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May 31, 2000

**VIA COURIER**

Dockets Management Branch  
Food and Drug Administration  
Department of Health and Human Services  
Room 1-23  
12420 Parklawn Drive  
Rockville, Maryland 20857

**Re: Citizen Petition to Remove False and Deceptive Labeling for Tylenol®  
Arthritis Extended Relief**

The Aspirin Foundation of America (“AFA”) hereby petitions the Food and Drug Administration (FDA) to order McNeil Consumer Products Company (“McNeil”) to discontinue making a false and misleading efficacy claim through the unapproved name of its product “TYLENOL® ARTHRITIS Extended Relief” and/or to take appropriate enforcement action to preclude McNeil’s continuing sale of a misbranded product.

Two years ago McNeil changed the name of Tylenol Extended Relief in a manner that adds an explicit claim that the product provides “extended relief” for arthritis. As explained herein, the new name for the product – TYLENOL ARTHRITIS Extended Relief – makes an inherently ambiguous and deceptive claim that the product provides “extended relief” for arthritis.

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The symptoms of arthritis include both pain and inflammation. Thus, for the claim of “arthritis extended relief” to be true, the product must relieve both the pain and the inflammation of arthritis. Acetaminophen, however, which is the sole active ingredient in TYLENOL ARTHRITIS Extended Relief, is solely a pain reliever and not an anti-inflammatory. Thus, the claim that Tylenol provides “ARTHRITIS Extended Relief” is false. McNeil has compounded this falsehood by prominently featuring the product name in advertising in a manner that suggests intentional deception, or at a minimum, conscious disregard for the likelihood that consumers will be misled.

This deception has been made possible because McNeil unilaterally revised the name of its product to add the central claim of efficacy in providing extended relief for arthritis *without FDA approval*. As we discuss below, a labeling change of this magnitude is not exempt from the pre-approval requirement as a simple “editorial or similar minor change.” 21 C.F.R. § 314.70(d)(3). It is quite clear that McNeil should have submitted a supplemental NDA to FDA for approval of the name change. *Id.* § 314.70(b)(3). Such approval would not have been forthcoming in any event, even if it had been applied for, because the claim that Tylenol provides “Extended Relief” for “Arthritis” is patently false and renders the product misbranded in violation of Section 502 of the Act. *See* 21 U.S.C. § 352.

Moreover, McNeil’s recent adoption of a deceptive product name is but the latest in an escalating campaign to persuade arthritic consumers to switch from anti-inflammatory medications to its acetaminophen product. That campaign has been replete with deceptive television and print advertising, some of which McNeil conceded to be inappropriate, and even

culminated in a consent agreement between McNeil and 19 state attorneys general over deceptive advertising directed to arthritis sufferers. Now that McNeil has moved from deceptive advertising to deceptive labeling, it is time for FDA to take action.

*Action Requested*

We urge FDA to declare TYLENOL ARTHRITIS Extended Relief misbranded and to direct McNeil to revise its labeling by removing false or misleading statements. McNeil should be prohibited from labeling TYLENOL ARTHRITIS Extended Relief as a treatment for arthritis, and should be required to disclose with sufficient prominence the limited efficacy of the product on any future packaging. Additionally, all advertising that mentions efficacy for arthritis for the "Extended Relief" product should carry an explicit disclaimer that the product is not effective to reduce or relieve inflammation and that it is effective only against the minor pain that accompanies arthritis. Such a disclaimer should be of the same prominence and conspicuousness as any oral or printed use of the word "arthritis," including use in the product name. Advertising for TYLENOL ARTHRITIS that does not carry such disclaimers may render the product misbranded by creating new claimed uses for the product that are not supported by FDA-approved labeling. *See* 62 Fed. Reg. 64075 (information disseminated by manufacturers in other contexts "can create new intended uses for the products, which must be reflected in approved labeling of the products").<sup>1/</sup>

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<sup>1/</sup> *See also United States v. Articles of Drug . . . Designated B-Complex Cholinol Capsules*, 362 F.2d 923 (3d Cir. 1966).

*Statement of Grounds*

**I. Background.**

**A. The 1994 NDA for Tylenol Extended Relief.**

In 1994 McNeil submitted a New Drug Application for an acetaminophen product that was to be called "Long Lasting Tylenol Extended Relief." FDA initially objected to the use of the term "Long Lasting" because of its ambiguity, and McNeil agreed to drop the term. The claimed indications for the product were as follows:

Indications: Extended Relief Tylenol caplets act quickly to provide temporary relief up to 8 hours from minor aches and pains of arthritis, headaches, menstrual cramps, backaches, and from the discomfort of fever due to colds and flu.

