Attachment I
Comments on Federal Register Notice

April 27, 2009

Agency for Healthcare Research and Quality: Proposed Collection of Information; "Understanding Patients' Knowledge and Use of Acetaminophen"

On February 26, 2009, the Agency for Healthcare Research and Quality (AHRQ) published a notice proposing a research project entitled "Understanding Patients' Knowledge and Use of Acetaminophen." This document is being submitted in response to the proposed research.

As stated in the supporting statement for the proposed study, acetaminophen-containing products are the most widely used analgesic/antipyretic drugs in the United States. A 2002 study on the patterns of medication use in ambulatory adults found that acetaminophen, as a single ingredient drug or as a component of a combination drug, was the most commonly used drug in the United States. (Kaufman et al. 2002). It is also well-recognized that such products present significant safety concerns, particularly with respect to accidental overdose and misuse. (Heubi et al. 1998, Larson 2005). It is, therefore, imperative that the packaging, labeling and related materials (e.g., advertising and promotional materials) for acetaminophen-containing products are clear and understandable to the majority of consumers, are factual and accurate, and represent the body of available medical information to ensure that consumers can make informed decisions regarding product selection and safe use.

While all acetaminophen-containing products identify acetaminophen's presence in product labeling within Drug Facts, and products often now identify acetaminophen on the front panel, there are many different over-the-counter (OTC) and prescription acetaminophen products covering a wide range of doses and indications. With so many choices, it would not be surprising that consumers may attempt to treat different conditions or symptoms with several products without realizing that all contain acetaminophen. Further complicating this issue is the fact that labeling for prescription products does not always identify acetaminophen as an ingredient, but instead employs the abbreviation APAP, which consumers are less likely to understand as acetaminophen. (FDA 2009) Improving

consumer awareness of acetaminophen – its presence in commonly used products, as well as dosing instructions and important warning information – is critical to ensuring the safe use of acetaminophen and to help reverse the trend of increasing acetaminophen-related toxicity discussed in the supporting statement.

For these reasons, we support the Agency's proposed research and respectfully submit the following comments:

Parent's Focus Group Questions

1. In Theme I: Knowledge, where it calls for the facilitator to hold up a bottle of acetaminophen, we recommend that the focus group participants see a bottle of Children's Tylenol brand of acetaminophen. Children's Tylenol is the leading market share brand of children's acetaminophen-containing products based on IRI data (as of March 22, 2009) with 37.1% market share; the next largest children's acetaminophen share is a compilation of the various store brand children's acetaminophen products (more than 20 different retailer brands) with a total market share of 10.3%. Because Tylenol users represent the largest body of acetaminophen users, it is critical to determine if they understand that Tylenol products contain acetaminophen and their perceptions about acetaminophen.

2. To maximize learnings from the proposed research, the parent's focus group should be limited to acetaminophen users. Parents who do not use acetaminophen-containing products are of limited use in identifying the issues, barriers and psychosocial factors surrounding how, when and why consumers use over-the-counter acetaminophen, which is the stated purpose of the research.

3. Many store brand acetaminophen-containing products use the term "non-aspirin" in the product name (e.g., Children's Non-Aspirin), which does little to inform the consumers that the products contain acetaminophen. We recommend adding questions to determine if consumers understand that the term "non-aspirin" pain

reliever means the product contains acetaminophen and the impact of this term on consumer behavior (e.g., would a parent be more likely to give both a Children's Tylenol product and a non-aspirin pain reliever to their child because it was not clear both contained acetaminophen?).

4. Acetaminophen has a relatively narrow therapeutic window, as liver injury may occur following a relatively small overdose. There appears to be an opportunity in Theme II: Beliefs about Benefits and Risks where probing questions may provide further information on consumer understanding of the therapeutic window for acetaminophen. Following the question on how much would you have to give your child to cause harm, it would be useful to ask why the parent believes the stated dose may cause their child harm and whether the stated dose is more than what is allowed on the label. There may be other opportunities, as well, and we encourage the Agency to review the questionnaire in its entirety to ensure this concept is fully covered.

