Safeguarding public health

UK Suspected Adverse Reaction Analysis

Swine Flu (H1N1) Vaccines – Celvapan and Pandemrix

26 November 2009

This report provides an overview of all UK reports of suspected adverse reactions to the new swine flu (H1N1) vaccines (Celvapan and Pandemrix) received by MHRA between Monday 15th October 2009 and Thursday 19th November 2009 (inclusive)[1]. These reports have been voluntarily submitted to MHRA by UK healthcare professionals and members of the public via the MHRA's 'Swine Flu ADR Portal' (www.mhra.gov.uk/swineflu) and the Yellow Card Scheme. It also includes all UK reports submitted by the Marketing Authorisation holders for Celvapan (Baxter) and Pandemrix (GSK) as part of their legal requirements.

The suspected adverse reactions listed in the attached Vaccine Analysis Prints have been coded using 'MedDRA' terminology[2].

It is important to note that a report of a reaction does not necessarily mean that it has been caused by the vaccine in question. We encourage reporters to report *suspected* adverse reactions i.e. the reporter does not have to be sure that the vaccine caused the reaction – a mere suspicion will suffice. Therefore, reports submitted to MHRA may be true adverse effects of the vaccine, psychogenic reactions related to the process of vaccination rather than to the specific vaccine itself (e.g. nervousness or anxiety about needles or vaccination); or they may be purely coincidental events that would have occurred anyway in the absence of vaccination (e.g. events due to underlying medical conditions). For this reason **this summary is not a list of known or proven adverse reactions to H1N1 vaccines and must not be interpreted and used as such**. A list of the recognised adverse effects of Celvapan and Pandemrix is provided in the product information for healthcare professionals (Summary of Product Characteristics) and patients (Patient Information Leaflet), copies of which are available on our website (www.mhra.gov.uk/swineflu).

Suspected adverse reaction reporting rates are highly variable and are dependent on many factors. Therefore these data cannot be used to determine the frequency of occurrence of adverse reactions to the H1N1 vaccines. Furthermore, the use of the two H1N1 vaccines available in the UK is expected to differ considerably in terms of the level of exposure and patient populations exposed (most will receive the Pandemrix brand). For these reasons **the data included in this report can not be used to directly compare the relative safety of Pandemrix and Celvapan.**

All reports of suspected adverse reactions to Celvapan and Pandemrix are closely monitored by a dedicated team of safety specialists at the MHRA. **Annex 4** to this document describes the processes involved in safety monitoring and outlines some of the factors to be considered in interpreting the data in this report.

[1] Suspected ADR data are released with a 1 week delay in order to ensure that MHRA has time to validate, extract and assess the data before publication.
[2] MedDRA - the Medical Dictionary for Regulatory Activities - is a standardised, medically validated adverse event terminology system used within the international medicines regulatory environment.

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Headline summary:

1. Up to and including Thursday 19th November 2009, MHRA has received a total of 936 UK reports of suspected ADRs to the H1N1 vaccines. The 936 reports include a total of 2515 suspected reactions (a single report may contain more than one reaction).

2. Reports of suspected adverse reactions to Pandemrix make up 89% (n=831) of all reports received for H1N1 vaccines to date. This is not unexpected given the *presumed* difference in the extent of use of the two vaccines[3]. The vaccine brand was not reported in 10% (n=93) of reports.

3. Two deaths following H1N1 vaccination have been reported in the UK to date. In both cases the patient had significant and chronic underlying medical conditions and there is no indication that the vaccine contributed to the deaths.

4. Further information on the type of suspected adverse reactions reported for each of the vaccines is provided in Annexes 1 (Celvapan), 2 (Pandemrix) and 3 (brand unknown).

5. As expected, the most frequently reported suspected adverse reactions are non-serious injection site reactions (e.g. pain, swelling, redness), or are well established minor adverse effects of many vaccines, including the swine flu vaccines (e.g. nausea, vomiting, dizziness muscle pain, fever, fatigue, headache, swollen glands, 'flu-like illness').

6. No new safety issues have been identified from reports received to date.

7. **The balance of benefits and risks for Celvapan and Pandemrix remains positive**

8. If identified, information on new and emerging safety signals will be provided in this report together with details of any resulting regulatory action or changes to prescribing advice deemed necessary.

[3] Data on relative usage of each vaccine are not currently available to MHRA. When such information is available, we will include it in these updates.

1. ADVERSE REACTION REPORTING TRENDS

Up to and including Thursday 19th November 2009, a total of 936 reports of suspected adverse reactions to H1N1 vaccines have been reported in the UK. These 936 reports include 2515 suspected reactions; a single report may include more than one suspected reaction.

A breakdown of the number of reports received by vaccine brand is provided in Table 1 below. The distribution of reports between Celvapan and Pandemrix is not unexpected given the presumed[3] difference in the extent of use of the two vaccines in the UK.

Table 1: Number of reports of suspected reactions received for Celvapan and Pandemrix in the UK

	Up to 5th November 2009		Up to 12th November 2009		Up to 19th November 2009	
Vaccine	**Number of Reports**	**Number of Reactions**	**Number of Reports**	**Number of Reactions**	**Number of Reports**	**Number of Reactions**
Celvapan	4	8	7	13	12	32
Pandemrix	172	412	449	1200	831	2224
Brand not reported	12	40	41	116	93	259
Total	**188**	**460**	**497**	**1329**	**936**	**2515**

Further information on the types of suspected adverse reactions reported for each of the vaccines is provided in **Annexes 1 (Celvapan), 2 (Pandemrix)** and **3 (brand unknown)** and in **Section 2** below.

2. ANALYSIS OF REPORTED SUSPECTED ADVERSE REACTIONS

2.1 Celvapan

A line-listing of all UK suspected reactions reported for Celvapan can be found in **Annex 1**.
Up to and including 19th November, twelve reports (of 32 suspected adverse reactions) have been received for Celvapan.

2.1.1 Nervous system disorders
The nervous system disorders system reported to date for Celvapan are generally non-serious and are recognised side-effects of the vaccine (dizziness; paraesthesia [pins and needles]). These cases are not indicative of serious neurological illness.

2.1.2 Symptoms of allergic or anaphylactic reactions
One case of swollen lips has been reported for Celvapan. The swelling was confined to the lips and was not indicative of a serious allergic reaction. Allergic reactions are recognised adverse effects of Celvapan.

2.1.3 Pregnant women
.One report of suspected a adverse reaction (injection site reaction) in a pregnant woman has been received for Celvapan in the UK to date. No adverse effects to the unborn baby were reported.

2.1.4 Children
No reports in children aged below 16 years have been received for Celvapan in the UK to date.

2.2 Pandemrix

Eighty-nine percent (831/936) of the total reports received for H1N1 vaccines in the UK to date are for Pandemrix. This most likely reflects greater usage of this vaccine in the UK to date[3]. A line-listing of all suspected reactions reported in the UK for Pandemrix can be found in **Annex 2**.

The most frequently reported reactions are generally non-serious; injection site reactions including pain, swelling, numbness, pins and needles (paraesthesia), and bruising; and symptoms that are common and recognised effects of many vaccines such as dizziness, headache, fatigue, flu-like illness, muscle aches, malaise, mild fever, swollen glands, nausea and vomiting.

2.2.1 Fatal reactions

Most people receiving the vaccine have serious and/or chronic underlying medical conditions which put them at greater risk of developing serious complications of swine flu. This is why it is important for these people to be vaccinated as a priority. Over the next few months, many of these patients will naturally suffer an exacerbation of their underlying illness, including death. Such events may occur shortly after vaccination and be reported as suspected side effects. It is important to bear in mind that this temporal association does not in itself mean that the vaccine was responsible for the event and that this may be coincidental. Such reports are fully evaluated by the MHRA.

