International Coordinating Group (ICG) on Vaccine Provision for Epidemic Control

Report of the Fifth Meeting

Geneva, Switzerland
8-9 December 1999

World Health Organization
Department of Communicable Disease Surveillance and Response

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Summary Report of the Fifth Meeting of the International Coordinating Group (ICG) on Vaccine Provision for Epidemic Meningitis Control
1. Opening and introduction

The fifth meeting of the International Coordinating Group on Vaccine Provision for Epidemic Meningitis Control (ICG) was held on 8 and 9 of December 1999 at WHO Headquarters in Geneva. Dr L. Martinez, Director of the Department of Surveillance and Response (CSR), welcomed the participants and opened the meeting.

Summarizing the history of the ICG, Dr L. Martinez stressed the fact that the success of the group relies on the cooperation and goodwill of a wide range of partners, in addition to the four agencies making up the Executive Sub-group of the ICG. The manufacturers of the products in the emergency stockpile, including Pasteur Mérieux Connaught, SmithKline Beecham Biologicals and Univec, have been essential partners. Donor governments came forward with the resources needed to set up the mechanism and continue to support its functioning. As part of a wider initiative, the ICG involves WHO Collaborating Centres and other partners, providing technical expertise in strengthening surveillance systems and the laboratory capacity to detect epidemics rapidly.

The objectives of the meeting were to prepare for the epidemic meningitis season 1999/2000 by reviewing the events of the last epidemic season. The lessons learned from that season will be applied in future work of the ICG. The meeting also considered the future role of the ICG, and how it has developed from crisis intervention, to a forum for the wider issues of epidemic meningitis preparedness. The meeting will make recommendations to shape the ICG's response both to epidemics in the coming season and, equally important, to prevent the crises that occurred in 1996.

Attention was drawn to the need to demonstrate how the ICG is an integral part of the overall WHO strategy for the control of communicable disease.

The meeting was co-chaired by Dr. M. Tailhaides, International Federation of Red Cross and Red Crescent Societies (IFRC) and Dr F. Varaine, Médecins sans Frontières (MSF).

2. Reports on the implementation of the regional plans for preparedness and control of epidemic meningitis (see Annex 2)

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.

a. WHO Regional Office for Africa (AFRO)

(Dr P. Lusamba)

Epidemic preparedness and response for meningococcal disease is part of the overall plan for epidemic preparedness and response for AFRO.
When taking population numbers into account, the countries that were most affected in 1999 by epidemics of meningococcal disease were Burkina Faso, Cameroon, Central African Republic, Guinea Bissau, Niger, Senegal and Chad. All together, in 1999, 26,784 cases and 3,547 deaths were reported to AFRO.

Following the outbreaks of meningococcal disease in 1996, AFRO began the process of defining five sub-regional blocks based on epidemiological and geographical coherence. Each block has its specific priority health problems, and meningococcal disease is identified among them in almost all five blocks of countries. Member States of the epidemiological blocks have committed themselves at ministerial level to adopting a sub-regional plan of action. These plans are at different stages of implementation and include the following activities:

- reinforcement of surveillance;
- standardization of case management;
- reinforcement of laboratory capacity;
- improvement of communication and information exchange;
- intensification of cooperation.

WHO AFRO is supporting the sub-regional blocks through:

- establishing sub-regional teams providing epidemiological and laboratory expertise;
- implementation of its programme on integrated disease surveillance (IDS);
- assessment of national surveillance systems;
- provision of guidelines.

b. WHO Regional Office for the Eastern Mediterranean (EMRO)

(Dr B. Sadrzadeh)

In EMRO, as well as in AFRO, preparedness and response of meningococcal disease is part of an integrated regional plan for preparedness and response. Sudan is the only country in the Region that is situated in the meningitis belt, and suffers epidemic waves at regular intervals. Meningococcal disease is endemic in many countries of the Region. Egypt, Morocco, Tunisia and Yemen are at particular risk of epidemics.

Because of the annual Hajj pilgrimage and socioeconomic and geopolitical changes, such as unplanned urbanization and civil strife, meningococcal meningitis is of great concern within the Region.

The regional plan for preparedness and control comprises, strengthening of surveillance systems and national laboratories support to national prevention and control activities, and the dissemination of information. Support has been given to the control of the epidemic of meningococcal meningitis in Sudan. Preventive vaccination strategies will continue to be carried out for high-risk groups in Sudan, Egypt, Saudi Arabia, Syria and Iran, and in accordance with the requirements relating to the Hajj. To improve the use
of surveillance information, the regional plan includes the weekly collection of data on meningococcal disease cases during the epidemic season, and a monthly distribution of this information to Member States.

