



## **System for Dosing and Dispensing Multiparticulate Formulations of Pediatric Drugs** **Request for Proposals (RFP)**

*The Institute for Pediatric Innovation (IPI) and Pfizer Independent Grants for Learning & Change (IGLC)*

**March 28, 2016**

**LOI Due Date: May 16, 2016**

### **I. Background**

The Institute for Pediatric Innovation (IPI) is a nonprofit organization focused on developing new medical devices and medicines specifically for children. The IPI team recognizes that pediatric healthcare is a niche – often neglected – market and forms relationships with various organizations to ensure that creative, feasible, and sustainable medical products become commercially available.

The mission of Pfizer Independent Grants for Learning & Change (IGLC) is to accelerate the adoption of evidence-based innovations that align the mutual interests of patients, healthcare professionals, and Pfizer, through support of independent professional education activities. The term “independent” means the initiatives funded by Pfizer are the full responsibility of the recipient organization.

The IPI and Pfizer are collaborating on an open innovation challenge to solicit and support innovative ideas for a system consisting of a package and dispensing device that will be used to deliver oral solid multiparticulate (MP) medicines to children. Parties entering the competition including the winning entity will retain ownership of related intellectual property, as Pfizer and IPI intend that the party submitting the winning design commercialize the design independently either directly or through a partner. The organization who submits the winning design will be awarded a seed grant to fund ‘proof of concept’ steps toward development of the device, and will have the opportunity for ongoing liaison with IPI to access its networks to explore follow-on funding opportunities.

Pfizer has developed a formulation technology that addresses taste, storage, and other factors essential for safe, accurate, and adherent administration of medicines to children in low-resource global health settings. The technology can reformulate a drug into a tasteless, non-gritty MP formulation (i.e. a powder) that can be taken directly, or sprinkled onto food or liquid for children to take.

This RFP is being issued by both organizations. IPI is the lead organization for review and evaluation of applications. A review committee, led by IPI, will make decisions on which proposals will receive funding. Grant funding will be provided by Pfizer. Up to \$50,000 is available for the award(s).

## II. Purpose

This RFP seeks to solicit proposals for the design of a system consisting of a package and dispensing device that can measure and administer the MP formulation in a child friendly but child-misuse resistant format and in doses relevant for therapy in low resource settings.

The main evaluation criteria are:

- Dosing accuracy
- Cost
- End user ease of use
- Cultural appropriateness

## III. Specific Area of Interest for this RFP

Children in low resource countries often do not receive the correct dose of medicine because pediatric formulations either are not available or existing formulations are not properly dosed. Several formulations of drugs are available commercially, each with their advantages and disadvantages. Liquid formulations are commonly used for the pediatric population for their ease of administration, but are limited by their need for large dosing volumes, bad taste and sometimes, cost of transport and requirement for a cold chain. Solid oral doses have better dosing volumes, but can be difficult for children to swallow.

The MP formulation brings together the advantages of both liquid and solid formulations – high dose flexibility and ease of administration – to facilitate the effective and safe administration of drugs for children in low resource settings. The dispensing device can be filled by the pharmacist or the device can be designed to work with a standard package, such as a bottle. The device should be able to be used for the duration of therapy with appropriate cleaning (if required) in between dose administration. The end user of the device will be a parent/caregiver who will administer the oral dose to the child.

*We intend to support a proposal for a **system** consisting of a package and device that can appropriately dose the multiparticulate (MP) formulation of pediatric medicines. The **package** is defined as what the MP comes in from the pharmacy (bottle, foil package, etc), while the **device** is defined as what measures and dispenses the MP. Applicants must specify their system (package and device) in their letter of intent (LOI). Applicants can use an existing package or design their own package, as long as it is clearly stated in the LOI. Devices, on the other hand, must be original ideas.*

## User Requirement Specifications

Dosing Requirements	Target	Comments
Deliverable Dose Range of formulated multiparticulate (not active dose)	~ 50-1,500 mg	The desire is for a single scalable design that can cover the entire range. Variants could include a series of similar devices or a single device with change parts.
Pediatric Age Range	0-18 Years	
Dose Administrator	Patient / Caregiver	In low resource settings, caregivers may not be able to read, so the device must be simple enough for them to use, with simple pictorial instructions if needed.
Dose Accuracy	+/- 10% of intended dose with no individual measurement exceeding +/- 15%	
Reproducibility	+/- 5%	
Dose Destination	Direct to mouth; Sprinkle on food or beverage, other caregiver/child friendly presentations acceptable	
In-Use Temp Range	15C-40C	
In-Use RH Range	30-75RH	

General Properties of the multiparticulates as they will be supplied. Designers may take these properties as given.

