Concomitant Administration of Varicella Vaccine with Combined Measles, Mumps, and Rubella Vaccine in Healthy Children Aged 12 to 24 Months of Age

B. Stück¹, K. Stehr² and H.L. Bock³

Varicella (chickenpox) is an extremely common and contagious disease, affecting almost all unvaccinated children living in the temperate regions of the world within the first few years of life. Although it is often considered benign and a normal part of childhood, there are nonetheless good reasons for attempting to prevent it through routine vaccination programs, as recommended since 1996 by the American Academy of Pediatrics and the Centers for Diseases Control Advisory Committee on Immunization Practices. The large number of children affected by varicella means that the absolute numbers of complications, although relatively infrequent on a per capita basis, are far from negligible. Before routine vaccination was introduced in the United States, there were approximately 4 million cases of varicella annually, of which almost 10,000 led to hospitalization and 90-100 were fatal. Doctors who are aware of the risk of serious complications are more likely to implement the recommendations for routine childhood immunization than those who are not, and this is particularly true for doctors who have personally seen death from chickenpox. Routine varicella vaccination also has economic benefits. Varicella causes substantial economic costs in lost working time, mainly as a result of parents taking time off work to care for their sick children. Economic analyses carried out in the United States, Germany, France, and Spain have predicted substantial social and economic gains resulting from routine varicella vaccination.

Measles, mumps, and rubella (MMR) vaccine is currently included in many routine vaccination programs as a single dose in the second year of life. This is also the recommended time for giving a varicella vaccine, so there could be logistical and economic advantages in giving a varicella vaccine at the same visit as the MMR vaccine, through elimination of the costs of

SUMMARY The reactogenicity and immunogenicity of three combined measles, mumps and rubella (MMR) vaccines and one administered with a varicella vaccine was studied in infants. The vaccines were Priorix™ (designated MeMuRu, Group 1), M-M-R II® (Group 2), Triviraten® (Group 3) and Priorix™ + a varicella vaccine, Varilrix™ (Group 4). Fever was greater in Group 2 (61.3%) compared to Group 1 (48.5%; p = 0.033) or Group 3 (37.1%; p = 0.009). Rash with fever was reported in Group 2 (4.8%) and Group 4 (3.3%), but not for Group 1. Anti-measles, -mumps and -rubella seroconversion was similar for Group 1 (96.1%, 96.1% and 100%, respectively), Group 4 (98% for all three), and Group 2 (91.5%, 93.6% and 97.9%) 60 days post-vaccination. GMTs for measles (3.053.7–3,412.2 mIU/ml), mumps (1,001.5–1,158.8 U/ml) and rubella (68.7–89.1 IU/ml) were similar for Groups 1, 2 and 4 at Day 60. Antibody persistence was noted 2 years post-vaccination. The MeMuRu + varicella combination showed no clinically relevant increase in reactogenicity and should facilitate introduction of a varicella vaccine into national immunization schedules.

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separate vaccination visits. Vaccines administered at different times increase the likelihood of missed doses; concomitant administration could therefore increase compliance with vaccination. Before routinely administering multiple vaccines concomitantly, it is important to ensure that simultaneous administration does not compromise immunogenicity or lead to unacceptable increases in reactogenicity. This study, therefore, aimed to provide preliminary data on the effects of giving GlaxoSmithKline Biologicals' live attenuated measles-mumps-rubella (MeMuRu) vaccine and GlaxoSmithKline Biologicals' live attenuated varicella vaccine simultaneously as separate injections. These were compared with the effects of MeMuRu vaccine and two established MMR vaccines given without a varicella vaccine.

MATERIALS AND METHODS

Study conduct and participants

This was an open, randomized study at seven centers in Germany, and was approved by the Ethics Committees of all participating centers. The parents or guardians of all infants enrolled gave written informed consent before any trial-related procedures were performed, and the study was conducted according to the Declaration of Helsinki and the Good Clinical Practice guidelines which applied at the time. The study participants were healthy children aged 12 to 24 months with no previous history of or vaccinations against measles, mumps, rubella, or varicella. Subjects were excluded if they used any investigational or non-registered drug or vaccine other than the study vaccines during the study period or within 30 days preceding the first dose of study vaccine. Other reasons for exclusion were an immuno-suppressive or immunodeficient condition, administration of chronic immunosuppressants or immunomodulatory drugs, administration of immunoglobulins and/or blood products within 3 months preceding the study period, a history of allergic reaction to any of the vaccine components, or an acute disease.

