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MEASLES, MUMPS AND RUBELLA VIRUS VACCINE LIVE
(Life measles, mumps and rubella virus)

21-05-2007

Pharmaceutical form(s)	Powder for fluid for injection
MAH(s)	**Sanofi Pasteur**
IBD/NBD	**01-04-1978 (Ireland)/02-12-1993**
PSUR	**5 year PSUR 01-01-2001 – 31-12-2005** **addendum 01-01-2006 – 04-05-2006** **6 months PSUR covering 05-05-2006 – 04-11-2006** **Bridging report 01-01-2001 – 04-11-2006**
RVG	17672, 18676=17672
ATC	J07BD52
Assessor	[redacted]
Date last NL SPC	19-08-2002
Zaak Nr	20702406 019
Coll Nr	20702406

INTRODUCTION

The MAH submitted a renewal.
In the cover letter the MAH states they want to replace their product MMR II by MMRvaxPro which contains recombinant albumin in stead of human albumin. MMRvaxPro was registered in centralised procedure on 5 May 2006 under MA number EU/1/06/337/001 → 013

In order to facilitate the handling of MMR II vs MMRvaxPro, the MAH state they would like to harmonize the PSURs submission, one PSUR will be generated to ICH E2C recommendations for MMR II and MMRvaxPro. The data lock point for MMR II PSURs is established as the date on which marketing authorization is granted in the EU for MMRvaxPro. The EBD of MMRvaxPro is 05.05.06 and thus the covering period is for the 1st 6-month PSUR: 05.-5.06 – 04.11.06 (enclosed to this application).
For purposes of the PSUR, a global descriptive analysis will be performed for all reports combined for MMR II whether or not there is a batch/lot number to identify either MMR II or MMRvaxPro. Additionally a descriptive presentation of the data by albumin status will be performed for the first PSURs after licensing. This will allow a review of adverse experiences by batch (HAS, rHA and unknown) while the transition from MMR II to MMRvaxPro occurs.

Also to avoid double submission of identical PSURs, after the submission in January (current PSUR under assessment) they will submit the common PSUR according to the cycle of MMRvaxPro and in scope of the MMRvaxPro PSUR submission of the CBG-MEB.

The MAH further states that in a few days they will submit a variation to completely update the SPC and PIL, according to the current CCDS to bring it in line with the approved SPC and PIL for MMRvaxPro.

The MAH submitted the following documents:

[redacted]

- Summary Bridging Report covering the period 01-01-2001 to 04-11-2006
- A PSUR covering the period 01-01-2001 to 31-12-2005
- An addendum report covering the period 01-01-2006 to 04-05-2006
- A PSUR covering the period 05-05-2006 to 04-11-2006 for MMRvaxPro

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Assessor's comment: The SPC has been amended to the current SPC for MMRvaxPro,
In addition, in our letter of the 9th of April 2003 the MAH was requested to closely monitor several adverse reactions and add others. This letter was not complied with until recently and this response will be assessed by another assessor.
The PSUR for MMRvaxPro is not assessed in this report because the product is registered centrally with another country than The Netherlands as reporter.

DATA REVIEW

World wide marketing authorisation status

At the time of the summary bridging report covering the period 01-01-2001 to 04-11-2006 measles, mumps and rubella virus vaccine live, MSD (under the worldwide Tradename of MMR II TM) had been registered in 56 countries and an application is pending in [redacted] In the Netherlands it has been authorised through the National Procedure.

Actions taken for safety reasons

During the covered period, no specific action was taken for safety reasons, neither by an authority nor by the MAH.

Changes to reference safety information

During the reporting period several amendments to the reference safety information were made. These amendments involved sections 4.1, 4.2, 4.4 and 4.8. The CCDS that was current at the end of the review period is appended in appendix 2 of the SBR. Also, the MAH replaced their product MMR II by MMRvaxPro which contains recombinant albumin in stead of human albumin. The CCDS appended to the SBR is the CCDS for MMRvaxPro vaccine that contains recombinant human albumin.

