Children differ from adults in many aspects of pharmacotherapy, including capabilities for drug administration, medicine-related toxicity, and taste preferences. It is essential that pediatric medicines are formulated to best suit a child’s age, size, physiologic condition, and treatment requirements. To ensure adequate treatment of all children, different routes of administration, dosage forms, and strengths may be required. Many existing formulations are not suitable for children, which often leads to off-label and unlicensed use of adult medicines. New regulations, additional funding opportunities, and innovative collaborative research initiatives have resulted in some recent progress in the development of pediatric formulations. These advances include a paradigm shift toward oral solid formulations and a focus on novel preparations, including flexible, dispersible, and multiparticulate oral solid dosage forms. Such developments have enabled greater dose flexibility, easier administration, and better acceptance of drug formulations in children. However, new pediatric formulations address only a small part of all therapeutic needs in children; moreover, they are not always available. Five key issues need to be addressed to stimulate the further development of better medicines for children: (1) the continued prioritization of unmet formulation needs, particularly drug delivery in neonates and treatment gaps in pediatric cancers and childhood diseases in developing countries; (2) a better use of existing data to facilitate pediatric formulation development; (3) innovative technologies in adults that can be used to develop new pediatric formulations; (4) clinical feedback and practice-based evidence on the impact of novel formulations; and (5) improved access to new pediatric formulations.
Drug formulations used in pediatric pharmacotherapy should be adapted to children’s needs to suit their age, size, physiologic condition, and treatment requirements. Such pediatric medicines are key to achieving safe and accurate dose administration, reducing the risk of medication errors, enhancing medication adherence, and improving therapeutic outcomes in children.

The use of inadequate drug formulations in children may pose problems not seen in adults, such as difficulty in swallowing conventionally sized tablets, safety issues with certain excipients that are acceptable in adult formulations, and adherence problems with unpalatable medicines. These issues have led to tragedies in the past, and they exist partly because only a small fraction of all marketed drugs are available in formulations that are age appropriate. As a result, many adult medicines are used off-label in children, a practice that carries additional health and environmental risks.

To strengthen the development of pediatric drug formulations, new legislation was introduced in the United States and Europe, and efforts for global collaboration were made by the World Health Organization (WHO). A number of innovative pediatric formulations have followed, but their actual effect on pediatric drug approvals remains to be seen, as clinical trials and marketing authorization take a substantial amount of time.

To optimize pharmacotherapy in children, it is important for clinicians to understand the background of the aforementioned problems as well as to gain insight into the challenges, developments, and potential solutions. The aim of the present review was to describe why there is a specific need for pediatric drug formulations and to illustrate the clinical consequences of the absence of suitable medicines for children. We will discuss the progress achieved so far and determine additional steps required to improve the development and availability of pediatric drug formulations.

THE NECESSITY OF PEDIATRIC DRUG FORMULATIONS

Diversity in Children

It has been well established that children are not small adults but rather a distinct and heterogeneous patient group with regard to pharmacotherapy. They often exhibit a different response to both active substance and excipients. Children present a continuum of growth and developmental phases as a result of their rapid growth, maturation of the body composition, and physiologic and cognitive changes during childhood.

Children differ from adults in many aspects of pharmacokinetics and pharmacodynamics, potential routes of administration, medicine-related toxicity, and taste preferences. Important pharmacokinetic differences between children and adults include the rate of gastric emptying and pH, gastrointestinal permeability, and the surface area available for drug absorption. Dissimilarities have also been reported in drug metabolism, transporter expression, biliary function, and renal clearance, resulting in differences in drug disposition and elimination. The largest deviation from adult pharmacokinetics is observed in the first 12 to 18 months, when organ functions are developing. In older children and adolescents, the pharmacokinetic parameters approach adult values and are thus easier to predict.

The effect of age on pharmacokinetics leads to different dosing requirements for different age groups. From birth to adulthood, the body size and weight of an average child increases up to 20-fold, and the magnitude of dose variation administered throughout childhood may be 100-fold. More dramatically, premature neonates admitted to the hospital can weigh as little as 500 g, further highlighting the need for dose variability. Maturation processes in children are not linear, and therefore doses in certain age subsets may be lower, identical to, or higher than in adults, depending on a drug’s metabolic pathway.

