A Desk Review of Existing Literature on Medicines for Children

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# ABBREVIATIONS

<table>
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<th>Abbreviation</th>
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<tr>
<td>AIDS</td>
<td>Acquired Immunodeficiency Syndrome</td>
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<td>BMC</td>
<td>Better Medicines for Children</td>
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<td>DTC</td>
<td>Drug and Therapeutics Committee</td>
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<td>EML</td>
<td>Essential Medicines</td>
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<td>EMLc</td>
<td>Essential Medicines List for Children</td>
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<tr>
<td>FDB</td>
<td>Food and Drugs Board</td>
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<tr>
<td>GHS</td>
<td>Ghana Health Service</td>
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<td>GOG</td>
<td>Government of Ghana</td>
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<td>GMP</td>
<td>Good Manufacturing Practices</td>
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<td>HIV</td>
<td>Human Immunodeficiency Virus</td>
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<td>IGF</td>
<td>Internally Generated Fund</td>
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<td>IRPs</td>
<td>International Reference Prices</td>
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<td>MDGs</td>
<td>Millennium Development Goals</td>
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<td>MOH</td>
<td>Ministry of Health</td>
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<td>NMP</td>
<td>National Medicine Policy</td>
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<td>ORS</td>
<td>Oral Rehydration Solution</td>
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<td>STGs</td>
<td>Standard Treatment Guidelines</td>
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<td>UNICEF</td>
<td>United Nations Children’s Fund</td>
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<td>WHA</td>
<td>World Health Assembly</td>
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<td>WHO</td>
<td>World Health Organization</td>
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EXECUTIVE SUMMARY

A review of relevant reports and literature held by the World Health Organization (WHO), the Ministry of Health (MOH), UNICEF, and others related to medicines for children was undertaken as part of the project “Better Medicines for Children” (BMC) in Ghana.

The BMC is a WHO-led project funded by the Bill and Melinda Gates Foundation for improving the availability, accessibility, and use of child-specific medicines in Africa and India. Ghana was one of the two countries selected from Africa for implementation of country specific interventions geared towards achieving this goal. The BMC project in Ghana forms part of the framework of the country’s programme of work meant to achieve Millennium Development Goals 4 and 6 for reducing child mortality. Ghana embraced the BMC project because of its relevance with respect to access to medicines for children. The project also seeks to address issues within countries pertaining to existing child health policies.

The literature review assessed the existing knowledge about the supply and use of paediatric medicines, in general, and the 38 medicines on the global and supplementary lists of children’s medicines, in particular. The review identified aspects of the pharmaceutical sector that need to be enhanced in order to ensure availability and affordability of child-specific medicines. The review also considered the impact of factors such as rational selection, affordable prices, sustainable financing, and reliable health and supply systems. Some issues arising from the review included:

- Approximately 30% of targeted child-specific medicines are produced by local pharmaceutical manufacturers, even though capacity exists to produce a further 68% of the 38 medicines on the global and country supplementary list.
- There is undue emphasis on the production of over-the-counter medicines as a result of high demand for this class of medicines and this has deterred local manufacturers from producing child-specific essential medicines.
- Only 20% of the 500 medicines listed in the Essential Medicines List (EML) are produced by local manufacturers.
- A restricted list of 16 medicines mandated by the Government to be produced locally only has two medicines specifically for children; namely, syrup chloroquine, which is no longer used, and paracetamol syrup.
- Corporate taxes on industrial pharmaceutical raw materials and other withholding taxes are a disincentive for expansion of production to other lines, such as essential medicines for children, which invariably are not in high demand.
- Local manufacturers could explore the use of platform technology (an innovative technology) to make child-specific formulations available that are flexible to use at point-of-administration.
- The Food and Drugs Board (FDB) is not adequately resourced to monitor quality and safety of locally manufactured medicines as part of an effort to assist these manufacturers in achieving international standards.
• The distribution networks of local manufacturers appear chaotic and unquantifiable, hence the potential for increases in medicines prices.

• Current activities by drug and therapeutics committees, as defined in the Ghana National Medicine Policy of 2004, do not indicate any active role in the promotion of rational use of medicines in children.

• Drug and therapeutics committees have a major role to play in ensuring the availability, affordability, and safety of child-specific formulations of essential medicines in all health-care facilities.

• Drug and therapeutics committees also have the role of ensuring that appropriately trained personnel manage children’s conditions in an effort to achieve rational prescribing and optimal use of medicines.

• The MOH has no clear policy for systematic training and retraining of paediatric prescribers.

• There are problems with communication between health-care implementers, providers, researchers, and policy makers, which often result in sub-optimal quality of prescribing and referrals.

• Persistent stock-out of medicines, limited numbers of medicines available for treatment of children, and inappropriate dosage forms, are some of the problems identified with irrational use of medicines for children.

• The bulk of medicines used in Ghana are imported and account for 70% of all drugs available in Ghana, and imposes a limitation on access because of high prices.

• Child-specific medicines for high-risk diseases and conditions, such as HIV/AIDS, tuberculosis, malaria and other conditions, are not easily available.

• Inconsistencies exist in price mark-ups for medicines in all sectors, thereby reducing access to medicines for children especially.

• There are currently no national standard treatment guidelines for children to support rational use of medicines in children.

• Examination of MOH national competitive bidding documents for 2003 revealed total purchases from local manufacturers to be 37% in total value, but these purchases constituted only 0.4% (solids) and 1.3% (liquids) of manufacturers’ installed capacity.