Discussion:
It was suggested that surveillance of the circulating meningococcal strains could be carried out amongst pilgrims attending the Hajj, and that the identification of virulent strains would help predict the likelihood of epidemics associated with returning pilgrims. Special vigilance may be indicated during years when the pilgrimage coincides with the dry season in the meningitis belt.

3. Reports from the ICG Executive Sub-group and the Member Agencies (see Annex 3)

a. World Health Organization (WHO)

(Dr M. Hardiman)

The WHO communicable disease cluster consists of three departments and two special projects, Roll Back Malaria and Stop TB. The department of Surveillance and Response (CSR), has activities relating to the strengthening of preparedness and response to epidemic diseases in general, as well as to specific epidemic prone conditions such as meningococcal disease.

Surveillance
- Reports of potential epidemics received from several sources are verified and reported on a weekly basis through the Outbreak Verification List.
- Support is given to the assessments of national and regional surveillance systems.
- Through the HealthMap programme UNICEF and CSR have provided a range of services and products relating to the use of GIS and mapping.
- A global database on meningococcal disease is being updated and distributed.
- Information on the clonal analysis of meningococci is collected.

Epidemic preparedness and surveillance training
CSR is supporting WHO regional offices in the preparation and carrying out of meetings, workshops and training, including the development of training material.

Laboratory strengthening
To strengthen laboratory capacity at national level and to upgrade professional skills of laboratory workers, CSR has overseen a programme of laboratory assessment and provision of basic reagents and training.
Control
During 1999 most direct involvement in control activities regarding meningococcal disease were related to the epidemic in Sudan. CSR has published Guidelines for Control of Epidemic Meningococcal Disease; the second edition was recently printed in English and French.

Operational Research
A document on Research priorities for the more effective use of vaccines for the prevention and control of meningococcal disease in the African meningitis belt is in the final stages of development.

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

(Dr M. Tailhades)

The activities implemented by the Sudanese Red Crescent Society (SRCS):

1. Political and financial issues
In 1993 donors stopped giving bilateral support to Sudan. This delayed the raising of funds to the epidemic, so NGOs and international organizations had to use their own funds to start the necessary activities. In January 1999 the epidemic was assessed and a plan of action was prepared. IFRC provided an information bulletin, plan of action and response activities such as health education, community mobilization, training of trainers and vaccination. In February 1999 the Task Force was set up and in early March the consolidated appeal was launched for 5.6 million US$. In April 1,790,000 doses of vaccine were distributed among seven eastern states. At the end of April the appeal was revised to vaccinate 2.5 million persons and purchase 60,000 doses of oily chloramphenicol. In May 900,000 doses of vaccine were procured. A training of the trainer workshop was given, and in July a disaster preparedness plan and manual, as well as a training curriculum, was developed.

2. Strengths and weaknesses
The cooperation between the Red Crescent volunteers and the Ministry of Health was good, and the volunteers were able to make a significant contribution to the activities. Through the participation in the activities, the profile of the Sudanese Red Crescent Society was enhanced. By July 1999 the IFRC/SRCS prepared a package of material, including a manual of epidemic control measures. The biggest strength in the way the epidemic was dealt with in Sudan was the good cooperation of the partners. However, there were also weaknesses encountered:

The preparedness plan of the IFRC/SRCS prior to the epidemic was weak. Initially the activities were hesitant and adequate planning was lacking. The response was delayed...
because it was decided to wait until the IFRC could be included in the consolidated appeal; which was only launched in March. More emphasis could have been placed on the health education aspects.

3. Disaster preparedness
Disaster preparedness requires a long-term commitment and at the same time has difficulty in attracting funds. The knowledge of the Red Crescent volunteers should be regularly updated. The manual on epidemic control measures proposes the establishment of a network at three levels. The overall responsibility of the preparedness plan and the coordination of the international activities will take place at SRCS Headquarters (Khartoum). The role of the state branch level of the IFRC will be to coordinate the activities at state level, and to act as focal points for interventions in the states. The pool of volunteers will be responsible for ground level preparation, early warning, health education and communication.

An appropriate level of epidemic preparedness would ensure a timely response to an epidemic. In order to achieve this, collaboration with other partners, especially with WHO country offices, would be necessary.

The Federation has initiated a disaster preparedness programme in West Africa. Through training in prevention of epidemics at regional level, capacity will be built to strengthen the government's action.

c. Médecins Sans Frontières (MSF)

(Dr F. Varaine)

Concerning the response to meningococcal meningitis epidemics, MSF’s main activities took place in three African countries: Sudan, Guinea-Bissau and Chad. MSF provided technical and logistical support consisting of the provision of medicines, vaccines and injection material. In total, 3 730 000 doses of vaccine have been supplied.

Other activities
A new manual for response to epidemics of meningococcal disease was finalized, expanding on some issues that were only covered briefly in the previous manual. Included in the new guidelines are issues on vaccination strategies and evaluation of intervention.
Furthermore, a study on the epidemiological thresholds of meningococcal disease has been carried out in Mali by Epicentre and the Division de l'Épidémiologie of the Ministry of Health in Mali. A project on epidemic preparedness is ongoing in Mali.