With the truncated name "Tylenol Extended Relief" and the indication quoted above, FDA approved the application on August 1, 1994.

The NDA for Tylenol Extended Relief included only a single study directed to osteoarthritis in the hip and knee (Study Number 87-746). However, as to this study, the reviewer (Dr. E. Douglas Kramer) stated: "In the absence of a placebo control, it is not possible to establish efficacy directly from this trial." Because of similarity with the results of placebo-controlled trials, however, the reviewer found that "it is likely that [the product] is effective in the treatment of OA pain and that the finding of no statistically significant differences between [regular] and [Extended Relief] APAP is not merely due to chance." In other words, the small-scale trial had demonstrated some probable pain relief, but had not directly proven efficacy with respect to osteoarthritis.

In keeping with the limited study results presented in its NDA, McNeil did not initially seek to claim that the product provided “extended relief” specifically for arthritis. Consequently, FDA did not approve any claim for extended relief for arthritis. Indeed, the sole reference to arthritis in the NDA was the claim that the product provides “*temporary* relief . . . from minor aches and pains of arthritis . . . .”

**B. McNeil’s long-term promotion of Tylenol to treat arthritis.**

McNeil’s current use of the deceptive product name “TYLENOL ARTHRITIS Extended Relief” is a dramatic expansion of the approved NDA for “Tylenol Extended Relief,” and is but the latest in a long series of marketing steps undertaken over the past eight years to promote Tylenol for the treatment of arthritis. This on-going promotion of Tylenol to treat arthritis began with a close marketing association between McNeil and the Arthritis Foundation – an association that ultimately resulted in charges brought by 19 state attorneys general against McNeil and the Arthritis Foundation for deceptive marketing tactics.<sup>2/</sup> The adoption of the TYLENOL ARTHRITIS Extended Relief brand name is McNeil’s latest, and possibly the most misleading, of these improper marketing techniques.

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<sup>2/</sup> See Exhibit 2, News Release from the Florida Attorney General, October 16, 1996 announcing the settlement of state charges involving \$2 million in payments and a consumer refund offer from McNeil.

**1. Alliance between Tylenol and Arthritis Foundation**

In 1994, at about the same time as it was pursuing its NDA for Tylenol Extended Relief – an NDA which, as discussed above, did not establish any “extended relief” efficacy with respect to arthritis – McNeil undertook the first of its multi-faceted marketing campaigns to establish Tylenol as a primary treatment for arthritis. The principal, and most deceptive, marketing tool in this campaign was an exclusive marketing alliance between McNeil and the Arthritis Foundation, a non-profit membership organization that disseminates public educational materials and advocates medical research regarding arthritis. Under the auspices of this alliance, McNeil placed print and television advertisements and distributed “informational brochures” regarding arthritis, prominently linking the Tylenol brand name with the Arthritis Foundation. *See Exhibit 3.* These advertisements strongly suggested that the Foundation endorsed Tylenol as a preferred medication for arthritis.

In 1996, McNeil went a step farther by cutting a deal with the Foundation to manufacture pain relievers branded as the “Arthritis Foundation Pain Reliever.” In advertising these products, McNeil informed consumers that the Foundation had “helped to create” the pain relievers and that McNeil would donate a portion of sales proceeds to fund arthritis research. In fact, the only aspect of the product the Arthritis Foundation “helped to create” was the label, and McNeil had guaranteed payment to the Foundation of at least \$ 1 million dollars each year, no matter how many units it sold.

That same year, McNeil was sued by 19 state attorneys general, who accused it of deceptive marketing through its production and sale of these “Arthritis Foundation Pain

Relievers.” As a press release from the attorneys general noted, “[t]hese drugs contain[ed] analgesics common to other pain relievers and were developed with no assistance from the Arthritis Foundation.” *See* Exhibit 2. Indeed, as the allegations noted, the “active ingredients [did] not represent any new analgesic formulation not already available on the OTC market . . . .”

