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December 23, 2002

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

Re: Docket No. 02N-0417  
Applications for FDA Approval to Market a New Drug: Patent Listing  
Requirements and Application of 30-Month Stays on Approval of  
Abbreviated New Drug Applications Certifying That a Patent Claiming a Drug  
Is Invalid or Will Not be Infringed. 67 Fed. Reg. 65,448 (October 24, 2002).

Dear Madam/Sir:

The Michigan for Affordable Pharmaceuticals (MAP) Coalition is a voluntary organization comprised of employers, union groups, health care providers and health care plans that support specific reform initiatives that will help contain pharmaceutical costs while ensuring access and improved health care overall. MAP commends the FDA for its rule proposed on October 24, 2002 thereby taking the necessary steps to tighten legal loopholes used by brand manufacturers to delay the approval of competing generic drugs. MAP would like to take this opportunity to offer its comments.

As we are certain you are aware, outpatient retail prescription drug expenditures in the US have increased over 17 percent annually in the last four years<sup>1</sup>. Timely availability of generic drugs is a critical element to offsetting the current rate of increases in prescription drug spending. MAP supports the FDA proposed rule to allow only one 30-month stay when a generic company challenges a patent and to set out rules for the listing of patents to ensure only appropriate patents are listed with the FDA.

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While the two key issues addressed by the FDA proposed rule will provide assistance in bringing generics to market in a timely fashion, MAP has additional suggestions for this proposed rule, which we have set forth in this letter.

In particular, Michigan residents are significantly affected by delays of generic drug availability because we fill more prescriptions per resident and spend more than twice as much on prescription drugs than other states<sup>ii</sup>. Soaring drug costs are leading to dire consequences - especially for the elderly and underprivileged who may need to choose between medication and other necessities of life.

The proposed FDA rule is a welcome step that will aid Michigan residents' access to affordable prescription drugs. In 2001, there were 3.1 billion prescriptions dispensed at US retail pharmacies with sales revenue totaling \$154 billion<sup>i</sup>. Of these 3.1 billion prescriptions, approximately 47 percent<sup>iii</sup> were dispensed with a generic medication, accounting for only about eight percent of total prescription drug expenditures<sup>iv</sup>. These telling statistics demonstrate how generic medications can provide a tremendous amount of savings for consumers.

#### Existing Incentives for Brand Manufacturers

We must first be clear and mention that MAP supports patents and the incentive they provide to companies for their innovation. However, we also believe that there must be balance to the incentive. The Hatch-Waxman amendment to the federal Food, Drug and Cosmetic act sought to obtain this balance. It provided incentives for drug companies to invest in pharmaceutical research and development while improving consumer access to more affordable generic medicines. Thus, since the enactment of the Hatch-Waxman amendment, spending on research and development increased from under \$2 billion<sup>v</sup> to over \$30 billion in 2001<sup>vi</sup>. Further, according to the Federal Trade Commission (FTC), the share of generic medicines dispensed increase from 19 percent to 47 percent<sup>iii</sup>.

In addition there are many incentives provided in US policy that give brand manufacturers reasons to invest in drug research and development. Examples include:

- The base 20 years of patent life given from the date the application is received by the US Patent and Trademark Office
- An additional six months exclusivity for performing pediatric studies\*
- Up to an additional five years patent extension to cover the regulatory review<sup>†</sup>
- Three years for new uses of existing drugs<sup>»</sup>

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\* Granted through the Food and Drug Administration Modernization act of 1997 and renewed by the Best Pharmaceuticals for Children Act of 2001

† 1984 Hatch Waxman Act (i.e. One half the sum of clinical study time plus FDA pre-market review time)

In addition to these incentives, the FDA review time for new drugs has decreased substantially from 26.9 months in 1993 to 14 months in 2001 <sup>vii</sup>. Along with the incentives mentioned above, the pharmaceutical industry realized other advantages.

- Since 1999 the US Patent and Trademark Office guarantees patent processing times to be less than three years <sup>viii</sup>, consequently allowing new drugs to come to market faster.
- Through the National Institutes of Health (NIH), there is federal tax money in the amount of \$23 billion a year dedicated to research <sup>ix</sup>, much of which goes into developing new drugs.
- Through a series of laws passed in the 1980's <sup>†</sup>, the federal government must transfer inventions to the private sector for commercialization. In fact, as noted in a MIT Sloan School of Management working paper, 11 of the 15 most significant new drugs introduced from 1970 to 1995, had federal research that supported their development <sup>v</sup>.

