

Submitted by the
CONSUMER HEALTHCARE PRODUCTS ASSOCIATION

BRIEFING BOOK

Joint Meeting of the Nonprescription Drugs Advisory Committee and Pediatric
Advisory Committee

May 17 – 18, 2011

[Docket No. FDA-2010-N-0002]

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EXECUTIVE SUMMARY

Introduction

On March 9, 2011, FDA announced a joint meeting of the Nonprescription Drugs Advisory Committee and the Pediatrics Advisory Committee to discuss use of over-the-counter (OTC) acetaminophen in children (Federal Register 2011). FDA intends to review pertinent pharmacokinetic, safety and efficacy data, and discuss whether new dosing information for OTC acetaminophen products should be added to the label for children less than 2 years of age. According to FDA's announcement, the committees will also discuss weight-based dosing for children 2 to 12 years of age. Lastly, the committees will discuss ways medication errors can be minimized.

Consumer Healthcare Products Association (CHPA) is the national trade association representing the leading manufacturers and distributors of OTC medicines and dietary supplements in the United States. CHPA's members manufacture and distribute OTC acetaminophen single-ingredient products for children and adults. **CHPA supports inclusion of dosing information for children less than 2 years of age on labels of OTC single-ingredient acetaminophen products intended for children, and the amendment of the OTC Internal Analgesics Monograph to reflect this labeling. Further, our members also support dosing based on weight as the preferred method for dosing children, and inclusion of this dosing information in the OTC Internal Analgesics Monograph.**

A priority goal of CHPA is to ensure that parents and caregivers have access to the best medicines possible, as well as informational resources to use them safely, appropriately, and in a cost-effective manner. CHPA has an interest and expertise in the subject matter of the advisory committee meeting and is providing background information for the committee to review prior to the meeting.

Use of Acetaminophen in Children

The antipyretic/analgesic acetaminophen is one of the most commonly used ingredients in the United States to treat pain and reduce fever. Estimates suggest that in any given week, approximately 12% of children up to 11 years of age have taken acetaminophen. The peak of acetaminophen use is among children 6 to 23 months of age. Acetaminophen has been available as an OTC medicine for more than 50 years, and its use as first-line treatment of febrile children is endorsed by leading medical associations in the U.S. and other countries.

The efficacy of acetaminophen in children has been confirmed in multiple published clinical trials. The efficacious dose for antipyretic activity is 10-15 mg/kg body weight with repeated dosing every 4 hours, if needed, to a maximum of 5 doses per 24-hour period.

Pediatric Product Forms

Pediatric acetaminophen products are currently sold for infants as liquid concentrated drops dosed with droppers (80 mg/0.8-1.0 mL). For children older than 2 years of age, acetaminophen is available as liquid suspensions or solutions dosed with cups (160 mg/5 mL) and chewable tablets (80 mg/tablet). CHPA members provide calibrated dosing devices with their liquid products. Suppositories are also available OTC for infants ages 6 months to 3 years (80mg/suppository), children age 3-6 years (160mg/suppository) and children age 6-12 years (325 mg/suppository).

Current Product Labeling

Dosing information for children less than 2 years of age was derived from clinical studies and has been provided to healthcare professionals for decades. Consumers have access to this information through their healthcare providers, pharmacists, and various educational websites (*See Table 1*). However, the FDA OTC Internal Analgesics Monograph does not provide dosing instructions for children under 2 years of age in the Drug Facts label of acetaminophen products.

Table 1. Example dosing information for children under 2 years of age provided by healthcare practitioners (www.parents.com)

Weight	Infant Drops (80 mg / 0.8 mL)
6-11 lbs	0.4 mL (1/2 dropper)
12-17 lbs	0.8 mL (1 dropper)
18-23 lbs	1.5 droppers

In order to give caregivers ready and direct access to this information, CHPA members urge FDA to modify OTC labeling regulations to add dosing instructions for children less than 2 years on product labels. This action would be consistent with the agency's decision to permit the inclusion of dosing instructions for children under 2 years of age in the Drug Facts label of the only other pediatric OTC single ingredient antipyretic/analgesic: ibuprofen.

For children 2 years of age and older, weight-based and age-based dosing information is included on labels of OTC acetaminophen products manufactured by CHPA members for infants and children, as shown in *Table 2* below.

Table 2. Example dosing information for children 2 years of age and older provided on product labels (www.tylenol.com)

Weight	Age	Infants' Concentrated Drops (80 mg in each 0.8 mL)
Under 24 lbs	Under 2 years	Ask a doctor
24-35 lbs	2-3 years	1.6 mL (0.8 mL + 0.8 mL)

Weight	Age	Children's Acetaminophen (160 mg in each 5mL or 1 tsp)
Under 24 lbs	Under 2 years	Ask a doctor
24-35 lbs	2-3 years	1 teaspoon or 5 mL
36-47 lbs	4-5 years	1 ½ teaspoons or 7.5 mL
48-59 lbs	6-8 years	2 teaspoons or 10 mL
60-71 lbs	9-10 years	2 ½ teaspoons or 12.5 mL
72-95 lbs	11 years	3 teaspoons or 15 mL

CHPA members have been adding weight-based dosing instructions to the Drug Facts label on a voluntary basis. CHPA encourages FDA to include these weight-based dosing instructions in the OTC Internal Analgesics Monograph. This would ensure that weight-based dosing, which is the preferred method, becomes a legally required labeling standard for pediatric acetaminophen products.

Medication Errors (Unsupervised Ingestions and Therapeutic Errors)

In the vast majority of situations, acetaminophen is used safely. Medication errors can be characterized as 1) accidental unsupervised ingestions (approximately 95% of cases) and 2) therapeutic errors (approximately 5% of cases). Unsupervised ingestions occur when products are left in sight of children, frequently with the child-resistant cap disengaged. Root causes of therapeutic errors are known and include confusion between different pediatric formulations, confusion over dosing directions, and measurement errors. A combination of education and changes to products and packages can improve the safe use of acetaminophen in children.

