International Coordinating Group (ICG) on Vaccine Provision for Epidemic Meningitis Control. Report of the Sixth Meeting

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World Health Organization
Department of Communicable Disease Surveillance and Response

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Summary Report of the Sixth Meeting of the International Coordinating Group (ICG) on Vaccine Provision for Epidemic Meningitis Control
1. Opening Address and Introduction to the objectives of the Meeting and Adoption of the Agenda (Annexes 1 & 3)

The sixth meeting of the International Coordinating Group on Vaccine Provision for Epidemic Meningitis Control (ICG) was held on 20 and 21 September 2000 at the Hotel Meridien, Heliopolis, Cairo at the invitation of the WHO Regional Office for the Eastern Mediterranean.

Dr Hussein Al-Gezairy, the WHO Regional Director welcomed the participants. In his opening address Dr Al-Gezairy described the achievements of the ICG since its inception in 1997 and emphasized the effective collaboration of many partners including commercial industry. Dr Al-Gezairy recognised the role of the ICG in responding to outbreaks in Sudan and finally, reminding the meeting of the power of immunisation as a tool in disease prevention, looked forward to the development of an effective conjugate meningococcal vaccine for use in routine programmes.

Dr B. Sabri, Director of Health Care Delivery, WHO/EMRO chaired the opening session and began by outlining the objectives of the meeting:

- to review the last year’s experience of epidemic meningitis: epidemiology, response actions and any lessons learned;
- to report on the relevant activities of the ICG partners and update on any new developments in related areas of operational research;
- to review the state of preparedness for the 2000/2001 epidemic meningitis season;
- to make recommendations on the continuing operation of the ICG and its partners responding to epidemic meningococcal meningitis.

The preliminary agenda was adopted by the meeting. During periods of the meeting when Dr Sabri would be unable to be present it was agreed that Dr E. Tikhomirov, WHO/HQ would chair the meeting.

2. Regional reports on the implementation of the Regional Plan for Preparedness and Control of Epidemic Meningitis (Annex 4)

Representatives from the WHO Regional Office for Africa, and the WHO Regional Office for the Eastern Mediterranean, presented progress in the implementation of the regional plans for preparedness and control of epidemic meningitis in their regions.

WHO Regional Office for Africa (AFRO)

(Dr A. Yada)

Epidemic preparedness and response for meningococcal disease is part of the overall plan for epidemic preparedness and response for AFRO.
Beginning with the West African countries in 1996, AFRO has defined six sub-regional blocks based on epidemiological and geographical coherence: West, Central, Southern, Horn, Great Lakes and Islands. The countries of each block have committed themselves at ministerial level to adopting a sub-regional plan of action that includes the strengthening of national surveillance systems and intercountry cooperation. WHO AFRO is supporting the sub-regional blocks through establishing sub-regional teams providing technical support and through the implementation of its programme on integrated disease surveillance (IDS).

WHO/AFRO maintains a central database of weekly reports from countries of the meningitis belt during the meningitis season.

In 2000 technical support in responding to epidemics of meningococcal disease has been provided to Chad, Benin, Rwanda and Ethiopia. Technical support can also involve the areas of epidemic preparedness (including contingency stocks), epidemic response and evaluation of interventions.

**WHO Regional Office for the Eastern Mediterranean (EMRO)**

(Dr E. El Samani)

Meningococcal disease is given great attention in the Eastern Mediterranean Region because Sudan, a large country with some 28 million population lies within the African Meningitis belt and experiences recurrent large epidemics. The 33 000 plus cases in 1999 were followed this year by more limited outbreaks resulting in 4031 cases and 328 deaths being reported. Other EMR Member States, Egypt, Morocco, Tunisia and Yemen, have experienced epidemics in the past.

The annual pilgrimage to the holy sites of Islam in the Kingdom of Saudi Arabia often coincides with the meningitis season of the African Meningitis Belt leading to concerns over disease transmission amongst both the crowded pilgrims and the Saudi nationals.

Over recent years some areas of the Eastern Mediterranean Region have seen changes that may favour the spread of meningococcal disease with unplanned urbanization and growing populations of refugees and displaced persons.

EMRO is working with Member States to develop national plans for epidemic preparedness and response and carries out missions to provide technical support. Laboratory diagnostics is being strengthened and links established with the WHO Collaborating Centres.

The dissemination of surveillance information is being improved through the introduction of a specific format for the monthly updating by Member States of weekly disease rates.

Within the Region a number of national authorities include immunisations as part of their efforts to prevent meningococcal disease: the Saudi Arabian authorities vaccinate all Hajis who can not provide evidence of recent meningococcal vaccination and undertake mass vaccination of the Saudi population every three years. Other Member States
selectively vaccinate high risk groups: school children, military recruits, travellers and
the contacts of meningitis cases.

Outside of that used in acute epidemic response 9.7 million doses of vaccine were used
in 1999-2000. A larger demand is anticipated for the coming year with Sudan requesting
12.5 million doses to continue to vaccinate those elements of the population not covered
in the epidemic response over the last two years. In addition five Member States have
indicated that they would require small amounts of the quadrivalent vaccine: more
expensive and in much shorter supply than the bivalent vaccine.

Discussion
Several participants were concerned to understand the advice offered to countries
regarding the holding of national preparedness (contingency) stocks of vaccine at the
country level. At present countries are encouraged to maintain small stocks for use in the
immediate response to an epidemic while awaiting the arrival of more substantial
amounts from the ICG stocks or elsewhere. A number of questions over these stocks
remain unanswered:

What is the appropriate size of the stock?
How to deal with stocks that are approaching expiry?
A number of suggestions have been made: for example stocks could be 10% of the total
target population for mass vaccination campaigns and that stocks could be held with the
manufacturers to avoid expiry problems. However there is a lack of clear guidance from
any authoritative source on this issue and this should be taken up in the meeting
recommendations.

