2011 Institute of Medicine (IOM) Report generated - Proposals for Updates to the Vaccine Injury Table (VIT)

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MMR- Adverse events

- Febrile Seizures
- Transient Arthralgia
- Measles inclusion body encephalitis (MIBE)

MMR – Febrile Seizures

What are febrile seizures?

- Associated with a fever
- Infants or children
- Last a minute or two (few seconds to more than 15 minutes)
- No long-term sequelae

MMR – Febrile Seizures

- The 2011 IOM committee concluded that the evidence convincingly supports a causal relationship between MMR vaccine and febrile seizures

- Information is not new with literature evidence going back to 1989

MMR – Febrile Seizures

Listing of relevant literature

- Farrington, P., S. Pugh, A. Colville, A. Flower, J. Nash, P. Morgan-Capner, M. Rush, and E. Miller. 1995. A new method for active surveillance of adverse events from diphtheria/tetanus/pertussis and measles/mumps/rubella vaccines. *Lancet* 345(8949):567-569.
- Miller, E., N. Andrews, J. Stowe, A. Grant, P. Waight, and B. Taylor. 2007. Risks of convulsion and aseptic meningitis following measles-mumps-rubella vaccination in the United Kingdom. *American Journal of Epidemiology* 165(6):704-709.
- Andrews, N., J. Stowe, E. Miller, and B. Taylor. 2007. Post-licensure safety of the meningococcal group c conjugate vaccine. *Human Vaccines* 3(2):59-63.
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- Ehrengut, W., and K. Zastrow. 1989. [complications after preventive mumps vaccination in west Germany (including multiple preventive vaccinations)]. *Monatsschrift Kinderheilkunde Organ der Deutschen Gesellschaft fur Kinderheilkunde* 137(7):398-402.

MMR – Febrile Seizures

Listing of relevant literature (evidence for justification)

- Fescharek, R., U. Quast, G. Maass, W. Merkle, and S. Schwarz. 1990. Measles-mumps vaccination in the frg: An empirical analysis after 14 years of use. II. Tolerability and analysis of spontaneously reported side effects. *Vaccine* 8(5):446-456.
- Chen, R. T., J. W. Glasser, P. H. Rhodes, R. L. Davis, W. E. Barlow, R. S. Thompson, J. P. Mullooly, S. B. Black, H. R. Shinefield, C. M. Vadheim, S. Michael Marcy, J. I. Ward, R. P. Wise, S. G. Wassilak, S. C. Hadler, E. Swint, J. R. Hardy, T. Payne, V. Immanuel, P. Benson, J. Draket, L. Drew, B. Mendius, P. Ray, N. Lewis, B. H. Fireman, J. Jing, M. Wulfsohn, M. M. Lugg, P. Osborne, S. Rastogi, P. Patriarca, and V. Caserta. 1997. Vaccine safety datalink project: A new tool for improving vaccine safety monitoring in the United States. *Pediatrics* 99(6):765-773.
- Parisi, G., A. Chiarelli, M. Brandani, and A. D'Onofrio. 1991. [transient alkaline hyperphosphatasemia in childhood. A report of 4 clinical cases and etiopathogenetic hypotheses]. *Minerva Pediatrica* 43(4):337-341.

MMR – Febrile Seizures

- Febrile seizures occurring after MMR vaccinations hold no long-term consequences
  - no risk of subsequent seizure or neurodevelopmental disability
  - no increased rate of epilepsy
- In comparison, post-vaccination syncope can lead to serious adverse events
- No VIT revisions proposed

MMR – Febrile Seizures

Listing of relevant literature

- Barlow, W. E., R. L. Davis, J. W. Glasser, P. H. Rhodes, R. S. Thompson, J. P. Mullooly, S. B. Black, H. R. Shinefield, J. I. Ward, S. M. Marcy, F. DeStefano, and R. T. Chen. 2001. The risk of seizures after receipt of whole-cell pertussis or measles, mumps, and rubella vaccine. *New England Journal of Medicine* 345(9):656-661.
- Vestergaard, M., A. Hviid, K. M. Madsen, J. Wohlfahrt, P. Thorsen, D. Schendel, M. Melbye, and J. Olsen. 2004. MMR vaccination and febrile seizures: Evaluation of susceptible subgroups and long-term prognosis. *Journal of the American Medical Association* 292(3):351-357.
- Ward, K. N., N. J. Bryant, N. J. Andrews, J. S. Bowley, A. Ohrling, C. M. Verity, E. M. Ross, and E. Miller. 2007. Risk of serious neurologic disease after immunization of young children in Britain and Ireland. *Pediatrics* 120(2):314-321.
- MMWR Morb Mortal Wkly Rep. 2008 May 2; 57(17):457 – 60. Syncope After Vaccination – United States, January 2005 – July 2007.