Due to this extensive variability in children, there is an obvious need for drug formulations tailored to children in all the target age groups. The International Conference of Harmonisation divides childhood into 5 age groups related to the developmental stages, derived from the physiologic and pharmacokinetic differences mentioned earlier. These groups (with age ranges) are: preterm newborn infants; term newborn infants (0–27 days); infants and toddlers (1–23 months); children (2–11 years); and adolescents (12–18 years in the United States or 12–18 years in the European Union).

The European Committee for Medicinal Products for Human Use further divides the age group “children” into “preschool children” (2–5 years), and “school children” (6–11 years) to more precisely reflect the children’s ability to accept and use different dosage forms. However, the classification of the pediatric population into age categories is to some extent arbitrary because children of the same chronologic age may still develop at different rates.

Age-Related Adherence to Pediatric Drug Formulations

Formulation acceptability and preferences facilitate medication adherence in children, and they are important factors in achieving the intended treatment outcomes. Formulation acceptability differs across age groups as children gradually develop their cognitive and
motor skills, and improve their ability to swallow medications. At certain ages, the dependence on caregivers also plays a role in the administration of pediatric dosage forms.1 Pain, discomfort, and an unnecessary burden on children and/or caregivers during drug administration should be minimized to assure adequate medication adherence. In older children and adolescents, lifestyle and peer pressure may also influence medication adherence and possible preferences for particular formulations. Taste attributes may be critical to ensure acceptable adherence to pediatric oral formulations. Because children have a low tolerance for disagreeable taste, the use of tasteless or palatable medicines can minimize the loss of medication from spillage and/or spitting.14,37,38 Taste preferences may differ between children and adults, as children prefer sweet and salty flavors, and dislike bitter and peppermint taste. These findings suggest that taste assessment should involve children early in the drug formulation development.35,38,39 Children’s communication about taste perceptions can be facilitated by using age-appropriate methods, scales, and measures.40 Alternative taste-screening methods may include adult taste panels with validated design for data transferability or predictive electrochemical sensor systems (so called “electronic tongues”).41,42

CLINICAL CONSEQUENCES OF THE ABSENCE OF SUITABLE PEDIATRIC DRUG FORMULATIONS

Potential Limitations of Pediatric Drug Formulations

Historically, the failure to appreciate the developmental changes in children has led to many adverse outcomes in clinical practice. Examples include infant deaths from choking on albendazole tablets, the lethal use of benzyl alcohol or diethylene glycol in sulfanilamide elixirs, and electrolyte imbalances caused by high contents of sodium or potassium in parenteral formulations.6–9 To prevent such tragedies and ensure adequate treatment of children of all ages, different routes of administration, dosage forms, and strengths are often needed for the same active substance.1 Table 1 illustrates the specific purposes, potential strengths, and weaknesses of various routes of administration and dosage forms for pediatric use.1,2,5,43–47 As in adults, the oral route is the predominant route of administration in children.1,12,44 Alternative nonoral routes of administration include rectal, dermal, nasal, pulmonary, and ocular routes.1,2 The selection for clinical use is influenced by the limitations of each dosage form. Oral solids are associated with the risk of choking or chewing and with limited dose flexibility, whereas palatability and dose uniformity may be challenging for liquid preparations.1,2,43,44 In addition, liquid forms raise issues regarding stability (chemical, physical, or microbiological) and the requirement for clean water; moreover, they can be bulky, impractical, and expensive to ship and store, particularly in lower income countries with hot and humid climates.48,49

The use of nonoral routes of drug administration may be hampered by difficult application, local irritation, fluid overload, electrolyte imbalance, or poor drug acceptability (Table 1).1,2,5,43–47 In neonates, intravenous administration may lead to volume overload. Moreover, measuring small dose volumes may cause large dosage variations and errors.47 Similarly, age-appropriate dosing volumes are important to ensure full dose ingestion for oral liquids.5

Another important concern in pediatric drug formulations are the excipients, frequently used as preservatives, sweeteners, fillers, solvents, and coating and coloring agents. Their selection for pediatric medicines is challenging because neither the inactive ingredients guide list of the US Food and Drug Administration nor the “generally regarded as safe” status has been validated for pediatric use.3,29,30,50 Little is known about the safety of excipients in children, and accepted daily and cumulative intakes of excipients have not been established. Anecdotal evidence suggests an association between some excipients commonly used in adult medicines and elevated toxicity and safety issues in children, especially neonates (Table 2).5,6–9,26,50–52 A recent example is the administration of lopinavir/ritonavir (Kaletra [Abbott Laboratories, Abbott Park, IL]) oral solution in premature newborns who were exposed to the risk of ethanol and/or propylene glycol toxicity. This situation resulted in a Food and Drug Administration drug safety communication and a change in the drug label in 2011.61 A number of recent studies in NICUs revealed systemic concentra-tions of excipients that were intolerable even in older age groups.54,62,63

