SCOTTISH EXECUTIVE

Chief Medical Officer Directorate

HAEMOPHILUS INFLUENZAE TYPE B (HIB) VACCINE FOR YOUNG CHILDREN CATCH-UP PROGRAMME

This letter explains a *Haemophilus influenzae* type b (Hib) vaccination catch-up programme, which will start on 5 November 2007 and continue until 3 March 2009. Following advice from the Joint Committee on Vaccination and Immunisation (JCVI), a Hib booster will be offered to young children who have not previously received one, so that these children are protected in line with older and younger children.

The eligible group includes children born on or between 4 April 2003, and 3 September 2005 who will be aged between two years and two months old and four years and seven months old at the start of the campaign. This cohort of children was too young to have had a booster as part of the 2003 Hib catch-up campaign, and too old to have received the new Hib/MenC booster vaccine at 12 months of age following its introduction in September 2006.

Key features of this campaign are that:

- the Hib booster will be offered as part of the pre-school immunisation programme by temporarily changing the pre-school booster vaccine to one that contains an additional Hib component;
- the current pre-school booster will be temporarily changed to Infanrix-IPV+Hib™ (or alternatively Pediacel™);
- during the course of this campaign, the age at which the pre-school immunisation is offered will be reduced - in areas where this is not already the case - to three years following completion of primary immunisation, that is normally between three years four months and three years six months of age;
- some older children in the cohort, who may have already received their pre-school immunisation, will need to be offered an additional appointment to be offered a Hib-containing vaccine.

From the Chief Medical Officer, the Chief Nursing Officer and the Chief Pharmaceutical Officer

Dr Harry Burns MPH FRCS(Glas) FRCP(Ed) FFPH
Paul Martin, RN RHV DMS MBA
Bill Scott, BSc MSc FRPharmS

St Andrew's House
Edinburgh EH1 3DG
Telephone 0131-244 2264
Fax 0131-244 3477

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For Action
Directors of Public Health
Immunisation Co-ordinators
Consultants in Public Health Medicine
Medical Directors of NHS Boards
General Practitioners
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For circulation to all Occupational Health Departments and Directors of Infection and Prevention Control
Consultant Paediatricians
Infectious Disease Consultants
Clinical Director, Health Protection Scotland
Chief Executive, NHS Health Scotland

Further Enquiries
Jacqueline Campbell (policy)
jacqueline.campbell@scotland.gsi.gov.uk
Margaret Johnston (vaccine supply)
margaret.johnston2@nhs.net
Dr Elizabeth Stewart (medical)
elizabeth.stewart2@scotland.gsi.gov.uk

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An explanation of the rationale of this campaign and further practical details are provided in the Annex to this letter. Information materials will also be provided, as described in Section 16 of the annex. A timeline is also provided at the end of the Annex, which provides a chronological summary of the changes described.

It is recognised that the scheduling requirements of this campaign may vary significantly by area, due to the local variations in the age at which children are offered their pre-school immunisation currently.

Details of the funding and service arrangements are given in Section 14 of the Annex.

We would like to take this opportunity to thank all those who will help deliver the national childhood immunisation programme for your continued and vital efforts in delivering immunisation to children.

Yours sincerely

DR HARRY BURNS
Chief Medical Officer

PAUL MARTIN
Chief Nursing Officer

BILL SCOTT
Chief Pharmaceutical Officer

ANNEX

Haemophilus influenzae type b (Hib) vaccine for young children

1. Background

Haemophilus influenzae type b (Hib) is a serious bacterial infection that can cause meningitis and septicaemia, and sometimes be fatal, especially in young children. Hib vaccine was first introduced into the routine childhood immunisation programme in 1992 for infants at two, three and four months of age, along with a catch-up programme. As a result, the rates of Hib disease fell dramatically.

In 2003, a catch-up campaign offered a booster dose of Hib vaccine to all children who were aged six months to four years old at that time. That campaign successfully met its aim of reducing the small but steady increase in cases of Hib disease in young children that had occurred since 1999. However rates of Hib disease in children have not yet returned to the very low levels seen in the mid 1990s.

Studies have shown that protection from the primary schedule of three doses of Hib vaccine wanes during infancy. A booster dose of Hib vaccine was, therefore, introduced into the routine childhood immunisation programme, on 4 September 2006, for all children at 12 months of age (as combined Hib/MenC vaccine). This booster extends protection against Hib infection through childhood and is expected to further lower rates of Hib disease.