MAP believes there are sufficient incentives and processes that offer brand-name drug manufacturers equitable reward for their innovations. Unfortunately, some brand manufacturers have used legal loopholes to extend their incentives beyond their exclusivity periods intended by the Hatch-Waxman amendment. Expansion of the proposed regulatory remedies could close these loopholes and increase the availability of generic drugs.

#### Additional Regulatory Remedies to Close Loopholes:

- Requirements that patent declarations include a statement that complete and accurate patent information has been filed.
- Requirements that brand manufacturers register their patents with the FDA within 30 days of approval.

Both of the above clarifications would ensure, through full disclosure, that complete information is available to all interested parties on a timely basis. A lack of patent information leads to unnecessary delays once a generic manufacturer attempts to bring a drug to market. Current law addresses timely reviews and conflicts of interest for those reviewing applications (21U.S.C. 355(j)(3)). In fact, (3)(j) specifically stipulates that "no action by the reviewing division may be delayed because of the unavailability of information from or action by field personnel unless the reviewing division determines that a delay is necessary to assure the marketing

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<sup>v</sup> 1984 Hatch Waxman Act (e.g. Includes new indications, new formulations or new combination of drugs previously sold separately)

<sup>†</sup> 1980 Stevenson-Wydler Technology Innovation Act and 1986 Federal Technology Transfer Act

of a safe and effective drug". Clarification should be added to ensure the same level of responsibility for other parties involved in the process.

- Required disclosure on citizen petitions to indicate whether the petitioner has received or will receive remuneration for filing the citizen petition.

Enactment of this proposed rule will limit the avenues by which brand manufacturers can delay the availability of generic drugs. We are concerned that brand manufacturers could invoke other available avenues of delay, which include the citizen petition process. In fact, FTC staff commented on FDA citizen petitions and suggested "that the FDA consider requiring notification of whether the citizen petitioner has received or will receive consideration for filing the citizen petition and identification of the party furnishing the consideration" <sup>iii</sup> since there is the potential to mask anti-competitive strategies.

#### Additional Legislative Remedies:

While MAP recognizes that the FDA proposed rule can only address issues that clarify current law, we look forward to legislation that would accomplish the following additional items.

- Method to address arrangements where brand-name manufacturers pay generic manufacturers to "park" 180-day exclusivity.

Current law allows for a 180-day exclusivity period for the first generic applicant that challenges a listed patent for a relevant brand-name drug. The grant of this exclusivity period then precludes the FDA from approving any other eligible generic applicants until the exclusivity period has run out. The law stipulates that the 180-day period begins running upon the first commercial marketing of the drug or when a court decision is made stating that the patents challenged are invalid or will not be infringed. However, in recent years brand manufacturers have entered into agreements with generic manufacturers that hold a 180-day exclusivity. These brand-generic arrangements result in extending the brand manufacturer's exclusivity. This holds off cost reductions that could be realized by the public. The FDA should implement a stipulation that generic applicants that enter into such agreements forfeit their 180-day exclusivity.

*Example: In 1997, the makers of Cardizem CD<sup>®</sup>, Hoechst Marion Roussel, Inc. entered into an agreement with Andryx Corporation to refrain from marketing their generic version of Cardizem CD. The agreement stated that Andryx Corporation would withhold its product from the market once it received FDA approval with its right to a 180-day exclusivity. In exchange, Hoechst Marion Roussel, Inc. paid Andryx Corporation \$89 million and successfully "parked" the 180-day exclusivity that should have started in July of 1998, thus delaying generic Cardizem CD market entry until June of 1999<sup>x</sup>.*

- Process for generic manufacturers to challenge listability of patents under Hatch Waxman.

In an attempt to delay generic competition, some brand manufacturers have improperly listed patents in the FDA's Orange Book in order to trigger a 30-month stay of approval from the FDA. A recent federal appeals court case stated that generic manufacturers are not allowed to challenge a patent listing in the Orange Book even if the listing is potentially frivolous because it does not meet patent requirements. Thus, generic manufacturers are subject to following FDA protocol that has the potential to be abused by brand-name manufacturers for patent listings already filed in the Orange Book.

*Example: On November 21, 2000 Bristol-Myers Squibb submitted a patent to the Orange book for their product Buspar<sup>®</sup> one day before their patent was due to expire. The patent was for a metabolite of Buspar that formed in a person's body once ingested. In February 2002, this action was considered by a federal judge in New York, who ruled that Bristol-Myers Squibb had improperly listed the patent and ordered the patent be delisted from the Orange Book. Unfortunately this improperly listed patent delayed generic Buspar from coming to market for 14 months<sup>xi</sup>.*

- Process for removal of improperly listed patents.