• Supplies from vertical programmes for diseases and conditions are limited and are not coordinated with standard supply chains. Additionally, these medicines are also not child-friendly.

• Government allocations for medicines constitute only 15% of its budget, which is woefully inadequate to provide access to health care for children.

• Donors’ in flows for medicines appear unreliable since these do not pass through the normal supply chain.

• Current information on the status of the National Health Insurance Scheme (NHIS) indicates that 65% of the population, particularly children, may be denied access to medicines if the current funding challenges facing the NHIS are not addressed.
TERMS OF REFERENCE

To undertake a desk review of reports and literature, held by the MOH, WHO, UNICEF, the Ghana Better Medicines for Children project working group and other stakeholders, related to medicines for children in Ghana, and prepare a report summarizing:

- existing knowledge about the supply and use of paediatric medicines
- aspects of the pharmaceutical sector that need to be enhanced to ensure better medicines for children

and covering:

- local manufacturing capacity
- availability and price strategy
- reports describing rational drug use in paediatric populations
- current activities of drug and therapeutics committees that may be relevant for medicines for children.

OBJECTIVES

The objectives of the report were to:

- review existing knowledge from a literature search about the supply and use of essential child-specific medicines
- identity aspects of the pharmaceutical sector that need to be enhanced to ensure access to child-specific medicines
- assess the impact of governance in the areas of reliable health and supply systems, rational selection, affordable prices and sustainable financing on access to child-specific essential medicines.

The medicines category used was the global list of core paediatric medicines and Ghana’s supplementary list of items selected at country level for their national importance - a total of 38 medicines.
INTRODUCTION

Since endorsement of World Health Assembly Resolution 60.20 on Better Medicines for Children in May 2007, an intensive campaign was launched, urging Member States to accelerate action to address the need for improved availability, affordability and access to safe, child-specific medicines. In 2007, following the resolution, Ghana developed a child health policy with the goal of reducing the mortality rate of children under 5 from 111 deaths per 1000 live births in 2006 to 40 deaths per 1000 live births by 2015 (2010 report GHS).

The BMC project is a WHO initiative, for implementation in Member States, to improve access to essential child-specific medicines. This project also forms part of the framework and mechanisms set in place to achieve MDGs 4 and 6 for reducing child mortality in the country (2010 report, GHS).

At the launch of the BMC project in Ghana on 15 April 2010, after deliberations among major stakeholders, the following challenges facing prescribers, dispensers and consumers were noted:

- Doses prescribed for children often do not match the bottle sizes of liquid formulations leading to additional expense for parents if they have to purchase an extra bottle.
- Purchasing extra bottles of medicines to complete the course of treatment leads to the same problem of cost and to wastage if the excess volume has to be discarded.
- Medicine quality can be compromised when the reconstitution process takes place outside a pharmacy by a non-qualified person.
- Wide variations exist in the type and accuracy of measures used for children’s liquid formulations and this can lead to inaccurate dosing.
- Most liquid formulations for children appear too bulky for easy transportation and carry the risk of breakages.
- De-formulation of tablets and contents of capsules to give to children is a widespread practice among parents and care-givers but often leads to inaccurate dosing due to the erratic dispersion of active ingredients. Therefore the consensus reached was that global trends for the manufacture of child-specific formulations should support flexible, easy to reconstitute dosage forms for use at the point of administration.

The stakeholders also affirmed that drug and therapeutics committees should be empowered to ensure the rational selection and use of child-specific medicines in all health-care institutions (2010, report). The availability and rational use of child-specific medicines of acceptable quality and safety are prerequisites for reducing morbidity and mortality among children (WHO, 2009).

Preliminary data from a multi-country study presented at the 2009 partners meeting on BMC, suggested that one of the problems with access is that if a paediatric dosage form of medicine exists it is substantially more expensive than an equivalent adult dosage form. For this reason countries prefer to use fractions of adult medicines to treat children. The risk with this approach
is that dividing adult dosage forms can result in inappropriate doses for children, leading to overdose and potential toxicity or underdose and potential inefficacy (WHO report, 2009). Examination of published and grey reports about manufacturing capacity for child-specific medicines identified challenges, such as the:

- paucity of high quality research in children, especially in settings associated with highest mortality;
- limited number of internationally certified manufacturers as well as the limited capacity for pharmaceutical product innovation;
- challenges of incentivizing product development in children in an environment of limited resources, slow licensing and uncertain markets as pertains in Ghana (WHO report, 2009).

Currently Ghana has no national essential medicines list for children (EMLc) and no national treatment guidelines for children (STGc).

In general, wide variations exist in medicines prices for both originator brands and generics and this is particularly so for children, although results from the recent survey indicated that child-specific essential medicines are not readily available in the country (W.G. Report, 2010).

The pharmaceutical sector comprises both public and private medicines supply and distributions outlets. There are about 8000 pharmacies and licensed chemical sellers in Ghana as well as private and mission health-care facilities that supply medicines through the private sector. Public sector medicines supply is through pooled procurement with distribution through Government regional stores to the institutions.

Ghana has a National Medicine Policy document, which was last updated in 2004. An implementation plan setting out activities aimed at achieving the Policy goals is not in place. The national standard treatment guidelines (STGs) were last updated in 2010.

The pharmaceutical sector is regulated by the Food and Drugs Board (FDB) and the Pharmacy Council (PC). The FDB is responsible for product licensing and marketing authorization for local pharmaceutical manufacture, and the PC for regulating the practice of pharmacy and approval of site locations for the distribution of medicines.