Vaccination

The vaccines used in this study were all commercially available. Subjects in Group 1 received an MMR vaccine designated Me-

MuRu (Priorix™, GlaxoSmithKline Biologicals) which contains the Schwarz measles strain, the RIT 4385 mumps strain and the RA 27/3 rubella strain. Subjects in Group 2 received an MMR vaccine (M-M-R II®, Merck, Sharpe and Dohme) which contains the Edmonston Enders measles strain, the Jeryl Lynn mumps strain and the RA 27/3 rubella strain. Subjects in Group 3 received a different MMR vaccine (Triviracet®, Berne) which contains the Edmonston-Zagreb measles virus, the Rubini mumps virus and the RA 27/3 rubella virus strain. Subjects in Group 4 received Priorix™, as above, and a varicella vaccine (Varilrix™, GlaxoSmithKline Biologicals) which contains the live attenuated Oka-strain of varicella. On Day 0 of the study, subjects received a subcutaneous dose (0.5 ml) of one of the above vaccines into the left upper arm (or two vaccines given concomitantly, one into the left and one into right upper arms for Group 4). The viral titers of each of the vaccines are shown in Table 1.

Reactogenicity: solicited local and general symptoms

Parents of the study subjects

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Viral titers/dose (CCID₅₀)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Measles</td>
</tr>
<tr>
<td>Priorix™ MMR vaccine (designated MeMuRu, administered to Groups 1 and 4)</td>
<td>10⁶⁻⁰</td>
</tr>
<tr>
<td>M-M-R II® MMR vaccine (administered to Group 2)</td>
<td>10³⁰⁰</td>
</tr>
<tr>
<td>Triviracet® MMR vaccine (administered to Group 3)</td>
<td>10⁶⁻⁰</td>
</tr>
<tr>
<td>Varilrix™ varicella vaccine (administered to Group 4)</td>
<td>-</td>
</tr>
</tbody>
</table>

*CCID₅₀ = median cell culture infective dose

1 Minimal viral titer as stated by the manufacturers

2 Plaque forming units
kept diary card records of solicited local (pain, redness, swelling) and general symptoms (fever - reported as $\geq 38.1^\circ C$ and $>39.5^\circ C$, suspected meningism, parotid/salivary gland swelling, skin rash/exanthema), and unsolicited symptoms or serious adverse events for up to 42 days after vaccination. The definition of Grade 3 (severe intensity) for solicited symptoms of fever, redness and swelling, and pain was: a rectal temperature $\geq 39.5^\circ C$, a diameter $>20$ mm for swelling or redness at the injection site, and pain preventing normal daily activities.

**Immunogenicity**

Blood samples (3 ml) were taken immediately before and 60-70 days after vaccination to measure the immune responses to each of the vaccine antigens. Antibodies against measles, mumps or rubella were measured by an enzyme-linked immunosorbent assay (ELISA) system (Enzygnost, Behring). Antivaricella antibodies were measured using an indirect immunofluorescence test (Pharmacia).

A subject with an antibody titer greater than the cut-off point was considered seropositive. The cut-off points for the assays were: 150 mIU/ml for measles, 231 U/ml for mumps, and 4 IU/ml for rubella. For varicella, samples showing no or barely visible fluorescence at the starting dilution (1:4) were considered seronegative. Seroconversion was defined as the appearance of detectable levels of antibody in the serum of subjects who were seronegative before vaccination. An immune response was considered to be a four-fold or greater increase of a previously positive antibody titer, or as a seroconversion in previously seronegative subjects. Geometric mean titers (GMTs) were calculated by taking the anti-logarithm of the mean logarithmic titer transformations. In order to calculate GMTs, half of the above cut-off values were used, i.e., 75 mIU/ml for measles, 115.5 U/ml for mumps, and 2 IU/ml for rubella and varicella.

**Persistence of antibodies**

In addition to the blood samples collected after 60 days, further blood samples were collected after 1 year and 2 years to assess the persistence of antibodies against measles, mumps and rubella.

