on spontaneous abortion using time-dependent covariates Cox models. Pharmacoepidemiol Drug Saf 2012; 21(8): 844-50

This is a paper on research methods but reports on different ways of analysing the association between spontaneous pregnancy loss and H1N1 vaccine using data from the VAMPSS study. This is included in a fuller review, below.

CONFERENCE PROCEEDINGS

Conference proceedings mostly identified abstracts from studies we were aware of already. One additional study was identified from Argentina:

Rubinstein F, Micone P, Bonott A, Wainer V et al. Influenza (H1N1) MF59-adjuvanted vaccine and adverse perinatal outcomes. A large cross-sectional multicentre study. Int J Gynecol Obstet. 2012; 119(Suppl 3): S386.

The abstract reports on a retrospective observational cohort study in which hospital charts from 49 hospitals were searched from September 2010 to May 2011 for deliveries, and consenting women were interviewed about vaccination status as well as confounders; Focetria was the H1N1 vaccine used in Argentina. The primary outcome was a composite of low birth weight, pre-term delivery or the occurrence of any major foetal or early neonatal event up to 7 days postpartum. Secondary outcomes included maternal and neonatal outcomes. Out of 30448 women, 7582 had been vaccinated. Logistic regression was applied to adjust for 'all potential confounders'. A reduction in risk of the composite endpoint was identified (RR 0.87; CI_{95} 0.82-0.97). Although this provides no suggestion of harm, the result needs to be interpreted with caution because, given that exposure status was only determined at delivery, the study will have suffered from immortal time bias. This will have impacted on the risk estimate for preterm delivery (less likely to have been vaccinated than term deliveries) as well as on foetal outcomes in babies born prematurely. We have contacted the

authors to assess feasibility and desirability of including this study in the meta-analysis. Inclusion will depend on the information available in the raw data regarding gestational age and confounders as well as whether information on individual outcomes rather than just the composite endpoint is available.

Review of papers identified in the latest literature review update and reporting on study results for possible inclusion in the meta-analysis

Studies reporting on foetal death

Nine studies reported on H1N1 vaccination and the risk of foetal death.[1-9] The main challenge in studying the association with pregnancy loss is the combination of:

- the fact that embryonic loss and early foetal loss is often not clinically recognised or recorded in the healthcare databases used for these studies;

- the difficulty in determining gestational age in the studies included;

- and the fact that the likelihood of exposure increases with increasing gestational age whereas the likelihood of the outcome (foetal death) decreases with increasing gestational age.

For these reasons it is imperative survival analysis techniques are applied using time dependent covariates in order to avoid immortal time bias, as has been illustrated nicely by Xu.[7] This has been implemented in four studies;[2,5-7] five did not use time-dependent modelling and consequently, these all report spurious reductions in risk of foetal death or spontaneous pregnancy loss.[1,3,4,8,9] The four studies that used time-dependent modelling all reported a neutral or reduced risk of foetal death (see Table 1 below). However, it must be noted that the Danish data capture mostly losses after 12 weeks gestation[5] and the Norwegian data include foetal death after 12 weeks only.[2] For the UK, only foetal death rates from gestational age 9 onwards were deemed reliable and some residual error may remain as a result of mis-estimation of gestational age.[6] However, various sensitivity analyses conducted by the authors of all studies to estimate the impact of any residual bias suggest an increase in risk of foetal death associated with H1N1 vaccination is unlikely based on their study data. For the meta-analysis, the question arises whether any pooled estimates will have added value over and above the individual hazard ratios. The meta analysis would provide a more precise result, but the bias in estimating gestational age remains and the more precise result might simply mean the hazard ratio is no more or less reliable but it is likely to become statistically significantly reduced from 1. This may be a spurious reduction in risk as a result of residual bias and before any pooled analyses are carried out, agreement on this issue will need to be reached between study contributors.

Table 1. Hazard of foetal death associated with H1N1 vaccination in pregnancy

Author	Location	HRadj	CI95
Haberg et al[2]	Norway	0.88	0.66-1.17
Pasternak et al[5]	Denmark	0.79	0.53-1.16
Sammon et al[6]	UK	0.74	0.62-0.88
Xu et al[7]	USA	0.79	0.19-3.23

Other pregnancy outcomes

Six studies reported on other pregnancy outcomes.[1,3,4, 8-10] These outcomes included preterm delivery,[1,3,4,8] babies born small for gestational age (SGA),[1,8,10] pre-eclampsia,[3,4,8] gestational diabetes,[3,8] and congenital malformations.[3,4] Three reported on low birth weight [3,8,9] but this is

considered uninterpretable without the context of gestational age and in this review we focus on the outcome of SGA.

