



SCOTTISH EXECUTIVE

Health Department

Dear Colleague

MMR VACCINE

Colleagues will be aware of renewed media interest in MMR and of the continuing concerns of some parents about the vaccine. Further to the DCMO/CNO/CPO letter issued on 22 December 2000⁽¹⁾, the purpose of this letter is to update you on the latest position about MMR vaccine. The letter covers the following points:

- Latest concerns about MMR
- Recent statements by independent advisory committees and professional bodies
- Preparation of information for health professionals and parents.

The latest concerns

There has been recent publicity given to an article concerning MMR vaccine and alleged long term health problems, especially inflammatory bowel disease (IBD) and autism. The article by Wakefield and Montgomery (entitled *Measles Mumps Rubella Vaccine: Through a glass, darkly*) appeared in the *Adverse Drug Reactions and Toxicological Reviews*⁽²⁾ on 21 January. Media interest has also recently focussed on the use of single antigen vaccines as opposed to the recommended combined MMR vaccine.

Statements by independent expert advisory committees and professional bodies

The Government's independent Expert Committees, the Committee on Safety of Medicines (CSM) and the Joint Committee on Vaccination and Immunisation (JCVI), both reviewed a draft of the article. They advised that the

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For action

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article contains no new data relevant to the safety of MMR vaccine, that its analyses are incorrect and that it has failed to mention other published work that does not support their argument⁽³⁾. A detailed critique can be found at www.doh.gov.uk/mmrresponse.htm. A summary of the CSM meeting held on 10 January 2001 can be found at www.open.gov.uk/mca/mcahome.htm.

The suggested link between MMR and inflammatory bowel disease (IBD) and autism has been thoroughly investigated. In the light of Wakefield and Montgomery's article, the CSM conducted a further detailed review of the information available at the time of MMR licensing from 1972 onwards and the subsequent safety data of MMR vaccine.

The view of both the JCVI and CSM remains that, on the scientific evidence available, there is no causal link between MMR vaccine, autism and bowel disease. This view is supported by the Medical Research Council (MRC) and World Health Organisation (WHO). The British Medical Association (BMA), Royal College of General Practitioners (RCGP), Royal College of Paediatrics and Child Health (RCPCH), Royal College of Nursing (RCN) and the Community Practitioner and Health Visitor Association (CPHVA) have recently issued the following collective statement: "We welcome this positive statement from the Chairs of these Expert Committees about MMR vaccine⁴. MMR is a safe and effective vaccine. By contrast, there is a real concern about having the vaccines separately, since children would be left unnecessarily at risk from these potentially serious diseases. We strongly recommend that children are protected with MMR⁽⁴⁾".

In addition the BMA Scotland, RCN Scotland, Royal College of Physicians of Edinburgh, RCGP Scotland, the Faculty of Public Health Medicine and the RCPCH, have issued a statement⁽⁵⁾ affirming their belief that there is no evidence of any causal link between the combined MMR vaccine and autism and rejecting the introduction of separate vaccines as a retrograde step. They emphasised that the overwhelming weight of scientific evidence on MMR reaffirms its safety while the use of separate vaccines leads to lower take up rates and an increased incidence of measles. It concludes that parents should continue to have their children vaccinated with MMR.


The overwhelming evidence from world-wide experience is that MMR remains the safest way to protect children against these three potentially serious diseases. The safety and efficacy of combined MMR is supported by a great body of evidence while there does not appear to be such evidence on safety and efficacy when the individual vaccines are given separately. Giving children separate vaccines unnecessarily exposes them to the risk of life-threatening infection. The WHO said on 24 January 2001: "WHO strongly supports the use of MMR vaccine on the grounds of its convincing record of safety and efficacy. The combination vaccine is recommended rather than monovalent presentation [single vaccines] when available and the disease burden justifies its use".