**Statistical analysis**

This study was considered exploratory and only descriptive statistical analyses were performed. A comparison was made between all four groups for the overall incidence of subjects who experienced local and general symptoms (incidence $\geq 1\%$), using Fisher’s exact test ($\alpha = 0.05$). If any statistically significant difference between the four groups was observed, then each group was compared with the other groups, again using Fisher’s exact test ($\alpha = 0.05$). This set of comparisons was designed to detect any significant differences between Groups 1, 2 and 3 or between Groups 1 and 4.

Seroconversion rates and GMTs for measles, mumps, rubella and varicella, along with their 95% confidence intervals (CIs), were calculated for initially seronegative subjects in each group after vaccination. The difference in seroconversion rates between groups was assessed using Fisher’s exact test ($\alpha = 0.05$). Differences in GMTs between groups were assessed using one-sided analysis of variance (ANOVA) ($\alpha = 0.05$).

**RESULTS**

**Patient disposition and characteristics**

A total of 272 subjects were randomized in a 1:1:1:1 ratio to receive an injection of the MeMuRu alone (Group 1) or one of the two MMR vaccines alone (Groups 2 and 3) or injections of MeMuRu and a varicella vaccine concomitantly (Group 4). A total of 265 subjects completed the initial 60-day study period; four subjects were lost to follow-up, two did not complete the study because of protocol violations, and one subject withdrew consent. Of the 272 subjects who were enrolled into the study, 261 were eligible for inclusion in the 42-day reactogenicity analysis and 203 for inclusion in the 60-day immunogenicity analysis. Eleven subjects were excluded from the reactogenicity analysis, mainly because of randomization failure (7 subjects received a vaccine other than their randomized vaccine). The main reason for exclusion from the immunogenicity analysis was lack of compliance with the blood-sampling schedule (56 subjects). A total of 172 subjects had serological data available at 1 year and 137 had available serological data after 2 years of the study.

The mean age of the 261 children included in the According-to-Protocol analysis was 15.4 months (range 11–23 months), of whom 148 (57%) were male and 113 (43%) female. There were no significant differences between the four treatment groups in terms of mean age or the percentages of males and females.

**Reactogenicity**

Incidence of solicited local
and general reactions are given in Table 2. Higher rates of fever were observed in subjects of Group 2 (61.3%; 17.7%) and Group 4 (59.0%; 19.7%), than in subjects of Group 1 (48.5%; 7.4%) or Group 3 (37.1%; 10.0%). A statistically significant difference ($p = 0.021$) was observed between the four groups for fever. A pairwise comparison of each with every other group revealed that the incidence of fever in subjects of Group 2 was significantly higher compared to those in Group 1 ($p = 0.033$) or Group 3 ($p = 0.009$). Although the concomitant administration of a varicella vaccine (Group 4) produced an increase of fever, it was within the same range as that observed in Group 2.

Rash was observed in the group given MeMuRu alone (Group 1) or MMR alone (Groups 2 and 3) with the highest rate (7.1% of subjects) in subjects of Group 3. Generalized rash with fever was reported for 4.8% of subjects in Group 2 and in 3.3% of subjects given MeMuRu + a varicella vaccine (Group 4), whereas no cases were reported for subjects given MeMuRu alone (Group 1). Concomitant administration of MeMuRu with varicella vaccines (Group 4) resulted in lower incidences of local reactions to MeMuRu (pain, redness and swelling) compared with MeMuRu alone (Group 1). Thus, no increase in local reactogenicity to MeMuRu occurred when combining the MeMuRu and varicella vaccines. No Grade 3 local symptoms were observed in any of the groups for pain, redness or swelling (Table 2). It is noteworthy that no cases of parotid swelling and no signs of suspected meningism, including febrile convulsions (both of which were solicited symptoms), were reported during the study.

### Immunogenicity

The immune response to measles, mumps and rubella at Day 60 was similar in subjects in Group 1 or Group 2 in terms of seroconversion rates (Fig. 1) and GMTs (Fig. 2). Seroconversion rates and antibody titers against measles, mumps and rubella in Group 4 were similar to those in Groups 1 and 2 (Figs. 1 and 2). Thus, the immune response to the MeMuRu vaccine used in Group 1 was unaffected by its co-administration with a varicella vaccine, and was similar to the control vaccine administered to Group 2. Seroconversion rates for mumps, as well as anti-measles and anti-mumps GMT, were lower in subjects in Group 3 than in the other groups.