*Id.*

McNeil settled these allegations, without admitting fault, by discontinuing manufacture of the product, paying \$250,000 to the National Institute of Arthritis and Musculoskeletal and Skin Diseases, and paying \$90,000 to each of the 19 states that had brought the allegations. *See id.*

## **2. The introduction of TYLENOL ARTHRITIS Extended Relief.**

Recently, McNeil made a second foray into the arthritis market through the unapproved relabeling of its existing Tylenol Extended Relief drug as an indication-specific arthritis drug. McNeil’s own website states that its new “TYLENOL ARTHRITIS Extended Relief” is a relaunch of the identical acetaminophen formulation previously marketed under the brand name “Tylenol Extended Relief.” *See* Exhibit 4. The website further states that the company renamed the product as TYLENOL *ARTHRITIS* Extended Relief to capitalize on research showing that more than half of the consumers who use the product, use it to relieve minor osteoarthritis pain. McNeil’s website essentially concedes that the product name is intended to convey a claim regarding the product’s efficacy, stating that the name change “makes

it easier to understand the product's benefits." Exhibit 4. Thus McNeil has admitted an intent to convey to consumers a message about efficacy through the product's name.

McNeil has attempted to leverage this misleading claim of "arthritis extended relief" with nationwide advertising variously claiming that TYLENOL ARTHRITIS Extended Relief provides "relief" of arthritis, is a "wonderful treatment" for arthritis, "works as well as the leading prescription," and is a "preferred therapy for the management of mild to moderate osteoarthritis of the hip and knee." These ads are even more deceptive than the ill-fated Arthritis Foundation Pain Reliever campaign, because they purposefully imply that TYLENOL ARTHRITIS Extended Relief does *more* than temporarily relieve minor arthritis pain. These ads communicate an unmistakable message that TYLENOL ARTHRITIS Extended Relief is an *all-around medicine* for the treatment of arthritis. By failing to inform consumers that acetaminophen, the sole active ingredient, provides no reduction in inflammation due to arthritis, McNeil misleads consumers into switching to Tylenol even if they are taking NSAID medications indicated for both pain relief and the reduction of inflammation.

Some prominent recent examples of this misleading advertising are discussed below.

**3. Recent false advertising for TYLENOL ARTHRITIS Extended Relief.**

McNeil's awareness of the misleading nature of its claims is demonstrated by its decision on at least two recent occasions to discontinue misleading advertising. The first occasion was its decision to withdraw certain extremely misleading and unlawful shelf-talkers

that it had distributed to pharmacists. The second occasion on which McNeil recently conceded that its advertising was inappropriate was its agreement to withdraw a television ad for the product upon being challenged by the AFA. When McNeil tried to reintroduce a slight variation of the ad, making minor revisions, the AFA again complained to the networks and the networks themselves discontinued airing the ad. Despite McNeil's defeat before the networks, AFA has recently learned that McNeil is making similarly misleading claims for the product in advertising on the Internet.

*a. McNeil's misleading shelf-talkers.*

A letter from McNeil addressed to all pharmacists carrying TYLENOL ARTHRITIS Extended Relief advised the pharmacists to remove two McNeil advertisements known as "shelf-talkers" from their shelves. (See Exhibit 5, hereto.) One shelf-talker claimed that TYLENOL ARTHRITIS Extended Relief provides "Arthritis relief that lasts up to 8 hours." The second shelf-talker claimed that TYLENOL ARTHRITIS Extended Relief is the "First choice among arthritis sufferers." *Id.* McNeil's letter to the pharmacists explained that McNeil had been "advised that the wording on these two promotional items does not conform to regulatory requirements." *Id.* Although McNeil did not explain what regulatory requirements it believed had been violated, we strongly suspect that McNeil had been informed that the shelf-talkers were misleading and therefore unlawful because they made no reference to the fact that TYLENOL ARTHRITIS Extended Relief is intended only for relief of minor arthritis pain. Both improperly claimed broader general "relief" (which implies relief of all arthritis symptoms,

including pain and inflammation) from arthritis. The correspondence can be viewed as an admission by McNeil that a claim of general arthritis "relief" is misleading to the public.

**b. *Misleading television commercials.***

McNeil has aired a series of television commercials that promote TYLENOL ARTHRITIS Extended Relief as providing "relief" or "treatment" of arthritis. A few of the commercials go so far as to claim that Tylenol "works as well the leading prescription medicine," despite the fact that the acetaminophen in Tylenol is not an anti-inflammatory like prescription-strength ibuprofen. (Storyboards for these commercials are contained Exhibit 6, hereto.)