Two reports of death following vaccination with Pandemrix have been reported in the UK to date. In both cases the patients had significant underlying medical conditions. There is no indication that the vaccine contributed to these deaths.

2.2.2 Nervous system disorders

The nervous system disorders reported in the UK for Pandemrix to date are generally non-serious events (headache, dizziness, lethargy, and somnolence) and are recognised adverse effects of the vaccine.

The reports of paraesthesia (pins and needles) and hypoaesthesia (numbness) are generally transient and localised to the injection site or to the injected limb. This is also true of the two cases of neuralgia (nerve pain). The case of trigeminal nerve paresis has been fully evaluated and a causal association between Pandemrix and the neuritis is unlikely.

Fainting episodes (syncope) very shortly after vaccination are not uncommon with any vaccination. This is not a side effect of the vaccine, but a 'psychogenic' response to the injection (usually because of fear or anticipation of the needle injection). The one report of loss of consciousness is being followed-up to establish if this was a fainting episode.

The case of eyelid ptosis (droopy eyelid) was associated with swelling of the eyelid and so is therefore most likely to be of allergic than neurological origin.

Two cases of convulsions have been reported. Both involve children and are discussed in further detail in section 2.2.5 below. Convulsions are listed as a potential rare side effect of flu vaccines in the product information for Pandemrix

The nervous system disorders reported to date for Pandemrix are not indicative of serious neurological illness. As with all suspected side effects, the MHRA continues to closely monitor nervous system disorders.

2.2.3 Symptoms of serious allergic or anaphylactic reactions

There have been a number of cases of potentially serious allergic reactions reported for Pandemrix to date. These include two cases of angioedema, 6 cases of facial swelling, and one case of pharyngeal oedema. Two cases of anaphylactic reaction have also been reported for Pandemrix to date but neither case appears to be a true case of anaphylaxis.

Anaphylaxis is a known, although very rare, risk with any vaccine and is thought to occur at a frequency of between one and ten cases per million doses of vaccine given. The prescribing information for swine flu vaccines warn of this possible risk and the need to ensure that appropriate medical treatment and supervision should always be readily available in case of a rare anaphylactic event.

At least 5 million doses of swine flu vaccine have now been given across Europe and there is currently no good evidence to suggest that there is a greater risk of anaphylaxis with Pandemrix vaccine, or that it causes more severe cases, than we would normally expect.

2.2.4 Pregnant women

Twenty six reports of suspected adverse reactions in pregnant women have been received. The gestation period at the time of vaccination ranges from 2 to 8 months.

With the exception of one case of possible reduced foetal movements for 24 hours (no adverse outcome) starting 12 hours following vaccination, all of these reports describe adverse effects for the mother only. All reports are non-serious and recognised side-effects of Pandemrix (injection site reactions and flu-like illness). To date we have received no reports of any adverse effects on the unborn baby or on the progression or outcome of pregnancy reported.

2.2.5 Suspected reactions reported in children

There are 55 reports of suspected adverse reactions to Pandemrix in children under the age of 15 years.

The majority of the reported suspected reactions in children are non-serious, recognised side effects of many vaccines including Pandemrix, or can be attributed to the process of vaccination rather than the vaccine itself. These reactions include injection site reactions, flu-like illness and psychogenic reactions.

One child experienced reactive arthritis (which can occur as a result of infection) and two others experienced seizures. A causal association between these events and the vaccine has not been established.

2.3 H1N1 vaccine brand unknown

A total of 93 reports (of 259 suspected reactions) have been reported for H1N1 vaccines in which the brand is not provided. The majority of suspected reactions are non-serious and are consistent with symptoms commonly experienced after any vaccination (flu-like illness, fever, injection site pain, headache, malaise, aches and pains, flushing, and nausea).

A line-listing of all suspected reactions reported in the UK for H1N1 vaccines in which the brand is not reported can be found in **Annex 3**.

2.3.1 Nervous system disorders

One case of an inability to move limbs (translated in our medical dictionary to 'paralysis'[2]) has been reported to date for H1N1 vaccine. Further information has been requested, however, initial assessment is that this may relate to a difficulty in moving the injected arms after vaccination, rather than a form of paralysis.

2.2.3 Symptoms of serious allergic or anaphylactic reactions

One case of swollen tongue and one case of anaphylaxis has been reported. The case of anaphylaxis occurred in a patient with a history of severe allergic reactions. Allergic reactions are recognised side-effects of flu vaccines.

2.2.4 Pregnant women

Four reports of suspected adverse reactions in pregnant women have been received for H1N1 vaccine where the brand of vaccine was not reported. These reports described adverse effects for the mother

only. All reports are non-serious and recognised side-effects of the vaccine. We have received no reports in which adverse effects on the unborn baby or on the progression or outcome of pregnancy are reported.

2.2.5 Suspected reactions reported in children

Eight reports of suspected adverse reactions to H1N1 vaccine in children under the age of 15 years have been received. The majority of children experienced flu-like illness and injection site reactions which are generally non-serious and are recognised side effects of H1N1 vaccines.

Two children experienced an allergic reaction – symptoms included facial swelling (including lips) and rash. As discussed above, allergic reactions are recognised side-effects of many vaccines including the H1N1 vaccines.

One child (aged under 5 years) experienced a febrile seizure on the same day as vaccination and was recovering at the time of the report. Febrile seizures are not uncommon in children under the age of 5-years.

2.4 Overall Conclusions

The vast majority of reports of suspected adverse reactions to H1N1 vaccines received to date are for Pandemrix. This is not unexpected given the presumed[3] greater usage of Pandemrix in the UK to date.

The most frequently reported suspected adverse reactions are non-serious and expected – i.e. injection site reactions (e.g. local pain, swelling, redness or bruising) and general symptoms including nausea, vomiting, dizziness, muscle pains, fever, fatigue, headache, swollen glands).

No new safety issues have been identified from UK data to date. The benefit – risk balance for Celvapan and Pandemrix remain positive.

ANNEX 1 - CELVAPAN

Drug Analysis Print
Drug Name: Celvapan

Run Date: Unspecified to 19 November 2009		
Total number of reactions: 32	**Total number of ADR reports:** 12	**Total number of fatal ADR reports:**

System Organ Class	Reactions	Fatal Reactions
Gastrointestinal disorders	3	0
General disorders and administration site conditions	9	0
Musculoskeletal and connective tissue disorders	4	0
Nervous system disorders	9	0
Respiratory, thoracic and mediastinal disorders	6	0
Skin and subcutaneous tissue disorders	1	0
Total	32	0

Glossary/Abbreviations

ADR - Adverse Drug Reaction

Age group - lists which age groups are included in the Drug Analysis Print - either ALL, Adolescent, Adult, Child, Elderly, Infant or Neonate

Data lock date - shows data on the database at this specified date and time

HLT - High Level Term - see definition of MedDRA

MEDRA - this stands for Medical Dictionary for Regulatory Activities, which is the internationally agreed list of terms used for Medicines Regulation. MedDRA groups related adverse drug reaction terms in a hierarchical structure whereby the 'preferred term' (PT) (e.g. tunnel vision) is grouped under the broader heading the 'high level term' (HLT) (e.g. visual field disorders). 'High level terms' are contained within the 'system organ class' (SOC) (e.g. eye disorders). The 'preferred term' is the most specific term on the Drug Analysis Print, while the 'system organ class' is the most general

Multi active constituent products - contain the drug constituent of interest plus one or more other drug constituents (e.g. co-codamol contains paracetamol and codeine)

NEC - appears in MedDRA and stands for Not Elsewhere Classified

NOS - appears in MedDRA and stands for Not Otherwise Specified

PBG - Product Brand Generic - this means drug brand name e.g. Amoxil is a PBG for the drug substance amoxic