Children born on or between 4 April 2003 and 3 September 2005 will not have been offered a Hib booster dose. They were too young to have had a booster as part of the 2003 Hib catch-up campaign and are too old to have received the new Hib/MenC booster vaccine at 12 months of age. This cohort of children will have lower levels of immunity against Hib compared to children who have had a Hib booster. It is estimated that UK-wide this additional Hib booster could prevent about thirty cases of Hib disease in this cohort.

JCVI has recommended that this cohort of children should be offered a Hib booster to protect them further through childhood, in line with the protection already offered to older and younger children. To minimise disruption, the Hib booster will be offered as part of the pre-school immunisation whenever possible.

2. Summary of campaign

- The cohort targeted will be children born on or between 4 April 2003 and 3 September 2005;
- The campaign will start on 5 November 2007 and will continue until 3 March 2009;
- Any older children in the cohort who may have already received their pre-school immunisation should be offered an additional appointment to receive the Hib/MenC vaccine (Menitorix™);

- Children who have not received their pre-school immunisation - the main body of the cohort - should be offered a Hib-containing pre-school booster at the time of their pre-school immunisation;

- The current pre-school booster will, therefore, be temporarily changed from DTaP/IPV (Infanrix IPV™) or dTaP/IPV (Repevax™) to DTaP/IPV/Hib, given as Infanrix-IPV+Hib™ (or alternatively as Pediacel™);

- The second dose of MMR will continue to be given with the pre-school booster.

- By the end of the campaign at the latest, and thereafter, all children should be routinely sent an appointment for their pre-school immunisation three years following completion of primary immunisation that is normally between three years and four months of age to three years and six months of age;

- In NHS Boards where children are currently offered their pre-school immunisation at a later age, Boards will need to bring forward the age at which children are invited in a phased manner during the campaign.

- Children who receive their third dose of the primary immunisation series later than recommended should have their pre-school immunisation with a minimum one year gap from the third primary immunisation, in accordance with the advice in the 2006 edition of *Immunisation Against Infectious Disease* (page 114, 282, 318, 371).

3. Explanation of the schedule

Providing a Hib booster at the pre-school immunisation visit, rather than separately, should help ensure high vaccine coverage. This arrangement will also help minimise additional work in primary care, as children will be given the Hib booster at the same time as their routine pre-school vaccinations and will not need an additional appointment or injection.

As the age at which the pre-school immunisation is currently offered varies by NHS Board, the implementation will have to be tailored accordingly at local level. Local planning for the implementation of this campaign is discussed further in Section 5.

Children who have already received their pre-school immunisations
A number of the older children in the cohort may have already attended for their pre-school immunisations. These children need an additional appointment so that they can be offered a Hib-containing vaccine.

Standardisation of the age at which children are offered their pre-school immunisation

'*Immunisation Against Infectious Disease* 2006' recommends that the pre-school booster is given three years after completion of primary immunisation, that is at three years and four months of age, or soon after.[1]

Almost all primary immunisations are completed by six months of age, therefore it is recommended that scheduling for pre-school booster vaccinations is standardised to three years and four months to three years and six months of age. This is in line with the recommendations in '*Immunisation Against Infectious Disease 2006'*, but is also a necessary part of this campaign, as explained below.

Reducing the age at which pre-school immunisation is offered is a necessary part of this campaign. If children are offered a pre-school immunisation at four and a half years of age, as is currently the case in some areas, the youngest children in the cohort would not receive their pre-school immunisation, and therefore their Hib booster, until 2010.

If the age at which the pre-school immunisation is offered is reduced in all NHS Boards, during the course of the campaign, to three years and four months, or soon after, then, by 3 March 2009,[2] all children in the cohort should have been offered a Hib booster.

This avoids a considerable delay or a separate catch-up campaign involving additional clinic visits and an additional injection for many children.

A locally phased campaign
In those NHS Boards not currently offering pre-school immunisation at the earlier age, this change may need to be introduced in a phased manner during the course of the campaign, as it involves the bringing forward of appointments for a substantial proportion of the cohort. It is, however, recommended that the bringing forward of the age at which pre-school immunisation is offered is carried out as soon as possible. This will allow earlier protection for more children in the cohort.