Although many countries target the population aged between 2 and 30 years during mass
vaccination campaigns, in practice vaccination can rarely be refused to those not falling
within this age group.

The usefulness of sharing the weekly surveillance information with other partners was
pointed out.

3. Reports from the ICG Executive Sub-Group (Annex 5)

a. International Federation of Red Cross and Red Crescent Societies
(IFRC)

(Dr B. Hersh)

The IFRC is a federation of 176 national societies. The secretariat in Geneva co-
ordinates the activities of the national societies which include over 105 million volunteers
and members and nearly 300,000 employees. The federation is concerned with the
development of national societies and the peace time coordination of relief work
following natural and technical disasters, as distinguished from its sister organization the
International Committee of the Red Cross and Red Crescent which is concerned with
situations of armed conflict. The national societies act as an auxiliary to the national health services focusing on health promotion and disease prevention in priority health problems as well as disasters including epidemics.

In 1999-2000 the IFRC was involved in responding to meningococcal epidemics in Benin, Cameroon, Chad, Central African Republic and Niger. An evaluation of these activities in Yaounde, Cameroon in June highlighted the following points as contributing to delayed response to epidemics:

- Late declaration by national authorities;
- Incomplete epidemiologic data;
- Incomplete/absent vaccination plans;
- Sub-optimal Red Cross/Red Crescent participation in ICG;
- Administrative delays in vaccine procurement (“Geneva lag-time”)

This last was to be addressed by establishing an outbreak response fund in Geneva so that activities could be implemented without waiting for the resources to be mobilised.

b. Médecins Sans Frontières (MSF)

(Dr F. Varaine)

Interventions by MSF in response to epidemics of meningococcal disease in 2000.

Technical and logistical assistance including the provision of vaccine and injection material was given to 4 African countries:

- Angola (MSF Belgium and France) 158,750 doses
- Niger (MSF France) 1,825,000 doses
- Central African Republic (MSF Spain) 320,000 doses
- Chad (MSF Belgium) 2,570,000 doses

In total 4,873,000 doses were delivered through MSF to these countries.

In following up on the recommendations of the 5th Meeting of the ICG in December 1999 MSF has carefully undertaken systematic evaluation of the epidemic responses. With Epicentre, MSF has undertaken a review of studies on the epidemic threshold. MSF has carried out an evaluation of the materials used in mass vaccination campaigns in order to make recommendations regarding their quality.

c. United Nations Children Fund (UNICEF)

(Dr A. Paganini/Dr J-M. Ndiaye)

UNICEF has been involved in procuring emergency materials for a number of countries experiencing epidemics of meningitis and the organization has been able to participate effectively in the ICG Executive Sub-group. This has raised the profile of meningitis and epidemic preparedness in UNICEF which is now considering mechanisms for providing
additional training to UNICEF personnel, national authorities and NGOs in preparing for and responding to epidemics.

These activities should not be vertical or disease specific but should link to and strengthen existing systems: for example responses requiring immunisation should be linked to the existing EPI programmes and to the GAVI initiatives to improve immunisation services in a number of countries.

d. **World Health Organization (WHO)**

(Dr. M. Hardiman)

Up until July there have been 36,384 cases and 3,770 deaths due to meningococcal disease reported to WHO in 2000. This is less than last year when the numbers were dominated by the large epidemic in Sudan which alone reported more than 33,000 cases. In the African Meningitis Belt widespread epidemics have occurred in Niger, Chad, the Central African Republic, more localised outbreaks in Benin, Ethiopia and Sudan. Outside of the Belt there have been recent localised outbreaks of meningococcal meningitis in Angola and Rwanda and there was a significant outbreak this year in Saudi Arabia associated with the Haj season.

Vaccine has not been in shortage over the last season and the ICG emergency stocks have only been called upon in three of the epidemics: Chad, Niger and the Central African Republic. The emergency stock of vaccine remains at a similar level to previous years: around 7.5 million doses. The stock of autodisable injection materials has been allowed to decline to a level of approximately 50% of that of the stock of vaccine. There are two reasons for this: firstly that in an emergency additional autodisable injection materials can be obtained quickly, and secondly many orders for vaccine from the ICG stocks are “bundled” with autodisable injection materials from non-ICG sources. It is important to stress that the differential in size of the stock in no way indicates a reduction in the ICG’s commitment or ability to “bundle” vaccine with safe injection materials.

The ICG Executive Sub-group has functioned effectively over the last year with consistent participation from all four partners. The collective decision making regarding the release of emergency stocks continues to work well using e-mail. The Group has met in Geneva on three occasions over the last year and produced two issues of the ICG Newsletter. In addition to the sharing of information and coordination of international response activities, the main issues addressed by the Sub-group this year have been:

- Quality of materials used in responses; MSF have evaluated the materials used in Sudan in 1999 and the ICG wants to apply the lessons learnt from this experience.

- Borrowing from ICG stocks; a process has been established which works to the benefit of manufacturers, the ICG and purchasers of vaccine.

- The need to replicate the effective role of the ICG in coordination at the international level at regional and particularly country level.
• To continue to provide “added value” to the emergency response to meningococcal epidemics, including supply issues outside of times of acute vaccine shortage.

Discussion:
The need for international responses to an epidemic to be delayed until the official declaration of the epidemic by national authorities was questioned. In most circumstances, where a country has a functioning national authority, the ICG partners only act upon the invitation of the national authority and it is therefore important that epidemics are officially acknowledged as early on as possible.

Dr Hersh reassured the meeting that the outbreak response fund being established in the IFRC was simply an immediately available source of funds and not a stockpile to replace or duplicate the ICG stocks.

On the issue of quality of response materials the need for training in the use of autodisable injection material was raised. It was agreed that health care workers became skilled at using these materials quite quickly and that training in safe injection techniques was the responsibility of the national EPI programmes. Becton-Dickinson produce training materials describing how to use their brand of autodisable syringes.