About 65% of the population had registered with the National Health Insurance via various mutual schemes throughout the country. Enactment of the National Health Insurance Act means that for registered members treatment is provided for various categories of health conditions, so they receive free services at the point of care. However medicines for children in the National Health Insurance List of Medicines are woefully inadequate. Examination of the October 2009 National Health Insurance Medicines List indicated only about 11% of medicines for children in all disease categories (N.H.I.A, 2009).

Medicines financing in the public sector is from the Government of Ghana (G.O.G), donors, payment for medicines and other services, (Internally Generated Funds (IGF)) and the National Health Insurance Schemes.
Access to medicines is a complex construct, because medicines should not only be available but affordable and acceptable to patients. (Robertson, 2009).

METHODOLOGY

The review assessed published literature from the MOH, WHO, UNICEF, reports from the Technical Working Groups constituted for the Better Medicines for Children project, interactions with key personnel of some local pharmaceutical manufacturers and pharmaceutical wholesalers. Other sources were grey reports from the MOH and others. Literature sources were reviewed in terms of their relevance to child-specific medicines, their supply, availability, affordability and rational use.

FINDINGS

A. Existing knowledge about the supply and use of paediatric medicines with regards to:

i. Local manufacturing capacity
ii. Information about availability and pricing strategy
iii. Reports describing rational use of medicines in paediatric populations
iv. Current activities of drug and therapeutics committees that may be relevant to medicines for children.

i) Local manufacturing capacity for formulations appropriate for children

According to the literature, the pharmaceutical market is very fragmented. Even though there are 34 registered local manufacturers, only 8 major ones account for 80% of the market share, the rest have not been consistent with their production. This assessment therefore focuses on the eight principal manufacturers.

The literature showed that almost all the companies meet the requirements for basic, Good Manufacturing Practices (GMP) assessment by the FDB for pharmaceutical production. Local manufacture accounts for only 30% of all essential medicines in the country. The remaining 70% come from importation both for the public and private sectors and a small percentage from vertical programmes for diseases and conditions. Ghana has a state system for medicines procurement in the public sector within a functioning procurement unit. The criteria used to guide the selection of medicines confine the circulation of essential medicines to specific and appropriate settings and levels of health-care delivery. The growth and capacity of local pharmaceutical production is marginal. Local pharmaceutical manufacture has been weighed down by the Government’s market policy, and lack of tax exemptions for raw materials, thereby adversely affecting production and competition (Grupper et al., 2005).
It was found that currently a list of 16 formulations of generic medicines have been mandated for local production and their importation would be forbidden in order to provide an incentive for local manufacturers (Appendix 3, List of Restricted Medicines) (PMAG, 2010). However paracetamol syrup is the only child-specific formulation among the 16. This situation should compel the Government to provide incentives to local manufacturers to expand the range of essential medicines for children. When similar action is taken for essential child-specific medicines, problems of access, price, availability and affordability would be addressed.

None of the manufacturers reviewed had plans to venture into new technology for producing child-specific essential medicines apart from the few over-the-counter products for the private sector. When occasionally money is allocated for research and development it is usually on a case-by-case basis and targeted towards new product lines. A case could therefore be made for innovative formulations to deliver optimal dosage in children especially with active support from Government. However, examination of a 2010 BMC Working Group survey of local pharmaceutical manufacturing capacity for the list of 38 children’s medicines, showed that 29% of the 22 manufacturers could produce antibiotics containing penicillin whilst 7 have future plans to expand production of this group of medicines. It was also found that none of the 22 manufacturers produce other beta-lactam antibiotics. A similar situation was found with medicines for treatment of tuberculosis and opioid analgesics (W.G. Report, 2010).

Quality assurance systems exist in most of the companies but FDB reports from the literature indicate poor documentation of processes. With the strengthening of the FDB in terms of equipment and human resource capacity much could be achieved in order to make these pharmaceutical manufacturers perform to high standards.

From the literature, most companies’ distribution networks appear chaotic and unquantifiable. This is because most of these manufacturers do not have an adequate number of wholesale outlets and defined distribution networks for their products. This situation increases the final price patients have to pay, and also does not promote access to medicines, especially for children (Grupper et al, 2005).

There was no documentation of any of the manufacturers having any systematic training in place for either professional or other key staff in terms of building capacity for human resource development. To venture into the production of child-specific medicines, there should be on-going training to acquire new knowledge and skills for staff, and training in the use of new technologies to attain international standards and competition in production. The number of professional staff in most of these companies is seriously inadequate, and will remain so unless active recruitment is pursued to bridge the gap and to make provision for succession planning (W.G. 2010).

All the manufacturers indicated that they have access to capital, either from their own resources, commercial banks or private funds, but none comes from foreign investment funds. The high cost of borrowing from local financial institutions, coupled with the unstable foreign exchange market, do not promote the necessary growth of local industries for them to venture into new formulations. High corporate taxes charged on
industrial raw materials and other withholding taxes all contribute to high medicine price, and these serve as a disincentive for expansion into other product lines, such as essential medicines formulations for children (ibid, 2005).

Most industrial raw materials are imported and the manufacturers usually source them individually. There is no established pooled procurement of these raw materials to ascertain the quality and achieve uniform standards of products which could possibly lead to a reduction in the final patient price. It is anticipated that if this trend continues without intervention to control the quality of active pharmaceutical ingredients, the production of child-specific medicines would fall short of standard requirements and the medicines would be unduly expensive and not accessible (Kinapharma & Dan Adams, 2010).

