World Health Organization

EXECUTIVE BOARD
120th Session
Provisional agenda item 4.9

EB120/37
21 December 2006

Progress in the rational use of medicines, including better medicines for children

Better essential medicines for children

Report by the Secretariat

1. The Health Assembly has adopted numerous resolutions on pharmaceutical issues, such as the rational use of drugs (most recently resolution WHA47.13), ethical criteria for medicinal drug promotion (resolution WHA41.17), the WHO Action Programme on Essential Drugs (resolution WHA45.27), the role of the pharmacist (resolution WHA47.12), the revised drug strategy (resolution WHA52.19), the WHO medicines strategy (resolution WHA54.11) with its global framework for expanding access to essential medicines, antimicrobial resistance (resolution WHA58.27) and public health, innovation, essential health research and intellectual property rights (resolution WHA59.24). However, to date no resolution has specifically mandated work on promoting better essential medicines for children. This report has been prepared in response to the request from a Member State that this matter should be considered by the Executive Board.

2. An estimated 10.5 million children under the age of five years die every year. Many of these deaths are from treatable conditions: the most common is pneumonia, but others include diarrhoea, HIV disease, AIDS and malaria. Two of the Millennium Development Goals focus on significantly reducing this unacceptably high level of child mortality. Goal 4 aims to reduce by two thirds, between 1990 and 2015, the mortality rate among children under five, and Goal 6 aims to have halted by 2015 and begun to reverse the spread of HIV/AIDS and to have halted by 2015 and begun to reverse the incidence of malaria and other major diseases. Recent data, however, suggest that few countries are on track to achieve these goals, even though effective interventions exist for many of the conditions, at least for adults. The interventions entail use of "essential medicines", that is, they satisfy the priority health-care needs of the population.[1] Many of these essential medicines, however, do not exist in dosage forms for children or, if they do, are not available in low- and middle-income countries. For example, antibiotics to treat pneumonia were available in less than 20% of cases in developing countries when last assessed (although recent data are lacking). Similar problems have been identified in a recent preliminary survey undertaken by WHO in relation to the availability of essential medicines such as co-trimoxazole suspension, used in the management of children with HIV.[2] Lack of availability of these essential interventions has been identified as a major reason for countries not making adequate progress towards the Millennium Development Goals.

[1] WHO Technical Report Series, No. 933, 2006.

[2] Meeting Report, Joint WHO–UNICEF Consultation on Essential Medicines for Children, Geneva, 9–10 August 2006, available at http://www.who.int/medicines/publications/UNICEFconsultation.pdf.

3. The reasons why medicines for children are not available have been described in several studies, and fall into four main groups: lack of scientific information; lack of appropriate drug development; relative market failure; and insufficient staff, knowledge and prescribing information for health-care professionals and other carers at the point of care in order to be able to ensure appropriate use of medicines for children.

4. Scientific information is lacking in several different areas. Many medicines have not been properly tested in children for efficacy and safety, and regulators therefore cannot approve their paediatric use. Hence, children are often treated as small adults when dose is being determined. Many concerns have been expressed about whether it is appropriate to carry out clinical trials of new medicines in children, in particular in developing countries. Fixed-dose combination products are an important example. For diseases such as malaria, HIV and tuberculosis, recommended treatment is with such combinations as it reduces the number of tablets patients have to take, which in turn improves adherence to treatment. However, since fixed-dose combination products have not been a priority for developed-country markets (because of the relatively small number of children there with those conditions), few studies have been done on their use in children. Development of fixed-dose combination products for paediatric patients therefore lags far behind the need for them in developing countries.

5. Similar failings exist in other major therapeutic areas such as treatment of chronic disease in children, including epilepsy and diabetes, and management of terminal diseases. In some cases the lack of available medicine is due to the absence of appropriate dosage forms of essential medicines for children. Although syrups are appropriate for small children under three years of age, other forms such as chewable low-dose tablets or small granules may be easier for children to swallow and easier for carers to administer. Few examples of these types of dosage forms currently exist.

