HIGH-LEVEL PANEL ON ACCESS TO MEDICINES

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For the executive committee of GPED
Section 1: Abstract (281 words)

Global Pediatric Endocrinology and Diabetes (GPED) is a non-profit organization that aims at improving the care of children in resource-constrained settings with endocrine disorders and with diabetes through advocacy, the provision of training and educational opportunities and the development of clinically relevant research studies initiated by local investigators.

The last 10 years have seen a major increase in capacity in Pediatric Endocrinology and Diabetes in low and middle income countries. However, because of the lack of access to very well known, affordable medicines, morbidity and mortality that could easily be prevented remain high.

A major objective of GPED is to facilitate access to essential medicines relevant to Pediatric Endocrine and Diabetes care in resource-constrained settings.

Through evaluation of the WHO model lists of essential medicines, of the national lists of essential medicines and through collaborations with many stakeholders, GPED has identified 5 key initiatives that would, if implemented, improve sustainable access to essential medicines in children.

- Use of a single national list of essential medicines that serves as the only reference for a country
- Build capacity in areas of medicine (such as Pediatric Endocrinology) in order to bring sustainable expertise within countries.
- Empower patients and families to advocate for their rights. Parent groups have proven a key, low cost factor in supporting access to medicines
- Facilitate registration of medicines at a regional level.
- Identify pharmaceutical companies that market specific medicines: there is presently to our knowledge no list of pharmaceutical companies producing a specific medicine.

We suggest that key international organisation work with stakeholders in order to implement these recommendations and facilitate the safe and sustainable access of essential medicines to the children who need them.
Section 2. Call for contributions (2880 words).

Promoting Sustainable Access of Essential medicines in Pediatric Endocrinology and Diabetes in Low and Middle Income Countries

1. Introduction

a. Global Pediatric Endocrinology and Diabetes

Global Pediatric Endocrinology and Diabetes (GPED) is a non-profit organization established in 2010 that aims at improving the care of children in resource-constrained settings with endocrine disorders and with diabetes through advocacy, the provision of training and educational opportunities and the development of clinically relevant research studies initiated by local investigators (1).

GPED is endorsed by all regional Societies for Pediatric Endocrinology (African Society for Paediatric and Adolescent Endocrinology [ASPAE], Arab Society for Paediatric Endocrinology and Diabetes [ASPED], AsiaPacific Paediatric Endocrine Society [APPES], Chinese Society for Pediatric Endocrinology and Metabolism [CSPEM], European Society for Paediatric Endocrinology [ESPE], Indian Society for Pediatric and Adolescent [ISPAE] Endocrinology, Japanese Society for Pediatric Endocrinology [JSPE], Pediatric Endocrine Society [PES], Sociedad LatinoAmericana de Endocrinología Pediátrica [SLEP]) and the International Society for Pediatric and Adolescent Diabetes (ISPAD). Through this endorsement, it is associated with the vast majority of the Pediatric Endocrinologists around the world.

Over the last 10 years, training programs that aim at increasing capacity in Pediatric Endocrinology in resource-constrained settings have been developed by several regional societies for Pediatric Endocrinology. With the increase in capacity, an increasing number of children are being diagnosed with endocrine conditions and diabetes, conditions that are easily managed with existing medicines.

A major objective of GPED is to facilitate access to essential medicines relevant to Pediatric Endocrine and Diabetes care in resource-constrained settings (2).

The purpose of this submission is

- To describe the work performed so far towards sustainable access to essential medicines in Pediatric Endocrinology and Diabetes in Low and Middle Income Countries (LMICs)
- To identify the barriers preventing access to essential medicines
- To propose a plan of action that will lead to sustainable access to essential medicines for the benefit of the patient and his/her family

b. Pediatric Endocrinology and Diabetes and Non-Communicable Diseases

Pediatric Endocrinology is a subspecialty of Pediatrics that focuses on the diagnosis and treatment of children with diseases of the endocrine system. This includes a.o. diabetes, obesity and its complications, disorders of sexual development, growth and puberty, thyroid diseases, diseases of the adrenal glands, calcium and bones. These conditions are part of the non-communicable diseases (NCD) group which today accounts for 63% of all deaths (3).