An evaluation of the quality of injection material has been carried out.

d. United Nations Children Fund (UNICEF)

(Dr. Voumard)

Besides activities in Sudan, UNICEF supported Kenya, Ghana and Eritrea in controlling meningococcal disease. UNICEF is especially involved at the country level providing response supplies such as vaccines, syringes and drugs.

UNICEF emphasised the advantages in working in a country level task force such as the one set up in Sudan. These structures provide a good opportunity for regional staff of UNICEF to cooperate with the Regional Offices of WHO.

### Meningococcal A/C vaccine, vials of 50 doses shipped by UNICEF during 1999

<table>
<thead>
<tr>
<th>Receiving Country</th>
<th>Suppliers</th>
<th>No of Vials</th>
<th>No of Doses</th>
<th>Value (US$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eritrea</td>
<td>PMC</td>
<td>5 575</td>
<td>278 750</td>
<td>42 618</td>
</tr>
<tr>
<td>Ghana</td>
<td>PMC</td>
<td>10 000</td>
<td>500 000</td>
<td>75 748</td>
</tr>
<tr>
<td>Kenya</td>
<td>PMC</td>
<td>4 500</td>
<td>225 000</td>
<td>34 087</td>
</tr>
<tr>
<td>Sudan</td>
<td>PMC/SB</td>
<td>72 800</td>
<td>3 640 000</td>
<td>565 056</td>
</tr>
<tr>
<td><strong>Grand Total</strong></td>
<td><strong>92 875</strong></td>
<td><strong>4 643 750</strong></td>
<td><strong>717 509</strong></td>
<td></td>
</tr>
</tbody>
</table>

Dr. Paganini, advisor for health emergencies, will participate in the ICG as the new focal point for UNICEF. In addition, the decentralized nature of UNICEF makes interaction between the UNICEF regional offices and ICG secretariat desirable.

e. ICG Secretariat

(Dr M. Hardiman)

**Introduction**

In 1999 nearly 60 000 cases of meningococcal disease have been reported so far. This is 22 000 more than in 1998, and it is also the first time that there is an increase in the
annual number of cases since 1996. With 32,000 cases the epidemic in Sudan accounts for the higher number of cases during 1999. Vaccine was not in short supply over the last year, and this is an important reason why the ICG has not contributed a high proportion of the total amount of vaccine that was supplied to Africa in this period.

I. Supplies
The ICG stock of emergency materials, as of December 1999, contains 6,395,000 doses of vaccine and 1,530,000 units of autodestruct syringes. The discrepancy between the syringes and the vaccine was arrived at intentionally; it was foreseen that the prices of the autodestruct syringes would go down allowing a new stock to be re-ordered at a better price. The intention now is to replenish the stock of autodestruct syringes for the coming epidemic season.

The ICG should consider whether a stock of almost 6.4 million doses of vaccine is sufficient for an emergency comparable to that in 1996. In 1997 there were 14 million doses of vaccine in the ICG-stock and 10 million of it were used in that year.

II. Other issues
In 1999 the Executive Sub-group of the ICG held 3 meetings, two newsletters were distributed and the role of the ICG was externally evaluated by a consultant from ISADE (Institucion Internacional para la Salud y el Desarrollo).

One of the important findings of the evaluation was the relative invisibility of the ICG: awareness of the role of the ICG is poor outside of the ICG partners themselves. Distribution of the newsletter may help to improve this but other possibilities should be explored.

Other issues that were addressed in 1999 are the following:

Quality of the supplied materials
- size of the vaccine packaging differs between the two manufacturers and significantly impacts upon logistics and transport costs;
- quality of the disposal boxes has been questioned;
- needles mounted on autodestruct syringes have become detached or blocked.

Shipment
- infrequent scheduled flights have made it difficult to ensure a rapid and simultaneous arrival of vaccines and injection material to certain locations.

Added value of purchasing through the ICG
The purpose of the ICG is not to control the market in emergency supplies for epidemic meningitis, but to ensure that sufficient supplies are available in emergency situations. In addition to ensuring availability, the advantages of purchasing supplies through the ICG are:

- 'bundling' and delivery autodestruct syringes and vaccines;
- quality of the vaccines and other supplies is assured (WHO certified);
- the decision to release material is based on an international consensus.

Follow-up issues of 4th ICG meeting
- Recommendation 4: Operational issues: even though the review and editing process has taken a long time, the document Research priorities for the more effective use of vaccines for the prevention and control of meningococcal disease in the African meningitis belt has been developed.

- Recommendation 5: Technical groups: most of the technical groups were not established due to lack of manpower and uncertainty regarding the desired output.

