

The Best Pharmaceuticals for Children Act

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Best Pharmaceuticals for Children Act

- ◆ Enacted January 2002, will sunset October 2007
- ◆ Continues exclusivity provision of FDAMA
- ◆ Purpose: pediatric labeling

Pediatric Research Equity Act (PREA)

- ◆ Codifies the 1998 Pediatric Rule into law
- ◆ Passed November 19, 2003
- ◆ Signed into law December 5, 2003

Pediatric Labeling

- ◆ Pre-approval: Pediatric Research Equity Act
- ◆ On-patent:
 - Best Pharmaceuticals for Children Act which continues the exclusivity provisions of FDAMA
 - Studies supported by the NIH Foundation
- ◆ Off-patent: Best Pharmaceuticals for Children Act

Best Pharmaceuticals for Children Act

◆ In pediatric oncology

- prioritize new drugs for study
- assure timely access to new treatments
- develop pre-clinical models of pediatric cancers

Best Pharmaceuticals for Children Act

- ◆ Mechanism to study on-patent drugs
 - referral to NIH Foundation
- ◆ Mechanism to study off-patent drugs

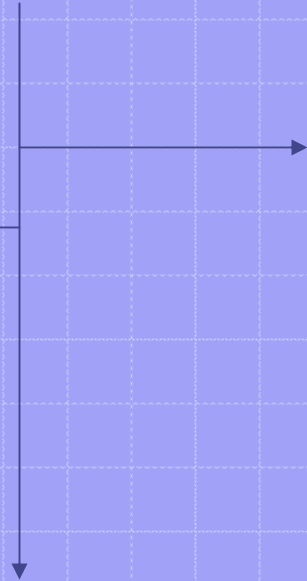
Master List of all Off-Patent Drugs
which lack adequate pediatric labeling
N=169

Consider for prioritizing:

- Availability of S/E data
- Are additional data needed?
- Will new studies produce health benefits?
- Reformulation?

Consultation with
experts in pediatric
practice and research

Develop, prioritize, publish an
Annual List
N=15-20



Priority List

- ◆ Developed by NIH
- ◆ In consultation with
 - Institutes and Centers of the National Institutes of Health
 - Federal Agencies
 - ◆ Food and Drug Administration
 - ◆ Centers for Disease Control and Prevention
 - pediatric subspecialists and subspecialty groups
 - committees of the American Academy of Pediatrics

Drugs on the Priority List: January 2003

FR 68: 13; Jan 21, 2003

- ◆ Azithromycin
- ◆ Baclofen
- ◆ Bumetanide
- ◆ Dobutamine
- ◆ Dopamine
- ◆ Furosemide
- ◆ Heparin
- ◆ Lithium
- ◆ Lorazepam
- ◆ Rifampin
- ◆ Sodium nitroprusside
- ◆ Spironolactone

Drugs on the Priority List: August 2003

FR 68: 156; Aug 13, 2003

- ◆ Ampicillin/sulbactam
- ◆ Diazoxide
- ◆ Isoflurane
- ◆ Lindane
- ◆ Meropenem
- ◆ Metoclopramide
- ◆ Piperacillin/
tazobactam
- ◆ Promethazine

Drugs on the Priority List: February 2004

FR 69:30; February 13, 2004

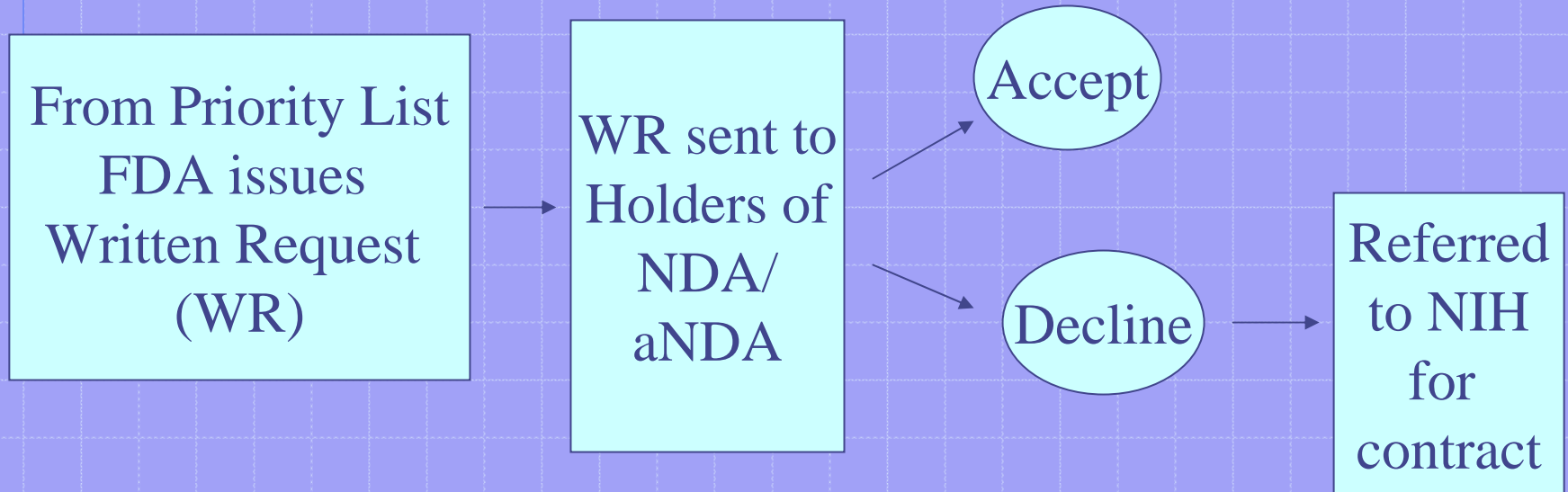
- ◆ Ampicillin
- ◆ Ketamine
- ◆ Vincristine
- ◆ Dactinomycin
- ◆ Metolazone