4. Reports from countries on 1999/2000 meningitis season (Annex 6)
a. Niger

(Dr Mamoudou Djingarey)

The significance of meningococcal disease to the country of Niger which lies in the middle of the African Meningitis Belt was described. The epidemic of 1994/95 caused over 43 000 cases and nearly 3 800 deaths.

So far in 2000 there have been 13 922 cases reported and 1 008 deaths. This year’s epidemic occurred in the two western departments of Tillabéri and Dosso (including the capital, Niamey) and in one district of the neighbouring department of Tahoua. The highest attack rates had been in Niamey. A National Epidemic Management Committee had been established in 1998 with the functions of:

• The elaboration and implementation of the national intervention plan;
• To coordinate the partners in epidemic management;
• To update standard treatment sheets when necessary;
• To study epidemic trends;
• Rapidly investigate any epidemic focus;
• To evaluate epidemic interventions.

Based on population estimates a need for 4 761 474 doses of vaccine and 71 626 vials of
oily chloramphenicol was identified. There were existing stocks of 570,000 doses of vaccine and 14,360 vials of chloramphenicol in the country, following the appeal for international assistance totals of 4,596,900 doses of vaccine (96% of estimated need) and 35,800 vials of chloramphenicol (50% of estimated need) were reached.

The following have been identified as strengths of the epidemic response:

- Pre-positioning of stocks;
- Surveillance;
- Public information;
- Vaccination and treatment free of charge;
- Weekly meetings of National Committee;
- International mobilisation through WHO Representative (WR)/Niger;
- Plan of action prepared in advance.

The following weaknesses were identified:

- Timeliness of surveillance data;
- Laboratory training;
- No national budget line for epidemic response;
- Co-ordination of arrival of supplies;
- Information on the vaccination status of individuals and communities.

To address some of these weaknesses a budget line has been established for 900,000,000 CFA and the international partners (including ICG sub-group representatives) will be invited to participate in the National Epidemic Control Committee. A plan to routinely vaccinate populations identified as “high risk” will be implemented.

Discussion:
The problem of how to make best use of remaining stocks of vaccine was raised: in Niger these may be used for the routine vaccination referred to above.

b. Saudi Arabia

(Dr Amin Mishkas)

Meningoccal disease has a special significance in the Kingdom of Saudi Arabia because of the several millions of pilgrims visiting the country every year often from countries with high endemic levels of meningococcal disease. Surveillance for infectious diseases has a long history in the Kingdom and since 1933 meningitis has been included in the surveillance system. Vaccination against serogroup A meningococcal disease began in 1975, bivalent A&C vaccine was introduced in 1986 and its use intensified in 1992 with annual vaccination for all people living in “high risk” areas (main pilgrimage sites) or in a “high risk” group. The outbreak in 2000 was the largest since 1989. So far there are 304 cases reported, 90% in people originating from outside the Kingdom of Saudi Arabia. 98 cases (32%) are confirmed as associated with *Neisseria meningitidis* serogroup W135 and 64 cases (21%) as serogroup A.

The control measures undertaken in response to the outbreak were:
• Intensify surveillance.
• Analysis of epidemiological data to guide control measures.
• Implement vaccination campaigns at:
  
  - Vaccination Centres:
    The area around the Holy Mosque (148 000 vaccinated)
    Hajis residential areas. (475 000 in Mecca, 162 000 in Medina
    and 375 000 at ports of entry to the Kingdom)
  
  - Identification and vaccination of defaulters

The outbreak was felt to have been effectively controlled but there remained a question
of how the international community should respond to this unusual outbreak involving
a serogroup not covered by the widely used A&C polysaccharide vaccine. The alternative
vaccine which includes 4 serogroup antigens is available in very limited quantities and
much more expensive.

Discussion:
Participants deferred the wider discussion of the implications of the serogroup W135
outbreak until the agenda item dealing with this issue.

It was questioned whether this outbreak of 304 cases should be described as an
“epidemic”, although the incidence of disease by no means reached the thresholds
established for detection of epidemics, these thresholds have been developed specifically
for use in countries of high endemicity in the African Meningitis Belt. Using the more
general definition of an epidemic being a grouping in time and place of an unusually high
level of disease the outbreak described could be considered an epidemic.

The cost effectiveness of using chemoprophylaxis in case contacts and Hajis was
questioned; in the Saudi Arabian situation a single dose of ciprofloxacin is used. Late
presentation of some cases, particularly amongst Hajis, was thought to be responsible for
the high case fatality rate noted during the outbreak. It was suggested that the
examination of the vaccination history of cases might provide useful insights into
effective prevention of disease.

c. Sudan

(Dr Ahmed El Tigani)

In 1998/99 Sudan had experienced the largest epidemic there since 1988/89, over 33 300
cases and 2 400 deaths were reported from that year. It was anticipated that there would
be further epidemics in 2000. A localised epidemic occurred in the south of the country
around the town of Juba in Bahr el Jebel State and smaller outbreaks reported from White
Nile, South Kordofan and Sennar States. These epidemics have resulted in around 4000
cases and 350 deaths so far this year.
10.7 million people were vaccinated in response to the epidemic in 1999 out of a total population at risk of 24.3 million. The Federal Ministry of Health wishes to continue vaccination to provide cover for the remaining population at risk. Currently the country has about 3 million doses of vaccine but only about 360,000 units of autodisable injection equipment.

Discussion:
It was noted that all 3 of the countries presenting on this agenda item practised some form of routine vaccination and it was suggested that this was carried out in the absence of clear epidemiological evidence for the effectiveness of such vaccination in preventing epidemics. The meeting was called upon to make a clear statement warning that such practices might divert resources from interventions with proven benefit. Some of the participants expressed the view that the routine vaccination of high “risk groups” (e.g. school children and military recruits) was justified and that countries should not be discouraged from this practice. The meeting agreed that the coverage achieved by the routine interventions described so far would not prevent epidemics, though would provide individual protection for an uncertain period for those vaccinated.

