

# Childhood drug studies show room for improvement

Report finds recent laws have enhanced US child medicine, but some drugs are still used without rigorous testing.

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Drug regulators need more authority to compel pharmaceutical companies to conduct timely, rigorous tests of medications in children, says a committee that examined US laws designed to boost the safety and efficacy of childhood treatments.

The US Institute of Medicine (IOM) convened the [committee](#) at the request of the US Food and Drug Administration (FDA) to look at two laws that are up for review this year by the US Congress. The committee, which issued its report today, concluded that these laws are spurring progress in childhood medicine, but that Congress could make them work better by making several changes to how studies are conducted in children, such as requiring clearer ethical justification, boosting their quality, encouraging more long-term studies and requesting more trials in newborn babies.

“These have been very worthwhile programmes that should be continued, but the next iteration of legislation ought to push for further improvement,” says Thomas Boat, vice-president for health affairs at the University of Cincinnati, Ohio, who chaired the IOM committee.

The committee found that since July 1998, paediatric studies required under two laws — the Best Pharmaceuticals for Children Act (BPCA) and the Pediatric Research Equity Act (PREA) — have resulted in new information that has changed the way that nearly 400 drugs are used in children.

“These laws have had a tremendous impact,” says paediatrician Daniel Frattarelli, a member of the American Academy of Pediatrics and chairman of the academy's Committee on Drugs.

Before the laws were passed, drug companies were reluctant to test treatments in children because such trials are expensive and difficult to conduct, and physicians could use drugs in children legally once they were approved by regulators. As a result, in 1973, almost 80% of drugs used in children were prescribed 'off label', meaning that there was no evidence-based information about how to use the drugs safely in children.

But drugs can behave differently in children than in adults. Physicians often found this out only after a drug that had been approved for adults caused unexpected — and sometimes fatal — complications in children.

For example, in the 1950s, physicians started using the antibiotic chloramphenicol in premature babies to prevent bacterial infections. Only after chloramphenicol-treated babies began dying did physicians organize clinical trials of the drug in newborns. The trials found that whereas less than 20% of untreated babies died, more than 60% of premature infants treated with chloramphenicol died because they could not rid their bodies of it as quickly as adults and older children could.

Today, information on how to use drugs correctly in children is available for about half of the drugs used in paediatrics.

“We've probably learned as much in the past 10 to 15 years as we did in the 60 to 70 years beforehand,” Frattarelli says.

Despite this, he points out, some areas of paediatric drug testing are still not up to scratch. For instance, the [American Academy of Pediatrics estimates](#) that almost 90% of the drugs routinely used in newborns “have never been adequately studied for safety, dosing, or efficacy” in babies. The academy has recommended that the FDA recruit more reviewers who are experts in treating babies, and that it should require more studies in infants who are less than one month old.

The academy has also noted that 78% of drug studies and 54% of studies on biological products (such as vaccines) required by law



Image Source/Corbis

Drugs can behave differently in children than in adults, so improvements to paediatric clinical trials are vital to boost safety.

under PREA after 2007 were either not completed, or were finished late. To prevent such delays, the IOM committee recommended that Congress should consider giving the FDA the power to punish drug companies who don't complete paediatric studies on time, and should ask firms to submit their plans for such trials earlier in the drug development process.

“Someone should be saying, 'yes, that's a legitimate reason for delay', or 'no, that's not gonna fly',” Frattarelli says.

The IOM committee also said that Congress could consider extending the authorization period for the paediatric drug laws, which are reviewed every five years. But Frattarelli points out that regular reviews have allowed Congress to continue to strengthen the laws. For instance, a review in 2007 led Congress to compel the FDA to release information to the public about studies done in children.

“We always find little tweaks that make the law work better, so I think it's a good idea to have a review period every so often,” Frattarelli says.

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