COATED MULTIPARTICULATE ATTRIBUTE	DESIRED STATE	RATIONALE
<b>Size</b>	Target $D_{[4,3]}$ : ~ 200-300 $\mu\text{m}$ Particle Size Range: 150-500 $\mu\text{m}$ Monodisperse $\geq 85\%$ yield at PSD range	Particle Size target around 250 $\mu\text{m}$ was specified based on the desire to have a non gritty feel in the mouth (i.e. good mouth feel). A narrow PSD improves content uniformity of the finished product which better enables volumetric dispensing of multiparticulates, if desired.
<b>Shape</b>	Highly spherical and symmetrical	A spherical/symmetrical core provides a better substrate for Wurster fluid bed coating and also improves flow properties of the multiparticulate.
<b>Dose Range</b>	~50 – 1,500mg with incremental steps	A wide dose range with many increments can be expected for pediatric drugs. It will be dependent on the number of efficacious doses required to cover the pediatric population.
<b>Friability</b>	Low, $\leq 0.5\%$ of the batch	Low friability is essential to ensure substrate can withstand the sieving and Wurster fluid bed coating processing. Also helps ensure minimal damage upon dispensing of the multiparticulates.
<b>Bulk Density (g/cc):</b> <b>Bulk Specific (cc/g):</b> <b>Tapped Density (g/cc):</b>	0.65 1.539 0.743	Powder can be manufactured, and will be supplied to consistent bulk density, enabling dosing by weight or volume.
<b>Known Sensitivities</b>	Moisture, Static	Product may be susceptible to clumping over long term storage when exposed to high RH conditions. Microspheres exhibit static behavior with some materials.
<b>Flow</b>	Flow Function Coefficient > 8 (high flowing)	Free flowing powder, displays excellent flow properties.

#### **IV. Practice gaps and barriers to closing them**

The vast majority of pediatric formulations today are oral solutions or suspensions and while these formulations still have their advantages, they also have their limitations. Some of the limitations of current oral solutions/suspensions are (i) palatability issues – namely poor taste and ability to efficiently taste mask the formulation (ii) may require refrigeration (iii) reliance on sugars and flavorants to overcome palatability issues (iv) need for preservatives (v) potable water sources to reconstitute powder for oral solutions [1-6]. A recent publication which discussed the formulation factors which affect acceptability of oral medicines in children stated, “Oral liquids are traditionally appraised as the first formulation of choice for children who cannot swallow tablets and capsules. In recent years, shortcomings of liquids are recognized mainly including challenges in taste masking, stability issues and the use of numerous excipients, particularly preservatives. There is a consensus to move away from oral liquids to other flexible oral solid dosage forms such as multiparticulates and dispersible tablets”[7].

Recognizing these limitations, and the desire to have a more robust pediatric approach, there has been a consistent desire from both the World Health Organization and regulatory agencies to develop a flexible oral multiparticulate based pediatric platform[2, 8-10]. The development of pediatric specific taste masked multiparticulates has progressed over the past 10 years with several examples of commercially available products on the market[3, 6, 11-14] and still others adapting the approach with compounds under development. A consistent limitation with the broader use of the approach appears to be in the delivery of the multiparticulate medication. The familiarity and ‘ease’ of dosing children with oral solutions/suspensions is a perceived barrier to entry for a novel pediatric platform and therefore, it is desired that proposed device solutions be deemed as ‘easy’ (or ideally easier) as current dose-flexible administration practices for liquid pediatric formulations. For those interested in additional background literature on the challenges of developing pediatric formulations the following references are provided.[1, 3-7, 11, 12, 14-27]

Properly dosing multiparticulates has the potential to offer personalized and precise medicine for each child. However, powder is more challenging to dispense than solid tablets, which have a fixed shape and dose. One of the biggest advantages offered by multiparticulates is increased dose flexibility to account for different children sizes. The dosage can be calculated using the weight of the child and the exact dose (usually in milligrams) can be dispensed as powder. This would be more precise than translating the dose into units of solid tablets. Having the exact dose would also eliminate fixed doses, which can be too high or too low compared to what the child actually needs.

#### **V. Letters of Intent/Proposals**

This RFP model employs a 2-stage process: Stage 1 is the submission of the Letter of Intent (LOI). If your LOI is selected, you will be invited to submit a full proposal. Stage 2 is the submission of the Full Proposal.