Interventions to Address Root Causes of Medication Errors

Consistent Labeling of Volumetric Measures

More than three years ago, CHPA members recognized an opportunity to reduce variability in dosing directions for liquid medicines given to children. In November 2009, the CHPA Board of Directors approved and adopted a voluntary guideline for labeling packages and dosing devices for these liquid products. The preferred unit for volumetric measures is milliliter (“mL”). Unnecessary markings are being eliminated from dosing devices. Doses listed on the label will

have corresponding markings on the dosing device. A calibrated dosing device will be provided with every liquid product labeled for use in children. These guidelines are currently being implemented on new and existing products, including all OTC children's acetaminophen products.

Product Formulations

CHPA members have voluntarily taken further action to reduce confusion with acetaminophen dosing to children. Beginning mid-2011 and continuing through early 2012, CHPA members will discontinue manufacturing concentrated infant drops and convert these products to the same concentration used today for children's (ages 2-11 years) acetaminophen products (160mg/5mL). This action is consistent with guidance from three advisory committees to FDA in June 2009 (vote of 36-1 in favor) to standardize acetaminophen liquid products to one concentration. In addition, these new products will be packaged with flow restrictors to make it difficult to ingest large amounts of liquid in the event of an accidental unsupervised ingestion. Dosing devices for infants will be calibrated oral syringes and for older children, calibrated dosing cups will be used. These important changes will be supported by outreach efforts to alert professionals to the change, with particular emphasis on pharmacists, pediatricians, physician assistants, and nurse practitioners.

Education

CHPA has a strong track record of sustained education to consumers regarding the safe and appropriate use of OTC medicines. Two initiatives in particular highlight CHPA's commitment to safe use of acetaminophen-containing medicines. In 2007, CHPA was an inaugural partner in the CDC-led PROTECT initiative, a public-private partnership to reduce medication errors in children. Through the PROTECT initiative, stakeholders approved voluntary labeling guidelines for liquid medicines; clear, consistent communication of measuring units and use of appropriate dosing devices (discussed earlier). Also, as part of PROTECT, an education campaign titled "Up and Away and Out of Sight," was developed and funded by industry members and approved by PROTECT members, to educate parents and caregivers on the safe storage of medicines. Professional and consumer organizations will use these materials to further multiply the messages about safe use and storage of medicines.

Specific to acetaminophen, CHPA is a founding member of the Acetaminophen Awareness Coalition. Started in 2009 by the American Pharmacists Association with CHPA, this group of stakeholders is committed to increasing consumer awareness of the ingredient acetaminophen, its safe use, and the potential hazards of overdose. Know Your Dose is an OTC and Rx acetaminophen awareness campaign supported by the coalition, designed to reach consumers and patients at various points of care—doctor's offices, hospitals, health centers, pharmacies, and in-store clinics—when acetaminophen and dosing decisions are likely to be top of mind.

The program has its own website, www.KnowYourDose.org, with information and educational materials for consumers and healthcare providers. The materials are intended to ensure consumers and patients have access to core educational messages at points during which they are most receptive—such as when they are thinking of their own healthcare and of their

medications—and when they have contact with healthcare providers should they have additional questions. Baseline awareness of acetaminophen was measured prior to the campaign. The coalition will resurvey both consumers and healthcare providers to ensure impact and to refine the program as needed.

Recommendations

Regarding the topics under discussion at the upcoming FDA Advisory Committee meeting on pediatric acetaminophen, CHPA and its member companies strongly support the following actions:

1. Amend the OTC Internal Analgesics Monograph to include dosing directions for children less than 2 years of age on OTC product labels
2. Amend the OTC Internal Analgesics Monograph to include weight-based dosing for children less than 12 years of age

The materials provided in this document reflect the collective work and views of the following CHPA member companies which currently market OTC products containing acetaminophen for children:

Aaron Industries
AccuDial Pharmaceutical
Actavis
GlaxoSmithKline
McNeil Consumer Healthcare
Novartis Consumer Healthcare
Perrigo Company
Prestige Brands Holdings

RECOMMENDATIONS BY MEDICAL ASSOCIATIONS

Acetaminophen is the mainstay of analgesic/antipyretic treatment in children of all ages. Leading medical groups and associations in the United States and other countries recommend acetaminophen to improve the overall comfort of febrile children and to reduce body temperature.

The American Academy of Pediatrics published in March 2011 a clinical report which summarizes recommendations related to the use of antipyretics in children. The report from the academy's Section on Clinical Pharmacology and Therapeutics and the Committee on Drugs concludes that acetaminophen doses of 10 to 15 mg/kg given every 4 to 6 hours orally are generally regarded as safe and effective. On the basis of a review of recent efficacy studies, the report states that approximately 80% of children experience a decreased body temperature within 30 to 60 minutes after acetaminophen administration (Sullivan et al. 2011). The American Academy of Pediatrics endorses 3 months as the lower age limit for acetaminophen use without supervision by a healthcare professional. Ibuprofen is recommended as an alternative to acetaminophen for the treatment of fever in children. However, the use of ibuprofen in children younger than 6 months is not recommended due to inadequate data in this age group. To promote child safety, the academy's report instructs that pediatricians should educate parents on the safe storage of antipyretics and advocate for a limited number of formulations, clear labeling of dosing instructions, and the inclusion of dosing devices for antipyretic products (Sullivan et al. 2011, <http://www.healthychildren.org>).

Consistent with the 2011 clinical report, the American Academy of Pediatrics provides specific recommendations and instructions on the use of acetaminophen both in a parent education book, "*Caring for your Baby and Young Child*," and on its website for parents, *healthychildren.org*. (AAP/Shelov et al. 2009, <http://www.healthychildren.org>). The parent education book provides caregivers with an acetaminophen dosage chart that explicitly advises to dose acetaminophen based on a child's bodyweight, and the chart states that age is provided for "convenience only." The pediatric dosing recommendations are divided into five weight ranges, starting from 6 to 11 pounds (representative of children up to 5 months old) and ending with 36 to 47 pounds (representative of 4 to 5 year olds). The dosage chart further spells out the different dosage instructions for different forms and concentrations of acetaminophen products, including infant drops, less concentrated liquids, and chewable tablets. These complex instructions reflect the challenge of providing clear dosage information to caregivers because they must be applied to different product forms and concentrations (*See Table 3*).