It is acknowledged that this aspect of the campaign will require a temporary increase in the size and/or number of clinics provided for childhood immunisation, though there will be no overall increase in the number of immunisation appointments required. By July 2008 it is recommended that the pre-school booster should be routinely offered to all children before their fourth birthday.

Any enquiries about the new schedule should be addressed to NHS Boards Immunisation Co-ordinators in the first instance. Immunisation Co-ordinators should

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[1] When primary immunisation has been delayed, the pre-school booster may be given at the scheduled pre-school immunisation visit, as long as this is at least one year since completion of primary immunisation.

[2] 3 March 2009 has been chosen as the end date for the campaign as this is the point by which the youngest children in the cohort would become three years six months old, by which time the vast majority of these children – except those whose primary immunisation has been delayed - should be eligible for their pre-school immunisation.

address queries to katherine.sinka@hps.scot.nhs.uk or elizabeth.stewart2@scotland.gsi.gov.uk.

4. Vaccines to be used

Children who have already received their pre-school immunisations
Children who have already received their pre-school immunisations should be offered a further vaccination with Hib/MenC (Menitorix™).

Single antigen Hib vaccines are not currently available and therefore Hib/MenC (Menitorix™) should be offered. Although the purpose of the campaign is to offer a Hib booster, the additional Men C component of Menitorix™ may offer some additional benefit to those children receiving it.

The main body of children in the cohort
The majority of children in the cohort will not yet have received their pre-school immunisations. For these children, the current pre-school booster will be temporarily changed from DTaP/IPV (Infanrix IPV™) or dTaP/IPV (Repevax™) to DTaP/IPV/Hib, given as Infanrix-IPV+Hib™ (or alternatively as Pediacel™).

We strongly recommend that preference is given to use of Infanrix-IPV+Hib™ for this campaign. Greater stocks of Infanrix-IPV+Hib™ are currently available for this use, and it is important that stocks of Pediacel™ be conserved for use in primary immunisation.

Please note that Infanrix-IPV+Hib™ should not be used for primary immunisation. Pediacel™ will continue to be used for this purpose.

'Off-label' use of vaccines
The manufacturer's Summary of Product Characteristics (SPC) for Infanrix-IPV+Hib™ gives an upper age limit of 36 months of age (and the SPC for Pediacel™ states an upper age limit for booster use as the fourth birthday). The SPCs do note that use of these vaccines should be in line with official national recommendations.

This use of these vaccines above their age limits is outside of the specifications in the manufacturer's SPC ('off-label'). The advice in this letter, which is based on an expert review and endorsed by JCVI, takes precedence over the specifications in the SPCs. Such circumstances are discussed on page 25 of '*Immunisation Against Infectious Disease* (2006)'.

The expert group has carefully considered the available data, including experience elsewhere in the world where similar vaccines are used in children of these ages, noted that Pediacel™ is frequently used 'off-label' in cases of uncertain or incomplete immunisation, and also carefully considered the issue discussed in Section 11.

JCVI advice is that the use of these vaccines 'off-label' is clinically appropriate. Further information concerning this advice will be provided with the Q&A (see Section 16) and can be found on the JCVI website at www.advisorybodies.doh.gov.uk/jcvi.

5. Planning the schedule for the campaign locally

As the age at which different areas currently schedule pre-school immunisations varies, the scheduling requirements for this campaign therefore need to be clarified locally.

To help in planning, NHS Boards will need to:

1. Assess the number of children in the cohort who will have received their pre-school immunisations before the start of the programme. The number of children in this group should be small for the majority of NHS Boards;

2. Provide, if necessary, extra immunisation capacity and establish the number of extra Menitorix*™* vaccine doses that may need to be ordered.;

3. Assess the number of children that form the rest of the cohort, i.e. those who have not received their pre-school immunisations. This is the majority of the cohort;

4. Assess the likely pace at which the age of pre-school immunisation can be lowered, based on the capacity of general practices to provide the necessary (temporary) additional clinic capacity.

6. Pharmacy issues

The comments in the final part of Section 4, regarding the ‘off-label’ use of Infanrix-IPV+Hib™ and Pediacel™ should be noted.

Thiomersal is not present in Infanrix/IPV+Hib™, Pediacel™ or Menitorix™

Infanrix-IPV+Hib™ (DTaP/IPV/Hib) vaccine is manufactured by GlaxoSmithKline.

