VISUAL DISTRACTION AS A MEANS OF ENHANCING CHILD RESISTANCE

By

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ABSTRACT

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Despite advances improving packaging safeguards in recent years, unintentional child poisonings remain an important public health concern. From 2001 to 2008, more than half a million children 5 or younger visited an emergency room in the U.S due to possible poisoning by medication [3]. Our study attempts to extend early stage processing (i.e. capture a child's attention in an area of the package away from the closure system) to extend the time before opening. To do so, we applied a lenticular graphic, or a "visual distracter," to pharmaceutical vials and blisters. Distracters alternated between a frowning facial icon and the words "keep away" as the packages were moved. Two hundred and seven children between the ages of 24 and 51 months were tested in pairs.

The results for the vials suggest the presence of a visual distracter to be a promising approach for prolonging time to opening (P=0.0375 ; Treatments that contained distracters [ME= 103.05 seconds SE 26.10]; Plain Treatment [ME=36.64 seconds SE 20.34]) and may be particularly effective in preventing younger children (24 to 40 months of age) (P=0.0356) from successfully opening vials (LSM=0.085 CI [0.0246, 0.2538]) as compared to their counterparts 42-51 months (LSM=0.2414 CI [0.0813, 0.5337]).

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“Try to be a rainbow in someone's cloud.” - Maya Angelou

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KEY TO ABBREVIATIONS

ASTM - American Society for Testing and Materials

CPSC - Consumer Product Safety Commission

CR - Child-resistant

CFR - Code of Federal Regulations

CDC - Centers for Disease Control and Prevention

CTTE - the most commonly poisoned

Non CR - Non child-resistant

OTC - Over-the-counter

PPPA - Poison Prevention Packaging Act

SBS - Solid Bleached Sulfate

SAS - Statistical Analysis System

IB - Inattentional Blindness

AB - Attentional Blink

UCL - Upper Control Limit

LCL - Lower Control Limit

RFID- Radio-frequency identification

CHAPTER 1

Introduction

Child Resistant Packaging (or special packaging) was developed to keep small children from accessing a number of household products, including: drugs, cleaning agents and other household chemicals. The definition of “special packaging” provided by The Poison Prevention Packaging Act (PPPA) is:

> “Packaging is designed or constructed to be significantly difficult for children under 5 years of age to open or obtain a toxic or harmful amount of the substance contained therein within a reasonable time, and not difficult for normal adults to use properly, but does not mean packaging which all such children cannot open or obtain a toxic or harmful amount within a reasonable time [1].”

1.1 International regulations and standards of Child Resistant packaging

Poisonings have been a recognized cause of injuries among children under 5 years of age since the 1950s. The first poison control center was established in Chicago in 1953 in order to provide specialized diagnoses and treatments. After that, the US Congress drafted the Hazardous Substances Labeling Act in 1960, one of the most important early, preventive attempts. This law stated that “hazardous substances" had to carry on their labels specific, cautionary statements[2]. Another activity geared to the prevention and control of childhood poisonings occurred in 1966. Largely due to growing concerns around overdoses of children from the ingestion of aspirin, manufacturers voluntarily began to restrict the number of children's aspirin tablets in a single container to 36, $1\frac{1}{4}$ grain tablets, in order to

decrease the possibility of a child obtaining a toxic dose [3].

Perhaps most impactfully, in 1970, the Poison Prevention Packaging Act (PPPA) was enacted under Congress and signed by the President with issues of unintentional poisoning among young children highly motivating this legislation. FDA was responsible for enforcing the PPPA until 1973, when jurisdiction was transferred to the newly formed Consumer Product Safety Commission (CPSC)[4]. Since then, "special packaging" has been required for a number of pharmaceutical products and household substances in order to protect children from serious injury or illness.

The PPPA authorized testing procedures that are detailed in Title 16 Parts 1700 through 1702 of the Code of Federal Regulations (CFR). During testing, sequential panels of 50 children between the ages of 42 and 51 months (up to maximum of four panels of 50 or a total of 200 children) are tested in pairs to determine whether packaging qualifies as child-resistant or not. The children are given 5 minutes to try to open the package. If they fail to open their package within that time period, the children are given another 5 minutes to attempt to open the packages. Prior to the second five-minute trial, an opening demonstration is provided by the tester, and children are instructed that they may use their teeth if they wish.

If 80% are not able to perform the task, the package can be considered child resistant. However, the package's accessibility is another important factor that must

be considered and tested. A panel of 100 adults aged 50-70 years without overt or obvious physical or mental disabilities are tested as well. Contrary to the child testing, these subjects must be able to open *and properly close* the packages in a 5 minute time period. This five minute period provides an opportunity for the adult to familiarize themselves with new innovation and gain an understanding of how the package needs to be manipulated. If successful, the individual will repeat the test, with a one minute trial. Upon the successful opening of the package in the second trial, a pass is granted for that individual's test. If 90% of subjects are able to open and close the child-resistant package during both of the trial periods, it is considered to have passed protocol.

The US protocol has served as the basis for this type of testing globally [5]. Differences in other test protocols around the globe relate primarily to the size and composition of the test group, duration of the tests and some analytical procedures. The United Kingdom (UK) was the first European Union country to utilize CR packaging; the second country after the United States. The test standards that are used around the globe are referenced in Table1.1.

Table 1.1 Worldwide standards or regulations of Child Resistant packaging

Country	Act and Standards	Year	Difference
United Kingdom	BS 5321	1975	The standards differed primarily in sample size, sample composition and stringency. Standard BS EN 862 covered blister packs and other non-reclosables, but excluded those which contained pharmaceuticals. Adult tests were incorporated as the concept of adult open ability assumed increasing importance. For example the latest version of ISO 8317 (2004) has changed the

Table 1.1 (cont'd)

	BS 6652 BS EN 28317 BS EN 862 BS EN ISO 8317 BE EN ISO 14375	1985 1989 1997 2000	adult age range from 45 to 65 years inclusive to 50-70 years inclusive.
Canada	the Hazardous Products (Hazardous Substances) Regulations Consumer Chemicals and Containers Regulations CSA Z76.1-99 CAS Z76.2-00	1979 1988 2003 2005	Within the context of a child-resistant requirement, CCCR recognizes that containers which require a tool to open, such as typical paint cans (cylindrical and metallic) or soup-type cans, are considered to be child-resistant by design. However, In child resistant test protocols such as the CFR 1700.20 children are suggested to use their teeth. Thus, using one's teeth does not constitute using a tool.
Germany	DIN 55559 DIN EN14375 DIN EN ISO 8317	1979 2003 2004	
Italy	Regulation only UNI EN 14375 UNI EN ISO 8317	1984 2004 2005	
Australia	The Australian Standard AS 1928: Child-Resistant Packaging Requirements	1985 2001	
Netherland	Following DIN	1985	
New Zealand	NZS5825	1991	
India	IS 14233	1995	The India standard IS 14233 " Packaging Pharmaceutical Products- child resistant, temper proof packaging for solid dosage forms-code of practice " is similar to BS 7236. The package test is not carried out with children but is a mechanical test.

International standards exist for both reclosable and non-reclosable packaging and marketing authorization holders are required to demonstrate compliance with these standards as part of their application. ISO 8317 (2004), which

is equivalent to DIN EN ISO 8317 (2004), is the international standard for reclosable child resistant packaging. EN 862 (2005), equivalent to DIN EN 862 (2006), is the international standard for non-re-closable, child resistant packaging for non-pharmaceutical products. Besides that, EN 14375 (2003) which has replaced DIN 55559 is the European standard for non-reclosable child resistant packages for pharmaceutical products. This standard is especially relevant for blister packs, stick packs and granule bags.

1.2 Unintentional poisoning of children

Despite advances improving packaging safeguards in recent years, the unintentional poisoning of children remains an important public health concern. According to research from Cincinnati Children's Hospital Medical Center and the University of Cincinnati reported in the *Journal of Pediatrics*, from 2001 to 2008, more than half a million children 5 or younger visited an emergency room due to possible poisoning by medication. Perhaps more alarming, this same report indicates a 22% increase in accidental drug exposures even though the population of children only increased by 8% during the study period [6]. What's worse, according to a medicine safety report from Safety Kids Worldwide, during 2012 there were 63,952 visits to emergency departments for children 4 and under involving exposure to a medicine, either because of unsupervised ingestion or as the a result of a dosing error[7]. That's one child every 8 minutes. Among these, approximately 64,000 children, three out of four were unintentionally poisoned by their parent's (39%) or

grandparent's (38%) medications. Data reported by the Centers for Disease Control and Prevention (CDC) in their latest report (2013) further suggests the gravity of this issue. "Among the cases of poison exposures, ED visits for medication poisonings are most common in children under 6 years of age" and "one out of every 180 two-year-olds visits an emergency department for a medication poisoning"[8](Figure 1.1)

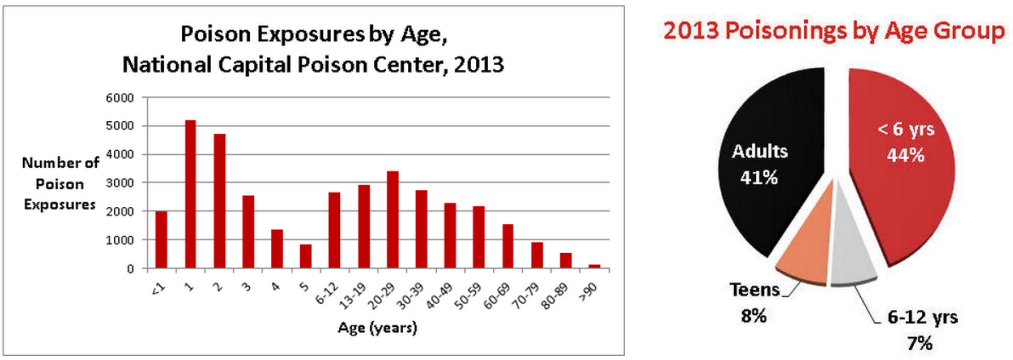


Figure 1.1 Poison exposures by age group (National Capital Poison Center, 2013)

Further compounding the aforementioned problems, are two other phenomena that cannot be ignored:

1. Children are becoming increasingly skillful at younger and younger ages [9]. Tablets, smartphones and gaming systems, many of which contain software applications and games intended for toddlers and preschoolers, have improved children's fine motor skills and made it easier for them to interpret symbols [10].

2. Children are around more medicine than ever before. The "typical" household is changing; increasing numbers of grandparents reside in homes with small children.

Data from the U.S. Census show that grandparents play a greater role than ever before in their grandchildren's lives. From 2005 to 2012, there has been a 23 percent increase in the number of grandparents living with their grandchildren, with

projections of 5.7 million in 2015 [11]. In 2012, more than seven million grandparents lived with their grandchildren. Seventy-four percent of grandparents who take care of young grandchildren take prescription medicine every day[12]. Perhaps more alarming, research from Safe Kids Worldwide suggests that grandparents commonly store medications in an easy-to-reach place, like on a nightstand or dresser (12%) where kids can get into it. They also found that 28% grandparents who regularly take care of grandchildren keep their medicine in easy-open containers or bottles with non-CR closures [13].

Every minute of every day, a concerned parent calls a poison control center after a young child is unintentionally overdosed. Even though an encouraging trend shows a 15% decline in the number of poison control center calls for medicine exposures in young children from 2009 (578,491 calls) to 2012 (489,742 calls) , this is still far too many children[14]. Protocol testing cannot guarantee that a child will never be poisoned because packages are child *resistant* not child *proof*. Thus, an effective design that decreases children's interest in packaging opening is the critical area this research focuses on.

CHAPTER 2

Current Design of Child-Resistant Packaging

According to the Poison Prevention Packaging Act (PPPA) of 1970, CR packaging is required to be difficult for young children to open within a reasonable time yet not pose an unreasonable burden for adults to use properly [15]. CR packaging was first mentioned in a publication (1959) written by researchers from Durham, NC who indicated the need to use “safety closures” for aspirin [16]. However, the concept was not widely adopted until 1970[17], when the United States enacted the Poison Prevention Packaging Act (PPPA). Requirements took effect in 1972, and the concept was originally applied to exclusively to drugs.

The CPSC defined special packaging as technically feasible, practicable and appropriate [18]:

> "Technical feasibility exists when technology exists to produce packaging that conforms to the standards. Practicability means that special packaging complying with the standards can utilize modern mass production and assembly line techniques. Appropriateness exists when packaging complying with the standards will adequately protect the integrity of the substance and not interfere with the intended storage or use."

In 1976, a Standard Classification of Child-Resistant Packages (ASTM D3475) was approved to define the type of motions, skills, or tools required for a particular type of child-resistant package. In the current edition, approved in 2003（D3475-03), thirteen categories of child-resistant packages were developed to organize the varying approach to child-resistant packaging intended for household use,

pharmaceutical, human healthcare , nutritional products and so on (Table 2.1).

Table 2.1 The ASTM classification of Child Resistant packages [19]

Type	Description
Type I	Reclosable Packaging-Continuous Thread Closure
Type II	Reclosable Packaging-Lug Finish Closure
Type III	Reclosable Packaging- Snap Closure
Type IV	Unit Non Reclosable Packaging-Flexible(Strip/Pouch)
Type V	Unit Non Reclosable-Rigid
Type VI	Unit Reclosable Packages
Type VII	Aerosol Packages
Type VIII	Non Reclosable Packages-Semi Rigid(Blister)
Type IX	Dispenser (Not intended to be removed)
Type X	Box or Tray Package
Type XI	Reclosable Packaging – Flexible
Type XII	Dispenser(may be removed)
Type XIII	Reclosable Packaging Semi Rigid(Blister)

In essence, there are five principle activities that have been used to develop child resistant packaging over the past several decades. These include: 1) requiring the user perform two deliberate and different simultaneous motions, 2) requiring the user to perform a hidden alignment, 3) requiring the user to have adult strength, 4) requiring the user to have an adult-sized finger or hand, and 5) requiring the user to have a tool [20]. This chapter presents a review of patents published in the US with CR features from 1970 to 2014, organized based on the previously mentioned activities for functionality. Packages have been included as examples below based on manufacturers' claims of child-resistance.

2.1 CR packages requiring the user perform two deliberate and different simultaneous motions.

The approach that requires two different simultaneous motions is commonly built into CR closures. The two most frequently used CR closure types are the press-

turn and squeeze-turn[21]. The "press and turn" closure is removed by applying downward force while simultaneously turning the cap. "Squeeze and turn" closures employ a free-rotating soft plastic over cap which engages an inner threaded cap or disengages a locking mechanism when sidewall pressure is applied. (Figure 2.1, 2.2)

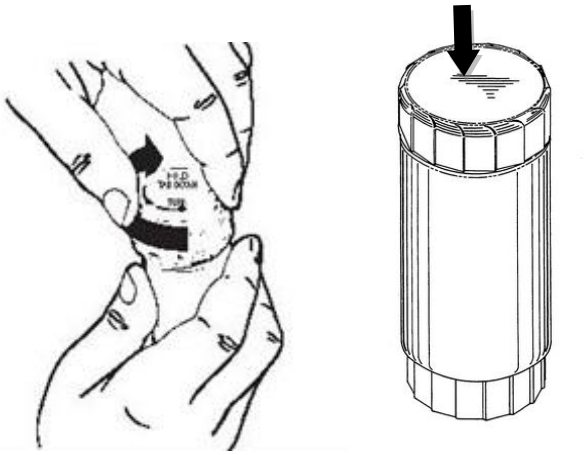


Figure 2.1 "Press and Turn" closure [22] (US5381912A, American Cyanamid Company.)

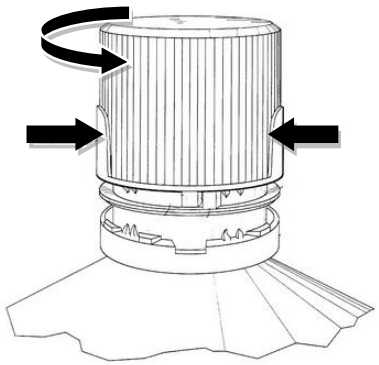


Figure 2.2 "Squeeze and Turn" CR closure with tamper indicating band [23] (US 5927527A, Rexam Plastics, Inc.)

Application of two dissimilar, simultaneous motions is not limited to systems of vials and caps; it is also applied to enhance child resistance in unit dose packaging. Blister packs have been designed to meet the CR requirement by performing dual motions for opening such as "press and pull" and "squeeze and pull" as well. An example of this approach is when a blister card is integrated into an outer container

(e.g. a paperboard carton or an injection molded outer shell) where access to the product is achieved by squeezing appropriate sections of the outer packaging while pulling simultaneously on the blister card it contains, exposing the blisters that contain the product. Subsequently, the product can be pushed through the lidding foil (Figure 2.3, 2.4).

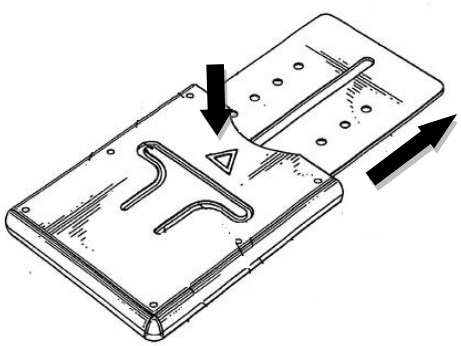


Figure 2.3 Blister pack container with “Press and Pull” release mechanism [24]
(EP 1562840B1, MeadWestvaco Corporation)

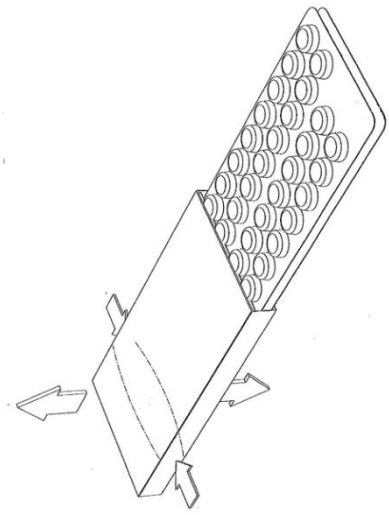


Figure 2.4 Side-Squeeze blister pack container [25]
(US 20110114512 A1, MeadWestvaco Corporation)

2.2 CR packages requiring the user to perform a hidden alignment.

“Combination-lock" closures use interrelated components formed into

closures which must be oriented specifically before the closure can be removed. A common example is the one-piece "line-up, snap-off closures" (Figure 2.5). A slight interruption of the threads on the container serves as an engagement point and a protrusion on the cap fits under the single thread. When the cap is turned, it becomes locked onto the container.