The uncertainty over the size and nature of emergency stocks was raised again in the context of Sudan’s request for 12 million doses of vaccine for the year 2000.

Treatment with oily chloramphenicol requires the administration of quite large volumes of drug by intra-muscular injection, the manufacturers were asked if any progress had been made in increasing the concentration of the drug in the vials to reduce the volume needed. It was explained that this was not feasible as any increase in the concentration of the drug would exacerbate problems of the drug precipitating out of its emulsified state and forming a sediment, making it very difficult to administer.

5. Epidemic meningitis Vaccines for Africa (EVA) Project update (Annex 7)

(Dr Luis Jodar)

The EVA project is a multi-partner initiative with the aim of developing and implementing an affordable conjugate meningococcal vaccine in Africa. The background to the project was outlined under the following headings:

a) The problem

The cyclic epidemics and their associated morbidity and mortality; many thousands of cases occur during the years of widespread epidemics and every year at least one or two countries from the African Meningitis Belt experience epidemics. These epidemics are associated with significant socio-economic and health service disruption.
b) The political commitment

Following the meningitis epidemics of 1996 and outbreaks of other diseases such as cholera and yellow fever there is a new political will to tackle epidemic diseases more effectively. This commitment has been demonstrated in the signing by government ministers, of protocols of cooperation for the control of epidemics between countries of the different African Sub-regions. In April 2000 representatives from 8 African countries issued a statement saying that the development of a meningococcal vaccine to prevent epidemics was a high priority for them.

c) The product

Current evidence suggests that a conjugate meningococcal vaccine will be immunogenic at all ages including children, that further immunisation provokes a booster response, that long term immunological memory is induced, that the immune response is protective against disease and is likely to also decrease nasopharyngeal carriage of the meningococcus. These characteristics mean that the vaccine has the potential to prevent epidemics.

d) The right time

New initiatives have been established to ensure that resources are available to prevent disease through immunisation include the Global Alliance for Vaccine and Immunisation (GAVI) and the Global Fund for Children’s Vaccines. Both GAVI and the Children’s Vaccine Programme (CVP) regard the EVA project as an important initiative for support. The ICG maintains the international focus on effective response to epidemics and can become a platform for developing the implementation strategy.

The Project strategy involves two strands: the business plan to develop the new product and an implementation plan to assure a market and effective use of the product. Negotiations with a number of vaccine manufacturers are currently in progress. It is expected that a product will be available in 3 to 7 years and the cost will be in the range of US$ 0.40 to $ 1.00 a dose.

The introduction strategy is likely to have at least two components: introduction into the routine infant vaccination schedules (EPI) accompanied by mass immunisation “catch-up” campaigns for older age groups. The vaccine will be introduced in 1-2 demonstration projects for careful evaluation before widespread introduction to the meningitis belt.

The presentation concluded that:

- Meningococcal epidemics cause substantial morbidity, mortality and disruption;
- Epidemic prevention is a high priority for African meningitis belt countries;
- Meningococcal conjugate vaccines can prevent and eventually eliminate epidemics;
- A meningococcal conjugate A or A/C vaccine is feasible, in a short-time at an affordable price - A model public/private partnership;
- The conjugate vaccine has the potential to be integrated in the EPI while protecting
against other disease of public health importance through combination vaccines;
- The conjugate vaccine has the potential to strengthen immunisation programmes, be sustainable and synergise with other disease control programmes.

**Discussion:**

It is estimated that the “long-term protection” associated with the new vaccine will last at least 10 years.

At the EVA meeting in April 2000 the representatives of African countries had expressed the desire that the new vaccine be manufactured in Africa. This option had been discussed with the vaccine manufacturers and if it were to be pursued would increase the complexity of development in a number of ways and delay the process.

It was pointed out that, although both GAVI and the Bill and Melinda Gates Foundation had expressed interest in the project, no commitment to any amount of funding had been made and that the Gates Foundation would not be committing to fund the whole project.

The cost estimates for the vaccine do not include the cost of injection material needed for its administration.

Some African countries have applied for and will receive funding from the GAVI initiative for the strengthening of their immunisation programmes. It is important that the introduction of this new vaccine, which will also receive support from GAVI, is effectively coordinated with these activities.

6. **W135 indications of spread and carriage study (Annex 8)**

a. **WHO/HQ**

(Dr M. Santamaria)

During March 2000, coinciding with Haj pilgrimage, Saudi Arabia health authorities recorded an increase in the number of cases of meningococcal disease. Furthermore they reported that a significant proportion of these cases were confirmed as being caused by *N. meningitidis* W135.

Subsequently, a number of countries around the world notified cases of meningococcal disease due to *N. meningitidis* W135. The increased reporting of cases due to a relatively unusual serogroup in Europe led to epidemiological studies with a view to identifying risk factors that could be associated with the W135 serogroup. The fact of having been a Haji in 2000 or having had contact with these Hajis was identified as a risk factor associated with subsequently developing W135 meningococcal disease.

In 2000 there were around 1.3 million of Hajis from all around the world travelling to
Saudi Arabia mainly during the first half of March 2000 (until 19.03.00). During this period, there were 41 cases of meningococcal disease notified in SAA with a significant proportion being due to \textit{N. meningitidis} W135. To the end of week 30 (30.07.2000) there was a total of 366 cases being notified in 14 countries that were either 1) confirmed by laboratory as N.mW135 or b) associated with international travel to SAA.

This event raises a number of important questions:

Does this signal a change in the virulence - and therefore epidemic potential - of the \textit{N.m} W135 ?

Does this signal a potentially extensive spread of this W135 strain leading to a global change in the dynamics of the carriage and/or the disease due to \textit{N.meningitidis}? 

What will be the impact of this event in the epidemiology of meningococcal disease?