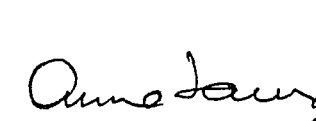
The Health Departments are aware that it has been suggested that the administration of licensed single rubella vaccine to children will allow practitioners to justify the importation of unlicensed measles and mumps vaccines. The UK Health Departments' publication *Immunisation against infectious disease*⁽⁶⁾ advises that rubella vaccine should be used for the protection of sero-negative women, and should not be used for immunisation of infants.


Information for health professionals and parents

The present scare stories clearly worry parents. In order to encourage parents to have their children protected with MMR and to ensure that factually accurate scientific information is available to help professionals assist parents in their decision making, the Scottish Executive is reviewing information resources for both health professionals and the public. Revised leaflets and factsheets are being prepared and will be issued as soon as possible. Posters will also be provided. In addition seminar packs will be provided for Immunisation Co-ordinators to allow them to provide further information to health professionals and answer any questions they may have. We would encourage all those involved in delivering primary care immunisations, including health visitors and practice nurses, to familiarise themselves with the revised material when it becomes available and hope that you will find it helpful. In the meantime, Annex 1 to this letter contains responses to some of the questions most frequently asked by parents and Annex 2 contains some facts and figures. We hope you find this helpful.

Yours sincerely


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- (3) Department of Health Press Release 2001/0027, 12 January 2001
<http://tap.ccta.gov.uk/doh/intpress.nsf/page/2001-0027>; Public Health Link
CEM/CMO/2001/1 (12 January 2001)
- (4) BMA Press Release *Joint professional statement on MMR* 12 January 2001
(<http://web.bma.org.uk/pressrel.nsf>)
- (5) BMA Scotland Press release 8 February 2001 <http://web.bma.org.uk/scotland>
- (6) UK Health Departments: *Immunisation against Infectious Disease*. London: HMSO, 1996

MMR QUESTIONS AND ANSWERS**Q1. General statement on safety of MMR vaccine**

A. The suggestion of an association between measles, measles vaccine, MMR vaccine, inflammatory bowel disease (IBD/Crohn's disease) and autism was made by researchers at the Royal Free Hospital, London, led by Dr Andrew Wakefield. Rigorous scrutiny by a number of independent expert advisory groups has established that the evidence does not support any such association.

Q2. What has the Government done on this concern?

A. The Government has ensured this issue has been thoroughly looked at. The view of our independent expert committees – the Joint Committee on Vaccination and Immunisation (JCVI) and the Committee on Safety of Medicine (CSM) - remains that, on the scientific evidence available, there is no causal link between MMR vaccine and long term health problems such as bowel disease or autism. This view is supported by non-government organisations such as the Medical Research Council (MRC) and World Health Organisation which recognises MMR as being a "highly effective vaccine which has such an outstanding safety record".

Q3. Does MMR cause autism and Inflammatory Bowel Disease?

A. No. Reviews by the CSM, a CSM Working Party, the MRC and the latest report from the MRC's group of experts did not identify a causal link between MMR and Measles/Rubella vaccines, autism and IBD. Such views are further reinforced by a study undertaken by Taylor et al in North Thames region, which found no evidence of a causal link between MMR and autism and also by recently published research from Finland (Patja et al) and the UK (Kaye et al).

Q4. What about the article published in the journal Adverse Drug Reactions and Toxicological Reviews on 21 January 2001 by Wakefield and Montgomery?

A. The Government's independent expert committees have reviewed the paper and have advised that: it contains no new data relevant to the safety of MMR vaccine; its analyses are incorrect; and it has failed to mention published work that does not support the hypothesis that MMR causes inflammatory bowel disease and autism.

Q5. Was MMR vaccine properly tested prior to licensing?

A. Five combined measles, mumps and rubella vaccines have been licensed in the UK. Three of these are still licensed and two are used in the national immunisation programme (Priorix and MMRII). In accordance with the principles of good clinical practice, the majority of clinical trials that supported licensure of these vaccines were sponsored by the company, were conducted by investigators experienced in the field, and were monitored by company personnel.

After careful review the Medicines Control Agency (MCA) rejects any suggestion that combined measles, mumps and rubella (MMR) vaccines were licensed prematurely. The MCA is confident that the licensing process was properly conducted on the basis of safety, quality and efficacy of the vaccines in adequate numbers of children.