MMR – Transient arthralgia

- Transient Arthralgia is a symptom with no long term effects
- The 2011 IOM committee concluded that the evidence favors acceptance of a causal relationship between MMR vaccine (rubella component) and transient arthralgia in women and children.
- The 2011 IOM committee concluded that the evidence is inadequate to accept or reject a causal relationship between MMR vaccine and chronic arthralgia.
- No VIT revisions proposed

MMR – Transient arthralgia

Listing of relevant literature (evidence for justification)

- Slater, P. E., T. Ben-Zvi, A. Fogel, M. Ehrenfeld, and S. Ever-Hadani. 1995. Absence of an association between rubella vaccination and arthritis in underimmune postpartum women. *Vaccine* 13(16):1529-1532.
- Ray, P., S. Black, H. Shinefield, A. Dillon, J. Schwalbe, S. Holmes, S. Hadler, R. Chen, S. Cochi, and S. Wassilak. 1997. Risk of chronic arthropathy among women after rubella vaccination. *Journal of the American Medical Association* 278(7):551-556.
- Tingle, A. J., L. A. Mitchell, M. Grace, P. Middleton, R. Mathias, L. MacWilliam, and A. Chalmers. 1997. Randomised double-blind placebo-controlled study on adverse effects of rubella immunisation in seronegative women. *Lancet* 349(9061):1277-1281.
- Mitchell, L. A., A. J. Tingle, L. MacWilliam, C. Home, P. Keown, L. K. Gaur, and G. T. Nepom. 1998. HLA-DR class II associations with rubella vaccine-induced joint manifestations. *Journal of Infectious Diseases* 177(1):5-12
- Best, J. M., J. E. Banatvala, and J. M. Bowen. 1974. New Japanese rubella vaccine: Comparative trials. *British Medical Journal* 3(5925):221-224.
- Mitchell, L. A., A. J. Tingle, L. MacWilliam, C. Home, P. Keown, L. K. Gaur, and G. T. Nepom. 1998. HLA-DR class II associations with rubella vaccine-induced joint manifestations. *Journal of Infectious Diseases* 177(1):5-12.
- Mitchell, L. A., A. J. Tingle, M. Grace, P. Middleton, and A. C. Chalmers. 2000. Rubella virus vaccine associated arthropathy in postpartum immunized women: Influence of preimmunization serologic status on development of joint manifestations. *Journal of Rheumatology* 27(2):418-423.

MMR-Vaccine-strain measles viral disease

In 2011, the Institute of Medicine, following an extensive review of the scientific and medical literature, concluded that the evidence convincingly supported a causal relationship between MMR vaccine and measles inclusion body encephalitis (MIBE) in individuals with demonstrated immunodeficiencies.

MMR-Vaccine-strain measles viral disease

Summary Justification for Proposed Changes to the VIT

- The current VIT has the injury “Vaccine-strain measles infection in an immunodeficient recipient” for vaccines containing measles virus.
- Since MIBE is one type of measles-associated disease, the proposal involves revision of the current injury to include MIBE.

MMR- Vaccine-strain measles viral disease

Justification for Proposed Changes to the Time Interval

- Based on 3 case reports the IOM reviewed, the time interval for MIBE is 4 – 9 months.
- Goon 2001 describes a patient with vaccine strain measles with onset of symptoms 8 days after vaccination.
- Angel 1998 describes a patient with vaccine-associated measles pneumonitis with onset of symptoms 11 months after vaccination.
- Proposal:
  - Broad interval of ≤ 12 months for those cases in which typing of vaccine strain was not performed.
  - If vaccine strain is identified, no time frame will be applicable.

MMR-Vaccine strain measles viral disease

Listing of relevant literature (evidence for justification)

- Bitnun, A., P. Shannon, A. Durward, P. A. Rota, W. J. Bellini, C. Graham, E. Wang, E. L. Ford-Jones, P. Cox, L. Becker, M. Fearon, M. Petric, and R. Tellier. 1999. Measles inclusion-body encephalitis caused by the vaccine strain of measles virus. *Clinical Infectious Diseases* 29(4):855-861.
- Baram, T. Z., I. Gonzalez-Gomez, Z. D. Xie, D. Yao, F. H. Gilles, M. D. Nelson Jr, H. T. Nguyen, and J. Peters. 1994. Subacute sclerosing panencephalitis in an infant: Diagnostic role of viral genome analysis. *Annals of Neurology* 36(1):103-108.
- Poon, T. P., V. Tchertkoff, and H. Win. 1998. Subacute measles encephalitis with AIDS diagnosed by fine needle aspiration biopsy - a case report. *Acta Cytologica* 42(3):729-733.
- Angel, J. A., P. Walpita, R. A. Lerch, M. S. Sidhu, M. Masurekar, R. A. DeLellis, J. T. Noble, D. R. Syndman, and S. A. Udem. Vaccine-associated measles pneumonitis in an adult with AIDS. Ann of Intern Med 129:104 – 106.