Table 3. American Academy of Pediatrics: Acetaminophen Dosage Chart
Excerpt from: CARING FOR YOUR BABY AND YOUNG CHILD: BIRTH TO AGE 5. Steven P. Shelov, editor in chief [et al.]. "American Academy of Pediatrics", A Bantam Book; 5th edition (October 2009).

Acetaminophen Dosage Chart

Age*	Weight †	Infant Drops 80 mg/0.8 mL	Children's Elixir 160 mg/5 mL	Chewable Tablets 80 mg tabs
0-5 mos.	6-11 lbs. (2.7-5 kg)	0.4 mL	-	-
6-11 mos.	12-17 lbs. (5.5-7.7 kg)	0.8 mL	½ tsp	1 tab
1-2 yrs.	18-23 lbs. (8.2-10.5 kg)	1.2 mL	¾ tsp	1½ tabs
2-3 yrs.	24-35 lbs. (10.9-15.9 kg)	1.6 mL	1 tsp	2 tabs
4-5 yrs.	36-47 lbs. (16.3-21.4 kg)	2.4 mL	1½ tsps	3 tabs

*Note: Age is provided as a convenience only. Dosing for fever should be based on current weight.

† Weight given is representative of the age range.

The American Academy of Family Physicians also recommends acetaminophen as the first-line treatment of fever in infants and children. On its website for consumers, *FamilyDoctor.org*, the American Academy of Family Physicians instructs parents to follow the label instructions or ask their doctor about the correct dosage for their child which depends on the child's weight and age (<http://www.aafp.org> ♦ <http://familydoctor.org>).

Consumer education guides provided by the Canadian Pediatric Society and the Royal Australian College of General Practitioners mirror the advice and instructions by U.S. organizations in that they also recommend acetaminophen as the first-line treatment of fever in children (<http://www.caringforkids.cps.ca/> ♦ <http://www.racgp.org.au/familyhealth>).

In the UK, the National Institute for Health and Clinical Excellence published a guideline in 2007 on the assessment and initial management of feverish illness in children younger than 5 years of age. The guideline concluded that both acetaminophen and ibuprofen are recommended for use in febrile children who appear distressed and unwell (NICE 2007).

In addition to its use as an antipyretic, acetaminophen is also recommended as the first-line treatment of pain associated with certain acute illnesses in children. A joint report by the American Academy of Pediatrics and the American Pain Society from 2001 endorses the use of acetaminophen in acute pain associated with pharyngitis, meningitis (headache), pelvic

inflammatory disease (pelvic pain), and otitis media (AAP & APS 2001). A 2004 joint clinical practice guideline of the American Academy of Pediatrics and the American Academy of Family Physicians on the diagnosis and management of acute otitis media confirmed acetaminophen as the recommended treatment for mild to moderate earache associated with this condition (AAP & AAFP 2004).

USE OF ACETAMINOPHEN IN CHILDREN

Acetaminophen is the most commonly used active ingredient taken by children. In a 2005-2006 telephone survey conducted by the Slone Epidemiology Center at Boston University, 12% of children up to the age of 11 years had taken acetaminophen in the previous week. The peak of acetaminophen use was among children 6 to 23 months of age (Vernacchio et al. 2009). While acetaminophen use in children is mainly initiated by parents or other caregivers, it also results to a significant extent from physician-initiated therapy. According to data from the Verispan, LLC: Vector One®: National (VONA) system which measures retail dispensing of prescriptions, 1.1 million acetaminophen-containing products were dispensed in 2005 as a prescription for children up to 5 years of age (FDA/Governale 2006). These results are consistent with a report from the National Center for Health Statistics which showed that during 2004 and 2005 antipyretics and non-narcotic analgesics were among the most commonly prescribed medications at ambulatory care visits for children under 15 years of age (Raofi et al. 2006).

Upper respiratory tract infection associated with fever is the most common reason for acetaminophen use in children. According to a study in more than 8,000 3-year-old children whose mothers were interviewed for the 1991 Longitudinal Follow-up to the National Maternal and Infant Health Survey, sore throat and cough with fever were the most common indications for which acetaminophen was used in this age group (Kogan et al. 1994). These findings are similar to data on acetaminophen recommendations by physicians. A 2008 office-based physician survey showed that acute respiratory infection was the most frequently reported indication in the overall population for which doctors recommended a single-ingredient acetaminophen product (FDA/Governale 2009).

Apart from routine or child health checks, acute upper respiratory infections are the most common reason why children are seen by a physician (Cherry et al. 2007). Fever associated with acute respiratory infections (common cold) is usually slight but can increase to 102° F in infants and young children (NIAID 2004). It is estimated that fever is the primary complaint for 30% of patients seen by pediatricians (Crocetti et al. 2001). Fever is also one of the main reasons for emergency department visits by children. Data from the National Center of Health Statistics show that children under 15 years of age made three and a half million visits to emergency departments in 2007 with fever as principal reason, accounting for 16% of all emergency department visits in this age group (Niska et al. 2010).

ROOT CAUSES OF MEDICATION ERRORS (UNSUPERVISED INGESTIONS AND THERAPEUTIC ERRORS)

Accidental Unsupervised Ingestions

Accidental unsupervised exposures and ingestions are the main cause of product-related non-therapeutic exposures in children. Unsupervised ingestions occur when curious young children expose themselves or self-ingest medicines or other products, usually in the home, that are not kept out of their reach. Approximately 60 to 70% of the poisonings involve the ingestion of oral prescription and OTC medications followed by cleaning products, preparations for external use, and personal care products. Children between 1 and 3 years of age are at greatest risk for unsupervised ingestions (Franklin & Rodgers 2008, Schillie et al. 2009).

In a study of 2004-2005 data from the National Electronic Injury Surveillance System (NEISS), unsupervised medication ingestions caused 97% of emergency department (ED) visits among children aged 1 to 5 years. The remaining 3% of ED visits resulted from therapeutic errors (Schillie et al. 2009). Among the 10 most commonly ingested medications were many of the most frequently used prescription and OTC medicines, including analgesics, antidepressants, and antihypertensives (Vernacchio et al. 2009, Kaufman et al. 2002).