Assessor's comment: Sections 4.2, 4.3, and 4.8 of the current Core Safety Information (CSI) provide more (relevant safety) information than the Dutch SPC. The MAH should note that a Core Safety Information can not contain information which is not included in at least every accepted national SPC. If the MAH deems it necessary to include this information in the CSI the MAH should submit an adequately supported application for inclusion of this information and a proposal to update the Dutch SPC. If correctly used the Core Safety Information cannot include information which is not accepted in all countries where a product is licensed.

Regarding section 4.8

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The MAH submitted an application for harmonisation of the SPC of MMR II with the SPC of MMRvaxPro. It was noted however, that the MAH had not included the adverse reactions Toxic Epidermal Necrolysis (TEN) and pancreatitis as asked in our letter of the 9th April 2003 coll 20221015. The assessor for the application for Type II variation to harmonize SPC of M-M-RII with the SPC of M-M-RvaxPro made the following conclusion: harmonisation of the SPCs is accepted provided that the MAH will still consider Toxic Epidermal Necrolysis (TEN) and pancreatitis to be included in the Dutch SPC of M-M-RII (i.e. the decision to include these adverse reactions or the justification not to include, as was stated in the response document of the MAH are still being awaited) and with respect to pancreatitis, the MAH should at least explain why this adverse event is included in the American SPC but not in the Dutch SPC, which is supported.

Patient exposure

The estimated number of marketed measles, mumps and rubella virus vaccine live, MSD doses distributed worldwide between 01-01-2001 and 04-11-2006 was estimated to be approximately [redacted] based on the assumption that each patient received one dose.

The estimated number of marketed measles, mumps and rubella virus vaccine live, MSD doses distributed worldwide from market introduction to 04-11-1006 was approximately [redacted] It was estimated that approximately [redacted] patients have been vaccinated based on the assumption that each patient received one dose.

Clinical trials:
It was estimated that about [redacted] patients received were enrolled in [redacted]-sponsored clinical trials between 01-01-2001 and 04-11-2006 who were treated with measles, mumps and rubella virus vaccine live, MSD.

Additionally approximately 830 patients were treated with measles, mumps and rubella virus vaccine live in a study sponsored by MedImmune entitled "safety and Immunogenicity of Concurrent LAIV (FluMist®) with measles-mumps-rubella (MMR ® II") and varicella (VARIVAX®) Vaccines in Infants 12 to 15 months of Age."

The MAH further states the estimated patient exposures are based on the availability of monthly drug distribution figures; hence the figures have been calculated for the period from 01-01-2001 to 31-10-2006.

Assessor's comment: All these patient exposure figures provided by the MAH are based on one single dose per patient but patient exposure is actually a lot lower because most patients receive a second dose and not all doses are used.

Adverse reactions

During the period under review for MMR II, there were 5419 reports with 6024 adverse drug reactions of which 1637 were serious unlisted. For an overview of serious and non-serious unlisted adverse drug reactions reported for MMR II, see appendix 1.

[redacted]

Assessor's comment: The MAH should include the adverse reactions nasopharyngitis, upper respiratory infection, viral infection, rhinorrhoea, diarrhoea, vomiting to the SPC if these are not already included in the current type II variation under assessment And the MAH should include the adverse reactions, collapse or shock-like state (hypotonic-hyporesponsiveness episode), dermatitis, decreased appetite, prolonged or abnormal crying, restlessness, drowsiness, fatigue, lethargy, dyspnoea, pain in extremity, insomnia to their SPC as these are also an issue with other vaccines.

Reports with a fatal outcome

During the period of the first PSUR a total of 60 spontaneous reports involving a fatal outcome were received. Of these 60 reports, 27 were use-during-pregnancy reports in which the pregnancy resulted in an elective abortion (6), spontaneous abortion (19), intra-uterine death (1) and twin pregnancy with foetal loss and retention of one foetus (1). The remaining 33 reports are summarized in appendix 2.

The MAH comments on these 33 remaining reports that 23 indicate that the patient died of underlying disease(s) or concurrent illnesses. Two reports concerned SIDS and in the remaining 8 reports a relationship between MMR II vaccine and death could not be established. Therefore, no new safety issues with fatal outcomes were identified.