6. Lack of appropriate drug development and relative market failure are closely linked. Manufacturers have been reluctant to undertake research and development into medicines for children, owing to the unpredictable and smaller market for these products. Even when appropriate dosage forms of medicines for children have been developed, they are often not available in low-income countries. This unavailability is mainly due to high prices, and inadequate capacity to procure and supply medicines. Weak procurement is one reason, as exemplified by the difficulties in procuring and distributing syrups for children – those steps need adequate warehouse capacity for shipping large volumes and bottles High prices are also a problem: procuring syrups can be up to 500% more expensive than comparable medicines for adults. In addition, in some countries, the national essential medicines list is used to guide reimbursement of medicines and, if essential medicines for children are not included on these lists, they may not be included on reimbursement schemes.

7. Lack of appropriate capacity and information for the effective use of medicines has been described for various important diseases. For example, recent data show that in some settings only 20% of carers can identify early signs of pneumonia, and only about half the children with suspected pneumonia receive appropriate treatment. In HIV and malaria, there is still uncertainty about the effective dose of some essential medicines in children under three years of age. In settings where only adult-strength tablets are available, there may be no way to provide an appropriate dose of a medicine for a child, even if that were known.

8. WHO has been working with governments, other organizations in the United Nations system, universities, the private sector, nongovernmental organizations and funding agencies on various aspects of improving access to essential medicines for children, and has reviewed some of the activities being undertaken by Member States. Important initiatives related to medicine development and regulation in North America have had some impact on the situation there and similar measures

will be implemented in Europe in 2007. However, these initiatives, which combine incentives and requirements for medicine development, are unlikely to solve the problem in developing countries without global action. There is evidence that limited regulatory capacity is a barrier to access to HIV treatment in some regions, resulting in delays in licensing new medicines for HIV. It is likely that the delays occur in licensing medicines for other diseases as well. In consultation with technical experts and key partners, WHO has begun to develop a comprehensive plan of work to improve access to essential medicines for children.

9. The WHO Model List of Essential Medicines is a vital instrument for promoting access to medicines generally. A review of the 14th Model List found at least 20 medicines that may be essential for children and are potentially available in developed-country markets but which are not listed, and a further 20 medicines that are likely to be essential for children but do not exist in appropriate dosage forms.[1] Work has begun to revise and update the List accordingly; this is an important first step in developing global standards but does not go far enough. Pharmaceutical manufacturers need to devise new dosage forms and strengths of medicines that can be used by children of different ages and that are easy to store, handle and administer. Standards for the ideal types of dosage forms of medicines for children should be established, including a description of the pharmaceutical specifications needed. Setting standards will assist the manufacturers of such products (including generics), and help to encourage increased supply and affordable prices. For medicinal product development, global standards must be set and capacity established for conducting appropriate, ethically-sound clinical trials in children in order to identify additional medicines that are effective and safe. Methods of monitoring the safety of medicines in children after a medicine has been approved need to be improved and tested. Initial technical consultations on the actions needed have taken place with experts and partners in pharmaceutical development.

10. Once appropriate and effective medicines are available, the capacity to use them correctly needs to be ensured. That, in turn, requires health workers to know the appropriate ways to prescribe, dispense and administer medicines for children. Examples show that training programmes for community health-care workers can increase the appropriate use of antibiotics in children with pneumonia. Other examples, however, demonstrate the need for further implementation of guidelines, such as those on ensuring the appropriate dose in vitamin A supplementation. Providing evidence-based prescribing information and guidelines at the point of care, through appropriate technology, is an essential strategy in improving use of medicines; WHO's treatment guidelines could serve as the basis of this approach. A review of WHO's existing treatment guidelines for children is being undertaken in order to ensure that they are evidence-based and fully meet the needs of Member States. WHO is also working with academic institutions, through the International Child Health Review Collaboration, on a dynamic process of updating the evidence underpinning these guidelines, and to enable health workers to participate in this process through Internet access.[2]

11. To undertake the activities needed to improve access to essential medicines for children, WHO, Member States, organizations in the United Nations system and other partners need to collaborate on a global approach. A two-phase approach is proposed: first, on the basis of existing regional expertise and experience; initial setting of global norms and standards on selection, quality, supply and procurement of essential medicines for children, and establishing appropriate financing systems; and

[1] Meeting Report, Joint WHO–UNICEF Consultation on Essential Medicines for Children, Geneva, 9–10 August 2006, available at http://www.who.int/medicines/publications/UNICEFconsultation.pdf.

