



**DEVICE CHALLENGE Q&A**  
**System for Dosing and Dispensing Multiparticulate Formulations of Pediatric Drugs**

**As of 05/02/16**

**\*This file includes questions received during the Q&A Session held on April 12<sup>th</sup> as well as questions received from individuals via email.\***

**Dosing**

**Question:** Is there a specified number of dosing steps?

**Answer:** There is flexibility in this requirement. Multiple different options may be viable, and the jury is interested in seeing your thoughts regarding this. Initial thinking was approximately 10-12 dosing steps would allow covering the wide body surface area (BSA) required for pediatric dosing but this will be dependent on each drug and its respective dosing regimen. So should be seen as a guide not a requirement.

**Question:** Does every dosing process have its own procedure for filling the system or should it be possible to fill the system once and have incremental dosing steps of the prefilled granulate?

**Answer:** This is open to the entrant to propose, either approach may be viable and we welcome thoughts/ideas.

**Question:** What is the dosage size?

**Answer:** The overall dosage is specified in the Request for Proposal under the "User Requirement Specification". This describes the dose we wish to deliver which is appropriate to almost any medication. The most critical aspect is that it must be able to measure out the appropriate amount according to the age and weight of the child.

**Question:** Can we build a relationship between number of particles and dose?

**Answer:** In theory yes, but in practice may be challenging. Unlike systems that work with larger (e.g. 1 mm size) multiparticulates or minitables, due to the significantly smaller size of the multiparticulates, the dose will likely involve 1000 or more particles. If a system could be designed to address the challenges posed in the RFP and function based on counting, it is possible this could work.

**Device**

**Question:** Are there special requirements on the used material for the device?

**Answer:** This is open to the entrant to propose.

**Question:** Are there any other already existing components we have to take account of?

**Answer:** Other than needing to work with the multiparticulates themselves, none that come to mind.

**Question:** Is it allowed to use additional tools (e.g. a funnel or tube) for the filling process of the dispensing device?

**Answer:** Yes

**Question:** What are the target unit costs for the device?

**Answer:** This is a parameter that could be optimized going forward, but should be seen as one to minimize as the intent of the device is for less developed/developing countries.

**Question:** What is the exact meaning of “cultural appropriateness”? Are there any specific requirements?

**Answer:** Further feedback on this question could be provided by the expert panel members going forward.

**Question:** Is it intended to replace the device with each drug reservoir (disposable)? How long is the intended period of use per device?

**Answer:** The cost of the device should be low enough that while it could be thrown away it could also be used repeatedly. For example, some therapies will only require 1 week of administration, while other therapies are for more chronic indications where longer duration of dosing would be needed. A device that can as easily be used in other situation (single dose or repeated dosing) is preferred.

**Question:** Are there special requirements regarding cleanability of the device?

**Answer:** Should be easy if needed at all.

**Question:** Is it intended to have the device single packed or will it be offered as a “starter kit” (primary packaging of the multiparticulate medicine included)?

**Answer:** Flexible, part of the design challenge.

**Question:** Is there a limitation of handling time for the device during each application?

**Answer:** Not formally, but the overall process should not be overly burdensome when compared to current dosing systems for example an oral liquid given by oral syringe.

**Question:** Are there limitations in weight and dimensions of the device? Should the device be portable or may it be stationary?

**Answer:** Smaller and portable is more preferred vs. a stationary dispensing device.

**Question:** Are transdermal devices on the table for pediatric treatments?

**Answer:** Transdermal is not part of the challenge. Just a way to measure out powder and get it into a child’s mouth in an accurate and pleasant way for all concerned.

**Question:** Would this technology replace/displace the need for oral liquid OTC medication drug delivery (Pediatric oral liquids for pain, cold-cough, etc.)?

**Answer:** Yes, we hope to replace the need for liquid formulations in a large number of cases. However, we expect liquids to continue to be important products.

**Question:** For the system, what is the intended region to which this system will be marketed?

**Answer:** We envision it as something to be used worldwide including low-resource settings.

**Question:** How long can the duration of therapy be this type of drug?

**Answer:** That would be specific to the drug. Good guidance would be to think of a typical course of antibiotics. The key is being able to easily, reliably and accurately measure out and dose to the child in

a child friendly manner. You need to consider both the device and the package. It is acceptable to use an existing package size or design your own.