### Persistence of antibodies

Persistence of antibodies against measles, mumps and rubella is shown in Table 3. Seroconversion rates (%) and GMTs (calculated as percentage of seroconverters for the 60-day period and on all 137 subjects with two-year data) are

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**Table 2** Reactogenicity: incidences of solicited local and general symptoms

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Percentage of subjects with symptoms</th>
<th>Overall p-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Group 1 (N = 68) Group 2 (N = 62) Group 3 (N = 70) Group 4 (N = 61)</td>
<td></td>
</tr>
<tr>
<td>Fever ≥ 38.1°C</td>
<td>48.5 61.3 37.1 59.0</td>
<td>0.021</td>
</tr>
<tr>
<td>Fever &gt; 39.5°C</td>
<td>7.4   17.7 10.0 19.7</td>
<td>-</td>
</tr>
<tr>
<td>Rash Total</td>
<td>4.4   4.8  7.1  4.9</td>
<td>0.916</td>
</tr>
<tr>
<td>Rash Generalized with fever</td>
<td>0.0 4.8 1.4 3.3</td>
<td>-</td>
</tr>
<tr>
<td>Pain Total</td>
<td>7.4   8.1  2.9  3.3</td>
<td>0.519</td>
</tr>
<tr>
<td>Pain Grade 3</td>
<td>0.0   0.0  0.0  0.0</td>
<td>-</td>
</tr>
<tr>
<td>Redness Total</td>
<td>11.8  14.5 7.1  3.3</td>
<td>0.124</td>
</tr>
<tr>
<td>Redness &gt; 20 mm</td>
<td>0.0   0.0  0.0  0.0</td>
<td>-</td>
</tr>
<tr>
<td>Swelling Total</td>
<td>4.4   1.6  1.4  3.3</td>
<td>0.598</td>
</tr>
<tr>
<td>Swelling &gt; 20 mm</td>
<td>0.0   0.0  0.0  0.0</td>
<td>-</td>
</tr>
</tbody>
</table>

N = number of subjects who returned symptom sheets
*Comparison of all four groups, *= not performed.

Group 1: MeMuRu (Pnorix\textsuperscript{TM}), Group 2: MMR (M-M-R II\textsuperscript{a}), Group 3: MMR (Triviraten\textsuperscript{a}), Group 4: MeMuRu (Pnorix\textsuperscript{TM}) + varicella vaccine (Varilix\textsuperscript{TM})
shown post-vaccination at Day 60, Year 1 and Year 2.

In Group 1, seropositivity for measles, mumps and rubella antibodies was 96.2%, 76.9% and 100%, respectively, after 1 year and 96.2%, 88.5% and 100%, respectively, at 2 years post-administration. The majority of subjects who had seroconverted at Day 60 remained seropositive at 1 and 2 years post-vaccination. The corresponding seropositivity rates in Group 4 were 97.2%, 86.1% and 97.2%, respectively, at 1 year and 97.4%, 94.7% and 100% at 2 years. Results for both Groups 1 and 4 were similar to those of Group 2 in terms of seroconversion and GMTs, although higher GMTs were observed at 2 years in Group 4 than in Group 1.

Subjects in Group 3 had similar seroconversion rates to those who received other measles-mumps-rubella vaccines for measles and rubella, but a markedly lower rate for mumps. Lower GMTs for measles and mumps were achieved at all time points following vaccination in Group 3.

The seroconversion rate for varicella when given with MeMuRu (Group 4) was 95.7% at Day 60, with a GMT of 41.2, rising to 136.3 at Year 2.