Issues for the fifth meeting of the ICG include:

- to review and endorse the Terms of Reference of the ICG;
- to recommend on any extension of the role of the ICG;
- to recommend effective ways of communication and raising awareness;
- to recommend on any further resource mobilization;
- to recommend on mechanisms of vaccine demand forecasting.

Discussion:
It was suggested that the ICG Executive Sub-group partners could improve their coordination and avoid duplication by consolidating a single set of guidelines instead of each partner producing his own.

4. Reports from countries on 1998/1999 meningitis season
(see Annex 4)

a. Sudan

(Dr A. El Tigani)

Almost half of Sudan is situated in the meningitis belt. At the beginning of December 1998 cases of neck stiffness and fever were reported from Kutum in North West Darfour State. The State Minister of Health was informed because meningococcal disease was suspected. Since spread of the disease was feared, the assistance from the Federal Ministry of Health was asked. A case definition was formulated.

Through lack of laboratory facilities, a month elapsed between the first suspected case and laboratory confirmation of the disease. The epidemic was declared in a district where there was a doubling of the cases in two consecutive weeks, compared to the same period 3 to 4 years ago. In January assistance from the WHO was asked. A task force was set up including the ICG partners and plans were developed to be implemented according to a number of potential scenarios for the spread of the epidemic. One of the
objectives of the task force was to ask the international community for support in the containment of the epidemic. The task force met twice a week and developed a strategy for the following topics:

- strengthening surveillance and laboratory capacity in order to monitor the outbreak;
- improving case management;
- an immunization campaign targeted to achieve the most rapid and effective response;
- ensure availability of resources;
- ensure effective management of epidemic response;
- disseminate public information and education;
- provide training of health staff and other personnel dealing with epidemic intervention.

The task force set up a sub-committee for surveillance. Its tasks were to decide on the population (denominator) data, data collection, surveillance forms etc.

In order to inform the public, 60 000 self-explanatory posters and 20 000 leaflets were distributed. People were also informed through the radio, television and mosques.

On 16 July 1999 the epidemic was declared over.

Discussion:
Attention was given to the preventive use of vaccines in Sudan which is only received by a small proportion of the population. More effective vaccines or vaccination strategies would need to be developed to provide herd immunity; any protection now has a short duration and would appear not to protect people against the epidemic waves coming approximately every eleven years. A preventive vaccination strategy was discussed between WHO and the Ministry of Health in Sudan. 30% of the population has been vaccinated in 1999 and the Ministry of Health plans to vaccinate another 30% of the population in 2000.

It was suggested that following the identification of the localized outbreak, pre-emptive vaccination in areas as yet unaffected by the disease might have provided greater protection of the population. However, it has been estimated that the current strategy of mass vaccination in populations where disease levels exceeded a predetermined threshold had successfully prevented a large number of cases.

b. Ethiopia

(Dr A. Moka)

Ethiopia is the third most populous country in Africa with 60 million inhabitants. Health indicators such as life expectancy and infant mortality rate are very poor, and publicly provided health services are only accessible to a limited proportion of the population.

Outbreaks of meningococcal meningitis occur most regularly in the north and west of the country but occasionally may spread to involve the whole country. On the last occasion when this occurred in 1988/1989 there were an estimated 46 000 cases. Since then
significant outbreaks have occurred in 1997 (547 cases, 19 deaths) and 1999 (175 cases, 8 deaths).

Response to these recent outbreaks included mass vaccination aimed at a population at highest risk (2-30 years of age, prisoners, pupils and military recruits). Case management and health education were also instituted. Vaccine was provided from central stores, current vaccine stocks are very limited and the Ministry of Health looks to WHO to procure additional vaccine when required.

Seventeen diseases in Ethiopia, including meningococcal meningitis, are under surveillance. Standard reporting forms for surveillance have been developed and are in use. Case definitions have been developed and meningococcal meningitis is reported on a weekly basis.

Since 1991 national guidelines for the prevention and control of meningococcal disease exist in Ethiopia. Epidemic committees have been established at national, regional and district levels and when an epidemic of meningococcal disease occurs these committees will become active.

There is a budget line for epidemic preparedness at central level, but the funds are so limited that it cannot satisfy the requests from the regions. On the other hand, regions are expected to have a budget line for epidemic preparedness, but there usually is no money available.

5. Evaluation of the ICG in the epidemic response role in Sudan (see Annex 5)

(Ms C. Schulte-Hillen, ISADE (Institución Internacional para la Salud y el Desarrollo))

Introduction
During the epidemic in Sudan, the ICG through its Executive Sub-group not only fulfilled a Coordinating role, but also gave guidance and support: assisting the Ministry of Health in carrying out a rapid situation assessment, formulating plans, creating a task force and providing appropriate technical support through the epidemic period.

