

Paula Botstein M.D.
Botstein Associates
544 Fourth Street
Brooklyn, NY 11215

Phone 718-499-9729
718-832-0992
Fax 718-832-1473
pbotstein@hotmail.com

718 499 9729
July 5, 2002

Docket No. 02N-0152
21 CFR Parts 201, 312, 314, and 601
ANPR

Obtaining timely pediatric studies of and adequate labeling for human drugs and biologics

Dockets Management Branch (HFA 305)
Food and Drug Administration
5630 Fishers Lane
Room 1061
Rockville, MD 20852

~~Submitted electronically to <fda.gov/dockets/ecomments>~~

Dear FDA people:

FDA's 1998 pediatric rule is a strong mechanism for ensuring that medicines are studied for children. This rule provides the long-term solution to drugs' not having adequate instructions for use in children. This pediatric rule should not be weakened nor its scope reduced.

The pediatric rule calls for medicines to be studied in children. Children get sick and need medicines, just as adults do. Although most disorders and diseases of children respond to the same medicines effective in adults, doses appropriate for children can only be determined through pediatric studies. Inappropriate dosing leads to lack of effectiveness or to toxicity. Figuring out suitable doses for the pediatric population may be simple or difficult, depending on the drug, but cannot be adequately done by an individual doctor using guesswork when faced with a sick patient. Clinical trials, which may consist of pharmacokinetic studies, are the answer. In addition, safety problems need to be evaluated or basic studies of the effectiveness of some uses of drugs need to be conducted for some drugs in children.

The pediatric rule and the Best Pharmaceuticals for Children Act (BPCA) are complementary and are both needed. This rule should not be changed because of the subsequent passage of the 2002 BPCA. Congress passed the BPCA in 2002 while leaving unaffected the 1998 FDA regulations known as the pediatric rule. Congress did not intend that FDA weaken the pediatric rule.

Benefits of the pediatric rule

A major benefit of the rule is that it kicks in early during a drug's development. The pediatric rule positions discussion and planning for studying a drug in children into early drug development by requiring that a sponsor's plans for pediatric study be discussed at routine drug development meetings with the FDA. Consideration of pediatric data and needs thus has become an intrinsic part of drug development.

The pediatric rule is obligatory on the part of manufacturers, although FDA can waive or delay its provisions when scientifically appropriate for a particular drug.

02N-0152

C 91

Under the pediatric rule, FDA may require a manufacturer to develop a pediatric formulation; this provision means that formulations usable in children, such as liquids for toddlers, will thus be available. This provision of the regulation is essential.

Results from the rule occur when a drug is approved or soon thereafter: around the time a drug is available for use by pediatric patients and labeling for sensible pediatric use is wanted.

Provisions of the pediatric rule applying to already-marketed drugs will be important particularly in those rare cases where pediatric use of an inadequately labeled drug presents potential or demonstrated serious problems of safety or inadequate effectiveness.

Limitations of the BPCA

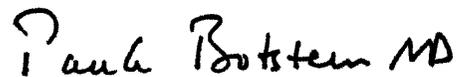
The BPCA and its precursor FDAMA create a financial incentive, a period of additional marketing exclusivity in return for a manufacturer's obtaining pediatric data. This financial incentive is valuable and has resulted in pediatric studies by those companies wishing to avail themselves of the opportunity. However, the BPCA is voluntary and sponsors will not use it for many drugs, as was the case with the FDAMA. The BPCA will preferentially be used for drugs with enormous profits from adult use. These drugs may not include those most needed for use in children.

Manufacturers may wait to obtain the marketing exclusivity offered by the BPCA until near the end of a drug's existing marketing exclusivity; as a result, a sponsor may delay pediatric studies until the drug has been marketed and used in children without labeling information for fifteen years or more.

Support for pediatric rule

I had a hand in the creation of the pediatric rule and in the implementation of FDAMA, while I worked in FDA's Center for Drug Evaluation and Research. The proposed pediatric rule generated unusually widespread and enthusiastic comment from many medical groups, patient groups, and others. In addition, many people outside the FDA or outside of CDER and CBER at the FDA expressed surprise that medicines were not already routinely assessed in children. Parents, aunts, uncles, grandparents and those who for other reasons care about the welfare of children viewed requiring pediatric studies of drugs as a real contribution to the health of children.