Drugs on the Priority List: January 2005

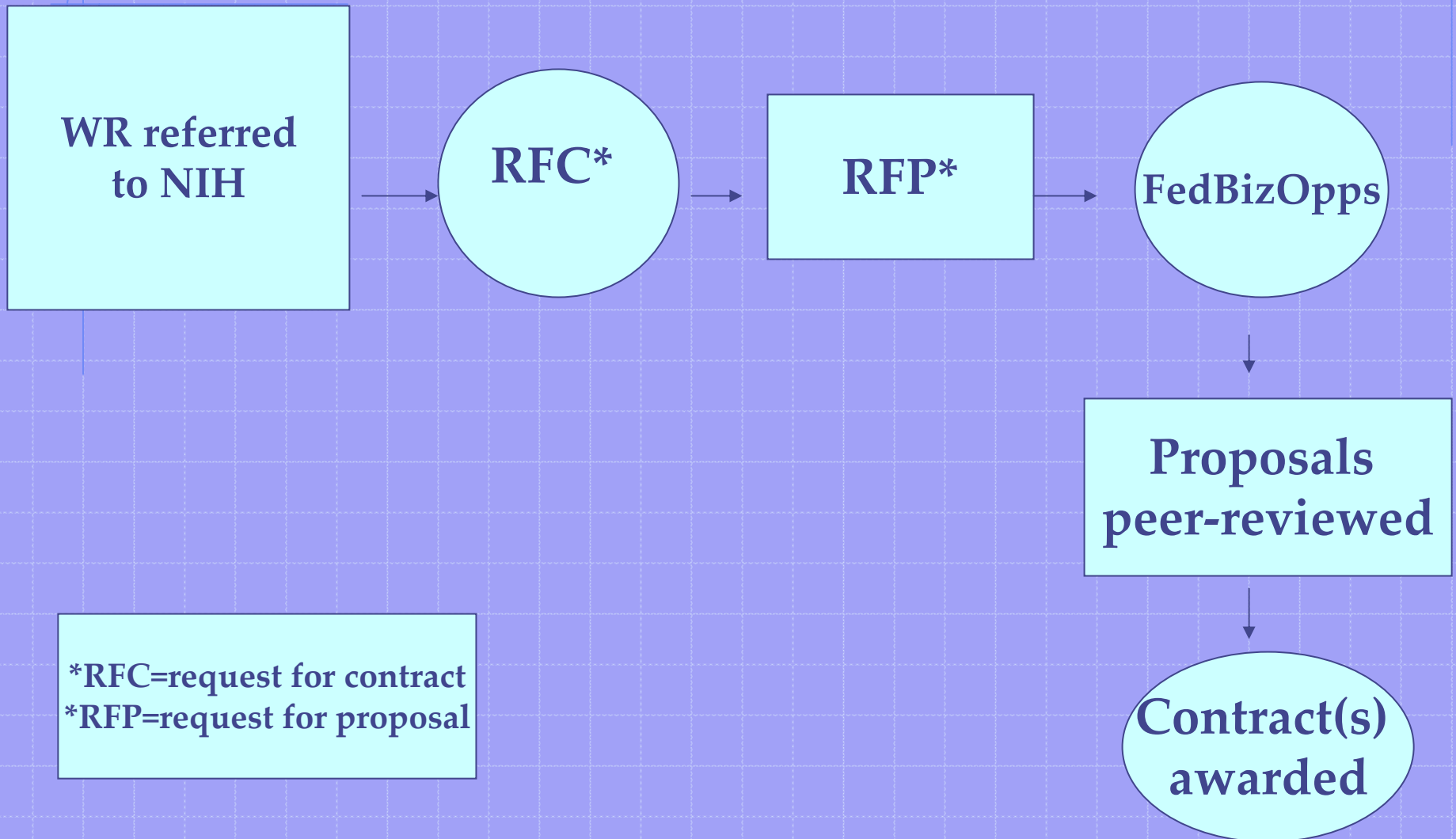
FR 70:3937; January 27, 2005

- ◆ Ivermectin
- ◆ Hydrocortisone valerate
- ◆ Hydrochlorothiazide
- ◆ Ethambutol
- ◆ Griseofulvin
- ◆ Methadone
- ◆ Hydroxychloroquine

FDA Issues a Written Request



Contracting Process



NIH: Process for Contracts

- ◆ NIH publishes the Request for Proposal (RFP) in FedBizOpps

Methods of Funding

- ◆ Grant
- ◆ Cooperative Agreement
- ◆ **Contract**

Post-Award

- ◆ Study performed (NIH holds IND)
- ◆ Data analyzed
- ◆ Results submitted to NIH, data published on the BPCA web site
- ◆ Results submitted to the FDA, placed on public docket, for labeling

Results So Far...



Written Requests Issued by FDA

- ◆ Lorazepam
 - Sedation
 - Status epilepticus
- ◆ Nitroprusside
- ◆ Azithromycin for Ureaplasma pneumonia
- ◆ Azithromycin for Chlamydia
- ◆ Baclofen
- ◆ Lithium

Written Requests Issued by FDA

- ◆ Lindane
- ◆ Rifampin for MRSA endocarditis
- ◆ Meropenem
- ◆ Vincristine
- ◆ Dactinomycin

Written Requests Declined by Industry

◆ Off-patent:

- Lorazepam (2)
- Nitroprusside
- Azithromycin for *Ureaplasma pneumonia*
- Azithromycin for *Chlamydia*
- Lithium
- Baclofen*
- Rifampin for MRSA endocarditis

Written Requests Declined by Industry

◆ Off-patent

- Meropenem
- Vincristine
- Dactinomycin

Written Requests Declined by Industry

◆ On-patent:

- Morphine
- Baclofen
- Bupropion
- Sevelamer
- Zonisamide
- Hydroxyurea
- Dexrazoxane
- Eletriptan

Written Requests Published in the Federal Register for Comment

- ◆ Azithromycin for Ureaplasma pneumonia/prevention of bronchopulmonary dysplasia
- ◆ Azithromycin for Chlamydia
- ◆ Rifampin for MRSA endocarditis
- ◆ Meropenem for complicated intra-abdominal infections