The prevalence of obesity and its metabolic complications such as Type 2 diabetes is increasing rapidly in children and these conditions affect millions of children in low and
middle income countries (LMICs). They are easily recognized and are managed through a collaboration between public health authorities and health professionals, including pediatric endocrinologists.

Other conditions such as Type 1 diabetes, congenital hypothyroidism, congenital adrenal hyperplasia and osteogenesis imperfecta, to name a few, affect many thousands of patients. Importantly, the prevalence of these conditions varies widely from country to country (for instance, congenital adrenal hyperplasia is much more prevalent in Northern Africa, likely because of increased consanguinity compared to other parts of the world) and prevalence is often under estimated (for instance, Type 1 diabetes was thought to be uncommon in many low income countries until proper screening led to more successful recognition of the disease). These conditions, if left untreated, are associated with mortality or severe morbidity. In contrast, early recognition and appropriate management most often with low cost medicines make it possible to prevent mortality and morbidity, assuming that appropriate medicines are available.

The last 10 years have seen a major increase in capacity in Pediatric Endocrinology and Diabetes in low and middle income countries. Training programs that take place directly in the region where capacity is needed have been developed. For instance, the PETCA (Pediatric Endocrinology Training Center for Africa) which was proposed by Dr Hochberg, founder of GPED, is an example of a successful capacity building initiative: more than 50 pediatricians from South Saharan Africa have attended an 18 month program in either Nairobi or Lagos and have now established a Pediatric Endocrinology center in their country of origin (4, 5). The responsibility of the organisation of the training centers is progressively transitioned from tutors working in high income countries (HIC) to local tutors, highlighting the sustainability of this program. This is a highly successful initiative that serves as a model for capacity building in other areas of interest.

c. The WHO Model List of Essential Medicines and the National Lists of Essential Medicines

A common aspect of pediatric endocrine conditions is that most medicines required for their management are well known, have often reached the “generic” status and are very affordable by HIC standards. However, they are often not readily available in many LMICs, causing morbidity and mortality that could easily be prevented.

The World Health Organisation (WHO) has released a list of medicines considered as essential for children (6) and for adults (7) which are updated on a regular basis. These lists are non-binding but are used as a template by most LMICs to decide which medicines will be made available at the national level.

Indeed, 117 (at the time of writing) LMICs have published a list that includes the medicines deemed essential at the national level. These lists are updated irregularly (8).

In addition, there are many limitations to these lists: firstly, an unknown number of countries have additional lists that are not easily accessed; secondly, the existence of public and private systems in many countries means that there is often more than one official list of medicines in a specific country; thirdly, the fact that a medicine is listed on the national list (8) (or on another list used in the country) does not necessarily mean that it is systematically available in pharmacies.
To clarify this problem, in a first step, after talking to Dr Hill (WHO Geneva), we have extracted a list of the medicines that are most commonly used in Pediatric Endocrinology and Diabetes and compared it to the WHO model lists of essential medicines for children (6) and adults (7). As shown in the Table, most of the medicines deemed relevant are included in the WHO list for children or adults.