Weaknesses in the functioning of the ICG in general and during the epidemic in Sudan:
- Because of the informal set up, the ICG Executive Sub-group depends on the commitment of individuals within the four agencies. There may be a lack of continuity in the dynamic of the group as the composition of the group changes.
- Being a member of the ICG Executive Sub-group as well as being a member of an international organization may mean that members are faced with conflicting mandates and functions.
- Lack of consistent coordination and leadership hampered the functioning of the task force. The leadership should be more explicit and accountability of the different actors' commitment needs to be reinforced.
- Internationally provided technical assistance could have been better coordinated and better integrated into the task force.
- The uncertainty of the amount of vaccine and other materials imported during the epidemic, and the lack of information concerning their actual storage (national, state and location level), increased wastage and made preparedness planning difficult.
- 46% of the vaccines used were purchased through the ICG. The ICG Executive Sub-group partners themselves were not consistent in their use of the ICG mechanism for the purchase of sensitive material; some members of the Executive Sub-group of the ICG did not use the ICG mechanism on all occasions.
- Externally, it is difficult to identify the specific activities belonging to the ICG because the actions of the four agencies in the Executive Sub-group are generally attributed to the individual organizations.

**Strengths in the functioning of the ICG:**
- The informal working arrangement is also an advantage, as an imposed rigid structure would not work; some of the partners would not want to participate in such a structure and individual agencies can make more rapid decisions than a complex bureaucracy.
- The four ICG members and the Ministry of Health formed the stable group of the task force and were able to achieve much.
- Broad representation in the task force of key international organizations participating in epidemic response was an important asset.
- International organizations, agencies and the Ministry of Health were able to mobilize important resources (financial, technical and political).

**Recommendations arising from the evaluation:**
1. Careful tracking of the purchase of vaccine and other materials and the quantity kept reserved stocks should be undertaken.
2. Re-negotiation of the price of the vaccine available to the ICG in order to encourage use of the ICG mechanism. There are other advantages in using the ICG, but a preferential price acts as the main motivation.
3. Direct quality assurance of sensitive material through the ICG partner organizations, including the definition of the characteristics of quality, packaging and practicality of ICG supplied/recommended products.
4. Ensure that oily chloramphenicol is used only for meningococcal disease. MSF has prepared guidelines on the withdrawal of oily chloramphenicol following the end of an epidemic. Improved monitoring of the use of supplies should be ensured, as well as better control on the stocks available at country level which would also reduce wastage.

**Discussion:**
It was generally agreed that the international coordination and the functioning of the task force had been of great benefit in the response to the epidemic in Sudan. The need to include coordination of technical response within the ICG mandate was raised.
6. Forecasting vaccine demand in 2000 (see Annex 6)

a. WHO Regional Office for Africa

(Dr P. Lusamba)

Within the WHO African Region the population living within the meningitis belt is 97 million. Outside the meningitis belt the number of persons considered to be at risk of getting meningococcal disease is 24 million. This makes a total of 121 million persons at risk in the WHO African Region.

The estimated number of people in the target group for vaccination in the region is 60,550,000. The current practice of advising that 10% of this should be held as an immediately available contingency stock would suggest that the region should have such stocks amounting to approximately 6,055,000.

The available information from countries is inadequate to make reliable estimations of the true size of the contingency stocks held. Also, in general there is an insufficient understanding of the importance of providing sound regular and timely epidemiological data.

Consideration needs to be given to the management of the contingency stocks in order to avoid wastage of vaccine through expiration of the product's shelf life, and to mechanisms to resource the maintenance of the contingency stock levels.

b. WHO Regional Office for the Eastern Mediterranean (EMRO)

(Dr E. El Samani)

During 1999, 11.5 million doses of vaccine were used in the WHO Eastern Mediterranean Region for non-epidemic purposes. This includes routine preventive vaccination (5.5 million) and use in association with the annually Hajj and Omra pilgrimage (1 million). From emergency stocks at national level 1 million doses were used; this represents 10 to 30% of the expected needs. Another 1 million was used from the emergency stock kept by the Regional Office. This stock is kept to anticipate epidemics. Three million doses were used by non-Ministry of Health Organizations. In addition, to control the epidemic in Sudan, 15 million doses of vaccine were used (17 million doses were available and 11 million people were vaccinated). In total 26.5 million doses of vaccine were used during 1999.

The needs for vaccine in 2000 are estimated to be 15 million for non-epidemic use (out of which 9 million will be for preventive use). As for epidemic use, 7 million is estimated to be used for the anticipation of a second epidemic wave in Sudan. Additional
vaccine may be needed should other countries experience epidemics in 2000. In total 22 million doses of vaccine are estimated to be needed.