**Question:** Is this device supposed to deliver the particulate directly into the child?

**Answer:** This is one area that we left open in terms of the solution. The intent of the challenge is for organizations to propose innovative ideas/methods of not only accurately determining the doses but also administering them.

**Question:** Where would the fill location be for the package?

**Answer:** The package can be prefilled by the manufacturer or by the pharmacist. However, we are open to other ideas. Clearly for a manufacturer, it's easy if you have an idea that permits the use of a standard packaging configuration (i.e. a bottle with a cap), and if your device can work with that in some fashion, that lowers the barrier to entry. On the other hand, if you have a truly innovative idea that requires a custom package, perhaps the advantages of your idea can justify the additional cost of the package.

**Question:** The device needs to be adjustable or not?

**Answer:** Yes, it should be adjustable to determine the dose or have some method of accurately dispensing the correct dose.

**Question:** Are there any concerns with over dosing based on user/caregiver confusion or lack of instructions? Does there need to be an inherent max dose size that can be dispensed? Assumption is that a Dr. or Medical personnel will initially set the device dosing.

**Answer:** The assumption that the medical personnel would set the correct dose is an area that I would leave open to creative ideas, so depending on the device, the dose may or may not be set by a pharmacist or doctor. Safety is a very high priority, so take the time to think through your design concepts and at least to the thought experiment about what a failure mode effects analysis would look like and how many ways it could be used wrong. Try to design it so that it cannot be used incorrectly.

**Question:** Can we use aqueous solvents or organic?

**Answer:** Either, as long as the residual solvent requirements are met at the end.

**Question:** How much family of bottles/sizes would be desired to connect to the dosing device? size range of that bottle family?

**Answer:** This is another flexible parameter. Smaller size is preferred for something affordable and portable for parent/caregiver to carry around with them.

**Question:** Are you looking at a device or process that won't cause a change in the particles?

**Answer:** Yes. If you crush the particles, it is very likely they will taste bad.

**Question:** Is there a need for cold chain?

**Answer:** No. The multiparticulates do not require cold chain storage.

**Question:** Should there be recycling capabilities for 3rd world countries? Or just in general?

**Answer:** Yes, that is a good idea but not required. The device should be inexpensive enough to be disposable or easily cleaned and reused/recycled

## Device Packaging

**Question:** What sort of "packaging" considerations might you be looking for? Tamper evidence? Assume child resistant?

**Answer:** These are certainly desirable features but we do not want to specify them in order to leave room for creativity.

**Question:** To what level do we have to reference existing packaging systems , i.e. brand, manufacturer, model?

**Answer:** If this is something that will pair well with an existing packaging configuration, that's a point in its favor. On the other hand, if you can make a substantially improved user patient experience by designing some kind of custom packaging, then that could be part of the design as well. We're open to ideas and encourage maximum creativity to try to get the best solution possible.

**Question:** Will the device and packaging need to be sterilized, if so, which method?

**Answer:** That would not be required.

## Multiparticulate

**Question:** How high is the tolerance of the bulk density? Are there any experiences, observations, values?

**Answer:** Our experience with the bulk density is that it typically is around 0.65 g/cc. While there may be some variation around this value, I would not classify it as a high degree of variation around the bulk density value.

**Question:** How high is the variation of volume (bulk and single dose) and weight within the defined range of temperature and humidity?

**Answer:** This is where the device or packaging will become important – being able to store the final device and package in zone IVb regions (i.e. 30C/75% RH which includes regions such as Africa) but still be able to maintain the accurate dosing and dispensing of the multiparticulates will be a key consideration. It is important to be able to maintain them in their free flowing form where humidity does not cause sticking or agglomeration.