Earlier this year, the AFA complained to ABC, NBC and CBS that the two TYLENOL ARTHRITIS Extended Relief commercials then on the air were misleading consumers by failing to disclose that TYLENOL ARTHRITIS Extended Relief was not indicated for the treatment of inflammation. The lack of such a qualification or disclaimer regarding inflammation was not only misleading, but potentially harmful to public health because the commercials explicitly claimed that TYLENOL ARTHRITIS Extended Relief "works as well as the leading prescription medication" (ibuprofen). As discussed at length above, prescription strength ibuprofen is an NSAID that acts to reduce inflammation, unlike acetaminophen.

For example, McNeil's "Mr. Moretti" commercial depicted an older woman who tells viewers that she has arthritis in her hands. *See* Exhibit 6. In the most recent script, which was terminated by the networks, the woman says she has "arthritis pain in her hands." A previous version, revised by McNeil in an incomplete effort to address the AFA's concerns, entirely omitted even this oblique reference to pain. In both versions, the woman tells viewers

that she went to the doctor and exclaims that “[n]ow I am on a wonderful treatment.”<sup>3/</sup> The announcer then intones that TYLENOL ARTHRITIS Extended Relief “works as well as the leading arthritis prescription, but is much gentler to your stomach.” At the same time, a small written super states that the comparison is “versus Prescription Ibuprofen.”

The failure of the commercial prominently to disclose the drug’s limitations to relief of minor pain, and not including inflammation, was materially misleading and inconsistent with FDA policy pertaining to marketing of analgesic medications for arthritis pain. Indeed, the prominence accorded the claim “ARTHRITIS Extended Relief” in the product name, coupled with the commercial’s references to “treatment” of arthritis and comparisons to prescription NSAIDs, rendered the commercial extremely deceptive.

A second commercial halted by the networks featured famous hockey player Wayne Gretzky and took the form of a mock public service announcement, informing viewers of important “information for healthy living.” See Exhibit 6. The commercial introduced Gretzky as a sufferer of “common arthritis,” but did not state whether “common arthritis” referred to osteoarthritis, rheumatoid arthritis, or both. It then went on to claim that the medicine in TYLENOL ARTHRITIS Extended Relief is “[t]he first choice of doctors for arthritis pain” and that “Tylenol works as well as the leading arthritis prescription, but is much gentler on your stomach.” The commercial closed by reminding viewers that “Tylenol House Call is brought to

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<sup>3/</sup> When considered in context -- the woman begins taking the Tylenol following a visit to her doctor -- the claim that she is “on” a “wonderful treatment” for arthritis can reasonably be interpreted to mean that TYLENOL ARTHRITIS is what her doctor has prescribed for the medical management of the long-term arthritic condition.

you by TYLENOL ARTHRITIS,” thus tying the concepts of arthritis closely together with the Tylenol brand.

Upon review of the Moretti and Gretzky advertisements in response to the AFA’s complaints, each of the three networks discontinued airing the offending advertisements. *See* Exhibit 7. The CBS television network instructed McNeil that it would not permit future advertising for TYLENOL ARTHRITIS Extended Relief unless the commercials made clear that Tylenol was effective only against the minor pain of arthritis. *See id.*

*c. The TYLENOL ARTHRITIS@ThirdAge.com Internet Promotion.*

McNeil is currently advertising TYLENOL ARTHRITIS Extended Relief in partnership with ThirdAge.com, an online site that bills itself as “the leading Web destination for first-wave baby boomers . . . provid[ing] unique resources, interactive guides and companions for ThirdAgers to enrich life and manage its transitions.” *See* Exhibit 8. The promotion includes a short survey for which participants are offered free samples of TYLENOL ARTHRITIS Extended Relief.

The site offers a purportedly educational quiz about osteoarthritis, entitled the “Joint Pain Barometer.” One question asks, “Which over-the-counter remedy relieves your joint pain and helps manage osteoarthritis with the minimum of side effects?” The three multiple choices are: (1) “a non-narcotic analgesic that contains acetaminophen, the medicine contained in TYLENOL ARTHRITIS,” (2) “aspirin or another non-steroidal anti-inflammatory drug, or NSAID, such as Ibuprofen,” (3) “I never feel enough joint pain to warrant taking a pill.” The favored answer, not surprisingly, is option (1), the TYLENOL ARTHRITIS, because “the

medicine in TYLENOL ARTHRITIS . . . is recommended by arthritis experts as the preferred therapy for the management of mild to moderate osteoarthritis of the hip and knee.” *Id.*

In another portion of the site, entitled “Arthritis Answers from the Experts,” Deborah Litman, M.D., an assistant clinical professor from Georgetown University answers the question “Is morning stiffness and pain in my fingers the beginning of osteoarthritis?” Dr. Litman advises readers that “the pain of osteoarthritis is best treated with acetaminophen, such as Tylenol.” *Id.* She goes on to state that “Sometimes other medications are used as well, *if* there is significant inflammation present.” *Id.* (emphasis added). By clicking through a link on Dr. Litman’s name, diligent readers will find that she has served as a “consultant to McNeil Consumer Healthcare.” *Id.*

The site thus promotes TYLENOL ARTHRITIS as a “therapy for the management” of osteoarthritis, and purports to advise readers that it is the first line recommended treatment for arthritis unless “significant inflammation” is present, in which case an anti-inflammatory may be used in addition to the Tylenol.

