

Adolescent Over-the-Counter (OTC) Drug Product Use: A Public Workshop
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This public workshop was sponsored by the Food and Drug Administration (FDA), the National Institutes of Health (NIH), and the Consumer Healthcare Products Association (CHPA).

Introduction

The purpose of this workshop was to gain an understanding of current use of OTC drug products by adolescents, including adolescent decision-making skills (compared with adult skills) and other factors influencing adolescent OTC drug product use. Information gathered at the workshop will be used to identify when it would be most appropriate for consumer studies on OTC drugs to enroll adolescents and to define the type of consumer research and study designs needed to support OTC drug product approval in the adolescent population. The workshop will help inform FDA in its efforts to assure the safe and effective use of OTC drug products by adolescents and provide guidance to NIH in developing clinical trials of OTC drug products in adolescents. The workshop will further understanding of the physiological and psychological differences and similarities between adolescents and adults, which may have an impact on adolescents' decisions about OTC drug use and may define research priorities for assessing the differences in drug use decisions. In addition, the workshop is aimed at designing efforts to encourage appropriate OTC drug product use by adolescents. It is hoped that such efforts will foster appropriate use when adolescents become adults.

OTC drugs are FDA-regulated drug products that are available without a prescription. Other health care products (for example, dietary supplements) were beyond the scope of the workshop. Adolescents use OTC drug products from a wide range of therapeutic categories (including fluoride toothpastes, acne drug products, and pain relievers) and with varying degrees of parental oversight. Although clinical and consumer behavior studies for OTC drugs have enrolled various populations, few studies have included adolescents. Therefore, limited information on adolescents' use of OTC drug products has been collected regarding the magnitude of their use, the types of products they use, factors that influence their use, and their ability to understand and follow directions provided on OTC labels. There is a need to learn more about adolescents' decision-making skills as they relate to the use of OTC drug products

The workshop addressed the following topics:

- Current OTC drug product use by adolescents
- The influence of adolescent neurocognitive development on decision-making skills and OTC drug product use by adolescents
- How best to communicate product information directed toward adolescents
- Future actions and research agendas, including studies regarding consumer behavioral issues
- Mechanisms to promote appropriate and optimal use of OTC drugs by adolescents.

Using Clinical Research to Inform Regulatory Decisions for OTC Drugs: Understanding Consumer Behavior

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Because there are both potential risks and benefits of OTC access, the benefits of availability of a drug without involvement of a learned intermediary must be weighed against the risks. The OTC product label is the critical tool for informing consumers as to the proper use of an OTC drug. It may be the sole source of information at the time of purchase and must guide all aspects of self-management of therapy related to both indication and drug use. Thus, design and validation of the OTC label is central to an OTC development program and regulatory decision making.

When a prescription drug is proposed for switching to an OTC product, key data are needed to demonstrate that the product's label is effective. Key messages must be identified, including indications, directions, and warnings for when not to use the drug and when to discontinue use. The wording for the key messages must be developed and organized into the proposed label.

An essential component of label development is determining whether a typical consumer understands the label. Label comprehension studies are a critical tool to answer this question. Typically, study participants are provided the proposed label(s) and asked a series of questions about the drug. Study recruitment is designed to enroll a population similar to consumers who would consider using the product. Enrolling the appropriate population allows generalizability of study results. One concern with label comprehension studies is whether they truly measure comprehension or a universal tendency toward "safe" response in a testing scenario. In addition, label comprehension may not translate to actually following instructions. These studies do not measure the safe and effective use of the OTC drug product.

A more relevant question for an OTC drug product label is: Does the proposed label guide consumer behavior in the use of the OTC candidate? Self-selection and actual-use studies are clinical trials that provide information about how consumers make decisions and use the drug in the real-world OTC setting. The major endpoints are whether consumers appropriately self-select and self-manage the course of therapy. The goal of these studies is to help predict marketplace consumer behavior. Ultimately, the results of clinical research will inform OTC regulatory decision making.

Currently, there is a need for the continued evolution of research methodologies for conduct of OTC trials. These trials should have prespecified objectives/hypotheses, predefined benchmarks of adequate comprehension/behavior rates, and robust statistical approaches. Specific questions about a specific switch necessitate specific trial designs. Because results for one population should not be extrapolated to another, concerns about a specific population require studying that population. There is a need for validation by bridging to postmarketing research of OTC drugs. Researchers need to recognize influences that cannot be incorporated into trial design, such as advertising, peer pressure, and misinformation and rumors about a drug's effects.

