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Ref. No _____

12 August 2011

Hilary Butler
25 Harrisville Road
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Dear Ms Butler

Thank you for your email of 19 July 2011 requesting information under the Official Information Act 1982 about the total and serious adverse events reported in association with Gardasil and how many doses have been administered since the beginning of the HPV vaccine program.

Since the beginning of the HPV program up to 20 June 2011, 404,389 people have received at least one dose of Gardasil vaccine in New Zealand.

Since Gardasil was approved for use in New Zealand the Centre for Adverse Reactions Monitoring (CARM) has received a total of 376 reports of *suspected* adverse reactions in association with Gardasil. The number of reports per year is shown in table 1. Reporters are encouraged to report suspected adverse reactions to medicines. This means that the reporter dose not have to be sure that the vaccine caused the reaction; therefore the reports may or may not be true adverse reactions to the vaccine. It is expected that a number of co-incidental events will be reported for all vaccines.

Table 1 number of reports received by CARM in association with Gardasil per year

Year	**Number of reports**
2007	5
2008	20
2009	211
2010	118
2011	22

Of the 376 reports CARM consider that 27 were serious according to the criteria:

- Congenital abnormality
- Died
- Hospitalisation or prolonged hospitalisation
- Life Threatening
- Intervention required to avoid permanent harm
- Persisting disability

It is important to note that serious is not the same as severe and that for two people having the same reaction one case may be considered serious and the other case non-serious.

Of the 27 serious reports the reasons for considering the report to be serious were as shown in table 2.

Table 2 Overview of serious reports

Seriousness	Number of reports
Non-serious	349
Hospitalisation	11
Life threatening	2
Intervention Required	2
Died	2
Congenital anomaly	0
Persisting disability	10

For the two reports of death, CARM considers that the death was not related to Gardasil in one report and of unknown relationship in one report.

When reviewing this data it is also important to note that for many reports information to support the diagnosis is not provided to CARM. Therefore although the report is coded with the reported suspected reaction it does not necessarily mean that the person actually had the reaction. This is particularly true of reports of convulsions which are often confused with faints.

It should also be noted that the final outcome of many cases is not known. For the cases of persisting disability not all the reported suspected reactions reported for that case were persisting at the time of the report.

As requested the reported serious reactions are outlined in table 3. The terms presented are those used by CARM.

Table 3 Suspected reactions reported in association with Gardasil

Number	Reactions	Other Reported Medicines	Outcome
Hospitalised cases			
1	Arthropathy, hypertension, myalgia, diabetes mellitus aggravated, uveitis	None reported	Not recovered at the time of report
2	Convulsions	None reported	Recovered
3	Vasovagal reaction, headache	None reported	Not recovered at the time of report
4	Leukaemia	None reported	Not recovered at the time of report
5	Headache, myalgia, tachycardia, fever, lymphopenia	None reported	Recovered

6	Leg pain, neuropathy, headache, chest pain, syncope	Microgynon 20ED	Not recovered at the time of report
7	Ataxia, photophobia, paraesthesia, behaviour abnormal, consciousness decreased	None reported	Not recovered at the time of report
8	Headache, nausea, fever, vomiting, urticaria	None reported	Not recovered at the time of report
9	Henloch-Schonlein Purpura	None reported	Recovered
10	Serum sickness-line disorder	Fluoxetine	Recovered
11	Paraesthesia	None reported	Not recovered at the time of report
Life-threatening			
12	Pallor, nausea, tongue swelling non-specific	None reported	Recovered
13	Rash pruritic angioedema circulatory failure hypotension	None reported	Recovered
Intervention Required			
14	Injection site abscess	None reported	Not recovered at the time of report
15	Genital wart	None reported	Unknown
Died			
16	Paraesthesia, cognitive function abnormal, muscle weakness, night sweats, sudden death	Depo-provera	Not applicable
17	Suicide	None reported	Not applicable
Persisting Disability			
18	Rigors, insomnia, anxiety, fatigue	None reported	Not recovered at the time of report
19	C-reactive protein positive, paraesthesia, headache, fever, myalgia	None reported	Not recovered at the time of report
20	Paraesthesia, lymphadenopathy, arthralgia, headache, muscle weakness	None reported	Not recovered at the time of report
21	Alopecia	Fluticasone, salbutamol, ferrous sulphate, Estelle 35	Not recovered at the time of report
22	Abdominal pain, pelvic inflammation	None reported	Not recovered at the time of report
23	Nausea, faintness, muscle weakness, twitching, memory loss	None reported	Not recovered at the time of report
24	Headache, dizziness, fever	None reported	Not recovered at the time of report
25	Headache	Noriday 28	Not recovered at the time of report

26	Neuropathy, headache, concentration impaired, behaviour abnormal, lethargy	Citalopram, metoclopramide	Not recovered at the time of report
27	Syncope, consciousness decreased	Budesonide/ eformoterol, salbutamol	Not recovered at the time of report

Please also see attached a copy of further information available on this issue published on the Medsafe website.

Yours sincerely

Dr Don Mackie
Chief Medical Officer
Clinical Leadership, Protection and Regulation Business Unit

MEDSAFE
NEW ZEALAND MEDICINES AND MEDICAL DEVICES SAFETY AUTHORITY
A BUSINESS UNIT OF THE MINISTRY OF HEALTH

Media Releases

Response to Emma Bailey from the Timaru Herald requesting information on the 31 serious cases reported in association with Gardasil vaccine

Please attribute to Dr Joanne Hart, Manager, Clinical Risk Management, Medsafe

Up to 31 January 2010 the Centre for Adverse Reactions Monitoring (CARM) had received 242 reports of suspected adverse events associated with the Gardasil vaccine. The World Health Organisation (WHO) and the International Conference on Harmonisation (ICH) have published a definition of serious events. Using the criteria outlined below CARM consider that 31 cases were serious.