In addition the addendum covering the period 01-01-2006 to 04-05-2006 in the narrative does not comment on cases reporting a fatal outcome.. The cumulative table of ADR terms that are serious and unlisted, reports: brain death (1), death (25), sudden death (1), SIDS (10) and intra-uterine death (4).

Overall, no new safety issues with a fatal outcome were identified

Assessor's comment: accepted

Studies

Newly analyzed studies
During the reporting period there were six newly analyzed studies that contained important safety information.

1. A randomized double-blind comparison of MMR II and Priorix™ In Infants 12 to 24 months of age.
2. A study of MMR™ II at Mumps Expirery Potency in Healthy Children 12 to 18 months of age.
3. A comparison of the safety tolerability, and immunogenicity of MMR™ II manufactured with Recombinant Human Albumin (rHA) versus MMR™ II Manufactured with pooled-Donor Human Serum Albumin (HAS) in Healthy Children 12 to 18 Months Of Age.
4. A Comparison of the Safety and Tolerability of a second Dose of MMR™ II Manufactured With Recombinant Human Albumin (rHA) Versus Serum Albumin (HAS) in Healthy Children
5. A comparison of the Safety Tolerability and Immunogenicity of MMR™ II Manufactured from the 2003 Measels Stock Seed versus Currently Licensed MMR™ II Manufactured From the 1967 Measels Stock Seed in Healthy Children 12 to 18 Months of Age.
6. Safety and Immunogenicity of the Simultaneous Administration of a Liquid Hexavalent Combined Vaccine (Hexavac®) and a Trivalent Measels Mumps Rubella combined Vaccine (MMR®II) in Healthy 12 Month Old Children.

Assessor's comment: The reported adverse drug reactions in the 6 studies published during the period under review are in line with the known safety profile of MMR II and revealed no new major safety issues.

Targeted safety study

In addition there was 1 targeted safety study (Protocol 011) for measles mumps and rubella virus vaccine live that had completed enrolment but had not been summarized entitled "A Open Randomised Comparative Multicenter Study of the Immunogenicity and Safety of MMR™II Manufactured with the Recombinant Human Albumin (rHA) and VARIVAX® When Administered Concomitantly by Intramuscular (IM) ROUTE AT Two Separate Injection Sites in Healthy Subjects 12 to 18 Months of Age". The MAH further comment on this study safety analysis will be provided in an upcoming PSUR.

Assessor's comment: although the MAH comments in the first PSUR (01-01-2001 to 31-12-2005) safety analysis on the study protocol 011 will be provided in the next PSUR, this analysis can not be found in the addendum or the one year PSUR submitted concomitantly. The MAH should provide the safety analysis for study protocol 011 within 3 months.

Published Studies

There were 9 published safety studies that described new and potentially important safety information.

1. Hviid A, Stellfeld M, Wohlfahrt J and Melbye M Childhood vaccination and type 1 diabetes *N Engl J Med 350(14): 1398-1404, Apr. 1, 2004*

2. Vestergaard M, Hviid A, Madsen K M, Wohlfahrt J, Thorsen P, Schendel D, Melbye M and Olsen J, MMR vaccination and febrile seizures: evaluation of susceptible subgroups and long-term prognosis *JAMA 292(3): 351-357, July 21, 2004*

3. Pool V and Russell M
Inadvertent administration of measles vaccine in early infancy: a review of safety data in the U.S. *Pharmacoepidemiol Drug Safety 13(Suppl. 1): S280-S280 (#556), July 2004 (in Soc. Proc.)*

4. Smeeth L, Cook C, Fombonne E, Heavey L, Rodrigues L C, Smith P G and Hall A J
MMR vaccination and pervasive developmental disorders: a casecontrol study *Lancet 364(9438): 963-969, Sept. 11-17, 2004*

5. Reisinger K, Wiedmann R, Sheaffer C, Malacaman E, Senders S, Marchant C, Giacoletti K, Shaw E, Schodel F and Musey L K Safety and immunogenicity of M-M-R II with recombinant human albumin (rHA) in children *Paper presented at the 42nd Annual Meeting of IDSA, September 30-October 3, 2004, Boston, Massachusetts, USA, Abstract 1024*