Products included in this print - this is a list of the products for which at least one suspected Adverse Drug Reaction (ADR) report has been received that specifies that product as a 'suspected drug' (i.e. suspected causal association with the reaction). It does not provide an exhaustive list of the products which contain the named drug substance

PT - Preferred Term - see definition of MedDRA

Reaction - defines which ADRs are included in the Drug Analysis Print - either ALL, Serious or Non-Serious

Reporter type - lists the reporter types which are included in the Drug Analysis Print - either Patient, Health Professional or ALL (i.e. both)

Report run date - the date the Drug Analysis Print was produced

Route of admin - lists the route of administration of the suspect drug for which reports are included in the Drug Analysis Print, e.g. ORAL only includes reports where the suspect drug was specified as having been taken by the oral route, or ALL which includes all routes of administration

Spontaneous - suspected ADR reports sent in to the Yellow Card Scheme are called spontaneous reports

Single active constituent products - contain only the drug substance of interest

System Organ Class (SOC) - this is the highest level in MedDRA which groups together reactions that affect similar systems/organs in the body

Drug Analysis Print
Drug Name: Celvapan

Reaction Name	Reactions	Fatal Reactions
SOC		
HLT		
PT		
Gastrointestinal disorders		
Nausea and vomiting symptoms		
Nausea	1	0
Vomiting	1	0
Oral soft tissue disorders NEC		
Lip swelling	1	0
Oral soft tissue signs and symptoms		
Gastrointestinal disorders SOC Total	3	0

Drug Analysis Print
Drug Name: Celvapan

Reaction Name	Reactions	Fatal Reactions
SOC		
HLT		
PT		
General disorders and administration site conditions		
Asthenic conditions		
Fatigue	2	0
Malaise	2	0
Febrile disorders		
Pyrexia	2	0
Injection and infusion site reactions		
Injection site pain	1	0
Pain and discomfort NEC		
Pain	1	0
Feelings and sensations NEC		
Thirst	1	0
General disorders and administration site conditions SOC Total	9	0

Drug Analysis Print
Drug Name: Celvapan

Reaction Name	Reactions	Fatal Reactions
SOC		
HLT		
PT		
Musculoskeletal and connective tissue disorders		
Muscle pains		
Myalgia	1	0
Musculoskeletal and connective tissue pain and discomfort		
Neck pain	1	0
Pain in extremity	1	0
Limb discomfort	1	0
Musculoskeletal and connective tissue disorders SOC Total	4	0

Drug Analysis Print
Drug Name: Celvapan

Reaction Name	Reactions	Fatal Reactions
SOC		
HLT		
PT		
Nervous system disorders		
Headaches NEC		
Headache	3	0
Neurological signs and symptoms NEC		
Dizziness	3	0
Paraesthesias and dysaesthesias		
Paraesthesia	2	0
Speech and language abnormalities		
Dysarthria	1	0
Nervous system disorders SOC Total	9	0

Drug Analysis Print
Drug Name: Celvapan

Reaction Name	Reactions	Fatal Reactions
SOC		
HLT		
PT		
Respiratory, thoracic and mediastinal disorders		
Coughing and associated symptoms		
Cough	2	0
Nasal disorders NEC		
Epistaxis	1	0
Upper respiratory tract signs and symptoms		
Rhinorrhoea	1	0
Oropharyngeal pain	2	0
Respiratory, thoracic and mediastinal disorders SOC Total	6	0

Drug Analysis Print
Drug Name: Celvapan

Reaction Name	Reactions	Fatal Reactions
SOC		
HLT		
PT		
Skin and subcutaneous tissue disorders		
Angioedemas		
Pruritus NEC		
Pruritus	1	0
Skin and subcutaneous tissue disorders SOC Total	1	0

ANNEX 2 - PANDEMRIX

Drug Analysis Print
Drug Name: Pandemrix

Run Date: Unspecified to 19 November 2009		
Total number of reactions: 2224	**Total number of ADR reports:** 831	**Total number of fatal ADR reports:** 2

System Organ Class	Reactions	Fatal Reactions
Blood and lymphatic system disorders	38	0
Cardiac disorders	17	0
Ear and labyrinth disorders	10	0
Eye disorders	27	0
Gastrointestinal disorders	249	0
General disorders and administration site conditions	752	1
Immune system disorders	6	0
Infections and infestations	26	0
Injury, poisoning and procedural complications	19	0
Investigations	40	0
Metabolism and nutrition disorders	12	0
Musculoskeletal and connective tissue disorders	368	0
Nervous system disorders	365	1
Pregnancy, puerperium and perinatal conditions	1	0
Psychiatric disorders	34	0
Renal and urinary disorders	4	0
Reproductive system and breast disorders	4	0
Respiratory, thoracic and mediastinal disorders	91	0
Skin and subcutaneous tissue disorders	131	0
Social circumstances	2	0
Surgical and medical procedures	1	0
Vascular disorders	23	0
Total	2220	2

Glossary/Abbreviations

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PT - Preferred Term - see definition of MedDRA

Reaction - defines which ADRs are included in the Drug Analysis Print - either ALL, Serious or Non-Serious

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Report run date - the date the Drug Analysis Print was produced

Route of admin - lists the route of administration of the suspect drug for which reports are included in the Drug Analysis Print, e.g. ORAL only includes reports where the suspect drug was specified as having been taken by the oral route, or ALL which includes all routes of administration

Spontaneous - suspected ADR reports sent in to the Yellow Card Scheme are called spontaneous reports

Single active constituent products - contain only the drug substance of interest

System Organ Class (SOC) - this is the highest level in MedDRA which groups together reactions that affect similar systems/organs in the body

Drug Analysis Print
Drug Name: Pandemrix

Reaction Name	Reactions	Fatal Reactions
SOC		
HLT		
PT		
Blood and lymphatic system disorders		
Lymphatic system disorders NEC		
Lymph node pain	2	0
Lymphadenitis	2	0
Lymphadenopathy	34	0
Blood and lymphatic system disorders SOC Total	38	0

Drug Analysis Print
Drug Name: Pandemrix

Reaction Name	Reactions	Fatal Reactions
SOC		
HLT		
PT		
Cardiac disorders		
Cardiac signs and symptoms NEC		
Cyanosis	1	0
Palpitations	7	0
Rate and rhythm disorders NEC		
Tachycardia	8	0
Supraventricular arrhythmias		
Atrial fibrillation	1	0
Cardiac disorders SOC Total	17	0

Drug Analysis Print
Drug Name: Pandemrix

Reaction Name	Reactions	Fatal Reactions
SOC		
HLT		
PT		
Ear and labyrinth disorders		
Hearing losses		
Deafness neurosensory	1	0
Inner ear signs and symptoms		
Tinnitus	4	0
Vertigo	1	0
Ear disorders NEC		
Ear pain	4	0
Ear and labyrinth disorders SOC Total	10	0

Drug Analysis Print
Drug Name: Pandemrix

Reaction Name	Reactions	Fatal Reactions
SOC		
HLT		
PT		
Eye disorders		
Conjunctival infections, irritations and inflammations		
Conjunctivitis	1	0
Eyelid movement disorders		
Blepharospasm	1	0
Eyelid ptosis	1	0
Lacrimal disorders		
Dry eye	1	0
Lacrimation increased	1	0
Lid, lash and lacrimal infections, irritations and inflammations		
Eyelid oedema	1	0
Ocular disorders NEC		
Eye pain	6	0
Eye swelling	3	0
Eyelid pain	1	0
Ocular infections, inflammations and associated manifestations		
Ocular hyperaemia	1	0
Ocular sensation disorders		
Asthenopia	1	0
Photophobia	1	0
Partial vision loss		
Visual acuity reduced	1	0
Visual acuity reduced transiently	1	0
Visual disorders NEC		
Vision blurred	5	0
Visual impairment	1	0
Eye disorders SOC Total	27	0