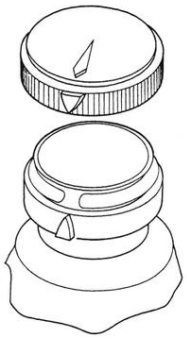


Figure 2.5 Combination-Lock closures which must be oriented before the closure can be removed [26](line-up, snap-off closures, Phoenix Closures Inc.)

Combination-locking mechanisms applied to blister packs are quite different. Combination-lock approaches require correct positioning of a series of tabs or keys. Locking tabs must all be shifted to unlocked positions in different directions so that they will no longer be interposed as barriers (Figure 2.6).

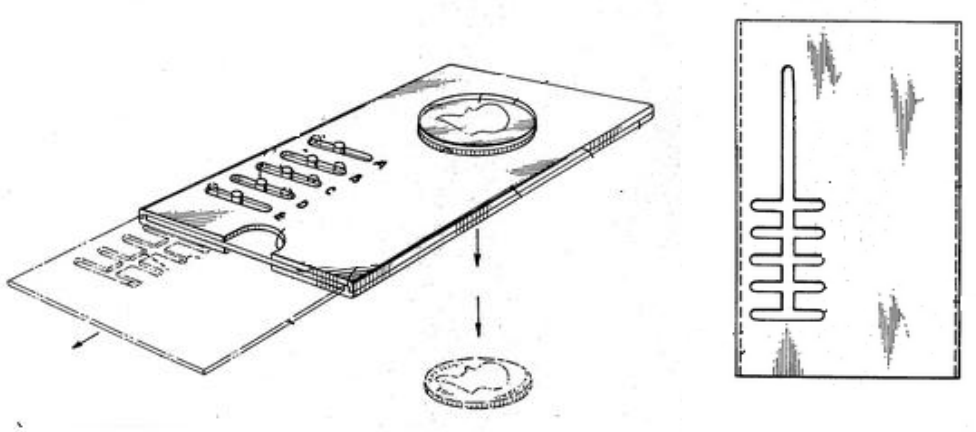


Figure 2.6 A Combination-Locked envelope type of approach to child resistance. This

security container requires alignment (of respective marks on the envelope container) is not originally designed for blister pack, but can hold medications [27].
(US 4187703 A, Product Dynamics, Ltd.)

2.3 CR packages requiring the user to have adult strength

Another approach to child resistance leverages the differences in strength that exists between children and adults. As indicated previously in this chapter, the most common CR closures necessitate pressing and/or turning actions, which thereby require strength from packaging users [28]. Once such example is blister packaging with safety backing (Figure 2.7). Not only does the design require sequential processes (remove the paper and then push the pill through the foil), the additional paper backing layer provides additional sealing engagement and significant pinch strength to be removed. By changing the gauge of the foil, further manipulations of force can be made regarding the necessary strength to push the dose through the backing material.

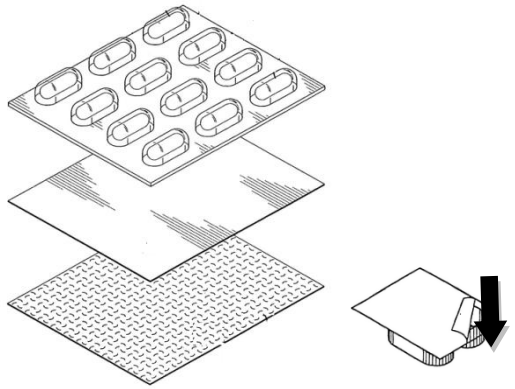


Figure 2.7 The blister package is formed by a receptacle substrate and an outer laminate[29] (US 8079475 B2，Sonoco Development, Inc.)

Many containers for hazardous chemicals leverage the difference in strength

paradigm. They require fingers that are fairly strong and agile (Hillman, U.S 4048050 and Heverly U.S4746008). However, this approach sometimes brings other issue by conflicting with senior-friendliness or accessibility for those with disabilities.

2.4 CR packages requiring the user to have an adult-sized finger or hand

Besides strength, anthropometrics, specifically hand size, is another physical characteristic that can be utilized to the benefit of CR designs. The closure or container can be developed with release elements only accessible by an adult-sized hand; for example, the package can be designed in such a way that a child's hand would not large enough to press both sides at the same time, while an adult's would. Figure2.8 provides an example of this approach. Here, adults are able to insert a single finger into the upper end of the cap in order to release its locking mechanism. The internal diameter of the cap is such that an infant or young child's finger is not large enough to displace all of the locking levers, and displacement of only a few of them is not effective to release the cap.

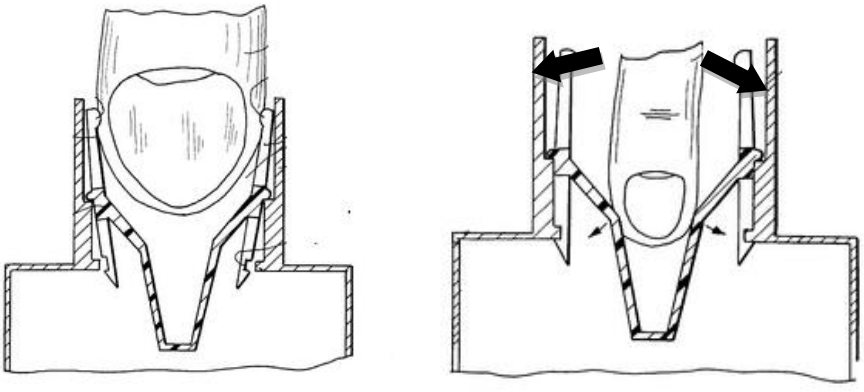


Figure 2.8 CR pill closure designed by considering the differences in finger size between adults and children [30]. (US 6112920 A, Lahaussois; Pierre)

This same approach has been taken with blister packaging. Figure 2.9 indicates this. In this blister, child-resistance is obtained by adding two actuating buttons that are spaced such that children would not be able to reach each with a single hand while adults would. Both locking buttons must be actuated at the same time in order to open the device. The spacing between the actuating members can be determined such that an adult's hand is large enough to actuate with one hand, but a child's hand is too small to do this (Figure 2.9).

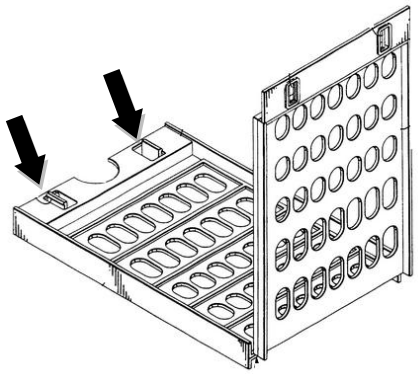


Figure 2.9 CR blister container with two spaced apart actuating buttons [31] (US 6338408 B1, Glaxo Group Limited)

2.5 CR packages requiring the user to have a tool

While the combination of dexterity, comprehension, and strength needed to open CR containers should be beyond that of young children, designers must also be sensitive to the fact that they must be readily understood and convenient for use by adults, many of whom may be frail or impaired. Another approach to enhancing child resistance is the development of designs that require access to, and the appropriate use of tools, such as a screwdriver or a coin. Figure 2.10 represents one design that leverages this approach.

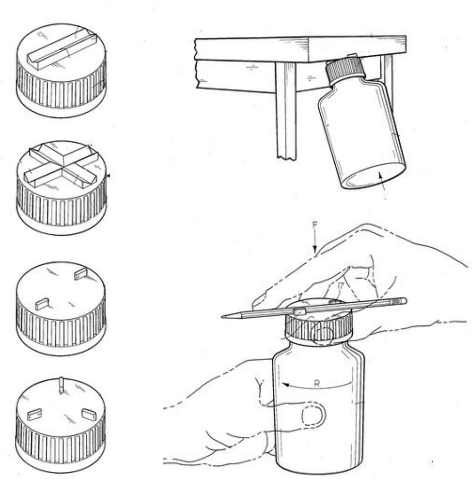


Figure 2.10 Child-Resistant closure with tooled access [32]
(US 4731512 A, Owens-Illinois Closure Inc.)

Some CR blister packaging is also designed that requires tooled access (Figure 2.11).

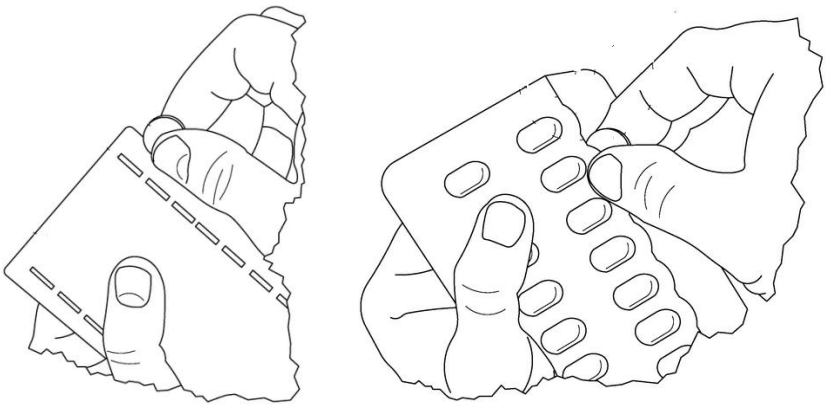


Figure 2.11 CR blister packaging with tooled access [33]
(US 8317026 B2, MeadWestvaco Corporation)

Appendix B contains a summary of the typical patents referencing child-resistant packaging published in the United States from 1970 to 2014. Among those reviewed, the majority of current CR designs focus on serving as a physical barrier (Table2.2). In contrast, in the past, little attention has been paid to the cognitive/perceptual features or how they may play a role in child resistance [34].

Table 2.2 Classification of motions, skills or tools required for a particular type of CR packages

1. Requiring the user perform two deliberate and different simultaneous motions	
Type	Description
Type I Reclosable Packaging-Continuous Thread Closure	1. Random push down while turning; no orientation of the push down force necessary. 2. Localized squeeze force while turning; the force must be applied to a designated location on the closure skirt. 3. Random squeeze while turning; no orientation of the squeeze force is necessary. 4. Holding a fitment while turning; two-handed operation is normally required. 5. Random lift while turning; no orientation of the lift force is necessary. 6. Localized lift of cap skirt or tab on closure while turning. 7. Localized push down while turning; force must be applied to a designated place on the top of the closure. 8. Localized push in while turning, force must be applied to designated place on closure. 9. Localized push back lever while turning, force must be applied to designated place on closure.
Type II Enclosable Packaging-Lug Finish Closure	1. Turn the top cap until stops, then push down and turn. 2. Turn the top cap until stops, then push down and turn. 3. Holding of fitment while turning; two-handed operation is normally required and no orientation of holding force is specified.
Type III Reclosable Packaging- Snap Closure	1. Downward pressure on top with simultaneous upward pull on edges. 2. Press to release and then lift hinged tab (dispensing cap); Press to release, follow by lifting force on tab (removable cap); Push up to release; Push in or up, or both, to release; Pull to release and lift hinged lid (dispensing cap). 3. Squeeze and lift two specific points simultaneously; Squeeze and lift one specific point simultaneously; Squeeze two points simultaneously to open 4. Squeeze two specific points simultaneously to unlock sides and then squeeze specific point on third side while lifting lids. 5.Random squeeze while turning and pulling up

Table 2.2 (cont'd)

Type VII Aerosol Packages	1. Localized squeeze while lifting removes over cap (actuates normally). 2. Hold fitment still while turning (actuates normally). 3. Hold fitment still while lifting (actuates normally) 4. Directional over cap-actuator requires sequential simultaneous pushing of locking device and actuator. 5. Press to release, lift hinged tab at center of the closure followed by an upward force on the tab to remove overcap (actuates normally). 6. Random push down while turning; no orientation of the downward force is necessary.
Type IX Dispenser (Not intended to be removed)	1. Finger pump (1) Directional pump must be oriented (by rotation to a second stop position) then pumped with finger; (2) Push tab while rotating directional pump to spray position, and then pump with finger. 2. Trigger pump (1) Press down on a point to release lock, rotate orifice to spraying position, and squeeze trigger;(2) Press in and up on orifice (lock cover) and squeeze trigger AFA Corp;(3) Push down on a point and slide it back to release lock, then rotate the orifice to the spraying position, and squeeze trigger.
Type X Box or Tray Package	1.Squeeze and slide to open 2. An asymmetrical neck bottle that uses a squeeze and slide cap. 3. Localized squeeze while lifting up, then pressing two tabs while lifting lid to open.
Type XI Reclosable Packaging – Flexible	1. Squeeze two specific points simultaneously, lift zipper tab and pull to open 2. Continuously threaded closure random squeeze while turning, no orientation of squeeze force is necessary.
Type XIII Reclosable Packaging Semi Rigid(Blister)	1.Press hold, pull out (parts remain together), push out 2.Press then flex and lift to open

2.Requiring the user to perform a hidden alignment

Type	Description
Type I Reclosable Packaging-Continuous Thread Closure	1. Set combination before turning 2. Align arrows, then push tab down, then turn.

Table 2.2 (cont'd)

Type III Reclosable Packaging- Snap Closure	1.Align two points then push up on tab or lip; Rotate then lift 2.Align two points, push down outer ring, then push up tab or lip
Type VII Aerosol Packages	1. Directional over cap-actuator must be oriented, and then pressed.
Type IX Dispenser (Not intended to be removed)	1. Line up arrows, and pull apart to open dispensing slot of a permanently attached two-piece unit. When the arrows are aligned, the two halves can be pulled apart to reveal a slot just large enough to dispense one tablet or capsule. 2. Combination lock, turning counterclockwise until it stops, then turning clockwise until arrow 1 on the closure aligns with the arrow on the bottle, and finally turning counterclockwise until arrow 2 on the closure aligns with the arrow on the bottle
Type X Box or Tray Package	1. Combination lock, multi-toggle, press down combination and slide or lift to open
Type XIII Reclosable Packaging Semi Rigid(Blister)	1. Slide blisters to align with holes in bottom of case, push out

3.Rrequiring the user to have adult strength

Type	Description
Type I Reclosable Packaging- Continuous Thread Closure	1 Pull tab then turn.
Type III Reclosable Packaging- Snap Closure	1. Lift locking tab then push up 2. Localized downward pressure to open
Type IV Unit Non Reclosable Packaging- Flexible(Strip/Pouch)	1. Oriented tear.
Type V Unit Non Reclosable- Rigid	1. Requires localized force
Type VII Aerosol Packages	1. Localized press down then pull up at arrow. 2. Localized push up to remove.
Type VIII Non Reclosable Packages-Semi Rigid(Blister)	1. Remove portion (tab), peel back, and push out. 2. Peel back Sharp. 3. Peel back and push out. 4. Center bend. 5. Push out. 6 Bend, peel off, peel back, and push out. 7.Bend, peel back, push out

Table 2.2 (cont'd)

4.Requiring the user to have an adult-sized finger or hand	
Type	Description
Type VII Aerosol Packages	1. Directional overcap-actuator which requires a finger longer than that of a child.
5.Requiring the user to have a tool	
Type	Description
Type I Reclosable Packaging-Continuous Thread Closure	1.Key or device required to open
Type III Reclosable Packaging- Snap Closure	1. Requires key device or fingernail or coin or other tool to open
Type VI Unit Non Reclosable Packaging-Flexible(Strip/Pouch)	1. Requires tool.
Type V Unit Non Reclosable-Rigid	1. Requires tool.
Type VII Aerosol Packages	1.Requires use of a key or device to open (actuates normally)
Type VIII Non Reclosable Packages-Semi Rigid(Blister)	1. Requires tool.

CHAPTER 3

Visual Distraction Approach

The potential efficacy of proposed Child-Resistant features not only depends on the differences in physical strength and manual dexterity between adults and children, but also relates to the differences in the ways adults and children think [60]. Children use different strategies for problem-solving than that used by adults. It has been suggested that children aged one to four do not generate possible solutions to the problems that they face and then systematically test those hypotheses as adults do [61]. Children typically make random attempts at "solutions", sometimes repeating incorrect attempts. It has been well-established that children ubiquitously use their senses to explore the environment [62] and that by 18 months of age they use that information to interact with the objects that they perceive [63]. Here, by applying a "visual distracter" to a non-functioning portion of the package (i.e. away from the opening feature), we attempt to increase the time that children interact with a non-functioning area of the package by extending early stage processing.

A number of possible technologies were considered for incorporation into the CR packages to serve as "visual distracters." Generally, basic design features such as color, orientation, size and direction of movement are capable of attention capture. More complex design factors such as, stereoscopic depth [64], 3D structure [65] and surfaces [66] are also capable of the same.

The lenticular image (Virtual Images, A Division of Travel Tags, Inc. Redlands, CA) applied in this study is a combination of multiple images overlaid with lenses of material, providing the observer with a sense of depth, movement, and change

(depending on how the input images differ). The lenses are accurately aligned with the interlaces of the image, so that light reflected off each strip is refracted in a slightly different direction, but the light from all pixels originating from the same original image is sent in the same direction[67]. The end result is that a single eye looking at the print sees a single whole image, but two eyes will see different images, leading to a stereoscopic, 3D perception.

3.1 Schematic face Icon captures attention

Research has suggested that faces can be detected and categorized very efficiently by the visual system. In 1992, Mack and Rock discovered the phenomenon of inattentional blindness (i.e. an observer fails to detect the unexpected presence of a stimulus in his/her visual field) and designed a paradigm to investigate the relationships between perception and attention. In the inattentional blindness (IB) paradigm, participants are asked to search a display for specific target among common objects. Faces and facial icons have been widely studied target objects of this paradigm. The time to find the target (e.g. the face) is measured as a function of the number of distracting elements in the display. In 1998, Mack and Rock tested this paradigm to compare the capture effect between schematic cartoon faces and scrambled faces. The scrambled faces were created by simply placing facial features, specifically representations of the nose, eyes and month, in a different location within the face contour. 88% of participants detected a "happy" face, compared to 27% for a scrambled face [68].

Dr. Stephen R.H. Langton furthered Mack and Rock's findings; specifically, he investigated whether faces are capable of capturing attention when in competition with other non-face objects [69]. Rather than testing subjects with defined targets ((i.e. a face)

in a visual search task, Dr. Langton conducted the experiments under conditions where the face was unrelated to the goal, meaning observers were neither searching for them nor expecting to see them. Researchers concluded that faces are preferentially attended over non-face items. In other words, one becomes aware of faces before other items [70].

