

(Document 1 of 2)

**CONFIDENTIAL**

**Merck Research Laboratories  
Worldwide Product Safety & Epidemiology**

**PERIODIC SAFETY UPDATE REPORT FOR:  
Measles, Mumps, and Rubella Virus Vaccine Live, MSD**

**01-Jan-2001 to 31-Dec-2005**

**International Birth Date: 01-Apr-1978 (Ireland)**

**Date of this Report: 17-Jan-2006**

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## **9.5 Drug Abuse and Misuse**

The term ‘Drug Abuse’ is herein interpreted in the context of *use that is illegal or addictive*, though it is acknowledged that this has limited utility when applied to vaccines, as contrasted with pharmaceuticals.

The term ‘Misuse’ is herein interpreted in the context of *use that deviates from what is recommended*, i.e., what is described in the CCDS or the package circular (Prescribing Information). Misuse is applied broadly to conditions of shipping, storage and administration, including doses given when contraindicated, at an inappropriate age, too soon or too late, by an incorrect route, etc. In MedDRA, ‘Misuse’ maps to the preferred terms of ‘Medication Error’, which includes such lower level terms as *expired drug, wrong drug administered, wrong patient, inappropriate schedule, expired drug, vaccine not stored properly*, etc.

During the reporting period for this PSUR, there were no reports of drug abuse and 1,359 spontaneous reports of product misuse (medication error) with measles, mumps, and rubella virus vaccine live were identified from health care providers. These reports consisted of the following: drug maladministration (409\*); inappropriate schedule of drug administration (210\*); medication error (no other term specified) (182\*); incorrect dose administered (15\*); incorrect drug dosage form administered (2); incorrect route of drug administration (265\*); poor quality drug administered (254\*); wrong drug administered (14\*); wrong technique in drug usage process (23\*). One-hundred-seventy-two reports (approximately 13%) of the 1,359 reports described adverse events, the majority of which are known side effects of measles, mumps, rubella virus vaccine live, MSD as described in the CCDS or complications of known side effects.

## **Conclusion**

The Company will continue to monitor reports of product misuse as part of the ongoing safety evaluation of measles, mumps, and rubella virus vaccine live.

## **9.6 Use During Pregnancy**

### **9.6.1 New Reports of Pregnancy Exposures Between 01-Jan-2001 and 31-Dec-2005**

During the reporting period of this PSUR, the Company received a total of 281 spontaneous reports of maternal exposure to measles, mumps, and rubella virus vaccine live during pregnancy identified from health care providers and consumers.

A prospective report of exposure during pregnancy is defined as a report for which the Company first learned of the exposure during the pregnancy and the outcome of the pregnancy may be subsequently reported. A retrospective report of exposure during pregnancy is defined as a report for which the Company first learned of the exposure after the outcome of the pregnancy was known.

Two-hundred forty-seven of the reports were prospective and the remaining 34 were retrospective reports. The pregnancy outcomes of these 281 reports are presented in Table 9.6.1.

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\* Thirteen patients were identified where 2 medication errors were reported for each. One patient had 3 medication errors reported.

**Table 9.6.1**  
**New Reports Received**  
**Summary of Pregnancy Exposures**  
**01-Jan-2001 to 31-Dec-2005**

	<b>Total Reports of Pregnancy Exposure</b>	<b>Live Births</b>	<b>Elective Abortions</b>	<b>Spontaneous Abortions</b>	<b>Fetal Death</b>	<b>Outcome Unknown</b>
<b>Prospective Reports</b>	247	34	4	11		198
<b>Retrospective Reports</b>	34	21 <sup>a</sup>	3	8	2 <sup>b</sup>	

<sup>a</sup> One report of limb hypoplasia congenital

<sup>b</sup> One report of a twin pregnancy w/ fetal loss and retention of one fetus.

#### **9.6.1.1 Prospective Reports**

The pregnancy outcomes of the 247 prospective reports of exposure to measles, mumps, and rubella virus vaccine live during pregnancy were: 34 live births, 4 elective abortions and 11 spontaneous abortions. The pregnancy outcomes of the remaining 198 reports are unknown.