Drug Analysis Print
Drug Name: Pandemrix

Reaction Name	Reactions	Fatal Reactions
SOC		
HLT		
PT		
Gastrointestinal disorders		
Diarrhoea (excl infective)		
Diarrhoea	35	0
Flatulence, bloating and distension		
Flatulence	1	0
Gastrointestinal and abdominal pains (excl oral and throat)		
Abdominal pain	9	0
Abdominal pain lower	4	0
Abdominal pain upper	14	0
Non-site specific gastrointestinal haemorrhages		
Haematochezia	1	0
Intestinal haemorrhages		
Rectal haemorrhage	1	0
Gastrointestinal signs and symptoms NEC		
Abdominal discomfort	2	0
Dysphagia	1	0
Stomach discomfort	2	0
Nausea and vomiting symptoms		
Nausea	97	0
Vomiting	59	0
Vomiting in pregnancy	1	0
Regurgitation	1	0
Oral dryness and saliva altered		
Dry mouth	6	0
Oral soft tissue disorders NEC		
Lip swelling	2	0
Oral soft tissue pain and paraesthesia		
Paraesthesia oral	5	0
Oral soft tissue signs and symptoms		
Hypoaesthesia oral	1	0
Acute and chronic pancreatitis		
Pancreatitis acute	1	0
Stomatitis and ulceration		
Mouth ulceration	1	0

Tongue disorders		
Tongue ulceration	1	0
Tongue signs and symptoms		
Swollen tongue	2	0
Tongue discolouration	1	0
Dental pain and sensation disorders		
Toothache	1	0
Gastrointestinal disorders SOC Total	249	0

Drug Analysis Print
Drug Name: Pandemrix

Reaction Name	Reactions	Fatal Reactions
SOC		
HLT		
PT		
General disorders and administration site conditions		
Application and instillation site reactions		
Application site pain	14	0
Application site pruritus	2	0
Application site reaction	2	0
Application site warmth	1	0
Application site haematoma	3	0
Asthenic conditions		
Asthenia	13	0
Fatigue	69	0
Malaise	49	0
Death and sudden death		
Death	1	1
Febrile disorders		
Pyrexia	132	0
General signs and symptoms NEC		
Influenza like illness	66	0
Irritability	1	0
Local reaction	24	0
Local swelling	3	0
Swelling	10	0
Induration	1	0
Inflammations		
Inflammation	2	0
Injection and infusion site reactions		
Injection site anaesthesia	1	0
Injection site erythema	11	0
Injection site haematoma	7	0
Injection site induration	3	0
Injection site inflammation	32	0
Injection site irritation	6	0
Injection site mass	1	0
Injection site pain	40	0
Injection site phlebitis	1	0

Injection site pruritus	6	0
Injection site rash	4	0
Injection site reaction	1	0
Injection site warmth	2	0
Injection site discolouration	1	0
Injection site swelling	22	0
Injection site discomfort	1	0
Oedema NEC		
Oedema peripheral	72	0
Pain and discomfort NEC		
Chest discomfort	16	0
Chest pain	7	0
Pain	32	0
Tenderness	5	0
Axillary pain	1	0
Non-cardiac chest pain	1	0
Administration site reactions NEC		
Venipuncture site swelling	1	0
Infusion site reactions		
Infusion related reaction	1	0
Feelings and sensations NEC		
Chills	52	0
Feeling abnormal	4	0
Feeling cold	3	0
Feeling hot	15	0
Peripheral coldness	4	0
Thirst	1	0
Feeling of body temperature change	5	0
General disorders and administration site conditions SOC Total	752	1

Drug Analysis Print
Drug Name: Pandemrix

Reaction Name	Reactions	Fatal Reactions
SOC		
HLT		
PT		
Immune system disorders		
Anaphylactic responses		
Anaphylactic reaction	2	0
Allergic conditions NEC		
Hypersensitivity	4	0
Immune system disorders SOC Total	6	0

Drug Analysis Print
Drug Name: Pandemrix

Reaction Name	Reactions	Fatal Reactions
SOC		
HLT		
PT		
Infections and infestations		
Bacterial infections NEC		
Cellulitis	5	0
Eye and eyelid infections		
Eye infection	1	0
Infections NEC		
Infection	2	0
Injection site abscess	1	0
Localised infection	1	0
Influenza viral infections		
Influenza	4	0
Lower respiratory tract and lung infections		
Bronchitis	1	0
Lower respiratory tract infection	3	0
Skin structures and soft tissue infections		
Skin infection	1	0
Upper respiratory tract infections		
Nasopharyngitis	4	0
Rhinitis	2	0
Viral infections NEC		
Sweating fever	1	0
Infections and infestations SOC Total	26	0

Drug Analysis Print
Drug Name: Pandemrix

Reaction Name	Reactions	Fatal Reactions
SOC		
HLT		
PT		
Injury, poisoning and procedural complications		
Anaesthetic complications		
Delayed recovery from anaesthesia	1	0
Gastrointestinal and hepatobiliary procedural complications		
Procedural nausea	1	0
Heat injuries (excl thermal burns)		
Heat oedema	1	0
Skin injuries NEC		
Contusion	6	0
Muscle, tendon and ligament injuries		
Muscle strain	1	0
Neurological and psychiatric procedural complications		
Procedural dizziness	1	0
Vaccination related complications		
Post vaccination syndrome	3	0
Vaccination complication	5	0
Injury, poisoning and procedural complications SOC Total	19	0

Drug Analysis Print
Drug Name: Pandemrix

Reaction Name	Reactions	Fatal Reactions
SOC		
HLT		
PT		
Investigations		
Carbohydrate tolerance analyses (incl diabetes)		
Blood glucose decreased	1	0
Physical examination procedures		
Body temperature decreased	1	0
Body temperature increased	32	0
Respiratory and pulmonary function diagnostic procedures		
Forced expiratory volume increased	1	0
Urinalysis NEC		
Blood urine present	1	0
Vascular tests NEC (incl blood pressure)		
Blood pressure abnormal	1	0
Blood pressure decreased	1	0
Heart rate and pulse investigations		
Heart rate increased	2	0
Investigations SOC Total	40	0

Drug Analysis Print
Drug Name: Pandemrix

Reaction Name	Reactions	Fatal Reactions
SOC		
HLT		
PT		
Metabolism and nutrition disorders		
Appetite disorders		
Anorexia	4	0
Decreased appetite	6	0
General nutritional disorders NEC		
Hyperglycaemic conditions NEC		
Hyperglycaemia	1	0
Total fluid volume decreased		
Dehydration	1	0
Metabolism and nutrition disorders SOC Total	12	0

Drug Analysis Print
Drug Name: Pandemrix

Reaction Name	Reactions	Fatal Reactions
SOC		
HLT		
PT		
Musculoskeletal and connective tissue disorders		
Arthropathies NEC		
Arthritis	1	0
Arthritis reactive	1	0
Bone related signs and symptoms		
Bone pain	1	0
Pain in jaw	1	0
Muscle infections and inflammations		
Myositis	2	0
Joint related signs and symptoms		
Arthralgia	68	0
Joint stiffness	3	0
Joint swelling	1	0
Musculoskeletal and connective tissue signs and symptoms NEC		
Sensation of heaviness	4	0
Mobility decreased	1	0
Musculoskeletal stiffness	17	0
Muscle pains		
Myalgia	84	0
Fibromyalgia	1	0
Muscle related signs and symptoms NEC		
Muscle spasms	6	0
Muscle twitching	2	0
Muscle swelling	1	0
Muscle tone abnormalities		
Muscle rigidity	1	0
Nuchal rigidity	1	0
Soft tissue disorders NEC		
Axillary mass	1	0
Tendon disorders		
Tendonitis	1	0
Muscle weakness conditions		
Muscular weakness	8	0
Musculoskeletal and connective tissue pain and discomfort		