According to the literature, the eight major companies’ installed capacities for oral liquids and tablets of the eight major industries were quantified as 16 billion litres for liquids, and 18 billion for tablets. However, examination of MOH national competitive bidding documents from 2003, revealed the total purchases from local manufacturers to be 118,000 litres of liquids and 230,000,000 tablets amounting to 37% in total value, but only 0.4% and 1.3% of the industries’ installed capacity. It becomes empirically clear that local manufacture is sustained by demand from the private sector and primarily by the over-the-counter market. It was also found that only 100 medicines (i.e. 20%) out of the 500 product forms on the essential medicines list (EML), are produced locally (Grupper et al., 2005).

There was no indication from the literature reviewed about future plans by local manufacturers to go into innovative formulations specifically for children because of the low demand for these formulations. A few manufacturers (29%) out of 22 manufacturers had budget allocated specifically for the new paediatric fixed-dose artemisinin combination therapy when Government changed the antimalarial drug policy. Sometimes the amount allocated for research and development was found to be on a case-by-case basis and was mainly for developmental work on other product lines, not necessarily paediatric products. This notwithstanding, a case can be made for appropriate formulations of essential medicines for children.

ii) **Information about the availability and price strategy**

Recognizing that better access to medicines is a prerequisite for improving health outcomes in children, in May 2007 the World Health Assembly passed resolution 60.20, which identified key steps for ensuring better medicines for children. The resolution urged the 193 WHO Member States: “to promote access to essential medicines for children through inclusion, as appropriate, of those medicines in national medicines lists, procurement and reimbursement schemes, and to devise measures to monitor prices.”

Given the paucity of data on the availability and cost to the patient of paediatric medicines in different health-care settings, WHO contracted a study in 2007 to document the extent to which key children’s medicines are currently included in national EMLs and STGs, to assess their availability in public and private health-care facilities and their
costs, where applicable, in 14 central African countries, including Ghana. The list of 17 medicines and 20 formulations can be found in Appendix 2.

Some of the findings of the study in relation to Ghana were:

- The facility survey had 75% of the tracer medicines in their EML, 75% in their STGs, but 40% of the tracer medicines at the central medical stores.

- Availability of these medicines by type of facility were:
  - Teaching Hospital: 50%
  - District Hospital: 60%
  - Primary Hospital: 45%
  - Retail Facility Pharmacy: 50%

<table>
<thead>
<tr>
<th>Medicines</th>
<th>Public sector facilities (price range in US$)</th>
<th>Retail pharmacy (price range in US$)</th>
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<tbody>
<tr>
<td>Amoxicillin suspension</td>
<td>0.44-2.13</td>
<td>0.27-4.16</td>
</tr>
<tr>
<td>Ceftriaxone injection 1 g</td>
<td>0.82-26.63</td>
<td>0.54-18.67</td>
</tr>
<tr>
<td>Cotrimoxazole suspension 200 mg+40 mg (100 ml)</td>
<td>0.27-4.16</td>
<td>0.27-5.62</td>
</tr>
<tr>
<td>Paracetamol syrup 120 mg/5 ml</td>
<td>0.27-2.71</td>
<td>0.27-2.85</td>
</tr>
<tr>
<td>Salbutamol inhaler 100 mg</td>
<td>1.30-7.25</td>
<td>2.07-7.45</td>
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The cost of these tracer medicines was difficult to assess because of the policy in most countries to supply medicines to children free of charge. However, the table above shows, in all the 14 countries, the price in US dollars of five selected children's medicines (amoxicillin suspension, ceftriaxone injection, cotrimoxazole suspension, paracetamol syrup and salbutamol inhaler).

The least available surveyed medicines were rifampicin syrup, vitamin A liquid, zinc 20 mg dispersible tablets, beclometasone inhalers and albendazole suspension. Spacer devices for use with salbutamol or beclometasone even though they were not included in the survey list were not available at the central medical stores in almost all the countries.

In general, the proportion of medicines in primary health-care facilities appeared to be lower, only 45% availability. The list of medicines selected for the survey were supposed to be stocked at primary care level and therefore their low availability should be of concern to policy-makers. While some common medicines in the survey list were available in the central medical stores, they were not found in the primary care facilities. This situation does not ensure even distribution.

Even though clinical trials have established the importance of suitable zinc formulations for reducing the severity of diarrhoeal illnesses in children, there was no affordable zinc preparation for children in any of the central medical stores and health-care facilities.
surveyed. During the survey, salbutamol inhalers were widely available but spacer devices for their effective use in children were not (WHO, 2007).

The survey revealed the absence of medicines for some priority diseases, such as HIV infections, tuberculosis and malaria, for children and this could be due to the existence of vertical programmes for these priority diseases. Sometimes these programme’s medicines supplies are not coordinated with standard supply chains in the country and are not child friendly.

In Ghana medicines supply and availability come from three sources, namely, local manufacturers, importation for both the public and private sectors, and from vertical programmes for selected diseases and conditions. However, local manufacture as a source of supply for children’s medicines had been found to be woefully inadequate because of lack of incentive from Government to encourage production.