Most of the studies enrolled children in the second year of life, although some enrolled children up to 13 years old. Details of adverse reactions were mostly recorded over 4-6 weeks post-injection because children returned for assessment of their response to the vaccines around this time. In clinical trials fewer than 200 children were followed for one year. However, post-marketing reporting of adverse reactions provides much additional information on the safety of these products.

- In 1972 the first measles, mumps and rubella combination vaccine was licensed in the UK (*MMR-I*). Information on protection in nearly 900 previously non-immune children and safety information on about 2,000 children was available.
- *MMR-II* replaced MMR-I in 1987. Detailed safety data were available for more than 800 children who received MMR-II in clinical trials.
- The approval of *Pluserix* in 1988 (not now licensed) was based on data from more than 600 children.
- The approval of *Priorix* in 1997 was based on trials in which almost 6000 children received the vaccine.
- The approval of *Immrvax* in 1989 (licensed but not in use in the UK) was based on clinical studies in which at least 6,400 subjects received the vaccine.

By the time the UK came to introduce MMR in 1988, there had already been substantial use in Scandinavia and the USA. Currently MMR is used in over 90 countries worldwide. Over 500 million doses have been given.

Q6. Has the safety of MMR been looked at in other countries?

A. Research conducted in Scandinavian countries has looked at measles infection and MMR vaccination in relation to reports of autism and Crohn's disease. In common with the latest information from the UK, no causal link was found between measles infection and MMR vaccination and either autism or Crohn's. For example, a study conducted in Gothenburg, Sweden over a ten year period during which time MMR vaccine was introduced into the childhood immunisation programme, showed that the incidence of autism was unaffected by the introduction of MMR.

Q7. Do some children develop autism after vaccination?

A. MMR vaccine is first given between the ages of 13 and 15 months. Autism is frequently diagnosed in the second year of life. This means that purely by chance, some children would have developed their autism around the time of vaccination. It certainly does not mean that MMR causes autism. Expert reviews do not show a cause and effect between MMR and autism.

Q8. Should MMR vaccine be given as 3 separate vaccines?

A. The UK has never recommended three separate injections. We are not aware of any country that recommends single vaccines rather than MMR. The policy is not based on financial considerations but on the best way to protect children. If there were any evidence of

real risk the Health Departments would act immediately. By contrast, separating vaccines puts children at risk and there is no evidence of a benefit over MMR. It is vital for children to be immunised with MMR or these three diseases will return.

Q9. What are the risks in using single vaccines?

- There is no convincing evidence of any additional benefit from using single vaccines instead of MMR.
- There is very considerable evidence for the safety of MMR vaccine. The WHO stated on 24 January 2001: "WHO strongly supports the use of MMR vaccine on the grounds of its convincing record of safety and efficacy. The combination vaccine is recommended rather than monovalent presentation [single vaccines] when available and the disease burden justifies its use".
- Separating the vaccines – it has been suggested, without any scientific evidence, that there should be a gap of at least 12 months between vaccines – leaves children at risk of infection whilst waiting between vaccines.
- Children would be left at risk up to age 3 from either measles (which is potentially a very serious disease) or rubella (with the risk to the unborn child this brings for unprotected pregnant women) or mumps (which, before MMR, was introduced was the main cause of viral meningitis).
- As six injections would be required rather than two, separating the vaccines exposes children to the risks of repeated reactions at the site of injection.

Q10. Can you get single measles and mumps vaccines privately?

A. The importation of unlicensed vaccine when a licensed alternative is available is restricted under the Medicines Act and this restriction applies equally to NHS and private sectors.

Q11. Why are single measles and mumps vaccines not available?

A. Although licenses for single measles and mumps vaccines do exist in the UK, no licensed single measles or mumps vaccines are manufactured for, or available for, the UK market. The MCA has restricted the importation of single measles and mumps vaccines on the grounds that under law, unlicensed medicines should not be imported when a safe and effective licensed alternative which meets a patient's needs – that is, MMR – is available. The MCA was also concerned about the evidence that the single mumps vaccine (Rubini strain) being imported was ineffective and that the mumps Urabe strain was less safe. Neither of these two vaccines can now be imported.