Development of OTC Drugs for Adolescent Patients: What Is Known and What Is Needed

Lisa Mathis, M.D., Associate Director, Office of New Drugs, Pediatric and Maternal Health Staff, Center for Drug Evaluation and Research, FDA

An early assumption about drugs for pediatric populations was that there were no significant differences in dosing, absorption, metabolism, elimination, and toxicity for children, adolescents, and adults. Another assumption was that because adolescents are about the same size as adults, researchers could simply extrapolate down to age 12 years and get studies on younger children. However, studies with prescription drugs have revealed that extrapolations cannot be made with adolescents. Adolescents are different with regard to physical, cognitive, psychological, and social development.

Given previous information learned from studies of prescription drugs, one of the challenges for drug development for adolescents is whether researchers can assume similar pharmacologic effects for adolescents and adults. Extrapolation from adults to adolescents must be supported by scientific rationale and supportive studies. To this end, FDA has developed an algorithm for determining the need for pediatric studies using the principle of scientific necessity/extrapolation. Another challenge is whether researchers can assume that behavioral issues for adolescents (12–16 years) are the same as those for adults.

The FDA has been given tools to encourage and require studies in the pediatric population. Although studies have demonstrated that adolescents are different from smaller children and adults, greater efforts must be made to assess differences in physical, cognitive, psychological, and social development to meet medical needs of adolescents. Additional information is needed regarding:

- Adolescent development, behavior, and decision making
- How these developmental differences affect actual use by adolescents
- Whether adolescents must be studied separately from adults
- Whether this age group should be subdivided (for example, 12–14 years, 14–16 years, older than 16 years)
- Factors that will help promote appropriate use of OTC drug products, including communication.

Adolescent Therapeutics: Health Literacy and Use of OTC Products

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Under the Best Pharmaceuticals for Children Act (BPCA) of 2002, activities focused on cataloging off-patent drugs, identifying those used in children, and characterizing dosing, efficacy, and safety. The 2007 BPCA reauthorization broadened the focus beyond drugs, charging NIH to identify needs and gaps in pediatric therapeutics, develop proposed pediatric study requests, and implement studies that are not undertaken by the pharmaceutical industry.

Identifying needs and gaps in pediatric therapeutics includes the use of OTC drugs by adolescents.

Using OTC drugs provides individuals with confidence about regulating their health. Self-medication with OTC drugs usually begins during early adolescence and increases with age. Usage may begin as young as 11 years of age. Children with chronic diseases such as asthma may begin self-medication as young as 9 years of age. Studies indicate that adolescents and young adults may not self-medicate correctly or effectively. For example, a study of analgesic use for dysmenorrhea showed that a substantial proportion of the adolescent participants inappropriately used OTC medications. Studies have also shown that medication use varies with age, gender, and symptom. Many adolescents appear to be unaware of the toxicity of OTC drugs.

An important component for correct and effective use of OTC drugs by adolescents is health literacy, which is defined as the degree to which individuals have the capacity to obtain, process, and understand basic health information and services needed to make appropriate health decisions. Elements of health literacy include critical thinking and problem solving, responsibility and productivity, self-directedness, and effective communication. A study of high school and college students showed that adolescents read OTC drug labels for information about symptoms treated, ingredients, dosing, and side effects. Adolescent use other sources for health information, such as parents, health professionals, and schools. Despite their access to and use of the Internet, adolescents are less likely than adults are to seek health information on the Internet.

Household Survey Data on the Adolescent Use of OTC Medicines

Michele Weissman, Senior Vice President, Panel Consulting

Information Resources, Inc. (IRI) Consumer Network™ Panel integrates key data sets at the household level to characterize consumer behavior. The data sets include demographic data, purchase information, and causal data. IRI's MedProfile IV Survey is a tool that can provide detailed information on individual household members' OTC drug use. The survey was used to gather data on (1) condition incidence in teens compared with the general population and (2) condition treatment choices for adolescents 18 years of age and younger. Analyses of the data revealed the following:

- Adolescents 18 years of age and younger overindex for acne but underindex for allergies and menstrual pain. For all of these conditions, adolescents 18 years of age and younger are most likely to choose an OTC remedy.
- Adolescents 12–17 years of age account for 38 percent of acne remedies' volume and have the highest penetration and usage rate. Different brands have very different age group usage profiles.
- Males 18 years of age and younger are the single largest user group for one branded remedy, but they have one of the lowest pills-per-user rates.
- Adolescents 18 years of age and younger account for only 7 percent of the total internal analgesics category volume, at a volume-to-population index of 28, and most brands are no exception. However, a top menstrual branded product nets 30 percent of its volume from females 12–17 years of age.