## **II. “TYLENOL ARTHRITIS Extended Relief” is Misbranded.**

As the culmination of an escalating campaign to capture the arthritis marketplace, the placement of a claim for relieving arthritis in the product name results in the misbranding of the product. In view of the multiple symptomatology of arthritis, the claim to provide “extended relief” for arthritis is fundamentally deceptive when made with reference to an acetaminophen product.

**A. The placement and prominence of the claim “ARTHRITIS Extended Relief” deceives consumers.**

The prominence with which the claim “ARTHRITIS Extended Relief” is expressed, in comparison with the largely inconspicuous statement of approved indication, deceives consumers and renders the product misbranded.

The law is clear that a false claim cannot be rendered lawful by an inconspicuous disclaimer contradicting in part the false claim. *See Smithkline Beecham Consumer Healthcare v. Johnson & Johnson-Merck Consumer Pharmaceuticals Company*, 906 F. Supp. 178 (S.D. N.Y. 1995) (a disclaimer or contradictory qualification placed in an ad will not remedy an ad which otherwise is false or misleading); *In re Stouffer Foods Corp.*, F.T.C. Dkt. No. 9250 (Sept. 26, 1994) (claim that frozen food is healthier because it “always contains less than 1 gram of sodium per entree” is misleading to consumers when a fine print footnote notes that 1 g is equivalent to 1000 mg, a relatively high sodium content).

The rule that a disclaimer or fine print cannot remedy an otherwise false claim applies equally where the claim is conveyed by the product name itself. *See In re Resort Car Rental System*, 83 F.T.C. 234 (July 31, 1973) (respondent “Dollar-A-Day Rent-A-Car” ordered to discontinue trade name because name conveyed false claim that cars could be rented for \$1, even though company disclosed much higher actual pricing structure in rental contracts); *In re Elliot Knitwear, Inc.*, 54 F.T.C. 1398 (Apr. 25, 1958) (Commission ordered respondent to discontinue brand name “Cashmora” on sweaters, which it found falsely implied cashmere content, even though labels contained accurate description of sweater fiber content in small print).

Here, the contrast between the prominence of the false claim – including its placement in the product name itself – and the minuscule disclaimer revealing the approved indication, is so great as to render the disclaimer of no legal or practical effect. An inconspicuous statement of indication which contradicts a prominent false claim of efficacy in relieving arthritis does not serve to eliminate the false message conveyed in the product name.

The overall effect of the product label for TYLENOL ARTHRITIS Extended Relief Caplets, with the degree of prominence and conspicuousness with which the words “ARTHRITIS Extended Relief” are presented, is to mislead consumers into believing that the product “relieves” arthritis. The two front panels of the outer package of TYLENOL ARTHRITIS Extended Relief bear the words “Tylenol” in 1/2-inch blue type face and “Arthritis” in 5/16-inch blue type face. *See* Exhibit 1. Immediately beneath the words TYLENOL ARTHRITIS, in black letters roughly 25% the size of the words “TYLENOL ARTHRITIS” are the words “Extended Relief Caplets.” Below that, in even smaller type are the words “Pain Reliever — Fever Reducer.” Only in very small type on the back panel in a section indicating uses does the package explain that the medication is indicated “For the temporary relief of the minor pain of arthritis . . . .” *Id.*

The label presentation of TYLENOL ARTHRITIS Extended Relief Caplets is inherently deceptive in failing to disclose the pain relief limitation with the same degree of prominence and conspicuousness as it gives to the claim “arthritis extended relief.” FDA labeling regulations applicable to OTC acetaminophen preparations sold as arthritis remedies require that the label “*prominently* bear[] a statement that the beneficial effects claimed are

limited to the temporary relief of minor aches and pains of arthritis and rheumatism . . . .” 21 C.F.R. § 310.201(a)(viii). The labeling regulations for aspirin and other salicylate-containing medications offered for sale as arthritis remedies similarly require that the product labels clearly state that beneficial effects are limited to “the temporary relief of minor aches and pains of arthritis and rheumatism.” 21 C.F.R. § 201.314(f). The latter regulations further require the qualifying phrase to appear “with the *same degree of prominence and conspicuousness* as the phrase ‘arthritis and rheumatism.’” *Id.* (emphasis added). Although the latter regulations do not explicitly apply to acetaminophen, the underlying basis for the requirement – to avoid consumer confusion about the extent to which the drug treats other arthritis symptoms – is particularly applicable to TYLENOL ARTHRITIS Extended Relief.

