

## **SAFEKIDS Initiative**

### **Frequently Asked Questions (FAQ)**

#### **What is the SAFEKIDS Initiative?**

The SAFEKIDS Initiative is a multi-year project aimed at making anesthesia safer for the millions of infants and young children who undergo anesthesia each year.

#### **Why was the SAFEKIDS Initiative launched?**

Early medical research suggests that some anesthetic drugs may be safer than others when used with infants and children younger than four years old. The health risks appear to be greater when children require repeated surgeries. The SAFEKIDS Initiative was launched to study existing anesthetic drugs and how they are used with children, including the dosage amounts and number of exposures. Information from these research studies will help determine if there are hazards to children. It will also help to improve the anesthetics currently in use or under development and develop new anesthetic drugs.

#### **Who is involved in the SAFEKIDS Initiative?**

The U.S. Food and Drug Administration (FDA) is concerned about the potential risks to public health identified by the early research studies. The FDA is partnering with many non-government organizations to learn more about the anesthetics and sedatives received by children each year. The FDA wants to make these drugs safer for children everywhere. The International Anesthesia Research Society is managing the SAFEKIDS Initiative and leading the fundraising to support the complex, multi-year research needed to make anesthetic drugs as safe as possible for children. Many medical societies, patient support groups, pharmaceutical companies, and other organizations will also be involved.

#### **How did the FDA become concerned about the safety of anesthetic drugs for infants and young children?**

The FDA's National Center for Toxicological Research (NCTR) has conducted research about the effects of anesthetics on the nervous systems of developing animals. This research has shown that exposure to some anesthetics and sedatives may cause memory and learning difficulties and other harmful changes in the central nervous systems of laboratory animals. There is not enough data to prove or disprove whether similar effects could occur in children.

#### **What is the National Center for Toxicological Research?**

The National Center for Toxicological Research is the FDA's internationally recognized research center. The NCTR conducts research to develop a scientific basis for the FDA's regulatory decisions, and to reduce risks associated with products regulated by the FDA. NCTR research evaluates the effects of potentially dangerous chemicals and identifies

what about those chemicals makes them dangerous. NCTR research also helps to assess risks to human health, which supports the FDA's goal of improving patient and consumer safety.

### **What did the animal studies show?**

In humans, the formation of brain structures and rapid brain growth starts during the third trimester of pregnancy and continues for up to three years.<sup>1</sup> In rats and mice, the comparable period of brain development is the first two weeks of life.<sup>2</sup> In the research studies, all of the anesthetics and sedatives commonly used in infants and children caused widespread loss of nerve cells and/or later abnormal behavior when administered during rapid brain growth in rodents.<sup>34567</sup> At this time, very limited data are available from studies of higher-level mammals, such as apes and monkeys. One study showed harmful effects to the nervous system in newborn monkeys given a commonly-used anesthetic.<sup>8</sup>

### **What are the known risks or concerns for humans?**

There are no studies that show anesthetic drugs cause harmful effects to the nervous systems of children. One study describes learning disabilities after multiple anesthetics administered in infants and children prior to four years of age, but not from a single anesthetic.<sup>9</sup> In that study, the researchers found that two exposures to anesthetics before age four increased the likelihood of future learning disabilities in reading, writing, and math by 50%. Three or more exposures created even greater risk for learning problems. Exposure times under two hours did not appear to be linked to learning difficulties.

### **Is it harmful for infants and young children to undergo anesthesia?**

The early research in animals has raised concerns about some anesthetic drugs that need to be investigated further to determine if they pose a hazard to infants and children younger than four years of age. However, dangers to infants and children from anesthesia are unproven at this point. There is no direct evidence that anesthetics are unsafe for children.

### **Should surgery requiring anesthesia for infants and young children be postponed?**

Children do not undergo surgery requiring anesthesia unless the surgery is essential to their health. If a child needs surgery, postponing that surgery until the child is older than four years of age would likely create far more risk than proceeding with anesthesia and surgery as soon as necessary. Currently, there is no scientific basis for delaying essential surgery. Parents of children requiring surgery should consult an anesthesiologist or other qualified physician for advice about an individual child's situation.

### **What additional research is being done?**

There are several research studies currently underway under the SAFEKIDS Initiative.

- Children’s Hospital, Harvard University (Boston, MA), is conducting a long-term study of neurodevelopment outcomes in pediatric patients administered regional or general anesthesia as neonates or infants.
- Arkansas Children’s Hospital Research Institute (Little Rock, AR) is researching the pharmacokinetics, pharmacodynamics, and neurotoxic effects of an anesthetic agent in infants undergoing various surgical procedures.
- Columbia University (New York, NY) is evaluating the effects of anesthetic exposure on neurocognitive, emotional and behavioral outcomes in pediatric patients.
- Mayo Clinic (Rochester, MN) is studying long-term cognitive development following exposure to general anesthetic agents during infancy.
- The NCTR is conducting non-clinical studies in non-human primates to assess the decline in mental function when young animals are exposed to anesthesia.
- The NCTR is researching the development of noninvasive ways of using imaging to measure structural changes in the human brain.

Other studies will be launched when the findings from these first studies are known and as funds to pay for additional research become available.

**Where and when will the results from these studies be published?**

Information from the research conducted under the SAFEKIDS Initiative will be published on the SAFEKIDS website at [www.iars.org/safekids](http://www.iars.org/safekids) and in other publications as soon as it becomes available. Press releases will be issued when research findings are published.

**How can I obtain more information?**

A reference list for medical professionals is included below. Current information about the SAFEKIDS Initiative can be found at [www.iars.org/safekids](http://www.iars.org/safekids). Parents of children requiring surgery or children who have undergone surgery should consult an anesthesiologist or other qualified physician.

**FAQ References**

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<sup>2</sup> Dobbing J, Sands J: Comparative aspects of the brain growth spurt. *Early Hum Dev* 1979; 3: 79-83

<sup>3</sup> Campagna JA, Miller KW, Forman SA: Mechanisms of actions of inhaled anesthetics. *N Engl J Med* 2003; 348: 2110-24

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- <sup>5</sup> Jevtovic-Todorovic V, Hartman RE, Izumi Y, Benshoff ND, Dikranian K, Zorumski CF, Olney JW, Wozniak DF: Early exposure to common anesthetic agents causes widespread neurodegeneration in the developing rat brain and persistent learning deficits. *J Neurosci* 2003; 23: 876-82
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- <sup>9</sup> Wilder RT, Flick RP, Sprung J, Katusic SK, Barbaresi WJ, Mickelson C, Gleich SJ, Schroeder DR, Weaver AL, Warner DO: Early exposure to anesthesia and learning disabilities in a population-based birth cohort. *Anesthesiology* 2009; 110: 796-804c

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3. Blaschke AJ, Weiner JA, Chun J: Programmed cell death is a universal feature of embryonic and postnatal neuroproliferative regions throughout the central nervous system. *J Comp Neurol* 1998; 396: 39-50