A study of 2001-2003 data from the National Poison Data System (NPDS) showed similar results in that unsupervised ingestions accounted for 94% of poison center calls involving ED visits of children up to 4 years of age. The remaining 6% of cases were therapeutic errors occurring at a home (Setlik et al. 2010).

An analysis of a data sample from nine U.S. poison centers showed that in the majority of unsupervised pediatric ingestions the medications were located in the kitchen or dining area (53%). In a significant number of the cases, the medications were in the bedroom (31%) or young children took them from a purse of an immediate family member or visitor (10%). In only 2% of the cases, the medications were stored in a bathroom medicine cabinet (Jacobson et al. 1989).

Therapeutic Errors

Two analyses using two different national databases examined the characteristics and root causes of therapeutic errors resulting in acetaminophen overdoses.

The results of the first analysis were presented by FDA at an advisory committee meeting in June 2009. The study, conducted by FDA's Center for Drug Evaluation and Research, was a review of the agency's Adverse Event Reporting System (AERS) on hepatic injury associated with acetaminophen-containing products. Over a 3.5-year period, 25 cases involved children up to 12 years of age. The mean age was 2.4 years. Twenty-two of the 25 children received only one acetaminophen-containing product, most commonly an OTC single-ingredient product. The following therapeutic error scenarios were found: administration of teaspoonfuls of medication instead of dropperfuls (n=4), administration of acetaminophen concentrated drops (100mg/mL) instead of acetaminophen suspension (32mg/mL) (n=3), misinterpretation of the dosing

instructions provided by a healthcare practitioner (n=3), and misinterpretation of the label instructions (n=2) (FDA/Manthripragada et al. 2009, FDA/Karwosky 2002).

The second analysis was as an examination of poison center cases published in April 2009 in *Clinical Toxicology*, the official journal of the American Academy of Clinical Toxicology, the American Association of Poison Control Centers, and the European Association of Poisons Centres and Clinical Toxicologists. The study queried NPDS for poison center cases from 2000 through 2004 in children 5 years of age and younger. Included were all cases in which the reason for the exposure was coded as “unintentional therapeutic error” and the medical outcome was “major effect” or “death.” Acetaminophen represented 25 of 238 medication-related cases. All of the consequential treatment errors occurred at home and with excessive doses of acetaminophen. Thirteen of the 25 cases occurred in children age 2 years or less. Twenty-two of the 25 cases occurred with single-ingredient acetaminophen formulations. Three cases involved single-ingredient acetaminophen and acetaminophen-containing cold medications given simultaneously. The following therapeutic error scenarios were found: confusion between different acetaminophen pediatric formulations (n=8), administration of adult dose (probably adult product) (n=4), simultaneous administration of multiple oral medications containing acetaminophen (n=3), simultaneous administration of oral and rectal acetaminophen products (n=2), and measurement error (n=1). Seven cases did not contain information on the reason of the error or the formulation given to the child (Tzimenatos et al. 2009, and personal communication).

In conclusion, both analyses show that consequential therapeutic errors involving acetaminophen use in children are rare, and that they are typically caused by parents being confused about how much to dose, how to dose, and which pediatric concentration to use.

CHPA MEMBER COMMITMENTS AND ACTIONS TO REDUCE UNSUPERVISED INGESTIONS AND THERAPUTIC ERRORS

The OTC medicine industry, under the auspices of CHPA, has engaged in a multi-pronged and long-term effort to reduce medication errors. In 1966, the industry formed the CHPA Educational Foundation, a nonprofit consumer-education entity, designed specifically to provide parents and other caregivers with the information they need to safely take and administer OTC medicines. Over the last 45 years, the foundation has launched programs on overall OTC safety, the Drug Facts label, information for targeted audiences, and ingredient-specific campaigns. Further, the foundation has a long history of partnering with various stakeholders—including the U.S. Food and Drug Administration—in order to address public health needs and to communicate as broadly as possible.

Formulation and Packaging Improvements

In June 2009, FDA convened a meeting of the Nonprescription Drug, Pediatrics and Drug Safety Advisory Committees to discuss acetaminophen safety. At that meeting, the committees were asked to vote on “Do you recommend that only one concentration of nonprescription acetaminophen liquid be available?” The vote was 36 to 1 in favor of this change. Committee members were not aligned on the single concentration. This vote recognizes that confusion between concentrations of acetaminophen in products for children has been demonstrated to be a root cause of medication error.

In response to this vote, and following significant investment in manufacturing equipment and validation, CHPA member companies are voluntarily converting the currently sold multiple concentrations of acetaminophen for infants and children to one single concentration of 160 mg/5 mL, the current children’s acetaminophen concentration. Infants’ product labels will continue to provide consumers with dosing directions for ages 2-3 years. Infant products will be sold with oral syringes for accurate dosing and ease of administration (vs. droppers provided with current products). Infant products will also be sold with flow restrictors, which will minimize product available in the event of an accidental unsupervised ingestion. Children’s products will continue to provide consumers with dosing directions for ages 2-11 years and will be sold with calibrated dose cups. These products will also be sold with flow restrictors.

Standardization of Volumetric Measures for Liquid OTC Medicines

Confusion about dosing directions has been cited as a root cause of medication errors. Current labeling regulations (OTC Drug Facts) do not specify standard dose-related volumetric measures. As a result, dosing directions may be provided in “spoon” or metric units, and any particular unit may have multiple acceptable abbreviations. A baseline survey of OTC liquid products (April 2009) found the following words associated with teaspoon: teaspoon, teaspoons, teaspoonful, teaspoonfuls, Teaspoon, and Teaspoons. Abbreviations for this one term are likewise numerous.