**Question:** Is it possible for the powder to get statically loaded?

**Answer:** This has not been evaluated.

**Question:** Is it allowed to compress the powder? Are there any experiences or evaluations on that topic?

**Answer:** Light compression of the powder may be acceptable, but higher compression forces may lead to damage of the taste masking coating on the microspheres. Microspheres have been successfully compressed into orally disintegrating tablets using standard tableting equipment, with some damage noted to the barrier coatings after compression. The coated microspheres withstand standard blending, screening, and encapsulation unit operations without any damage observed.

**Question:** Since we don't have access to the real MP, what can we use to mimic the density and the flow of the MP? Salt or coffee? Any other ideas?

**Answer:** An inactive excipient that has similar properties to the drug loaded multiparticulates is microcrystalline cellulose multiparticulates, sold under the trade name of “cellets 200”.

If you go to their website (<http://www.cellets.com/>) , and click “contact” and select your region of the world, it will provide contact information about how to obtain some of the excipient.

Cellets 200 are in approximately the same particle size range as “ideal” multiparticulates as defined in the RFP, and display similar properties from a material handling perspective.

Link to an informational brochure on the cellets  
website: [http://www.cellets.org/download/cellets\\_english.pdf](http://www.cellets.org/download/cellets_english.pdf)

**Question:** Do we need to keep the particles in the solid state? Can they be suspended in a gel system?

**Answer:** It is up to the solver to propose but pH should be a factor to consider. It would be undesirable to dissolve the multiparticulates in the carrier or to have the multiparticulates begin to dissolve in the carrier (e.g. gel). The multiparticulates may typically contain a pH dependent reverse enteric membrane which will dissolve below pH 5.5.

**Question:** Do you want to focus only on multiparticles / pellets? Or would you accept minitables as well?

**Answer:** Focus is only on Multiparticulates.

**Question:** How elastic these particles are if you force them through a syringe?

**Answer:** Yes, you can suspend them and put through a syringe. You can take an oral syringe, load it with the powder and it will freely flow out of the syringe. If you invert the syringe even without applying pressure they will empty from the syringe free flowingly.

**Question:** While a specific drug hasn't been identified, do you have any target/indicative treatments that would lend themselves to this administration method? This could impact the risks and requirements of accuracy and repeatability.

**Answer:** We're very interested in identifying drugs that would be used in the under-resourced developing world healthcare market, such as those for pneumonia, sepsis, antiretrovirals, and diarrhea. However, we do believe the formulation technology is applicable in US and Europe, so the full range of existing generic drugs and new proprietary drugs are also relevant. We have representatives from the Bill & Melinda Gates Foundation who will be part of the jury that is going to judge these entries, so that will be part of the analysis about where this could meet world needs as well as needs of the branded pharmaceutical industry. All drugs are potentially in scope.

**Question:** Will this be for prescription drugs only?

**Answer:** No. For example, consumer health over the counter could be a very big market.

**Question:** What is the size of these particles?

**Answer:** Please refer to the table on page 4 of the RFP. The average particle size of the multiparticulates is around 250 micron (um) in diameter. There is a distribution of sizes centered around this value.

**Question:** How many micrograms is the weight of each particle?

**Answer:** Please refer to table on page 4 of the RFP.

**Question:** How sensitive are the particles to humidity? Do you consider that primary stability will require a high barrier level?

**Answer:** This is where the device or packaging will become important – being able to store the final device and package in zone IVb regions (i.e. 30C/75% RH which includes regions such as Africa) but still be able to maintain the accurate dosing and dispensing of the multiparticulates will be a key consideration. It is important to be able to maintain them in their free flowing form where humidity does not cause sticking or agglomeration.

**Question:** For the dose range, is that the dose of the MP or the drug or are they one and the same?

**Answer:** The table in the RFP has a range of material mass to be delivered, which can be considered the mass of the powder.

**Question:** What stage of development is the primary particulate technology at? Have you conducted clinical trials with any molecules?

**Answer:** The multiparticulate technology is a commercial technology. Pfizer has commercial products using this technology.

**Question:** Have you tested this system in simulated saliva?

**Answer:** Yes, it is one of the standard testing parameters to ensure minimal drug release.

**Question:** Is there any known incompatible material to contain the MP?

**Answer:** None to date.

#### Challenge Process

**Question:** Who will study the stability in the device? Is this part of the grant?

**Answer:** That would be stage 2. The Initial proof of concept is showing a device that can accurately determine and dispense the right dose. Then, following onto that is studying the interactions.