Importation of medicines was estimated to account for 70% of all supplies with a tendency for them to be more expensive and impose a limitation to access. This is because of the generally weak pricing mechanisms for medicines which are not enforceable. Also there are inconsistencies in price mark-ups for medicines across all sectors. Supplies from vertical programmes are limited and are not coordinated with standard supply chains in the country hence their non-availability in most primary health-care facilities. Some of the children’s medicines formulations that were not available are nevirapine syrup, artemisinin-based combination therapies (ACTs), zinc sulphate dispersible tablets, Vitamin A capsules and rifampicin syrup (WHO, 2007).

The 2010 BMC Working Group survey of 38 medicines’ availability and pricing strategy indicated, that:

- mean availability of originator medicines in the public sector were 3.0%, while the generic ones were 19.3%; in the private sector originator medicines were 10.3%, and generics 17.4%. In the mission sector originator medicines were 5.7% and the generic ones were 21.7%.
- prices patients had to pay were calculated to be three times more than the International Reference Prices (IRP), almost 101.9% (WG, 2010).

The conclusions of the survey were that child-specific medicines in the list of 38 were not readily available in the country. It can be inferred that essential child-specific medicines to treat common ailments in children are not available and this should be of concern to policy-makers and Government.

iii) **Existing knowledge about paediatric medicines with regard to reports describing rational drug use in paediatric populations**

The 2007 survey report on 14 African countries, including Ghana, clearly defined the major causes of death in children as pneumonia, diarrhoea, malaria, neonatal pneumonia and sepsis. There are effective treatments for these diseases. However, a review of countries’ progress towards achieving the United Nations’ MDG for reducing child
mortality, carried out in 2006, found no data to describe the coverage or availability of antibiotic treatment for pneumonia, an intervention said to be relevant in 60 countries. Data on the availability of oral rehydration therapy and anti-malarials were given for only 50 and 31 countries respectively (Robertson, 2009). The delivery of optimal health care to children is limited by the scarcity of skilled human resources in all countries, according to the same report. The development of tools, such as clinical practice guidelines and algorithms for case management, is a useful way of achieving focused training to address the gaps in and scarcity of skilled human resources.

Strategies to enhance adherence and compliance to medicines use in children need to be defined in relation to both short-term and chronic illness.

- Communication and record-keeping among health-care workers were identified as problems in relation to medicines use in children.
- The potential value of alternative routes of administration of medicines as a strategy to enhance adherence needs to be further investigated.
- It has been documented that age-appropriate devices to administer medicines to infants and children are essential to ensure safety and accuracy. In the 2007 survey for instance, salbutamol inhalers were widely available but spacer devices for their effective use in children were unavailable. Salbutamol syrup and tablets were widely available but these oral forms are rarely used in developed countries because of their limited effectiveness. Clinical trials have also established the importance of zinc formulations for reducing the duration and severity of diarrhoeal illness, but zinc sulphate preparations were conspicuously absent in both public and private sector health facilities in the survey (Robertson, 2009).

The persistent problems of stock-outs of medicines, the limited number of medicines available for treating children and inappropriate dosage forms were all problems identified with rational use of medicines. There were also communication problems between health-care implementers, providers and researchers and policy-makers resulting in sub-optimal quality of prescribing and referrals (WHO, 2009).

iv) **Current activities of drug and therapeutics committees that may relevant to medicines for children**

The role of the drug and therapeutics committee is to optimize rational medicine use by evaluating the clinical use of medicines, developing the policies for managing medicine use and administration and managing a formulary system. The DTC has the responsibility to promote rational medicine use through education of professional staff, patients and their care-givers. The committee also has broad responsibilities for determining what medicines should be available at what cost and how they should be used. There had been a series of training workshops organized in the regions for clinical teams with the aim of promoting the role of DTCs in various health-care institutions. Some of the practical demonstrations of DTC’s activities include field trips to assess medicines use indicators (GHS Report, 2010). However activities of DTCs do not include
B. Aspects of the pharmaceutical sector that need to be enhanced to ensure better medicines for children

i) Local manufacturing capacity and supplies

• Even though the local manufacturing industry is fragmented, it may well be described as consolidated because it is primarily moved by a few industries and said to be viable. It has been documented that 20% of the product mix of local manufacturers are in the essential medicines list (EML). These 20% medicines were products which Government provided concessions on the Active Pharmaceutical Ingredients (APIs). It is therefore logical to infer that more concessions would result in an increase in the share of locally produced medicines including medicines for children. Government would only be willing to invest in domestic Pharmaceutical manufacture when data on revenues accruing from operations of the local industry are made available in order to measure the financial impact of domestic production on the country’s economy, (Grupper et al, 2005).
• No local pharmaceutical manufacturer had been selected through WHO’s pre-qualification criteria to produce medicines for disease conditions funded by the Global Fund. A major constraint also facing the local industry is under utilization of manufacturing capacity by more than 50% (GTZ, 2007). Local manufacturers should therefore consolidate to be able to access the potential of their market before requesting pre-qualification as it would not be useful to invest money to upgrade their facilities when sales cannot justify investment. It is expected that consolidation and expansion would result in greater use of capacity and lowering of production costs and in turn this would be translated into improved access for consumers.

• Another option for the Government to improve output in domestic production would be to reduce corporate taxes for manufacturers who have high sales. Access to the Ghana stock exchange should be facilitated for domestic manufacturers to make them more viable. Foreign companies should be encouraged to strategically partner with local manufacturers for technology transfer to enhance production of medicines for children (ibid, 2007).

• The justification for specialized dosage forms for children is to ensure absorption, distribution, metabolism and excretion of medicines, which differ in children compared to adults and they also influence the efficacy, toxicity and dosing regimens required in children for outcomes of therapy, (UNICEF Report, 2010).

