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The Essentials of Essential Oils

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Key points

- Essential oils have been used for centuries as medicine and are now much more readily available and inappropriately advertised for the treatment of specific diseases.
- There is very little reliable evidence in favor of using essential oils in pediatrics, except for peppermint in the treatment of irritable bowel syndrome and a combination of tea tree oil and iodine for molluscum contagiosum.
- With the increased access to essential oils, there have been more cases of toxic exposures to children.

INTRODUCTION

Essential oils (EOs) are the basic components of aromatherapy, with records of their use in the practice of herbal medicine dating from 4500 BC. The composition and potency of each EO can vary depending on the part of the plant from which they are extracted. EOs are a mixture of hydrocarbons, terpenes, phenols, and aldehydes; 1 oil can contain 80 to 300 different hydrocarbons [1]. Historically, EOs have been used in a variety of applications including perfumes, food flavorings, aromatics, paints, cleaners, and medications. Many studies have reported mechanisms of action with clinical effects of specific EOs described herein. However, data are limited and most evidence is not high quality.

MANUFACTURING AND MARKETING

Manufacturers of EOs distill the hydrocarbon components from the desired part of the plant. Thus, the word "essential" refers to the essence of the plant

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that is distilled, instead of an invaluable active ingredient. Manufacturers describe their products as ranging from cosmetic grade C, food grade B, to therapeutic grade A. However, there is no regulatory body that determines these quality standards; the determinations are made by each manufacturer [1]. Although many companies conduct testing, safety, and treatment studies on their EOs, the studies are designed and funded by the companies themselves, which introduces bias and questions regarding validity.

Numerous brands are available for consumer purchase including doTERRA, Plant Therapy, Young Living, and Rocky Mountain Oils. Most of these companies function with a multilevel marketing system with no store, and products only available through an approved member. Although multilevel marketing is a legitimate sales model, multilevel marketing sales people are motivated by commissions, which can lead to overzealous marketing.

THE LAW

EOs are covered by the Dietary Supplement Health and Education Act of 1994. Thus, they are not regulated by the US Food and Drug Administration and do not have any other government agency oversight. Although the act specified that companies cannot "claim to treat, prevent, cure, mitigate, or diagnose disease," many EO manufacturers violate this act with claims on their websites. Manufacturers are allowed to make claims of "structure or functional help," such as their product "improves prostate health" or "maintains a healthy immune system."

Critically, they are not required to show safety or to report adverse events. It is the responsibility of the by the US Food and Drug Administration to prove the product is unsafe, thereby enabling the removal of products from market. With companies growing at a remarkable rate, this task is challenging.

OILS MOST COMMONLY USED (BOX 1)

Clove oil

Historically, clove oil has been combined with zinc for use as a tooth sealant and an analgesic; 60% to 90% of the content is eugenol, which is the active ingredient [1,2]. Eugenol works by blocking certain ion channels and inhibiting prostaglandin synthetase, which contributes to its antiinflammatory effects. Its

Box 1: Most commonly used EOs

Clove
Eucalyptus
Lavender
Nutmeg
Peppermint
Tea Tree

effects are similar to benzocaine. For these reasons, it is used as a skin anesthetic [1].

Thomassen and colleagues [3] reported in 1991 that clove oil can deplete glutathione, resulting in hepatotoxicity in rats. Toxic effects from human ingestion are altered mental status, increased anion gap resulting in a metabolic acidosis, coagulopathy, and hypoglycemia. Common reactions include contact dermatitis, skin irritation, and allergic reaction [1].

Eucalyptus oil

Eucalyptus oil is historically and currently used to treat the common cold. It reduces mucous secretions by inhibiting tumor necrosis factor-α and IL-1β and it decreases tracheal muscle contractions by potentiating acetylcholine. The oil inhibits potassium-induced contraction of airway smooth muscle, thereby enabling it to act as a myorelaxant [1]. These actions could be beneficial to patients with asthma or chronic obstructive pulmonary disease.

There are case reports of altered mental status, slurring of speech, nausea, vomiting, and seizures or coma when the oil is used topically in excess or ingested owing to its rapid absorption through the gastrointestinal (GI) tract. One teaspoon is toxic in children when ingested; however, inhaled or topical exposure is rarely toxic [1].