Researchers have also examined how the emotional affect of the icon influences attention. In 1999, a face detection effect was explored by Shelly-Tremblay and Mack who addressed that smiley face icons were detected more readily than scrambled or inverted faces [71]. In 2005, Fox et al. used both fearful and happy faces to investigate the effect of these specific facial expressions on attentional blink (AB). Attentional blink (AB) is a phenomenon observed in rapid serial visual presentation (RSVP); when presented with a sequence of visual stimuli in rapid succession at the same spatial location on a screen, a participant will often fail to detect a second salient target occurring in succession if it is presented between 180-450 ms after the first one[72]. When using schematic faces as the second target to explain the diminished AB effect, Fox et al. indicated that anxious individuals take longer to disengage their attention from negative facial expressions of angry and fear, but not from the positive facial expression of happy or neutral [73]. A similar study was conducted by testing participants under normal emotions recently. Miyazawa and Iwasaki evaluated the influence of positive effect on attentional blink with schematic faces by comparing the positive face icons (happy faces) with negative face icons (angry faces) [74]. Researchers stated that positive and negative faces were comparable in their power to capture attention in both upright and inverted orientations.

On the other hand, the attention capture of emotional faces was also studied

across different age group. In general, infants and younger children direct their gaze toward emotional faces [75, 76, 77]. Infant are able to detect emotional faces during the first six months of life, and sustained visual attention emerges from six months to three years of age [78]. According to the research results from LoBue and DeLoache, eight to fourteen-month-old infants preferentially look more quickly at angry faces than happy ones. Research in 3-year-old children has also indicated that emotional facial expressions, especially fear expression, can capture spatial attention [79]. This provides one possible explanation about the present of "Mr. Yuk". In the United States, schematic face stickers were once used commonly referred to as "Mr. Yuk" to warn children to stay away from the poisonous substance[80] (Figure 3.1).

Figure 3.1 Mr. Yuk is a created by the Children's Hospital of Pittsburgh, and widely employed in the United States in labeling of substances that are poisonous if ingested.

Results suggest that facial icons (regardless of the emotion being conveyed) readily capture attention and are easily interpreted.

3.2 Motion captures attention

In 2003, Franconeri and Simons reported that several types of motion are capable of capturing attention. These include unidirectional translational motion and oscillatory translation [81]. Specifically, whereas simulated looming motion (a dynamic

increase in object size) captures attention, simulated receding motion (a decrease in object size) does not. However, at the same time, researchers Abrams and Christ argued that capture by motion onset, not by specific types of motion, is more parsimonious than the behavioral urgency hypothesis Franconeri and Simon offered [82]. Researchers compared attentional capture for items that recently began to move, recently stopped moving, were continuously moving, and never moved. All the results were consistent with a single conclusion: Motion itself does not capture attention, but the onset of motion does. Abrams and Christ believed motion onset is important because it is indicative of the presence of an animated object.

In 2005, Franconeri and Simon presented a new experiment and found that motion strongly captured attention, even in the absence of a motion onset. They concluded that dynamic events capture visual attention [83]. While some dynamic signals may capture more attention than others (Franconeri and Simon 2003), it is also possible that motion accompanied by a motion onset capture attention more strongly than does motion alone. Also, since there is now little evidence of a qualitative division between dynamic events that capture attention and those do not (e.g. receding motion), a receding stimulus would attract attention if the size change were large enough.

3.3 Color change captures attention

Adding color to a label has been noted to increase its ability to attract attention because a color is distinguishable from background and surrounding colors[84].Visual search studies have shown that attention can be top-down, biased to a specific target color, so that only items with this color or a similar color can capture attention[85].Both Young in 1991 and Braun et al. in 1994 provide significant evidence that labels printed in

red (compared to black) led to improved noticeability [86, 87]. However, this issue is quite controversial. Some visual searches indicated that color singletons do attract attention automatically [88, 89, 90]. However, studies conducted by Jonides & Yantis (1988), Hillstrom & Yantis (1994), Todd & Kramer (1994) have shown that designs featuring singleton color fail to elicit attentional capture effects in the absence of any goal-directed prioritization [91,92,93].

The conception of color, symbolically and emotionally, varies from region to region, culture to culture. Certain hues have the power to automatically trigger a certain response in us at a subconscious level such as the national flag, college mosaic or luxury brand. Also, there are no foolproof rules about exact color meaning and individuals are usually aware of both the positive and the negative implications when using particular colors [94]. For an example, Red stands for both cupid and the devil because it is associated with both love and war. Yellow is widely used for warning labels in western countries since it is associated with hazard or emergency, while in the Asian, especially China, Korea and Japan, yellow represents honor and royalty. Thus, since color symbolism is generated within various cultures, there are many disagreements when it comes to specifics.

In contrast to the literature that examines the effect that a single color has on attention capture, there is less debate in the literature that studies the effect of color change on invoking involuntary attention capture. In 1999, findings of Gellatly, Cole, and Burton's experiment suggest that equiluminat color changes were capable of capturing attention [95]. Studies which followed indicated equiluminant color change cues guide attention in the cue-target paradigm [96, 97]. In 2005, researchers Lu, S and

Zhou, K investigated the attention capture by color changes in a real stimulus-driven fashion. Participants were asked to search for a targeted letter in a search display in which an element underwent a sudden color change. The presented results demonstrated that when the target was located inside the color-changed item, reaction times (RT) were rapid and influenced little by display size, providing evidence that the color-changing item clearly captured strong attention in the presented visual search task. [98].

CHAPTER 4

Hypothesis and Design Justification

4.1 Identify ways to prevent unintentional poisoning, with a focus on children 24-41 months of age.

Specifically, we apply the idea that opening time can be extended by attracting the attention of children to a non-working component of drug packages (both vials and blisters).

To examine this hypothesis, we tested children 24-51 months of age. Although this age group differs from that commonly used for protocol (42-51 months of age), we have chosen it because children 24 months of age are the most commonly poisoned[99]. During this stage of child development, children are predisposed to explore their surroundings; they learn quickly by watching, and although they are not as strong as adults, they are noted to creatively employ the use of their teeth, table edges, or other tools around them. Their hands and fingers are smaller than those of adults, and their teeth and fingernails can slide under and into gaps. Additionally, the taste sense of children from 6 months through 4 years has not fully developed, further increasing the potential for unintentional ingestion of all kinds of objects[100].

4.2 Identify ways to distract children's attention from opening features.

The stage that begins at two and continues to the age of six is called "Early Childhood"[101]. According to Piaget's Theory of Cognitive Development, children aged two to six years old easily generate intuitive thoughts that tend to propose the questions of why and how come. During this stage children are eager to explore the external environment. Children's motor, speech, vision and hearing develop rapidly, especially

vision. Information about the surroundings is principally obtained through vision rather than audition during the early childhood stages of development [102]. As such, we propose the addition of a visually-based distractive device on a non-working component of drug packaging has the potential to add time before opening.

4.3 Identify ways to improve the visual attraction of lenticular image.

Lenticular images (Virtual Images, A Division of Travel Tags, Inc. Redlands, CA) were created containing a frowning facial icon which changes to the words “keep away”. Conception of the distracter design leveraged the insights regarding facial icons, motion and color from the field of visual perception discussed previously (Figure 3.2).

Figure 4.1 The visual distracter employed a schematic facial icon (unhappy face), looming motion (a dynamic increase in object size) and color change (red to yellow).

CHAPTER 5

Material and Methods

In order to measure the efficacy of visual distraction as a child resistant (CR) feature, we conducted testing with children aged of 24 to 51 months. Two types of packages were tested: a PRX 40-dram (green) pharmaceutical vial outfitted with a reversible cap that could be secured as a push-and-turn or in a non-CR format (Tri State Distribution; Sparta, TN), and a unit dose system, specifically a paperboard wallet containing foil-backed blisters (MeadWestvaco, Richmond, VA).

5.1 Materials

5.1.1 Packaging

PRX™ reversible caps were affixed to vials (Tri State Distribution, Inc, Sparta, TN) (height 9.5 cm [3.7"], diameter 4.6 cm [1.8"], top 4.2 cm [1.7"]) for testing. Package sizes were chosen/created to accommodate the lenticular graphic (diameter 1.7"), which had been created in a moderate size with the theory that it would enhance attraction. The lenticular was not only sized for attention, but also so that it could be hidden within both vials and blisters systems.

Vials were filled with 14 placebos (lactose monohydrate excipient) and closed in a non CR manner during all testing, whereby instructions for opening are listed as "caution, not child-resistant" (Figure 5.1).

Figure 5.1 Dram-40 size PRX™ reversible vial

The second package tested was a paperboard wallet (SBS 12pt thickness) containing foil backed blisters (MeadWestvaco, Richmond, VA). The blisters were (length 15.3cm [6"], width 5.8cm [2.3"], thickness 0.83cm [0.3"]). A single placebo dose (lactose monohydrate excipient) was sealed into each of the 14 blister cavities on a single card (Figure 5.2).

Figure 5.2 Paperboard wallet containing foil backed blisters (see Appendix C)

5.1.2 The visual distracter

A lenticular image (Virtual Images, A Division of Travel Tags, Inc. Redlands, CA) was customized such that it contained a frowning facial icon which changed to the words "keep away." as the packages moved. The textual element of the design gives the illusion

of motion; when viewed from different angles, the words appear to zoom in and out. (Figure 5.3)

Figure 5.3 The lenticular distracter containing holographic facial icon and text

5.2 Testing Methods

5.2.1 Recruitment, screening and consent

Participants for the testing were recruited by Great Lakes Marketing (Toledo, OH, USA). Great Lakes Marketing's database lists over 600 test locations (daycares, preschools, etc.) which they regularly collaborate with. Thus, specifically for this research, Great Lakes helped us distribute information (see Appendix E) through its substantial network, gather consent forms and schedule identified participants.

To participate in the testing, children had to be between 24 and 51 months of age, have the written consent of a parent or guardian (see Appendix F) and the verbal consent of the child based on our assent script (see Appendix G). As with CPSC protocol testing, children were prescreened for physical or mental impairments that impacted their ability to open packages.

5.2.2 Test Procedure

Visual distracter (present and absent) was crossed with package type (vial and blister), for a total of four treatment conditions (vial with and without distracter and blister with and without distracter). Children were primarily tested in pairs, though, on occasion three children would be available without the benefit of a fourth (e.g. a participant did not show or a sibling that had not been registered and met screening criteria would be available). As such, on a few rare occasions, three children were tested simultaneously. Test partner was recorded and included in the subsequent analysis. Each child was provided a single package that was identical in treatment to their test partner(s).

Children were shown into one of three identical testing rooms at the Great Lake facility by testers from Michigan State University. Each child was seated on a small carpet square (in accordance with permission granted RE: digital recording. See Figure.4.4) that was positioned in front of a screen which contained a one way mirror through which testing was video recorded (Figure 5.5). Cameras were hidden in order to reduce the distraction that taping can induce.

Figure 5.4 The color of carpet squares corresponded to whether or not parents had approved the viewing of testing for presentation purposes (green squares for those who permitted it and red for those that did not wish to allow this)

Figure 5.5 Corrugated screen with CDC advertisement was located in the corner of the testing room (see Appendix D).

Prior to testing, a member of the research team went through a verbal assent process with the children (see Appendix F). Children that gave an indication (verbal or otherwise) that they did not wish to participate were excused from the study. Parents were asked to limit their comments, “I know that we want to as parents help our children as much as possible, but we need to see what they do on their own. So please resist the urge to coach them or try to help them anyway." Each child in the pair was handed a package and asked, “Please do whatever you would like with this package.”

Testing was stopped at three minutes, or when the child had opened the package in a way that would enable access to the product, whichever came first.

5.3 Analysis Method

Data analysis was primarily based on information gathered from video review. Appendix H dedicates the detail data coding applied in the experiment. Dependent variables for analysis included: the binary response, opened (yes/no) and the continuous response, time to successful opening.

A generalized linear mixed model was fitted to the binary response "successful opening" (yes/no). Fixed effects included age group (non-protocol age 24-41 months and protocol age 42-51 months), treatment (package (vial or blister) x distractor (present or absent)) and their 2 way interaction. Random effects included room (nested with tester) as an overall blocking factor as well as the kids nested within treatment.

Over dispersion was evaluated using the maximum-likelihood based fit statistic Pearson Chi-Square/DF. The final statistical model used for inference was fitted using residual Pseudo-Likelihood. Kenward-Roger's approach was used to estimate degrees of freedom and to correct estimated standard errors. The model was fitted using the GLIMMIX procedure of SAS (Version 9.2, SAS Institute, Cary, NC) implemented using Newton-Raphson with ridging as the optimization technique. Estimated least square mean probability of opening and corresponding standard errors for levels of the fixed effects of interest are reported in Chapter 5, Analysis and Conclusions. Relevant pairwise comparisons were conducted using a Tukey-Kramer or Bonferroni adjustment, as appropriate in each case, to avoid inflation of Type I error rate due to multiple comparisons.

As to the variable response, "time to open", a general linear mixed model was employed. For this case, responses included in the analysis were limited to cases where

the packages were successfully opened within the three minute time period. Fixed effects included age group (non-protocol age 24-41 months and protocol age 42-51 months), treatment (package (vial or blister) x distractor (present or absent)) and their 2 way interaction. Random effects included room (nested with tester) as an overall blocking factor as well as the pair of kids nested within treatment.

Model assumptions were checked using studentized residuals. Kenward Roger's procedure was used to estimate degrees of freedom and adjust estimates of standard errors. The model was fitted using the GLIMMIX procedure of SAS (Version 9.2, SAS Institute, Cary, NC) implemented using Newton-Raphson with ridging as the optimization technique. Estimated least square means and corresponding 95% confidence intervals (LCL and UCL) for levels of the fixed effects of interest are reported after back transformation. Relevant pairwise comparisons were conducted using either Tukey-Kramer or Bonferroni adjustments, as appropriate in each case, to avoid inflation of Type I error rate due to multiple comparisons.

Extra criteria were analyzed to determine the effect of children's involvement (See the coding "Involved in…"). A child was assumed to have no involvement with test packages if the subject did nothing or passively held the package throughout the entire 3 minute test period. A generalized linear mixed model was fitted to the binary response "package involvement" (yes/no). Fixed effects included age group (non-protocol age 24-41 months and protocol age 42-51 months), treatment (package (vial or blister) x distractor (present or absent)) and their 2 way interaction. Random effects included room (nested with tester) as an overall blocking factor as well as the pair of kids nested within treatment.

CHAPTER 6

Data Analysis

In the experiment, a total of 207 subjects tested two package types (pharmaceutical vials and blisters) at two levels (with and without distracters). Treatments were rotated as subjects were recruited in an attempt to generate an equal number of subjects by treatment. Table 6.1 presents gender and age frequency by treatment type.

Table 6.1 Working group crossed with gender and age

Treatment	Subjects	24-41months		42-51 months*	
		Female	Male	Female	Male
Vial Plain	54	18	16	9	11
Vial with Distracter	54	18	19	9	8
Blister Plain	49	16	18	11	4
Blister with Distracter	50	17	13	5	15

*42-51 month is the protocol age required by the Consumer Products Safety Commission (CPSC) as required by 16 CFR 1700.20. 24-41 months is outside protocol age but has been noted to be at the greatest risk for poisoning due to unintentional ingestion of medication.

6.1 Vial

6.1.1 Dependent variable: probability of opening for vials

Opening results for the 108 children who tested vials are presented in Table 6.2.

Table 6.2 Opening frequency and percentage of children testing vials with and without distracters by age group and gender*

Treatment	Age Group				Gender Group			
	24-41 Months		42 -51Months		Female		Male	
	Frequency	Percentage	Frequency	Percentage	Frequency	Percentage	Frequency	Percentage
Plain Vial	12	42.9%	5	17.9%	9	32.1%	8	28.6%
Vial with distracters	4	14.2%	7	25%	3	10.7%	8	28.6%
	16	57.1%	12	42.5%	12	42.8%	16	57.2%

There was evidence for a significant interaction of age group x treatment on the probability of opening (P=0.0489) whereby protocol aged children (42-51 months of age) were more likely to open a vial containing a distracter than younger children. This effect was not evident when comparisons were made with the plain vials (Table 6.3, Figure 6.1).

Table 6.3 Mean estimates of probability of opening (with CI) by treatment and age group in vial tests

Treatment	Age Group	Mean Estimates (%)	LCL (%)	UCL (%)
Distracter	24-41 Months	8.5	24.64	25.38
Plain	24-41 Months	38.7	15.58	68.34
Distracter	42-51 Months	30.9	14.53	54.05
Plain	42-51 Months	24.14	8.13	53.37

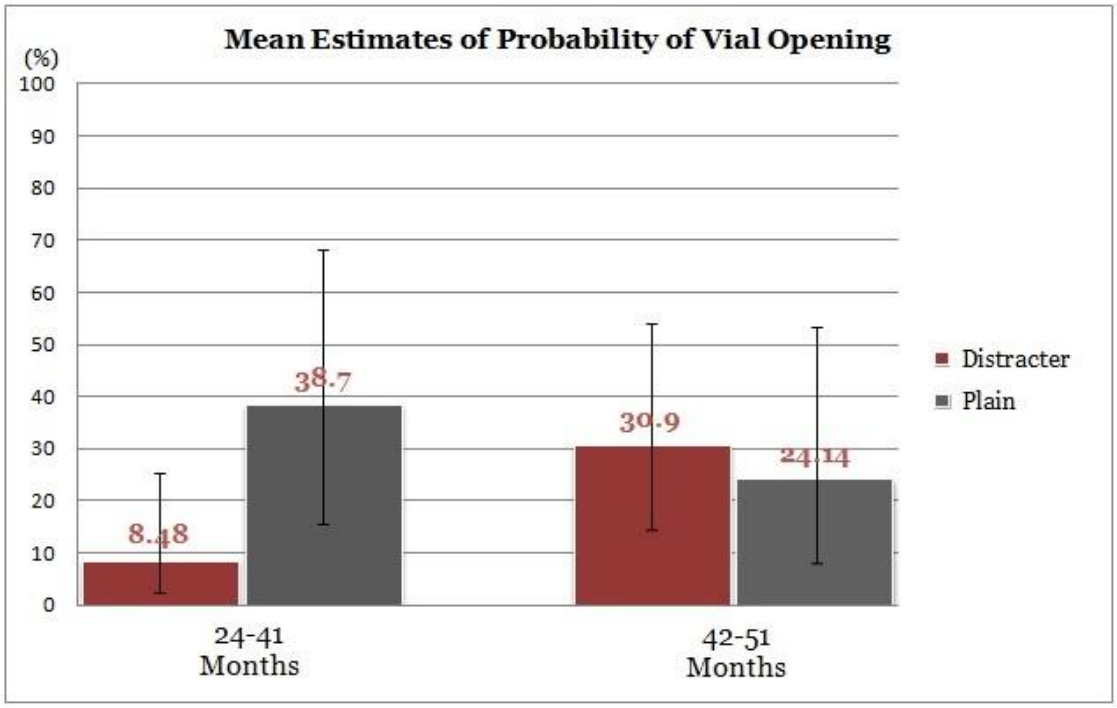


Figure 6.1 Mean estimates of probability of opening (with CI) by treatment and age group in vial tests

6.1.2 Dependent variable: time to opening for vials

Of the 108 participants tested with vials, 28 (26%) resulted in successful openings. For successful trials, time to opening was treated as a dependent variable and data was analyzed (Table 6.4).