6. Miller E, Andrews N, Grant A, Stowe J and Taylor B No evidence of an association between MMR vaccine and gait disturbance *Arch Dis Child 90(3): 292-296, Mar. 2005*

7. Machado CM, de Souza V A U F, Sumita LM, da Rocha IF, Dulley FL and Pannuti CS
Early measles vaccination in bone marrow transplant recipients *Bone Marrow Transplant 35(8): 787-791, Apr. 2005*

8. Asatryan A, Pool V and Chen R T Sensorineural hearing loss following measles-mumps-rubella vaccination: Vaccine Adverse Event Reporting System, United States, 1991-2004 *Pharmacoepidemiol Drug Safety 14(Suppl. 2): S200-S200 (#401), Aug. 2005 (Paper presented at the 21st International Conference on Pharmacoepidemiology and Therapeutic Risk Management,*

August 21-24, 2005, Nashville, Tennessee, USA)

9. Ray P, Hayward J, Michelson D, Lewis E, Schwalbe J, Black S, Shinefield H, Marcy M, Huff K, Ward J, Mullooly J, Chen R, Davis R and Vaccine Safety Datalink Group Encephalopathy after whole-cell pertussis or measles vaccination: lack of evidence for a causal association in a retrospective casecontrol study *Pediatric Infectious Disease Journal 25(9): 768-773, September 2006*

Assessor's comment: Overall the studies do not reveal new safety issues requiring updating of the SPC. However, study 8, Sensoryneural hearing loss (SHL) following measles-mumps-rubella vaccination does conclude that there might be a very rare link between MMR and SHL. Six reports of deafness were received during the period under review. The SPC currently mentions the ADRs "neurale doofheid" and "otitis media" which is considered sufficient.

Overall safety evaluation

Efficacy-related information

During the reporting period, reports of lack of efficacy for measles, mumps and rubella virus vaccine live, MSD received by the MAH did not suggest a hazard to the treated population.

Late-breaking information

The MAH states there was no important or new late-breaking information that would alter the currently known safety profile as described in the current CCDS of measles, mumps and rubella virus vaccine live, MSD.

CONCLUSION

Assessment of the PSUR's covering the period of 01-01-2001 to 04-11-2006 led to the following conclusions:

- Sections 4.2, 4.3, and 4.8 of the current Core Safety Information (CSI) provide more (relevant safety) information than the Dutch SPC. The MAH should note that a Core Safety Information can not contain information which is not included in at least every accepted national SPC. If the MAH deems it necessary to include this information in the CSI the MAH should submit an adequately supported application for inclusion of this information and a proposal to update the Dutch SPC. If correctly used the Core Safety Information cannot include information which is not accepted in all countries where a product is licensed.

- Regarding section 4.8. The MAH submitted an application for harmonisation of the SPC of MMR II with the SPC of MMRvaxPro. It was noted however, that the MAH had not included the adverse reactions Toxic Epidermal Necrolysis (TEN) and pancreatitis as asked in our letter of the 9th April 2003 coll 20221015. The assessor for the application for Type II variation to harmonize SPC of M-M-RII with the SPC of M-M-RvaxPro made the following conclusion: harmonisation of the SPCs is accepted provided that the MAH will still consider Toxic Epidermal Necrolysis (TEN) and pancreatitis to be included in the Dutch SPC of M-M-RII (i.e. the decision to include these adverse reactions or the justification not to include, as was stated in the response document of the MAH are still being awaited) and with respect to pancreatitis, the MAH should at least explain why this adverse event is included in the American SPC but not in the Dutch SPC. This conclusion is supported.

- The MAH should include the adverse reactions nasopharyngitis, upper respiratory infection, viral infection, rhinorrhoea, diarrhoea, vomiting to the SPC. And the MAH should include the adverse reactions, collapse or shock-like state (hypotonic-hyporesponsiveness episode), dermatitis, decreased appetite, prolonged or abnormal crying, restlessness, drowsiness, fatigue, lethargy, dyspnoea, pain in extremity, insomnia to their SPC as these are also an issue with other vaccines.

- Although the MAH comments in the PSUR (01-01-2001 to 31-12-2005) safety analysis on the study protocol 011 will be provided in the next PSUR, this analysis can not be found in the addendum or the one year PSUR submitted concomitantly. The MAH should provide the safety analysis for study protocol 011 within 3 months.