As part of a multiple stakeholder efforts to help prevent accidental, unsupervised medication ingestions and overdoses in children, CHPA members companies adopted voluntary guidelines to improve the consistency and standard format of volumetric measures within the dosing

directions on the outer packaging and immediate container label, as well as on the dosing device for OTC oral liquid drug products with dosing directions for children, defined as ≤ 12 years of age. While research evidence is limited, the guidelines represent the integration of stakeholder communications and standards, including those from authoritative bodies and professional organizations, as well as knowledge gained from consumer experience and research with OTC medicine products.

Findings from an industry-wide survey (April 2009) of OTC oral liquid drug products with dosing directions for children suggested potential areas to improve the consistency and standard format of volumetric measures:

- Dosing Directions
 - Representation in a dosing chart versus running text
 - Volumetric measures: unit types and standards, abbreviations, formats, and style
 - Decimals and fractions
- Dosing device accompanying the product
 - Consistency with labeling dosing directions

The guideline document may be found at:

http://www.chpa-info.org/scienceregulatory/Voluntary_Codes.aspx#volumetricmeasure

Key points include the following:

1. Provide a statement(s) that 1) encourages a consumer to select the right dose, 2) use the dosing device that accompanies the product, and 3) keep dosing device with product/do not discard dosing device
2. Provide a definition of any volumetric unit of measure specified in the product's dosing directions using the following abbreviations and full text exactly:
 - a. "mL = milliliter"
 - b. "tsp = teaspoonful"
3. If space permits, use a dosing table format to provide dosing directions
4. Use milliliter as the preferred unit of measure in the dosing directions
5. Avoid use within labeling dosing directions of the following: tablespoon, cubic centimeters, cc, dram, fluid ounce, Fl. Oz., and dropper(ful).
6. Provide a calibrated dosing device with all products
7. Provide graduated markings on the dosing device that include dosage(s) specified in the dosing directions
8. Use contrasting graduated markings (e.g. etched or printed) so as to aid the readability of the measured liquid

These guidelines are currently being implemented on new and existing products, including children's liquid acetaminophen products.

MINIMIZING ACCIDENTAL UNSUPERVISED MEDICINE INGESTIONS

While many of CHPA's efforts through the CDC collaborative PROTECT initiative (See page 5) address the administration of medicines in order to reduce therapeutic errors, such as inclusion of dosing devices with OTC products and the voluntary volumetric measures guideline outlined above, CHPA is moving forward with an educational campaign to address the overwhelming cause of medicine-related pediatric emergency-department (ED) visits: unsupervised medicine ingestions.

As part of the private-public partnership with the Centers for Disease Control and Prevention, CHPA and other organizations have taken a systematic approach to the issue of reducing medication errors. This partnership—the PROTECT initiative—initially undertook a root-cause analysis across the entire medicine category. This analysis clearly points to unsupervised medicine ingestions by children as the leading cause of all medicine-related, pediatric ED visits.

Educational Campaign: Up and Away and Out of Sight

The mission of the educational campaign was borne from these insights. To further understand the levels of awareness and the attitudes among parents and other caregivers, CHPA and the CDC conducted focus groups in 2010 on behalf of the initiative. The focus groups took place in Oakbrook Terrace, Illinois; Chicago, Illinois; and Atlanta, Georgia. The groups were heavily weighted toward mothers, with fathers and grandmothers also represented. There was one group of Latinas and one group of African-American mothers. Education and income levels were varied.

The focus groups confirmed that crucial caretaking audiences are generally aware of the need for safe medicine storage and the danger that unsafe storage may pose. Their behaviors, however, often are influenced by whether or not they need to take a particular product daily. Daily products, such as certain prescription medications and vitamins, typically are kept in a location that is in plain sight, as a visual cue to remember to take the product. This attitude was verbalized in almost every group and thus informed the campaign's main goal to serve as a reminder of the importance of safekeeping and the risks of unsafe storage for every medication.

The educational campaign—Up and Away and Out of Sight—is designed to remind parents and other caregivers of the need for safe medicine and vitamin storage. It has a core set of messages, developed with the assistance of two plain-language experts from the CDC. The messages describe what safe storage is, the importance of using child-resistant caps, and behaviors that contribute to engendering respect for medicines among children. A final message was crafted to give parents a resource—the national poison control helpline—should prevention efforts fail. These draft messages were tested and refined based on the focus groups' feedback. These messages were integrated into various educational products and put through three rounds of reviews among the PROTECT participants as well as an external health literacy professional. PROTECT participants include CDC, FDA, healthcare professional societies, consumer advocates, poison control representatives, academics, and health literacy experts.

The campaign will officially launch in spring 2011. Components include a pamphlet, public service announcements (PSA), digital outreach, and partner communications. Already CHPA has begun communicating Up and Away's safe storage messaging through a PSA in *PARADE Magazine* (October 2010, *see next page*), educational workshops with the National Head Start Association (April 2010 and April 2011), and a webinar with the National Association of Child Care Resource and Referral Agencies (August 2010).

Measurements and Evaluation

Evaluation is an important element of the campaign. In addition to social media and media metrics to understand the reach of the initiative, CDC is taking leadership in assessing awareness, attitudes, and behaviors and impact moving forward.

- CDC will work with the American Association of Poison Control Centers to design a protocol to track the number of calls to poison control reporting unsupervised medicine ingestions by children age 5 and younger.
- The CDC Medication Safety team will conduct an annual analysis of the National Electronic Injury Surveillance System: Cooperative Adverse Drug Events Surveillance System (NEISS-CADES) data of ED visits of children age 5 and younger caused by unsupervised medicine ingestions.
- CDC will ensure that the nationally representative HealthStyles Survey includes questions regarding safe medicine storage awareness and behaviors. The baseline survey will be conducted in June 2011, with questions repeated yearly to assess shifts in awareness, attitudes, and behaviors.



Quick

can you spot the medicine
before your 2-year-old does?

It's important. Every year, 60,000 children wind up in emergency rooms because they have gotten into medicines outside of their parent or caregiver's sight.

Remember to put every medicine and vitamin away—out of reach and out of sight—every time you use them. If your child ever takes a medicine out of your supervision, call the local poison control helpline at 800.222.1222 for help.

Keep your kids safe by keeping medicines safely out of their reach and sight.