Lavender oil

Lavender oil has multiple uses: as a mood enhancer, anxiolytic, pain control, insect repellant, and for its antimicrobial effects. In vitro and in vivo studies in rats found that lavender oil inhibits mast cell degranulation and histamine release. One of the added benefits includes the ability to inhibit prostaglandins and leukotrienes. These analgesic and antiinflammatory properties support lavender oil as a possible therapeutic agent [4]. There is also evidence that it has antimicrobial activity against methicillin-resistant *Staphylococcus aureus*, vancomycin-resistant enterococcus, and other bacteria [1].

However, lavender oil is rapidly absorbed through the skin and commonly causes a contact dermatitis [5]. It also has dose-dependent estrogenic and antiandrogenic effects. A well-documented side effect is gynecomastia [6].

Nutmeg oil

During the Middle Ages, nutmeg was used as a digestive aid and to treat cholera and rheumatic disease. However, the scarlet-colored aril around the seed was used as an abortifacient. Unfortunately, it was often toxic to the mother as well as her unborn infant. Historically it has also been used as a natural high, providing the feeling of giddiness, detachment, or impending doom. Currently, mace spray is made from the aril [1].

Myristicin is currently being investigated as the possible psychoactive component of the oil; otherwise, the pathophysiology of nutmeg is largely unknown [1]. Side effects include tachycardia, reflexive bradycardia, nausea, vomiting, delirium, and dry mouth [1,7].

Peppermint oil

Peppermint oil is used for oral care, candy, cosmetics, and beverages. It is also used to treat upper respiratory infections, itching, inflammatory bowel syndrome, and as an anesthetic. Menthol is the main component, making up 29% to 48% of the oil [8].

Menthol acts as a smooth muscle relaxant through its actions on ion channels. At temperatures of 46° to 82°F, peppermint oil stimulates the calcium channels providing a warming sensation. Its action on sodium channels causes analgesia. By these mechanisms, it decreases peristalsis within the GI tract and alleviates symptoms of rhinitis. However, prolonged use can cause a reflexive increase in congestion [1]. Other properties of menthol include stimulating bile flow and helping relieve gas through burping or flatulence [8].

Although this oil is rapidly absorbed through the skin and GI tract, it is rarely toxic. Side effects include abdominal pain, hypersensitivity, rash, muscle tremor, and bradycardia. Menthol relaxes the lower esophageal sphincter, which worsens gastroesophageal reflux [8]. The dermatitis and hypersensitivity primarily result from topical use. It is speculated that neonates with glucose-6-phosphate deficiency cannot conjugate menthol, resulting in worsened jaundice [9].

Tea tree oil

Australian Aborigines inhaled crushed tea tree leaves in their hands to treat colds and applied tea tree poultices to wounds for its antimicrobial effects. There are also stories of "healing lakes," where tea tree leaves had fallen and steeped [1].

Investigations in the 1920s found the oil to be bactericidal and antiinflammatory. Later studies showed its specific lipophilic hydrocarbon disrupts lysosomal membranes, resulting in lysis in a hypertonic medium. It also inhibits tumor necrosis factor-α, IL-1α, IL-10, and prostaglandin E. There is speculation that it may function as a topical antiseptic and an in vitro bactericidal agent for staphylococcal and *Escherichia coli* species [1].

Tea tree oil is very allergenic, and its adverse effects include skin irritation. Repeated exposure can cause gynecomastia, and ingestion can cause altered mental status, ataxia, and slurred speech within 30 minutes [1].

OILS THAT ARE HIGHLY DANGEROUS TO CHILDREN (BOX 2)

Camphor Oil

Camphor oil is an abortifacient, a contraceptive, and a lactation suppressant. It has also been used as a cold remedy, antidiarrheal agent, and antiseptic. In the

Box 2: Most dangerous EOs

Camphor

Oil of wintergreen

19th and 20th centuries, this oil was used as a cardiac stimulant in patients with chronic heart failure during flu epidemics [1].

It is rapidly absorbed through the GI tract, skin, and mucous membranes, and can also cross the placenta and blood–brain barrier [1]. The name is similar to castor oil, which is purported to help induce labor; camphor and castor oil have been confused before with the mother accidently ingesting camphor oil causing serious injury to her and her unborn child. Toxicity occurs 5 to 90 minutes after ingestion, with nausea, vomiting, vertigo, headache, altered mental status, seizures, and hepatotoxicity. Symptoms can also occur from other exposures such as inhalation and dermal application [1,10]. One tablespoon can be fatal in children if ingested [1].