Successful proposals will describe a **system** consisting of a package and device, as well as a detailed plan to develop a functional prototype to reliably and accurately measure and administer relevant amounts of the drug MP formulation. Proposals must include how the MP will be administered to the child’s mouth, the final destination. The device and its administration of drug must be child friendly and must accommodate flexible dosing options. Use of the device cannot compromise the integrity of the MP. Proposals must describe how the device will directly measure and administer the MP and how this mechanism will work for a range of doses. Lastly, proposals need to discuss a clear path to commercialization, providing mechanisms to reduce the novel device to practice.

Successful applicants will be able to describe the challenges that exist for patients and caregivers administering medicines in low resource settings and how their device design has taken those into account. The end user specifications must be clear and culturally appropriate. The device must be easy to use and robust in terms of

accuracy as well as physical state. For example, the device must be rugged and sturdy enough to withstand and remain functional in high temperatures and humidity, which are often present in low resource settings. Most low resource settings will not have access to electricity, so a successful device would not depend on electricity.

Pfizer and IPI are particularly interested in supporting proposals that understand the unique circumstances the device will ultimately be used in, as well as the steps required for commercialization. This knowledge is critical for creating an appropriate device that will be adopted into the existing system. Criteria for success should be identified and coupled with strategies to overcome potential obstacles, including unit price, purchase and distribution avenues, and failure modes of the device.

## **VI: Potential outcomes and metrics**

Milestones, metrics and/or outcomes are expected.

## **VII. RFP key information**

<b>Total awards</b>	Up to \$50,000 will be awarded to meritorious proposals.
<b>Specific area of interest</b>	System for Dosing and Dispensing Multiparticulate Formulations of Pediatric Drugs
<b>Website</b>	<a href="http://www.pfizer.com/responsibility/grants_contributions/device_challenge">http://www.pfizer.com/responsibility/grants_contributions/device_challenge</a>
<b>Target settings</b>	Pediatric populations in low resource settings
<b>Geographic scope</b>	<input checked="" type="checkbox"/> United States <input checked="" type="checkbox"/> International LOIs may be submitted from anywhere in the world, but the content of the LOIs should focus on low resource settings such as those found in Africa, India, China, and South America.
<b>Recommended format</b>	Research proposal and path to commercialization plan
<b>Selection criteria</b>	Applicant submissions will be evaluated on: <ul style="list-style-type: none"> <li>• Dosing accuracy over a range of relevant doses to children of all ages</li> <li>• Appropriateness for low resource settings (low cost, end user ease of use, cultural relevance)</li> <li>• Commercialization plan and feasibility</li> </ul>
<b>Key dates/deadlines</b> Please note all deadlines are midnight Eastern Time (New York, GMT -5).	<b>March 28, 2016</b> — RFP released <b>April 12, 2016</b> – Live Q&A Session (click <a href="#">here</a> to Register) <b>May 16, 2016</b> — Letters of Intent (LOIs) due <b>June 10, 2016</b> — Applicants notified; LOIs invited to submit full proposal <b>July 22, 2016</b> — Full proposals due <b>August 19, 2016</b> — Applicants notified; full proposals chosen <b>August 26, 2016</b> — Funded projects start

## **VIII. How to Apply:**

### **Letter of Intent (LOI)**

The LOI is a brief concept document that describes the proposed project at a high level. The Review Committee will select LOIs that are best aligned with the purpose of the RFP. All applicants will be notified with either an acceptance or a refusal. Successful applicants will be asked to submit a full proposal for funding consideration.

### **Submission requirements**

1. The LOI should be no more than three (3) pages, single spaced, using Calibri 12-point font and 1-inch

margins. It should contain the following information about the proposed project:

- a. Project title
  - b. Organization(s) involved
  - c. Project Lead (named individual)
  - d. High-level project description, including
    - i. System components of package and device
    - ii. Description of how the proposal builds on existing work, projects, or concepts
    - iii. Anticipated challenges and solutions
    - iv. Expected outcome and how the impact of the project will be evaluated
  - e. Deliverables and dissemination strategies
2. LOIs exceeding three (3) pages will **NOT BE REVIEWED**.
  3. Submit the LOI online via the Pfizer IGLC website
    - a. Please go to the website at [www.pfizer.com/independentgrants](http://www.pfizer.com/independentgrants) and click on the button “Go to the Grant System.”
    - b. If this is your first time visiting this site, you will be prompted to take the *Eligibility Quiz* to determine the type of support you are seeking. Please ensure you identify yourself as a first-time user.
    - c. Select the “Device Challenge” area.
  4. Complete all required sections of the online application and upload your LOI.

A website has been created to provide additional details about the device challenge. Please click [here](#) to visit this site.

### **IX. Full proposals**

A limited number of applicants will be invited to submit a full proposal of no more than 10 pages, accompanied by a line-item budget. The full proposal guidance will be shared with those invited to move forward.