- Preference for OTC remedies and affinities for particular brands within a category (although not necessarily for a category) show that the teen market is a viable one, in some cases without even direct targeting.

Teen Surveys on Marketed OTC Products

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Overall, the influences affecting the use of OTC products and product brands among teens vary according to the product in question. The influence of parents on teen OTC product and brand selection is key but varies by product category. A comparison of these influences on teens' use of acne treatment products and dental care products serves to demonstrate those differences.

A 2007 survey of the market for acne products among teens 13–17 years of age found that the use of OTC acne medications is most heavily influenced by the severity of the condition, the recommendations of family and peers, and the gender and age of the teen. This product category reflects a high level of teen involvement in product selection. Advertising appears not to be a particularly influential factor in brand selection. As might be expected, the use of OTC acne medication correlates to the severity of the condition. Both the age and gender of the teen affect the level of involvement in OTC acne treatment brand use.

A 2007 survey of the market for dental care products among teens 13–17 years of age found the use of dental care products is most heavily influenced by how serious teens are about maintaining good oral hygiene and the recommendations of their dentists or hygienists. Dental product brand use, however, is largely the result of the brand provided and used by adults in the household. Adolescent girls are somewhat more involved in brand selection of these products than are boys.

FDA Review of Prescription-to-OTC Consumer Studies Involving Adolescents

Bindi Nikhar, M.D., Medical Officer, FDA

The current health climate has fostered an increased interest in self-medication. There may be more OTC drugs available to adolescents, and the number of adolescents using OTC drugs may increase. Literature reports suggest that adolescent use of OTC medications starts around 11–12 years of age and increases with age. However, there is limited information regarding magnitude and patterns of use. Factors influencing use of OTC drugs may include parents, peers, media, social circumstances, and socioeconomic status. Adolescent decision-making skills and risk-taking behaviors regarding use of OTC drugs are not well studied. In addition, consumer studies (such as label comprehension, self-selection, and actual use) for prescription-to-OTC drug switches have often excluded adolescents. Enrolling adolescents in consumer studies presents numerous study design challenges and limitations (for example, recruitment, informed consent and assent, follow-up, and dropout).

There are several clinical implications about OTC drug use by adolescents. Because adolescents may be less aware than adults are about toxicities of OTC drugs, there are safety concerns (for

example, overdose). Clinical diagnosis may be confounded by overlooking OTC medications (adolescents may not be as forthcoming as adults about their use of OTC drugs).

The process of switching a drug from prescription to OTC requires a New Drug Application (NDA). Considerations for a switch include adequate self-recognition of the condition, successful self-treatment of the condition, and safe and effective use of the product. Switch candidates must demonstrate an acceptable margin of safety based on prior prescription marketing experience and adequate labeling (OTC labels are generally targeted to 8th grade literacy levels). Self-treatment and self-monitoring should occur with minimal physician supervision. The benefits of the drug should outweigh its risks.

Consumer studies of OTC drug use by adolescents should consider the following:

- The primary motivation to self-select an OTC drug in adolescent age groups appears to be related to the underlying disease process.
- Purchase decisions by adolescents may be independent of self-selection and may be dependent on available funds and other influences.
- Adolescents may have less comprehension than adults have on some communication objectives.
- Follow-up is not optimal, and dropout rates are higher for adolescents.
- The number of FDA studies and the number of patients enrolled have been inadequate to allow determination of adolescent comprehension and decision making regarding use of OTC drugs.

Potential research topics for adolescents and OTC drug use include:

- The age at which self-administration of OTC medications starts and patterns of use
- Knowledge of potential toxicities of OTC drugs
- Decision making about self-selection and purchase
- Identifying relevant situations where differences in information processing and decision making between adolescents and adults warrant consumer studies (label comprehension, actual use) in adolescent age groups
- Methods of overcoming study design challenges involving adolescents.