The urgent need to understand these safety concerns has led to a collaborative effort by the United States and the European Union to create a STEP (Safety and Toxicity of Excipients for Pediatrics) database. Its aim is to improve systematic data collection on excipient toxicity and tolerance in children,64–66 A similar initiative, ESNEE (European Study of Neonatal Exposure to Excipients), has developed a platform for the systematic assessment of excipients in neonates.67

Concerns Over Off-label and Unlicensed Use of Medicines in Children

Pediatric drug development is associated with numerous challenges, including methodologic and ethical requirements for pediatric trials, high developmental costs, and a small and fragmented market.3,4,50,68–71 As a result of these challenges, there have only been limited research efforts to adapt medicines according to pediatric needs. Thus, only
<table>
<thead>
<tr>
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<tr>
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<td>First-pass effect</td>
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<td>Acceptability from term birth</td>
<td>Instability of multidose preparations</td>
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<td>• Suspensions</td>
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<td>Age-appropriate dosing volume for full-dose ingestion (&lt;5 mL in younger and &lt;10 mL in older age groups)</td>
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<tr>
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</tr>
<tr>
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<td>Ease of administration</td>
<td>Risks of administration without prior dispersion/dissolution</td>
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<tr>
<td>• Powders, granules, sprinkles, multiparticulates, mini-tablets</td>
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<td>Ability to swallow intact dosage forms</td>
</tr>
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<td>Size considerations</td>
</tr>
<tr>
<td>• Suppositories</td>
<td></td>
<td>Limited bioavailability (minor absorption area, lack of active drug transporters, small fluid volume for dissolution)</td>
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<tr>
<td>• Rectal liquids</td>
<td></td>
<td>Frequent stooling in breast-fed infants, uncontrolled defecation in infants</td>
</tr>
<tr>
<td><strong>Topical, transdermal</strong>&lt;sup&gt;1,2,5&lt;/sup&gt;</td>
<td>Provision of constant blood levels</td>
<td>Unintended systemic absorption/toxicity risk in neonates (large skin surface area, thickness, hydration, perfusion)</td>
</tr>
<tr>
<td>• Transdermal patches</td>
<td>Painless and easy administration of bolus</td>
<td>Natural barrier for penetration of many drugs</td>
</tr>
<tr>
<td>• Medicated plasters</td>
<td>Sustained drug delivery</td>
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<td>• Ointments/creams/gels/liquids</td>
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<td>Good nasal transmucosal bioavailability</td>
<td>Deliberate removal of patches/plasters</td>
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<tr>
<td>• Solutions, drops</td>
<td>Needle-free access to systemic circulation</td>
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</tr>
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<td>• Semisolid dosage forms</td>
<td>Irritation of the mucosa</td>
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<tr>
<td><strong>Pulmonary</strong>&lt;sup&gt;1,2,5&lt;/sup&gt;</td>
<td>Avoidance of hepatic first-pass metabolism</td>
<td>Increased deposition in upper/central airways (small airway diameter)</td>
</tr>
<tr>
<td>• Metered dose inhaler with spacer/facemask</td>
<td>Painless application</td>
<td>Decreased total lung deposition (reduced motor abilities/low inspiration volume)</td>
</tr>
<tr>
<td>• Nebulizers (older children)</td>
<td></td>
<td>Device use critical to improve inhaled doses</td>
</tr>
<tr>
<td>• Dry powder inhalers (older children)</td>
<td></td>
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</table>
one-third of all medicines approved by the European Medicines Agency over the period of 1995 to 2005 were licensed for use in children.\textsuperscript{11,23,72} Higher but still unsatisfactory rates were reported in New Zealand (35%), Australia (38%), and the United States (54%).\textsuperscript{23,73,74} The pediatric market has focused mostly on only a limited number of therapeutic areas, such as antiinfectives, hormones, and medicines for the respiratory and central nervous system.\textsuperscript{75} Meanwhile, there are hardly any dermal preparations and medicines specifically aimed at younger age groups for the cardiovascular system, sensory organs, and cancers.\textsuperscript{25} Moreover, especially in younger children and neonates, even authorized pediatric medicines may not always be age appropriate with respect to dosing, suitability of dosage forms, and excipients.