Drugs Proposed by the Children's Oncology Group

- ◆ Doxorubicin
- ◆ Daunorubicin
- ◆ Methotrexate

Contracts

◆ Contracts awarded

- Lorazepam: sedation in ventilated patients
- Lorazepam: status epilepticus
- Nitroprusside: controlled hypotension
- Ketamine: pre-clinical toxicology studies
- Vincristine: pediatric malignancies
- Dactinomycin: pediatric malignancies
- Lithium: acute mania in bipolar disease

RFPs developed

- ◆ Azithromycin (IV) for Ureaplasma pneumonia and prevention of BPD
- ◆ Azithromycin (PO) for treatment and prevention of Chlamydia trachomatis pneumonia and conjunctivitis
- ◆ Meropenem for complicated intra-abdominal infections
- ◆ Baclofen (PO) for spasticity related to cerebral palsy

Coordinating Center

◆ Purpose:

- Coordinate patient enrollment
- Coordinate, monitor data collection
- Report adverse events and other data (usually blinded) to Data Safety Monitoring Board (DSMB)
- Analyze, organize results into a supplemental NDA for submission to FDA

◆ Contract awarded to Premier Research, Philadelphia, Pennsylvania

Questions from NIH to the Pediatric Subcommittee of the Oncology Drug Advisory Committee

- ◆ Prioritization process for deciding which off-patent drugs should be studied
 - Health benefit
 - ◆ Number of patients affected
 - ◆ Lack of other drugs that treat the disease
 - ◆ Severity of the disease

Questions

- ◆ Other drugs that should be studied
 - Antineoplastics
 - Supportive Care
 - ◆ Anti-emetics
 - ◆ Anti-infectives
 - ◆ Analgesics
 - Other

Summary

- ◆ Work in Progress
- ◆ Partnership with FDA
- ◆ NIH responsible for
 - prioritizing list
 - providing input on the Written Request
 - sponsoring clinical studies in children that will produce improvement in pediatric therapeutics