Stability applies to the condition under which particles would be stored in their original packaging. If the device is only used momentarily to measure out particle and dose, then there is no need for stability studies in the device.

**Question:** Are you open to other ideas than a device?

**Answer:** Yes, as long as it meets the user requirements in the RFP.

**Question:** How many design concepts can be submitted in the letter of intent?

**Answer:** There is no limit to the amount of concepts but please submit as separate letters of intent.

**Question:** What is the overall timing for implementation for the dispensing device to be in the field? How much time is allowed for development? -This would be after the August award

**Answer:** There is not a firm deadline. It will depend on how the device needs to be developed and how the resources to develop it can be accumulated. Ideally, we would like to be able to see something that can be in use in a 3 year period.

**Question:** Is it possible to submit several LOIs or is it limited on one per person/company?

**Answer:** Yes several are welcomed! If an organization has multiple approaches to the challenge, submitting more than one LOI is welcomed. However, each LOI is limited to one approach.

**Question:** Are you looking for an organization (or group of organizations) that will take the device all the way to market launch, or would you also consider organizations who might design the device and then find a route to market?

**Answer:** This is flexible. It might not be reasonable to expect an entrepreneur to have the wherewithal to take a device from concept to full commercialization; there could be a number of intermediate steps. We know there are organizations out there that have capability to do that, but we also think the challenge should be open to those who have a good idea, but I should hasten to add that you need more than a good idea. You actually need to envision a reasonable and practical path to market.

**Question:** You mention in the RFP that IPI has some funding options for the winning design firm. What does that mean? Is that actual real dollars through grants (i.e. WHO, Clinton Foundation) or simply just sources of capital that the winner would be able to access but negotiate essentially “on the open market”.

**Answer:** The \$50,000 seed grant is just that—a seed. More funding would be needed to develop the device for commercialization. It is our intention to stimulate an external party to develop a device that they can use to build a sustainable business based on being able to sell their device to big pharmas, small pharmas, consumer products, NGO’s,...everyone. Different organizations will have different appetites for how to take it on. We plan to engage in discussion of how to facilitate the winning design after it is awarded. There are many potential pathways. Other Big Pharma have expressed interest in our Pediatric Platform. In addition, the Bill and Melinda Gates Foundation is very interested in getting medicines to children in Low Resource Settings and are represented on the Challenge jury. It is our hope that a device that can meet the needs of several constituencies could provide a viable business opportunity for the right company.

**Question:** What concept “maturity” are you guys looking for in the LOI and Proposal?

**Answer:** The Challenge is a contest to flush out the best concepts. Mature is better but novelty is not discouraged. We do not necessarily expect to get fully-developed concepts at the LOI stage. The LOI format will force some limitations on what can be provided. Entrants who are invited to submit full proposals will have the opportunity to develop their ideas further. It will be up to the individual entrants to decide how much effort is worth putting in for the potential rewards.

**Question:** We are one of those Design Consultancies where our model is one where a client engages us to design against a specific problem and funds us appropriately. I am assuming there is no fee for services associated with this initiative but instead the \$50k Grant for winning design(s), along with resulting IP, is the payout for participating?

**Answer:** The fee for service is not contemplated during the design challenge. The \$50K grant is a seed grant to get the project started. We recognize that projects will require further funding to get to market. The challenge winner will own their own intellectual property and commercialization rights, so we hope that some combination of seed grant, owning the IP and commercialization rights, and publicity of being the challenge winner will enable winning entrant to garner funding for their idea.

**Question:** Can visual concepts be added within the pages for the letter of intent, or only text?

**Answer:** Visual concepts can be added to an appendix and will not count towards the page limit.

*If you have any additional questions regarding this RFP, please send them to Amanda Stein ([amanda.j.stein@pfizer.com](mailto:amanda.j.stein@pfizer.com)) and Winnie Wong ([Winnie.wong@pediatricinnovation.org](mailto:Winnie.wong@pediatricinnovation.org)) with the subject line “Multiparticulate Device RFP”.*