[2] Duke T. et al. Accessing and understanding the evidence. *Bulletin of the World Health Organization, 2006; **84** (12):922.*

secondly, creation of comprehensive regional and country programmes based on the plan of work referred to in paragraph 8 above, for implementing strategies to ensure development, availability, and appropriate use of medicines, supported by innovative technology.

ACTION BY THE EXECUTIVE BOARD

12. The Executive Board is invited to consider the following draft resolution:

> The Executive Board,
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> Having considered the report on progress in the rational use of medicines, including better medicines for children,[1]
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> RECOMMENDS to the Sixtieth World Health Assembly the adoption of the following resolution:[2]
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> > The Sixtieth World Health Assembly,
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> > Having considered the report on progress in the rational use of medicines, including better medicines for children;
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> > Recalling resolutions WHA39.27, WHA41.16 and WHA47.13 on the rational use of drugs, WHA41.17 on ethical criteria for medicinal drug promotion, WHA43.20 and WHA45.27 on the WHO Action Programme on Essential Drugs, WHA47.12 on the role of the pharmacist in support of the WHO revised drug strategy, WHA49.14 and WHA52.19 on the revised drug strategy, WHA54.11 on the WHO medicines strategy, and WHA58.27 on improving the containment of antimicrobial resistance;
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> > Recognizing the efforts of WHO in collaboration with governments, other organizations in the United Nations system, universities, the private sector, nongovernmental organizations and funding agencies in areas related to improving access to better medicines for children;
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> > Aware of the core components of WHO's global framework for expanding access to essential medicines;
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> > Wishing to promote evidence-based selection and use of medicines for children by health providers and carers;
> >
> > Aware that there are regional initiatives to address inadequate access to essential medicines for children;

[1] Document EB120/37.

[2] See document EB120/37 Add.1 for the administrative and financial implications for the Secretariat of this resolution.

Wishing to ensure better access to essential medicines for children as a prerequisite for achieving health outcomes as set out in the Millennium Development Goals;

Aware that the lack of access to essential medicines of assured quality continues to pose significant risks of high morbidity and mortality in children, especially those under five years of age;

Recognizing that many countries do not have the requisite capacity to regulate and control medicines for children;

Aware that many manufacturers of essential medicines have neither developed nor produced appropriate dosage forms and strengths of medicines for children;

Concerned that there is insufficient investment in the clinical trials, development and manufacture of medicines for children;

1. URGES Member States:

(1) to ensure that appropriate medicines are developed for the diseases that affect children, and that high-quality clinical trials for these medicines are conducted in an ethical manner;

(2) to promote access to essential medicines for children through inclusion of those medicines in national medicine lists, procurement and reimbursement schemes, and to devise measures to monitor and reduce prices;

(3) to take steps to identify appropriate dosage forms and strengths of medicines for children, and to encourage their manufacture and licensing;

(4) to enable rapid licensing of appropriate, high-quality and affordable medicines for children with innovative methods for monitoring the safety of such medicines;

2. REQUESTS the Director-General:

(1) to set global standards for, and promote global consistency in, clinical trials of essential medicines for children, to select such medicines by means of evidence-based clinical guidelines, and to promote adoption of these standards by Member States and international financing bodies, with initial focus on treatments for HIV/AIDS, tuberculosis, malaria and chronic diseases;

(2) to promote the development of international norms and standards for quality and safety of formulations for children, and the regulatory capacity to apply them;

(3) to make available evidence-based treatment guidelines and independent information on dosage and safety aspects of essential medicines for children, and work with Member States to implement these guidelines in order to promote rational use by prescribers and patients, providing information through appropriate technologies;

(4) to collaborate with governments, other organizations in the United Nations system, donor agencies and nongovernmental organizations in order to ensure adequate financing for securing better access to medicines for children;

(5) to report to the Health Assembly through the Executive Board on progress achieved, problems encountered and specific actions needed to further promote better access to medicines for children.

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