Session 1
Pediatric Formulations Research: NIIH Perspectives

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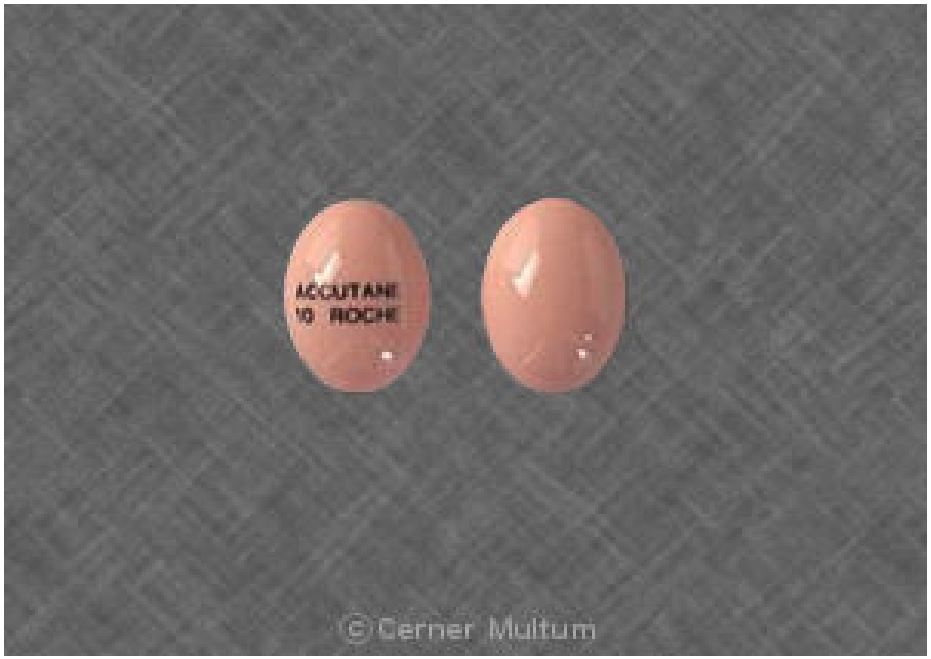
Pediatric Needs

- Parity with adults?
- Commercially available dosage forms
- Dose accuracy
- Acceptable frequency of dosing
- Palatability and swallowability not preventing medication (re)administration
- Minimal use of excipients

Hydroxyurea 500 mg
Dose: 20 mg/kg
Indication: Sickle cell disease in 9-17 month olds

Isotretinoin 10 mg
Dose: 160 mg/m2
Indication: Neuroblastoma in 2 year olds



Meropenem 500 mg Vial
Dose: 10 mg/kg
Indication: Abdominal infection in premature neonates

Atropine autoinjector and pralidoxime chloride autoinjector

- **Atropine** autoinjector
  - 2 mg in 0.7cc
- **Pralidoxime** autoinjector (2-PAM)
  - 600 mg in 2cc

https://chemm.nlm.nih.gov/antidote_nerveagents.htm

http://www.phe.gov/Preparedness/legal/boards/naccd/Documents/healthcare-prep-wg-20151311.pdf

Extemporaneous Compounding

- Neonatal Abstinence Syndrome (NAS)
  - Extemporaneous compounding of morphine, methadone with ethanol

FDA Approves 3-D–Printed Drug

The US Food and Drug Administration green lights the first medicine produced by a 3-D printer for use in the human body.

By Jef Akst | August 4, 2015

APRECIA PHARMACEUTICALS

At first glance, SPRITAM looks like any other pill. But the drug, developed by pharmaceutical company Aprecia, is actually layers of powder laid down by a 3-D printer. Its approval this week (August 3) by the Food and Drug Administration (FDA) for the treatment of epilepsy marks the first 3-D–printed drug to reach the US market, according to a company press release.

SPRITAM is a branded version of the generic anticonvulsant drug levetiracetam. The tablet is designed to dissolve more quickly in the human body than existing pills, and it can provide custom and uniform doses, as well as better taste-masking options, according to the company.

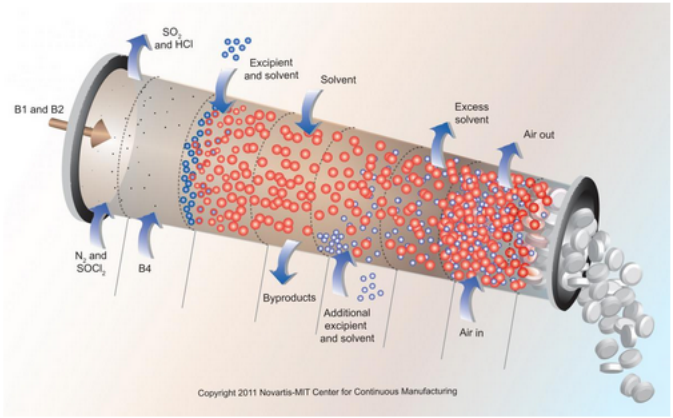
http://www.the-scientist.com/?articles.view/articleNo/43672/title/FDA-Approves-3-D-Printed-Drug/

About Us

The Novartis–MIT Center for Continuous Manufacturing is a 10–year research collaboration aimed at transforming pharmaceutical production. Combining the industrial expertise of Novartis with MIT's scientific and technological leadership, the Center develops new technologies to replace the pharmaceutical industry's conventional batch–based system with a continuous manufacturing process. Continuous manufacturing will benefit patients, healthcare providers, and the pharmaceutical industry by:

- Accelerating the introduction of new drugs through efficient production processes
- Requiring the use of smaller production facilities with lower building and capital costs
- Minimizing waste, energy consumption, and raw material use
- Monitoring drug quality on a continuous basis rather than through post–production, batch–based testing
- Enhancing process reliability and flexibility to respond to market needs

Initial research is conducted primarily through PhD programs at MIT laboratories and involves MIT faculty members, students, postdoctoral fellows, and staff scientists. Novartis then applies the research to industrial–scale projects and pilots new manufacturing processes using its own pharmaceutical products. Novartis has committed its manufacturing and R&D resources and $65 million to the Center over the next 10 years.



https://novartis-mit.mit.edu/

http://www.npr.org/sections/health-shots/2016/05/23/478576727/inventing-a-machine-that-spits-out-pills-a-whole-new-way

NIH-FDA Formulations Platform

- Inter-Agency Agreement with FDA 2010-2012
- Develop an open-source, technically feasible platform based on chemical structure, to produce orally dissolvable solid dosage forms that are stable at high temperatures/humidity, taste-masked, with good oral absorption, in suitable dosage increments, with minimal excipients
- https://bpca.nichd.nih.gov/collaborativeefforts/initiatives/Documents/Formulations_Platform_Report2.pdf

Development of Appropriate Pediatric Formulations and Pediatric Drug Delivery Systems (PAR 13-345/346)

- Development of innovative technologies and platforms for oral pediatric formulations , including taste masking and the use of novel excipients;
- Use of a materials science approach to overcome solubility limitations of pediatric drugs, increase bioavailability, decrease excipients' exposure, and provide effective taste masking;
- Development of neonatal parenteral formulations with minimal excipients;
- Development of long acting pediatric formulations by combining APIs and proprietary nanocarriers;
- Development of novel approaches for oral mucosal, transdermal, nasal, and pulmonary drug delivery systems and device technologies.

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