Table 6.4 Average opening time by distracter presence and age group in vial tests

	Vial with Distracter		Plain Vial	
	24-41 Months	42- 51 Months	24-41 Months	42- 51 Months
Average (Sec)	103.05	36.64	94.59	45.09
Standard Error	26.10	20.34	23.16	19.17

A generalized linear mixed model was fitted to the continuous response "time to successful opening" (in seconds restricted to successful cases only; n=28). Data supports evidence for a main effect of age group and treatment on time to successfully open. Whereby, older children opened vials significantly faster (45.1 seconds SE 19.17) than their younger counterparts (94.6 seconds SE 23.16) (P=0.0356). Treatment also proved to be a significant treatment for the response variable time to successful opening (P=0.0375) whereby, treatments that contained distracters took significantly more time to open (ME= 103.05 seconds SE 26.10) than those without (ME=36.64 seconds SE 20.34).

Estimated least square means and corresponding 95% confidence intervals (LCL and UCL) for levels of the fixed effects of interest are also reported after back transformation. (Table 6.5, Figure 6.2)

Table 6.5 Mean estimates of opening time (with CI) by treatment and age group in vial tests

Treatment	Age Group	Mean Estimates	LCL	UCL
Distracter	24-41 Months	140.87	58.3332	223.41
Plain	24-41 Months	48.32	-8.7395	105.38
Distracter	42-51 Months	65.221	-2.6441	133.09
Plain	42-51 Months	24.96	-31.573	81.4983

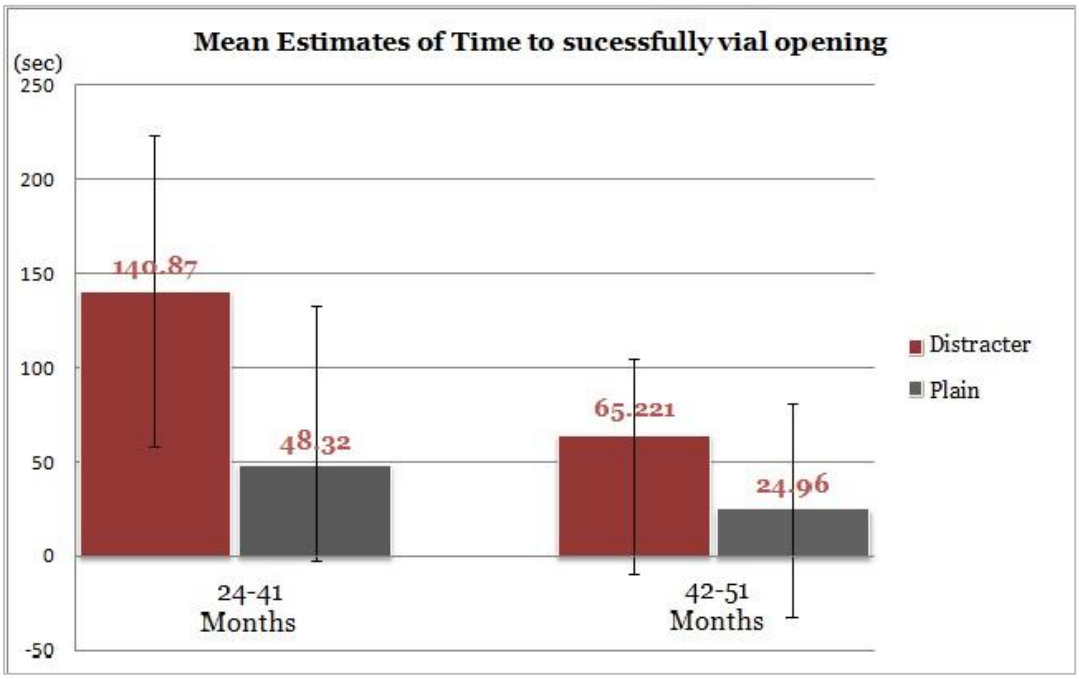


Figure 6.2 Mean estimates of opening time (with CI) by treatment and age group in vial tests

6.1.3 Dependent variable: Involvement with a vial package

Among the 108 subjects that tested vials, 88 were defined as being actively involved with the packaging. Table 6.6 show the group distribution crossed the treatment and age.

Table 6.6 Frequency of children actively involved in vial tests

	Involved with package		Not Involved with package	
	24-41 Months	42-51 Months	24-41 Months	42-51 Months
Plain Vial	29	13	5	5
Vial with Distractor	31	15	6	4
Total	60	28	11	9

Analysis provided no evidence for any effects of treatment (P>0.90), nor difference in age group (P=0.35) on the probability of involvement with the package.

6.1.4 The study of children's behavior in vial tests

Task analysis was used to analyze video recordings. For each treatment, researchers identified common motions that the children employed (e.g. hold, play, twist cap, pull blister, etc.) and calculated the number of times children exhibited each action during the 3 minute time period. Typical actions were defined for both vials and blisters. Twelve categories were defined for the PRX 40-dram vials (Table 6.7)

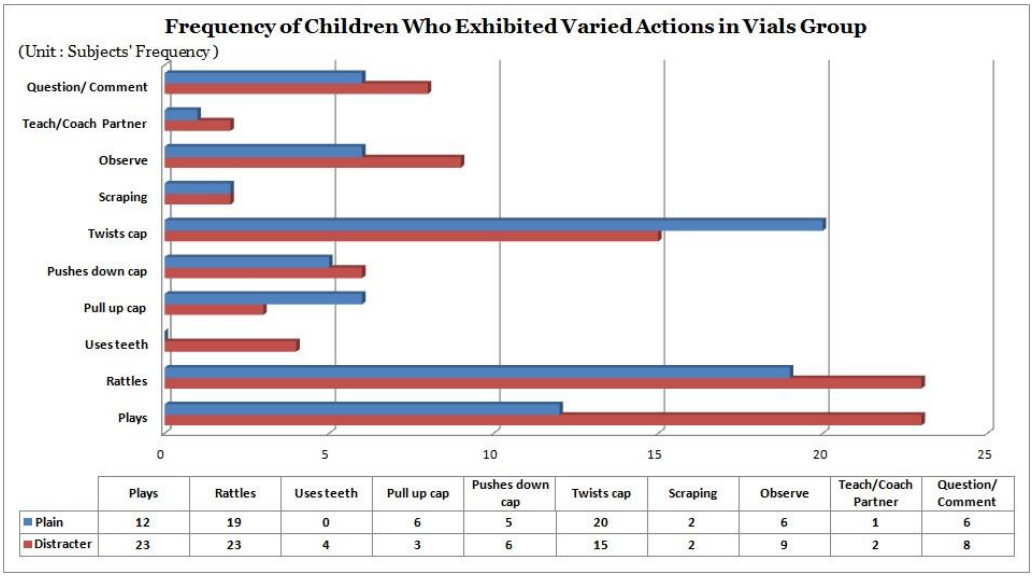
Table 6.7 Typical child actions for a vial package

Category	**The child…**
Plays	Is playing with the package with no intention of opening
Rattles	Is shaking the package
Uses teeth	Tries to pull up the cap with his/her teeth
Pull up cap	Pulls up the cap
Pushes down cap	Pushes down the cap

Table 6.7 (cont'd)

Twists cap	Holds the cap and makes a twisting movement
Scraping	Scrape the cap or the bottom of vials
Observe	Observe anything related to sample such as distracter, label, logo or the content inside
Teach/Coach Partner	Coach partner to open the vials, look the distracter or just follow him/her
Question/ Comment	Ask partner-, tester or his /her parents about the medicine-, package or the distracter

Figure 6.3 offers a bar chart representing the frequency of the behaviors were exhibited by the 88 subjects that actively involved with vials. Almost all of the 88 subjects offered some form of active behavior; 42 children (47.7%) rattled vials and 25 children (28.4%) played the package as a toy (cap, rolling ball, train .etc.), while 35 children (39.8%) twisted the caps. The children with plain vials were likely to rattle (45.2%) and twist caps (47.6%), while the children tested in distracter treatment are more likely to play (50%) and rattle (50%).



	Plays	Rattles	Uses teeth	Pull up cap	Pushes down cap	Twists cap	Scraping	Observe	Teach/Coach Partner	Question/ Comment
Plain	12	19	0	6	5	20	2	6	1	6
Distracter	23	23	4	3	6	15	2	9	2	8

Figure 6.3 Frequency of children who exhibited varied actions in vials group

Also, as indicated by Figure 6.3, 14 children of the 88 who were provided vials were categorized by researchers as commenting or asking questions about vials. More children are found in the actions such as observe, question or comment when we compared the vials with distracter treatment (36.9%) to the plain vials treatment (28.6%). Among those 14 children, 4 children commented or questioned about the distracter specifically (See the comment examples of No 37, 175, 176 208).

The following statements were comments of subjects; they were identified by the subject number.

"What's on the bottom? .... Picture..... See...picture" (No37)

"Look, it is candy." (No.47)

"What's inside (turned to his mom), what's it?" (No51, 110,)

"Why is medicine inside?" (No 58)

"Is this a medicine?" (No.82)

"I do not know what is inside, but I would like to open." (No.116)

"Mom (handed the package to other) can you open? Can you help me?" (No.143)

"What is it? (Obverse the label and the content inside) "(No.170)

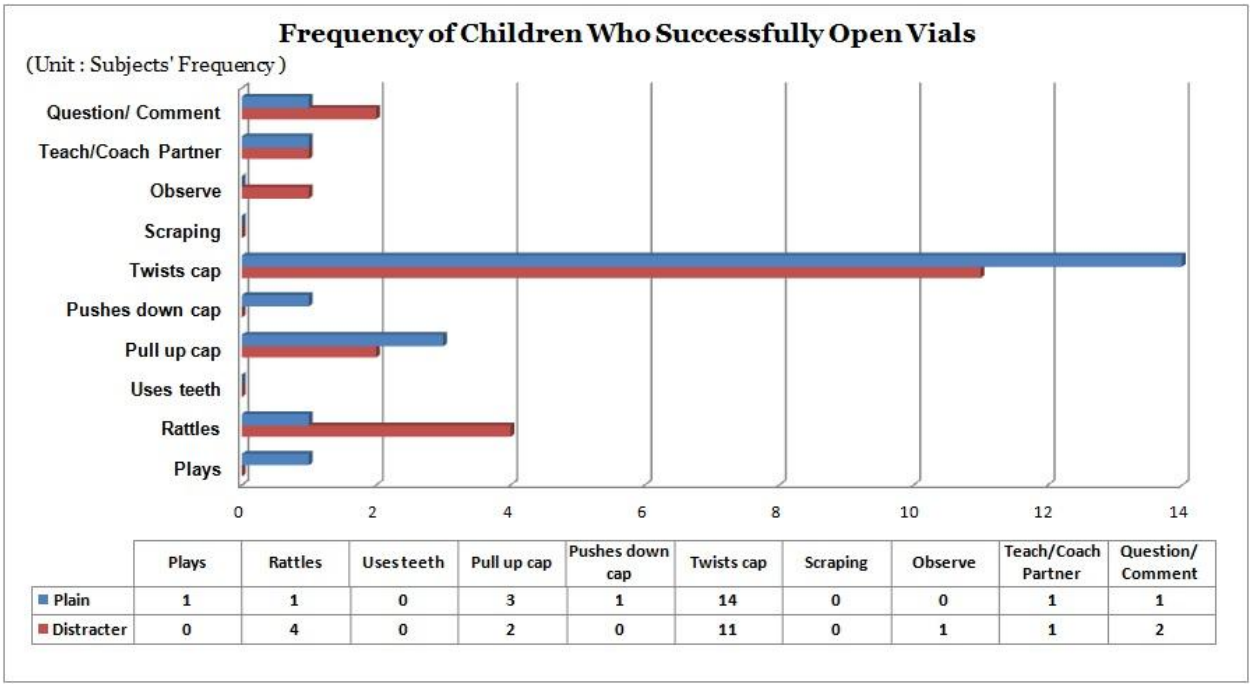
"Look, mom, (Pointed at the sticker) what is it?" (No.175, 176 208)

"I cannot open it." (No.192)

"I can open it!!" (No.199)

"I can help you (coached the partner) I can open that." (No.198)

A behavior summary was also conducted for those 28 children (17 children in plain treatment while 11 children in distracter treatment) who opened their vials successfully. Not surprisingly, twisting (89.2%) and pulling up the cap (17.8%) were the main actions that led to vial opening (Figure 6.4), with three children opening their vials by pulling up the cap directly. Even though four children tried to use teeth during the experiment, none of them were successful in their opening attempts.



	Plays	Rattles	Uses teeth	Pull up cap	Pushes down cap	Twists cap	Scraping	Observe	Teach/Coach Partner	Question/ Comment
Plain	1	1	0	3	1	14	0	0	1	1
Distracter	0	4	0	2	0	11	0	1	1	2

Figure 6.4 Frequency of children who successfully open vials

6.2 Blister

6.2.1 Dependent variable: probability of opening for blister packages

The opening frequencies for the 99 subjects who tested blisters by gender and age are summarized in Table 6.8.

Table 6.8 Open frequency of children testing blisters with and without distracters

Actions of Children in the blister tests	Blister with Distracter		Plain Blister	
	24-41 Months	42-51 Months	24-41 Months	42-51 Months
1. Failed to open the wallet*	29	18	33	12
1.1 Opened the wallet but did not unfold the blister	*1*	*2*	*0*	*1*
1.2 Opened the wallet , unfolded the blister but not peel the foil	*7*	*10*	*0*	*1*
2. Open the wallet, unfolded the blister and punctured or peeled the foil	1	2	1	3

* 1.1 and 1.2 are the sub-situations included in the category 1: Failed to open the wallet.

Despite the fact that the system of test was non-CR, of the 99 children that tested blister treatments, only 7 were successful in opening their package. This was largely due to the fact that children did not seem to recognize that the blister card was held inside a sleeve and could be easily removed.

There was no evidence for any of the tested effects at $\alpha=0.05$.

6.2.2 Dependent variable: time to opening for blister packages

For successful opening trials for blister packages (n=7), time to opening was treated as a dependent variable and data was analyzed (Table 6.9).

Table 6.9 Average opening time by distracter presence and age group in blister tests

	Blister with Distracter		Plain Blister	
	24-41 Months	42- 51 Months	24-41 Months	42- 51 Months
Average (Sec)	173.00	160.00	193.00	128.33
Standard Error	29.06	20.54	29.05	16.77

A generalized linear mixed model was fitted to the continuous response "time to successful opening" (in seconds restricted to successful cases only; n=7). Analysis provided no evidence for any effects at α=0.05.

6.2.3 Dependent variable: Involvement with a blister package

Among the 99 subjects that tested blisters, 91 (92%) were defined as being actively involved with the packaging. Table 6.10 show the group distribution crossed the treatment and age. Analysis provided no evidence for any effects at P=0.05.

Table 6.10 Frequency of children actively involved with blisters during testing

	Involved with the blister package		Not Involved with the blister package	
	24-41 Months	42-51 Months	24-41 Months	42-51 Months
Plain Blister	28	15	6	0
Blister with Distractor	28	20	2	0
Total	56	35	8	0

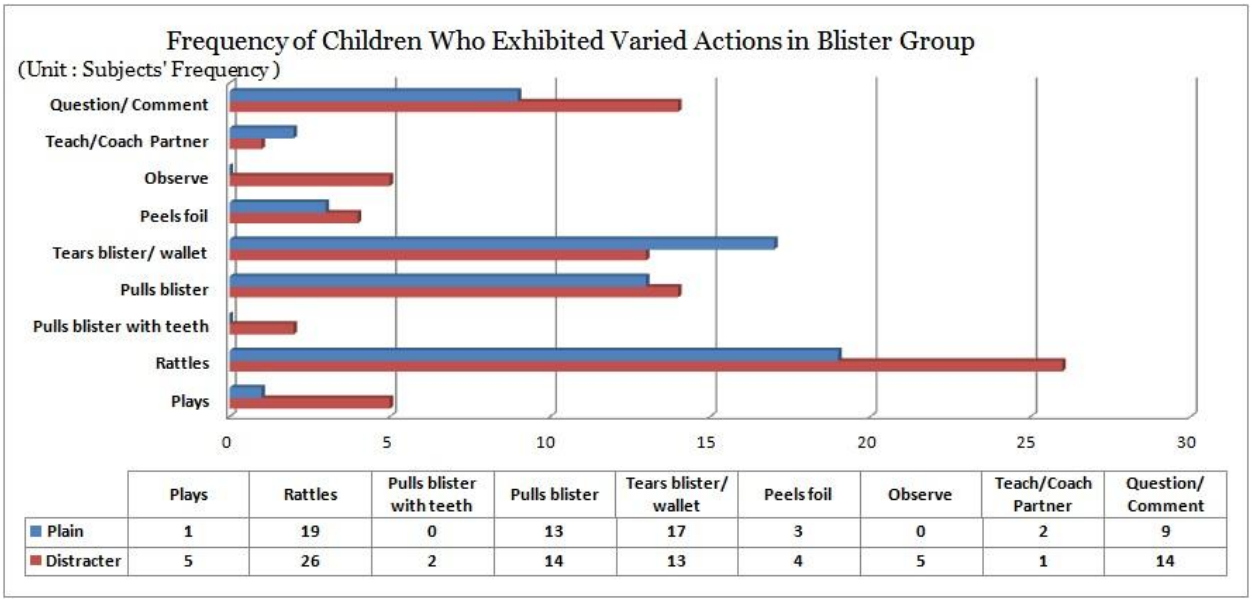
6.2.4 The study of children's behavior with blister packaging

Task analysis was used to analyze video recordings. For each treatment, researchers identified common motions that the children employed (e.g. hold, play, twist cap, pull blister, etc.) and enumerated the participants that exhibited a particular action during the 3 minute time period. Eleven categories were defined for the foil-backed blisters (Table 6.11).

