Pediatric Formulation Development – Industry Perspective on Palatability Challenges & Opportunities

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Challenges and Strategies to Facilitate Formulation Development of Pediatric Drug Products
CERSI Workshop in collaboration with EuPFI & IQ Consortium
Hyattsville, MD
June 8-9, 2016

Pfizer
WORLDWIDE RESEARCH & DEVELOPMENT
PharmaTherapeutics Pharmaceutical Sciences

Acknowledgements

Pfizer UK

- Cram, Anne
  - EuPFI
- Coupe, Alastair
  - Innovate UK Pediatric Consortium
- Bennett, Jo
- Carmody, Alan
- McGovern, James
- Contreras, Lourdes
- Turnbull, Neil
- English, Cheryl
- Ogilvie, Ron
- Simmons, Joanna
- Forbes, Claire

Pfizer US

- Santangelo, Matt
- Herbig, Scott M
- Shanker, Ravi M
- Heimlich, John H
- Hausberger, Angie

Pfizer US

- Murdande, Sharad
- Prpich, Andrew
- Ciringh, Yangzhen
- Nixon, Phil
- Korsmeyer, Richard
- Thombre, Avi
- Sagawa, Kazuko

Pfizer Global Pediatric Center of Excellence

- Thompson, Charlie
- Darsey, Edress

Institute of Pediatric Innovation (IPI)

Others I am sure I have missed…

Outline

- **Why is palatability important?**
- **What makes developing a palatable formulation challenging?**
- **What can be done?**

Why is palatability important?
Bartlett Household Example 1

Why is palatability important?
Bartlett Household Example 2

Why is Taste of Medicines Important?

- **Even the best medicine won't work unless the child takes it!**
- **A 2003 survey of pediatricians conducted by the American Association of Pediatrics found**
  - Unpleasant taste was the biggest barrier for completing treatments in pediatrics[1]
- **Average compliance rate in children is ~58%, with major factors attributed to formulation and palatability[2]**

[1]Ayenew, Z., V. Puri, L. Kumar and A. K. Bansal (2009). "Trends in pharmaceutical taste masking technologies: a patent review." Recent Pat. Drug Delivery Formulation **3**(1): 26-39.

[2]Matsui, D. (2007). "Current issues in pediatric medication adherence." Paediatr Drugs **9**(5): 283-288.

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Challenges in developing pediatric formulations

- **Diverse patient group**
  - Birth to age ~ 18
  - Size/Weight change over 20 fold
  - Dose adjustment >3-4 fold
  - Ability to take and preference of dosage form varies across the wide age range
- **Palatability**
  - Cultural and geographical preferences
  - Restrictions related to use of excipients (type and quantity)
  - Taste assessment vs. compliance
    - How do you know when you are “good enough?”
  - What palatability information should you use to drive formulation development?
    - Adult Healthy Volunteers
    - Trained Adult Taste Panel
    - Pediatric Patients
    - In vitro
- **Keeping in mind, palatability is only one part of dosage form acceptability!**