Adolescent OTC Drug Use: Overview of Federal Trade Commission (FTC) Regulatory Authority

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A memorandum of understanding between FTC and FDA specifies that FTC has primary jurisdiction over advertising and that FDA has primary jurisdiction over labeling. Core violations in labeling of OTC drug products include false statements, omissions of material facts, and unsubstantiated efficacy and safety claims. FTC jurisdiction and analysis are not affected by compliance with FDA structure/function analysis, use of “FDA disclaimer,” or the classification of the article (for example, food, drug, or dietary supplement).

The FTC Act prohibits unfair or deceptive acts or practices in or affecting commerce and the dissemination of any false advertisement for the purpose of inducing the purchase of food, drugs,

devices, services, or cosmetics. Elements of deception include a representation, omission, or practice that is likely to mislead a reasonable consumer under the circumstances. The representation, omission, or practice must be “material.” Deception does not require knowledge of falsity, intent to deceive, actual deception, or substantial consumer injury. A false advertisement is an advertisement that is “misleading in a material respect.” A false advertisement need not contain any “false” statements.

In its analyses, FTC views an advertisement from the perspective of the target audience (for example, adolescents). An interpretation is presumed reasonable if it is one the respondent intended to convey. An interpretation may be reasonable even though it is not shared by a majority of consumers in the relevant class or by particularly sophisticated consumers. Where an advertisement conveys multiple implied messages, only one of which is misleading, a seller is liable for the misleading interpretation even if nonmisleading interpretations are possible. The primary evidence of advertisement meaning is the advertisement itself.

Many OTC drug products intended for use by adolescents have not been tested. There are no safety data or efficacy data for these products. For advertising directed at adolescents, FTC enforcement activities focus on the following:

- Efficacy of treatments for attention deficit/hyperactivity disorder
- Safety of sports and muscle-building products
- Safety of herbal street drug knock-offs
- Efficacy of cold remedies
- Growth enhancements
- Weight loss products.

Brain and Behavioral Development in Adolescence

Laurence Steinberg, Ph.D., Distinguished University Professor of Psychology, Temple University

Different brain systems mature at different times during the adolescent decade. The socioemotional system, which is linked to processing of emotions, social information, and reward and punishment, undergoes major changes in early adolescence around the time of puberty. The changes result in increased attentiveness to rewards, increased sensation-seeking, increased/easier emotional arousal (both positive and negative emotions), and increased attentiveness to social information. The cognitive control system is associated with working memory, logical reasoning, planning, and regulating impulses. This system develops gradually from preadolescence to the mid-20s. Its changes result in better impulse control, better emotion regulation, more foresight, more planning ahead, and better reasoning. The result of this differential development is that an “accelerator” is activated before a good “braking” system is in place.

Adolescence is a time of a still-maturing cognitive control system and still-maturing connections between socioemotional and cognitive control systems. As a result, individuals mature intellectually before they mature socially and emotionally. Intellectual abilities increase in early adolescence but plateau around age 16. Psychosocial maturity is stable from age 10 to age 14; it then steadily increases from age 14 into the late 20s. This maturity is reflected in gains in impulse control, delay of gratification, planning, future orientation, resistance to peer influence, risk perception, and risk aversion. However, certain situations (for example, social and emotional arousal) may exacerbate age differences in decision making. Middle adolescence is a period of heightened vulnerability to emotional and behavioral problems due to a timing gap between normative development of two brain systems. This differential development has implications for adolescent self-regulation and risk-taking behavior.

Adolescents' Concepts of Health and Wellness

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The World Health Organization defines health as a state of complete physical, mental, and social well-being and not merely the absence of disease and infirmity. Health is also defined as the actualization of inherent and acquired human potential through goal-directed behavior, competent self-care, and satisfying relationships with others while adjustments are made as needed to maintain structural integrity and harmony with relevant environments.

Early adolescents define health according to functional ability (running, performing sports), a good physique, and absence of illness. Adolescents define wellness in the context of friends and social groups, exercise, and food. Older adolescents define health according to health risk—avoidance behavior (not smoking, not using drugs), health-promoting behavior, and holistic integration. Socioemotional connections and physical activity are major components of health.

Adolescents, however, are not as knowledgeable about health and wellness as they perceive. They are somewhat knowledgeable about nutrition and eating disorders but are less knowledgeable about sleep and exercise. Adolescents who report health risks often do not consult a physician about risks. Although they may prefer information from a physician, adolescents are concerned about privacy issues and lack of provider availability. Sources of information may depend on the health scenario. For example, when seeking information about pneumonia, an adolescent may seek a parent or physician. For information about initiating sex, an adolescent may prefer a partner or friend.