Oil of Wintergreen

Touted to help with rheumatism, inflammation, myalgias, and upper respiratory infections, wintergreen oil is another highly dangerous EO. With its minty smell and taste, it carries a high risk of accidental ingestion by children. It is rapidly absorbed by the GI tract and skin with 12% to 20% transdermal absorption within 10 hours. Quicker absorption occurs if heat is applied or if the skin is inflamed, broken, or an occlusive dressing is applied.

Wintergreen oil is metabolized by CYP450 which converts it to salicylic acid. This conversion can cause aspirin toxicity, with 1 teaspoon of ingested oil being the equivalent of 7 g of aspirin. Transdermal application has caused deaths in children [11]. Signs of toxicity with this oil are similar to salicylate toxicity: nausea, vomiting, tinnitus, fever, hyperpnea, and tachypnea [1].

TREATMENT AND LABORATORY TESTS

Measurement of EO levels in the blood of patients with suspected toxicity is generally not available or useful. Blood samples are sent to outside laboratories that take a long time to return results, so they are not generally used to guide treatment. Treatment usually is supportive, with laboratory measurements made as needed. Local poison control centers should be contacted immediately for specific treatments and if any further specific monitoring for the patient is needed.

THE EVIDENCE OF EFFICACY

As described elsewhere in this article, limited data exist on the pharmacology and therapeutic effects of EOs. The few extant randomized, controlled studies are described.

Evidence for anxiolysis

A double-blind, placebo-controlled, randomized study was done by Ndao and colleagues [12] in 2012 to evaluate the effects of inhalation of bergamot EO on the anxiety, nausea, and pain of 37 patients ages 5 to 21 years old undergoing stem cell transfusion; the parents were also included [13,14]. The placebo was a scented shampoo that did not contain EOs.

Children were assessed before infusion, at infusion completion, and 1 hour after infusion using validated anxiety, pain, and nausea scales (Spielberger State-Trait Anxiety Inventory, Children's Behavioral Style Scale, visual analogue scale, and the Emotionality Activity Sociability and Impulsivity instrument). Parents were assessed with the Spielberger State-Trait Anxiety Inventory for parents before, during, and after the infusion as well. The children were randomized into 2 groups: 20 into the placebo group and 17 into the experimental group controlling for age, transplant type, and amount of dimethyl sulfoxide in grafts. Dimethyl sulfoxide is added to stem cells as a cryoprotectant and has been associated with nausea and vomiting owing to its unpleasant odor [15].

The investigators concluded that bergamot EO did not significantly reduce transitory anxiety and may have contributed to persistent anxiety after transfusion, with children in the treatment group experiencing greater anxiety 1 hour after the transfusion ($P = .05$). In the treatment group, reported pain was higher at baseline ($P = .04$), but it decreased in both groups and was not significantly different 1 hour after the infusion.

Nausea was significantly greater in patients in the treatment group upon completion of transfusion ($P \leq .01$) and 1 hour after the transfusion ($P = .03$). Parental anxiety declined in both groups; however, the difference between groups was not significant. This study indicates that there is no benefit of aromatherapy with bergamot EO for decreasing anxiety, nausea, or pain in children receiving stem cell infusions, and in their parents.

Nord and Belew (2009) [7] conducted a single-blinded, randomized, controlled, prospective clinical trial to determine the effectiveness of combined aromatherapy with lavender and ginger EOs in lessening postoperative distress in children. Forty-eight children (from <1 to 21 years old) were assigned to aromatherapy with lavender and ginger EOs, and 46 were assigned to placebo, which was aromatherapy with jojoba EO, which has no known effects and a light scent.

All children received standard care in addition to EO inhalation (EO on cotton ball taped on the subject's hospital gown) and topical administration (EO placed over a pulse point and covered with a nonocclusive adhesive bandage). Parents completed the Faces, Legs, Activity, Cry, Consolability tool as a measure of pain and distress before anesthesia was administered and after surgery when they were reunited with their children. Parent satisfaction was assessed by asking, "In your opinion, do you think the aromatherapy enhanced the patient's overall comfort?", "Would you choose to use aromatherapy for future health care comfort measures?", and additional open-ended comments were encouraged.