OTCsafety.org

Public service announcement in *PARADE Magazine*, October 2010

CHPA EDUCATIONAL ACTIVITIES REGARDING ACETAMINOPHEN

Acetaminophen is found in both prescription and OTC pain-relief and fever-reducing medicines. It is the most commonly used active ingredient and present in over 600 medications. Following the June 2009 FDA advisory committee, CHPA worked with the American Pharmacists Association to create the Acetaminophen Awareness Coalition, a forum for stakeholders to convene and work together to address acetaminophen-related issues and educational needs.

The Acetaminophen Awareness Coalition was formed in August 2009 and formalized in January 2010. The goal of the coalition is to educate consumers and patients on how to use medicines containing acetaminophen appropriately and to help change behaviors that could lead to an unintentional acetaminophen overdose. Through outreach to healthcare professionals, patients, and consumers, the coalition works to ensure that acetaminophen is used only as directed or labeled.

Members of the Acetaminophen Awareness Coalition

The coalition includes the following organizations:

- Alliance for Aging Research
- American Academy of Nurse Practitioners
- American Academy of Physician Assistants
- American Pain Foundation
- American Pharmacists Association
- CHPA Educational Foundation
- National Association of Boards of Pharmacy
- National Association of Chain Drug Stores
- National Consumers League
- National Community Pharmacists Association
- National Council on Patient Information and Education
- FDA and the CDC are special advisors to the coalition

Awareness and Attitudinal Research

It should be noted that the goal of the coalition is to affect behaviors in order to prevent unintentional overdose. To help understand behaviors and effective tools to change them, the coalition conducted research.

In late 2009, CHPA fielded surveys on behalf of the coalition (Binder 2009). The surveys polled adults to assess awareness and attitudes concerning both prescription acetaminophen-containing medicines in general. The prescription survey involved 900 prescription acetaminophen users and its companion survey involved 1000 nonprescription users.

The overall objectives of the surveys were to:

1. Establish a quantitative baseline for Rx and OTC acetaminophen attitudes and knowledge
2. Identify attitude and knowledge items that could pose risk to be addressed through Acetaminophen Awareness Coalition efforts
3. Seek to identify a meaningful sub-group where risk-oriented attitudes or less knowledge may be more prevalent

Taken as a whole, the surveys found Rx and OTC acetaminophen products are important to many consumers, leading to a considerable investment of time and attention to relevant information. For example:

- Almost six in 10 OTC consumers (57 percent) have taken acetaminophen medications in the past six months (either alone or in a combination medicine).
- Virtually all consumers seek out important information about their new acetaminophen medicines. For example, 92 percent of OTC users and 95 percent of Rx users report they look for directions for how much of the medicine to take. 90 percent of prescription users and 81 percent of OTC users report they look on the label for warnings about possible side effects.
- Acetaminophen users rely heavily on the label for determining how much of a medicine—Rx and OTC—to take. Eighty-seven percent of both OTC and Rx users report they always or most times look at the instructions on the product label to determine how much to take.
- Many users will also seek out information on how much medicine to take from healthcare professionals at least occasionally: 79 percent of Rx users report they always, most times, or sometimes consult with their doctor for this purpose, and 40 percent of OTC users report they always, most times, or sometimes consult with their doctor or nurse.

Both OTC and Rx users express a fairly high level of general awareness with acetaminophen products, including risk. For example, 87 percent of OTC users and 84 percent of Rx users strongly or somewhat agree acetaminophen products are serious medicines and can do serious harm if misused.

One risk-oriented knowledge gap that the survey may have revealed is a lack of in-depth ingredient awareness. In most cases, less than one-half of users were able to correctly identify the active ingredients in medicines they reported using (unaided, open-ended recall). Rx users were especially prone to have problems with unaided, open-ended active-ingredient recall. Approximately two-thirds of survey participants showed also a lack of awareness of risks associated with acetaminophen medicines (no difference between OTC and Rx products).

The vast majority of individuals responded that they would seek out extensive information when they take a new acetaminophen medicine for the first time. No specific demographic or sub-group could be identified as being at greater risk.

Know Your Dose Campaign

Overall, the survey provided insights to guide the direction of the Acetaminophen Awareness Coalition's core educational messages to:

- Emphasize the importance of reading and following label directions.
- Know if your medicines contain acetaminophen.
- Never take two medicines that contain acetaminophen at the same time.
- Reassure consumers that, when used as directed, medicines containing acetaminophen are safe and effective, but taking more than directed—an overdose—can cause serious liver injury.

The coalition has created the Know Your Dose campaign to reinforce the educational messages for appropriate acetaminophen use. The home of the campaign, as well as the coalition, is KnowYourDose.org.

As the Know Your Dose campaign is specifically focused on utilizing healthcare providers as trusted messengers of healthcare information, a point-of-care strategy was designed with materials that providers will find useful and easy to distribute. Information cards have been developed by the coalition for placement in doctors' offices, at pharmacy counters, and at in-store health clinics. A cardboard holder also has been crafted to contain the cards and make displaying them easier for the provider (*See next page*). A wall poster has been developed, as well as a thirty-second video for use on in-store and clinicians' office closed circuit television channels. All materials are available at no cost to providers and are also available electronically.

The launch of the KnowYourDose.org website is April 2011. The campaign elements will begin distribution in May 2011. In addition to the coalition members, a great deal of targeted outreach has been conducted, with a number of other groups lining up to participate in this educational campaign. Anticipated partnering organizations include various disease groups, health clinic organizations, and associations that help the underserved with health information. In addition, a number of for-profit pharmacy chains also have expressed interest in making educational resources available to their customers.

As the campaign moves forward, measurements of reach and distribution will be collected and distributed to members of the coalition. In addition, the baseline survey conducted with David Binder Research will be repeated in order to assess the campaign's effects on ingredient awareness, attitudes, and behaviors.

ACETAMINOPHEN is in more medicines than you might think



ACETAMINOPHEN is the most common drug ingredient in America. It is found in more than 600 different types of prescription and over-the-counter medicines, including pain relievers, fever reducers, and sleep aids as well as cough, cold, and allergy medicines.

