of cyclophosphamide, these only serve as a short-term solution to the problem and have clear limitations. Capsules can be made at appropriate dosages from the active principle powder as this is stable for 70 days when manufactured in 10 and 25 mg capsules (Bouligand et al., 2005). However, these capsules cannot be prepared in each hospital taking care of children with cancer as it requires specialist pharmaceutical equipment. In addition, there is still a need to open the capsules for children who cannot swallow them. Cyclophosphamide IV formulation may be used as a liquid alternative for oral administration. However, it is stable for only 14 days at +4 °C in glass containers protected from light (Paci. in-house personal review; Beijnen et al., 1992) and the bioavailability of these in-house preparations is unknown.

As such, a major goal of the project is to develop child-appropriate oral liquid formulation of cyclophosphamide. The intent is to improve oral treatment for children with cancer who are due to receive protracted daily administration of cyclophosphamide in children.

A cyclophosphamide IV dosage form (Endoxan®) is available at 20 mg/ml. This IV dosage form is widely used orally in children (off label use) with a good acceptability. Using cyclophosphamide is safe for the environment since this is an inactive pro-drug that requires liver enzymatic by CYP450 to generate alkylating moieties.

Then, we propose to develop a drinkable solution of cyclophosphamide, with an easy and fast reconstitution with the following objectives:

- to develop a drinkable solution allowing easiness of use and flexibility of administration doses depending on the age and body surface of kids
- to guarantee good tolerance of the formulation using well tolerated and agreed excipients for paediatrics
- to insure physical and chemical stability during storage and use as well as relevant safety of handling and use in ambulatory treatment situations
- to control accuracy and reproducibility of doses delivery with a suitable formulation and appropriate dosing device
- to have a manufacturing process allowing industrial scale for commercial supply
- to guarantee regulatory compliance

The goal is to have appropriate physical properties of the dosage form for a reliable manufacturing process.

Depending on the critical parameters encountered (reconstitution time and physical characteristics of powder for reliable process, stability of cyclophosphamide), 4 development options are envisaged:

- A simple distribution of the API in vials together with aroma
- A dry blend formulation combining API with excipients
- A powder granulation formulation consisting in associating excipients to the API under humid conditions followed by a drying phase.
- A hydrodispersible tablet formulation having the property to dissolve immediately (within one minute) when in contact with water.

Depending on feasibility results and mainly cyclophosphamide stability in solution, the cyclophosphamide dosage form should consist in:

- A cyclophosphamide solution for multiple administrations
- Or hydrodispersible tablets of several dosage strengths leading to an oral solution when dissolved in water at the time of administration.

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Current administration practices and preferred formulations of children's medicines in Tanzania: Summary of survey findings

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1. Introduction

It is estimated that up to 8.1 million children die every year, many of them from treatable conditions (You et al., 2010). This astounding statistic is, in part, due to the lack of pediatric drug formulations for many common infectious diseases that, in turn, cause a majority of these deaths. Even when pediatric formulations do exist, their availability in clinical settings may be variable. Con-

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Table 1
Parents/caregivers' and children's stated preferences for medicine taste.

	Parent/caregivers ($N = 194$)	Children ($N = 101$)
Sweet	155 (79.9%)	83 (82.2%)
Bitter	2 (1.0%)	0 (0%)
No taste	13 (6.7%)	6 (5.9%)
No preference	24 (12.4%)	12 (11.9%)

sequently, healthcare workers are often forced to dispense adult forms of medicines with instructions on how to achieve the desired pediatric dose. Use of medicines in such a manner is likely to lead to inaccurate dosing resulting in potentially reduced efficacy (due to under-dosing) and/or safety issues (due to excessive doses). Formulations, including their qualitative features of form and taste, help to determine whether the dose will be successfully delivered to pediatric patients; however, information on how best to prepare and administer drug formulations for children is often lacking (Nunn and Williams, 2005).

Clearly, more qualitative and quantitative data are needed from diverse settings about parent/caregiver, patient and provider behavior to define the current challenges and address barriers to treatment access and adherence (Craig et al., 2009). Information about what parent/caregiver, provider and patient preferences are, or would be, can guide the creation of optimal formulations of pediatric medicines. Therefore, we conducted a cross-sectional survey of parents/caregivers, children, and healthcare workers throughout Tanzania to assess current practices of administration and determine formulation preferences for children's medicines.

2. Methods

We conducted a cross-sectional survey of parents/caregivers, children, and healthcare workers throughout Tanzania to determine preferences for children's medicines. Both rural and urban settings were sampled. Data collection was conducted between 17 May and 6 July 2010. We stratified analyses by setting, parent/caregiver education, healthcare worker level and pediatric age group.

3. Results

A total of 202 parents/caregivers, 206 children, and 202 healthcare workers and were interviewed and had complete data. Parents/caregivers and children expressed a strong preference for sweet tasting medicines (Table 1).

Reports by parents/caregivers of children vomiting their medicines and disliking the taste were common. Most parents/caregivers and healthcare workers prefer syrups for young children. Parents/caregivers and healthcare workers had similar thresholds for the maximum number of tablets children at different ages can take. Most findings persisted across sub-group stratifications.

4. Discussion

Parents/caretakers, children and healthcare workers in Tanzania have clear preferences for pediatric medication taste and formulations. Despite their preferences for child-friendly formulations, most are receiving crushed/broken or whole pills to swallow. Their responses should be used to inform development, manufacturing, and marketing of pediatric medications for resource-limited settings.

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