To eliminate any ambiguity regarding the degree of prominence required for the disclaimer, the FDA should apply the same labeling standard to acetaminophen products as is already imposed on NSAID medications – that the disclaimer appear “with the same degree of prominence and conspicuousness as the phrase ‘arthritis and rheumatism.’” Allowing acetaminophen products latitude to omit this important qualification is potentially harmful to public health and provides an unfair competitive advantage to acetaminophen producers, particularly in light of McNeil’s recent marketing emphasis on TYLENOL ARTHRITIS Extended Relief as a “treatment” for arthritis that should be compared to prescription medications.

Despite the absence of a comparable regulation for acetaminophen products, the label of TYLENOL ARTHRITIS Extended Relief is itself deceptive to consumers. FDA is fully

empowered to take action to halt this deception and need not modify the regulation before proceeding. Indeed, it is incumbent on the agency to bring this misbranding to a stop.

**B. Inflammation is an important symptom of arthritis.**

McNeil has argued, in defense of its misleading television advertising, that **TYLENOL ARTHRITIS Extended Relief** is intended for osteoarthritis and that osteoarthritis is only rarely characterized by inflammation. The medical community disagrees. Inflammation plays an important role in osteoarthritis, and the failure to address it while claiming to provide relief for arthritis is indefensible.

A recent conference sponsored by the Case Western University School of Medicine examined what it viewed as a current and important debate – namely, whether “osteoarthritis [is] a chronic inflammatory condition or a pain syndrome.” (Exhibit 9, hereto.) The conference report cites a symposium at the recent American College of Rheumatology annual meeting, in which members of the College in attendance were asked whether they considered osteoarthritis to be primarily a chronic inflammatory condition or primarily a pain syndrome. Of the 392 audience members, who represented a cross section of practicing and academic arthritis specialists from around the world, 58.2% (228 doctors) held the opinion that osteoarthritis is primarily a chronic inflammatory condition. The remaining 41.8% (164 doctors) believed it to be primarily a pain syndrome. *Id.* While this survey does not end the debate as to whether osteoarthritis is “primarily” an inflammatory condition or a pain syndrome, it does

indicate the widespread view in the medical community that inflammation is an important element of osteoarthritis.

Another report has called osteoarthritis the “consequence of life events at the joints, [which] can be regarded as the sequel to any joint insult, be it traumatic, congenital deformity, mechanical derangement or inflammatory (and inflammation attendant on the inception may promote the first stage and, at later stages, be responsible for many of the symptoms attributable to OA [osteoarthritis]).”<sup>4/</sup> Some authors have suggested that appropriate anti-inflammatory treatment of symptomatic joints early in the detectable course may be a better treatment than mere palliative analgesic therapy. *Id.*

The important role of inflammation in osteoarthritis has already led to a revision in the American College of Rheumatology 1995 Guidelines:

For many years, OA treatment options were limited, with physicians generally able to prescribe little more than standard analgesics or traditional anti-inflammatory agents. A recent explosion in available new pharmacologic treatments has brought new hope for OA patients, offering therapeutic options not even dreamed of a decade ago.

But along with these advances has come a debate over whether OA treatment should focus on symptoms or on the underlying cause of the disease. This ongoing clinical controversy is rooted in the issue of whether OA is considered to be an inflammatory disorder or pain syndrome. Of import in this debate is the increase in research into new treatments for this condition, and a treatment paradigm that has been shifting in recent years. The Guidelines Committee for the American College of Rheumatology (ACR) published new OA treatment protocols as recently as 1995, but rapid advances in therapy during the last 4 years have led to revision of these guidelines that will be published soon. . . .

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<sup>4/</sup> G.E. Erlich, *Treatment Decisions, Side-Effect Liability and Cost-Effectiveness in Osteoarthritis*, *Inflammopharmacology*, 1996, vol. 4, pp. 137-140 (Exhibit 10).