This lack of pediatric formulations often leaves health care professionals no alternative but to use adult medicines in an off-label or unlicensed manner. The trend is widespread: in the European Union, 45% to 60% of all medicines are given to children off-label. This trend is also true for 90% of medicines administered to neonates and infants, particularly in PICUs.\textsuperscript{26} Not surprisingly, off-label use is common for antiarrhythmics, antihypertensives, proton pump inhibitors, H\textsubscript{2}-receptor antagonists, antiasthmatic agents, and some antidepressants.\textsuperscript{27} In the United States, two-thirds of medicines used in pediatrics are off-label, worldwide, this proportion is up to three-quarters.\textsuperscript{77}

### Risk Management of Compounding and Manipulation of Medicines for Children

Alternative treatment options are often used to make unavailable drugs accessible for children and/or to adjust drug doses according to individual patient needs. These options include the modification of administration routes (eg, oral use of parenteral formulations); manipulation of adult dosage forms (eg, diluting liquid formulations); segmenting tablets and suppositories, cutting patches, and dispersing open capsules or crushed tablets in water, liquid, or food; or extemporaneous dispensing (ie, compounding medicines from ingredients within pharmacies).\textsuperscript{5,78}

Administering medicines in this way is difficult and unsafe because limited data are available to validate stability, bioavailability, pharmacokinetics, pharmacodynamics, dosing accuracy, tolerability, and reproducibility.\textsuperscript{79–84} A documented example is the crushing of Kaletra tablets for pediatric administration, which resulted in reduced bioavailability and drug exposure in children.\textsuperscript{85} All these manipulations may compromise drug efficacy and/or safety, as well as create risks for the environment and individuals handling the dosage forms, particularly in the case of mutagen and cytotoxic compounds.\textsuperscript{79–84}

Producing a medicine by extemporaneous dispensing may be the only option for some children to receive a certain medicine in a suitable dosage form. In such situations, the risks can be reduced by applying sound quality assurance systems. Pharmacists should ensure that good manufacturing principles are implemented, adequate raw materials and formulae are used, and stability studies are validated and conducted by certified laboratories. Moreover, because practices and guidelines for extemporaneous formulations differ greatly among practitioners, there is an urgent need for a standardization of commonly applied compounding practices.\textsuperscript{78,86} Existing networks, resources, and guidelines should be stimulated to provide appropriate information on the standards of practice for extemporaneous formulations.\textsuperscript{78,84} However, the available information may not always be easily transferable to a local situation or may not be exclusively focused on children.\textsuperscript{87}

### PROGRESS IN DEVELOPING PEDIATRIC DRUG FORMULATIONS

#### New Frameworks for the Development of Pediatric Drug Formulations

To overcome the aforementioned challenges, a new pediatric regulatory environment has been created to stimulate the development and availability of age-appropriate medicines for children.\textsuperscript{16–19} The intended long-term aim is to integrate pediatric needs into overall drug development, so that each new component is systematically evaluated for its potential use in children. Initial progress has been made by combining legal requirements with incentives for companies to test, authorize, and formulate medicines for use in children. Over the past decade, the Best Pharmaceuticals for Children Act and the Pediatric Research Equity Act in the United States, and the Pediatric Regulation in the European Union, have fueled an increasing number of pediatric clinical trials and innovations in pediatric drug formulations.\textsuperscript{22,24}

Nonetheless, therapeutic areas addressed by the industry seem to be more aligned with adult drug development than with unmet public health needs in children.\textsuperscript{22,68,88,89} To guide the efforts toward significant therapeutic benefits for children, the US and European Union government...
agencies have produced priority medicines lists, highlighting areas with substantial off-label use in children and gaps in pediatric data.90,91 Simultaneously, a WHO initiative ("Make Medicines Child Size") has drawn attention to the fact that the lack of medicines most acutely affects children living in developing countries.20,92 A focus on the development of suitable dosage forms to treat diseases of high burden in childhood in low-resource settings could greatly reduce childhood morbidity and mortality.92 There have been comprehensive WHO activities to improve access to and use of safe and appropriate pediatric medicines. These activities include establishing a model list of essential medicines for children and a list of priority life-saving medicines for women and children, developing model formularies for children, updating childhood treatment recommendations, and including pediatric medicines in the prequalification process.95–97