Back pain	15	0
Musculoskeletal pain	14	0
Neck pain	12	0
Pain in extremity	93	0
Musculoskeletal chest pain	1	0
Musculoskeletal discomfort	5	0
Limb discomfort	22	0
Musculoskeletal and connective tissue disorders SOC Total	368	0

Drug Analysis Print
Drug Name: Pandemrix

Reaction Name	Reactions	Fatal Reactions
SOC		
HLT		
PT		
Nervous system disorders		
Acute polyneuropathies		
Polyneuropathy	1	0
Cerebellar coordination and balance disturbances		
Balance disorder	1	0
Disturbances in consciousness NEC		
Lethargy	23	0
Loss of consciousness	1	0
Somnolence	9	0
Syncope	6	0
Dyskinesias and movement disorders NEC		
Hypokinesia	2	0
Headaches NEC		
Headache	169	0
Sinus headache	3	0
Tension headache	2	0
Mental impairment (excl dementia and memory loss)		
Disturbance in attention	1	0
Migraine headaches		
Migraine	14	0
Migraine with aura	1	0
Narcolepsy and hypersomnia		
Hypersomnia	2	0
Neurological signs and symptoms NEC		
Dizziness	51	0
Dizziness postural	3	0
Head discomfort	1	0
Presyncope	2	0
Neuromuscular disorders NEC		
Paraesthesias and dysaesthesias		
Burning sensation	1	0
Hyperaesthesia	2	0
Paraesthesia	33	0
Paralysis and paresis (excl cranial nerve)		

Monoplegia	1	0
Peripheral neuropathies NEC		
Neuropathy peripheral	1	0
Seizures and seizure disorders NEC		
Convulsion	2	0
Epilepsy	1	1
Sensory abnormalities NEC		
Dysgeusia	4	0
Hypoaesthesia	11	0
Neuralgia	2	0
Sensory loss	1	0
Speech and language abnormalities		
Aphonia	2	0
Dysphasia	1	0
Transient cerebrovascular events		
Transient ischaemic attack	1	0
Tremor (excl congenital)		
Tremor	8	0
Trigeminal disorders		
Facial neuralgia	1	0
Trigeminal nerve paresis	1	0
Nervous system disorders SOC Total	365	1

Drug Analysis Print
Drug Name: Pandemrix

Reaction Name	Reactions	Fatal Reactions
SOC		
HLT		
PT		
Pregnancy, puerperium and perinatal conditions		
Foetal complications NEC		
Foetal hypokinesia	1	0
Pregnancy, puerperium and perinatal conditions SOC Total	1	0

Drug Analysis Print
Drug Name: Pandemrix

Reaction Name	Reactions	Fatal Reactions
SOC		
HLT		
PT		
Psychiatric disorders		
Affect alterations NEC		
Affect lability	1	0
Anxiety symptoms		
Nervousness	1	0
Behaviour and socialisation disturbances		
Confusion and disorientation		
Confusional state	1	0
Disorientation	4	0
Deliria		
Delirium	1	0
Dissociative states		
Dissociation	2	0
Disturbances in initiating and maintaining sleep		
Insomnia	13	0
Fluctuating mood symptoms		
Mood swings	1	0
Increased physical activity levels		
Restlessness	2	0
Mood alterations with depressive symptoms		
Tearfulness	1	0
Mood disorders NEC		
Parasomnias		
Nightmare	2	0
Perception disturbances		
Hallucination	1	0
Sleep disorders NEC		
Sleep disorder	3	0
Speech articulation and rhythm disturbances		
Stereotypies and automatisms		
Head banging	1	0
Psychiatric disorders SOC Total	34	0

Drug Analysis Print
Drug Name: Pandemrix

Reaction Name	Reactions	Fatal Reactions
SOC		
HLT		
PT		
Renal and urinary disorders		
Bladder and urethral symptoms		
Pollakiuria	1	0
Urinary tract signs and symptoms NEC		
Renal pain	3	0
Renal and urinary disorders SOC Total	4	0

Drug Analysis Print
Drug Name: Pandemrix

Reaction Name	Reactions	Fatal Reactions
SOC		
HLT		
PT		
Reproductive system and breast disorders		
Menstruation and uterine bleeding NEC		
Metrorrhagia	1	0
Reproductive tract signs and symptoms NEC		
Pelvic pain	1	0
Breast signs and symptoms		
Breast pain	1	0
Breast swelling	1	0
Reproductive system and breast disorders SOC Total	4	0

Drug Analysis Print
Drug Name: Pandemrix

Reaction Name	Reactions	Fatal Reactions
SOC		
HLT		
PT		
Respiratory, thoracic and mediastinal disorders		
Breathing abnormalities		
Dyspnoea	15	0
Hypoventilation	1	0
Tachypnoea	2	0
Bronchospasm and obstruction		
Asthma	2	0
Wheezing	5	0
Coughing and associated symptoms		
Cough	11	0
Productive cough	4	0
Nasal disorders NEC		
Epistaxis	2	0
Nasal congestion and inflammations		
Nasal congestion	2	0
Nasal inflammation	1	0
Rhinitis allergic	1	0
Pharyngeal disorders (excl infections and neoplasms)		
Pharyngeal oedema	1	0
Pharyngeal hypoaesthesia	1	0
Paranasal sinus disorders (excl infections and neoplasms)		
Sinus congestion	3	0
Upper respiratory tract signs and symptoms		
Rhinorrhoea	9	0
Sneezing	4	0
Throat irritation	1	0
Oropharyngeal pain	26	0
Respiratory, thoracic and mediastinal disorders SOC Total	91	0

Drug Analysis Print
Drug Name: Pandemrix

Reaction Name	Reactions	Fatal Reactions
SOC		
HLT		
PT		
Skin and subcutaneous tissue disorders		
Angioedemas		
Angioedema	2	0
Apocrine and eccrine gland disorders		
Cold sweat	6	0
Hyperhidrosis	15	0
Night sweats	2	0
Sweat gland disorder	3	0
Bullous conditions		
Erythema multiforme	1	0
Dermal and epidermal conditions NEC		
Pain of skin	3	0
Skin discolouration	2	0
Skin discomfort	1	0
Skin reaction	6	0
Swelling face	6	0
Hypoaesthesia facial	2	0
Dermatitis and eczema		
Dermatitis allergic	1	0
Skin irritation	1	0
Erythemas		
Erythema	12	0
Rash erythematous	1	0
Papulosquamous conditions		
Rash papular	1	0
Photosensitivity conditions		
Photosensitivity reaction	2	0
Purpura and related conditions		
Purpura	1	0
Skin injuries and mechanical dermatoses		
Skin vasculitides		
Vasculitic rash	1	0
Urticarias		
Urticaria	6	0

Pruritus NEC		
Pruritus	3	0
Rash pruritic	2	0
Pruritus generalised	9	0
Rashes, eruptions and exanthems NEC		
Rash	21	0
Rash generalised	10	0
Rash macular	5	0
Rash maculo-papular	5	0
Rash morbilliform	1	0
Skin and subcutaneous tissue disorders SOC Total	131	0

Drug Analysis Print
Drug Name: Pandemrix

Reaction Name	Reactions	Fatal Reactions
SOC		
HLT		
PT		
Social circumstances		
Dependents		
Sick relative	1	0
Disability issues		
Impaired driving ability	1	0
Social circumstances SOC Total	2	0