Do community protection measures need to be re-oriented?

Do recommendations for international travel need to be re-considered?

With a view to addressing the above issues, the WHO is supporting several initiatives. These include operational research projects (e.g. carriage studies; prevalence of strains causing disease) and enhanced surveillance to monitor the situation.

b. Morocco

(Dr K. Bin Kaddour)

Morocco has a population of around 29 million persons, large distances separate the population centres. The last major epidemic of meningococcal disease was in 1989 when 1915 cases were reported. Since then the annual number of cases has dropped to around 400 with serogroups B and A predominating amongst the small proportion of cases for which serogrouping is performed.

During the period October 1999 to July 2000 there was a slight rise in the number of cases of bacterial meningitis reported for the months of April, May and June, corresponding to the post pilgrimage period. During this time there has been one case of W135 meningococcal disease in a 72 year old man returning from pilgrimage to Saudi Arabia. The onset of disease was 2 days after his return to Morocco and he died on 21\textsuperscript{st} April, 19 days later. The confirmation of the serogroup was by antigen detection. There were two further cases of meningococcal disease amongst returned pilgrims; one was confirmed serogroup C and the other unknown. A further 2 Moroccan pilgrims were amongst the cases reported by the Saudi Arabian authorities during their stay at the pilgrimage sites: the serogroups are unknown.

The current strategy for control of meningococcal disease in Morocco is based on:

- Early warning: immediate case-by-case notification;
- Rapid intervention: investigation, chemoprophylaxis and vaccination;
- Adoption of WHO’s new case definitions;
- Preparation and distribution of surveillance standards;
- Preparation and implementation of an emergency readiness and response
plan.

Following the concern over cases of W135 meningococcal disease amongst returned pilgrims and their close contacts the Ministry of Health, in collaboration with WHO, is undertaking a field survey amongst the households of returned pilgrims (further details of the study protocol are given in Annex 8).

Following the events linked to the 2000 pilgrimage the Ministry of Health intends to:

- Strengthen laboratory diagnosis of meningococcal strains;
- Strengthen surveillance for the disease amongst pilgrims and both during the pilgrimage and after return to Morocco;
- Introduce the tetravalent vaccine for pilgrims and possibly more widely;
- Strengthen response systems in post pilgrimage months;
- Examine the feasibility of other preventive actions: e.g. chemoprophylaxis, accommodation conditions during pilgrimage.

In implementing these measures the Ministry of Health will coordinate with WHO and the Saudi Arabian health authorities.

c. Oman

(Dr S. Al Lamki)

Meningococcal disease is seen as an important public health issue in Oman and rapid reporting of cases (within 24 hrs) is part of the national surveillance system established in 1991. Oman has adopted an epidemic threshold of 3 or more confirmed cases from one village (Hara) within one week. The actions implemented immediately on crossing the threshold include:

- Screening of family/neighborhood contacts by nasopharyngeal swabbing for carrier state;
- Carriers treated till negative;
- Chemoprophylaxis with Rifampicin;
- If serotype known then vaccination with A/C vaccine may be implemented.

Protocols have been developed for cases management, laboratory diagnosis and community action. There is a mandatory requirement for pilgrims travelling to Saudi Arabia to receive bivalent meningococcal A&C vaccine 2 weeks prior to departure.

Reported cases of meningococcal disease in Oman had been declining in number in the period 1991 to 1999. By June 2000, 22 cases had been reported, the highest number since 1991, almost all these cases occurred in the period immediately following on from the Haj pilgrimage. Of the 22 cases 12 were confirmed as serogroup W135, 3 as group A and 1 as group B. Nineteen of the cases were in returned pilgrims or their close family contacts.

A study of nasopharyngeal carriage of \textit{N. meningitidis} amongst returned pilgrims and
their close family contacts is being instituted. The basic study protocol and methods are similar to those being used in Morocco. Unfortunately the study implementation was delayed by a number of factors including the need to relocate the study area from Muscat to another region because of difficulty in tracing pilgrims in the capital.

**Discussion:**
This topic provoked a lively discussion amongst the participants who expressed clear concern over possible implications this year’s Haj associated W135 outbreak may have for the protection of pilgrims in future years and on the epidemiology of epidemic disease in the world in general.

The following points were made regarding the information that is available:

- The meeting has no clear understanding of the significance of the emergence of different genetic clones of *N. meningitidis* as opposed to different serogroups;
- The carriage studies described will not answer some of the important questions facing the international community;
- Further studies may need to be planned to take place during the next Haj season;
- Surveillance data, including the submission of samples to WHO collaborating centres for characterisation of isolates, is crucial to monitoring and understanding the situation and ultimately guiding actions.

Regarding the recommendations for protection of travellers:

- The only WHO recommendation at present is in the “International Travel and Health – Vaccination Requirements and Health Advice” publication, where both bivalent and quadrivalent vaccines are advised for travellers to epidemic areas. The choice of which vaccine is left to the national authority or individual;
- That currently the US market represents 90% of sales of quadrivalent vaccine with only small quantities being sold beyond that for traveller vaccinations;
- The amounts of vaccine produced are not expected to increase without a very clear forecast of increased market potential;
- The cost of quadrivalent vaccine, although much higher than bivalent vaccine is small when compared to the total costs for a pilgrim undertaking the Haj pilgrimage.

The need for an expert meeting to consider the research issues and current evidence for a need to change the existing recommendations was agreed.

7. **Technical Issues**

a. **Contingency stocks**

(Dr M. Santamaria)

In response to the recommendation made by the last ICG meeting efforts had been made to examine the issue of contingency stocks of emergency materials in order to provide clearer guidance to national authorities on the issue. Progress had been difficult as there
is a paucity of data published or unpublished on the use of emergency stocks. Currently countries make their own decisions on the contents, size and organisation of any contingency stocks held for epidemic response. There are a number of epidemic prone diseases for which it is suggested that such stocks may play a useful role, including yellow fever, cholera, diphtheria, influenza in addition to meningococcal meningitis.

