Abstract. It is generally agreed that satisfactory safety and effectiveness of pharmaceutical products for children and adolescents have not yet been established. This applies in particular to anti-cancer drugs and even to those having successfully been used for many years in multidrug chemotherapy protocols for childhood cancer. For example, nephroblastoma or Wilms’ tumor is one of the typical and frequent forms of childhood cancer occurring at a median age of about 3 years. Standard therapy for Wilms’ tumor is the combination of vincristine and actinomycin D; survival is about 85%. For actinomycin D, the summary of product characteristics states that one contraindication is children aged below 6–12 months. If this would be considered and respected it would mean that a substantial proportion of children with Wilms’ tumor would not be treated and thus a proven curative therapy would be withheld. The current situation in pediatrics is that off-label use has become a common practice: in private practice about 20% of prescriptions are off-label, in children’s hospitals approximately 40%–50% with 50%–70% in pediatric oncology and more than
90% in neonatology (Conroy et al. 1999, 2000, 2003; Turner et al. 1996, 1998; McIntyre et al. 2000). These conditions are more or less tolerated by the authorities although they are beyond legality. The reason is that appropriate clinical trials like those in adults have not been conducted in children and drugs have therefore not been licensed.

8.1 Peculiarities of Childhood and Adolescence

Childhood and adolescence are characterized by different phases of maturation and differentiation of organs, the immune system, and the central nervous system (Brochhausen and Seyberth 2000). The most immature individuals are preterms with their specific problems such as surfactant deficiency, persistent fetal circulation, immaturity of the brainstem, lack of autoregulation of circulation, and incomplete vascularization of the retina, which result in problems of pulmonary adaptation, pulmonary hypertension, persistent ductus arteriosus, bronchopulmonary dysplasia, and retinopathy of prematurity. Newborns have a large body surface area and a high content of body water and fat. In infants, the immune system is still incompetent, the myelinization of nerves incomplete, and the maturation of metabolic processes still in progress. School children have a lower growth rate and are becoming increasingly independent. Finally, in adolescents puberty starts with again a higher growth rate, and emotional instability is common.

Hence, children are not simply small adults, and for pharmacology and drug dosing this means that drug doses cannot merely be converted from adults according to body weight or body surface area.

8.2 Reasons for the Lack of Clinical Trials in Children

Children, and in particular research in children, are quite strictly protected by law. Thus, the general conditions for clinical trials are much more complicated than in adults because the legal conditions frequently hamper pharmaceutical studies, in particular those that have no direct implications for the individual child. Frequently, ethical reasons do not allow clinical and/or pharmaceutical studies in children, and there are ethics committees that require the consent of the patient and not just the