Drug Analysis Print
Drug Name: Pandemrix

Reaction Name	Reactions	Fatal Reactions
SOC		
HLT		
PT		
Surgical and medical procedures		
Therapeutic procedures NEC		
Anaphylaxis treatment	1	0
Surgical and medical procedures SOC Total	1	0

Drug Analysis Print
Drug Name: Pandemrix

Reaction Name	Reactions	Fatal Reactions
SOC		
HLT		
PT		
Vascular disorders		
Circulatory collapse and shock		
Circulatory collapse	2	0
Peripheral circulatory failure	1	0
Neurogenic shock	1	0
Haemorrhages NEC		
Vascular hypertensive disorders NEC		
Hypertension	4	0
Peripheral vascular disorders NEC		
Flushing	2	0
Hot flush	8	0
Vasculitides NEC		
Vasculitis	1	0
Vascular hypotensive disorders		
Hypotension	2	0
Site specific vascular disorders NEC		
Pallor	2	0
Vascular disorders SOC Total	23	0

ANNEX 3 – H1N1 vaccine (brand unknown)

Drug Analysis Print
Drug Name: H1N1 Vaccine

Run Date: Unspecified to 19 November 2009		
Total number of reactions: 259	**Total number of ADR reports:** 93	**Total number of fatal ADR reports:**

System Organ Class	Reactions	Fatal Reactions
Blood and lymphatic system disorders	1	0
Cardiac disorders	1	0
Eye disorders	3	0
Gastrointestinal disorders	34	0
General disorders and administration site conditions	83	0
Immune system disorders	2	0
Infections and infestations	6	0
Injury, poisoning and procedural complications	1	0
Investigations	6	0
Metabolism and nutrition disorders	1	0
Musculoskeletal and connective tissue disorders	41	0
Nervous system disorders	39	0
Psychiatric disorders	10	0
Respiratory, thoracic and mediastinal disorders	5	0
Skin and subcutaneous tissue disorders	24	0
Social circumstances	1	0
Vascular disorders	1	0
Total	259	0

Glossary/Abbreviations

ADR - Adverse Drug Reaction

Age group - lists which age groups are included in the Drug Analysis Print - either ALL, Adolescent, Adult, Child, Elderly, Infant or Neonate

Data lock date - shows data on the database at this specified date and time

HLT - High Level Term - see definition of MedDRA

MEDRA - this stands for Medical Dictionary for Regulatory Activities, which is the internationally agreed list of terms used for Medicines Regulation. MedDRA groups related adverse drug reaction terms in a hierarchical structure whereby the 'preferred term' (PT) (e.g. tunnel vision) is grouped under the broader heading the 'high level term' (HLT) (e.g. visual field disorders). 'High level terms' are contained within the 'system organ class' (SOC) (e.g. eye disorders). The 'preferred term' is the most specific term on the Drug Analysis Print, while the 'system organ class' is the most general

Multi active constituent products - contain the drug constituent of interest plus one or more other drug constituents (e.g. co-codamol contains paracetamol and codeine)

NEC - appears in MedDRA and stands for Not Elsewhere Classified

NOS - appears in MedDRA and stands for Not Otherwise Specified

PBG - Product Brand Generic - this means drug brand name e.g. Amoxil is a PBG for the drug substance amoxic

Products included in this print - this is a list of the products for which at least one suspected Adverse Drug Reaction (ADR) report has been received that specifies that product as a 'suspected drug' (i.e. suspected causal association with the reaction). It does not provide an exhaustive list of the products which contain the named drug substance

PT - Preferred Term - see definition of MedDRA

Reaction - defines which ADRs are included in the Drug Analysis Print - either ALL, Serious or Non-Serious

Reporter type - lists the reporter types which are included in the Drug Analysis Print - either Patient, Health Professional or ALL (i.e. both)

Report run date - the date the Drug Analysis Print was produced

Route of admin - lists the route of administration of the suspect drug for which reports are included in the Drug Analysis Print, e.g. ORAL only includes reports where the suspect drug was specified as having been taken by the oral route, or ALL which includes all routes of administration

Spontaneous - suspected ADR reports sent in to the Yellow Card Scheme are called spontaneous reports

Single active constituent products - contain only the drug substance of interest

System Organ Class (SOC) - this is the highest level in MedDRA which groups together reactions that affect similar systems/organs in the body

Drug Analysis Print
Drug Name: H1N1 Vaccine

Reaction Name	Reactions	Fatal Reactions
SOC		
HLT		
PT		
Blood and lymphatic system disorders		
Lymphatic system disorders NEC		
Lymphadenopathy	1	0
Blood and lymphatic system disorders SOC Total	1	0

Drug Analysis Print
Drug Name: H1N1 Vaccine

Reaction Name	Reactions	Fatal Reactions
SOC		
HLT		
PT		
Cardiac disorders		
Cardiac signs and symptoms NEC		
Rate and rhythm disorders NEC		
Tachycardia	1	0
Cardiac disorders SOC Total	1	0

Drug Analysis Print
Drug Name: H1N1 Vaccine

Reaction Name	Reactions	Fatal Reactions
SOC		
HLT		
PT		
Eye disorders		
Ocular disorders NEC		
Eye pain	2	0
Visual disorders NEC		
Vision blurred	1	0
Eye disorders SOC Total	3	0

Drug Analysis Print
Drug Name: H1N1 Vaccine

Reaction Name	Reactions	Fatal Reactions
SOC		
HLT		
PT		
Gastrointestinal disorders		
Diarrhoea (excl infective)		
Diarrhoea	9	0
Diarrhoea haemorrhagic	1	0
Gastrointestinal and abdominal pains (excl oral and throat)		
Abdominal pain lower	1	0
Nausea and vomiting symptoms		
Nausea	12	0
Vomiting	3	0
Oral soft tissue disorders NEC		
Lip swelling	1	0
Oral soft tissue signs and symptoms		
Hypoaesthesia oral	3	0
Stomatitis and ulceration		
Mouth ulceration	3	0
Tongue signs and symptoms		
Swollen tongue	1	0
Gastrointestinal disorders SOC Total	34	0

Drug Analysis Print
Drug Name: H1N1 Vaccine

Reaction Name	Reactions	Fatal Reactions
SOC		
HLT		
PT		
General disorders and administration site conditions		
Application and instillation site reactions		
Application site pain	2	0
Asthenic conditions		
Asthenia	1	0
Fatigue	10	0
Malaise	2	0
Febrile disorders		
Pyrexia	20	0
General signs and symptoms NEC		
Influenza like illness	9	0
Local reaction	2	0
Local swelling	1	0
Swelling	2	0
Injection and infusion site reactions		
Injection site erythema	1	0
Injection site inflammation	4	0
Injection site irritation	1	0
Injection site pain	3	0
Injection site rash	1	0
Injection site swelling	5	0
Oedema NEC		
Oedema peripheral	4	0
Pain and discomfort NEC		
Chest discomfort	2	0
Pain	3	0
Feelings and sensations NEC		
Chills	7	0
Feeling hot	1	0
Feeling jittery	1	0
Peripheral coldness	1	0
General disorders and administration site conditions SOC Total	83	0

Drug Analysis Print
Drug Name: H1N1 Vaccine

Reaction Name	Reactions	Fatal Reactions
SOC		
HLT		
PT		
Immune system disorders		
Anaphylactic responses		
Anaphylactic reaction	1	0
Allergic conditions NEC		
Hypersensitivity	1	0
Immune system disorders SOC Total	2	0

Drug Analysis Print
Drug Name: H1N1 Vaccine

Reaction Name	Reactions	Fatal Reactions
SOC		
HLT		
PT		
Infections and infestations		
Herpes viral infections		
Herpes zoster	1	0
Infections NEC		
Infection	1	0
Influenza viral infections		
Influenza	2	0
Upper respiratory tract infections		
Nasopharyngitis	1	0
Viral infections NEC		
Meningitis viral	1	0
Infections and infestations SOC Total	6	0