Discussion:
The need to further refine forecasting methods was highlighted. However, it was pointed out that much progress had been made in terms of establishing contingency stocks in countries. The lack of information on contingency stocks available is a worrying sign. There is a concern about wastage of vaccine held at country level, while rotation of the stocks by the manufacturers ensures that there is no wastage of the supplies of the ICG.

7. Update from manufacturers of meningococcal vaccines, oily chloramphenicol and injection material

a. Pasteur Mérieux Connaught International

(Dr P. Laturnus)

In 1999, 25 million doses of meningococcal vaccine were distributed from Pasteur Mérieux Connaught (PMC) to the meningitis belt. This is a low figure compared to last year and was limited to a small number of countries. In the rest of the world the demand has been stable.

The issue of forecasting is important, but more important is something we have already achieved, transparency and openness in the purchase and supply of vaccine. The mechanism and teamwork of the ICG has created a high level of transparency and coordination resulting in reduced duplication of effort and vaccine wastage.

The lack of information about the vaccine stocks held in countries is a continuing problem for forecasting demand. It is important for the ICG preparedness role that we continue to focus on anticipating needs and demands for vaccine.

b. SmithKline Beecham Biologicals Manufacturing s.a.

(Mr J.-B. Simeon)

The epidemic in Sudan has been the major challenge during the 1999 meningitis season. Thanks to efficient communication between SmithKline Beecham Biologicals Manufacturing (SB) and the ICG secretariat, a smooth supply of vaccine was maintained in the face of large demand for product.

Now that the ICG is well established and it has demonstrated its effectiveness during outbreaks, the ICG should look at appropriate levels of emergency stock to be kept at manufacturers' facilities. Since 1997, when they were first put in place, stocks have been slowly depleted. The situation on the meningitis front has stabilized for the past three years, but a target stock for potential future threats ought to be defined. The ICG could then consider rebuilding stocks during the quiet period, i.e. the summer months. At
present the basis of determining the size of such a contingency stock has not been
determined: should this be based on theoretical populations at risk or take into
consideration the number of persons that have already received vaccination in recent
years?

One of the roles of ICG is to maintain and administer a central stock in order to ensure
that meningococcal vaccine is available at short notice in case of declared epidemics. It
is not to act as a purchasing agency in the context of routine or limited scale
procurements by member countries. SB has always made sure that pricing of
meningococcal vaccine to ICG is appropriate, stable, consistent with worldwide trends
and in line with the objective of crisis management.

c. S. N. Laboratories Lafran

(Dr A. Itani)

There is a growing tendency for countries to set up contingency stocks of oily
chloramphenicol on their own behalf. This is a positive development making it easier to
prepare for emergencies. Because it is important that the stocks at national level
increase, the ICG should convince and encourage countries to raise their national stocks.

During 1999 Lafran was able to provide oily chloramphenicol at or low prices. Lafran
receives requests to prepare large amounts of vials during the period immediately
proceeding the meningitis season, which should be available by January. For Lafran the
best period to prepare large amounts of vials is the period between April and November.
A longer planning period would allow for lower prices.

d. Chiron Vaccines

(Dr G. Breghi)

Chiron Vaccines is now able to again supply vaccines to help fight meningococcal
meningitis on a large scale. The AC polysaccharide vaccine is back in production and
can be supplied in substantial quantities, provided enough lead-time is given to plan for
these operations.

A file has been submitted in the United Kingdom for a meningococcus C conjugated
vaccine. Such a vaccine is capable of inducing immunological memory, and is effective
also in infants, unlike the current polysaccharide vaccines. A project to develop a MenA
conjugate vaccine was started a few years ago. The first generation vaccine was effective
but not optimal. The second generation conjugate vaccines for MenA have been
developed which are ready to go into clinical trials.

Conjugate vaccines will in the future allow a different approach towards vaccination.
The ICG is encouraged to consider what role it should take in the introduction of the new
conjugate vaccines for meningococcal disease.
The broad composition of the ICG has allowed it to find practical solutions to problems regarding the use of vaccine for rapid response in epidemics. Extension of the ICG to a wider range of health problems should be considered. It would also be advisable for the ICG to pool resources to develop a MenA conjugate vaccine.

**Discussion:**

Since the establishment of the ICG, the price for a dose of vaccine has dropped significantly. It is believed that the ICG receives the most preferential price for their vaccine, and it was emphasised that the ICG role is to ensure the availability of emergency stocks and not to interfere with the pricing mechanism. Part of the significant added value for countries ordering through the ICG is obtaining vaccine at a preferential price. If the ICG cannot offer a better price than the open market, purchasers will be less motivated to use the ICG-mechanism. It was felt that any price negotiations regarding the supplies should take place in a different forum.

Vaccine manufacturers stressed that it would be more effective to establish the emergency stocks during the quiet season for meningococcal disease. The manufacturers already try to anticipate likely demand for their products and therefore take a certain risk, but the difficulty is to decide how big this risk should be.