**DISCUSSION**

In this study, the incidence of fever, defined as a rectal temperature ≥ 38.1°C and > 39.5°C, was notably higher than those reported in previous trials. In three studies which compared the vaccine given to Group 1 with the vaccine given to Group 2, incidences of fever (≥ 38.1°C) were 24.7-28.2%, 11 31.3% and 35.6%, 12 and 38.0 and 39.7%, respectively. 13 In a fourth study which compared MeMuRu with the
Table 3  Persistence of antibodies against measles, mumps, rubella and varicella

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Time*</th>
<th>Measles</th>
<th></th>
<th>Mumps</th>
<th></th>
<th>Rubella</th>
<th></th>
<th>Varicella</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>N</td>
<td>%</td>
<td>GMT (mIU/ml)</td>
<td>N</td>
<td>%</td>
<td>GMT (IU/ml)</td>
<td>N</td>
<td>%</td>
</tr>
<tr>
<td>Group 1</td>
<td>Day 60</td>
<td>51</td>
<td>96.1</td>
<td>3,294.5</td>
<td>51</td>
<td>96.1</td>
<td>1,158.8</td>
<td>51</td>
<td>100</td>
</tr>
<tr>
<td></td>
<td>Year 1</td>
<td>26</td>
<td>96.2</td>
<td>2,422.8</td>
<td>26</td>
<td>78.9</td>
<td>471.0</td>
<td>26</td>
<td>100</td>
</tr>
<tr>
<td></td>
<td>Year 2</td>
<td>26</td>
<td>96.2</td>
<td>1,950.1</td>
<td>26</td>
<td>86.5</td>
<td>424.7</td>
<td>26</td>
<td>100</td>
</tr>
<tr>
<td>Group 2</td>
<td>Day 60</td>
<td>47</td>
<td>91.5</td>
<td>3,412.2</td>
<td>47</td>
<td>93.5</td>
<td>1,001.5</td>
<td>47</td>
<td>97.9</td>
</tr>
<tr>
<td></td>
<td>Year 1</td>
<td>30</td>
<td>88.7</td>
<td>1,952.5</td>
<td>30</td>
<td>86.7</td>
<td>708.4</td>
<td>30</td>
<td>96.7</td>
</tr>
<tr>
<td></td>
<td>Year 2</td>
<td>32</td>
<td>90.6</td>
<td>1,693.4</td>
<td>32</td>
<td>87.5</td>
<td>907.9</td>
<td>32</td>
<td>96.9</td>
</tr>
<tr>
<td>Group 3</td>
<td>Day 60</td>
<td>55</td>
<td>96.4</td>
<td>797.7</td>
<td>55</td>
<td>19.8</td>
<td>533.9</td>
<td>56</td>
<td>100</td>
</tr>
<tr>
<td></td>
<td>Year 1</td>
<td>37</td>
<td>100</td>
<td>688.7</td>
<td>38</td>
<td>23.7</td>
<td>176.1</td>
<td>38</td>
<td>100</td>
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<tr>
<td></td>
<td>Year 2</td>
<td>40</td>
<td>97.5</td>
<td>485.2</td>
<td>41</td>
<td>48.8</td>
<td>345.7</td>
<td>41</td>
<td>100</td>
</tr>
<tr>
<td>Group 4</td>
<td>Day 60</td>
<td>49</td>
<td>98.0</td>
<td>3,053.7</td>
<td>49</td>
<td>98.0</td>
<td>1,108.8</td>
<td>49</td>
<td>98.0</td>
</tr>
<tr>
<td></td>
<td>Year 1</td>
<td>36</td>
<td>97.2</td>
<td>2,462.8</td>
<td>36</td>
<td>86.1</td>
<td>731.0</td>
<td>36</td>
<td>97.2</td>
</tr>
<tr>
<td></td>
<td>Year 2</td>
<td>38</td>
<td>97.4</td>
<td>2,627.2</td>
<td>38</td>
<td>94.7</td>
<td>1,316.9</td>
<td>38</td>
<td>100</td>
</tr>
</tbody>
</table>

*Note: Day 60 data is for the 203 subjects (FP) for immunogenicity analysis. Year 1 and Year 2 data refer to those subjects for whom two-year data is available.

Group 1: MeMuRu (Priorix™), Group 2: MMR (M-M-R ii™), Group 3: MMR (Trivaris™), Group 4: MeMuRu (PrioRx™) + varicella vaccine (Varivax™)

Vaccine given to Group 3, fever incidences were 23.5% and 16.8%. The incidence of Group 3 fever (>39.5°C) was mostly less than 7%, although incidences of 9.5% and 11.5% were reported in one study. In the present study, the incidence of Grade 3 fever ranged from 7.4%-19.7%.