MMR-Vaccine strain measles viral disease

Listing of relevant literature (evidence for justification)

- Mawhinney, H., I.V. Allen, J.M. Beare, J.M. Bridges, J.H. Connolly, M. Haire, N.C. Nevin, D. W. Neill, J. R. Hobbs. 1971. Dysgammaglobulinaemia complicated by disseminated measles. *British Medical Journal* 2:380 – 381.
- Mihatsch, M.J., H. Ohnacker, M. Just, P.W. Nars. 1972. Lethal measles giant cell pneumonia after live measles vaccination in a case of thymic alymphoplasia Gitlin. *Helv Paediat Acta* 27: 143 – 146.
- Goon, P., B. Cohen, L. Jin, R. Watkins, G. Tudor-Williams. 2001. MMR vaccine in HIV-infected children – potential hazards? *Vaccine* 19:3816 – 3819.

MMR- Vaccine-strain measles viral disease

Current VIT

- Vaccine:

  Vaccines containing measles virus (e.g., MMR, MMRV,MR, M)
- Injury (Time Interval):
  - A. Thrombocytopenic purpura (7 – 30 days)
  - B. Vaccine-Strain Measles Viral Infection in an immunodeficient recipient (6 months)
  - C. Any acute complication or sequela, including death, of above events that arose within the time period prescribed (Not applicable)

Proposed VIT

- Vaccine:

  Vaccines containing measles virus (e.g., MMR, MMRV,MR, M)
- Injury (Time Interval):
  - A. Thrombocytopenic purpura (7 – 30 days)
  - B. Vaccine-Strain Measles Viral Disease in an immunodeficient recipient
    - Vaccine –strain virus identified (Not Applicable)
    - If strain determination is not done or if laboratory testing is inconclusive (≤ 12 months)
  - (b) Any acute complication or sequela, including death…of above events…

MMR- Vaccine-strain measles viral disease

- Current VIT

Vaccines containing measles virus (e.g., MMR, MMRV,MR, M)	Injury	Time Interval
	Vaccine-Strain Measles Viral Infection in an immunodeficient recipient	0 - 6 months

MMR- Vaccine-strain measles viral disease

- Proposed VIT

Vaccines containing measles virus (e.g., MMR, MMRV,MR, M)	Injury	Time Interval
	Vaccine-Strain Measles Viral Disease in an immunodeficient recipient • Vaccine –strain virus identified • If strain determination is not done or if laboratory testing is inconclusive	Not Applicable ≤ 12 months

MMR- Vaccine-strain measles viral disease

Current QAI

- Vaccine-strain measles viral infection is a disease caused by the vaccine-strain that should be determined by vaccine-specific monoclonal antibody or polymerase chain reaction tests.

Proposed QAI

- This term is defined as a measles illness that involves the skin and/or other organs (such as the brain and lungs).
- Measles virus must be isolated from the affected organ or histopathologic findings characteristic for the disease must be present.
- Measles viral strain determination may be performed by methods such as polymerase chain reaction test and vaccine-specific monoclonal antibody.
- If strain determination reveals wild-type measles virus or another, non-vaccine-strain virus, the disease shall not be considered to be a condition set forth in the Table.
- If strain determination is not done or if the strain cannot be identified, onset of illness in any organ must occur within 12 months after vaccination.

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MMR- Vaccine-strain measles viral disease

Justification for proposed QAI

- Science
  - Isolation of measles virus from the affected organ and/or characteristic histopathologic findings
  - Identification of vaccine-strain measles virus by PCR or specific monoclonal antibody
  - Diseases in persons with immunodeficiencies
- ACCV Guiding Principles
  - Presumption of causation to cases in which the vaccine-strain is undetermined or testing is inconclusive
    - Only 1 out of 3 cases of MIBE showed vaccine-strain virus

MMR- Vaccine-strain measles viral disease

Vaccine	Injury	Time Interval
Vaccines containing measles virus (e.g., MMR, MMRV,MR, M)	Vaccine-strain Measles viral disease in an immunodeficient recipient • Vaccine strain virus identified • If strain determination is not done or if laboratory testing is inconclusive	Not applicable ≤ 12 months

This term is defined as a measles illness that involves the skin and/or other organs (such as the brain and lungs). Measles virus must be isolated from the affected organ or histopathologic findings characteristic for the disease must be present. Measles viral strain determination may be performed by methods such as polymerase chain reaction test and vaccine-specific monoclonal antibody. If strain determination reveals wild-type measles virus or another, non-vaccine-strain virus, the disease shall not be considered to be a condition set forth in the Table. If strain determination is not done or if the strain cannot be identified, onset of illness in any organ must occur within 12 months after vaccination.