The next PSUR covering the period, 01-01-2006 to 31-12-2008 should be submitted within 60 days after data lock point.

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APPENDIX 1: Table 1: Serious and non-serious unlisted ADRs spontaneously reported during the period 01-01-2001 to 04-11-2006 (total ≥ 5 times). [redacted]

SOC	Serious	Non-serious	Total reports
Infections and infestations			
Bronchitis	3	7	10
Cellulitis	13	15	28
Croup infectious	2	3	5
Gastroentritis	5	17	22
Infection	6	6	12
Injection site cellulitis	5	3	8
Laryngitis	3	3	6
Measles post vaccine	2	3	5
Meninigitis	5	0	5
Nasopharyngitis	15	47	62
Pharyngitis	10	13	23
Pneuminia	13	4	17
Sepsis	5	0	5
Tonsilitis	7	7	14
Upper respiratory tract infection	10	34	44
Urinary tract infection	3	5	8
Varicella	2	12	14
Viral infection	16	12	28
Viral rash	4	6	10
Blood and lymphatic system disorders			
Anaemia	3	2	5
Leukopenia	3	3	6
Neutropenia	4	2	6
Thrombotic thrombocytopenic purpura	5	0	5
Metabolism and nutrition disorders			
Anorexia	8	12	20
Decreased appetite	5	24	29
Dehydration	7	1	8
Diabetes mellitus	8	0	8
Diabetes mellitus insulin dependent	15	0	15
Psychiatric disorders			
Abnormal behaviour	11	12	23
Agression	1	5	6
Agitation	5	3	8
Anxiety	2	5	7
Asperger's syndrome	5	0	5
Attention deficit/hyperactivity disorder	4	2	6
Autism spectrum disorder	12	0	12
Crying	13	41	54
Decreased activity	0	5	5
Dysphemia	3	2	5
Insomnia	3	6	13

[redacted]

Persenonality change	3	2	5
Personality disorder	7	1	8
Restlessness	5	3	8
Screaming	4	7	11
Sleep disorder	3	8	11
Staring	0	5	5
Nervous system disorders			
Aphasia	8	2	10
Autism	163	0	163
Balance disorder	8	13	21
Cerebellar ataxia	7	0	7
Dyskinesia	1	6	7
Encephalitis post measles	13	0	13
Epilepsy	6	2	8
Hemiparesis	7	0	7
Hemiplegia	5	0	5
Hypoaesthesia	2	7	9
Hypotonia	18	12	30
Hypotonic-hyporesponsive episode	4	2	6
Lethargy	6	22	28
Loss of consciousness	8	3	11
Meningism	3	2	5
Mental retardation severity unspecified	11	0	11
Migraine	3	3	6
Movement disorder	3	2	5
Nervous system disorder	8	3	11
Petit mal epilepsy	5	2	7
Psychomotor hyperactivity	3	3	6
Somnolence	10	10	20
Speech disorder	20	8	28
Speech disorder developmental	6	2	8
Status epilepticus	6	0	6
Stupor	6	2	8
tremor	9	11	20
Eye disorders			
Eye disorder	2	3	5
Eye irritation	2	6	8
Eye pain	1	5	6
Eye pruritus	1	4	5
Eye rolling	5	1	6
Eye swelling	3	9	12
Eyelid oedema	6	6	12
Lacrimation increased	3	4	7
Ocular hyperraemia	3	3	6
Strabismus	1	4	5
Visual disturbance	4	5	9
Ear and labyrinth disorders			
Deafness neurosensory	6	0	6
Ear pain	0	10	10
Tinnitus	2	3	5

[redacted]