A number of factors might have led to the higher incidence of fever reported here. The present study conducted in Germany, commenced in November, and influenza infections are more common in the winter and can sometimes be of epidemic proportions, leading to an increased incidence of fever symptoms. Two studies using similar methodologies reported incidences of fever of 27-38% in one study and 38-39% in the other. The site chosen to measure temperature can also influence assessment of fever. Mean rectal temperature readings were significantly higher (p < 0.001) than axillary temperature measurements in children beyond the neonatal period. In the four trials involving Priorix, three used a temperature sensitive pad placed on the forehead to monitor temperature, whereas the other trial monitored rectal temperature. These factors might explain the higher incidences of fever noted in the present trial.

The results for other solicited local and general reactions (rash, pain, redness and swelling) were generally similar to other studies in which these symptoms were recorded, although the incidence of generalized rash with fever was higher in the present study, for the reasons already postulated. No pain, redness or swelling symptoms rated as Grade 3 were reported during the present study. Severe pain was either absent or occurred with very low incidence in the previously published studies. In two studies, a notable amount of redness >20 mm (7.5% and 8.2%) was noted in the subjects given the Group 2 vaccine, though none was reported in Groups 1 or 4 in the present study. Swelling >20 mm was also either absent or occurred with low incidence in the subjects who received the Group 2 vaccine in these two studies, and was again absent from Groups 1 and 4 in the present study. Thus, co-administration of MeMuRu and a varicella vaccine did not lead to an increase in local and general symptoms. No cases of parotid swelling or signs of suspected meningism, including febrile convulsions, were observed during the present study.
Previous publications reported that anti-mumps seroconversion rates and GMTs, as well as anti-measles GMTs, were lower in subjects vaccinated with Trivirac,\textsuperscript{14-19} and this vaccine was also less immunogenic against mumps and measles in the current trial. Seroconversion rates and GMTs were similar in Groups 1, 2 and 4 in the present study, and were in accordance with previously published reports.\textsuperscript{1-13} Additionally, the values for seroconversion rate and GMT for varicella in subjects given MeMuRu + a varicella vaccine were similar to those observed after simultaneous but separate administration of the Group 2 vaccine and a varicella vaccine in children aged 12-19 months.\textsuperscript{22}

Other studies in which MeMuRu and a varicella vaccine were administered by separate injections, but given at the same visit, demonstrated the effectiveness of combined MeMuRu and varicella vaccination.\textsuperscript{22-24} The present study showed that the immunogenicities of MeMuRu and a varicella vaccine were not affected or compromised by their co-administration. Varicella vaccination is administered together with an MMR vaccine as part of a routine vaccination schedule in the USA.\textsuperscript{25} Our findings suggest that a varicella vaccine may be concomitantly administered at the same visit as a MMR vaccine such as MeMuRu in European countries and in other regions where an anti-varicella vaccine is not presently administered as part of a routine vaccination schedule.

Although there was variation in the numbers of subjects with serological data available at Day 60, 1 Year and 2 Years, this study provides some information regarding persistence. The persistence of antibodies against measles, mumps and rubella was similar in the Me-

MuRu, MeMuRu + varicella vaccine and Group 2 subjects at 2-years post-administration, with seropositive responses in > 85% of subjects. A similar persistence of antibodies against measles, mumps and rubella has been reported at 1-year after vaccination with MeMuRu or the Group 2 vaccine.\textsuperscript{13} We observed similar rates of persistence of antibodies against measles, mumps and rubella in Groups 1 and 4 as well as maintenance of a high rate of seroconversion and high GMTs for varicella in Group 4.

In conclusion, this exploratory study in 272 healthy children found that the concomitant administration of MeMuRu and varicella vaccines was well tolerated and did not result in any clinically relevant increase in reactogenicity. The reactogenicity and immunogenicity observed was within the same range as that induced by the vaccine administered to Group 2 (MMR alone). The immune response to MeMuRu was not compromised by concomitant administration of a varicella vaccine in the contralateral arm and the immune response to a varicella vaccine was also as expected from this vaccine, suggesting that concomitant administration of a varicella vaccine with a MeMuRu vaccine can be performed in countries where varicella vaccination is not currently part of a routine vaccination schedule.

**ACKNOWLEDGEMENT**

The editorial assistance of Dr. C.L. McCoy is greatly appreciated.

**REFERENCES**