Q12. Other countries

A. No country in the world recommends MMR be given as 3 separate vaccines. MMR is used in 93 countries around the world. Over 500 millions doses have been given worldwide. Single rubella vaccine is available in the UK as it is recommended for women who are not immune. France has been mentioned as a country where single vaccines are given. However, the position is that in France children are given single measles vaccine from 9 months of age **IF** they are in a nursery and there is a risk of a measles outbreak. These children then receive 2 further MMR vaccinations, at the same time as the UK. France does not recommend single mumps vaccine.

Q13. Situation in Japan

A. Japan immunises against measles and rubella separately because they do not have a suitable MMR vaccine. However, Japan has suffered from endemic and epidemic measles. Between 1992-97, there were 79 measles deaths in Japan. There have been no deaths from acute measles in the UK since 1992. There is no recent data on congenital rubella syndrome (CRS) prevention in Japan. Between 1997 and 99, there were no cases of CRS in England and Wales detected through active surveillance.

Q14. MMR vaccine contains 3 viruses in one: is this too much for young children?

A. Evidence shows that babies' and young children's immune systems cope daily, without difficulty, with many different challenges from the wild viruses and bacteria that are found virtually anywhere. In addition, the three vaccines in MMR work at different speeds, so they don't all impact on the child at once. Splitting MMR into separate doses may be harmful because it exposes children unnecessarily to potentially serious diseases.

Q15. Consequences of fall in MMR vaccine uptake

A. MMR vaccine uptake has fallen over the past few years at age two and has now stabilised at around 88% in England which is too low to maintain sufficient levels of protection in the population especially against measles (95% is needed). Uptake in Scotland is higher at nearly 93% but still falls short of the 95% needed to provide sufficient levels of protection in the community. The UK as a whole is very close to the point where serious outbreaks of measles will occur as in Ireland where there have been deaths from measles. Mumps and rubella may not be far behind. Every child who is not immunised is at risk and also increases the risk of a return of these potentially very serious diseases. The latest scientific evidence shows MMR remains the safest way to protect children against these diseases.

Q16. Why is population protection ("herd immunity") important?

A. High population protection is important because if someone incubating measles has contact with others in a community, measles will not spread as the chances of being in contact with someone who is not immune are small. This is an important way of protecting vulnerable children with poor immunity who cannot be immunised, eg children with leukaemia or on immunosuppressive treatments.

Q17. If MMR does not cause autism then what does?

A. Autism is a highly complex but poorly understood mental disorder, the precise causes of which are often difficult to pinpoint. At present the nature of these factors and influences are not known. However, there is much research under way to try to establish answers. The Medical Research Council (MRC) is one organisation which is investing some £6.4m into projects to research autism and its causes.

In addition, further information can be found on each of the following web sites:

www.immunisation.org.uk

www.doh.gov.uk

www.open.gov.uk/mca

MMR KEY FACTS

1. Measles, Mumps and Rubella Seriousa. *Measles*

- Complications in 1 in 15 cases.
- Meningitis/Encephalitis 1 in 1,000
- Deaths 2 or 3 per 1,000 (US 1990s experience).

b. *Congenital Rubella*

- causes birth defects, eg blindness, deafness, mental retardation and heart disease
- pregnant women who catch rubella in early pregnancy have 90% chance baby will have birth defects

c. *Mumps*

- complications include viral meningitis and encephalitis
- commonest cause of viral meningitis in under 15s prior to immunisation
- pre MMR resulted in 1,200 hospital admissions a year in England and Wales

2. MMR Effectivea. *Measles*

1960s - Before vaccination ½ million notifications and 100 deaths each year in UK

1968 - Measles vaccine introduced
 - Measles notification fell to < 100,000 (UK) by 1988; <10,000 in Scotland
 - But still killed 13 children each year up to 1988 (UK)