5. The supporting statement indicates that there are literature reports of intentional overdose with acetaminophen in adolescents. We recommend including questions to determine if parents are aware of reports of attempted suicide by adolescents with acetaminophen and whether this knowledge impacts consumer behavior. This could be accomplished by modifying Theme V: Related Experiences to add a question about someone taking too much of this medicine on purpose (see comment 10 under Adult Focus Group questions below). A positive response would result in a follow-up question on whether this changed how they used the product.

6. In Theme VI: Labeling and Packaging, one of the probe questions for the bottle label asks about the number of pills in each bottle. The majority of acetaminophen products for young children is in liquid form (e.g., suspensions) rather than in pill form. We propose that the question be modified accordingly, perhaps to ask how many doses are in each bottle. Children's acetaminophen liquids/suspensions are often supplied with a device for dosing (e.g., a dosing cup or syringe). The ease of

use of the supplied dosing device may impact a parent's ability to properly dose their child, and we would recommend including questions to determine if the parent uses the device provided and, if they do, its ease of use.

Adult Focus Group Questions

7. In Theme I: Knowledge, where it calls for the facilitator to hold up a bottle of acetaminophen, we recommend that the focus group participants see a bottle of Tylenol brand of acetaminophen. Tylenol is the leading market share brand of acetaminophen-containing products based on IRI data (as of March 22, 2009) with 17.4% market share; the next largest adult acetaminophen share is a compilation of the various store brand children's acetaminophen products (more than 20 different retailer brands) with a total market share of 5.7%. Because Tylenol users represent the largest body of acetaminophen users, it is critical to determine if they understand that Tylenol products contain acetaminophen and their perceptions about acetaminophen.

8. To maximize learnings from the proposed research, the adult focus group should be limited to acetaminophen users. Adults who do not use acetaminophen-containing products are of limited use in identifying the issues, barriers and psychosocial factors surrounding how, when and why consumers use over-the-counter acetaminophen, which is the stated purpose of the research.

9. Many store brand acetaminophen-containing products use the term "non-aspirin" in the product name (e.g., Extra Strength Non-Aspirin), which does little to inform the consumers that the products contain acetaminophen. We recommend adding questions to determine if consumers understand that the term "non-aspirin" pain reliever means the product contains acetaminophen and the impact of this term on consumer behavior (e.g., would they be more likely to take both a Tylenol product and a non-aspirin pain reliever because it was not clear both contained acetaminophen?).

10. As noted, acetaminophen has a relatively narrow therapeutic window, as liver injury may occur following a relatively small overdose. There appears to be an opportunity in Theme II: Beliefs about Benefits and Risks where probing questions may provide further information on consumer understanding of the therapeutic window for acetaminophen. Following the question on how much would someone have to take to cause harm, it would be useful to ask why the consumer believes the stated dose may cause harm and whether the stated dose is more than what is allowed on the label. There may be other opportunities, as well, and we encourage the Agency to review the questionnaire in its entirety to ensure this concept is fully covered.

11. The supporting statement indicates that there are literature reports of intentional overdose with acetaminophen in adolescents. We recommend including questions to determine if consumers are aware of reports of attempted suicide by adolescents with acetaminophen and whether this knowledge impacts consumer behavior. This could be accomplished by modifying Theme V: Related Experiences to determine if the question asked about someone taking too much on purpose or by probing afterward if this was on purpose. Positive responses would result in a follow-up question on whether this changed how they used the product.

Physician/Pharmacist Interview Script

As mentioned in the previous sections, the supporting statement indicates there are literature reports of intentional overdose with acetaminophen in adolescents and further indicates that it is important to understand adolescent use of OTC acetaminophen in order to reduce the opportunity for intentional and unintentional misuse. Doctors and pharmacists may be an important contact point or resource for consumers who have direct or indirect experience with acetaminophen overdose. As such, the physician/pharmacist interviews should specifically solicit information about the potential intentional overdose, and the following comments make specific recommendations with regard to this topic:

12. We recommend adding a series of questions asking if the physician or pharmacist has heard from a patient or customer that they, or someone they know, intentionally overdosed on acetaminophen; the outcome, if known; and if the person who overdosed was an adult, adolescent or child.