Preterm delivery

Unfortunately, none of the studies reporting on the association between H1N1 vaccination and the risk of preterm delivery used survival techniques when analysing their results. This is a problem because most vaccinations occurred in the 2nd and 3rd trimester and prematurely born babies will have had less time *in utero* for their mother to have been eligible for vaccination in pregnancy. This results in immortal time bias with consequently spuriously reduced risks of premature delivery identified in all studies except for the study from Denmark. However, because the German study[4], the Novartis observational study,[3] the Danish study, and to some extent the Swedish study (18% missing) all have the date of vaccination recorded, it may be possible to resolve this issue in the meta-analysis.

Babies born SGA

All studies reported a neutral or reduced risk of babies being born SGA. Discrepancies in results in this association between 2nd and 3rd trimester deliveries[1,10] suggest there may be residual error here as a consequence of the immortal time bias; this is difficult to establish without analyses stratified by gestational age and authors have been contacted with a request for more detail on this matter. Summary results are presented in Table 2 below:

Table 2. Summary results from all studies reporting on the association between A/H1N1 vaccination in pregnancy and babies being born small for gestational age

Author	Location	RR_{adj}	CI_{95}
Fell *et al* [1]	Ontario, Canada	0.90 (10th centile)	0.85-0.96
		0.81 (3rd centile)	0.72-0.92
Kallen *et al* [8]	Sweden	1.04 (10th centile)	0.92-1.17
Pasternak *et al* [10]	Denmark	0.97 (10th centile)	0.89-1.05

Congenital malformations

All except for the Canadian studies reported on a composite endpoint of all major birth defects combined. The Canadian study did not report on birth defects,[1] the Taiwanese study reported one malformation in the exposed group (n=202 births in 198 pregnancies): severe coarctation of the aorta with aortic hypoplasia.[9] The risk estimates for the remaining studies are summarised in Table 3 below. None of the risk estimates are significantly different from 1, which is reassuring although it should be noted that different birth defects have different aetiologies and assessing birth defects as an aggregate endpoint may make it impossible for associations with specific birth defects to be identified. However, the German study and the spontaneous reporting data thus far do not highlight any specific birth defects, which is reassuring.

Table 3. Summary results from all studies reporting on the association between A/H1N1 vaccination in the first trimester of pregnancy and congenital malformations

Author	Location	RR_{adj}	CI_{95}
Heikkinen *et al* [3]	Argentina, Italy, the Netherlands	1.33	0.88-2.00
Oppermann *et al* [4]	Germany	0.92	0.58-1.46
Kallen *et al* [8]	Sweden	1.01	0.83-1.23
Pasternak *et al* [10]	Denmark	1.21	0.60-2.45

References

1 Fell DB, Sprague AE, Liu N, Yasseen AS et al. H1N1 influenza vaccination during pregnancy and fetal and neonatal outcomes. American Journal of Public Health 2012; 102:e33-e40

2 Haberg S, Trogstad L, Gunnes N, et al. Risk of fetal death after pandemic influenza virus infection or vaccination. N Eng J Med 2013;268:333-40

3 Heikkinen T, Young J, van Beek E, Franke H et al. Safety of MF59-adjuvanted A/H1N1 influenza vaccine in pregnancy: a comparative cohort study. Am J Obst Gynecol 2012; 207 (3): 177.e-177.e8

4 Oppermann M, Fritzsche J, Weber-Schoendorfer C, Keller-Stanislawski B et al. A(H1N1)v 2009: a controlled prospective cohort study on vaccine safety in pregnancy. Vaccine 2012; 30(30): 4445-4452.

5 Pasternak B, Svanstrom H, Molgaard-Nielsen D, Krause TG et al. Vaccination against pandemic A/H1N1 2009 influenza in pregnancy and risk of fetal death: cohort study in Denmark. BMJ 2012; 344: e2794

6 Sammon CJ, Snowball J, McGrogan A, de Vries CS. Evaluating the hazard of foetal death following H1N1 influenza vaccination; a population based cohort study in the UK GPRD. PLoS ONE 2012; 7(12)

7 Xu R, Luo Y, Chambers C. Assessing the effect of vaccine on spontaneous abortion using time-dependent covariates Cox models. Pharmacoepidemiol Drug Saf 2012; 21(8): 844-50

8 Kallen B, Olausson PO. Vaccination against H1N1 inflenza with Pandemrix ® during pregnancy and delivery outcome: a Swedish registry study. BJOG 2012; 119(13): 1583-1590

9 Lin T-H, Lin S-Y, Lin C-H, Lin R-I et al. AdminFlu S ® influenza A (H1N1) vaccine during pregnancy: the Taiwanese Pharmacovigilance Survey. Vaccine 2012; 30(16): 2671-2675

10 Pasternak B, Svanstrom H, Molgaard-Nielsen D, Krause D et al. Risk of adverse fetal outcomes following administration of a pandemic influenza A(H1N1) vaccine during pregnancy. JAMA 2012; 308 (2): 165-174