1988 - MMR introduced (+ MR campaign 1994)
 - Measles notifications fell to <10,000 by 1993 (UK); <3,000 in Scotland
 - and approximately 1 death per year by 1993 in UK

1996 - 2nd dose of MMR introduced – no measles deaths in Scotland from 1996 till present

b. *Congenital Rubella*

1970-79 – 454 cases of congenital rubella births in GB: 15 in Scotland (1976-79)

1980-89 - 333 cases of congenital rubella births in GB: 12 in Scotland

1990-99 – 46 cases of congenital rubella births in GB; 4 in Scotland

3. Two Doses of MMR Needed

- 90% protected by 1st dose with 90% uptake
- 2nd dose protects those not protected by 1st dose and opportunity for those who missed 1st dose to be immunised.

4. Safety of MMR – Main Scientific Evidence

a. Autism

Main evidence refuting link between MMR and Autism

- UK data - study by Taylor et al, Lancet 1999. (Royal Free and CDSC.) Studied immunisation records of approximately 500 autistic children born between 1979-1998. No clustering of onset of concern after MMR given. MMR did not affect age at diagnosis. No sudden “step up” or change in trend after introduction of MMR. Concluded finding did not support a causal association between MMR and autism.
- Taylor found that reports of autism increasing before MMR introduced
- Paper published on 24 February 2001 shows autism continues to rise in recent years despite constant uptake of MMR. Kaye et al BMJ, 24 February 2001

Supporting evidence which does not support a link between MMR and autism (but does not refute it)

- Finnish study (Patja et al, December 2000). 1.8 million individuals immunised with 3 million doses since 1982. No case of inflammatory bowel disease or autism detected during long follow up (1982-96)
- Finnish study (Peltola, Letter to Lancet 1998) (note this paper uses the same dataset as above). Those vaccinees for whom gastrointestinal symptoms reported, traced to check prevalence of autism. Out of 31 children with GI symptoms none developed autism.
- Swedish data shows incidence of autism did not rise over decade when MMR introduced (Gilberg and Heijbel 1998).

- Fombonne, Lancet 1998 – retrospective analysis of 201 autistic children at Maudsley Hospital, London born post 1987 – and likely to have had MMR – none had inflammatory bowel disease (IBD).

b. **Crohn's/Inflammatory Bowel Disease (IBD)/Ulcerative Colitis**

Main evidence refuting link between MMR and (IBD), Crohn's, Ulcerative Colitis

- Numerous laboratory studies failed to find evidence of viral particles in GI tissues (Aszal et al 2000, B.WHO; vol 78)
- Finnish data. Peltola and Heinonen, Lancet 1986. Twin study – double blind, placebo controlled cross over study provides strong evidence of lack of diarrhoea following MMR up to 3 weeks post vaccination.

Supporting evidence

- Incidence of Crohn's Disease started to rise before measles vaccine introduced in 1968 and MMR in 1988
- Eedes, Nottingham 1991. Compared MMR and measles vaccine. No difference in GI disorders between two groups.

5. **Opinion of Expert Groups**

The total body of scientific evidence has been assessed by the following expert groups who have all advised no link between MMR and autism or bowel disease.

- Committee on Safety of Medicines (CSM)
- Joint Committee on Vaccination and Immunisation (JCVI)
- Medical Research Council Expert Group
- Working Party of CSM – detailed evaluation of >100 children's records

Their views endorsed by WHO.

6. **Support for MMR from Professional Bodies**

MMR has support from the following professional bodies:

- RCGP and RCGP Scotland
- RCPCH
- Faculty of Public Health Medicine
- RCP Edinburgh
- BMA and BMA Scotland
- Royal College of Nursing
- Royal Pharmaceutical Society
- UNISON
- SENSE

7. No Other Country Recommends Choice of Single Vaccines

In France measles alone is given to children under 1 year if attending nursery school. They receive MMR as well - 2 doses - at approximately same age as given in UK, ie Measles given as well as MMR in France not instead of it.