13. Pack size limitations and mandatory blister packaging were implemented in the United Kingdom in 1998 in response to increasing concerns about intentional overdose with acetaminophen. A number of articles have been published (Bateman et al. 2003, Chan 2000; Gorman et al. 2007, Greene et al. 2006, Gunnell et al. 2000, Hawton et al. 2001, Hawton et al. 2004, Hughes et al. 2003, Mariarie 2007, Morgan and Majeed 2005, Morgan et al. 2005a, Morgan et al. 2005b, Morgan et al. 2007, Prince et al. 2000, Robinson et al. 2000, Sheen et al. 2002, Turvill et al. 2000) on the effectiveness of the new requirements, and a majority of the data indicate that use of blister packaging for acetaminophen and restricting the amount that can be purchased at one time is associated with a reduction in intentional acetaminophen overdose and its subsequent liver damage and death. Given similar concerns about intentional acetaminophen overdose in the United States, we recommend that a question related to the quantity of pills in a bottle be included for Question 5 when packaging and labeling are discussed. Alternatively, this could be included as a question in relation to legislation/policy under Question 6 with reference to the UK experience.

14. Following recent restrictions on sales of over-the-counter products containing pseudoephedrine and restrictions on sales of other consumer products to children and adolescents (e.g., cigarettes), we recommend that Question 6 be supplemented with a probing question on whether limiting purchase of acetaminophen-containing products to adults would help reduce intentional overdose in adolescents.

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2. Chan, Improvements in packaging of drugs and chemicals ,ay reduce the likelihood of severe intentional poisonings in adults. Human Exp. Toxicol. 19; 387-391, 2000.

3. Food and Drug Administration (FDA). Federal Register 74:18731-3, April 24, 2009.

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6. Gunnell et al, Use of paracetamol for suicide and nonfatal poisoning: Worldwide patterns of use and misuse. Suicide Life Threat Behav. 30; 313-320, 2000.

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McNeil

Consumer Healthcare

April 27, 2009

Doris Lefkowitz
Reports Clearance Officer
Agency for Healthcare Quality and Research
540 Gaither Road
Rockville, MD 20850

RE: Proposed Agency Information Collection Activities
Understanding Patients' Knowledge and Use of Acetaminophen
***Federal Register* 74(5): 8798-8799**

Dear Ms. Lefkowitz,

McNeil Consumer Healthcare, a major US manufacturer of analgesic drug products, markets a comprehensive line of Tylenol® (acetaminophen) brand single-ingredient and combination-ingredient products for adults and children, as well as acetaminophen-containing products under the Sudafed® and Benadryl® brand names for adults. McNeil also markets Motrin® (ibuprofen) products for use by adults and children, as well as St. Joseph® aspirin (81 mg) for use by adults only.

McNeil is committed to encouraging scientifically appropriate and adequate labeling as well as educational material that include consistent and clear language for consumer use. As such, McNeil has interest in ensuring that the current information collection activity provides an opportunity to gain useful consumer and healthcare professional insights regarding the use of OTC pain medications and provides the comments herein.

The Agency for Healthcare Quality and Research (AHRQ) has requested comment on a proposed qualitative survey to preliminarily identify issues that relate to the misuse and overdose of over-the-counter (OTC) acetaminophen, the results of which will be used in the design of a more comprehensive survey.[1] AHRQ requests comment on four areas of the proposed information collection activity. McNeil is specifically providing comments in two of the four areas: (a) Whether the proposed collection of information is necessary for the proper performance of AHRQ health care research, quality improvement and information dissemination functions, including whether the information

[1] *Federal Register*. "Agency Information Collection Activities: Proposed Collection; Comment Request." February 26, 2009: 8798-8799.

improvement and information dissemination functions, including whether the information will have practical utility and (c) Ways to enhance the quality, utility, and clarity of the information to be collected.

AHRQ Comment Request: (a) Whether the proposed collection of information is necessary for the proper performance of AHRQ health care research, quality improvement and information dissemination functions, including whether the information will have practical utility.