Presentation
Infanrix-IPV+Hib**™** is supplied as a single dose pre-filled syringe and vial. The DTaP/IPV portion is presented as a slightly milky liquid in the pre-filled syringe. The Hib portion is presented as a powder in the vial. There are two separate needles included in the pack - a green needle (21g x 38 mm) for reconstitution and a blue needle (23g x 25 mm) for administration. Instructions for reconstitution of the vaccine are given in Section 7 of the package leaflet.

The vaccine is provided as a single dose pack.

This vaccine should <u>not</u> be used for primary immunisation.

Dosage
A single dose of 0.5ml should be given when a child is eligible for their pre-school booster, i.e. at least three years after completion of primary immunisation.

Pediacel™ (DTaP/IPV/Hib) is manufactured by Sanofi Pasteur MSD.

Presentation
Pediacel™ is supplied as a suspension in a single dose vial. The vial should be shaken well before the vaccine is drawn up in a syringe for administration.

The vaccine is provided as a single dose pack.

Dosage
A single dose of 0.5ml should be given when a child is eligible for their pre-school booster, i.e. at least three years after completion of primary immunisation.

This information does not alter guidance regarding primary immunisation using Pediacel.

Menitorix™ (Hib/MenC vaccine) is manufactured by GlaxoSmithKline.

Presentation
Menitorix is supplied as a vial of white powder and a 0.5ml pre-filled syringe containing a clear colourless solvent. It is supplied with two separate needles, a green needle (21g x 38 mm) for reconstitution and a blue needle (23g x 25 mm) for administration. Instructions for reconstitution of the vaccine are given in Section 7 of the package leaflet. The vaccine is provided as a single dose pack.

Dosage
A single dose of 0.5ml should be given to those children who have already received their pre-school booster and need to be recalled to be offered a Hib antigen-containing vaccine.

This information does not alter previous guidance regarding giving the Hib/MenC booster at 12 months of age using the same vaccine.

7. Vaccine supply

Supplies of Infanrix-IPV+Hib™ and Menitorix™ should be ordered from the vaccine holding centres in the usual manner.

Pediacel™ is also available to order in the usual way, although you are reminded that preference should be given to the use of Infanrix-IPV+Hib™ for pre-school immunisation. As noted in Section 4, although the use of either Infanrix-IPV+Hib™ or Pediacel™ is acceptable, we recommend that preference is given to Infanrix-IPV+Hib™. Stocks of Infanrix-IPV+Hib™ are currently available and it is important that stocks of Pediacel™ be conserved for use in primary immunisation.

Any vaccine supply queries should be addressed to the vaccine holding centres in the first instance. Vaccine holding centres should address supply queries to Margaret.johnston2@nhs.net.

8. Vaccine stock management

Please review the amount of Repevax™ and Infanrix IPV™ being held locally. If possible, stocks of these vaccines should used by the start date of the campaign. Any remaining supplies of Repevax™ and Infanrix IPV™ should be held under cold chain conditions and the vaccine holding centre should be contacted for further advice.

9. Consumables

Needles will need to be ordered to administer Pediacel™ vaccine and should be obtained in the usual manner.

10. Administration

Vaccines are routinely given intramuscularly into the upper arm of older children. This is to reduce the risk of localised reactions, which are more common when the vaccine is given subcutaneously. For individuals with a bleeding disorder, however, vaccines should be given by deep subcutaneous injection to reduce the risk of bleeding.

These vaccines must not be mixed as a single injection with any other concurrently administered vaccine.

11. Reporting of adverse reactions

Infanrix-IPV+Hib™, Pediacel™ and Menitorix™ vaccines all carry a black triangle symbol (▼). This is a standard symbol added to the product information of a vaccine/medicine during the earlier stages of its introduction to encourage reporting of all suspected adverse reactions.

Doctors, nurses, pharmacists or parents can report a suspected adverse reaction to the Commission on Human Medicines (CHM) using the Yellow Card spontaneous reporting scheme (www.yellowcard.gov.uk).

Vaccines containing acellular pertussis (aP) antigens generally cause fewer adverse reactions than those containing whole cell pertussis. However, booster doses of aP vaccines, *if they follow primary immunisation with an aP vaccine,* have been associated with an increased risk of extensive local limb swelling. Although this may occur with a fourth aP dose, as is the case in the UK, it is thought to be more common when giving a fifth dose of an aP containing vaccine, as occurs elsewhere in the world.