<table>
<thead>
<tr>
<th>List of Medicines</th>
<th>WHO EML</th>
<th>National lists</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Adrenal</strong></td>
<td></td>
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</tr>
<tr>
<td>Hydrocortisone, and/or Prednisone, and/or Prednisolone (PO)</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Dexamethasone (PO)</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Fludrocortisone (PO)</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Hydrocortisone (IV/IM)</td>
<td>x</td>
<td>x</td>
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<tr>
<td><strong>Thyroid</strong></td>
<td></td>
<td></td>
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<tr>
<td>L-Thyroxine (PO)</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Propylthiouracil (PTU), Methimazole/Carbamazole (PO)</td>
<td>x</td>
<td>x</td>
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<tr>
<td>Beta Blocker (Propranolol) (PO)</td>
<td>x</td>
<td>x</td>
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<tr>
<td><strong>Diabetes</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Insulin Short Acting Human and/or Analogues (SQ)</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Insulin Long Acting Human and/or Analogues (SQ)</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Insulin Pre-mix (SQ)</td>
<td></td>
<td></td>
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<tr>
<td>Glucagon (SQ/IM)</td>
<td>x</td>
<td>x</td>
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<tr>
<td>Metformin (PO)</td>
<td>x</td>
<td>x</td>
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<tr>
<td>Sulfonylurea (any) (PO)</td>
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<td>x</td>
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<tr>
<td><strong>Water metabolism</strong></td>
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<td></td>
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<tr>
<td>Vasopressin analogs (SC/IV)</td>
<td></td>
<td></td>
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<tr>
<td>Desmopressin (DDAVP) (Nasal spray/IN/SubLingual/PO)</td>
<td>x</td>
<td>x</td>
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<tr>
<td><strong>Gonads</strong></td>
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<tr>
<td>GnRH analogues (IM)</td>
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<tr>
<td>Testosterone (PO, transdermal, topical gel, IM)</td>
<td></td>
<td>x</td>
</tr>
<tr>
<td>Medroxyprogesterone (PO)</td>
<td></td>
<td>x</td>
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<tr>
<td>Estrogen (17b Estradiol or Ethinylestradiol) (PO)</td>
<td></td>
<td></td>
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<tr>
<td>Oral Contraceptives (Ethinylestradiol and Progestagen) (PO)</td>
<td></td>
<td>x</td>
</tr>
<tr>
<td>IM Contraceptives (Medroxyprogesterone or other) (IM)</td>
<td></td>
<td>x</td>
</tr>
<tr>
<td><strong>Bone/Calcium</strong></td>
<td></td>
<td></td>
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<tr>
<td>Calcitriol/1 α vitamin D</td>
<td></td>
<td></td>
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<tr>
<td>Vitamin D2/D3</td>
<td>x</td>
<td>x</td>
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<tr>
<td>Calcium (PO)</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Calcium (IV)</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Biphosphonates (PO or IV)</td>
<td></td>
<td></td>
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<tr>
<td><strong>Hypoglycemia</strong></td>
<td></td>
<td></td>
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<tr>
<td>Diazoxide</td>
<td></td>
<td></td>
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<tr>
<td>Somatostatin</td>
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</tbody>
</table>

In a second step, we have compared the WHO model lists with the national lists to determine the extent to which individual countries included medicines relevant to Pediatric Endocrinology and Diabetes. Figure 1 shows the percent of countries in South and Central
America that include medicines relevant to Pediatric Endocrinology and Diabetes in their national lists. Interestingly, many of these medicines are present in these countries.

In a third step, we have looked into each of the countries for which a WHO national list was available and distinguished between the highest and the lowest income countries (9) (Figure 1).

![Figure 1](image)

The Figure clearly shows differences, with more medicines included in the list of the richest countries (open bars) compared to the poorest countries (solid bars).

2. Understanding and overcoming the specific barriers preventing access to essential medicines and identifying sustainable solutions

a) Policy incoherence

By policy incoherence, we understand a lack of structure in the processes that, if appropriately standardized, would greatly facilitate access to essential medicines. We have identified several key issues that affect access to essential medicines. For each of them, we describe a specific situation and how it impacts access. We also propose a sustainable solution.

i. Differences between countries in the registration process of a medicine.

Europe, with the creation of the European Medicine Agency (EMA) (10) has made it possible for all European countries to abide by a single process for the registration of medicines. This is unique in the world to our knowledge. In LMIcs, the process of registration, in particular for medicines that are needed in relatively small quantities, such as those relevant to Pediatric Endocrinology and Diabetes, is often perceived by pharmaceutical companies as slow, cumbersome, expensive and inefficient. Interestingly, the Gates Foundation has initiated a project that aims to cut drug registration times by 50 in sub Saharan Africa by 2018 (11). This should serve as an incentive for pharmaceutical companies to support markets that are perceived as being small and we suggest that such an initiative should be extended to other groups of countries/regions.
ii. **Lack of standardization of the national model lists of essential medicines**