As stated in the FTC study, Generic Entry Prior to Patent Expiration, "currently, the FDA does not review the propriety of patents listed in the Orange Book, and courts have ruled that generic applicants have no private right of action to challenge those listings. As a result, there is no mechanism to delist an improperly listed patent from the Orange Book. The lack of such mechanism may have real world consequences in that the FTC is aware of at least a few instances in which a 30-month stay was generated solely by a patent that raised legitimate listability questions"<sup>iii</sup>.

*Example: Following the Orange book delisting of the patent for Buspar's metabolite, as ordered by a federal judge in New York as described above, an appeal was filed by Bristol-Myers Squibb. As a result of the appeal, a federal appeals court ruled that under existing law (Hatch-Waxman), the generic company has no right to delist a patent in the Orange Book<sup>xi</sup>.*

- Requirement that brand-name companies and first generic applicants provide copies of certain agreements to the FTC.

As mentioned previously, situations may arise where some brand-name manufacturers and generic manufacturers enter into agreements that would "park" the 180-day exclusivity, thus evoking anti-competitive practices. This requirement

would deter companies from engaging in behavior that violates antitrust laws and leaves that determination up to the FTC.

In summary, Michigan businesses and residents already spend twice the national average on prescription drugs and the economic downturn deepens the strain on employers, hospitals, residents and the State itself to pay for prescriptions. In addition, the federal government is now considering a Medicare drug benefit for which it is estimated that in 2002 seniors will use \$80 to \$85 billion worth of prescription drugs<sup>1</sup>. In the next 3 years, 17 brand-name medications face patent expiration that could bring an immediate annual savings of \$400 million or more to Michigan residents if generic competition is not delayed. By ensuring the timely availability of generic drugs, Michigan residents, businesses, employers and the State of Michigan will be able to afford prescription medications today and in the future. Your review and consideration of these comments is greatly appreciated.

Questions concerning these comments may be directed to Timothy Antonelli at (248) 448-7372 or [tantonelli@bcbsm.com](mailto:tantonelli@bcbsm.com).

Sincerely,

Michigan for Affordable Pharmaceuticals Coalition

cc: Michigan Congressional Delegation

## References

<sup>i</sup> National Institute for Health Care Management, *Prescription Drug Expenditures in 2001: Another Year of Escalating Costs*, [cited November 2002] available online @ [www.nihcm.org](http://www.nihcm.org).

<sup>ii</sup> The Henry J. Kaiser Family Foundation, *State Facts Online*, [cited July 10, 2002] available online @ [www.statehealthfacts.kff.org](http://www.statehealthfacts.kff.org).

<sup>iii</sup> The Federal Trade Commission, *Generic Drug Entry Prior to Patent Expiration: An FTC Study*, [cited November 2002] available online @ [www.ftc.gov/opa/2002/07/genericdrugstudy.htm](http://www.ftc.gov/opa/2002/07/genericdrugstudy.htm).

<sup>iv</sup> Blue Cross Blue Shield Association, *Medical Cost Reference Guide*, [cited April 2002] available online @ [bluweb.bcbs.com](http://bluweb.bcbs.com).

<sup>v</sup> Blue Cross Blue Shield Association, *Prescription Drug Costs: Federal Regulation of the Industry (Full Report)*, [cited November 2002] available online @ [bcbshealthissues.com/issues/drugprices/report/toc.vtml](http://bcbshealthissues.com/issues/drugprices/report/toc.vtml).

<sup>vi</sup> The Pharmaceutical Research and Manufacturers of America (PhRMA), *Annual Report 2001-2002*, [cited November 2002] available online @ [www.phrma.org](http://www.phrma.org).

<sup>vii</sup> US Food and Drug Administration Center for Drug Evaluation and Research, *Approval Times For Priority And Standard NDAs Calendar Years 1993-2001*, [cited November 2002] available online @ [www.fda.gov/cder](http://www.fda.gov/cder).

<sup>viii</sup> National Institute for Health Care Management, *Prescription Drugs and Intellectual Property Protection: Finding the Right Balance between Access and Innovation*, [cited November 2002] available online @ [www.nihcm.org](http://www.nihcm.org).

<sup>ix</sup> National Institutes of Health, *An Overview*, [cited November 2002] available online @ [www.nih.gov](http://www.nih.gov).

<sup>x</sup> Families USA, *Class Actions: Collusion and Anticompetitive Practices*, [cited November 2002] available online @ [www.familiesusa.org](http://www.familiesusa.org).

<sup>xi</sup> National Institute for Health Care Management, *A Primer: Generic Drugs, Patents and the Pharmaceutical Marketplace*, [cited November 2002] available online @ [www.nihcm.org](http://www.nihcm.org).