In a meeting on epidemic preparedness in Ouagadougou in 1996 it was decided to base the size of contingency stocks of meningococcal vaccine on a calculation of 10% of the total population at risk and on this basis the suggested stocks for countries in 1997 were calculated. It has proved very difficult to follow up on those calculations in a meaningful way. Over subsequent epidemic seasons vaccine has entered countries from various sources and either been added to the stocks or used in epidemic response. Obtaining the information from countries about current stocks of vaccine has proved increasingly difficult. Some countries now hold stocks considerably larger than the original calculations while in others it may be uncertain how much vaccine is in fact held following vaccine distribution to the regions and districts.

The situation with regard to contingency stocks would vary from country to country: some countries have much greater planning and logistic capacity, while others face more serious emergency needs, unfortunately these two elements do not always coincide.

**Comments from the manufacturers of emergency materials**

The manufacturers represented at the meeting were asked to comment on available stocks of emergency materials under this agenda item.

The vaccine manufacturers confirmed that the ICG held contingency stocks of some 3.8 million doses with SmithKline Beecham and 3.3 million doses with Aventis Pasteur.

UNIVEC currently has 3.6 million units of auto-disable injection material with the ICG forwarding agents in Frankfurt and Becton Dickinson could supply their auto-disable injection material to anywhere it was needed and production capacity would be doubled in the coming year.

Lafran will produce 100,000 vials of oily chloramphenicol including 25,000 vials as part of the ICG pre-paid stock. IDA holds a stock of 30,000 vials and has the capacity to produce 300 units of 100 vials within a 3 week period.

**Discussion**

The meeting participants generally acknowledged the need for and value of emergency stocks, and voiced a variety of opinions and concerns regarding the stockpiles needed in preparation for epidemics of meningococcal disease. The importance of materials for case management as well as for vaccination was pointed out.

Despite the differences in ability to forecast demand, it was suggested that closer links be explored with the logistics and management systems used by national authorities for the routine EPI immunisations. The issue of how to deal with expiring stock was raised again: re-sale with the support of the WHO regional offices to a purchaser with
immediate needs, or use in some type of pre-emptive vaccination programme were suggested as potential solutions.

Stocks maintained at a central, manufacturer or international level would be better looked after than stocks sent to peripheral levels. It was also suggested that central stocks could facilitate the re-sale of stocks from a country that did not experience an epidemic to a country that had urgent needs. It is easier to collect and maintain data on fewer, more centralised stockpiles than supplies that have been widely dispersed. IDA expressed their commitment to supporting effective access to emergency materials and would support countries in procuring, maintaining and dispatching stocks.

Again there were calls for a technical analysis of the issue to provide guidance on the size and nature of contingency stocks.

b. Epidemic Thresholds (Annex 9)

(Dr R. Lewis)

As recommended by the last ICG meeting Epicentre/MSF had organised a meeting to review the WHO recommendations on the epidemic thresholds used to guide response actions during epidemics in the African Meningitis Belt. The threshold was based on weekly incidence rates with the purpose of providing an “early” alert and guiding the implementation of appropriate response actions.

The meeting had taken place in Paris on 20 June with the participation of research partners from CDC, Cermes, Mali; Niger and WHO (AFRO &HQ). After presentations of the research evidence available to inform the recommendations, a number of working groups discussed the issues in depth and brought back their conclusions for incorporation into the new guidance. The outputs from the meeting are a report in French and an agreed text for the new recommendation in English and French, this latter has been published in the Weekly Epidemiological Record1 (Annex 9).

The new recommendation describes two types of threshold weekly incidence:

- **The alert threshold** is used to: (1) sound an early warning and launch an investigation at the start of an epidemic; (2) check epidemic preparedness; (3) start a vaccination campaign if there is already an epidemic in a neighbouring area; and (4) prioritize areas for vaccination campaigns in the course of an epidemic;

- **The epidemic threshold** is used to confirm the emergence of an epidemic so as to step up control measures, i.e. mass vaccination and appropriate case management.

A different type of threshold, needed for populations of less than 30 000, where weekly incidence rates are inherently unstable, is also described.

The advantages of the new recommendations are that they are:

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• More sensitive, increasing time for intervention;
• Designed to minimize false alarms;
• Context-specific (population size, level of risk);
• Taking account of new information;
• Action-oriented;
• Easy to calculate.

However the successful application of these new recommendations depends upon the:

• Quality of surveillance: completeness, timeliness;
• Responsiveness of health systems and personnel;
• Judgement and decisions of health authorities;
• Political commitment: in “declaring” an epidemic;
• Training of health personnel.

Discussion
The increased level of sophistication in the new recommendations makes them more complex than the previous guidance; in order for their application to result in improved detection and response to epidemics, they will have to be carefully disseminated and health care workers trained in their use.

Concerns were expressed about the use of small numbers of cases to alert or detect epidemics in small populations given the difficulties in obtaining accurate diagnosis especially in remote areas.

The availability of additional guidance in terms of case management and public health actions other than vaccination was raised: both MSF and WHO have produced practical guidelines covering these issues.

c. Community Based Surveillance (Annex 10)

(Dr B. Hersh)

The Red Cross and Red Crescent societies focus on trying to fill the gap between the communities and the formal health sector. The organisation is moving away from a role as a “health service provider” to developing community orientated health promotion. Continuing support to the formal health sector is complimented by strengthening individuals, families and communities to make decisions related to health.