Drug Analysis Print
Drug Name: H1N1 Vaccine

Reaction Name	Reactions	Fatal Reactions
SOC		
HLT		
PT		
Injury, poisoning and procedural complications		
Skin injuries NEC		
Vaccination related complications		
Vaccination complication	1	0
Injury, poisoning and procedural complications SOC Total	1	0

Drug Analysis Print
Drug Name: H1N1 Vaccine

Reaction Name	Reactions	Fatal Reactions
SOC		
HLT		
PT		
Investigations		
Carbohydrate tolerance analyses (incl diabetes)		
Blood glucose abnormal	1	0
Physical examination procedures		
Body temperature increased	4	0
Heart rate and pulse investigations		
Heart rate increased	1	0
Investigations SOC Total	6	0

Drug Analysis Print
Drug Name: H1N1 Vaccine

Reaction Name	Reactions	Fatal Reactions
SOC		
HLT		
PT		
Metabolism and nutrition disorders		
Appetite disorders		
Anorexia	1	0
Metabolism and nutrition disorders SOC Total	1	0

Drug Analysis Print
Drug Name: H1N1 Vaccine

Reaction Name	Reactions	Fatal Reactions
SOC		
HLT		
PT		
Musculoskeletal and connective tissue disorders		
Joint related signs and symptoms		
Arthralgia	9	0
Joint stiffness	3	0
Musculoskeletal and connective tissue signs and symptoms NEC		
Musculoskeletal stiffness	3	0
Muscle pains		
Myalgia	9	0
Muscle related signs and symptoms NEC		
Muscle tone abnormalities		
Nuchal rigidity	1	0
Soft tissue disorders NEC		
Axillary mass	1	0
Musculoskeletal and connective tissue pain and discomfort		
Musculoskeletal pain	1	0
Pain in extremity	13	0
Limb discomfort	1	0
Musculoskeletal and connective tissue disorders SOC Total	41	0

Drug Analysis Print
Drug Name: H1N1 Vaccine

Reaction Name	Reactions	Fatal Reactions
SOC		
HLT		
PT		
Nervous system disorders		
Cerebellar coordination and balance disturbances		
Balance disorder	1	0
Disturbances in consciousness NEC		
Lethargy	1	0
Loss of consciousness	1	0
Headaches NEC		
Headache	17	0
Migraine headaches		
Migraine	2	0
Neurological signs and symptoms NEC		
Dizziness	7	0
Paraesthesias and dysaesthesias		
Burning sensation	2	0
Paraesthesia	1	0
Paralysis and paresis (excl cranial nerve)		
Paralysis	1	0
Seizures and seizure disorders NEC		
Febrile convulsion	1	0
Sensory abnormalities NEC		
Hypoaesthesia	1	0
Speech and language abnormalities		
Dysarthria	1	0
Tremor (excl congenital)		
Tremor	3	0
Nervous system disorders SOC Total	39	0

Drug Analysis Print
Drug Name: H1N1 Vaccine

Reaction Name	Reactions	Fatal Reactions
SOC		
HLT		
PT		
Psychiatric disorders		
Confusion and disorientation		
Confusional state	1	0
Deliria		
Delirium	1	0
Disturbances in initiating and maintaining sleep		
Insomnia	2	0
Mood disorders NEC		
Parasomnias		
Nightmare	1	0
Perception disturbances		
Hallucination	1	0
Psychotic disorder NEC		
Acute psychosis	1	0
Sleep disorders NEC		
Sleep disorder	1	0
Speech articulation and rhythm disturbances		
Stereotypies and automatisms		
Head banging	2	0
Psychiatric disorders SOC Total	10	0

Drug Analysis Print
Drug Name: H1N1 Vaccine

Reaction Name	Reactions	Fatal Reactions
SOC		
HLT		
PT		
Respiratory, thoracic and mediastinal disorders		
Coughing and associated symptoms		
Cough	3	0
Upper respiratory tract signs and symptoms		
Oropharyngeal pain	1	0
Respiratory tract disorders NEC		
Respiratory disorder	1	0
Respiratory, thoracic and mediastinal disorders SOC Total	5	0

Drug Analysis Print
Drug Name: H1N1 Vaccine

Reaction Name	Reactions	Fatal Reactions
SOC		
HLT		
PT		
Skin and subcutaneous tissue disorders		
Angioedemas		
Apocrine and eccrine gland disorders		
Cold sweat	1	0
Hyperhidrosis	2	0
Bullous conditions		
Blister	1	0
Erythema multiforme	1	0
Dermal and epidermal conditions NEC		
Skin reaction	3	0
Swelling face	2	0
Dermatitis and eczema		
Dermatitis allergic	1	0
Erythemas		
Erythema	2	0
Rash erythematous	2	0
Pruritus NEC		
Pruritus	1	0
Pruritus generalised	2	0
Rashes, eruptions and exanthems NEC		
Rash	4	0
Rash macular	2	0
Skin and subcutaneous tissue disorders SOC Total	24	0

Drug Analysis Print
Drug Name: H1N1 Vaccine

Reaction Name	Reactions	Fatal Reactions
SOC		
HLT		
PT		
Social circumstances		
Disability issues		
Bedridden	1	0
Social circumstances SOC Total	1	0

Drug Analysis Print
Drug Name: H1N1 Vaccine

Reaction Name	Reactions	Fatal Reactions
SOC		
HLT		
PT		
Vascular disorders		
Circulatory collapse and shock		
Peripheral vascular disorders NEC		
Flushing	1	0
Vascular hypotensive disorders		
Vascular disorders SOC Total	1	0

ANNEX 4

MEDIA BRIEFING

H1N1 SWINE FLU VACCINE SAFETY MONITORING

Summary

1. As with all medicines and vaccines on the UK market, the Medicines and Healthcare products Regulatory Agency (MHRA) has the responsibility for monitoring the safety of the pandemic H1N1 swine flu vaccine.

2. With any new vaccine programme, a key challenge we face in safety monitoring is teasing out real side effects from background medical conditions that would have occurred regardless of vaccination.

3. This document outlines the existing processes MHRA has in place to monitor the safety of any new vaccine and how we plan to tailor these to the swine flu vaccine programme.

4. We aim to achieve real-time analysis and transparency of the emerging data through regular public reports. These notes are intended to assist in the understanding of our processes and data that we collect.

Pandemic vaccine safety and need for monitoring

5. The swine flu vaccines being used in the UK have been licensed for use by European regulators following a thorough review of their manufacturing quality, the immunity they induce and their safety. This was based on information from clinical trials of prototype H5N1 ('bird flu') strain vaccines which have been studied over several years, as well as trials using the current H1N1 swine flu strain.

6. As with any vaccine, the swine flu vaccines will cause side effects in some people. The most common side effects will be injection site reactions (pain, swelling, and/or redness), headaches, dizziness, muscle aches, mild fever and fatigue. These side effects will mainly be mild and last only 2 to 3 days. Some of these symptoms may be similar to a mild flu-like illness, although we should stress that the vaccines cannot cause swine flu itself.

7. Because clinical trials are relatively limited in size, very rare side effects might not be identified until the vaccines have been used on a wide scale in large numbers of people. The swine flu vaccines are not unique in this regard and this applies to any new medicine or vaccine. This is why the MHRA has in place robust systems for post-licensing safety monitoring.

What systems are in place in the UK?

8. The Yellow Card Scheme underpins safety monitoring in the UK. Through this Scheme, healthcare professionals and members of the public voluntarily submit reports of suspected side effects to the MHRA. Drug companies also

submit such reports as part of their legal requirements. Safety scientists at MHRA carefully evaluate “signals” of suspected safety issues; it is important to point out that just because a Yellow Card has been sent does not necessarily mean that the vaccine caused the reaction - it may be coincidental or due to an underlying medical condition.