Based on the presenting symptoms and the physician's judgment, simple analgesics and NSAIDs are primary considerations in first-line treatment of OA. Mild to moderate pain frequently responds to acetaminophen, while patients with more severe pain frequently respond better to NSAIDs, particularly when inflammation presents in the form of joint swelling, tenderness, and stiffness. Intra-articular corticosteroids are also used intermittently.

Moskowitz, R.W., *et al.*, Issues in Osteoarthritis Care: Concepts and Controversies, *Medscape, Rheumatology Treatment Updates*, 2000, Exhibit 9.

The evidence is therefore clear that inflammation is a potentially significant element of osteoarthritis. There is no evidence that consumers understand that treating arthritis pain with acetaminophen will not also treat this other major symptom of the disease. In view of the prominent label claim that McNeil's product will provide "Extended Relief" for "Arthritis," it is necessary that the label be modified either to drop any reference to arthritis-specific relief, or prominently to disclaim relief of inflammation. If the packaging is not clarified, it will continue to mislead and confuse its targeted arthritic consumers.

McNeil has exacerbated this deception by representing that this product "works as well as the leading arthritis prescription," which McNeil identifies as ibuprofen. Ibuprofen relieves both pain and inflammation, as do other arthritis medications. McNeil's ads have suggested, however, that arthritic consumers switch from a prescription medication (which is indicated for both pain and inflammation) to their acetaminophen product (which is indicated only for temporary relief of minor pain). The effect of the recommended switch may be to encourage consumers to self-medicate without their doctor's approval and despite the fact that

the doctor may have prescribed a different NSAID medication for treatment of both pain and inflammation.

**C. McNeil's claim of efficacy violates the terms of its approval.**

By changing the name of its product, McNeil has effectively expanded its efficacy claim significantly beyond that which was approved in the NDA. As presently marketed, TYLENOL ARTHRITIS Extended Relief is plainly misbranded, in violation of 21 U.S.C. § 352. The statute states in relevant part that “[a] drug or device shall be deemed to be misbranded if its labeling is false or misleading in any particular.” 21 U.S.C. § 352(a). Because the product provides no relief for arthritis inflammation, the label is literally false.

The offense of “misbranding” includes publication of misleading “labeling or advertising,” taking “into account (among other things) not only representations made or suggested by the statement, word, design, device, or any combination thereof, but also the extent to which the labeling or advertising *fails to reveal facts material* in the light of such representations . . .” 21 U.S.C. § 321(n).

It is axiomatic that to secure FDA approval for a drug, a manufacturer must demonstrate that the product is safe and effective for each of its “intended” uses. *See Washington Legal Foundation v. Henney*, 202 F.2d 331 (D.C. Cir. 2000). To the extent that the product’s label or advertising makes claims for the product that conflict with those uses specified as intended in the approved NDA, FDA has considered those claims to broaden the uses “intended” by the manufacturer. If off-label uses are promoted by the manufacturer, they can

render the drug misbranded. *See* 62 Fed. Reg. 64075 (information disseminated by manufacturers in other contexts “can create new intended uses for the products, which must be reflected in approved labeling of the products”); *see also United States v. Articles of Drug . . . Designated B-Complex Cholinol Capsules*, 362 F.2d 923 (3d Cir. 1966) (unapproved statements in promotional brochures can result in misbranding); *United States v. General Nutrition, Inc.*, 638 F.Supp. 556 (W.D.N.Y. 1986) (oral statements by sales representatives can render product a misbranded “drug” instead of nutritional supplement).

In order to protect public health, the Act’s misbranding provisions have been broadly construed. As the Supreme Court has stated “[t]he high purpose of the Act [is] to protect consumers who under present conditions are largely unable to protect themselves in this field.” *Kohler v. U.S.*, 335 U.S. 345, 349, 69 S. Ct. 106, 109 (1948). A demonstration that *any* representation is either false or misleading has been held sufficient to establish misbranding. *See, e.g., United States v. Sene X Eleemosynary Corp. Inc.*, 479 F. Supp. 970, 980 (S.D. Fl. 1979) (court found drug misbranded for failure to bear adequate directions for use).<sup>5/</sup>

There is little doubt that McNeil has promoted the product in a manner that implies more than the approved indication of temporary relief of minor arthritis pain. Its nationwide advertising campaign, which has taken place over several media and over many years, has attempted to position Tylenol as the preferred overall medication for arthritis. These

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<sup>5/</sup> The word “misleading” in § 352(a) is intended to broaden the scope of the Act to “to cover situations in which, although a claim is not technically false, or even if literally true, the drug or device may nevertheless be misbranded if the total effect of the labeling is to deceive or mislead.” *United States v. An Article of Device, Consisting of One Device, More or Less, Labeled in part: “The Ellis Microdynameter”*, 224 F. Supp. 265, 268 (E.D. Penn. 1963).

advertisements have claimed that Tylenol is a physician-preferred “treatment” and “therapy” for arthritis, encouraging consumer switching from NSAIDs, while uniformly failing to mention that the product does not reduce inflammation.