The table below demonstrates the contrasting “traditional” role of the Red Cross/ Red Crescent societies with the vision for the next 10 years:

<table>
<thead>
<tr>
<th>Traditional Red Cross/Red Crescent</th>
<th>Red Cross/Red Crescent 2010</th>
</tr>
</thead>
<tbody>
<tr>
<td>Activities duplicate/substitute those of the</td>
<td>Activities complement those of the formal</td>
</tr>
</tbody>
</table>
formal health system (mostly at the primary level, but also secondary and tertiary levels, e.g. blood supply) | health system where RC/RC have comparative advantages
---|---
Volunteers seen mainly as health care providers - first aid (reactive/emergency role) | Volunteers seen mainly as enablers of behavioural change (pro-active role)
Volunteers' "loyalty" to the RC/RC | Volunteers’ "loyalty" to the household/community
Working on its own | Working in partnerships

With these goals, 53 African Red Cross/Red Crescent societies have developed the African Red Cross/Red Crescent Health Initiative (ARCHI) 2010. Using its national, regional and global structures and some 2 million volunteers the initiative focuses on priority public health issues in the areas of:

- Disease prevention;
- Health promotion;
- Disaster preparedness;
- Disaster response.

RC/RC volunteers are being trained to carry out surveillance for clusters of syndromes of public health importance including meningococcal disease. This surveillance will be carried out in the communities in which the volunteers live and in the case of meningococcal disease they will be trained to recognise and report on clusters of people ill with fever and rash. Other syndromes that will be identified include: watery diarrhoea, bloody diarrhoea, acute flaccid paralysis and jaundice.

It is anticipated that such surveillance will not only detect outbreaks that do not present to the formal health care system but will provide communities with the information needed to institute rapid response actions.

d. **Evaluation of Response (Annex 11)**

(Dr F. Varaine)

MSF had presented a number of indictors proposed for use in evaluating the response to meningococcal epidemics at the ICG meeting in 1998 in Bamako, Mali. Using the examples of the outbreaks in Sudan (1999) and Niger (2000) Dr Varaine presented how these indicators had been implemented in the field.

The first area covered was case management. The effectiveness of treatment is measured primarily by the Case-Fatality Rate (CFR). It was noted how the CFR fell over the course of the epidemic in Niger, and how it varied between different groups that received
treatment from health personnel with different levels of qualification. Access to appropriate case management had been estimated by the coverage with treatment kits, and the timeliness by the delay between a district crossing the alert threshold (5 cases / 1000,000 pop / week) and the arrival of specific treatment supplies. This later also showed that treatment supply took longer to arrive in the small health units than in hospitals. In Sudan the cost of each treatment was averaged at 25 Euro per treated case.

Vaccination was assessed by coverage, timeliness, prevented cases, safety and resource expenditure. In Sudan although the overall coverage of the target population in 4 states was 32%, in the urban areas, which were prioritized as being at highest risk, the coverage was 80%. There had been a median delay of 4 weeks between a district crossing the alert threshold and vaccination campaigns being implemented in the state. Using formulae to calculate the number of cases prevented in 9 Sudanese towns that generally achieved high coverage rates, it was estimated that some 54% of the potential cases were prevented through mass vaccination. A similar proportion of cases were calculated to have been prevented by the vaccination campaign in Niamey, Niger in 2000. Accidental exposure to blood through needle-stick injuries is a hazard of vaccination campaigns, 24% of the health care workers surveyed reported some injury; all exposures were related to the handling of the safety boxes used for syringe disposal. The costs of vaccination in Sudan were estimated at 0.6 Euro per dose.

On the basis of the evaluations carried out recommendations had been made regarding the maintenance of regional stock of specific treatments, training of health personnel and the design of safety boxes.

**Discussion**

The participants congratulated the presenter on the excellent implementation of the evaluation criteria developed. The differences in the CFR between grades of health care personnel could be explained by case –mix. The resistance to use oily chloramphenicol injections in the cities, where there might be expected to be easy access to hospital based treatment was noted. The use of the “alert” threshold rather than the “epidemic“ threshold to calculate delays was questioned: in Sudan where there was already an established epidemic under way the “alert” threshold would become the threshold for implementing response actions including vaccination. The importance of disseminating the information contained in this presentation was voiced.

**e. Interaction with NIDs**

(Dr J-M. Ndiaye)

Mass vaccination campaigns are planned to avoid the difficulties associated with the wet season and the timing of NIDs has sometimes coincided with outbreaks of meningococcal disease. In Ghana an NID coincided with an outbreak of both yellow fever and meningitis. The usual result is delayed implementation of the emergency response.

The participants recognised the global priority of polio elimination but expressed the view that the immediate threat to human life posed by an epidemic of meningococcal
disease was a more urgent priority. It was a difficult decision to take but emergency campaigns should not be delayed or displaced by NIDs. It was suggested that the public fear of meningitis could be used to increase the participation in NIDs if the campaigns could somehow be combined. The practical difficulties in combining the campaigns were thought to be significant.

f. Epidemic Forecasting (Annex 12)

a) NASA

(Dr N. Rosenstein)

It had not been possible for anyone from the NASA Environment and Health Initiative at the Goddard Space Flight Center to participate in the meeting and Dr Rosenstein from CDC, Atlanta, had generously agreed to present the basic outline of their work in epidemic prediction to the ICG.

The project aims to link environmental parameters that can be observed through remote, satellite sensing to health events, such as disease patterns and epidemics. Examples of where results are already becoming available include environmental risk mapping for Dengue in SE Asia and Malaria in Africa.

It is hoped that by overlaying remotely sensed data on surface temperature, rainfall, dust and vegetation it will be possible to develop models that give a better understanding of the dynamics of climate-disease interactions. The goal is to produce practical early warning systems for disease outbreaks and tools to improve the surveillance of disease.

The current programme will look at the potential for such developments for the following diseases:

- Malaria
- Rift Valley Fever
- St. Louis Encephalitis Fever
- Dengue Fever
- Ebola
- Influenza
- Meningitis
- Asthma
- Bartonellosis
- Cholera

b) Liverpool School of Hygiene and Tropical Medicine

(Dr A. Molesworth)

The Meningitis Forecasting Project aims to explore associations between the environment and the occurrence of epidemic meningitis and thereby establish potential risk markers for epidemics in the Sahel.
The research is intended to increase knowledge for governments and relief organisations at the national and local levels, which may be used to improve epidemic preparedness and timely response strategies.