The first children to have routinely received primary immunisation with an aP-containing vaccine, Pediacel™, will become eligible for their pre-school immunisation in the latter part of 2007. It is, therefore, expected that after this time some children who have received primary immunisation with Pediacel™ may develop transient limb swelling reactions following pre-school immunisation with Infanrix-IPV+Hib™ (or Pediacel™). It is important to note that such reactions would also be expected in these children after receiving Repevax™ or Infanrix IPV™.

These reactions usually develop within 24 hours of vaccination and resolve, without sequelae, within around five days. If a child presents with signs of extensive limb swelling following pre-school booster vaccination, it is important to carefully consider whether this may be a recognised injection site reaction, rather than caused by local infection.

Cases of limb swelling reported in the UK so far in association with Repevax™ or Infanrix IPV™ have ranged from redness and swelling up to several inches around the injection site to swelling from shoulder to elbow. Several cases have presented with blistering around the site of swelling. In up to 20% of cases of extensive local swelling, the children have been given systemic antibiotics in the absence of obvious laboratory or other evidence of infection. A presumptive diagnosis of cellulitis has also been reported in several cases. Based on the information available, it is assumed that, due to unfamiliarity with this kind of local reaction, these cases have been incorrectly diagnosed and treated as infections as a precaution.

Further details are available from the MHRA website: www.mhra.gov.uk ('Local reactions associated with pre-school d/DTaP-IPV boosters', 20 Jan 2006).

12. Data issues

The temporary addition of a Hib booster to the pre-school immunisation programme for this cohort of children will impact on SIRS. The functionality of the SIRS system will be amended to support the new vaccine schedule.

13. Patient Group Directions

Patient Group Directions (PGDs) may be used for licensed vaccines being used outside the specifications of the manufacturers' Summary of Product Characteristics (SPC) ('off-label' use). PGDs for Menitorix™ and Pediacel™ are currently in use and may require amendment for this campaign.

A template PGD for the use of Infanrix-IPV+Hib in this campaign will be provided as part of the information materials described in Section 16.
The use of Patient Group Directions (PGD) is described in detail in '*Immunisation Against Infectious Diseases* 2006 (page 35 to 39), available at www.dh.gov.uk/greenbook.

14. Funding and service arrangements

Vaccine costs will be met centrally.

Payments to contractors

There will be no in-year amendment to the Childhood Immunisation Scheme Directed Enhanced Specification (DES) for 2007.

Where the delivery of the HiB catch-up results in children being recalled for an additional immunisation visit, payments will be made to contractors through a separate (national) Directed Enhanced Service (DES). This is different from the arrangements in place in England, where payments will be made through Local Enhanced Services.

A circular will be issued by the Primary and Community Care Directorate later this month describing these arrangements.

15. Consent

Consent must be obtained before administration of all vaccines. Further guidance is given in '*Immunisation Against Infectious Diseases* 2006 (pages 7 to 15) available at www.dh.gov.uk/greenbook. There is no legal requirement for consent to be in writing.

Health professionals involved in immunisation must ensure that:
- parents/carers should have access to information about the new vaccine
- that there is sufficient opportunity for them to discuss any issues arising
- and that they are properly informed of the benefits of the new vaccine, the possible side effects and how to treat them.

16. Information for parents and healthcare professionals

To support the Hib booster campaign, NHS Health Scotland will produce a leaflet for parents, and a Q&A factsheet for professionals.

Sample copies of the leaflet and factsheet will be sent to general practices, community pharmacies, health promotion departments, NHS24 call centres and local immunisation co-ordinators in October. These resources should be shared with the primary care teams involved in giving and advising about immunisation. GPs should order the required quantities of the parent leaflet from their local health promotion department as with other immunisation resources. These should then be distributed by the local SIRS departments or GPs, in line with existing local arrangements, to the relevant cohort, alongside the regular publication *Pre-school immunisations: a guide to vaccinations for 3 to 5 year olds,* where appropriate.

Copies of these resources can be ordered from your local health promotion department or from publications@health.scot.nhs.uk. They will also be available to view and download from www.healthscotland.com/immunisation.

Hib booster 2003- 09 timeline