Table 6.11 Typical child actions for a blister package

Category	The child…
Plays	Is playing with the package with no intention of opening
Rattles	Is shaking the package
Pulls blister with teeth	Pulls the blister with the teeth while holding the plastic shell
Pulls blister	Is holding the paper wallet with one hand and pulling the blister with the other
Tears blister/ wallet	Is trying to pull apart paper wallet or the carton of the plastic shell
Peels foil	Is trying to peel the foil off the blister
Observe	Observe the label, logo or the content inside
Teach/Coach Partner	Coach partner to open the vials, look the distracter or just follow him/her
Question/ Comment	Ask partner , tester or his /her parents about the medicine , package or the distracter

Data described below represent the number of children that exhibited a given behavior from the 91 children tested with blisters. The analysis of what kept children focused revealed different opening strategies and behaviors for each package. Note that during the 3 minute period, no opening suggestions and demonstration were provided by testers.



	Plays	Rattles	Pulls blister with teeth	Pulls blister	Tears blister/ wallet	Peels foil	Observe	Teach/Coach Partner	Question/ Comment
Plain	1	19	0	13	17	3	0	2	9
Distracter	5	26	2	14	13	4	5	1	14

Figure 6.5 Frequency of children who exhibited varied actions in blister group

Figure 6.5 offers a bar chart of typical behavior exhibited by the 91 subjects that involved with blister treatments. Because so few children accessed the distracter, we chose not to enumerate these behaviors by treatment, but left the behaviors in aggregate. Active children focused on tearing the blister/wallet (30 subjects 32.9 %) or pulling the blister (27 subjects 29.6%).

For the blister group, the majority of children tested failed to see the attached sticker because seldom of them could break the outside wallet. Still, the bar chart reflected children's attitude to the package itself since there are 23 children questioned or commented on the blisters. Among those 23 children, 3 children commented or questioned about the distracter specifically (See the comment examples of No 135, 136 165).

The following statements were comments of subjects; they were identified by the subject number.

"What's inside (turned to his mom), what's it?" (No.3, 157)

"It is a vitamin!" (No 20,173,174)

"Is this a medicine box?" (No.30)

"I do not know what it is, maybe is vitamin in it." (No.36)

"I know, it is medicine." (No.61)

"I see it at home.... it is medicine." (No. 71,152,164)

"This is a package... (Excited) it is my package!" (No.79)

"Look, (Pointed at the sticker) what is it?" (No.135)

"Can you get the stick off for me (ask his mom for help)? (No.136)

"I did it all by myself! (Tearing and pulling out the blister) (No.162)

"I gonna open it... wow... look... the sticker." (No.165)

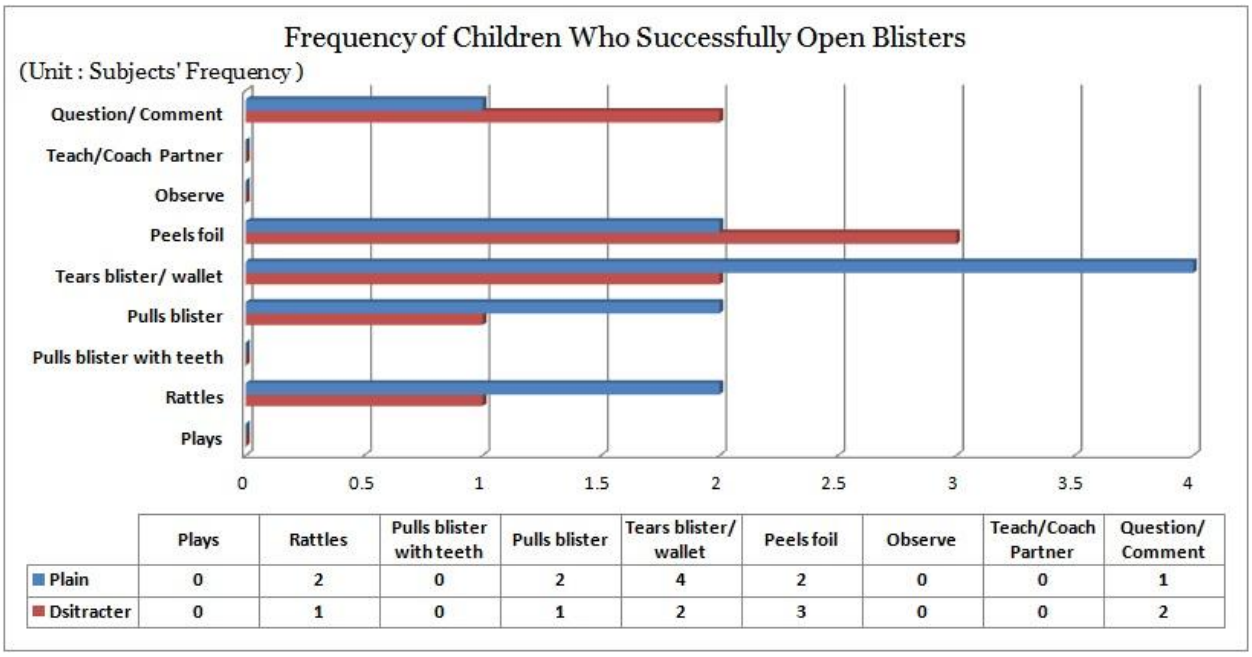
"How to open it...I cannot." (No.177)

"I cannot eat it ...I do not want to eat it." (No 179)

"Can I open it (ask the tester)?" (No.181)

The behavior summary was also conducted for the children who opened the blister successfully (Figure 6.6). Seven children were successful in pulling the blister out and peeling or puncturing the foil, enabling access to package contents. Typical actions were: tearing the wallet and rattling the blister simultaneously (3 subjects),

manipulating the foil side and trying to peel the foil (5 subjects). Interestingly, the use of teeth (2 subjects) was not among the behaviors that resulted in successful opening. Tearing (6 subjects 85.7%) and Peeling (5 subjects 71.4%) are the main actions leading to open the blister. The children who are likely to rattle (3 subjects 42.9%) or pull out (3 subjects 42.9%) the package are easier to get the blister out of the wallet.



	Plays	Rattles	Pulls blister with teeth	Pulls blister	Tears blister/ wallet	Peels foil	Observe	Teach/Coach Partner	Question/ Comment
Plain	0	2	0	2	4	2	0	0	1
Dsitracter	0	1	0	1	2	3	0	0	2

Figure 6.6 Frequency of children who successfully open blisters

CHAPTER 7

Results and Discussion

7.1 Results

1. When a distracter was present in the vial group, younger children (24-41 months) were less likely to open the vials than older children (P=0.035). However, there was no evidence for any treatment effects (distracter present vs. absent) on probability of opening for either age group (P=0.107).

2. Overall, for children in both age groups, time to open vials (for those that were successfully opened) was prolonged when the vial had a distracter relative to a plain vial(P=0.0375).

3. There was no evidence for any effect of treatment on the probability of opening blister (P=0.6522) and time to open (P=0.8196). This is largely due to the fact that so few children were successful in removing the blister card from the paperboard wallet that contained it. As such, very few children (3 subjects) were even exposed to the distracter leaving the study under-powered.

7.2 Limitations

No evidence of significance was found related to any of the results for blisters. This could be attributed to the very limited number of children who successfully peeled or punctured the foil, exposing the product (7 subjects 7%). This was likely due to the difficulty children had in removing the wallet from the outer paperboard shell.

A significant limitation of the study involved coaching from the parents. Since testers reminded parents not to guide or help their children during testing, theoretically, all the experiments were conducted without any opening demonstration. However, since parents were allowed to stay in the testing room or some disruptive guiding (15 out of 207 subjects) was provided which definitely affected the behavior of the children. The following statements were comments of parents; they were identified by the subject number.

Baby, can you show me how to open it? (No.43)

Good trying! I know you can open it. I just want to see how you open it (No.44, 122)

Hey, try to open it. ... Yeah she win! She opens it! (No.120)

Do you want to see the inside of this box? Show me... open it.....Did you open it? go back... open it (No.205)

7.3 Future Study

7.3.1. The results for the vials suggest that the presence of a distractive device, potentially extends early stage processing, and is, therefore, a promising approach for prolonging time to opening. Further, data suggest that the addition of a visual distracter may be particularly effective in preventing young children, who tend to be perceptual processor and are at higher risk for unintentional exposure from opening. However, this approach would be an "attractive nuisance" if it were to be so effective that it drew this vulnerable age group to the hazard. Further study is needed to determine if this is the case.

To address this issue, a behavior study is proposed, with the objective of determining if the visual distracter attracts attentions. To study this issue, we propose the following.

Subjects aged in 24-51 months will be asked to test two levels of package (vial and unit of use), each with three placements of distracter (none, visible and hidden). Each child will be shown all three treatments simultaneously (distracter absent, visible and hidden) for a given package type (vial and blister). The three packages will be placed next to one another on a shelf set; position of the treatment (e.g. A1, A2, A3 or B1, B2, B3- see Figure.7.1) on the shelf will be counterbalanced across subjects to minimize any effect of positioning. Children will be instructed, "I am going to show you three packages. I would like you to pick one; please pick up only your favorite package." After this instruction, the packages are dropped into place and time will start.

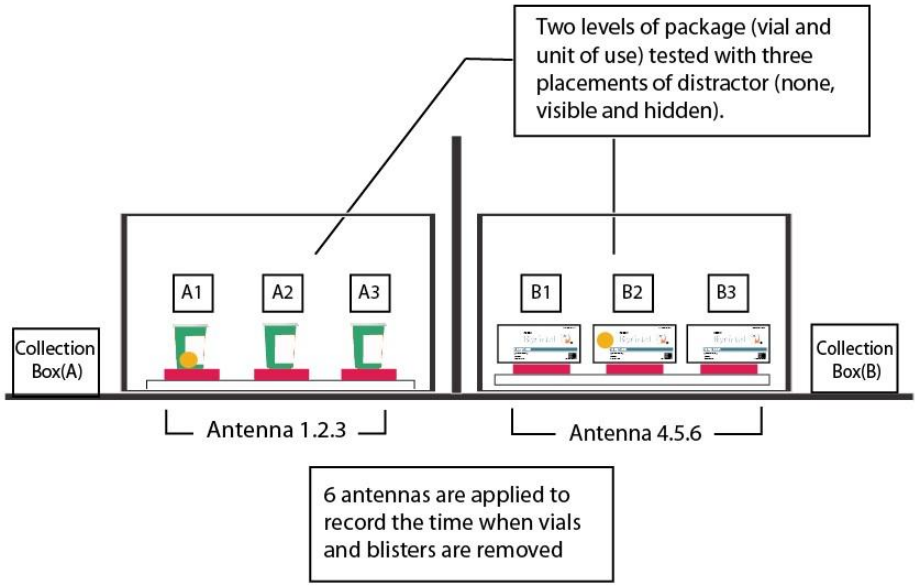


Figure 7.1 RFID system (Children will be tested one at a time and will be asked to choose their favorite on two occasions, once from a set comprised of vials and another time from a set comprised of blisters. Order of presentation of the top treatments position within the set will be counterbalanced.)

RFID tags will be used to record the exact time when subjects pick up or put down a package. For the vials, RFID tags are attached to the bottom of the inside of vials in order to be in close proximity to the reader, which employs a near field technology; for the blisters, RFID tags will be attached to the inside wall of the wallet (Figure 7.2) . Upon the removal of the package, the RFID reader ceases to read its tag, providing us with an accurate removal time, as well as an electronic record of which package was removed first.

Figure 7.2 The RFID tag placement for both vials and blisters

7.3.2. For clear results, a similar research study could be conducted using a non-wallet covered blister. It is advised to conduct the test with same sample size to be a comparison.

7.3.3. There is a little known about the interface between packaging and children. It seems that some children are likely to be a follower while some always want to coach their partners. Thus, studies aimed to link child development concepts and package usability is advised.

7.3.4. Besides visual distraction, it is also recommended distractive devices based on other senses, such a sound, could be developed. Based on the former project conducted by HUB Research Group of Michigan State University in 2005, sight and sound has the potential to affect a child's resolve to enter packages. Rattling vials provoked more questions and comments from children. Thus, combing acoustic perception with package design may be another potential solution to explore.

7.3.5 How to realize the visual distracter as a printable label should be determined in detail. Considering the cost of 3D lenticular sticker, a research project aimed to apply the 3D printing label onto pharmaceutical package is advised.

APPENDICES

APPENDIX A Lists of the substances that require special packaging (1700.20)

Table A1 Lists of the substances that require special packaging (1700.20)

Substance	Description
Aspirin	Any aspirin-containing preparation for human use in a dosage form intended for oral administration
Furniture Polish	Nonemulsion type liquid furniture polishes containing 10 percent or more of mineral seal oil and/or other petroleum distillates and having a viscosity of less than 100 Saybolt universal seconds at 100 °F.
Methyl salicylate	Liquid preparations containing more than 5 percent by weight of methyl salicylate, other than those packaged in pressurized spray containers.
Controlled drugs	Any preparation for human use that consists in whole or in part of any substance subject to control under the Comprehensive Drug Abuse Prevention and Control Act of 1970
Sodium and/or potassium hydroxide.	Household substances in dry forms such as granules, powder, and flakes, containing 10 percent or more by weight of free or chemically unneutralized sodium and/or potassium hydroxide, and all other household substances containing 2 percent or more by weight of free or chemically unneutralized sodium and/or potassium hydroxide
Turpentine	Household substancesin liquid form containing 10 percent or more by weight of turpentine
Kindling and illuminating preparations.	Prepackaged liquid kindling and/or illuminating preparations, such as cigarette lighter fuel, charcoal lighter fuel, camping equipment fuel, torch fuel, and fuel for decorative or functional lanterns, which contain 10 percent or more by weight of petroleum distillates and have a viscosity of less than 100 Saybolt universal seconds at 100 °F.
Methyl alcohol	Household substances in liquid form containing 4 percent or more by weight of methyl alcohol (methanol), other than those packaged in pressurized spray containers
Sulfuric acid.	Household substances containing 10 percent or more by weight of sulfuric acid, except such substances in wet-cell storage batteries
Prescription drugs	Any drug for human use that is in a dosage form intended for oral administration and that is required by Federal law to be dispensed only by or upon an oral or written prescription of a practitioner licensed by law to administer

Table A1 (cont'd)	
Ethylene glycol	Household substancesin liquid form containing 10 percent or more by weight of ethylene glycol
Iron-containing drugs	Noninjectable animal and human drugs providing iron for therapeutic or prophylactic purposes, and containing a total amount of elemental iron, from any source, in a single package, equivalent to 250 mg or more elemental iron in a concentration of 0.025 percent or more on a weight to volume basis for liquids and 0.025 percent or more on a weight to volume basis for liquids and 0.05 percent or more on a weight-to-weight basis for nonliquids(e.g., powders, granules, tablets, capsules, wafers, gels, viscous products, such as pastes and ointments, etc.)
Dietary supplements	Dietary supplements that contain an equivalent of 250 mg or more of elemental iron, from any source, in a single package in concentrations of 0.025 percent or more on a weight-to-volume basis for liquids and 0.05 percent or more on a weight to-weight basis for nonliquids (e.g.,powders, granules, tablets, capsules, wafers, gels, viscous products, such as pastes and ointments, etc.)
Solventsfor paint or other similar surface-coating material.	Prepackaged liquid solvents (such as removers, thinners, brush cleaners, etc.) for paints or other similar surface-coating materials (such as varnishes and lacquers), that contain 10 percent or more by weight ofbenzene (also known as benzol), toluene(also known as toluol), xylene (also known as xylol), petroleum distillates(such as gasoline, kerosene, mineral seal oil, mineral spirits, naphtha, and Stoddard solvent, etc.), or combinations thereof, and that have a viscosity of less than 100 Saybolt universal secondsat 100 °F.,
Acetaminophen	Preparations for human use in a dosage form intended for oral administration and containing in a single package a total of more than one gram acetaminophen
Diphenhydramine	Preparations for human use in a dosage form intended for oral administration and containing more than the equivalent of 66mg diphenhydramine base in a single package
Glue removers	Household glue removers in a liquid form containing more than 500 mg of acetonitrile in a single container.
Permanent wave neutralizers	Home permanent wave neutralizers, in a liquid form, containing in single container more than 600 mg of sodium bromate or more than 50 mg of potassium bromate.
Ibuprofen	Ibuprofen preparations for human use in a dosage form intended for oral administration and containing one gram (1,000 mg) or more of ibuprofen in a single package
Loperamide	Preparations for human use in a dosage form intended for oral administration and containing more than 0.045 mg of loperamide in a single package (i.e., retail unit)

Table A1 (cont'd)	
Mouthwash	Mouthwash preparations for human use and containing 3 g or more of ethanol in a single package
Lidocaine	Products containing more than 5.0 mg of lidocaine in a single package (i.e., retail unit)
Dibucaine	Products containing more than 0.5 mg of dibucaine in a single package (i.e., retail unit)
Naproxen	Naproxen preparations for human use and containing the equivalent of 250 mg or more of naproxen in a single retail package
Ketoprofen	Ketoprofen preparations for human use and containing more than 50 mg of ketoprofen in a single retail package
Fluoride.	Household substances containing more than the equivalent of 50 milligrams of elemental fluoride per package and more than the equivalent of 0.5 percent elemental fluoride on a weight-to-volume basis for liquids or a weight-to-weight basis for non-liquids
Minoxidil	Minoxidil preparations for human use and containing more than 14 mg of minoxidil in a single retail package
Methacrylic acid	Liquid household products containing more than 5 percent methacrylic acid (weight-to-volume) in a single retail package
Over-the-Counter Drug Products.	Any over-the-counter (OTC) drug product in a dosage form intended for oral administration that contains any active ingredient that was previously available for oral administration only by prescription
Hazardous substances	All prepackaged nonemulsion-type liquid household chemical products that are hazardous substances as defined in the Federal Hazardous Substances Act (FHSA), and that contain 10 percent or more hydrocarbons by weight and have a viscosity of less than 100 SUS at 100 °F
Drugs and cosmetics	All prepackaged nonemulsion-type liquid household chemical products that are drugs or cosmetics as defined in the Federal Food, Drug, and Cosmetics Act (FDCA), and that contain 10 percent or more hydrocarbons by weight and have a viscosity of less than 100 SUS at 100 °F