McNeil requests that the following be considered AHRQ in the proposed qualitative survey:

1) ***Both Rx-acetaminophen combination and OTC acetaminophen containing products should be included in the information collection activity to understand consumer behavior associated with concomitant use.***

FDA has identified the wide variety and availability of both OTC and prescription drug products that contain acetaminophen as a factor which may have resulted in potentially fatal or life threatening unintentional overdoses in adults.[2] A recent CDC publication reports that estimated rates for emergency department visits (per 100,000 drug uses/week) is higher for prescription acetaminophen containing products compared to single-ingredient products (10.25 vs 0.87) or compared to non-narcotic acetaminophen combination products (10.25 vs. 0.62).[3] Additionally, the Institute for Safe Medication Practice published the observation that when acetaminophen is included on the label of a prescription drug, it may be abbreviated as "APAP."[4] The information collection activity in development provides a potential opportunity to understand consumer perception and the awareness of prescription acetaminophen and understanding of the use of the "APAP" abbreviation on the OTC label.

2) ***Focus group research such as that proposed by the AHRQ qualitative survey has been useful for the design of education programs but should not be used in policy decisions or recommendations regarding packaging or labeling.***

Focus group research in the proposed information collection activity may be useful to understand the thinking of a group and has been useful for the design of education programs.[5] Such research may provide directional insight for future

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[2] Food and Drug Adminsitration. *Safety Concerns Associated with Over-the-Counter Drug Products Containing Analgesic/Antipyretic Active Ingredients for Internal Use.* January 22, 2004. http://www.fda.gov/cder/drug/analgesics/sciencepaper.htm (accessed April 10, 2009).

[3] Willy, M., J. Kelly, P Nourjah, D. Kaufman, D. Bednitz, and J. Staffa. "Emergancy department visits attributed to select analgesics, United States 2004-2005." *Pharmacoepidemiology and Drug Safety* 18, no. 3 (2009): 188-195.

[4] Institute for Safe Medication Practices. "Don't Hide the Acetaminophen." *Pennsylvania State Board of Pharmacy.* 2007-2008. http://www.dos.state.pa.us/bpoa/lib/bpoa/20/phabd/pharmacy07-08.pdf (accessed April 10, 2009).

[5] Gibbs, A. "Focus Groups." *Social Research Update* 19(1997) http://sru.soc.surrey.ac.uk/SRU19.html (accessed April 24, 2009)

research, learning about opinions and attitudes, pilot testing materials for assessments and generating recommendations[6] but it is not a scientific, controlled assessment of individualized behavior and should not be used in policy decisions or recommendations regarding packaging or labeling.

AHRQ Comment Request: (c) Ways to enhance the quality, utility, and clarity of the information to be collected.

McNeil requests that the following be considered by AHRQ in the proposed qualitative survey:

1) ***The product(s)and packaging being demonstrated in the AHRQ study should be representative of those on the OTC market.***

The packaging and presentation of the product (even with the same active ingredient) can vary by manufacturer. Different manufacturers of the same active ingredient label the products with differences in prominence of active ingredients on the package. Examples of various labeling are provided in Attachment A. Such variations should be controlled for in both the preliminary information collection activity and any subsequent research and conclusions should be product specific. Any survey should take various products (both adult and pediatric) into account as consumers may have multiple products in house from different manufacturers at a given time. To eliminate bias and obtain reliable results, survey information should be gathered using representative packaging from all types of products, not just one brand or product type. In addition, the participant should be permitted to refer to the product package while answering the survey questions since the package information would be available to the consumer at the decision to use.

2) ***During interviews with pharmacists and physicians, retail-practice, community setting pharmacists should also be included in the study population so as to have a representative sample of sources of medication information often utilized by consumers.***

As background, "**Aim 2**" of the proposed AHRQ study proposes to qualitatively explore experiences and practices of key professional informants, including physicians and pharmacists, with respect to communicating information regarding the administration and risks of OTC acetaminophen to consumers and patients. As published in the *Federal Register*, the current information collection activity design recruits pharmacists from hospitals and clinics but overlooks the retail-practice, community setting pharmacist. Consumers often rely on the retail-practice pharmacist as a source of information. A recent survey conducted by the American Pharmacists Association found that retail pharmacists make on-

[6] University of Waterloo. "Focus Group – Quick Guides." (2003) http://www.ahs.uwaterloo.ca/hsg/documents/QUICK_GUIDE_-_focusgroupsDS.pdf (Accessed on April 24, 2009)

average 35 recommendations for OTCs per week and 83% of these patients purchase the pharmacist recommended product.[7] Failing to include the retail-practice pharmacist in the AHRQ interview population will not provide a representative sample of sources of consumer medication information upon which to base future surveys or educational materials.

