

## ATTACHMENT 1

**Agency Name: Food and Drug Administration**

**Docket Number: 2006N-0062**

**Regulatory Information Number (RIN): RIN 0910-AF14**

### **1. PARTITIONING OF THE REGULATIONS TO IMPROVE READABILITY**

Partitioning of the regulation as follows is recommended to improve readability:

- Entity (Company-Sponsored) and Investigator-Sponsored expanded access.
- Differentiation of requirements for New Molecular Entities and for approved products being studied in new indications.

### **2. APPLICABILITY**

#### **2.1 General Comment**

- It is not clear if this expanded access regulations apply to both unapproved drugs and approved drugs under investigation in new indications.
- Is this regulation applicable to instances where the drug is approved and marketed for one or more indications but is being studied in clinical trials for the purpose of licensing in a new indication that is “serious or immediately life threatening”?

#### **2.2 Individual Patients, Including in Emergencies**

FDA may request the company engage in a treatment IND protocol if 10 or more patients, within a relatively short time, have been included under Emergency Use INDs. Although the company may have agreed to these “individual uses” of the drug, further expanding and publicizing this use through expanded access may create supply and resource constraints that may impact ongoing clinical trials. This is true especially for early stage and/or orphan drugs. There is a concern that this uncontrolled use of the drug by investigators inexperienced in the use of investigational drugs could adversely affect the drug’s development, slowing down time to approval and/or result in unfavorable patient outcomes.

#### **2.3 Intermediate-sized Patient Populations**

The same comment applies in this case and critical drug shortages may occur.

#### **2.4 Larger Populations, Treatment IND = No Change**

The evidence for allowing a large-scale treatment IND is such that the drug supply issue identified in 1 and 2 above is less likely. These treatment INDs appear to be better defined in scope than the proposed alternatives. Treatment INDs also occur at a time in

## ATTACHMENT 1

**Agency Name: Food and Drug Administration**

**Docket Number: 2006N-0062**

**Regulatory Information Number (RIN): RIN 0910-AF14**

development when approval is predictable. Have there been any drugs approved for a treatment IND that did not subsequently receive approval?

### **3. ADVERSE EVENT REPORTING UNDER EXPANDED ACCESS**

- In instances of an approved drug being studied in a new indication, adverse event reporting should be limited to serious and unexpected adverse events as defined in ICH Guideline (E2A) – Clinical Safety Data Management: Definitions and Standards for Expedited Reporting.
- For New Molecular Entities adverse event reporting should be limited to serious adverse events and deaths unless there are specific adverse events related to an identified safety concern that may impact risk benefit assessment.

### **4. REIMBURSEMENT**

The proposed regulation states, “Sponsors are strongly encouraged to include individual expanded access protocols under their own INDs.” In what situations will FDA allow investigators to sponsor the individual patient access protocols?

### **5. COSTS OF THE PROPOSED RULE**

Baxter believes that FDA has significantly underestimated the costs associated with company-sponsored expanded access INDs or protocols which may involve more time and resources on the part of the company in terms of management, of providing product, data collection, monitoring, verification, and summarization that will meet FDA’s desire to improve information collected under expanded access.

### **6. WHAT DOES “CONDUCT A CLINICAL TRIAL OF THE EXPANDED ACCESS USE” MEAN?**

“FDA will consider whether to request that a potential sponsor submit an intermediate-size patient population IND or protocol for the expanded access use and, possibly conduct a clinical trial of the expanded access use.”

### **7. EMERGENCY USE INDS**

Given Baxter’s recent experience with Emergency Use INDs the “agreement to submit an expanded access submission within 5 working days of the FDA’s authorization of the expanded use” is unrealistic. Baxter could not agree or commit to this short time period

## ATTACHMENT 1

**Agency Name: Food and Drug Administration**

**Docket Number: 2006N-0062**

**Regulatory Information Number (RIN): RIN 0910-AF14**

knowing the difficulties we have had collecting the required information from investigators under Emergency Use INDs (30 days was the average to obtain this information with repeated follow up).

### **8. HOW DOES FDA DEFINE “MONITORING” IN THESE INSTANCES?**

The proposed regulation states, “The sponsor is responsible for monitoring the expanded use protocol to ensure that licensed physicians comply with the protocol and the regulations applicable to investigators 312.315(d)(2)”. How does FDA define “monitoring” in these instances?