Adolescent Decision Making

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To understand how adolescents use OTC drug label information to make decisions on appropriate use, investigators need to understand how adolescents process information. There have been no systematic studies comparing adult and adolescent decision-making competence (DMC). Studies focused on probability assessment have shown no differences between adults and adolescents. In addition, these studies have shown biases in probability assessment for both adolescents and adults.

A study of adolescent DMC measuring skills identified by decision-making theory (for example, probability assessment, value assessment) showed that better DMC scores correlated with fewer risk behaviors. These results hold even after controlling for socioeconomic status and general cognitive ability. Future activities could examine age effects on DMC, identify levels (or ages) at which people have good DMC, develop interventions to teach DMC (recognizing that DMC may not be used and that adolescents may need domain-specific messages), and adjust domain-specific messages, depending on DMC.

Effective interventions should have a theoretical basis that represents what experts know and that takes an interdisciplinary approach. They should be based on formative research with members

of the intended audience, using wording that adolescents understand, presenting decision contexts relevant to adolescents, and addressing decision-relevant gaps and misconceptions. Interventions should provide information and behavioral skills training. Existing interventions often lack the features of effective interventions and are often ineffective (if they are evaluated).

Adolescents and adults may have comparable DMC. However, a systematic study is lacking. Adolescents can make better decisions if provided with effective risk communication. Effective risk communication requires content that is evidence-based and useful to adolescents.

OTC-Relevant Lessons from the National Youth Anti-Drug Media Campaign

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The goal of the National Youth Anti-Drug Media Campaign was to prevent and reduce teen drug use by raising awareness and changing attitudes, intentions, and behavior. The campaign's outreach activities and continuous advertising served as reinforcement. Use of the media conferred status on issues and ideas; delivered clear, consistent, credible antidrug messages; informed, educated, and inspired; refuted myths and countered prodrug messages; and identified, linked, and promoted local resources. Three lessons were learned: understand the challenges (media and social environments; behavioral issues), know your audience (be sensitive to topic and adult "agendas" and shifting attitudes and beliefs), and invest in research (formative/process, performance tracking).

Over the past 5 years, adolescent abuse of prescription and OTC drugs has been increasing. Teens are abusing prescription and OTC drugs because they believe that these drugs provide a medically safe high. They believe the drugs are "safer" because they are manufactured by professionals, prescribed by doctors, and "you know what you're getting." A 2005 study of teens showed that 31 percent believed there was "nothing wrong" with using prescription drugs without a prescription and 29 percent believed prescription painkillers are not addictive. The lessons learned from the National Youth Anti-Drug Media Campaign can be applied to adolescent prescription and OTC drug use/abuse campaigns. Although parents, in general, are not getting enough information about prescription and OTC drugs, they can provide the biggest voice in educating adolescents regarding the use/abuse of these drugs.

Factors Promoting Safe and Effective Use of OTC Drugs by Adolescents: The Role of Parents and Parent-Adolescent Communication

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Common interventions to promote safe and effective adolescent OTC drug use include legal/policy-based strategies; strategies that alter the environment, context, or product itself; and educational/counseling strategies. Educational/counseling approaches include school-based, clinic-based, Internet/Web-based, and parent-based approaches, as well as the use of public service announcements (PSAs).

Disadvantages to parent-based approaches are that they generally do not work in dysfunctional families, they require parents' knowledge of OTC drugs, and adolescents are more peer-oriented than parent-oriented. However, parent-based approaches can be tailored to the needs and characteristics of the adolescent, allow flexible timing, and can be implemented in the context of a family's values. Parents have a broader role than just providing technical information. Key parenting dimensions include parent-adolescent communication, parental monitoring and supervision, parent-adolescent relationship satisfaction, and parental discipline strategies.

When considering information sources, adolescents focus on three key dimensions: expertise, trustworthiness, and accessibility. Although different sources can send the same message, an adolescent's differing perception of the sender's level of expertise may result in different behavioral responses. Message content may affect adolescent risk behavior and OTC drug abuse, depending on perceived advantages/disadvantages; norms, peer influence, self-concept, images, and social prototypes; emotions and affect; self-efficacy; and high-risk situations.