APPENDIX B. The mainly published design patents of Child Resistant packaging in United State from 1970 to 2014

Table B1 The mainly published design patents of Child Resistant packaging in United State from 1970 to 2014

Patent Name	Year	Patent Number	Inventors	Category	Description	CR principle
Dispensing pill package or similar article[29]	1970	US D217900 S	Burton J. Gray	Unit dose	A dispensing pill package or similar article includes the outer sheath with the inner carrier	Requiring two-steps opening procedure
Safety locking closure[35]	1971	US 3623622 A	Sullivan Peter	Closure	A safety locking closure comprising a base portion and a cap hinged to the base. The base has an aperture giving access to the container and the cap swing to close or open the aperture. It requires a two- step opening procedure.	Requiring two-steps opening procedure
Two-part telescopic safety container[36]	1974	US 384407 A	R Buie	Container	The inner and outer cylindrical containers each have a closed end disposed remotely opposite one another for preferably thumb and forefinger compression together against an internal combined locking and moisture-seal spring device	Requiring "Squeeze and Turn"
Repturable blister pill package with safety backing[37]	1975	US 3921805 A	Newton L compere	Blister	The pill package is secured to the blister sheet a laminated backing sheet having at least one strong flexible polyester layer so that the pill cannot be forced through the package unless the backing sheet is first peeled away.	Requiring two-steps opening and adult's strength

Table B1 (cont'd)						
Triple-sealed closure for retaining liquids[38]	1975	US 3888373 A	Gach Peter P.	Closure	The closure cap includes an outer skirt and inner skirt and an intermediate skirt. The inner skirt is engaged within the container neck to form a first seal. Pluralities of concentric members depend from the container cap and engage the top of the container neck to form a second seal. An integral annular sealing ring is positioned between the intermediate skirt and the container to form a third seal.	Requiring three-steps opening
Pill packaging for opening only by a predetermined procedure[39]	1977	US 4011949 A	Robert J, Braber, Paul L, Weber	Blister	A packaging construction includes a pair of laminated layers, one layer having a pocket for receiving product and a cut-out space from the pocket, the other layer extending across both the pocket and cut-out, and a line of weakening for severing the layers to expose a finger-grip portion.	Performing a hidden alignment and requiring adult's strength
A sandwich style foil-backed blister package[40]	1978	US 4125190 A	John H. Davie Jr, Martin E. Hulick, Stephen J	Blister Wallet	A foil-backed blister sheet is sandwiched between upper and lower sheets formed by folding a single die-cut card. Blisters project through holes in the upper sheet, and the blister contents are removed by pushing them through the foil backing and through holes in the lower sheet.	Requiring three-steps opening

Table B1 (cont'd)						
Dial type child resistant dispenser[41]	1981	US 4298125 A	Walter G. Berghahn, Jack Weinstein	Dispenser	Tablets are dispensed by pushing the tablet pockets with enough force to rupture the sheet material.	Requiring adult's strength
Reversible child resistant closure[42]	1983	US 4406376 A	Walter G. Berghahn	Closure	A reversible child resistant closure having a child resistant and a non-child resistant mode of use. The closure is characterized by its low profile and tab that extends outwardly from the closure; this tab being engageable from below when closure is rotated into the appropriate position on the container.	Requiring "Press and Turn"
Child resistant tray[43]	1985	US 4561544 A	Randy F. Reeve	Container	A tray which slidably engages a lid and is locked in a fully closed position as a spring arm on the tray urges a locking detent on the arm into engagement with a locking aperture located in an adjacent side wall of the lid.	Requiring different simultaneous motions and adult's hand size
Child resistant hinge top closure[44]	1989	US 4821898 A	Ned J. Smalley	Closure	Pressing by the thumb on the tab while holding the package in the same hand ruptures the scores and deflects the tab inwardly for ready access to an exposed edge of the formed slot; and pressure on the edge opens the cover cap.	Requiring different simultaneous motions
Child resistant push-pull dispensing closure[45]	1990	US 4979648 A	Gary V. Montgomery, Alexander Mark	Closure	When the sleeve is pushed toward the base member to a READY position, the cap can be gripped for opening movement.	Requiring " Push and Pull"

Table B1 (cont'd)						
Bend 'n peel child resistant/tamper evident blister package[46]	1991	US4988004 A	Thomas D. Intini	Blister	It is reinforced by a backing sheet made of a material which separates into strata on tearing and adhered to a rupturable film closing article containing pockets. The backing sheet is provided with tabbed tear strips overlying the pockets	Requiring three-steps opening and adult's strength
User friendly child-resistant blister packages[47]	1994	US 5310060 A	John M. Bitner, Craig T. Vanderburg, Curtis E. Hart	Blister	The blister package has pull tabs which are designed to be pulled away from, rather than towards, article receiving pockets. A young child or user of the blister package can only access one article-receiving pocket at a time, whether deliberately or inadvertently.	Requiring " Push and Pull"
Convertible child-resistant blister package[48]	1998	US 5758774 A	Wayne T. Leblong	Blister	A blister package which can be converted from child-resistant to nonchild-resistant at the user's discretion.	Requiring two-steps opening
Child-resistant tear-open synthetic resin bag[49]	1998	US 5826985 A	Frank C. Goodman, Robert T. Seeley, Robert J. Dempsey	Bag	One end closure of the bag is provided with a tear-propagating slit which can be readily manipulated by an adult to tear off a corner of the bag and thereby form a pour spout for dispensing the contents of the bag in a controlled manner.	Requiring adult's strength and tooled access
Squeeze and turn flip top child resistant package[50]	1998	US 5779072 A	John D. Krebs	Closure	When the closure is squeezed and turned, the flip top is released; and wherein the closure is adaptable to either cylindrical or other cross sections of containers.	Requiring "Squeeze and Turn"

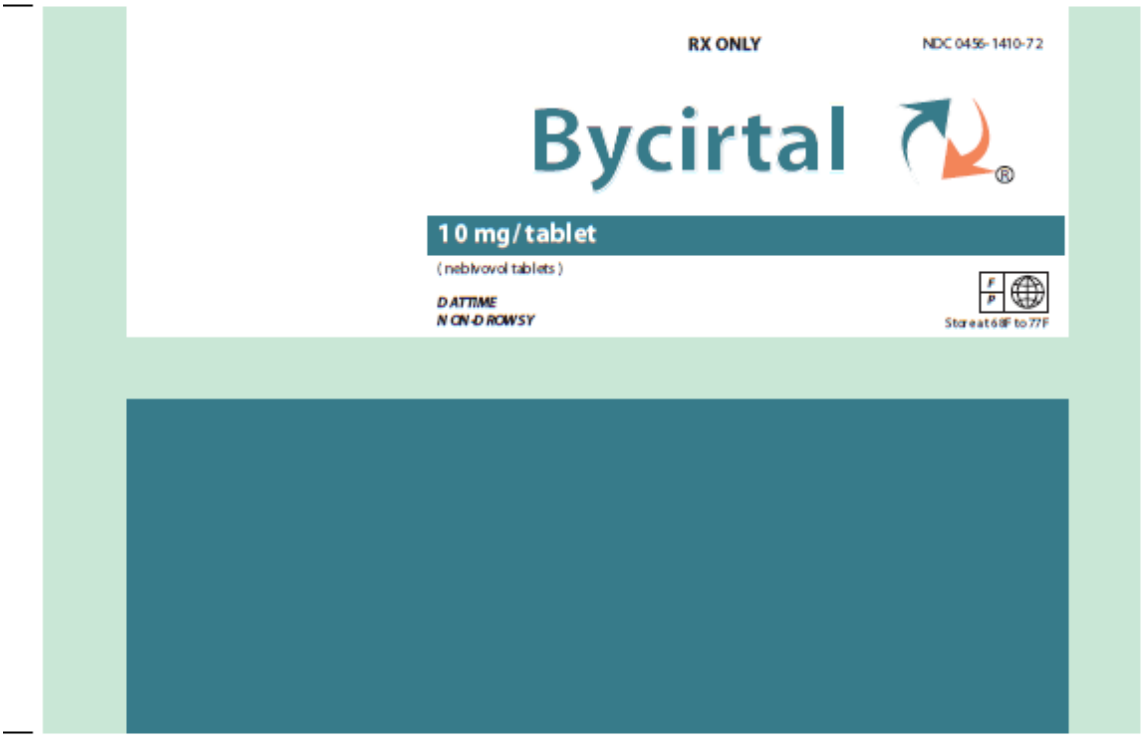
Table B1 (cont'd)						
Directional push and peel easy to open child resistant blister package[51]	1999	US 5894930 A	Lynn Faughey, Kelley Rowles, Charles T. Love	Blister	The blister is opened by pushing on the pre-formed cavity and score area to easily break the land area and free the backing closure sheet at the score forming a pull allowing for easy access to separate and pull the backing material towards the product cavity and thus exposing the product cavity.	Requiring two-steps opening
Unit dose packaging system (udps) having a child resistant locking feature[52]	2001	US6230893B1	Meredith McHugh Karow	Unit dose	A two piece paperboard package that houses a unit dose product on an internal slide card within an outer paperboard shell. This package may have one or more internal or external lock(s) that prevent the slide card from being pulled out without triggering some type of lock release mechanism.	Requiring two-steps opening and tooled access
Anti back off screw on closure[53]	2001	US6296130 B1	Michael J. Forsyth,	Closure	Screw on caps for bottles that have an anti back off feature formed on a hinged tab of the cap engaging detent teeth below the threads on the bottle. The hinge has a unique configuration that enables the tab to snap into and hold a gripping position while avoiding temporary distortion or creep.	Requiring adult's strength

Table B1 (cont'd)						
One hand opening child resistant blister pack container[54]	2004	US6679381 B1	Randall G. Bush	Blister	A blister pack container having child resistant characteristics yet, this can be opened with one hand. the finger pads can be unlocked with an inward and downward force thereby opening the container.	Requiring adult's hand size
Child-resistant flip-top dispensing closure and package[55]	2006	US7404495B2	Wing-Kwong Keung	Closure	A child-resistant dispensing closure includes a base having a deck with a dispensing opening and a peripheral skirt.	Requiring adult's strength
Friction surface for push and turn child resistant closure[56]	2010	US7815061B1	Clayton Robinson, William J. Shankland	Closure	For removal of the combined closure, both downward and counter-clockwise rotational force is applied to the over cap. The use of a highly frictional material more readily imparts rotational force on the under cap when utilized as depicted herein.	Requiring " Push and Turn" and adult's strength
Non-removable closure with integral RFID[57]	2010	US7772981B1	Phil Lambert, Mark Branson	Closure	A non-removable closure having a radio frequency identification, RFID, circuit integral therein. The RFID may be active or passive and may be integral with the top wall or side wall of the closure.	Requiring tooled access
Flip-top dispensing system with a child resistant latch mechanism[58]	2011	US7861873 B1	Jason Bragg, Mark K. Branson, Clifton C. Willis	Closure	A child resistant dispensing system having a flip-top closure. The flip-top closure has a push button positioned in the skirt of the flip-top lid wherein an opposed squeeze disengages the child resistant latch mechanism.	Requiring " Push and squeeze"

Table B1 (cont'd)						
Child resistant blister package housing with tooled access[59]	2011	US7926660B2	Steve Jones, Rodney Dixon	Blister	A packaging blank includes a first panel and a second panel. The first panel defines at least one blister aperture and at least one tool portion. The second panel defines at least one tab strip and at least one tool access portion. The at least one tab strip is at least partially severable from the packaging blank.	Requiring tooled access

APPENDIX C. Graphic drawing- blister wallet

Figure C1 Graphic drawing- blister wallet



APPENDIX D. Specification of camera hidden box

Figure D1 Specification of camera hidden box

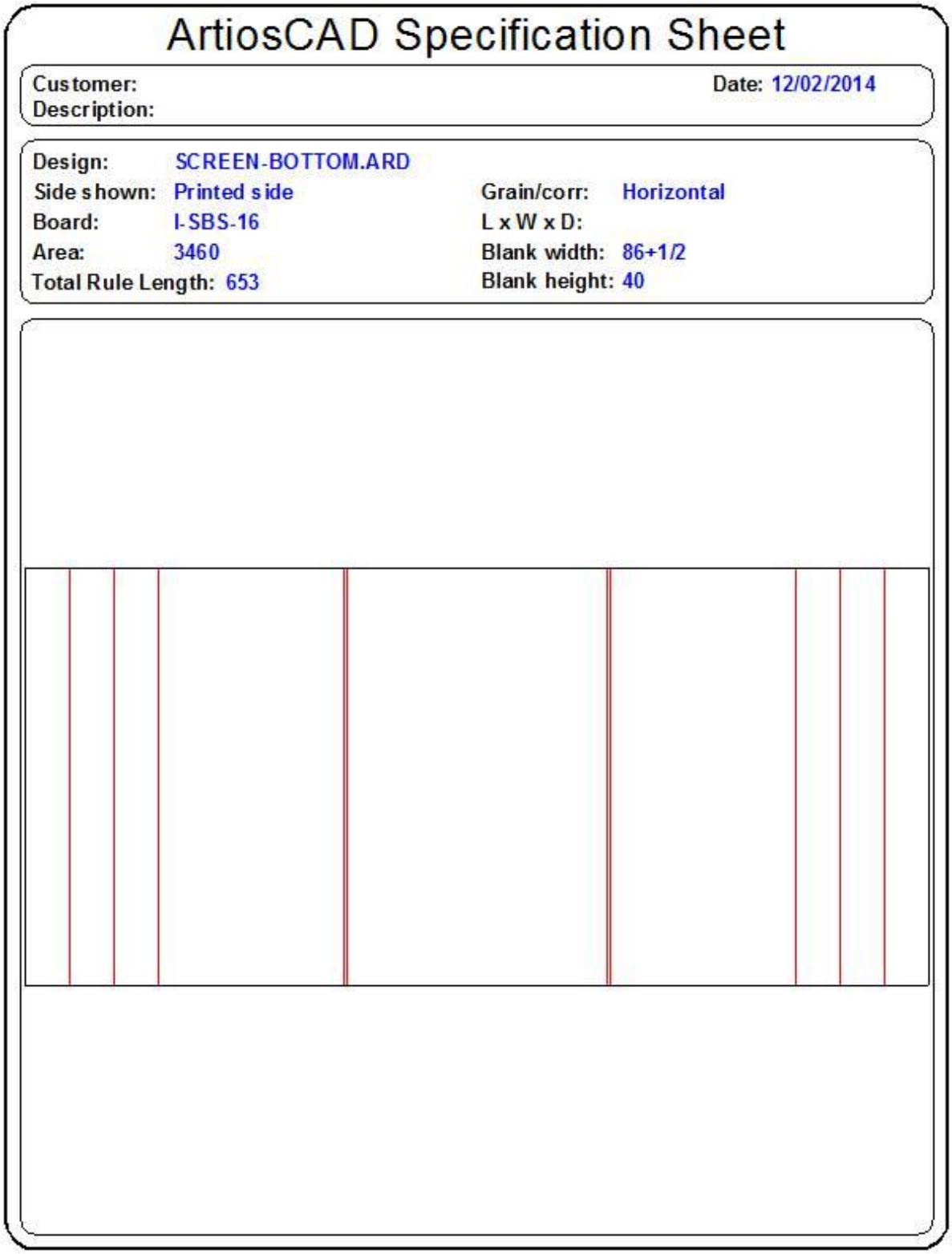


Figure D1 (cont'd)

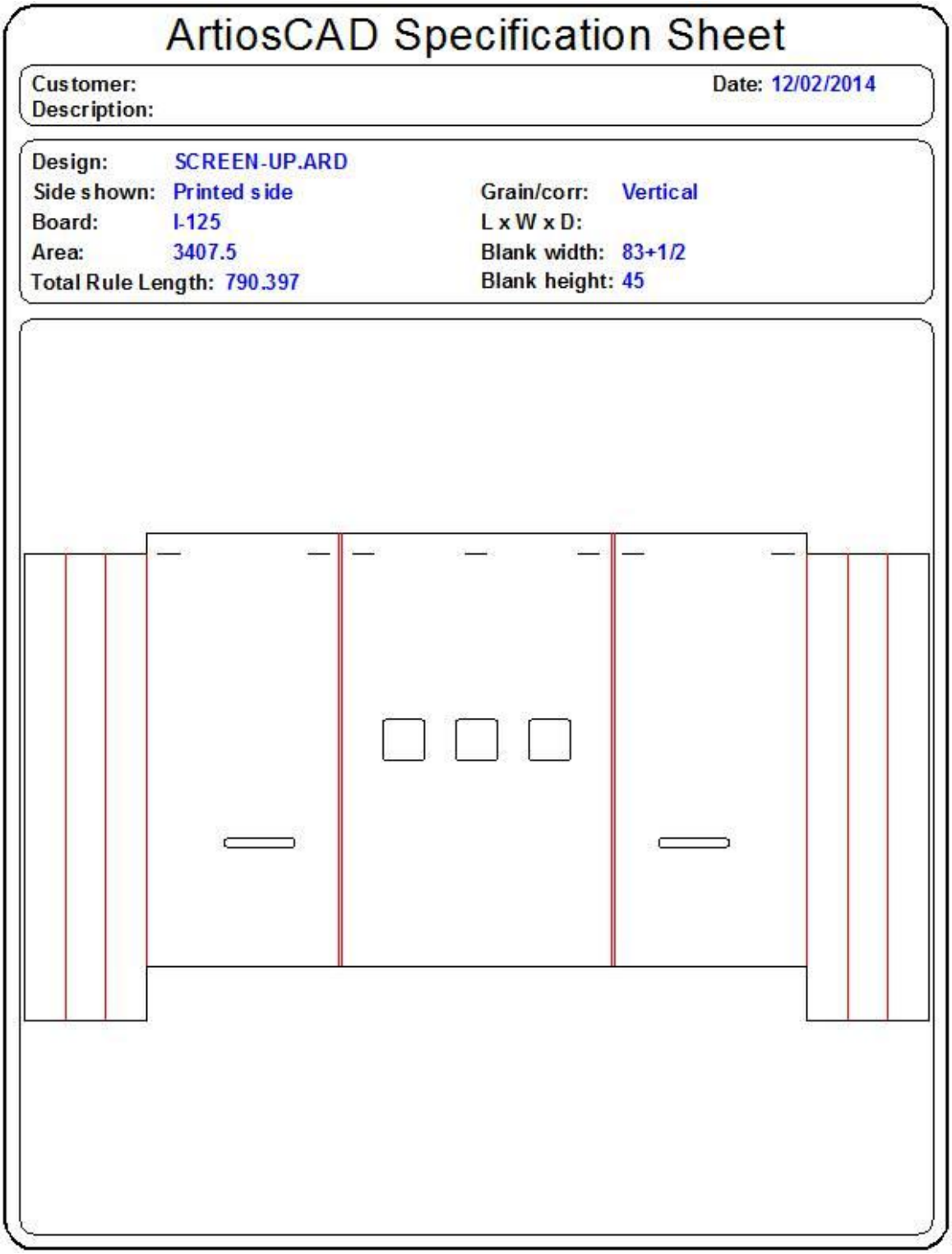
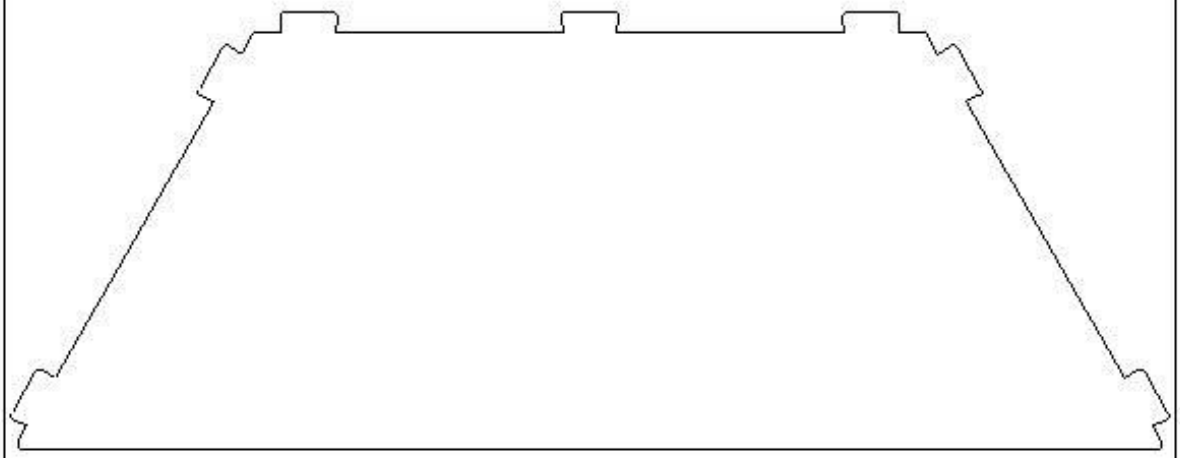