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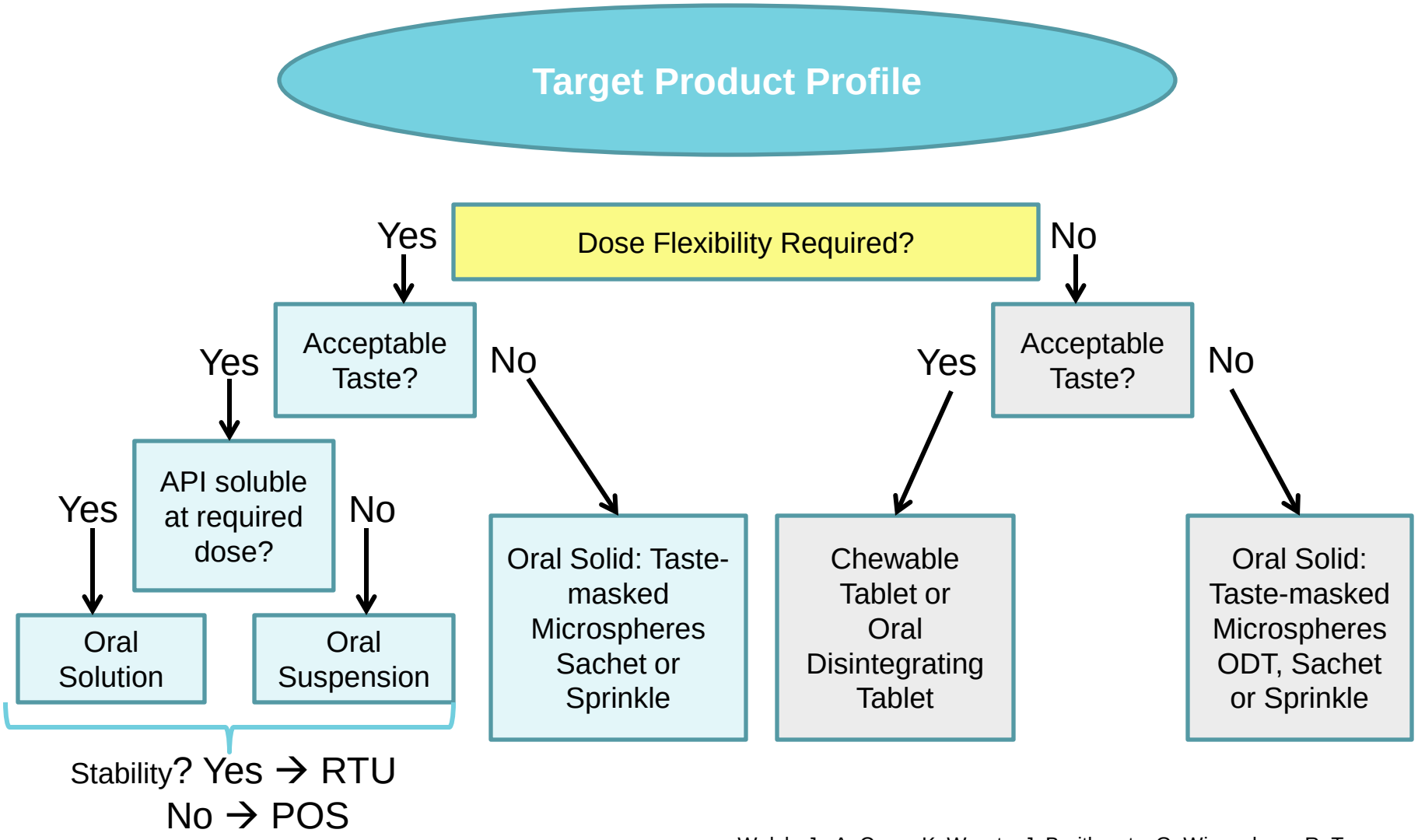
Pediatric Oral Dosage Form Decision Tree

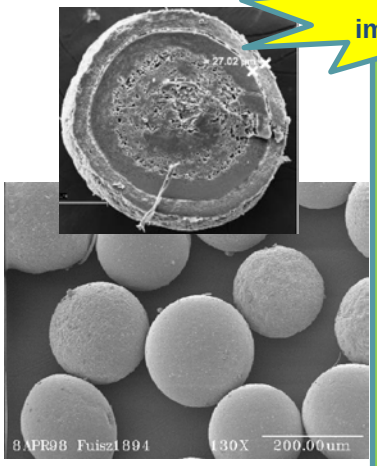


Walsh, J., A. Cram, K. Woertz, J. Breitkreutz, G. Winzenburg, R. Turner and C. Tuleu (2014). "Playing hide and seek with poorly tasting paediatric medicines: Do not forget the excipients." Adv. Drug Delivery Rev. **73**: 14-33.