Furthermore, the present reward system has not proved to be an adequate incentive for investment in off-patent drug research.69,89 This tendency may be linked to prescription reimbursement rules that attach little value to old medicines, even if they include new child-friendly formulations.69 To generate more interest in off-patent medicines, new public funding opportunities in academia and small- and medium-sized enterprises have been provided by both the US Eunice Kennedy Shriver National Institute of Child Health and Human Development Pediatrics Formulation Initiative and the EU’s Seventh Framework Program for Research.98–100 However, new technologies developed from these initiatives must be adopted by the industry and marketed so they can realize their full potential.

There is also increased recognition that the selection of appropriate pediatric formulations requires a risk/benefit analysis on a case-by-case basis.1,2 Taking into consideration the heterogeneity of children and specific characteristics of each dosage form (Table 1), the industry has recently proposed a composite assessment tool to guide optimal formulation choices for individual patients.44 This structured framework is based on 3 pre-determined criteria for each drug formulation: product efficacy and ease of use (eg, dose flexibility, drug acceptability, convenient handling, correct use), patient safety (eg, bioavailability of active substances, safety of excipients, medication stability, risk of medication errors) and patient access (eg, product manufacturability, affordability, development, production speed).41 The choice between alternatives is based on a quantitative scoring system for each pharmaceutical formulation option.44 This individualized approach to optimal formulations can also be replicated in clinical settings if the selection criteria include relevant aspects of patient care.

### Novel Oral Pediatric Formulations

Recent progress in pediatric drug development mostly concerns oral formulations.22,101 Until recently, liquid formulations were preferred for younger children because of their easy and simple dosing across age subgroups.5,102 In 2008, a WHO expert forum proposed a paradigm shift toward pediatric oral solids in view of stability problems and the high transportation and storage costs involved in liquid formulations.92 From then on, flexible oral solid dosage forms, such as oral dispersible tablets and/or tablets used to prepare oral liquid preparations suitable for younger children, have become the recommended pediatric dosage forms worldwide. In 2009, Coartem Dispersible (Novartis International AG, Basel, Switzerland, and Medicines for Malaria) was launched to offer flexible artemisinin-based combination therapy for children (5–35 kg) with a cure rate comparable to that of the Coartem tablet.103,104

For oral medicines requiring precise dose measurement, a new flexible platform technology was proposed to produce solid multiparticulate dosage forms (eg, mini-tablets, pellets) and dosage forms dispersible in liquids or sprinkled on food.92 This platform technology has the potential flexibility to construct fixed-dose combination products, especially for chronic diseases such as HIV or tuberculosis.105–107

Table 3 illustrates some of the quality-certified, innovative oral pediatric dosage forms brought to market, including much needed heat-stable formulations and fixed-dose combination products for low-resource settings.97,104,108–116 Current surveys reveal that novel oral solids may be used in children at an earlier age than previously anticipated.5,117,118 Initially, in 2009, Thomson et al119 demonstrated that 46% of 2-year-old children and 86% of 5-year-old children could swallow innovative 3-mm mini-tablets without choking or aspiration. The age limit was further decreased in an exploratory study which demonstrated that children aged 6 to 12 months were capable of swallowing uncoated, drug-free, 2-mm mini-tablets and accepted them better than sweet liquid formulations.120,121 For infants aged <2 years, a new promising development is the orally disintegrating mini-tablet, which combines mini-tablets and fast-dissolving dosage forms.111

A complementary research area is the development of pediatric dosing devices, which facilitate the accurate and consistent administration of oral pediatric formulations.5,122 New devices generally assist the oral delivery of liquids to small children by using modified feeding bottles and pacifiers with medicines placed in a reservoir; help improve the palatability of oral solutions by using a dose-sipping technology, or
help increase product stability by using a pulp-spoon with a single dry dose of medicine (see Table 4 for more detailed examples).3,116,122

**FUTURE STEPS**

The ideal pediatric formulation should have flexible dosage increments and minimal excipients, be palatable, safe and easy to administer, and be stable with regard to light, humidity, and heat. Nevertheless, a significant number of drug formulations are unsuitable for children, which leads to unsafe off-label and unlicensed use of adult medicines. Recent initiatives promoting pediatric drug development have made some initial progress in the neglected area of pediatric formulations. Most efforts have focused on age-appropriate oral solid preparations, which enable dose flexibility, easier administration, and better acceptance in children. Despite these advances, the new pediatric formulations are still only a small part of the full therapeutic arsenal needed to serve all pediatric patients.