In summary, in order for the proposed by AHRQ data collection activity to be of optimal value in the development of future consumer education programs, McNeil requests specific additional considerations and improvements be made in the study design and survey instrument.

Thank you for this opportunity to provide comments. Please contact my office if you have any questions or require further clarification.

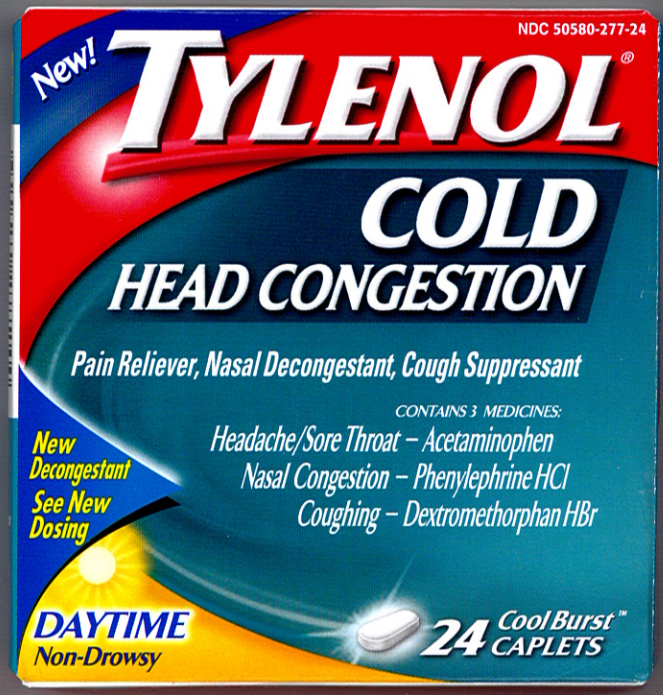
Sincerely,

Patricia Straight
for

Lynn Pawelski
Vice President – Regulatory Affairs
McNeil Consumer Healthcare
215-273-7731

Attachments
A: Representative Labels of OTC Acetaminophen Containing Products
B: Copies of References