• There is also the problem of packaging and labelling of medicines for children. Since medicines are generally given to children by care-givers, clear and concise labelling in an appropriate format and standardized packaging are essential to ensure adherence to therapy. Therefore there is a need for capacity development at local level, to ensure that medicines are produced specifically for children, at affordable prices and that they are used rationally (ibid, 2010).

• Government and donors should provide support to the local industry by the promotion of rational use of child-specific medicines’ education since medicines for children aged 0-6 months would need proper education with administration and use and this responsibility lies with the health care provider. That way medicine prices would reduce considerably and used rationally for optimal therapeutic outcomes (Kinapharma, 2010).

• When considering optimal frequency of dosing in terms of adherence and clinical outcomes, government could lobby industry to consider innovative ways of achieving these outcomes with appropriate dosage forms especially when assured of a ready market (ibid, 2010).

• Government should consider a policy not to allow the importation of a selected list of essential medicines on the list of 38 to be produced by local manufacturers (ibid).

• Local manufacturers could explore the use of platform technology (multiparticulate solid, including those that could be dispersed to form a liquid dose), rather than focusing on oral liquids. It is anticipated, that this will allow production of ‘tailored’ doses and strengths as well as preparations of a range of dosage forms, such as tablets or capsules (WHO, 2009).
• A report from the Working Group on local manufacturing capacity indicated that capacity exists to produce child-specific medicines on the list of 38, with an increase from 30% to 68% (Boateng, 2010).

ii) **Medicine availability and price strategy**

Ghana has both a centralized and decentralized procurement system for public sector medicine supply. The mapping of partners involved in Ghana’s medicine supply management system shows clearly that there are manageable partners and the system is streamlined. However, a large part of investments in medicine supply go outside the MOH procurement systems and this increases the potential for poor coordination and inefficient use of resources. It was reported that storage, stock management and distribution activities are inadequately financed relative to supply of medicines. Also, the link between supply data and health needs is weak for determining and setting health priorities, and this could lead to wastage of the scarce resources available for health services.

These problems affect medicines for children as well. The MOH should identify information gaps in the supply chain, mobilize resources for underserved programmes, such as child-specific essential medicines, and reschedule procurement priorities in this area. Development partners should also target child-specific essential medicines in their plans, target gaps in the supply management system for these products and share information among partners to facilitate coordination in medicines procurement and distribution.

Since duties, tariffs and mark-ups significantly contribute to the final price of medicines, (30-40% taxes and tariffs, 50-200% for mark-ups), there is a need to develop price guidelines for medicines in general, and paediatric medicines specifically, for all sectors and to enforce compliance with a maximum mark-up policy. Another option is for Government to implement a policy of generic prescribing and dispensing to promote uniformity in pricing of essential medicines for children. Support by Government for local manufacturing of essential medicines for children could also improve access and make these medicines affordable.

iii) **Current activities of drug and therapeutics committees**

The role of DTCs in health facilities is to promote rational use of medicines. However examination of current literature on DTC activities did not indicate any active role in the promotion of rational use of medicines in children. This could be due to lack of a national EMLc and STGs for children. Regardless of this, the MOH should institute ongoing training and re-training for paediatric prescribers to ensure optimal use of medicines in children. The national medicine policy (NDP, 2004) clearly states the functions of DTCs but legislative instruments have not been developed to enforce the establishment of functional DTCs with accompanying sanctions for non-compliance. Therefore, MOH/GHS should facilitate the process for ensuring the establishment of functional DTCs in all health-care institutions. It is also anticipated that with such committees in
place, the selection process for procurement of medicines would make adequate provision for child-specific medicines, improve access and promote better management of childhood diseases. Institutions that have functional DTCs could develop local treatment guidelines and formularies, using the current WHO Model Formulary as a basis for adaptation.

CONCLUSION

The review found that globally research on child-specific medicines had not been actively undertaken and supported in the past. Also, the pharmaceutical industry had not been provided with any incentives to produce innovative child-specific formulations that would deliver the optimal dosage. Regulatory institutions set up to monitor quality and safety of medicines had not been adequately resourced and had often omitted medicines for children in their activities.

One of the reasons child-specific medicines have become a critical issue on the world agenda is the short range of age groups in terms of dosage. Unlike adults where dosages remain the same between 15 and 65 years, dosage ranges for children may be 0-2 years, 3-6 years and 6-12/15 years. Children cannot be thought of as small adults - their rapidly changing physiological and co-morbid conditions, such as malnutrition, mean that their pharmacokinetic and pharmacodynamic profiles are very different from those of adults. There are also major differences in pharmacokinetic properties, such as absorption, distribution, metabolism and excretion of medicine, between children and adults and these influence the efficacy, toxicity and dosing regimens related to children. Other factors to be considered are the proportion of body fat, protein, extra cellular water content, organ size and body surface area which vary throughout the child’s growth period. A child’s changing age, weight and physiological status affect the most optimal way to measure the correct dosage of medicine. Medicines are given by care-givers, and clear and concise labelling in an appropriate format and packaging are all essential to ensure adherence to therapy.

This literature review underlines the need for Government to channel more resources into research and manufacture of child-specific medicines, especially within the local pharmaceutical industry. Increased resources are essential to produce and make available this therapeutic category of medicines in order to deliver optimal dosages and achieve the desired therapeutic outcomes.
REFERENCES


Boateng K. Situation analysis of the domestic production of essential medicines in paediatric dosage forms in Ghana. 2010.