There already exists a substantial body of evidence to link meningococcal epidemics to environmental factors: the geographic distribution of disease, the seasonal patterns and the recent extension of the epidemics to new areas. A number of environmental factors have been proposed as linked to epidemics including: absolute humidity, rainfall, dust storms and temperature.

The project has collected time series data on the occurrence of disease from a number of sources. It is now examining the associations between this disease data and three types of environmental data: meteorological (data from ground-based weather stations), modelled (interpolated ground-based data) and satellite (remotely sensed data).

The data collection is now largely complete and will be analysed over the coming months with the aim of identifying factors that predict the size, timing and site of epidemics of disease.

At this stage it is concluded that the distribution of epidemic meningitis in Africa can be established using environmental criteria and that it may be possible to predict where epidemics are likely to occur. The prediction of epidemics in time is likely to be complicated by the interaction of other risk-factors (e.g. immunity, vaccination, introduction of new strains).

Discussion:
The ICG had been in contact with Stone Environmental, a further research group interested in the environmental prediction of meningococcal disease and a brief description of their study aims was read out for the information of the meeting.

The ICG participants were enthusiastic in their interest in this research and warmly encouraged the presenters to keep the ICG informed of progress. Some of the difficulties of defining an epidemic or an epidemic prone country were discussed. Human behaviour was suggested as an important “other risk factor” that might complicate the use of environmental parameters to predict outbreaks.

8. Review and Update of the ICG Terms of Reference

The participants reviewed the current ICG Terms of Reference and with the exception of some minor changes to the wording (underlined below) agreed that they remained valid for the coming year.

Revised Terms of Reference for the International Coordinating Group on Vaccine Provision for Epidemic Meningococcal Disease (ICG)

1. Review the meningococcal disease situation and the control measures that have been undertaken;
2. Review new information on cost-effectiveness of meningococcal vaccine strategies and vaccination policies;

3. Update country estimates of needs for emergency stocks of vaccine, drugs and injection material and project the amount and timing of global aggregate demand;

4. Determine the amount of vaccine, drugs and injection material to be kept in the ICG stocks for emergency preparedness;

5. Monitor vaccine, auto disable injection material, and oily chloramphenicol availability;

6. Review regularly the criteria for vaccine distribution in emergency situations;

7. Maintain the current mandate of the ICG Executive Sub-group;

8. Review national reports on vaccine use and other response measures implemented;

9. Identify short-, medium- and long-term financial strategies to ensure the availability of sufficient vaccine, drugs and injection material;

10. Provide information through ICG partners to countries on how to access the ICG emergency stock;

11. Continue advocacy with international community and development agencies for preparedness and response to meningococcal disease outbreaks;

12. Periodically disseminate information on the meningococcal disease situation and the ICG activities.

9. Recommendations and Closing Remarks

The participants of the 6th meeting of the International Coordinating Group on Vaccine Provision for Epidemic Meningitis Control (ICG) made the following recommendations:

1. The key to controlling meningococcal disease outbreaks is the timely implementation of mass vaccination campaigns achieving the highest possible coverage. Unless coverage is maintained at very high levels and vaccination is repeated every 3 years, routine mass vaccination will not prevent epidemics and can be an inefficient use of resources. Therefore, the ICG strongly discourages the use of mass vaccination campaigns as a strategy to PREVENT epidemics, unless the appropriate coverage and frequency can be realistically achieved.

2. ICG Executive Subgroup should continue to lead efforts to:
   • evaluate methods to determine the appropriate size and nature of contingency stocks for countries;
   • provide information to countries concerning the potential benefits and
provides of maintaining contingency stocks;
- provide guidance for mechanisms for flexible management of vaccine stocks.

3. During meningitis outbreaks which coincide with planned NIDs, precedence should be given to life-saving epidemic response activities, fully exploiting potential synergies between meningitis control and polio eradication programmes. Where possible NIDs should be scheduled to take place outside the meningitis season.

4. All ICG partners should strongly reinforce existing efforts to assure that vaccines and antibiotics are administered in a safe manner. Vaccines should only be administered using auto-disable injection material by appropriately trained personnel. All partners should be committed to providing “bundled” vaccine and injection material.

5. ICG Executive Sub-group should continue close collaboration with the EVA project partners to define the appropriate role for the ICG in developing implementation strategies for the conjugate meningococcal vaccine.

6. WHO should continue to closely monitor the epidemiology of meningococcal serogroups other than A and C, including W135. WHO should convene a group of “experts” as soon as possible to consider changes in the disease epidemiology, research needs and potential implications for disease control strategies. WHO should continue to work closely with vaccine manufacturers to monitor availability of both bivalent and quadrivalent vaccines.

7. Current vaccine recommendations in the WHO International Travel and Health Guidelines (Yellow Book) remain valid.

8. ICG welcomes the revised WHO epidemic threshold recommendations and calls upon the ICG partners to assist WHO in the dissemination of this information and to encourage and support national authorities to conduct appropriate training in their application before the next epidemic season.

9. WHO should convene an informal consultation to discuss forecasting methods and to encourage the development of practical tools for country use.

10. In order to improve the quality and effectiveness of outbreak response, ICG strongly encourages the systematic evaluation of interventions based on precise indicators and sharing of the lessons learned.

Before closing the meeting the participants expressed their warm appreciation for the many years of tireless and technically excellent work undertaken by Dr E. Tikhomirov both in the ICG and in the wider international efforts to understand and control meningococcal disease. Although Dr Tikhomirov is retiring from his present position leading the bacterial group in WHO’s Epidemic Disease Control team, it was hoped that he would continue to contribute to future ICG meetings.