Cardiac disorders			
Cyanosis	13	4	17
Tachycardia	7	8	15
Vascular disorders			
Circulatory collapse	5	0	5
Flushing	2	7	9
Hypotension	9	3	12
Pallor	14	31	45
Respiratory, thoracic and mediastinal disorders			
Asthma	14	4	18
Dyspnoea	32	13	45
Epistaxis	7	6	13
Nasal congestion	2	4	6
Pharyngeal erythema	4	9	13
Respiratory disorder	6	8	14
Rhinorrhoea	7	28	35
Tonsillar hypertrophy	4	3	7
Wheezing	10	6	16
Gastrointestinal disorders			
Abdominal pain	13	17	30
Abdominal pain upper	1	4	5
Constipation	5	9	14
Gastrointestinal disorder	6	5	11
Pancreatitis acute	5	0	5
Parotid gland enlargement	3	17	20
Salivary hypersecretion	5	1	6
Skin and subcutaneous tissue disorders			
Cold sweat			
Dermatitis	1	5	6
Drug eruption	1	10	11
Ecchymosis	3	2	5
Eczema	1	16	17
Henoch-Schonlein purpura	7	3	10
Periorbital oedema	2	4	6
Petechiae	13	10	23
Rash pruritic	1	28	29
Rash rubelliform	1	5	6
Rash vesicular	1	10	11
Skin induration	0	6	6
Skin lesion	2	7	9
Skin nodule	1	4	5
Skin warm	1	9	10
Swelling face	10	13	23
Immune system disorders			
Immune system disorder	4	1	5
Musculoskeletal and connective tissue disorders			
Back pain	3	2	5
Joint effusion	3	2	5
Juvenile arthritis	6	1	7

[redacted]

Muscle spasms	5	2	7
Muscular weakness	5	4	9
Musculoskeletal stiffness	3	12	15
Neck pain	4	5	9
Pain in extremity	4	21	25
Polyarthritis	3	2	5
Reproductive system and breast disorders			
Epididymitis	3	2	5
General disorders and administration site condition			
Abasia	2	5	7
Adverse drug reaction	3	3	6
Adverse event	5	17	22
Asthenia	24	27	51
Chest discomfort	3	2	5
Chest pain	2	4	6
Chills	5	12	17
Developmental delay	25	2	27
Drug ineffective	0	12	12
Fatigue	9	23	32
Feeling abnormal	2	11	13
Feeling hot	1	10	11
Gait disturbance	33	29	62
General symptom	3	4	7
Hyperpyrexia	3	10	13
Hyperthermia	3	4	7
Inflammation	0	5	5
Influenza like illness	1	9	10
Injection site bruising	1	6	7
Injection site mass	0	26	26
Injection site nodule	0	5	5
Injection site oedema	5	23	28
Injection site pruritus	2	8	10
Injection site urticaria	2	25	27
Injection site vesicles	1	7	8
Injection site warmth	1	18	19
Local swelling	2	6	8
Mass	1	8	9
No adverse drug effect	0	91	91
No adverse effect	0	688	688
Oedema	3	15	18
Pain	1	29	30
Swelling	3	10	13
Tenderness	0	6	6
Investigations			
Antibody test negative	0	9	9
Blood amylase increased	1	4	5
Measles antibody negative	0	10	10
Mumps antibody test negative	0	30	30
Rubella antibody negative	0	10	10
Weight decreased	2	3	5
Injury, poisoning and			

[redacted]

procedural complications			
Accidental exposure	0	47	47
contusion	1	5	6
Drug administration error	0	409	409
Drug exposure during pregnancy	0	231	231
Drug exposure via breast milk	0	11	11
Expired drug administrated	0	241	241
Fall	7	3	10
Inappropriate schedule of drug administration	1	200	201
Incorrect dose administered	0	14	14
Incorrect route of drug administration	3	257	260
Medication error	0	179	179
Vaccination complication	2	7	9
Wrong drug administered	1	12	13
Wrong technique in drug usage process	0	22	22
Surgical and medical procedures			
Abortion induced	5	0	5
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous	17	0	17
Social circumstances			
Learning disability	4	1	5
Total			

[redacted]

[redacted]