The distress scales after surgery were lower for the children in the lavender/ginger EO group, although the difference was not statistically significant. There were no differences between the 2 groups in parental responses to questions. However, more than 78% of the parents in both groups stated that they would choose to use aromatherapy interventions in the future.

Nord and Belew (2009) [7] identified several limitations: parents who agreed to participate were likely biased in their beliefs about EOs and were more accepting of the treatment than the general population; parental bias may have influenced the Legs, Activity, Cry, Consolability scores; and variations in length of surgery case (and therefore length of EO exposure) was not controlled for; and jojoba oil was not a valid placebo because its effects have not been well-investigated.

Evidence for pain control

Soltani and colleagues (2013) [16] evaluated the effect of aromatherapy on pain in children in a single-blinded, randomized, controlled, prospective clinical trial. The investigators measured the effect of lavender EO on posttonsillectomy pain [5].

Forty-eight posttonsillectomy patients (ages 6–12 years old) were randomly assigned to a treatment or a control group. After surgery, all patients received acetaminophen as needed to relieve pain. The treatment group also inhaled lavender EO every 6 hours (4 droplets were rubbed on their palms and patients were instructed to inhale it for 3 minutes). The frequencies of acetaminophen use, nocturnal awakening owing to pain, and pain intensity (measured via visual analogue scale) were documented for 3 days after surgery. The control group received the acetaminophen only.

The treatment group required significantly less acetaminophen on all 3 postoperative days ($P < .05$), but there were no significant differences between groups in pain intensity and frequency of nocturnal awakening. The investigators concluded that aromatherapy with lavender EO can decrease analgesics usage after tonsillectomy in children. However, the study had major limitations, including the small sample size, the lack of a placebo in the control group, the lack of double-blinding, and the lack of control for the size of drop used.

Evidence for molluscum contagiosum

Markum and Baillie (2012) [17] conducted a double-blinded, randomized, controlled, prospective trial to compare the effectiveness of topical application of EOs: (1) tea tree oil, (2) a combination of tea tree oil and organically bound iodine, and (3) iodine alone (as the control) for the treatment of molluscum contagiosum in children. Tea tree oil and iodine are both known as topical antiseptics [18,19].

Fifty-three children (mean age, 6.3 $\pm$ 5.1 years) diagnosed with molluscum contagiosum were randomized to receive 1 of the 3 treatments. Children or their parents were instructed to apply their assigned treatment topically to the affected area twice daily and the results were documented after 30 days of treatment. Successful treatment was defined as more than a 90% decrease in the number of lesions. Forty-eight children completed the study.

The treatment was successful in 16 of 19 children treated with a combination of tea tree oil and iodine, 3 of 16 children treated with tea tree oil alone, and 1 of 18 treated with iodine alone. Two children treated with iodine only had worsening of lesions. Side effects were limited and included 4 cases of a

mild, noninfectious erythema around the base of lesions, and included children from all 3 therapy groups.

The investigators concluded that the combination of tea tree oil and organically bound iodine is a safe and effective treatment for molluscum contagiosum in children. The response within 30 days is a therapeutic improvement given that molluscum contagiosum typically requires 12 to 30 months to resolve spontaneously, and can require tissue destruction for treatment (curettage, cryotherapy, laser, topical caustics, etc).

The mechanism by which tea tree oil and iodine worked synergistically is unclear, but the authors proposed that it could be due to the lipophilic properties of tea tree oil allowing further penetration of the iodine into skin. A major limitation of the study is that the length of infection before treatment was not specified.

Evidence for treatment of lice

Greive and Barnes (2017) [19] conducted an assessor-blinded, randomized, multicenter, controlled, prospective clinical trial in Australia to compare the safety and efficacy of a head lice treatment containing Australian eucalyptus oil and *Leptospermum petersonii* (lemon-scented tea tree) oil versus pyrethrins and piperonyl butoxide in children [19]. Ninety-seven children (ages 6 months to 11 years old) were randomized to have 1 of the 2 treatments applied per manufacturer instructions: MOOV Head Lice Solution (eucalyptus oil and *L petersonii*) which was applied 3 times with 1 week between applications (at days 0, 7, and 14); Banlice Mousse (pyrethrins and piperonyl butoxide), which was applied twice with 1 week between applications (at days 0 and 7). Banlice Mousse is a leading product for treating head lice in Australia, but contains a neurotoxin. Effective treatment was defined as the absence of live lice, adults, or nymphs identified by wet combing 1 week after the final treatment.