### **X. Questions**

If you have questions regarding this RFP, please direct them in writing to the Grant Officer for this clinical area Amanda Stein ([amanda.j.stein@pfizer.com](mailto:amanda.j.stein@pfizer.com)) and to the IPI coordinator Winnie Wong ([winnie.wong@pediatricinnovation.org](mailto:winnie.wong@pediatricinnovation.org)) with the subject line, “**Multiparticulate Device RFP.**”

### **XI. Terms and conditions**

1. Complete **TERMS AND CONDITIONS** for Certified and/or Independent Professional Healthcare Educational Activities are available on submission of a grant application on the IGLC website at [www.pfizer.com/independentgrants](http://www.pfizer.com/independentgrants).
2. This RFP does not commit Pfizer or IPI to award a grant or to pay any costs incurred in the preparation of a response to this request.
3. Pfizer reserves the right to accept or reject any or all applications received as a result of this request or to cancel in part or in its entirety this RFP, if it is in the best interest of Pfizer to do so.
4. Pfizer and IPI reserve the right to announce the identity of the organization and nonconfidential details of successful grant application(s) by whatever means ensures transparency, such as on the Pfizer or IPI website, in presentations, and/or in other public media.
5. For compliance reasons and in fairness to all applicants, all communications about this RFP must come exclusively from Pfizer IGLC or the IPI. Failure to comply will automatically disqualify applicants.
6. The awardee(s) will retain intellectual property rights to their design, subject to the following provisions:

- a. Applicants that submit proposals in response to this RFP shall retain all intellectual property rights to the information they provide, and Pfizer and IPI will treat such information in confidence subject to standard limitations. All Reviewers will be bound by confidentiality agreements and any inventive contributions reviewers make will be considered as works for hire and assigned to IPI and to applicants.
  - b. In the event there are applicants that provide similar or overlapping proposals, IPI may in its judgment attempt to promote collaboration between the applicants, while ensuring all applicants retain their IP.
  - c. Notwithstanding, applicants will be advised and must agree in advance that, if their project is selected for funding, they will grant a license (Worldwide, Non-exclusive, Royalty-free, paid up, perpetual, irrevocable) to any intellectual property or work products necessary for IPI, Pfizer, or their respective affiliates to reproduce, publish, distribute, disseminate, adapt, modify, create derivatives of, or otherwise use the winning Device.
  - d. No applicant will obtain rights to Pfizer or IPI intellectual property as a result of participating in the device challenge.
7. U.S. Foreign Corrupt Practices Act: Grantee Organization acknowledges that it has not and will not directly or indirectly offer or pay, or authorize such offer or payment, of any money or anything of value to improperly or corruptly seek to influence any government official. Note: Additional documentation requirements could be required of an applicant prior to an approval of a grant.
  8. Sunshine Act: To comply with the Federal Physician Payments Sunshine Act, Grantee Organization must provide names and other required information of the US-licensed physicians and US teaching hospitals (Covered Recipients, as defined by Centers for Medicare and Medicaid Services) to whom the Grantee Organization furnished payments or other transfers of value stemming from the original independent grant awarded by Pfizer. This includes compensation, reimbursement for expenses, and meals provided to faculty (planners, speakers, investigators, project leads, etc.) and “items of value” (items that possess a value on the open market, such as textbooks) provided to faculty and participants, if such faculty and/or participants meet the definition of “Covered Recipient”. Such required information is to be submitted during the reconciliation process or earlier upon Pfizer’s request in order to meet certain Sunshine Act reporting commitments. The parties agree that, pursuant to this Agreement, Pfizer will not make any payments directly to any physician, and all payments shall be directed to Grantee Organization. The parties further agree that all payments made pursuant to this Agreement will be considered research payments under the Federal Physician Payments Sunshine Act.
  9. Food and Beverage Clause: No portion of a Pfizer independent grant will be used for food and/or beverage for learners and/or participants in any capacity. Grantee Organization will be required to certify during final grant reconciliation that the funds were not used for food and/or beverage for learners and/or participants.

## **XII. Transparency**

Consistent with our commitment to openness and transparency, Pfizer publicly reports its grants and support for medical and patient organizations in the United States. A list of all LOIs selected to move forward may be publicly disclosed, and whatever emanates from this RFP is in the public domain. In addition, all approved full proposals, as well as all resulting materials (e.g., status updates, outcomes reports, etc.) may be posted on the website. Grantees Organizations may be required to submit periodic quarterly reports and/or updates.

Issued RFPs are posted on the Pfizer IGLC website at [www.pfizer.com/independentgrants](http://www.pfizer.com/independentgrants) and are emailed to all registered organizations and users in our grants system.



### XIII. References

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