FDA should now fully implement and support its pediatric rule: the rule offers the long-term promise of drugs adequately labeled for use in millions of children.

A handwritten signature in black ink that reads "Paula Botstein MD". The signature is written in a cursive, slightly slanted style.

Paula Botstein M.D.

Paula Botstein M.D.
Botstein Associates
544 Fourth Street
Brooklyn, NY 11215

Phone 718-499-9729
718-832-0992
Fax 718-832-1473
pbotstein@hotmail.com

July 5, 2002

Docket No. 02N-0152
21 CFR Parts 201, 312, 314, and 601
ANPR

Obtaining timely pediatric studies of and adequate labeling for human drugs and biologics

Dockets Management Branch (HFA 305)
Food and Drug Administration
5630 Fishers Lane
Room 1061
Rockville, MD 20852

I submitted comments electronically
to the doc. management website but
the formatting got messed up.
Here is the correct document.

Paula Botstein MD

FedEx USA Airbill
Express

8290 3231 5052

0215

Form
10 No

SPR32

FedEx Copy

1 From

Date 7/5/02 Sender's FedEx Account Number 2355-6941-8

Sender's Name P. Botstein Phone 718 499-9729

Company BOTSTEIN ASSOCIATES

Address 544 4TH ST

City BROOKLYN State NY ZIP 11215

2 Your Internal Billing Reference

3 To

Recipient's Name Dochets Management Board Phone 301 827-428

Company HFA 305, FDA

Address 5630 Fishers Lane, Room 1061

To "HOLD" at FedEx location, print FedEx address. We cannot deliver to P.O. boxes or P.O. ZIP codes.

City Rockville State MD ZIP 20852



0184036945

4a Express Package Service

- 1 FedEx Priority Overnight Next business morning
- 5 FedEx Standard Overnight Next business afternoon
- 6 FedEx First Overnight Earliest next business morning delivery to select locations
- 3 FedEx 2Day Second business day FedEx Envelope rate not available Minimum charge One-pound rate
- 20 FedEx Express Saver Third business day
- 77 NEW FedEx Extra Hours Later drop-off with next business afternoon delivery to select locations

Packages up to 150 lbs.
Delivery commitment may be later in some areas.

4b Express Freight Service

- 7 FedEx 1Day Freight* Next business day
- 8 FedEx 2Day Freight Second business day
- 83 FedEx 3Day Freight Third business day

Packages over 150 lbs.
Delivery commitment may be later in some areas.

* Call for Confirmation

5 Packaging

- 6 FedEx Envelope*
- 2 FedEx Pak* Includes FedEx Small Pak, FedEx Large Pak and FedEx Sturdy Pak
- 1 Other Pkg Includes FedEx Box, FedEx Tube, and custom pkg

* Declared value limit \$500

6 Special Handling

- 3 SATURDAY Delivery Available only for FedEx Priority Overnight and FedEx 2Day to select ZIP codes
- 33 SUNDAY Delivery Available only for FedEx Priority Overnight to select ZIP codes
- 1 HOLD Weekday at FedEx Location Not available with FedEx First Overnight
- 31 HOLD Saturday at FedEx Location Available only for FedEx Priority Overnight and FedEx 2Day to select locations

Include FedEx address in Section 3.

Does this shipment contain dangerous goods? One box must be checked.

- No Yes As per attached Shipper's Declaration
- 6 Dry Ice Dry Ice, 9, UN 1845 x kg Cargo Aircraft Only

Dangerous Goods (incl. Dry Ice) cannot be shipped in FedEx packaging or with FedEx Extra Hours service.

7 Payment Bill to:

- 1 Sender Acct. No. in Section 1 will be billed
- 2 Recipient
- 3 Third Party
- 4 Credit Card
- 5 Cash/Check
- Enter FedEx Acct. No. or Credit Card No. below. Obtain Recp. Acct. No.

FedEx Acct. No.
Credit Card No.Exp.
Date

Total Packages	Total Weight	Total Declared Value*	Total Charges
1		\$.00	
			Credit Card Auth

*Our liability is limited to \$100 unless you declare a higher value. See the FedEx Service Guide for details.

8 Release Signature

Sign to authorize delivery without obtaining signature.

By signing you authorize us to deliver this shipment without obtaining a signature and agree to indemnify and hold us harmless from any resulting claims

406