Message timing and context are important. With regard to OTC drug use, parental messages should include information on medicating conditions, indications, how to use a drug properly, warnings and what to do if an adverse event is experienced, when to stop using a drug, and joint monitoring plans. Parents who deliver the message should remember: Listen, do not lecture (use the Socratic method if possible), give respect to get respect, and apply the eight-factor theory of communication styles.

Health Literacy Among Adolescents and Young Adults

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According to the Institute of Medicine, 78 million U.S. adults (36 percent) do not have "the capacity to obtain, process, and understand basic health information and services needed to make appropriate health decisions." These adults have "basic" or "below basic" skills. Among adults with "below basic" skills, many are English-speaking (52 percent), White, non-Hispanic (37 percent), employed (40 percent), and graduated from high school or college (45 percent). Low health literacy is estimated to cost the U.S. health care system \$25 billion to \$70 billion per year.

Studies have shown that poor health outcomes are associated with low adult health literacy and that poor child preventive care is associated with low adult health literacy. Children of adults with low health literacy are twice as likely to be uninsured, lack a regular pediatrician, and lack a medical home. They are more likely to use urgent health services, particularly children younger than 5 years of age.

Several measurement tools have been used to estimate health literacy among adolescents and young adults, including the Rapid Estimate of Adolescent Literacy in Medicine (REALM-Teen), the Test of Functional Health Literacy for Adults (S-TOFHLA), and the National Assessment of Adult Literacy (NAAL). Using these tools, studies have assessed health literacy in adolescents (12 years of age and older) through young adults (up to 34 years of age). The rate of low health literacy in these studies ranged from 22 percent to 37 percent. In a study of adolescents' self-report of their health literacy, 22 percent reported difficulty understanding health information.

Factors known to influence adolescent use of OTC medication include social factors (ethnicity/generational status, peers/family), system factors (mass media, insurance and access, medication cost/packaging/marketing), and individual factors (gender, illness type and severity, parent/child health literacy).

A research agenda for adolescent health literacy includes:

- Better tools to measure adolescent health literacy
- Understanding the relationship between health literacy and health behaviors
- Understanding the relationship between health literacy and medication use
 - Adherence and error rates among adolescents with chronic illness
 - Moderating effects of medication cost and packaging
- Interventions to reduce literacy-related health disparities
 - Improving doctor–adolescent communication
 - Health-information kiosks to deliver tailored messages
 - Enhanced health literacy curricula in schools
 - Social marketing in mass media (for example, billboards, films, the Internet)
 - Electronic health information delivery systems.

Teen Marketing and Psychology Research

Cornelia Pechmann, Ph.D., Professor of Marketing, The Paul Merage School of Business, University of California, Irvine

Studies such as *Monitoring the Future, 2006*, have shown that adolescents' use and abuse of prescription and OTC drugs appears to be relatively low. It is not known whether the data collection in such studies has been adequate, and therefore, the full extent of the problem may not be known. The reasons for use and abuse may be similar across drugs, and user/abuser groups may be similar across drugs. Additional research is needed to compare the use, misuse, and abuse of OTC drugs and illicit drugs.

Marketers readily target adolescents with youth-focused media. Media selection is quantitative and research-based. They often use young and “edgy” role models to appeal to adolescents. Marketers try to persuade adolescents that using their products will lead to peer acceptance. Marketers likely target some OTC drug advertisements at adolescents, and they have tools and expertise to do so. Marketers likely use youth-oriented media and role models and peer-acceptance messages. Adolescents are likely responsive to OTC advertisements, encouraging marketers to continue to target them. Additional research is needed to compare adolescent-targeted OTC advertisement campaigns with tobacco and alcohol advertisement campaigns.

Some industries regulate adolescent-targeted advertising. Industry regulations include the Beer Institute Advertising and Marketing Code and the Cigarette Advertising and Promotion Code. OTC industry compliance with self-regulation is unknown, and the effects of self-regulation on drug use are unknown. The OTC drug industry can adopt voluntary marketing regulations, if specific problems are identified. Research is needed to determine the effects of voluntary regulations.

PSAs by the government or the OTC drug industry can be effective at informing adolescents about OTC abuse or misuse. However, because some PSAs do more harm than good, they must be carefully crafted and pretested. Research is needed to determine the need for PSAs, the type of PSAs, and the potential effectiveness of PSAs regarding OTC drugs and adolescents.