#### **9.6.1.2 Retrospective Reports**

The pregnancy outcomes of the 34 retrospective reports of exposure to measles, mumps, and rubella virus vaccine live during pregnancy were: 21 live births, 3 elective abortions, 8 spontaneous abortions, and 2 fetal (intra-uterine) death.

#### **9.6.2 Congenital Anomalies**

During the reporting period of the PSUR, in all of the new reports of exposure to measles, mumps, and rubella virus vaccine live during pregnancy, there were no prospective reports of congenital anomalies and 1 retrospective report of congenital anomalies. In WAES [REDACTED], information was received concerning a 22-year-old female who was vaccinated with the first dose of dose of measles virus vaccine live (+) mumps virus vaccine live (+) rubella virus vaccine live (second generation) one month before the beginning of her pregnancy. At 29 weeks gestation, an echography was performed and a congenital anomaly (i.e., a pathology of the fetus' lower limbs) was observed. At 40 weeks gestation, the patient gave birth by Cesarean to a male with an "ectromelia consisting of hypoplasia of the fibula." The male infant was evaluated: Apgar score test = 9/10, weight = 4,270 g, height = 50 cm, and cranial perimeter = 37 cm.

##### **Comment**

Among the pregnancy reports with known outcomes, 1 retrospective report of congenital anomalies has been received during the reporting period. It is not known whether measles, mumps, and rubella virus vaccine live can cause fetal harm when administered to a pregnant woman or can affect reproductive capacity. Therefore, the vaccine should not be administered to pregnant females; furthermore, pregnancy should be avoided for three months following vaccination. The CCDS includes text stating that exposure to

mumps infection during the first trimester of pregnancy may increase the rate of spontaneous abortion.

### **9.6.3 Previously Identified Reports**

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During the reporting period of this PSUR, follow-up information was received concerning the outcomes of 8 previously identified reports in which women were exposed to measles, mumps, and rubella virus vaccine live during pregnancy and in which the pregnancy outcomes were unknown at the time of previous PSURs (prospective reports). In the 8 reports with follow-up information, 4 pregnancies resulted in normal healthy newborns, 3 reports involved patients who were lost to follow-up and 1 report involved a patient who underwent an elective abortion.

**Table 9.6.3**  
**Summary of Pregnancy Exposures from Previously Identified Reports**  
**(Follow-up Information Received)**  
**01-Jan-1999 to 31-Dec-2003**

	<b>Total Reports of Pregnancy Exposure</b>	<b>Live Births</b>	<b>Elective Abortions</b>	<b>Lost to Follow-Up</b>
<b>Prospective Reports</b>	8	4	1	3

#### **Comment**

Merck & Co., Inc. will continue efforts to obtain outcome information for all reports of exposure to measles, mumps, and rubella virus vaccine live during pregnancy.

### **9.6.4 Use During Lactation**

During the reporting period of this PSUR, 7 reports of exposure during lactation involving measles, mumps, and rubella virus vaccine were identified. In 3 of the 7 reports, there were no adverse effects reported. One report (WAES [REDACTED]) concerned a male infant who was breast fed by his mother, who had been vaccinated with a dose of measles, mumps, rubella virus vaccine live on 25-Oct-2002. Subsequently, after breast feeding, the infant "broke out with measles like rash" for 2 days.

The remaining 3 reports were obtained from a published literature article entitled, "Adverse Outcomes Associated with Postpartum Rubella or MMR Vaccine". In 2 of the 3 reports (WAES [REDACTED]), 15-month-old males were breast fed by their mothers who were vaccinated post-partum with a dose of measles, mumps, rubella virus vaccine live. The infants did not experience any adverse events due to possible vaccine exposure from breast milk. Both infants were reported to have developed normally during the first year of life. At 15-months of age, both infants were vaccinated with a dose of measles, mumps, rubella virus vaccine live and were diagnosed with autism. The third report (WAES [REDACTED]) involved a 4-day-old male patient whose mother was vaccinated with a dose of measles, mumps, rubella virus vaccine live in the postpartum period after his birth in May 1993, on his fourth day