When used as directed, acetaminophen is safe and effective. But there is a limit to how much you can take in one day. Taking more acetaminophen than directed is an overdose and can lead to liver damage.

Follow three simple steps when using acetaminophen:

▶ **ALWAYS READ AND FOLLOW THE LABEL**

Never take more medicine than the label says. Taking more acetaminophen than directed is an overdose and can lead to liver damage.

▶ **KNOW IF YOUR MEDICINES CONTAIN ACETAMINOPHEN**

It is important to check the active ingredients in all of your medicines to see if they contain acetaminophen. On over-the-counter medicines the word "acetaminophen" is listed on the front of the package or bottle and in the active ingredient section of the Drug Facts label. On prescription labels, acetaminophen is sometimes listed as "APAP," "Acetam," or other shortened versions of the word.

▶ **NEVER TAKE TWO MEDICINES THAT CONTAIN ACETAMINOPHEN AT THE SAME TIME**

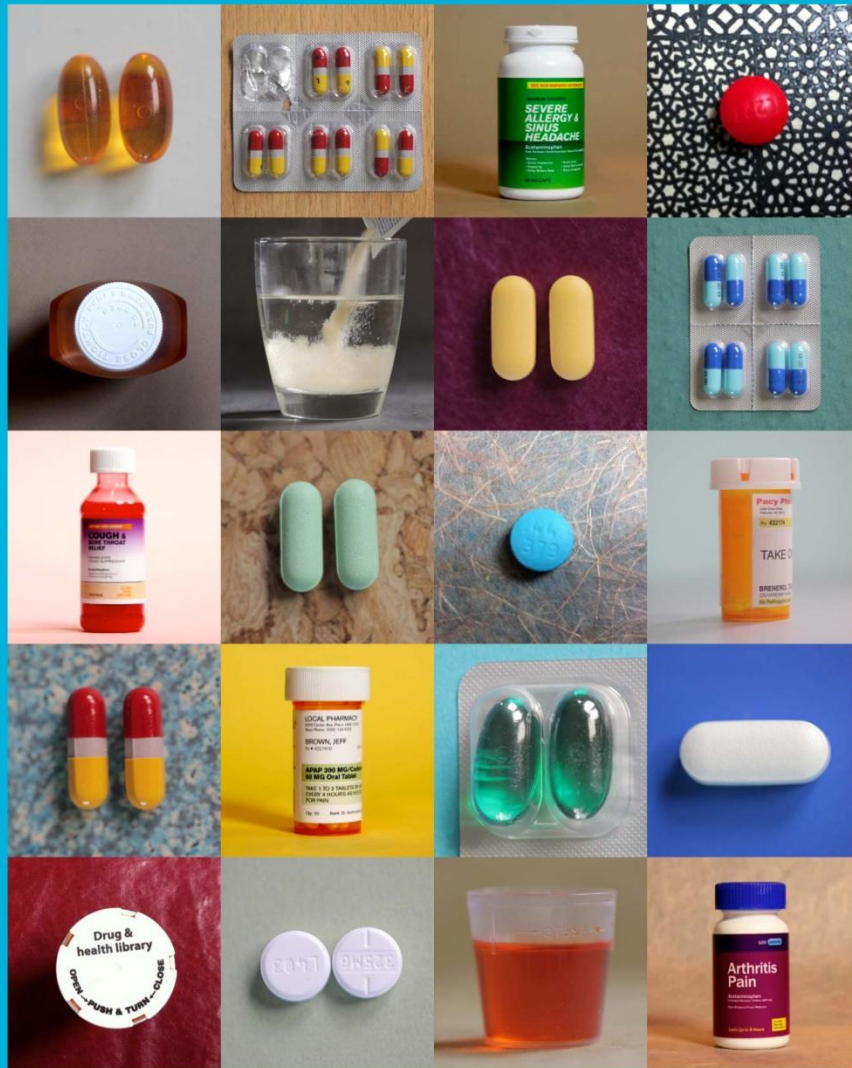
You can take too much acetaminophen if you use more than one medicine that contains acetaminophen at the same time. Always check the labels of your prescription and over-the-counter medicines to see if they contain acetaminophen.

For more information, talk to your healthcare professional or visit

KnowYourDose.org
Acetaminophen Awareness Coalition



The Acetaminophen Awareness Coalition has produced a number of materials for consumers and patients on the appropriate use of acetaminophen. Those materials include a two-sided information card and a holder, to make display and distribution easier for healthcare providers.



ACETAMINOPHEN

is in more medicines than you might think

It's the most common drug ingredient in America, found in more than 600 different prescription and over-the-counter medicines, including pain relievers, fever reducers and sleep aids as well as cough, cold and allergy medicines. On prescription labels, acetaminophen is sometimes listed as "APAP," "Acetam," or other shortened versions of the word. When used as directed, acetaminophen is safe and effective, but there is a limit to how much you can take in one day. Taking more than directed is an overdose and can lead to liver damage. So know your dose – always read and follow the label and never take two medicines that contain acetaminophen at the same time.

For more information, talk to your healthcare professional or visit KnowYourDose.org
Acetaminophen Awareness Coalition

The Know Your Dose Campaign also includes a wall poster (pictured above) for display in providers' offices.

REFERENCES

AAFP / American Academy of Family Physicians. FamilyDoctor.org. Fever in Infants and Children.

Available online at:

<http://familydoctor.org/online/famdocen/home/children/parents/common/common/069.html>

Accessed April 06, 2011.

AAP / American Academy of Pediatrics. Shelov PS (editor-in-chief) [et al.]. Caring for Your Baby and Young Child: Birth to Age 5. A Bantam Book. Fifth edition / October 2009.

AAP / American Academy of Pediatrics. HealthyChildren.org. Medications Used to Treat Fever.

Available online at: [http://www.healthychildren.org/English/health-](http://www.healthychildren.org/English/health-issues/conditions/fever/pages/Medications-Used-to-Treat-Fever.aspx)

[issues/conditions/fever/pages/Medications-Used-to-Treat-Fever.aspx](http://www.healthychildren.org/English/health-issues/conditions/fever/pages/Medications-Used-to-Treat-Fever.aspx) Accessed April 06, 2011.