The following 5 priorities have been identified as critical for the further development of appropriate pediatric formulations. The first key issue is the continuous prioritization process that focuses on unmet public health issues...
and ensures that drug development aligns with the true clinical needs in children. Special attention should be paid to innovations that improve drug delivery in neonates, fill treatment gaps in pediatric cancers, and treat diseases of high burden in developing countries.124,90,91,84,123

Second, better use of existing data are required to facilitate pediatric drug development. Some innovative scenarios under investigation include preliminary “enabling” formulations that bridge existing adult formulations and potential pediatric market formulations, adjustments of adult in vitro gastrointestinal models to study drug bioavailability in children, and refined criteria for the extrapolation of adult efficacy data to the pediatric population.124–126

Third, future research on pediatric formulations could potentially benefit from existing or innovative technologies under development in adults.127 Novel experimental treatments of adult cancers, infections, and asthma have used nanoparticle-targeted therapy, novel smart polymer-based drug delivery systems, new chemical entities (eg, dendrimers), and remote triggering devices. These treatments may have significant applications in children, and the identification of appropriate animal models for pediatric preclinical studies should be a research priority.128–130

Fourth, ongoing technologic advances need to be accompanied by relevant patient outcome studies and clinical feedback on efficacy, safety, patient acceptability, preferences, and adherence regarding new formulations; currently, such studies and feedback are lacking.131 Practice-based evidence on the impact of novel formulations, generated by health care professionals and caregivers, could provide further support for the development of pediatric medicines with clear clinical advantages.

The fifth priority concerns finance. Because innovative technologies are costly, the ultimate challenge is to make these new pediatric formulations available on the market and in daily practice.22,89,132 Their commercial viability might be improved by an increased market size (eg, global scale, inclusion of geriatric patients and adults with swallowing difficulties); new incentive schemes (particularly for off-patent drugs), such as limited exclusivity and premiums, funding, and tax breaks; and public–private partnerships that support the development of orphan drugs and other less profitable niches.69,98–100

In sum, to reach these goals, it is essential that there is a committed collaboration between stakeholders that extends across disciplines and geographic regions. Moreover, this collaboration should have the innovative potential to further shape the pediatric drug development agenda and thus to close the adult–child medicine gap.

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We acknowledge Dr Richard Laing (WHO) for his advice on the progress analysis and recommendations for improving pediatric drug formulations.

REFERENCES


**POUTINE:** Church Street is a pedestrian street that runs through the heart of downtown Burlington, Vermont. During the summer and fall, the street is crowded with food vendors selling all kinds of different foods. However, as required by city ordinance, street vendors may only sell foods that do not directly compete with restaurants on or immediately adjacent to Church Street. That is the reason no food vendors sell pizza or hamburgers. Just recently, though, I noticed a new vendor on the street selling poutine, a Canadian dish made of French fries and nuggets of curd cheese smothered in gravy. As reported in The Wall Street Journal (In Search Of: May 2, 2014), poutine is not classically associated with fine dining. In fact, there is a debate as to whether something such as “great poutine” even exists. Still, the dish seems to exploding in popularity, moving from humble trucks stops and cafes in rural Quebec to fine dining establishments in New York and Chicago. The roots of poutine are a bit mysterious. Some say the dish was created in the mid-20th century after a cook in Warwick, Quebec, mixed the ingredients together with vinegar in a waxed paper bag and after the resultant explosion, labeled the concoction a “maudite poutine”—a blasted mess. Most aficionados report the “best” poutine includes very fresh cheese curds, crisp French fries, and homemade brown gravy—preferably one that would do justice to a fine rib roast. Recently, restaurateurs have begun experimenting with all sorts of additional ingredients, but classic poutine has only three. Regardless of the quality of the ingredients, however, the dish is certainly not light. Still, it is a wonderful guilty pleasure that I partake of at least once a summer. Now I will not have to travel to a particular small town in upstate New York or Montreal, my traditional spots for poutine, but can savor the dish right here in my own town.

*Noted by WWR, MD*
Pediatric Drug Formulations: A Review of Challenges and Progress
Verica Ivanovska, Carin M.A. Rademaker, Liset van Dijk and Aukje K. Mantel-Teeuwisse

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