As mentioned above, our research has demonstrated that the available national lists of medicines were often outdated, presented in different formats, difficult to find and not representative of the actual situation in a country. For instance, GPED is supporting an African country where congenital adrenal hyperplasia is very common but where fludrocortisone, a very affordable life-saving medicine for this condition (0.15 Euro/tablet), is not included in the national list of medicines posted on the WHO website. This means that it cannot be imported legally in the country. It is presently imported through a variety of unreliable and costly channels. However, in this country that has a quite generous National Health System, fludrocortisone is included in a different list that is specific to hospitals. Practically, this means that a non-registered product can be imported and covered by the National Health system, provided that a request is sent to the Ministry of Health and that suitable pharmaceutical companies are identified. GPED is presently working to facilitate this process.

In another African country (where fludrocortisone is not part of the national list of medicines), a major academic center is registered as a non profit organisation. That means that if a medicine is shipped to the institution itself (instead of a patient or pharmacy), it easily crosses the border.

Ultimately, in both cases, formal registration of fludrocortisone would be the best sustainable solution.

iii. **Lack of engagement of the pharmaceutical industry**

In response to many individual requests, GPED has attempted to liaise with appropriate pharmaceutical companies or directed Health Authorities in specific countries towards pharmaceutical companies. This is a very difficult task because of the lack of interest and the fact that a single list of existing pharmaceutical companies, the medicines they make, the countries in which they are operating and how they can easily be contacted is not available. We suggest that such a list should be mandated. It would greatly facilitate progress towards access to essential medicines.

iv. **Unstructured capacity building**

The success of programs such as the PETCA (4, 5) and other programs has shown that locally trained specialists greatly improve the quality of healthcare and the recognition of easily treatable conditions that were previously left undiagnosed. However, these physicians now face the lack of access to essential medicines. They are however well-positioned to serve as advocates for their patients and liaise with their national health authorities. They serve as local experts to advise the government on the type and quantity of medicines that are needed. For instance, GPED has organized a symposium in an African country with local pediatric endocrinologists (trained through the Maghreb School (12)) and patients/families with congenital adrenal hyperplasia. This has resulted in the support from the health authorities (with a high ranking representative attending the symposium) and we are presently following up with the Health Ministry, in collaboration with the patient groups and physicians, to streamline access to this essential medicine. We suggest that training programs of physicians that develop a specific expertise and involvement of parent groups should be integral part of a strategy of access to medicines.
v. Lack of involvement of the community, patients and families

Empowering patients and families has proven to be an important step towards achieving sustainable access to medicines: Caring and Living As neighbours (CLAN) (13), is a non profit organisation founded by Dr K Armstrong that seeks to improve child health in LMICs. Although this organisation is not specifically dedicated to pediatric endocrinology, one the initiatives consists in improving access to fludrocortisone and hydrocortisone for patients with congenital adrenal hyperplasia and of bisphosphonates for patients with Osteogenesis Imperfecta in several countries in Asia. The process is ongoing and depends on the specificities of each country. CLAN emphasizes the central role of the family and the community to achieve its goals. The involvement of the patients and families has proven to be a key step towards improving the care of children, through better education and advocacy.

b) Impact on public health

Thanks to the progress made in the prevention and treatment of communicable diseases, NCDs now become the most important cause of mortality (3). Access to essential, affordable medicines in pediatric endocrinology and diabetes will markedly improve the quality of life of the patients, prevent morbidity and mortality and decrease the cost associated with raising handicapped children both at the family and society levels. For instance, in Uganda, young men with type 2 diabetes are admitted to hospital for limb amputation, secondary to vascular complications of Type 2 diabetes. Type 2 diabetes went unrecognized in adolescence and irreversible complications (gangrene of the leg requiring amputation) were the first sign of the disease. Recognition and treatment of Type 2 diabetes with insulin would prevent these complications that impact the long term survival of the whole family by removing the capacity of the main bread winner to provide for his family.