By adding the word “ARTHRITIS” to the product name, McNeil is building on a longstanding marketing campaign designed to lead consumers to believe that TYLENOL ARTHRITIS Extended Relief relieves both pain and inflammation associated with arthritis. This efficacy claim is patently false, since acetaminophen only relieves minor aches and pains of arthritis. Thus, McNeil has, without approval, expanded the efficacy claimed on labeling for its product to encompass a relief it cannot provide. TYLENOL ARTHRITIS Extended Relief should thus be considered misbranded under the Act.

**D. McNeil failed to obtain FDA approval for the indication change, as required by FDA regulations.**

McNeil has violated of 21 C.F.R. § 314.70(b)(3) by simply renaming Tylenol Extended Relief as “TYLENOL ARTHRITIS Extended Relief” without obtaining FDA’s approval of a supplemental NDA. FDA regulations clearly provide that such approval is needed.

The applicable regulation states that “an applicant shall submit a supplement [to an approved NDA application], and obtain FDA approval of it, before making . . . [a]ny change in labeling, except one described in paragraphs (c)(2) or (d) of this section.” 21 C.F.R. § 314.70(b)(3). The only exception that is arguably relevant is paragraph (d)(3), which allows “[a]n editorial or similar minor change in labeling” to be made without FDA approval. The

regulations provide that one example of such a minor labeling change would be adding the name of a distributor to the label.

McNeil's insertion of the word "Arthritis" into the product name is far more than a simple editorial change. It effectively adds an indication – the "Extended Relief" of arthritis – that was not approved in the NDA and for which no data were submitted by McNeil. Moreover, it specifically targets the product to arthritic consumers who are not informed by the package label or otherwise that the product is ineffective at reducing inflammation. In sum, the name change cannot be "editorial" in nature, because it introduces a patent falsehood to the product label.

### **III. Conclusion.**

McNeil has long sought to position its acetaminophen product as a premier OTC medication for arthritic consumers. In order to build market share, it has embarked on a multifaceted marketing campaign over many years to promote Tylenol Extended Relief as an arthritis medicine. Despite the fact that FDA approved Tylenol Extended Relief only for the temporary relief of minor aches and pains associated with arthritis, McNeil has renamed the product (without FDA approval) as "TYLENOL ARTHRITIS Extended Relief."

This name change carried the unmistakable, and undeniably false, claim that the product "relieves" arthritis. Moreover, McNeil has supported the name change with a massive advertising campaign claiming that TYLENOL ARTHRITIS Extended Relief is a "treatment" or

“therapy” for arthritis, while at the same time either omitting entirely or obfuscating the fact that the “relief” provided by the product is limited to minor pain.

The FDA should declare TYLENOL ARTHRITIS Extended Relief to be misbranded and should require McNeil to revise its labeling by removing false or misleading statements. TYLENOL ARTHRITIS Extended Relief does not “relieve” arthritis, because it does not reduce inflammation. The product name and the advertising campaign conducted by McNeil in support of the product are false, misleading, and ultimately injurious to public health.

#### ***Environmental Impact***

Petitioner claims a categorical exclusion from the preparation of an environmental assessment pursuant to 21 C.F.R. § 25.30 (General), 21 C.F.R. § 25.31 (Human drugs and biologics), 21 C.F.R. § 25.32 (Foods, food additives, and color additives), 21 C.F.R. § 25.33 (Animal drugs), and 21 C.F.R. § 25.34 (Devices and electronic products).

#### ***Economic Impact***

Information regarding economic impact will be submitted if requested by the Commissioner following review of the petition.

#### ***Certification***

The undersigned certifies, that, to the best knowledge and belief of the undersigned, this petition includes all information and views on which the petition relies, and

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that it includes representative data and information known to the petitioner which are unfavorable to the petition.

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**EXHIBITS**

**Attached to Citizen Petition  
Food and Drug Administration  
May 31, 2000**