Johnson & Johnson

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June 21, 2001

VIA FEDERAL EXPRESS

Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, Maryland 20852

Re: Comments to Docket No. 00N-1269
Proposed Rule; Requirements on Content and Format of Labeling for Human Prescription Drugs and Biologics; Requirements for Prescription Drug Product Labels

Dear Sir or Madam:

These comments are submitted on behalf of the pharmaceutical companies of the Johnson & Johnson family of companies. With approximately 99,000 employees, Johnson & Johnson, is the world's most comprehensive and broadly based manufacturer of health care products, as well as a provider of related services, for the consumer, pharmaceutical and professional markets. Johnson & Johnson has more than 190 operating companies in 51 countries around the world, selling products in more than 175 countries. In the year 2000, Johnson & Johnson invested $1.9 billion of a total $2.9 billion research and development spent on pharmaceutical development, which represents an 18.6% increase from 1999. Johnson & Johnson is the seventh largest pharmaceutical and the second largest biotechnology company in the world. Its subsidiaries manufacture and sell prescription medicines include antifungals and anti-infectives, family planning products, and drugs for psychiatry and mental health, pain management, cardiovascular disease, cancer, arthritis and gastrointestinal disorders.

We are keenly interested in FDA's proposal to amend its regulations governing the format and content of labeling for prescription drugs and biologic products and agree with the Agency's stated objectives of making the labeling "easier for health care practitioners to access, read, and use." We agree with and support the comments of the Pharmaceutical Research and Manufacturers of America ("PhRMA") on this subject dated June 14, 2001, and would like to expand upon two specific items of those comments as follows.

I. Highlights of Prescribing Information

We join PhRMA in strongly opposing the addition of a "Highlights" section to the approved product labeling. The approved product labeling is a distillation of complex data

00N-1269

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designed to provide current information about the safe and effective use of prescription products to health care professionals. In addition to the often protracted labeling negotiations with FDA, sponsors spend a considerable amount of time carefully analyzing the available data to ensure that the labeling is medically appropriate and reflects the most current knowledge about a product. The underlying objectives of the proposed rule – to make the labeling easier to access, read and use - are best and most appropriately served by the adoption of a standardized index system, the reorganization of the labeling sections to place more critical information first, and the further highlighting of key text through special formatting, which are all attributes addressed by the proposed rule.

In contradistinction, to include a further distilled summary of important prescribing information in an additional "Highlights" section will not further the objectives of the proposed rule and will have a detrimental public health impact. We believe that cognitive theory and actual research would support the proposition that inclusion of a "Highlights" section would encourage practitioners to rely improperly on that section and not consult all the crucial information contained in the comprehensive labeling. We also believe that cognitive theory supports the proposition that a reader will likely favor summarized information and ignore comprehensive information even with a contrary instruction. FDA itself acknowledges in its proposed "highlights reminder" that "Highlights" do not include all of the information needed to prescribe a drug safely and effectively. Yet the proposed rule would structure labeling in a manner that would inevitably distract from the full prescribing information and lead practitioners to not read the comprehensive information that is needed for safe and effective prescribing. This result does not serve a public health goal.

In addition, we join PhRMA in expressing our grave concern over the product liability implications of FDA's proposal. Virtually every pharmaceutical product liability case involves allegations that important information is missing from the labeling or that risk or other information disclosed was not sufficiently prominent. This exposure will be significantly increased by inclusion of a "Highlights" section based on claims about the alleged inadequacy of that section and purported inconsistencies between the information condensed for that section and the comprehensive prescribing information. This concern is not merely "speculative" as the Agency suggests. In fact, claims have been brought in highly analogous situations. For example, plaintiffs have alleged that a "product overview" section in the Physicians Desk Reference (which is similar in concept to the "Highlights" section proposed by FDA) did not contain sufficient information regarding certain side effects, was misleading when compared to the actual prescribing information, and would lead practitioners to ignore the actual prescribing information.