Figure D1 (cont'd)

ArtiosCAD Specification Sheet

Customer:
Description:
Date: 12/02/2014

Design:	SCREEN-TOP.ARD		
Side shown:	Printed side	Grain/corr:	Horizontal
Board:	I-SBS-16	L x W x D:	
Area:	533.21	Blank width:	42.934
Total Rule Length:	126.977	Blank height:	16.213



APPENDIX E. Advertisement

Figure E1 Advertisement

Opportunity for children aged age 2 - 4 ½ to participate

in a research project on medical packaging

Visual distraction as a means of enhancing child resistance

Data suggests that there has been a recent increase in childhood poisonings from accidents involving drug products (both prescription and OTC) in homes. We would like to test the idea that fewer openings will happen and it will take children longer to open packages (buying parents more time) if visual images are added to drug packages to distract attention away from a package's opening feature. During the experiment, we will watch young children (aged age 2 - 4 ½) interacting with different medication packaging. These packages will contain safe, non-medical items in case children open them.

Research will take place at Great Lakes Marketing (3361 Executive Parkway Toledo, OH 43606 419-481-1039) and will take approximately 20 minutes. Parents must give permission for their child to participate. Children will also be asked if they want to participate. Children will be videotaped so that researchers can observe/analyze what kinds of packaging children are most attracted to. Children will not be identified by name, and parents may choose to not allow for presentation of the recordings in classrooms and conferences.

To participate in this study your child must:

- Be 2 years to 4 ½ years old
- Have your permission to be videotaped
- Have your signed permission (in the form of the official, signed consent accompanying this document)
- Have **no known food allergies**

Figure E1 (Cont'd)

Verbally agree to participate after a brief explanation of what we want them to do

In exchange for the child's participation, parents will receive $20 and children will receive $30. If at any time your child is uncomfortable with the testing or wishes to discontinue the process, they may discontinue participation without penalty (i.e. you and your child will still receive the incentive).

If you have questions or comments regarding this study, please Laura Bix at bixlaura@msu.edu or phone 517-355-4556. **To schedule testing please call Penny at Great Lakes Marketing at 419-481-1039.**

APPENDIX F. Consent form

Figure F1 Consent form

PARTICIPANT INFORMATION STATEMENT AND CONSENT FORM

Visual distraction as a means of enhancing child resistance

- Does a visual distracter lengthen time to open?

Your child is invited to participate in a research study of packaging designs. We are investigating whether the addition of a "visual distraction" on packages can enhance child resistance. In other words, can we draw the attention of a child away from the opening feature of a drug package by adding an interesting image that is far from the opening? If the idea is successful, it would add valuable time prior to opening. Despite the fact that child resistant closures are required on many products, according to National Electronic Injury Surveillance System data 56,000 children under the age of five are treated in emergency rooms after overexposure to medications. That is more than for car accidents!

The Michigan State University School of Packaging and Great Lakes Marketing are conducting a two-part study to investigate the use of visual distracters as a means of enhancing child resistance.

Your child is being asked to participate in Stage II of this study. During Stage II, we are testing whether (or not) the addition of a distracter adds time to open, or prevents opening of a package that is otherwise easily opened.

To participate, your child must:

Have no known food allergies

Be between age 2 - 4 ½ at the time of testing

Have your permission to be video taped

Verbally agree to participate after a brief explanation of what we want them to do

Figure F1 (cont'd)

Research will take place at Great Lakes Marketing and will take approximately 20 minutes. Children will be seated on a yellow carpet square or a red carpet square (in accordance whether or not you grant permission to show their video tapes for educational and conference purposes). We will provide them with a brief explanation of what we will be doing, and ask them if they would like to help us. Children that indicate that they do not want to participate will be escorted by a teacher back to their room. Those who indicate willingness to participate will be handed a package (that may or may not contain a distracter) and asked to do whatever they would like with it.

After the testing is over, your child will be thanked and told that these types of packages usually contain medicine and other things that they should never touch without their parents' permission because what is inside could hurt them. We will also provide you information from the Centers for Disease Control and Prevention (CDC) about how best to store medications in order to ensure your child's safety.

Participation is voluntary. Refusal to participate will involve no penalty or loss of benefits to which you or your child are otherwise entitled. You have the right to say no. You may change your mind at any time and withdraw. You may choose not to answer specific questions.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov. This Web site will not include information that can identify you. All testing will be videotaped to record your child's thoughts regarding the package and to serve as a backup indicator of time to select. Data will only be tracked by participant number, and will not be tied to your child's name. Any audible reference to your child's name will be removed prior to any public display of the video (provided you grant permission). Collected data (stored by subject number) will be held for a minimum of three years on password protected computers in the packaging HUB lab (currently room 159). Only the MSU appointed researchers and the Institutional Review Board will have access to the research records at MSU.

In exchange for the child's participation, you will receive $20 and your child will receive $30. If at any time your child is uncomfortable with the testing or wishes to

Figure F1 (cont'd)

discontinue the process, they may discontinue participation without penalty (i.e. you and they will still receive the incentive.

There is little immediate risk to your child in participating in this research. All tested packages will contain placebo product (a harmless lactose (milk based) pill). However, there is a chance that exposing your child to prescription drug packages will inspire their curiosity about them. In order to mitigate this risk, we are debriefing your child about the importance of never touching products of this type and sending home "Up and Away" information from the CDC about how to properly store any medications that you have in your home with this consent form. Please always store medications with closures securely fastened in a location not accessible to young children.

If your child is injured as a result of this study to a point that requires medical attention, and you have insurance for medical care, your insurance carrier will be billed in the ordinary manner. As with any medical insurance, any costs that are not covered or in excess of what are paid by your insurance, including deductibles, will be your responsibility. The University's policy is not to provide financial compensation for lost wages, disability, pain or discomfort unless required by law to do so. This does not mean that you are giving up any legal rights you may have.

If you have concerns or questions about this study, such as scientific issues, or to report an injury, please contact Dr. Laura Bix, Associate Professor of Packaging at 448 Wilson Road # 153 Michigan State University 48823 at 517-355-4556 or bixlaura@msu.edu.

If you have questions or concerns about your child's role and rights as a research participant, would like to obtain information or offer input, or would like to register a complaint about this study, you may contact, anonymously if you wish, the Michigan State University's Human Research Protection Program at 517-355-2180 or e-mail irb@msu.edu or regular mail at 408 W. Circle Drive, 207 Olds Hall, MSU, East Lansing, MI 48824.

Figure F1 (cont'd)

Signing below indicates voluntarily agreement to have your child participate in the study examining the effect of visual distracters on their desire to enter a package.—

Signing below also indicates that you agree to have your child videotaped during these sessions.

---------- ----------

Print the name of your child here Your child's birthdate

---------- ----------

Signature of Parent or Legal Guardian Date

PLEASE INITIAL ONE OF THE FOLLOWING AS WELL- and Sign that you have received the CDC information regarding safe storage practices (below)

☐ I grant permission to have edited portions of the video tapes of my child shown for the purposes of education and conferences where people may gain insights from the learnings that occur as a result of this research. I understand that any audible reference to the child's name will be removed.

☐ I DO NOT grant permission to have edited portions of the video tapes of my child shown. I understand that he/she will still be taped, but that only MSU researchers and IRB personnel from MSU will have access to these tapes for the purpose of verifying the timing of the selection of the packages. Researchers will not use the last names of children, and data will only be identifiable by subject number. My child's privacy will be protected to the maximum allowable extent of the law.

I have received the CDC Up and Away information about safe medication storage practices (attached).

_____

(Sign Here)

APPENDIX G. Assent script

Assent Script- children between 2 - 4 ½ year olds

Researcher :
Hi, are you guys (state name from consent form) and (state name from consent form)? Good. I need your help with a project that I am working on. My name is (researcher name), and I am here from Michigan State University to try to learn about you guys and what you think of packaging.
Today, I am going to ask you to help me with a few things. I have some packages in this basket. I am going to hand it to you and ask you to do whatever you would like with it. Does that make sense? Do you want to help me with this? Great, let's get started.

(In order to limit the coaching or helping from parents, a friendly reminder is needed to the parents before testing)
I know that we want to as parents help our children as much as possible, but we need to see what they do on their own. So please resist the urge to coach them or try to help them anyway.

(Start the stopwatch after children take over the packages)

(1) if they open the vials/blisters successfully, we do not need to continue the test: Thank you. Please give it back to me.
(2) If they say something about not wanting to touch the packages because they are told not to touch medicine:
Ok, I am very glad you know not to touch these types of packages and you are right.

(After three minutes)
Ok, thank you! Now, I need get the vials/blisters back. Can you put them into the basket again?

(After testing of one pair, debrief is needed to the children)
OK, I would like to thank you guys very much for helping me today. I want to let you know that these types of packages can have medicine inside them. You should never touch these types of packages without your mom or dad's permission. It could hurt you. Will you promise me not to touch this type of package at home unless your mom and dad is there and say it is OK?

APPENDIX H. Data coding category

Table H1 Data coding category

Factors	Description	Vials	Blisters
Subjects	Define the unique number of each kid	√	√
Partner	Specify the subject number who takes the testing with	√	√
Pairs	Define the unique number of each pair	√	√
Room	Specify the tester by the Room number who conducts the testing. 1=Room A; 2=Room B; 3=Room C.	√	√
Tape	Capture whether the video document is legally released to the public (This column is not related to the data analysis, just for reference only). 1=Yes, 2=No.	√	√
Gender	Specify the gender (Girl/ Boy) of each subject. 1= Male, 2=Female.	√	√
Age*	Specify the age (by month) of each subject	√	√
Age Group	Specify the age group of each subject. 42 to 51 month is belonging to protocol group. 1= Non-protocol group, 2=Protocol group.	√	√
Package	Specify the packaging type (Vial/ Blister) that the subject is tested.1= Vial, 2=Blister.	√	√
Distracter	Capture whether the package is designed with a distracter or not.1=No, 2=Yes.	√	√
Treatment	Define the number of different treatment combinations. 1= Plain Vial, 2=Vial with distracter, 3=Plain Blister, 4=Blister with distracter.	√	√
Open	Note the fact whether a subject open the package or not.1=No, 2=Yes.	√	√
Time to open	Record the opening time if a subject opens the package successfully.	√	√
Distracter Exposure	Specify whether the distracter is exposure / partly exposure to a subject. 1=No, 2=Yes partly (open the wallet but not unfolded the blister), 3=Yes totally (open the wallet and unfolded the blister).		√
Involved in…	Specify whether a subject is involved positively to the test / shows some interested to the package. 1= No interested in package (Do nothing / Passive hold all the time /Cry all the time), 2=Yes.	√	√

Table H1 (cont'd)			
Noticing distracters	Rank different levels whether a subjects Notice the distracter or not. 1= No at all (Do nothing / Passive hold all the time /Cry all the time), 2= Do some action related to the package but not with the distracter, 3=Comment it; 4= Play it.	√	√

* Inclusion of age in the model as a quantitative explanatory covariate was evaluate but not pursued in the final model as the shape of the functional relationship between age and time to open was not clear.

APPENDIX I. Up and Away brochure

Figure I1 Up and Away brochure

Figure I1 (cont'd)

Know the facts.

More than **60,000** young children end up in emergency departments *every* year because they got into medicines while their parent or caregiver was not looking.

Families take medicines and vitamins to feel well or stay well. Any kind of medicine or vitamin can cause harm if taken in the wrong way or by the wrong person, even medicine you buy without a prescription. All medicines and vitamins should always be kept up and away and out of your child's reach and sight.

Figure I1 (cont'd)

Protect your child. Here's how.

**Put medicines and vitamins up and away—
out of reach and out of sight.**

Children are curious and put all sorts of things in their mouths. Even if you turn your back for less than a minute, they can quickly get into things that could hurt them.

Pick a place your children cannot reach

Find a place in your home that is too high for children to reach or see. Different families will have different places. Walk around your house and decide on the safest place to keep your medicines and vitamins.

Put medicines and vitamins away every time

Always put *every* medicine and vitamin away *every* time you use it. This includes medicines and vitamins you use *every* day. Never leave them out on a kitchen counter or at a sick child's bedside, even if you have to give the medicine again in a few hours.

Make sure the safety cap is locked

Always relock the safety cap on a medicine bottle. If the medicine has a locking cap that turns, twist it until you hear the click or you cannot twist anymore. Remember, even though many medicines and vitamins have safety caps, children may be able to open them.

Figure I1 (cont'd)

Teach your children about medicine safety

Tell your children what medicine is and why you must be the one to give it to them. Never tell children medicine is candy to get them to take it, even if your child does not like to take his or her medicine.

Tell guests about medicine safety

Ask houseguests and visitors to keep purses, bags, or coats that have medicines in them up and away and out of sight when they are in your home.

Be prepared in case of an emergency.

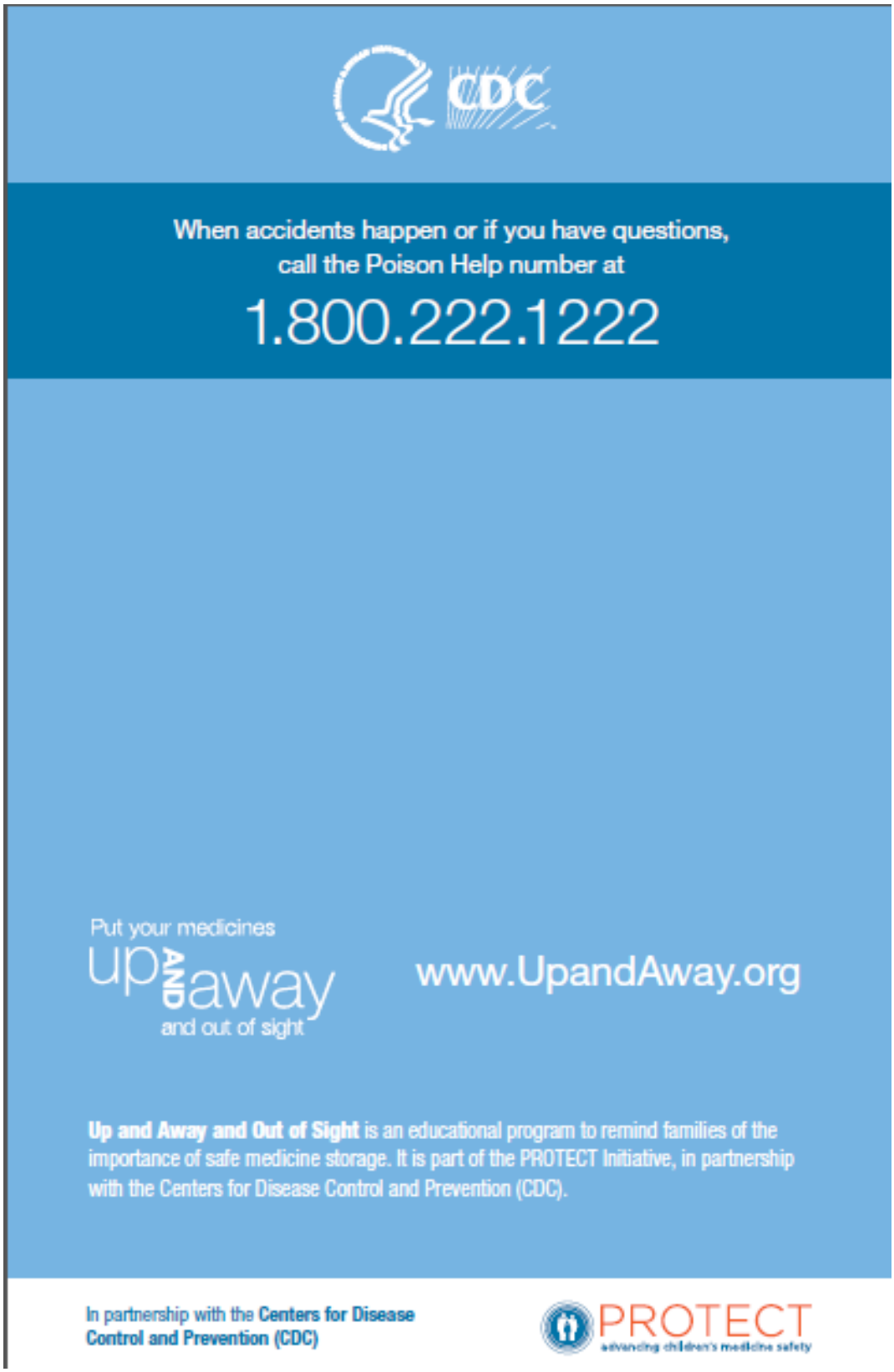
Program the Poison Help number into your phone

1.800.222.1222

right away if you think your child might have gotten into a medicine or vitamin.