Pediatric Dosage Form Technologies: Small Molecule Pediatric Products -- oral

Ready to Use (RTU) Oral Solution or Oral Suspension
Dosed using a syringe, dosing cup, or dosing spoon

Powder for Oral Solution or Powder for Oral Suspension (POS)
Constituted with water by the Pharmacist
Dosed using a syringe, dosing cup, or dosing spoon



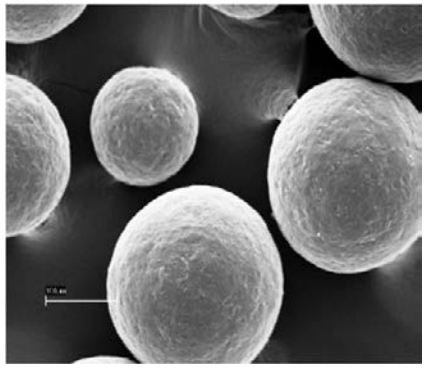
Being implemented!

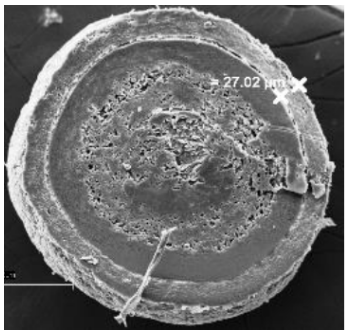
Taste-masked Microspheres

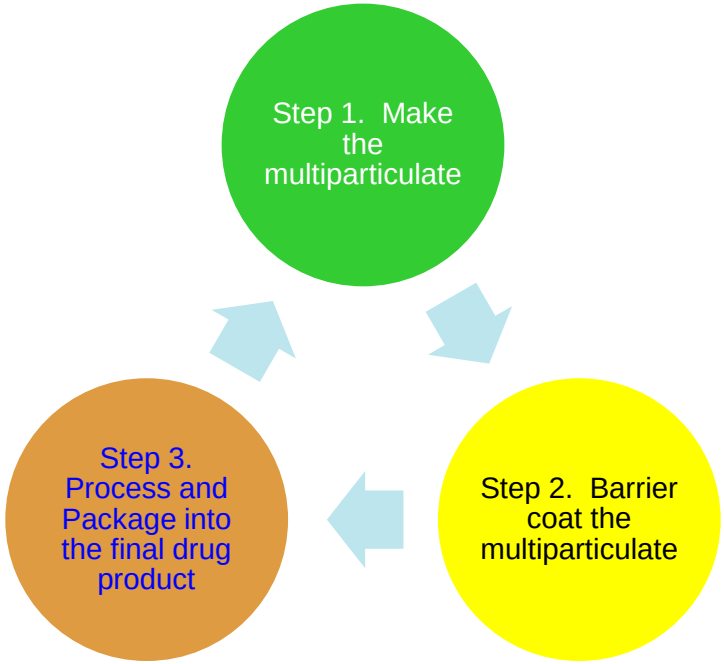
- Prevent drug release until the microspheres clear the mouth – achieve “taste neutral” profile
- Spherical coated multiparticulates
- Stability in Zone 4 (global)
- Reduce/Eliminate the need for flavors, sugars, preservatives
- Packaging include bottles, sachet, capsules (other presentations are also possible)
- Potential dosing with or without water

Pediatric Multiparticulate Platform Summary

- **Oral Multiparticulates provide an excellent platform for pediatric medicines**
  - Ideal substrate for taste masking
  - Dose Flexibility
  - Reduce/Eliminate need for preservatives, sweeteners, flavorants, dyes, etc
  - May be dosed w/wo water
- **To be successful three main focus areas**
  a) Multiparticulate
  b) Barrier Coating
  c) Dosing and Administration, Device/Packaging
     - Running Open Innovation Challenge to generate ideas on the best way to accurately dispense and administer the multiparticulates