**8. Reports on progress in operational research (see Annex 7)**

**a. EPICENTRE**

(Dr R. Lewis)

**Meningococcal meningitis threshold studies in Togo and Mali**

**Introduction**

Meningitis incidence thresholds are used to identify epidemics early but the level recommended for meningitis belt countries, 15 cases / 100 000 inhabitants / week averaged over two consecutive weeks, has proven to be less than satisfactory. With this threshold, interventions often start too late, as it can take 2-3 weeks to mount an effective response.

**Objectives of the study**

- evaluate the usefulness of the currently recommended threshold for the detection of meningitis epidemics and explore other potential thresholds;
- consider time constraints in the evaluation of selected epidemic thresholds.

**Methods**

Meningitis case data were collected from all health centres in northern Togo for 1990-1997 and the Segou region of Mali for 1989 - 1998. The ability of different incidence thresholds to predict an epidemic was determined. An epidemic was defined as more than or equal to 100 cases / 100 000 inhabitants per year. To assess the performance of different thresholds, sensitivity, specificity, and negative and positive predictive value
were calculated by comparing the number of times the threshold was crossed with the actual number of epidemics that occurred. The time available for intervention was defined as the number of weeks elapsed between the time a given threshold was crossed and the peak of the epidemic.

**Results**

Major meningitis epidemics swept the region in 1996 and 1997. In the Togo study, an incidence of 7 and 10 cases / 100 000 inhabitants / week had the best sensitivity, specificity, positive predictive value and negative predictive value. In Mali, threshold levels of 10 or 11 cases / 100 000 inhabitants / week had the best sensitivity and negative predictive value.

In Togo, thresholds of 7 and 10 cases / 100 000 inhabitants / week left 5.4 and 4.2 weeks on average before the epidemic peak in a district. With the recommended threshold of 15 cases / 100 000 inhabitants / week averaged over two consecutive weeks, the time available for intervention was only three weeks. In Mali thresholds of 10 and 11 cases per 100 000 left 3.2 and 3 weeks before the epidemic peaks, while current recommendations left only 2 weeks between crossing the threshold and the peak of the epidemic.

**Conclusions**

The use of a lower threshold should increase the time available for intervention in comparison with current recommendations and could increase the number of cases prevented. A threshold of 10 cases / 100 000 inhabitants / week could be used as a starting point. WHO should continue to review its recommendations regarding meningitis epidemic thresholds.

**Discussion:**

It was emphasised that a number of methods of determining an epidemic threshold could be employed: in addition to absolute rates of disease the doubling of numbers of cases in a population in consecutive weeks or in comparison to the same week in previous years can indicate the start of an epidemic. The widely accepted threshold of 15 cases per 100 000 for two weeks was felt to be applied too rigidly. Once again it was emphasised that any epidemic threshold is dependent upon the availability of an effective surveillance system.

Underreporting or loss of data in the surveillance chain will decrease the sensitivity of the threshold. Because surveillance data is vital for the determination of threshold levels, improvement of surveillance should be sustained.

But even when used with a more sensitive threshold, the impact of polysaccharide vaccine is limited, so there should be a lobby for the development of conjugate vaccine.

A participant suggested that longer-term prediction of epidemic likelihood could be based upon identification of circulating strains, medium-term predictions on carriage rates of the organism and short-term predictions on 'epidemic thresholds'.
b. World Health Organization

(Dr E. Tikhomirov)

Research priorities for the more effective use of vaccines for the prevention and control of meningococcal disease in the African meningitis belt

One of the recommendations of the 4th ICG meeting was to hold a consensus meeting on priority research to improve the use of meningococcal vaccine. A review paper on this subject has been prepared by a WHO consultant, which was circulated to experts in the field for comments.

The integration of these comments has resulted in a final draft which cannot yet be published or presented, as it contains reference to unpublished data and is subject to ongoing discussions.

Gaps in current knowledge are identified in the field of epidemiology, vaccine science and operational issues. The paper also identifies ongoing research that may fill some of these gaps. The next steps are to reach an agreement on the research priorities with the research community and to develop a plan of work identifying implementing partners and resources.

9. Update on current vaccine issues (see Annex 8)

World Health Organization

(Dr L. Jodar)

Epidemic meningitis vaccines for Africa (EVA)-project

Background
The constraints of using polysaccharide vaccine for routine protective use are well known. Conjugate vaccines provide protection during early childhood and induce immunological memory that persists into adult life. The disadvantages of current polysaccharide vaccine are the short duration of protection with a single dose, the need for four dose schedules, the capacity of the EPI programme to accommodate such a schedule and the costs.