9. A special on-line interface of the Yellow Card Scheme has been set up to receive reports of suspected adverse reactions to the swine flu vaccines (as well as antiviral medicines); the ‘Swine Flu Adverse Reaction (ADR) Portal’. This is accessed via www.mhra.gov.uk/swineflu and provides a simple and, most important, quick way of getting this information into the MHRA’s safety monitoring system. For those without internet access, postal Yellow Card reports can still be submitted.

10. This Swine Flu ADR Portal allows the MHRA safety scientists to access suspected side effect reports in real-time which will allow us to identify any new risks as soon as they emerge. Please refer to the annex for a screenshot of the Portal.

11. As well as analysing data from the Portal, the MHRA will review safety data from all available sources including those from other countries. The MHRA is also working with the two manufacturers on active safety surveillance in several thousand vaccinees in designated GP practices.

What will the MHRA do with the data it collects?

12. The main objective of the safety monitoring process is to identify any new risks that may emerge as the vaccines are used. Such risks could include a new side effect, an apparent change in the nature of a known side effect, identification of factors that increase the chances of having a side effect, batch-related problems or issues related to inappropriate use of the vaccines.

13. The MHRA will use advice from independent experts, including that of the Commission on Human Medicines (CHM), in assessing any identified risks. We will also work closely with our European and International counterparts in such evaluation.

14. If a new risk is confirmed, this will be fed into the ongoing evaluation of the balance of benefits of vaccination versus risks. If deemed necessary, regulatory action would be taken to minimise risk and support safe use (e.g. adding warnings to the vaccine licence, sending out communications to healthcare professionals and patients, restricting its use).

15. As well as confirming new risks, an equally important objective of monitoring will be to quickly rule out risks – i.e. to confirm that the vaccine is not responsible for a suspected side effect and to provide reassurance on its safety. This is discussed further below.

16. The MHRA will analyse all the data collected via the Portal on an ongoing basis. For particular[1] events of interest, we will employ a method known as 'observed versus expected' analysis to establish quickly if certain medical events are being reported more frequently after vaccination than might be expected to occur in the population without vaccination.

What information will we provide to the public on vaccine safety?

17. We have a transparent process. On a weekly basis, we will produce an up to date summary of the safety experience, including reports of suspected side effects, on our website (www.mhra.gov.uk/swineflu). At present, we intend to follow a similar format to our weekly summary of cervical cancer vaccine (human papillomavirus; HPV) vaccine safety which the public and media are already familiar with (www.mhra.gov.uk/hpvvaccine).

What side effects do we expect to see?

18. In the coming few months, more than 12 million people in the priority groups will be offered the vaccine. Drawing from recent experience with immunisation campaigns, we would expect to receive around 12 to 18,000 reports over the first few months. This is an estimate and the figures could be more or less.

19. As with any vaccine, we expect to see the following broad categories of suspected side effects reported to us.

- The most common will be injection site reactions
- Other common side effects reports will be other 'well-recognised' reactions (e.g. headaches, dizziness, muscle aches, mild fever and fatigue).
- Less commonly, we expect to see mild allergic-type reactions (e.g. mild rashes, localised/generalised itching). Serious allergic reactions (such as anaphylaxis) will be very rare.
- It will not be uncommon for immediate events which are not due to the vaccine itself, but due to fear or anticipation of the needle injection, to be reported. We call these 'psychogenic' events and they can typically involve fainting and associated symptoms.

20. The final category of suspected side effect will be either new side effects or coincidental medical conditions which are not due to the vaccine (see below).

Understanding the data reported to MHRA

21. It is important to fully understand that the data reported via the Yellow Card Scheme/Swine Flu ADR Portal relate to *suspicions*, from the reporters, that the vaccine may have caused the side effect. A 'suspected' side effect is not 'proof' of a side effect.

[1] MHRA has a list of certain medical conditions that will kept under close review using this 'observed vs expected' analysis – this list will be continually updated as new data emerge

22. Although some reports may be true side effects, some may also be entirely unrelated, coincidental ('background') medical events that would have happened anyway without vaccination.

Distinguishing real side effects from coincidental medical events

23. Most of the 12 million people offered the vaccine in the coming months have serious and/or chronic underlying medical conditions which puts them at greater risk of developing serious flu-related complications or even death. This is why it is so beneficial for these people to be vaccinated as a priority.

24. Over the next few months, many of these patients will naturally suffer an exacerbation of their existing illness. As in any influenza season, swine flu will also worsen underlying illness in many of these patients. Regardless of underlying illness, such patients may also develop other medical conditions, especially those that can be caused by other circulating pathogens.

25. Inevitably, as we vaccinate so many of these people, at a time when swine flu is also causing illness, some people will develop these medical conditions not long after receiving the vaccine. This temporal association in itself does not mean that the vaccine caused the condition. The challenge we therefore face is distinguishing these 'background' events from those that may have been caused by the vaccine. The 'observed versus expected' analysis described above is one of the tools that will help us to make this distinction.

Example – Guillain Barre Syndrome (GBS)

26. GBS is a very rare, neurological condition that can cause paralysis. It naturally occurs at a frequency of around 1 case per 100,000 people every year in the UK. It can occur in healthy individuals, either spontaneously or after certain infections. Studies have shown that flu-like illness can also cause up to an 18-fold increase in the risk of developing GBS.

27. GBS was an identified risk with swine flu vaccines used in the United States in 1976 - it is thought that 1 extra case of GBS occurred with every 100,000 doses of vaccine. The exact reason why the 1976 vaccines caused GBS remains unknown and modern flu vaccines have not been found to cause GBS. We have no reason to suspect that the current swine flu vaccines will cause GBS but, obviously, we will closely monitor this.

28. With the normal background frequency of GBS outlined above, if we vaccinate 12 million people over the next 3 months we can expect to see around 20 cases of GBS occurring naturally within one month of vaccination. A proportion of these cases are likely to be reported to the MHRA as suspected side effects, even when the vaccine played no role in causing the GBS. Indeed, although modern seasonal flu vaccines do not cause GBS, the MHRA has received more than 90 reports of GBS as suspected side effects to

seasonal vaccines over the past 20 years. These were likely to be coincidental 'background' events.

29. Following on from the GBS example, we can also expect to see, by chance, large numbers of serious medical events due to underlying illness (e.g. heart attacks, cardio-respiratory arrests, strokes etc) amongst the vaccinated priority population, and also fatalities.

Frequency of side effects

30. Although we intend to analyse the data reported to us in the context of the number of people vaccinated, this will not allow us to determine the frequency at which side effects are occurring. This is because suspected side effects may not actually have been caused by the vaccine, and for those which may be true side effects, all cases may not be reported to us.

31. For this reason, and because the vaccines will be given to different patient groups, the data reported via our ADR Portal must not be used to compare the relative safety of each vaccine.

Conclusion

32. The MHRA considers vaccine safety to be of paramount importance. We have proactive and robust systems in place to monitor the safety of this important immunisation programme and to ensure the benefits of vaccination continue to outweigh any risks.

33. For the reasons outlined in this document, we can possibly expect GBS and other serious events to be reported to us as *suspected* side effects when these priority groups are immunised. Our role is to establish quickly whether these 'observed' events are simply due to the 'expected' background frequency in the time after vaccination, or whether the vaccine may carry an additional risk of these conditions.

34. Going forward, our data on the suspected side effects reported via the Swine Flu ADR Portal will be made available on our website. To ensure that appropriate information is provided to the public during this important immunisation programme, each one of us has a responsibility to communicate these data appropriately. We must ensure that the data are not misinterpreted or misused and that balanced and informed communications are provided to the public.