In a major move, the European Medicines Agency (EMA) announced today it is revoking or revising most product class waivers that allow companies to bypass the requirement to test new drugs in pediatric populations before they can be authorized.

**Background**

Companies are often reluctant to conduct clinical studies in children over ethical concerns and fear of adverse events occurring during trials. These reservations have...
created a gap in the number of products authorized with specific indications and doses for children

While there are clear ethical issues and risks in conducting clinical research on children, such testing is critically important in determining whether drugs are safe and effective in pediatric populations at a given dosage.

For more on the ethical issues related to clinical study in children, see Focus feature article "The Ethics of Regulatory Mandates for Pediatric Research"

When a drug lacks specific dosage information for children, doctors are left to guess at what an appropriate amount might be. This ultimately leads to children taking unsubstantiated dosages of drugs, or dosages based on anecdotal evidence, sometimes with potentially dangerous or life-threatening consequences.

**Paediatric Regulations**

To ensure medicines are adequately tested in pediatric populations, the *Paediatric Regulations*, which entered into force in 2007, require companies to complete a paediatric investigation plan (PIP), unless they meet the criteria for one of three waivers described in Article 11 of *Regulation (EC) No 1901/2006*:

1. "Production of the information referred to in point (a) of Article 7(1) shall be waived for specific medicinal products or for classes of medicinal products, if there is evidence showing any of the following:
   a. that the specific medicinal product or class of medicinal products is likely to be ineffective or unsafe in part or all of the paediatric population;
   b. that the disease or condition for which the specific medicinal product or class is intended occurs only in adult populations;
   c. that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments for paediatric patients.

2. The waiver provided for in paragraph 1 may be issued with reference either to one or more specified subsets of the paediatric population, or to one or more specified therapeutic indications, or to a combination of both."
The logic behind offering these waivers is fairly straightforward: Some diseases don't affect children and some classes of product are likely to be unsafe or ineffective in children, so it would be unethical to study them in those populations.

However, despite the new regulatory requirements, some critics have said the number of clinical studies involving children remains low, and have called for reforms to the waiver system.

Waiver Reform

Since 2007, EMA's Paediatric Committee (PDCO) has periodically reviewed the list of waivers, and revoked two class waivers in 2008 and 2009.

This makes today's announcement by far the most sweeping revision to the pediatric waiver system to date. In total, EMA is revoking eight class waivers and revising 15 others, leaving only nine classes unaffected.

The eight revoked class waivers include drugs intended to treat several cancers, Parkinson's and Huntington's among others.

During a press conference this morning, PDCO vice chair Dr. Koenraad Norga and Dr. Jordi Llinares, head of product development scientific support at EMA, said that revising the class waiver list would "stimulat[e] research into the use of medicines in children and increase[e] medicines authorised for use in children."

Since the Paediatric Regulations entered into force, EMA says it has approved nearly 800 PIPs. Now, "companies developing medicines that are no longer subject to a class waiver … will need to have a PIP" or request a product-specific waiver.

When asked how the revised list would stimulate development for new medicines in children, Llinares answered, "It is extremely clear, if we are revoking or revising waivers, we are telling the sponsors they have to" develop their products for children.