APPENDIX 2: REPORTS WITH A FATAL OUTCOME

Age	Cause of death	Other events reported and medical history
13m/M	Aspiration, gastritis	Patient died in sleep 8 days after vaccination.
14m/F	Multi-organ failure	Possible immunodeficiency. Development of encephalitis, seizures, and combined immunodeficiency. Patient developed pneumonitis, hepatitis, and multiple organ failure
18m/M	Bacterial sepsis	Possible coning (axial displacement of the cerebellar tonsils through the foramen magnum). Sepsis with DIC
15m/FM	Cardio-respiratory arrest	Reactive airway disease. Concomitant therapy included varicella virus vaccine live and streptococcus pneumoniae vaccine
12m/M	Cardio respiratory arrest	Gastroentritis and chronic obstructive airway disease and prematurity. Concomitant therapy included varicella virus vaccine live and haemophilus b conjugate vaccine, albuterol and fluticasone propionate.
12m/F	Bacterial sepsis, cardio-respiratory arrest, dehydration,erythema multiforme, fever, lethargy, measles, meningitismeningoccoccal, shock, vomiting	Allergies, eczema amd hematoma on the forehead. Concomitant therapy varicella virus vaccine live, and streptococcus pneumonia vaccine. Doubtfull meningococcal meningitis infection. Possible vibrio infection from ingesting infected raw fish (Asia)
5y/F	Yellow fever	History of low birth weight, diarrhea, bronchitis and aseptic meningitis 3 months before. Patient concomitantly received separate vaccine of yellow fever virus vaccine life. Probable cause was vaccine virus for yellow fever.
11y/F	Death	Epilepsy and subacute sclerosing panencephalitis consistent with wild type measles visus from vaccine or an old measles infection.
25y/M	Death	Death was attributed to accident or suicide. [redacted] Follow-up indicated no connection between vaccinations and death.
14m/M	Acute respiratory distress syndrome, cyanosis, encephalopathy, fever, neurological examination abnormality, viral infection, lower respiratory tract infection	History of varicella. Five days post vaccination the patient presented with febrile syndrome and respiratory difficulty. Two days later followed by post food vomiting, cyanosis and respiratory distress and neurological trouble (shifty eyes). The first diagnoisis was infectious pneumopathy associated with an infectious pulmonary pathology from probable viral origin.No autopsy was performed.
7y/M	Subaute sclerosing panencephalitis	Subacute sclerosing panencephalitic process assessed as related to the MMRII vaccineation by the reporter.
18m/F	Sudden infant death syndrome	Patient developed common cold with fever after vaccination and was found with face downward in pillow.
2y/M	Wolf-Hirschhorn syndrome	It was reported that 35% of children with Wolf-Hirschhorn die before the age of 2 years. Autopsy revealed no indication for any other explanation for death than WH
18m/F	Sepsis	History of coli infection of urinary tract at 2 months of age and various infections especially respiratory and otitis media. Patient developed fever, vomitiong and blue reddish rash in groppins but was spreading generalized. No neck stiffness

[redacted]

		was reported. Patient had received previously vaccination against BCG, diphtheria, tetanus x3 and polio 1 and 2 without reactions
18m/M	Pneumonia	Autopsy showed inflammation of the lungs and respiratory system. Reporter assessed the event as unrelated to MMRII vaccination.
18m/M	Sepsis	Mild head trauma. Vomiting, diarrhea and later convulsions and bad peripheral blood circulation, superficial breathing increased heart rate, hypotoneness of extremities. CT scan revealed edema general. Cause of death was unclear. Reporter thought the patient might have developed sepsis and there was no causal relationship to the vaccine.
1y/F	Sepsis	Diagnosis was sepsis was assessed as not related to MMR II
18m/F	Cerebral hemorrhage thrombocytopenia	Low platelet count was first attributed to an idiopathic reaction. Investigation showed large intra cerebral hemorrhage and bone puncture showed a toxic influence on the bone marrow. Case was assessed as possibly related to MMR II.
25m/M	Sudden infant death syndrome	Patient had 2 episodes of uncomplicated fever convulsions, conjunctivitis and respiratory infection. Patient was found with on his back with blue lips and vomit in pharynx. The autopsy showed no certain cause of death and death was classified as borderline SIDS.
Unk/F (adult)	Death	Encephalitis in patient receiving MMR ii while in the hospital for unknown reason.
Unk/M	Death	Patient had unknown immunodeficiency. Following vaccination with MMR II patient developed morbiliform rash and fever which disappeared and returned after 3-4, then a serious illness (not stated which in PSUR comments) days. Diagnosis of hematophagocytic syndrome and Epstein Barr. Cause of death was unknown.
12y/F	Brain compression	History of intern hydrocephalus and sign of meningoencephaitis. Post vaccination the patient developed fever and numbness in arm and legs and vomiting. Autopsy showed big swollen, fluid-filled and slightly asymmetric brain with thick membrane and compressed under side.
18y/M	Meningitis bacterial	Cocomitant medication included hepatitis A (inactive), hepatitis B (rHBsAg (yeast), pneumococcal vaccine 23 polyvalent (MSD), tuberculin purified protein derivative, influenza virus vaccine and meningococcal ppolysaccharide vaccine.. Event reported inc;ded rash on feet that spread to the face over a few hours, 3 days of coughing and sore throat. Symptoms progressedt o severe respiratory distress and shock. Autopsy showed cause of death was Neisseria Meningitidis Septicemia.
Unk/M	Airways obstruction	Premature of 28 weeks sufferer of a rare stomach disorder. Secondary suspect therapy included poliovirus vaccine inactivated. A consultant neurosurgeon at a hospital thought the immunization could have depressed the patient's natural instinct to attempt to reject the milk
Unk/M	Subacute sclerosing panencephalitis	Information received from a newspaper article concerned a patient who developed subacute sclerosing panencephalitis over the 18 months following vaccination with MMR II. Patient died at the age of 18 from subacute sclerosing panencephalitis/.
22y/F	Lupus-Like syndrome,	Information was received from a newspaper article concerned an army reservist who concomitantly received