Danadams Pharmaceuticals Limited and Kinapharma Limited. Personal interactions with the Chief Executive Officer and General Manager, Accra, September 2010.


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The Daily Graphic, 17 November 2010.


**APPENDIX I: BETTER MEDICINES FOR CHILDREN PROJECT -- LIST OF CORE AND SUPPLEMENTARY COUNTRY MEDICINES**

<table>
<thead>
<tr>
<th>List*</th>
<th>No</th>
<th>Medicine (Name must be unique)</th>
<th>Medicine strength</th>
<th>Unit presentation</th>
</tr>
</thead>
<tbody>
<tr>
<td>G 1.</td>
<td>Amoxicillin clavulanic acid, suspension</td>
<td>125 mg/5 ml</td>
<td>/ml</td>
<td></td>
</tr>
<tr>
<td>G 2.</td>
<td>Amoxicillin dispersible tablet</td>
<td>250 mg</td>
<td>/tab</td>
<td></td>
</tr>
<tr>
<td>G 3.</td>
<td>Amoxicillin suspension</td>
<td>250 mg+62.5 mg</td>
<td>/ml</td>
<td></td>
</tr>
<tr>
<td>G 4.</td>
<td>Amoxicillin/clavulanic acid, dispersible tablet</td>
<td>125 mg+31.25 mg/5 ml</td>
<td>/ml</td>
<td></td>
</tr>
<tr>
<td>S 5.</td>
<td>Amoxicillin/clavulanic acid, suspense</td>
<td>250 mg+125 mg</td>
<td>/tab</td>
<td></td>
</tr>
<tr>
<td>G 6.</td>
<td>Artemether + lumefantrine, dispersible tablet</td>
<td>20 mg+120 mg</td>
<td>/tab</td>
<td></td>
</tr>
<tr>
<td>S 7.</td>
<td>Artesunate/amodiaquine, dispersible tablet</td>
<td>25 mg+75 mg</td>
<td>/tab</td>
<td></td>
</tr>
<tr>
<td>S 8.</td>
<td>Azithromycin, powder</td>
<td>200 mg/5 ml</td>
<td>/ml</td>
<td></td>
</tr>
<tr>
<td>G 9.</td>
<td>Beclometasone, inhaler</td>
<td>100 mcg/dose</td>
<td>/dose</td>
<td></td>
</tr>
<tr>
<td>G 10.</td>
<td>Benzylpenicillin injection</td>
<td>600 mg=1 million IU</td>
<td>/vial</td>
<td></td>
</tr>
<tr>
<td>G 11.</td>
<td>Carbamazepine chewable tablet</td>
<td>100 mg</td>
<td>/tab</td>
<td></td>
</tr>
<tr>
<td>G 12.</td>
<td>Carbamazepine suspension</td>
<td>100 mg/5 ml</td>
<td>/ml</td>
<td></td>
</tr>
<tr>
<td>S 13.</td>
<td>Carbamazepine tablet</td>
<td>200 mg</td>
<td>/pack</td>
<td></td>
</tr>
<tr>
<td>G 14.</td>
<td>Ceftriaxone injection</td>
<td>500 mg vial</td>
<td>/vial</td>
<td></td>
</tr>
<tr>
<td>G 15.</td>
<td>Chloramphenicol injection</td>
<td>1 gram vial</td>
<td>/vial</td>
<td></td>
</tr>
<tr>
<td>G 16.</td>
<td>Cotrimoxazole dispersible tablet</td>
<td>100 mg+20 mg (also expressed as 400 mg+80 mg)</td>
<td>/tab</td>
<td></td>
</tr>
<tr>
<td>G 17.</td>
<td>Diazepam rectal solution</td>
<td>2.5 mg/ml</td>
<td>/ml</td>
<td></td>
</tr>
<tr>
<td>G 18.</td>
<td>Ferrous salt, suspension</td>
<td>30 mg Fe/5 ml</td>
<td>/ml</td>
<td></td>
</tr>
<tr>
<td>G 19.</td>
<td>Gentamicin injection</td>
<td>10 mg/ml</td>
<td>/ml</td>
<td></td>
</tr>
<tr>
<td>G 20.</td>
<td>Ibuprofen tablet</td>
<td>200 mg</td>
<td>/tab</td>
<td></td>
</tr>
<tr>
<td>G 21.</td>
<td>Isoniazid, scored tablet</td>
<td>50 mg</td>
<td>/tab</td>
<td></td>
</tr>
<tr>
<td>S 22.</td>
<td>Mebendazole tablet</td>
<td>500 mg</td>
<td>/tab</td>
<td></td>
</tr>
<tr>
<td>G 23.</td>
<td>Morphine immediate release tablet</td>
<td>10 mg</td>
<td>/tab</td>
<td></td>
</tr>
<tr>
<td>G 24.</td>
<td>Morphine oral solution</td>
<td>10 mg/5 ml</td>
<td>/ml</td>
<td></td>
</tr>
<tr>
<td>G 25.</td>
<td>Oral rehydration solution (ORS) sachet</td>
<td>600 ml</td>
<td>/sachet</td>
<td></td>
</tr>
<tr>
<td>G 26.</td>
<td>Oral rehydration solution (ORS) sachet To make 1 litre</td>
<td>To make 1 litre</td>
<td>/sachet</td>
<td></td>
</tr>
<tr>
<td>G 27.</td>
<td>Paracetamol suspension</td>
<td>Or 125 mg/5 ml</td>
<td>/ml</td>
<td></td>
</tr>
<tr>
<td>G 28.</td>
<td>Phenobarbital injection</td>
<td>200 mg/ml</td>
<td>/ml</td>
<td></td>
</tr>
<tr>
<td>G 29.</td>
<td>Phenobarbital oral liquid</td>
<td>3 mg/ml (also expressed as 15 mg/5 ml)</td>
<td>/ml</td>
<td></td>
</tr>
<tr>
<td>G 30.</td>
<td>Phenytoin chewable</td>
<td>50 mg</td>
<td>/tab</td>
<td></td>
</tr>
<tr>
<td>G 31.</td>
<td>Phenytoin suspension</td>
<td>25 or 30 mg/1 ml</td>
<td>/ml</td>
<td></td>
</tr>
<tr>
<td>G 32.</td>
<td>Procaine penicillin injection</td>
<td>1 gram = 1 million IU</td>
<td>/vial</td>
<td></td>
</tr>
<tr>
<td>S 33.</td>
<td>Quinine injection</td>
<td>300 mg/ml</td>
<td>/ml</td>
<td></td>
</tr>
<tr>
<td>G 34.</td>
<td>Salbutamol inhaler</td>
<td>100 mcg/dose</td>
<td>/dose</td>
<td></td>
</tr>
<tr>
<td>G 35.</td>
<td>Spacer device</td>
<td>/</td>
<td></td>
<td></td>
</tr>
<tr>
<td>G 36.</td>
<td>Vitamin A capsules</td>
<td>100,000 IU</td>
<td>/tab</td>
<td></td>
</tr>
<tr>
<td>S 37.</td>
<td>Vitamin K1 injection (water soluble)</td>
<td>1 mg</td>
<td>/ml</td>
<td></td>
</tr>
<tr>
<td>G 38.</td>
<td>Zinc dispersible tablet</td>
<td>20 mg/10 mg</td>
<td>/tab</td>
<td></td>
</tr>
</tbody>
</table>