The results were statistically significant with 83% versus 36% cure rates in the eucalyptus oil and *L petersonii* group and pyrethrins and piperonyl butoxide group, respectively. As a secondary measure, the investigators immersed eggs for 10 seconds in the eucalyptus oil and *L petersonii* solution or water and monitored hatch rates. No body louse eggs hatched after 10 days immersion in the eucalyptus oil and *L petersonii* solution, whereas 24%, 76%, 92% and 92% of eggs hatched after 7, 8, 9 and 10 days, respectively, after immersion in water.

The investigators concluded that the eucalyptus oil and *L petersonii* solution was safe, effective, and superior to the pyrethrins and piperonyl butoxide. A major limitation was that the eucalyptus oil and *L petersonii* solution was applied 3 times, whereas the pyrethrins and piperonyl butoxide was only applied 2 times.

Evidence for apnea in premature infants

Edraki and colleagues (2013) [20] conducted a randomized, controlled, prospective clinical trial to study the efficacy of olfactory stimulation by vanillin in preventing apnea in premature newborns, a concept first proposed by Marlier and colleagues [21]). The proposed mechanism is passage of vanillin through the nasal mucosa and into the brain, where it reportedly affects the

respiratory center [21]. Thirty-six newborns were randomized into experimental and control groups. The experimental group received olfactory stimulation by saturated vanillin solution, which was placed on a cotton ball in the newborn's incubator, with no skin contact. The control group received no interventions. Apnea, arterial blood oxygen saturation, and heart rate were continuously monitored for 5 days.

The experimental group had a statistically significant decrease in the number of apnea episodes ($P = .001$) and a 3.1-fold decrease in apnea compared with the control group. The authors suggested that the vanillin decreased newborn distress, which subsequently prevented apnea related to stress, and they recommended its use. A major limitation of the study was the lack of controls to determine if the vanillin or olfactory stimulation alone produced the results.

Evidence for irritable bowel syndrome

Peppermint oil is used to treat a variety of ailments, including headaches, muscle pain, and abdominal distress. Most studies regarding the efficacy of peppermint oil in alleviating abdominal symptoms have been done in adults. Pittler and Ernst (1998) [22] conducted a critical review and metaanalysis on adult studies that used peppermint oil to treat irritable bowel syndrome; of the 8 studies that met criteria, 5 were double-blind, placebo-controlled, randomized clinical trials. Their analyses revealed "a significant ($P < .001$) global improvement of irritable bowel syndrome symptoms in patients treated with peppermint oil compared with placebo." However, the authors identified many limitations, including a lack of consistent diagnostic criteria, publication bias, length of treatment, and carry-over effects (only 1 trial had a washout period). Because of these limitations, the authors concluded that it is still not clear if peppermint oil alleviates symptoms of irritable bowel syndrome in adults [8].

A randomized, double-blind study by Kline and colleagues [23] indicated the efficacy of peppermint oil in children with irritable bowel syndrome. The investigators used enteric-coated peppermint oil capsules, which release the oil in the small bowel versus the stomach owing to the pH-dependent coating. The placebo was a capsule of arachis oil. Fifty children (ages 8–17 years) recruited from the University of Missouri, Georgetown University, and a private practice in Charleston, South Carolina, had previously been diagnosed with irritable bowel syndrome using the 2 most accepted criteria for diagnosis, either Manning or Rome. Forty-two children who met the criteria and who had symptoms and pain the prior 2 weeks were randomized to the treatment or placebo group, with weight-based dosing. Children maintained a journal of symptoms and clinicians ranked the severity of pain and the improvement in symptoms from day 1 to day 14.

Significantly more children in the peppermint oil versus placebo group reported a change in the severity of symptoms (76% vs 19%, respectively; $P < .001$) and improvements in symptoms (71% vs 43%; $P < .002$). There was no improvement in other symptoms, including gas, urgency, or features of stool, and children reported no side effects from the peppermint oil [23].