II. Proposed Restrictions on Data not included in the "Indications and Usage" and "Dosage and Administration" Sections

We join PhRMA in opposing the proposed restrictions on the inclusion of *in vitro* data and other data on indications, uses, and dosing that are not included in the "Indications and Usage" and "Dosage and Administration" sections, with respect to data that is scientifically valid and potentially relevant for the purpose of making prescribing decisions. FDA should not depart from its long-standing policy of including information in the labeling from studies that are scientifically sound and provide relevant information to the prescriber. Inappropriate use of this data in promotion can be addressed through FDA's existing legal authority and not at the expense of eliminating from the labeling scientific information that is otherwise factual and non-misleading. Both legally and from a public policy perspective FDA stands on firmer ground when it allows for the disclosure of truthful and non-misleading information in a context that permits the health care professional to make an appropriate and independent judgment about the significance of the information. We respectfully submit that eliminating valuable and clinically significant information from the labeling runs counter to FDA's stated goal of providing more informative labeling for practitioners and patients.

For instance, FDA proposes that *in vitro* data for anti-infective drugs where such data have not been shown to be pertinent to clinical use by adequate and well-controlled clinical studies, only be included in the prescribing information when the Agency has specifically granted a waiver. Currently, the labeling for anti-infective drug products contains two lists of organisms: (a) those for which there are adequate and well-controlled clinical studies (commonly known as the "clinically indicated organisms") and (b) those for which there are insufficient clinical data (usually due to the low frequency of isolation), but are pathogens associated with approved clinical indications and are documented to be >90% susceptible in the United States (commonly called the "*in vitro* only" section). The proposal to delete from labeling the "*in vitro* only" listing would deprive clinicians and microbiologists of valuable information on less frequently isolated pathogens, which is precisely the type of information a practitioner may seek in the package insert. This view is reflected in the comments of the Infectious Diseases Society of America ("IDSA") dated March 21, 2001:

> [A]s physicians weigh decisions and make judgments in their practice of medicine, it is important that *all relevant data be available to them.* Removing *in vitro* data from PIs poses problems that our member physicians believe, ultimately, will impact negatively on physician decision-making and patient care. Of particular concern, our members believe that FDA's action will impede physicians' ability to determine appropriate anti-infective therapy for patients with drug resistant or unusual infections. (emphasis added)

Echoing our view about the disclosure of truthful and non-misleading data with the appropriate contextual information, IDSA continues:

> In our view, this *in vitro* information is too valuable to be excluded from the PI, *but we agree that every effort should be made to clarify the limitations of this information while continuing to make it available to the clinician.* (emphasis added)

FDA can address the potential misuse of this information in promotion or otherwise through its existing legal authority. FDA's "Points to Consider in the Clinical Development and Labeling of Anti-Infective Drug Products (1992)" ("PTC") provides a clear statement of the Agency's position with respect to promotion of an anti-infective drug product for specific infections other than those listed in the Indications and Usage section of the product labeling. PTC at 9. In addition, the Points to Consider document outlines a mechanism for keeping the labeling current in recognition that microorganism susceptibility patterns can change with time. PTC at 14.

Moreover, it is unclear whether FDA has considered the impact of this proposed policy shift on the Agency's own ability to determine testing limits for commercial *in vitro* susceptibility testing devices for new drugs without the inclusion of *in vitro* data in the labeling. As reflected in the comments of Dr. Sally T. Selepak, Microbiology Reviewer, Center for Devices and Radiological Health (see Comment #23), FDA uses both the "clinically indicated organisms" and the "*in vitro* only" sections of the labeling of anti-infective drug products to select or establish organisms to be tested, Quality Control organisms, and interpretative criteria, in the Agency's review and clearance of susceptibility test devices.[1] The FDA reviewer further observes:

> The removal from the "Microbiology" section of the *in vitro* data would be too restrictive to establish performance for IVD [*in vitro* diagnostic] devices. Testing of organisms listed only in the "Indications and Usage" section may provide little evaluable data since these organisms are already known to be susceptible to the drug. With only a susceptible category to review, performance for laboratory testing cannot be established. If or when resistance develops in the select group of organisms, the IVD device may not be able to detect the resistance. The ability of an IVD device to detect resistance or even the trending toward the development of resistance is of high concern to the growing health threat of antimicrobial resistance.

* * *

[1] See also, Food and Drug Admin., *Guidance on Review Criteria for Assessment of Antimicrobial Susceptibility Devices* (March 8, 2000).