Program the number into your home and cell phones so you will have it, when you need it.

Figure I1 (cont'd)



APPENDIX J. Up and Away tip sheet

Figure J1 Up and Away tip sheet

up AND away
and out of sight

Up and Away Medication Safety Tip Sheet

Medicines and vitamins help families feel well and stay well, but children are curious; to keep them safe, parents and caregivers must practice safe medicine storage. All medicines and vitamins should always be kept up and away and out of your child's reach and sight – *every* time they are used. The following tips can help:

- ✓ **Store medicines in a safe location** that is too high for young children to reach or see.
- ✓ **Never leave medicine or vitamins out** on a kitchen counter or at a sick child's bedside, even if you have to give the medicine again in a few hours.
- ✓ **Always relock the safety cap on a medicine bottle.** If it has a locking cap that turns, twist it until you hear the click or you cannot twist anymore.
- ✓ **Tell children what medicine is** and why you must be the one to give it to them.
- ✓ **Never tell children medicine is candy so they'll take it**, even if your child does not like to take his or her medicine.
- ✓ **Remind babysitters, houseguests, and visitors** to keep purses, bags, or coats that have medicines in them up and away and out of sight when they are in your home.
- ✓ **Program the Poison Help number 1-800-222-1222 into your home and cell phones** so you will have it when you need it.

To help remember to take your medicines or vitamins when they are no longer out in plain view, use the following tips:

- ✓ Write a note to yourself, and put the note somewhere you will see it: examples include the family bulletin board, refrigerator, bathroom mirror, or next to your keys.
- ✓ Set a daily reminder for yourself. For example, you could send yourself an e-mail or set the alarm on your watch or cell phone.
- ✓ Take your medicine or vitamins at the same time every day, if possible.
- ✓ Use a medicine log to keep track each time you take or give medicine.

BIBLIOGRAPHY

BIBLIOGRAPHY

[1] US Consumer Product Safety Commission. “Poison Prevention Packaging Information.”2007.

[2] Consumer Product Safety Act (1972). 15 USC-Public Law 92-573 36 Stat 1670. US 1972: 1051-84.

[3] Wright, V., & Hopkins, R. (1976). Administration of antirheumatic drugs. Annals of the rheumatic diseases, 35(2), 174-176.

[4] Meyer, M. E., & Schuna, A. A. (1989). Assessment of geriatric patients' functional ability to take medication. Annals of Pharmacotherapy, 23(2), 171-174.

[5] Bix, L., De La Fuente, J., Pimple, K. D., & Kou, E. (2009). Is the test of senior friendly/child resistant packaging ethical? Health Expectations, 12(4), 430-437.

[6] Bond, G. R., Woodward, R. W., & Ho, M. (2012). The growing impact of pediatric pharmaceutical poisoning. The Journal of pediatrics, 160(2), 265-270.

[7] US. Consumer Product Safety Commission. NEEISS Estimates Query Builder. 2014.

[8] Franklin, R. L., & Rodgers, G. B. (2008). Unintentional child poisonings treated in United States hospital emergency departments: national estimates of incident cases, population-based poisoning rates, and product involvement. Pediatrics, 122(6), 1244-1251.

[9] Krum, AJ. In Parenting, 2000; p.25-26.

[10] De la Fuente, C. J. (2006). The use of a universal design methodology for developing child-resistant drug packaging (Doctoral dissertation, Michigan State University).

[11] US. Census. B10050 Grandparents living with own grandchildren, 2005 American Community Survey 1-Year Estimates.

[12] US. Census. B10050 Grandparents living with own grandchildren, 2006-2012 American Community Survey 1-Year Estimates.

[13] Ferguson, R. W., & Mickalide, A. D. (2012). A Report to the Nation on Home Safety: The Dangers of TV Tip-Overs. Washington, DC: Safe Kids Worldwide.

[14] Mowry JB et al. 2012 Annual Report of the American Association of Poison Control Centers’ National Poison Data System (NPDS): 30th Annual Report. Clinical Toxicology. 2013; 51: 949-1229.

[15] Guidance on Compliance with the Medicines (Child Safety), Regulation 2003, MHRA; John Trepper, VP Perrit Labs “Blister Packaging and Harmonisation” May 2000

[16] Arena, J (1959). Safety Closure Caps. Journal of the American Medical Association, 134:1187-8

[17] Gray, B. J. (1970). U.S. Patent No. D217, 900. Washington, DC: U.S. Patent and Trademark Office.

[18] Smialek, J. E., Monforte, J. R., Aronow, R., & Spitz, W. U. (1977). Methadone deaths in children: a continuing problem. JAMA, 238(23), 2516-2517.

[19] ASTM D3475 - 14 Standard Classifications of Child-Resistant Packages

[20] VERE, M. (1976). Variety of child-resistant closures available. ASTM special technical publication, (609), 20-28.

[21] Yam, K. L. (Ed.). (2010). The Wiley encyclopedia of packaging technology. John Wiley & Sons.

[22] Hirsch, E. M., & Walker, L. A. (1995). U.S. Patent No. 5,381,912. Washington, DC: U.S. Patent and Trademark Office.

[23] Branson, M. K., Luker, C. E., Minnette, J. C., Montgomery, G. V., & Rudolph, E. (1999). U.S. Patent No. 5,927,527. Washington, DC: U.S. Patent and Trademark Office.

[24] Harrold, J. E. (2002). U.S. Patent No. 6,460,693. Washington, DC: U.S. Patent and Trademark Office.

[25] Gelardi, J. A. (2010). U.S. Patent Application 12/943,140.

[26] Ekkert, L. (1993). U.S. Patent No. 5,271,512. Washington, DC: U.S. Patent and Trademark Office.

[27] Ippoliti, R. J., & Nelson, J. J. (1980). U.S. Patent No. 4,187,703. Washington, DC: U.S. Patent and Trademark Office.

[28] Berns, T. (1981). The handling of consumer packaging. Applied ergonomics, 12(3), 153-161.

[29] Davis, B., & McArthur, D. (2011). U.S. Patent No. 8,079,475. Washington, DC: U.S. Patent and Trademark Office.

[30] Lahaussois, P. (2000). U.S. Patent No. 6,112,920. Washington, DC: U.S. Patent and Trademark Office.

[31] Anderson, G. J. (2002). U.S. Patent No. 6,338,408. Washington, DC: U.S. Patent and Trademark Office.

[32] Barriac, J. J. (1988). U.S. Patent No. 4,731,512. Washington, DC: U.S. Patent and Trademark Office.

[33] Loftin, C. S., & Rigby, W. R. (2012). U.S. Patent No. 8,317,026. Washington, DC: U.S. Patent and Trademark Office.

[34] Norman, D. A. (1988). The psychology of everyday things. Basic books.

[35] "SAFETY LOCKING CLOSURE." U.S. Patent 3,623,622, issued November 30, 1971.
[42] R Buie (1974)"CHILD RESISTANT SAFETY CONTAINER." U.S. Patent 3,844,407, issued October 29, 1974.

[36] Compere, N. L. (1975). U.S. Patent No. 3,921,805. Washington, DC: U.S. Patent and Trademark Office.

[37] Gach, P. P., & Montgomery, G. V. (1975). U.S. Patent No. 3,888,373. Washington, DC: U.S. Patent and Trademark Office.

[38] Braber, R. J., & Weber, P. L. (1977). U.S. Patent No. 4,011,949. Washington, DC: U.S. Patent and Trademark Office.

[39] Davie Jr, J. H., Hulick, M. E., & Verespy Jr, S. J. (1978). U.S. Patent No. 4,125,190. Washington, DC: U.S. Patent and Trademark Office.

[40] Berghahn, W. G., & Weinstein, J. (1981). U.S. Patent No. 4,298,125. Washington, DC: U.S. Patent and Trademark Office.

[41] Berghahn, W. G. (1983). U.S. Patent No. 4,406,376. Washington, DC: U.S. Patent and Trademark Office.

[42] Reeve, R. F. (1985). U.S. Patent No. 4,561,544. Washington, DC: U.S. Patent and Trademark Office.

[43] Smalley, N. J. (1989). U.S. Patent No. 4,821,898. Washington, DC: U.S. Patent and Trademark Office.

[44] Mark, A., & Montgomery, G. V. (1990). U.S. Patent No. 4,979,648. Washington, DC: U.S. Patent and Trademark Office.

[45] Intini, T. D. (1991). U.S. Patent No. 4,988,004. Washington, DC: U.S. Patent and Trademark Office.

[46] Bitner, J. M., Hart, C. E., & Vanderburg, C. T. (1994). U.S. Patent No. 5,310,060. Washington, DC: U.S. Patent and Trademark Office.

[47] Leblong, W. T. (1998). U.S. Patent No. 5,758,774. Washington, DC: U.S. Patent and Trademark Office.

[48] Dempsey, R. J., Goodman, F. C., & Seeley, R. T. (1998). U.S. Patent No. 5,826,985. Washington, DC: U.S. Patent and Trademark Office.

[49] Krebs, J. D. (1998). U.S. Patent No. 5,779,072. Washington, DC: U.S. Patent and Trademark Office.

[51] Faughey, L., Love, C. T., & Rowles, K. (1999). U.S. Patent No. 5,894,930. Washington, DC: U.S. Patent and Trademark Office.

[52] Karow, M. M. (2001). U.S. Patent No. 6,230,893. Washington, DC: U.S. Patent and Trademark Office.

[53] Forsyth, M. J., Webster, C. A., Martin, D. S., Black, J. P., & Seaman, B. R. (2001). U.S. Patent No. 6,296,130. Washington, DC: U.S. Patent and Trademark Office.

[54] Bush, R. G. (2004). U.S. Patent No. 6,679,381. Washington, DC: U.S. Patent and Trademark Office.

[55] Keung, W. K. (2008). U.S. Patent No. 7,404,495. Washington, DC: U.S. Patent and Trademark Office.

[56] Robinson, C., & Shankland, W. J. (2010). U.S. Patent No. 7,815,061. Washington, DC: U.S. Patent and Trademark Office.

[57] Branson, M., & Lambert, P. (2010). U.S. Patent No. 7,772,981. Washington, DC: U.S. Patent and Trademark Office.

[58] Bragg, J., Branson, M. K., & Willis, C. C. (2011). U.S. Patent No. 7,861,873. Washington, DC: U.S. Patent and Trademark Office.

[59] Becker, C., Dixon, R., Jones, S., Loftin, C., & Rigby, W. (2011). U.S. Patent No. 7,926,660. Washington, DC: U.S. Patent and Trademark Office.

[60] Hunter, R.M., Hunter, M.M., Berg, C.A., Cudney, S.A., Warford, B., and Flaherty, R.J. (1989, January). Cognitive skill based child-resistant medicine container. Bozeman, MT: Ywllowstone Environmental Science, Inc.

[61] Robert M. Hunter and Mary M. Hunter (1991). Child-Resistant Products can be Adult Friendly, Children's Environments Quarterly. Children's Safety Research.Vol. 8, No. 3/4, pp. 71-81

[62] Ruff, H. A., & Kohler, C. J. (1978). Tactual—visual transfer in six-month-old infants. Infant Behavior and Development, 1, 259-264.

[63] Cognitive Development . California Infant/Toddler Learning & Development Foundations. California Department of education. http://www.cde.ca.gov/sp/cd/re/itf09cogdev.asp

[64] K. Nakayama, G.H. Silverman (1986). Serial and parallel processing of feature conjunctions Nature, 320, pp. 264–265

[65] J.T. Enns, R.A. Rensink (1991).Preattentive recovery of three-dimensional orientation from line drawings. Psychological Review, 98, pp. 335–351

[66] J.J. He, K. Nakayama (1992).Surfaces vs. features in visual search. Nature, 359, pp. 231–233

[67] Morrison, H. B. (1997, October). Depth and Image Quality of Three-Dimensional, Lenticular-Sheet Images. In Proceedings of the Human Factors and Ergonomics Society Annual Meeting .Vol. 41, No. 2, pp. 1338-1342

[68] Mack, A., Pappas, Z., Silverman, M., & Gay, R. (2002). What we see: Inattention and the capture of attention by meaning. Consciousness and cognition, 11(4), 488-506.

[69] Langton, S. R., Law, A. S., Burton, A. M., & Schweinberger, S. R. (2008). Attention capture by faces. Cognition, 107(1), 330-342.

[70] O'Regan, J. K., & Noë, A. (2001). A sensorimotor account of vision and visual consciousness. Behavioral and brain sciences, 24(05), 939-973.

[71] Shelley-Tremblay, J., & Mack, A. (1999). Metacontrast masking and attention. Psychological Science, 10(6), 508-515.

[72] Raymond JE, Shapiro KL, Arnell KM (1992). "Temporary suppression of visual processing in an RSVP task: an attentional blink?" Journal of experimental psychology. Human perception and performance 18 (3): 849–60

[73] Fox, E., Russo, R., & Georgiou, G. A. (2005). Anxiety modulates the degree of attentive resources required to process emotional faces. Cognitive, Affective, & Behavioral Neuroscience, 5(4), 396-404.

[74] Miyazawa, S., & Iwasaki, S. (2010). Do happy faces capture attention? The happiness superiority effect in attentional blink. Emotion, 10(5), 712.

[75] Bornstein, M. H., & Arterberry, M. E. (2003). Recognition, discrimination and categorization of smiling by 5 - month - old infants. Developmental Science, 6(5), 585-599.

[76] Vaish, A., Grossmann, T., & Woodward, A. (2008). Not all emotions are created equal: the negativity bias in social-emotional development. Psychological bulletin, 134(3), 383.

[77] Montague, D. P., & Walker-Andrews, A. S. (2001). Peekaboo: a new look at infants' perception of emotion expressions. Developmental psychology, 37(6), 826.

[78] Colombo, J. (2001). The development of visual attention in infancy. Annual review of psychology, 52(1), 337-367.

[79] Puliafico, A. C., & Kendall, P. C. (2006). Threat-related attentional bias in anxious youth: A review. Clinical Child and Family Psychology Review, 9(3-4), 162-180.

[80] Hingley, A. T. (1997). Preventing childhood poisoning. In Preventing childhood poisoning. FDA.

[81] Franconeri, S. L., & Simons, D. J. (2003). Moving and looming stimuli capture attention. Perception & psychophysics, 65(7), 999-1010.

[82] Abrams, R. A., & Christ, S. E. (2003). Motion onset captures attention. Psychological Science, 14(5), 427-432.

[83] Franconeri, S. L., & Simons, D. J. (2005). The dynamic events that capture visual attention: A reply to Abrams and Christ (2005). Perception & Psychophysics, 67(6), 962-966.

[84] Gill, R. T., Barbera, C., & Precht, T. (1987, September). A comparative evaluation of warning label designs. In Proceedings of the Human Factors and Ergonomics Society Annual Meeting (Vol. 31, No. 4, pp. 476-478).

[85] Ansorge, U., & Becker, S. I. (2014). Contingent capture in cueing: the role of color search templates and cue-target color relations. Psychological research, 78(2), 209-221.

[86] Young, S. L. (1991, September). Increasing the noticeability of warnings: Effects of pictorial, color, signal icon and border. In Proceedings of the Human Factors and Ergonomics Society Annual Meeting (Vol. 35, No. 9, pp. 580-584).

[87] Braun, C. C., Sansing, L., Kennedy, R. S., & Silver, N. C. (1994, October). Signal word and color specifications for product warnings: an isoperformance application. In Proceedings of the Human Factors and Ergonomics Society Annual Meeting (Vol. 38, No. 17, pp. 1104-1108)

[88] Cave, K. R., & Wolfe, J. M. (1990). Modeling the role of parallel processing in visual search. Cognitive psychology, 22(2), 225-271.

[89] Duncan, J., & Humphreys, G. W. (1989). Visual search and stimulus similarity. Psychological review, 96(3), 433.

[90] Wolfe, J. M. (1994). Visual search in continuous, naturalistic stimuli. Vision research, 34(9), 1187-1195.

[91] Hillstrom, A. P., & Yantis, S. (1994). Visual motion and attentional capture. Perception & Psychophysics, 55(4), 399-411.

[92]Yantis, S., & Jonides, J. (1990). Abrupt visual onsets and selective attention: voluntary versus automatic allocation. Journal of Experimental Psychology: Human perception and performance, 16(1), 121.

[93] Todd, S., & Kramer, A. F. (1994). Attentional misguidance in visual search. Perception & Psychophysics, 56(2), 198-210.

[94] David McCandless (2012). Visual Miscellaneum: The Bestselling Classic, Revised and Updated: A Colorful Guide to the World's Most Consequential Trivia.

[95] Gellatly, A., Cole, G., & Blurton, A. (1999). Do equiluminant object onsets capture visual attention?. Journal of Experimental Psychology: Human Perception and Performance, 25(6), 1609.

[96] Lambert, A., Wells, I., & Kean, M. (2003). Do isoluminant color changes capture attention?. Perception & psychophysics, 65(4), 495-507.

[97] Snowden, R. J. (2002). Visual attention to color: Parvocellular guidance of attentional resources?. Psychological Science, 13(2), 180-184.

[98] Lu, S., & Zhou, K. (2005). Stimulus-driven attentional capture by equiluminant color change. Psychonomic bulletin & review, 12(3), 567-572.

[99] Franklin, R. L., & Rodgers, G. B. (2008). Unintentional child poisonings treated in United States hospital emergency departments: national estimates of incident cases, population-based poisoning rates, and product involvement. Pediatrics, 122(6), 1244-1251.

[100] Wilkerson, R., Northington, L., & Fisher, W. (2005). Ingestion of Toxic Substances by Infants and Children What We Don't Know Can Hurt. Critical care nurse, 25(4), 35-44.

[101] Berk, L. E. . Chapter 2 - Child Development (8th Ed). 2006.

[102] Crone, E. A., & Richard Ridderinkhof, K. (2011). The developing brain: from theory to neuroimaging and back. Developmental Cognitive Neuroscience, 1(2), 101-109.