In summary, the studies of EOs being used to treat various ailments are generally limited owing to small sample sizes and many have inadequate control groups. However, the studies provide much-needed data that can help to guide recommendations on this growing and controversial topic.

NATIONAL POISON CONTROL DATA

The increasing popularity and availability of EOs have resulted in increasing numbers of exposures and toxicities. The American Association of Poison Control Centers annual report reveals 20,109 case mentions of EO exposures in 2016, of which 18,997 were single exposures (Table 1) [24]. A majority of the exposures were listed as miscellaneous EO, with the other most commonly listed oils being tea tree (22%), followed by eucalyptus (6%), and then cinnamon (3%) and clove oils (2.7%). In 2016, 70% of all calls to poison control for an exposure to an EO were for a child less than 6 years old. For all ages, 93.6% of calls were for an unintentional exposure and 9.6% needed treatment in a health care facility.

Of all exposures, 20% had minor effects that were "minimally bothersome . . . usually resolve[d] rapidly" [24] and had no permanent effects. One out of every 100 people exposed had moderate to major effects (Table 2). All of these exposures had similar side effect profiles listed under the individual oil information described elsewhere in this article. Moderate effects were "more pronounced, more prolonged or more of a systemic nature than minor symptoms. Usually some form of treatment is or would have been indicated." Again, the symptoms left no permanent effects and were not life-threatening. Major effects were "life-threatening or resulted in significant residual disability or disfigurement" [21]. There were no reported deaths owing to an EO exposure.

Table 1
American Association of Poison Control Centers 2016 and 2017 annual report from clinical toxicology

Age, y	Total exposures in 2016, n (%)	Total exposures in 2017, n (%)
<6	13,264 (69.8)	15,249 (69.1)
6–12	756 (3.9)	853 (3.9)
12–19	420 (2.2)	553 (2.5)
>20	3722 (19.5)	4403 (20.0)
Unknown age[a]/adult of unknown age[b]	835/716 (4.4%/3.7)	1010/891 (4.6%/4)

[a]Unknown age of patient involved in exposure (child or adult).
[b]Adult of unknown age: listed as an adult but their exact age was not listed. A majority of the calls that did not have an exact age listed were adults.
Data from Gummin DD, Mowry JB, Spyker DA, et al. 2017 Annual report of the American Association of Poison Control Centers' National Poison Data System (NPDS): 35th Annual Report. Clin Toxicol (Phila), 2018 in press.

Table 2
Examples of side effects associated with EO exposures, American Association of Poison Control Centers Annual Report, 2017

Minor	Moderate	Major
Mild GI symptoms	Acid–base disturbance	Repeated seizures or status
Drowsiness	High fever	Cardiovascular instability
Skin irritation	Disorientation	Cardiac or respiratory arrest
Transient cough	Isolated brief seizures	Esophageal stricture
	Minor creatinine elevations	Renal failure
	Hypoglycemia with confusion	Rhabdomyolysis

Data from Gummin DD, Mowry JB, Spyker DA, et al. 2017 Annual Report of the American Association of Poison Control Centers' National Poison Data System (NPDS): 35th Annual Report. Clin Toxicol (Phila), 2018 in press.

There was a 16% increase in single exposure calls from 2016 to 2017 (an increased from 18,997 to 22,068, respectively); the types of oils in the exposures were similar between years. Between 2016 and 2017, there was a 15% increase in children less than 6 years old being exposed (see Table 1). Ninety-four percent of exposures were unintentional with 9.3% of people needing treatment at a health care facility. Minor effects were reported in 15.2% of all cases and moderate to major outcomes were reported in 0.8% of cases. There were no deaths reported in 2017.

In summary, EOs have a long history of usage for their possible medicinal effects. Although the pharmacology and potential treatments applications are being studied, large, blinded, randomized studies are needed to clarify their efficacy and safety.

Potentially effective EOs are peppermint in the treatment of irritable bowel syndrome and a combination of tea tree oil and iodine in the treatment of molluscum contagiosum. The other studies with significant positive effects have too many limitations to draw reliable conclusions or there are already available effective and safe treatments. However, there needs to be better defined regulations of the EOs before true testing can occur if the results are to be reliably reproduced. Safety is a particularly important issue with children given their high risk of unintentional exposures and toxicities. Most importantly, EOs must be handled as potential poisons and stored out of a child's reach.

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