Based on the foregoing discussion, we respectfully request that the proposal for a "Highlights" section be eliminated in the final rule and that FDA abandon consideration of restrictions on the inclusion in the labeling of *in vitro* data and other data on indications, uses, and dosing that are not included in the "Indications and Usage" and "Dosage and Administration" sections. We appreciate the opportunity to comment on the proposed rule and look forward to your thoughtful consideration of the issues raised here and in the comments of PhRMA.

Sincerely,

Freddy A. Jimenez (by V. Margiotta)

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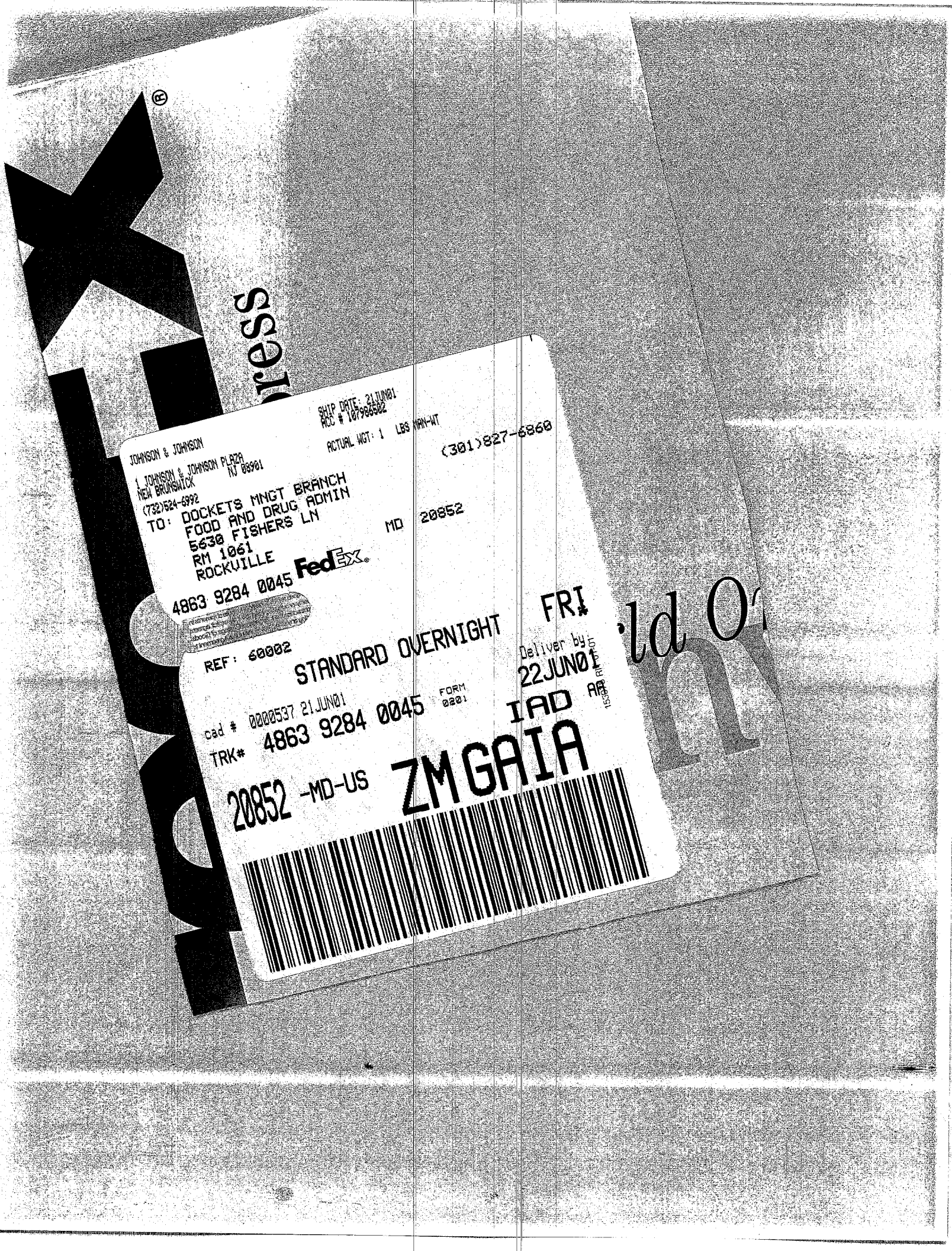
General Attorney
Johnson & Johnson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