The impact of conjugate vaccine on any herd immunity is unknown, but there are expectations that it could have a significant effect on carriage rates. Through herd-immunity the vaccine has the potential to change the epidemiology of the disease without reaching the highest coverage rates. A meningococcal serogroup A vaccine offers unique opportunities to meet a public health need of the African meningitis belt. The political commitment exists in these countries to tackle what is perceived to be a high risk of disease; furthermore the technology and know-how is available.
The largest epidemics are more or less confined to around 16 countries of the meningitis belt. Manufacturers find this relatively small and resource limited market commercially uninteresting.

Completed trials of A conjugate vaccines in Africa have indicated the potential of such products to induce long-lasting immunological responses. However, the major manufacturers are no longer planning to produce an A or A/C conjugate vaccine and concentrate instead on the production of quadrivalent vaccines.

WHO is therefor developing a project involving the establishment of a not-for-profit company (NFP) which, in alliance with commercial firms, can take forward the development of a vaccine for the African meningitis belt. Three options are under consideration.

1. **Alliance between NFP and a major vaccinate company**
   The NFP company purchases bulk conjugate vaccine from a major pharmaceutical company and will be responsible for quality control, clinical and regulatory development and other licensure activities.

2. **Manufacturing vaccine, in part at the NFP**
   The NFP purchases bulk polysaccharide vaccine and carrier protein and develops a manufacturing facility to perform the conjugation chemistry and other downstream activities.

3. **Full manufacturing facility**
   The NFP builds or acquires a manufacturing facility with fermentation and purification capability, as well as conjugation chemistry and all downstream facilities.

This is not a theoretical approach, but will result in a concrete and focused initiative with a business plan. It will focus on the development of a single product which will be specifically designed for the African meningitis belt.

The project will be taken forward through a meeting to be held in April 2000, at which the introduction and implementation of this strategy will be decided amongst the partners involved, including the governments of meningitis belt countries. The business plan is being developed and will be available at the meeting.

**Discussion:**
The proposal to produce a conjugate meningococcal vaccine for use in the epidemic prone countries of Africa was welcomed by all the participants. The Regional Offices for Africa and the Eastern Mediterranean were particularly enthusiastic to ensure the progress of this project. There was some discussion of the pros and cons of the three business-plan scenarios presented, but it was recognized that the ICG was not the forum to offer clear direction to this project. It was pointed out that conjugate vaccines had been shown to be immunogenic but their ability to block an epidemic has yet to be demonstrated. The ICG welcomed the discussion of this proposal and looks forward to the results of the meeting in spring 2000.
Recommendations

The participants of the 5th meeting of the International Coordinating Group on Vaccine Provision for Epidemic Meningitis Control (ICG) made the following recommendations:

1. The four Executive Sub-group members of the ICG should affirm their commitment to the new terms of reference of the ICG (see page 21);

2. The members of the Executive Sub-group of the ICG should identify a single contact person to ensure the day-to-day work of the Executive Sub-group of the ICG;

3. The Executive Sub-group of the ICG should oversee issues concerning the items that have been purchased through the ICG, and should ensure that appropriate follow up action is taken when needed;

4. The partners of the Executive Sub-group of the ICG should continue negotiating with the manufacturers on issues such as price, quality and availability of the products purchased through the ICG;

5. The Executive Sub-group of the ICG should investigate shipment options to ensure a timely delivery of epidemic response items at an optimal price;

6. The next meeting of the ICG should take place in September / October 2000;

7. Each member of the Executive Sub-group of the ICG should coordinate and report progress on the following technical issues:

   IFRC  - Epidemic preparedness and surveillance at community level
   MSF   - Epidemic thresholds
   MSF   - Evaluation of interventions
   UNICEF - Interaction between National Immunization Days and epidemic intervention
   WHO   - Security stock of vaccine at country level
   WHO   - Demand forecasting, epidemic trend analysis

8. The Executive Sub-group of the ICG should continue to produce an ICG newsletter, ensure a wider dissemination and encourage feedback.
Revised terms of Reference
Executive Sub-Group of the International Coordinating Group on Vaccine Provision for Epidemic Meningitis Control

A sub-group of the International Coordinating Group on Vaccine Provision for Epidemic Meningitis Control to review requests for meningococcal vaccine, drugs and injection material and to coordinate their allocation through the following activities:

- Review inventory of existing stocks in countries;
- Review availability from manufacturers;
- Review requests and compare with criteria for allocation;
- Seek complete information to back up requests from countries;
- Advise on the amount to be allocated;
- Monitor distribution of epidemic response items by countries and partners;
- Review financial resources for procurement.

Provide technical support in the following technical areas when needed:

- Initial situation assessment
- Surveillance and monitoring
- Plan of intervention
- Vaccination strategies
- Case management
- Evaluation
- Resource mobilization
Terms of Reference

The revised Terms of Reference, endorsed by the meeting in Geneva on 8 and 9 December 1999, are given below.

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, autodestruct 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 meningitis outbreaks;

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