[7] Amercian Pharmacists Association. "Annual OTC Survey." *Pharmacy Today*, February 2009: 4-23.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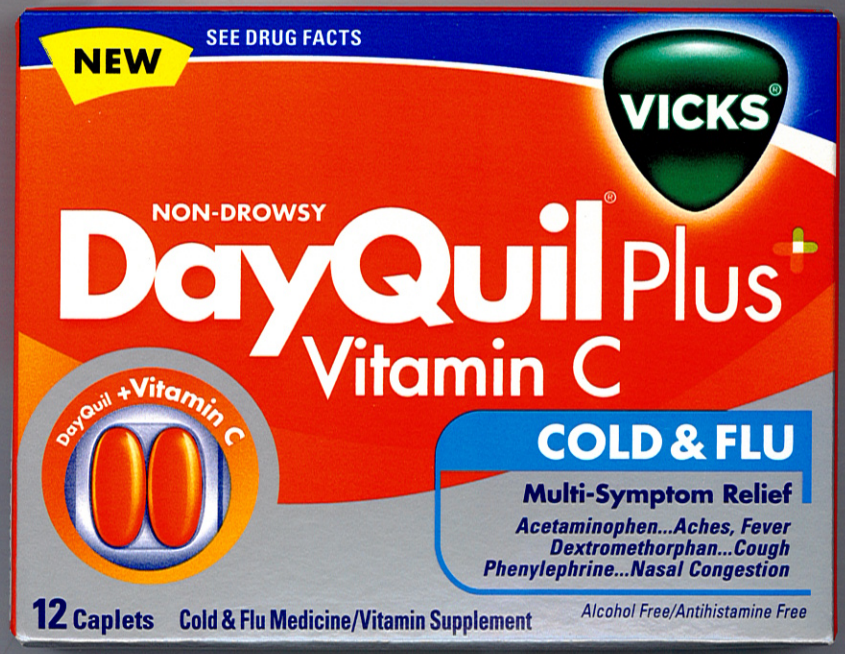
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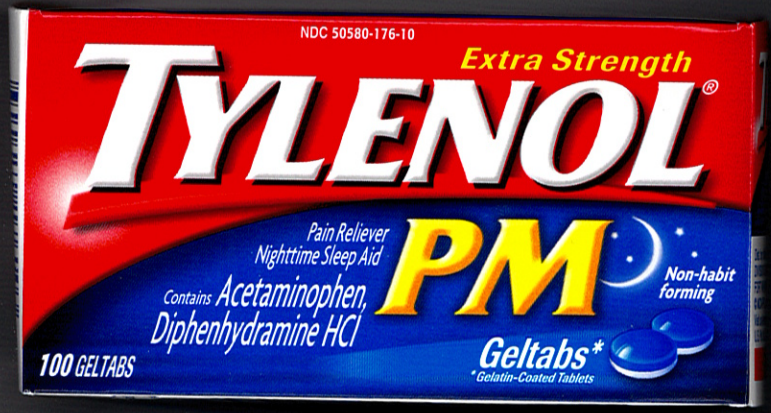
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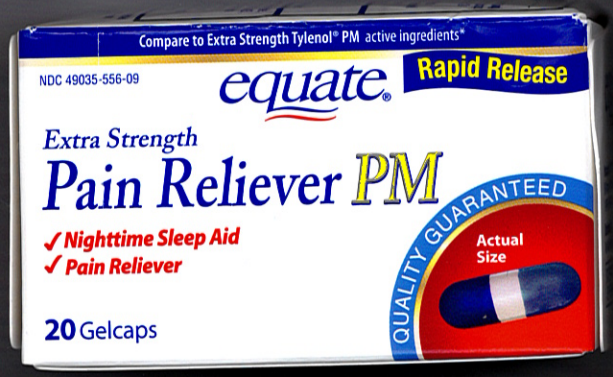
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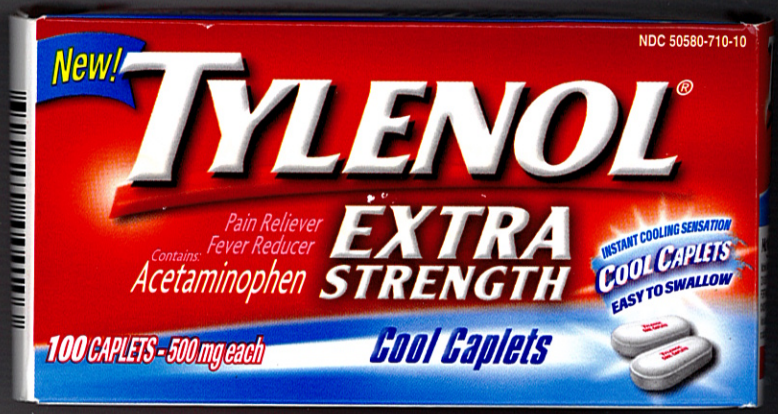
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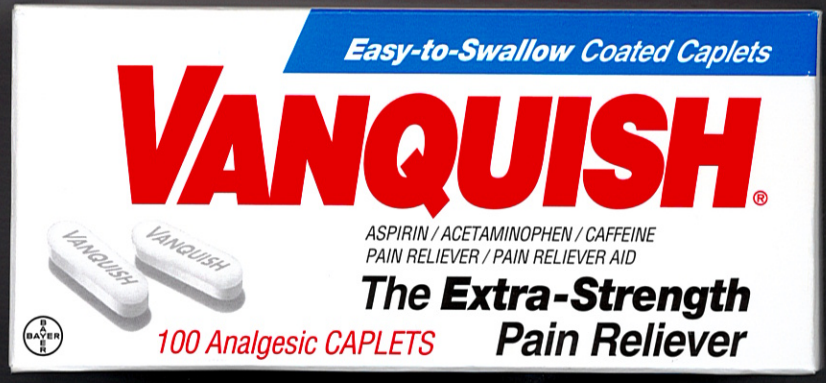
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