S=Supplementary list item
G=Global list item
APPENDIX II: LIST OF MEDICINES USED IN THE 2007 WHO SURVEY OF 14 AFRICAN COUNTRIES, INCLUDING GHANA

<table>
<thead>
<tr>
<th>No</th>
<th>Generic name</th>
<th>Dosage form</th>
<th>Strength</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Albendazole,</td>
<td>chewable tablets 200 mg</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Albendazole</td>
<td>suspension 100 mg/5 ml</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Amoxicillin</td>
<td>suspension 125 mg/5 ml</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>Artemether + lumefantrine</td>
<td>tablets 20 mg+120 mg</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>Beclomethasone</td>
<td>inhaler 50 microgram per dose</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>Ceftriaxone</td>
<td>injection 250 mg vial</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>Ceftriaxone</td>
<td>injection 1 gram vial</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>Cotrimoxazole</td>
<td>suspension 200 mg+40 mg/5 ml</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>Isoniazid</td>
<td>tablet 100 mg</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>Mebendazole</td>
<td>chewable tablet 100 mg</td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>Mebendazole</td>
<td>suspension 100 mg/5 ml</td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>Nevirapine</td>
<td>syrup 50 mg/5 ml</td>
<td></td>
</tr>
<tr>
<td>13</td>
<td>Nystatin</td>
<td>drops 100,000 I.U./ml</td>
<td></td>
</tr>
<tr>
<td>14</td>
<td>ORS</td>
<td>sachet</td>
<td></td>
</tr>
<tr>
<td>15</td>
<td>Paracetamol</td>
<td>syrup 120 mg/5ml</td>
<td></td>
</tr>
<tr>
<td>16</td>
<td>Rifampicin</td>
<td>syrup 100 mg/5ml</td>
<td></td>
</tr>
<tr>
<td>17</td>
<td>Salbutamol</td>
<td>inhaler 100 microgram/dose</td>
<td></td>
</tr>
<tr>
<td>18</td>
<td>Vitamin A</td>
<td>capsules 100,000 I.U (30 mg)</td>
<td></td>
</tr>
<tr>
<td>19</td>
<td>Vitamin A</td>
<td>liquid preparation 50,000 I.U, per dose</td>
<td></td>
</tr>
<tr>
<td>20</td>
<td>Zinc dispersible</td>
<td>tablets 20 mg</td>
<td></td>
</tr>
</tbody>
</table>
APPENDIX III: RESTRICTED DRUGS

As part of the Government’s drive to increase the manufacturing capacities of local pharmaceutical firms, the importation of some selected drugs on the Essential Drugs List has been restricted. Importation of the finished products listed below is not permitted. Only the raw materials can be imported for local manufacture.

1. Capsules:
   a. Ampicillin
   b. Chloramphenicol
   c. Oxytetracycline
   d. Chlordiazepoxide
   e. Tetracycline
   f. Indomethacin

2. Syrups:
   a. Chloroquine
   b. Paracetamol

3. Tablets:
   a. Aspirin
   b. Chloroquine
   c. Diazepam
   d. Paracetamol
   e. Ephedrine
   f. Phenobarbitone
   g. Prednisolone dexamethasone
   h. Folic acid
   i. Vitamin B Complex
   j. Paracetamol/aspirin/caffeine combinations
   k. Aspirin/caffeine combinations,
   l. Paracetamol/caffeine combinations
   m. Paracetamol/codeine combinations