[redacted]

	pulmonary haemorrhage	hepatitis B, smallpox vaccine, anthrax vaccine and typhoid vaccine. Events reported included aches, fever which worsened to resemble lupus. Patient eventually died from bleeding in the lungs. Army said death was probably or possibly related to vaccines but did not single out one.
34m/F	Salivary gland cancer	Definitely not related to MMR II
8y/M	Measles pneumonia	Information from a published article concerned a patient with acute lymphoblastic leukaemia on chemotherapy. According to the autopsy cause of death was clearly the recent measles infection causing giant cell pneumonia with diffuse damage to the lining epithelium of the respiratory tract from tracheal to alveolar levels. The authors stated they believed that the patient with leukaemia had depression of T-cell function as a result of chemotherapy and further believe that the patient developed measles in part because he received only a single dose of vaccine but was fatal because of the immunosuppression.
12m/M	Brain death, complex partial eizures, brain edema, hypertension	Information concerned a case in litigation. Patient was concomitantly vaccinated with a first dose of varicella virus vaccine life. On vaccination day post vaccination the patient developed various symptoms including a body rash, low grade fever, fussiness, decreased activity, not eating, slight diarrhea and episodes of vomiting. Pediatrician diagnosed patient to be encephalopathic and in status epilepticus. Condition worsened and spots worrysoem for measles developed. Approximately two weeks later a MRI showed a large region of cortical thickening consistent with encephalitis and a hemorrhage of the left posterior lobe. Patient improved and almost five months later virology and serology tests revealed no infectious etiology. Patient died approximately 1 and a half months later after an increase in seizures and decreasing mental status with hypertension. Encephalitis may be temporally related to MMR II but there was no direct evidence this was the cause of the event.
13 y/M	Acute lymphocytic leukaemia	Not related to vaccine according to reporter
Appr 13m/M	Encephalitis post measles	Patient had primary immunodeficiency and defected clinical antiviral T cell function. Brain biopsy was consistent with vaccine strain measles.
20m/M	Cardiac arrest, sepsis, respiratory distress	Case concerned a patient with chronic lung condition who was concomitantly vaccinated with a first dose of MMR II and a first dose of varicella virus vaccine live. Physicians thought overwhelming unrecognized sepsis or congestive heart failure was the cause of death but not the vaccines.
6y/F	Myocarditis, pyrexia, vomiting and abdominal pain.	Patient had received a second dose of MMR II and experienced vomiting, abdominal pain fever later followed by hemodynamic failure and cardiogenic shock and viral myocarditis. The patient died 15 days post vaccination. The health authority considered acute myocarditis, fever, abdominal pain and vomiting to be disabling.

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