c) Impact on human rights

The UN Convention on the Rights of the Child (14) clearly states the right of the child to live “without discrimination of any kind, irrespective of the child's or his or her parent's or legal guardian's race, colour, sex, language, religion, political or other opinion, national, ethnic or social origin, property, disability, birth or other status”. Access to essential medicines is a key aspect of these rights. Specifically, in Pediatric Endocrinology, access to cheap, readily available medicines that have been used for decades in HICs contributes to achieve this goal by addressing severe, preventable complications: diabetes (renal insufficiency, foot gangrene), congenital hypothyroidism (mental retardation), osteogenesis imperfecta (bone fractures and severe physical disabilities), congenital adrenal hyperplasia (ambiguous genitalia) to name a few.

d) Implementation

The recommendations below are consistent with the SDG #3 (15) which include:

- Achieve universal health coverage, including financial risk protection, access to quality essential health-care services and access to safe, effective, quality and affordable essential medicines and vaccines for all
- Substantially increase health financing and the recruitment, development, training and retention of the health workforce in developing countries, especially in least developed countries and small island developing States
We suggest the following actions to achieve the proposed goals (Figure 2). Although our submission focuses on Pediatric Endocrinology and Diabetes, we propose that this model can be used in other areas of medicine that face the same issues. Importantly, in our domain, the cost of the medications is NOT the most important issues. Most of the medicines listed in Table 1 are very affordable.

i. **Support** the use of a single national list of essential medicines that serves as the only reference for a country.

*Recommendation:* build on the existing framework (WHO model list of essential medicines) and support single national lists that will clarify the availability of medicines in specific countries and highlights the specific needs of the country. Promoting a single format, regular updating and a single depositary would go a long way towards simplifying a complex system.

ii. **Build capacity** in areas of medicine (such as Pediatric Endocrinology) in order to bring sustainable expertise within countries.

*Recommendation:* Establish international credentials. Support regional training programs of health professionals that develop specific expertise that is relevant to the country. Specifically, ensure that the training meets the local needs and that it is properly accredited. This will help clarify the magnitude of the problem associated with one condition and will help ensure that medicines are used appropriately.

iii. **Empower patients and families** to advocate for their rights. Parent groups have proven a key, low cost factor in successful initiatives such as those from CLAN (13)

*Recommendation:* Support circulation of information and educate families. GPED is presently identifying booklets for different conditions and translating them in various languages in a culturally appropriate manner. Patients become advocates for their own health. Parents support groups have proven to be a very valuable source of progress in accessing appropriate care.

![Diagram](http://www.who.int/mediacentre/areas/access/en/)

*Figure 2. Adapted for Pediatric Endocrinology from:* [http://www.who.int/medicines/areas/access/en/](http://www.who.int/medicines/areas/access/en/)*
iv. **Facilitate** registration of medicines at a regional level.

**Recommendation:** Create a working group (partnership that includes international organisations such as WHO, funding agencies such as the Gates Foundation, Health Authorities and pharmaceutical companies) to identify and engage groups of countries with similar interests to create a mutually beneficial, fast and efficient process for the registration of medicines. Groups could be formed according to WHO regions or sub-regions to build on an existing framework. Easy registration process, understanding country’s needs and clear national policy will make small markets more attractive and more affordable.

v. **Identify** pharmaceutical companies that market specific medicines: there is presently to our knowledge no list of pharmaceutical companies producing a specific medicine.

**Recommendation:** Partner with organisations such as the International Federation of Pharmaceutical manufacturers and Associations (16) to ensure that a list of manufacturers, their products, quality assurance and geographical areas of activity is kept up to date. Provide incentives (clear registration process, needs assessment of a country, quality assurance support) to engage the pharma industry.

GPED believes that implementation of the above recommendations will improve policy coherence, simplify processes and ultimately benefit children and families in a sustainable and affordable fashion.

Respectfully submitted,

Dr Jean-Pierre Chanoine, MDPhD
Secretary General
Global Pediatric Endocrinology and Diabetes

February 28, 2016
Section 3. References and Bibliography

3. NCD Child. www.ncdchild.org/understand.html
PERMISSION TO PUBLISH

If my contribution is shortlisted for consideration by the High-Level panel, I understand and accept that I give permission for the contribution to be made public on the High-Level Panel’s website. *

YES