Design of Consumer Research in Adolescents

Julie Aker, B.S., M.T. (ASCP), President and CEO, Concentrics Research

In clinical research, investigators attempt to understand how a drug reacts physiologically in the person. In consumer research, however, investigators attempt to understand how a person reacts behaviorally with a drug. Research on adolescents' use of OTC drug products focuses on label comprehension, self-selection, actual use, and postapproval studies. Actual-use trials are designed to simulate "real life" and assess safety in an unsupervised OTC environment. There must be a balance between simulating the real-life experience and gathering useful information. Actual-use trials require a protocol, review by an institutional review board, informed consent, recruitment and enrollment, and data collection and analysis. These trials follow FDA guidance for industry regarding investigations of medicinal products in the pediatric population.

Actual-use studies have shown that parents purchase OTC drugs for children up to 15 years of age. Adolescents begin purchasing occasionally from 16 to 18 years of age. Purchases tend to increase when adolescents leave home. Older teens will purchase OTC drugs if they have to, but they prefer not to spend their money on these products. Parents generally make usage decisions for children up to 15 years of age. Adolescents begin making usage decisions around 16–18 years of age and generally follow usage guidelines that they have observed or been taught. Older teens are still largely influenced by what they have observed or been taught, but there is increasing influence from friends and coworkers.

Challenges for consumer research include label size and format, label comprehension and self-selection, assessing misuse and abuse in a study, and controlling for the influence of observation and peer experience. Potential solutions begin with the label, which should have clear and consumer-friendly language. The label should clearly state the drug's purpose and indications and should have simple, clear instructions. The label should be clear about benefits, risks, when to use the drug, and when to stop taking the drug. Potential solutions beyond the label include literacy and self-selection testing, education, postapproval studies, or surveillance of misuse/abuse and adverse events.

Summary and Conclusions

Research tools exist for preapproval studies of OTC-relevant behaviors, and these tools can be applied to adolescents. There is a need to focus on interpreting data gathered with these tools because the intent to heed is not uniformly high; some key messages are not well understood, particularly by adolescents with lower health literacy; and determinants of behavior are not clear.

Adolescents differ from adults with regard to their biology, physiology, behaviors/decision making, and neurodevelopment. Correlation between structure and function provide the scientific

foundation to the concept of maturation of decision making, which is relevant to judgment and risk taking in adolescents. It is not clear whether age is a reliable surrogate for maturation of decision making. Environmental factors such as peer presence interact with host factors, which may precipitate the need for new label warnings/messages.

With regard to OTC use with therapeutic intent, it is not clear whether there is a problem (that is, an absence of evidence is not evidence of absence). If there is a problem, is it one of judgment or one of knowledge/misconception? If there is a problem, its magnitude is a product of the frequency of nonheeding and the risk associated with the specific nonheeding. Nonheeding may not necessarily constitute a public health problem. The data on adolescent OTC drug use are characterized by breadth but not depth. Focusing only on use with therapeutic intent is likely to mask the heterogeneity of OTC drug use/abuse.

There is a mandate from the public (Congress) to understand factors specific to pediatric/adolescent use of drugs, and there is a need to understand the public health issues to apply the new learnings about the population and differentiate drug abuse from errors with therapeutic intent. Issue-specific interventions include broad public communications (for example, drug abuse campaign for effective elements) and drug-specific labeling to address adolescent behaviors identified.

Potential Components for Clinical Research About Adolescent OTC Drug Product Use

Potential components for clinical research about adolescent OTC drug product use include:

- Magnitude and patterns of use
- Surveillance studies of adverse events/overdose
- Potential for misuse and abuse
- Magnitude and patterns of misuse and abuse
- Dosage to produce adverse events
- Potential for harm under normal conditions
- Effects of chronic use
- Effects of misuse and abuse
- Safety profiles
- Drug–drug interactions (OTC drug products with prescription drugs, illicit drugs, and alcohol)
- Products with wrong dosing
- Products that are not effective
- Products that need new warnings/safety signals
- Self-selection and self-management
- Barriers to self-management (that is, inability to use products safely and responsibly)
- Dosing according to chronological age versus developmental stage
- Illnesses, diseases, and conditions that may be contraindications to OTC use
- Safety and efficacy in special populations
- Pharmacokinetics/pharmacodynamics as a function of chronological age and developmental stage.