A serious adverse event or reaction is any untoward medical occurrence that:

- Results in death
- Is life-threatening
- Requires inpatient hospitalization or prolongation of existing hospitalisation
- Results in persistent or significant disability/incapacity
- Requires intervention to prevent permanent disability/ incapacity
- Results in a congenital anomaly

In addition CARM considers that cases where the patient attended an Emergency Department or after-hours clinic to be serious.

Reporters are encouraged to report suspected adverse events to vaccines. In other words the reporter does not have to be sure that the vaccine caused the reaction, a mere suspicion will suffice. Therefore the reports received may be true adverse reaction to the vaccine, they may be events related to the process of vaccination rather than to the specific vaccine itself, or they may be coincidental events which have occurred post-vaccination but which would have occurred anyway even if vaccination had not taken place (e.g. they may be due to an underlying medical condition).

The term "severe" is not synonymous with serious, "severe" is used to describe the intensity (severity) of a specific event (as in mild, moderate or severe); the event itself, however, may be of relatively minor medical significance (such as headache).

Since the definition of a serious case is based on the outcome for the patient it is possible to have cases which mention the same type of events but can be defined as serious and non-serious in different cases.

Table 1. An overview of the 31 serious cases

	Number of reports
Death	1
Life-threatening	1
Intervention required	1
Hospitalisation	4
Persisting disability	4
Emergency department attendance	20

Please note that suspected adverse event 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 vaccines or medicines.

There was one report of sudden death, 6 months after the final vaccination. The cause of death is as yet undetermined.

The single life threatening report was of severe hypersensitivity reaction involving tongue swelling.

The intervention report described an injection site abscess that required surgical draining.

The four reports of hospitalization refer to:

1. Systemic symptoms including diabetes and eye problems, both of which had been diagnosed prior to vaccination.
2. Convulsions 2 weeks following vaccination
3. Fainting episodes resulting in overnight observation
4. Leukaemia reported, but not attributed to vaccination.

The four reports of persisting symptoms all refer to event still present at the time of reporting at least one month after vaccination.

1. Three reports describe general symptoms of muscle aches, headache and fatigue
2. One report of hair loss.

The 20 reports of emergency department attendance include:

1. Nine reports of collapse/syncopal episodes (faints).
2. Seven reports of allergic-type symptoms such as rash
3. Two reports of convulsion-like episodes, occurring immediately following immunization and lasting longer that usually observed with a faint.
4. One report of severe arm pain and swelling
5. One report of Bell's Palsy (face paralysis) starting within one day of vaccination that may have been due to a recent infection.

A full summary of the 31 cases is given in the following table.

Table 2. Details of Reports Classified as Serious by CARM

Report	Reactions	Reason Regarded as Serious	Patient Outcome at Time of Report
1	Arthropathy Hypertension Myalgia Diabetes mellitus aggravated Uveitis	Hospitalisation	Not yet recovered
2	Convulsions	Hospitalisation	Recovered
3	Vasovagal reaction Headache	Hospitalisation	Not yet recovered
4	Leukaemia	Hospitalisation	Not yet recovered
5	Consciousness decreased Hypotension Nausea Pupillary reflex impaired Mydriasis	Emergency department attendance	Recovered
6	Rash maculo-papular	Emergency department attendance	Recovered
7	Absences	Emergency department attendance	Recovered
8	Flushing Nausea Urticaria	Emergency department attendance	Recovered
9	Papular rash	Emergency department attendance	Recovered
10	Consciousness decreased Malaise Gait abnormal	Emergency department attendance	Recovered
11	Vasovagal reaction Muscle contractions involuntary Tremor Tachycardia	Emergency department attendance	Recovered
12	Consciousness decreased Apnoea Hypotension Mydriasis	Emergency department attendance	Recovered
13	Vasovagal reaction Somnolence Cyanosis peripheral Consciousness decreased Muscle contractions involuntary	Emergency department attendance	Recovered

Report	Reactions	Reason Regarded as Serious	Patient Outcome at Time of Report
14	Nausea Bronchospasm Dyspnoea	Emergency department attendance	Recovered
15	Dizziness Headache Rash Angiodema	Emergency department attendance	Recovered
16	Angiodema Pruritis Injection site erythema	Emergency department attendance	Recovered
17	Chest pain	Emergency department attendance	Recovered
18	Bells palsy Face oedema	Emergency department attendance	Not yet recovered
19	Arm pain Pain neck/shoulder Injection site inflammation	Emergency department attendance	Unknown
20	Convulsions grand mal	Emergency department attendance	Recovered
21	Fever Headache Dizziness Chest tightness	Emergency department attendance	Recovered
22	Dizziness Hypoaesthesia Temperature changed sensation Respiratory disorder	Emergency department attendance	Recovered
23	Syncope	Emergency department attendance	Recovered
24	Rash pruritic	Emergency department attendance	Recovered
25	Pallor Nausea Tongue swelling non-specific	Life threatening event	Recovered
26	Injection site abscess	Intervention required to prevent persisting disability	Not yet recovered
27	Rigors Insomnia Anxiety Fatigue	Persisting disability	Not applicable

Report	Reactions	Reason Regarded as Serious	Patient Outcome at Time of Report
28	C-reactive protein positive Paraesthesia Headache Fever Myalgia	Persisting disability	Not applicable
29	Paraesthesia Lymphadenopathy Arthralgia Headache Muscle weakness	Persisting disability	Not applicable
30	Alopecia	Persisting disability	Not applicable
31	Paraesthesia Cognitive function abnormal Muscle weakness Night sweats Sudden death	Died	Not applicable

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