AAP & AAFP American Academy of Pediatrics and American Academy of Family Physicians. Clinical Practice Guideline. Diagnosis and Management of Acute Otitis Media. Pediatrics. 2004; 113:1451-1465.

AAP & APS American Academy of Pediatrics and American Pain Society. The assessment and management of acute pain in infants, children, and adolescents. Pediatrics. 2001; 108:793-797.

Binder D. Research for CHPA and Acetaminophen Survey – OTC users. December 2009.

Cherry DK, Woodwell DA, Rechtsteiner EA. National Ambulatory Medical Care Survey: 2005 Summary. Advance Data From Vital and Health Statistics, No. 387. June 29, 2007.

CPS / Canadian Pediatric Society. Caring for Kids.cps.ca. When Your Child is Sick. Fever and

Temperature Taking. Available online at: <http://www.caringforkids.cps.ca/whensick/Fever.htm>

Accessed April 06, 2011.

Crocetti M, Moghbeli N, Serwint J. Fever Phobia Revisited: Have Parental Misconceptions About Fever Changed in 20 Years? Pediatrics. 2001;107:1241-1246.

Federal Register March 9, 2011. Docket No. FDA-2011-N-0002, OC 201138. Joint Meeting of the Nonprescription Drugs Advisory Committee and the Pediatric Advisory Committee; Notice of Meeting. Pages 12972-12973 [FR Doc. 2011-5284] [OFR PUB] Meeting on May 17, 2011.

FDA / Governale LA. Office of Surveillance and Epidemiology. OTC and Prescription Combination APAP Use. November 30, 2006. Available at:

<http://www.fda.gov/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/DrugSafetyandRiskManagementAdvisoryCommittee/ucm161515.htm> Accessed April 06, 2011.

FDA / Governale LA. Office of Surveillance and Epidemiology. OTC and Rx Acetaminophen Market Overview Years 2004 – 2008. June 29, 2009. Available at: <http://www.fda.gov/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/DrugSafetyandRiskManagementAdvisoryCommittee/ucm171562.htm> Accessed April 06, 2011.

FDA / Karwoski CD. Division of Drug Risk Evaluation. Briefing Document Acetaminophen Containing Products, Safety Issue: Hepatotoxicity. August 02, 2002. Available at: http://www.fda.gov/ohrms/dockets/ac/02/briefing/3882b1_02_C-Acetaminophen%20Hepatotoxicity.pdf Accessed April 06, 2011.

FDA / Manthripragada A et al.. Office of Surveillance and Epidemiology. Characterization of Acetaminophen Overdose and Related Hepatotoxic Events. June 29, 2009. Available at: <http://www.fda.gov/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/DrugSafetyandRiskManagementAdvisoryCommittee/ucm171562.htm> Accessed April 06, 2011.

Franklin RL, Rodgers GB. Unintentional Child Poisonings Treated in United States Hospital Emergency Departments: National Estimates of Incident Cases, Population-Based Poisoning Rates, and Product Involvement. *Pediatrics*. 2008;122:1244-1251.

Jacobson BJ, Rock AR, Cohn MS, Litovitz T. Accidental Ingestions of Oral Prescription Drugs: A Multicenter Survey. *American Journal of Public Health*. 1989; 79:853-856.

Kaufman DW, Kelly JP, Rosenberg L, Anderson TE, Mitchell AA. Recent Patterns of Medication Use in the Ambulatory Adult Population of the United States. *The Slone Survey*. *JAMA*. 2002; 287:337-344.

Kogan MD, Pappas G, Yu SM, Kotelchuk M. Over-the-counter Medication Use Among US Preschool-age Children. *JAMA*. 1994; 272:1025-1030.

NIAID / National Institute of Allergy and Infectious Diseases. The Common Cold. December 2004. Available at: http://www.idph.state.ia.us/adper/common/pdf/abx/tab4_niaid_common_cold.pdf Accessed April 06, 2011.

NICE / National Institute for Health and Clinical Excellence. National Collaborating Centre for Women's and Children's Health. Feverish Illness in Children: Assessment and Initial Management in Children Younger Than 5 Years. London (UK): May 2007. Available online at: <http://www.nice.org.uk/nicemedia/live/11010/30523/30523.pdf> Accessed April 06, 2011.

Niska R, Bhuiya F, Jianman Xu. National Hospital Ambulatory Medical Care Survey: 2007 Emergency Department Summary. *National Health Statistics Report*, No. 26, August 6, 2010.

Raofi S., Schappert SM. Medication Therapy in Ambulatory Medical Care: United States, 2003-04. *Vital Health Statistics* 13. 2006; 163:1-40.

RACGP / The Royal Australian College of General Practitioners. Family Doctor Home Advisor. Fever in Children. Available online at:

http://www.racgp.org.au/familyhealth/Fever_in_children_child

Accessed April 07, 2011.

Schillie SF, Shehab N, Thomas KE, Budnitz DS. Medication Overdoses Leading to Emergency Department Visits Among Children. *American Journal of Preventive Medicine*. 2009; 37:181-187.

Setlik J, Ho M, Bond CR. Emergency Department Use After Pediatric Pharmaceutical Ingestion: Comparison of Two National Databases. *Clinical Toxicology*. 2010; 48:64-67.

Sullivan JE, Farrar HC, and the Section on Clinical Pharmacology and Therapeutics, and Committee on Drugs (American Academy of Pediatrics). Clinical Report—Fever and Antipyretic Use in Children. *Pediatrics*. 2011; 127:580-587.

Tzimenatos L, Bond GR, Pediatric Therapeutic Error Study Group. Severe Injury or Death in Young Children From Therapeutic Errors: A Summary of 238 Cases From the American Association of Poison Control Centers. *Clinical Toxicology*. 2009; 47:348-354.

Vernacchio L, Kelly JP, Kaufman DW, Mitchell AA. Medication Use Among Children <12 Years of Age in the United States: Results From the Slone Survey. *Pediatrics*. 2009; 124:446-454.