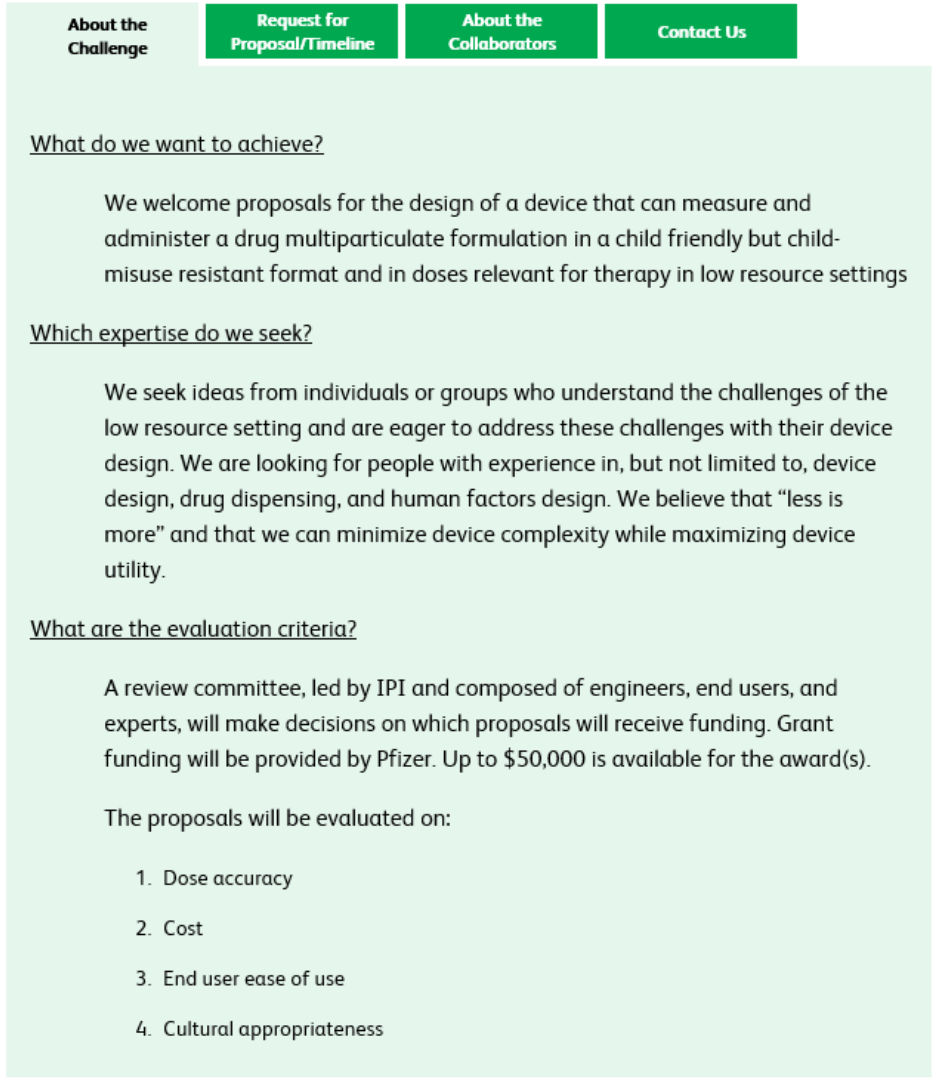
Institute of Pediatric Innovation and Pfizer collaborate on open innovation pediatric device challenge

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

The Institute for Pediatric Innovation (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

Expect to announce awardee ~ August 2016



www.pfizer.com/responsibility/grants_contributions/device_challenge

Conclusions & Opportunities

- Connecting taste assessment evaluations with compliance data would be very helpful
- Providing taste evaluation feedback early in adult clinical development can help guide technology selection
- Oral Multiparticulates provide an excellent platform for pediatric medicines
- Still working on –
  - What is the “ideal” barrier membrane?
  - What is the “best” way to dispense and administer a free flowing, non gritty, tasteless powder?