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Re: **Over-the-Counter Drug Products; Public Hearing**
Docket No. 00N-1256
65 Fed. Reg. 24704 (April 27, 2000)

The Pharmaceutical Research and Manufacturers of America (PhRMA) submits these comments following the public hearing on regulation of over-the-counter (OTC) drug products held by FDA on June 28-29, 2000. These post-hearing comments supplement the testimony provided by PhRMA at the hearing.

PhRMA represents the country's leading research-based pharmaceutical and biotechnology companies, which are devoted to inventing medicines that allow patients to lead longer, healthier and more productive lives. Investing over \$26 billion this year in discovering and developing new medicines, PhRMA companies are leading the way in the search for cures.

One issue raised by FDA's hearing notice, and discussed at the hearing, is whether FDA can switch a drug from prescription to nonprescription status without the support, and even over the objection, of the holder of the approved new drug application (NDA) for the prescription drug. This issue is of vital interest to PhRMA's members, because prescription drugs discovered and developed by PhRMA members are the source of virtually all major new OTC drugs.

Pharmaceutical Research and Manufacturers of America

As summarized in our earlier testimony and discussed in greater detail below, FDA does not have the statutory authority to switch a drug over the objection of the NDA holder without following the adjudicatory hearing process set forth in section 505(e) of the Federal Food, Drug, and Cosmetic Act. The "switch regulation" procedure in section 503(b)(3) is an anachronism that has not been used by FDA for almost thirty years and never over the objection of an NDA holder. It was not intended by Congress to override section 505(e), and firmly established principles of administrative law and procedural due process preclude FDA from applying it in derogation of the NDA holder's hearing rights. Forced switches also would violate the NDA holder's proprietary rights in the safety and effectiveness data contained in an application and protected under the Drug Price Competition and Patent Term Restoration Act of 1984 (the Hatch-Waxman Amendments) and would represent poor public health policy. For all these reasons, FDA should reject any effort to switch a drug over the NDA holder's objection and should not initiate such a proceeding on its own.

I. FDA Cannot Switch a Prescription Drug Using Informal Rulemaking Without the NDA Holder's Consent.

A. FDA Must Follow the Hearing Process in Section 505(e) to Switch a Drug Over the Objection of the NDA Holder.

An approved NDA licenses the sponsor to market the drug product in accordance with the labeling described in the approved application, including the "Rx only" legend for a prescription drug. A change in any of the conditions set forth in the NDA under which the drug may be lawfully sold amounts to a modification or withdrawal of the NDA.

Section 505(e) of the FD&C Act establishes an adjudicative procedure for withdrawing or modifying an approved NDA. Under section 505(e), FDA is authorized, "after due notice and opportunity for hearing to the applicant, [to] withdraw approval of an application" if the agency makes a finding specified in the law. 21 U.S.C. § 355(e). The procedural requirements of section 505(e) are implemented through detailed agency regulations. 21 C.F.R. § 314.200. If FDA wishes to remove the Rx legend from an approved drug without the consent of the sponsor, it must follow the statute and its own regulations, and make one of the findings set forth in section 505(e). Since there would be no question presented in the switch process of the safety or effectiveness of the drug when labeled for prescription use, the only such finding that even arguably would support a forced switch is that the Rx legend renders the labeling "false or misleading."

FDA's authority to issue a switch regulation under section 503(b)(3) does not and cannot override a sponsor's hearing rights under section 505(e). As an initial matter, we note that FDA has not used this authority to switch a drug for almost thirty years, the last time being in 1971. After that, FDA turned to the OTC Drug Review as the principal mechanism for switch, and in fact withdrew existing switch regulations in 21 C.F.R. § 310.201 when the drugs in question became subject to final monographs. See, e.g., 60 Fed. Reg. 52507 (Oct. 6, 1995) (removal of switch regulation for sodium fluoride and sodium monofluorophosphate in connection with anti-caries monograph); 59 Fed. Reg. 4218 (Jan. 28, 1994) (removal of doxylamine succinate in connection with cough-cold monograph); 58 Fed. Reg. 49898 (Sept. 23, 1993) (removal of tolnaftate in connection with topical anti-fungal monograph). Beginning in the mid-late 1980s, as the

OTC Drug Review wound down, the agency has used the NDA process for virtually every switch (a few, such as 1% hydrocortisone, were done through the monographs). FDA's attempted reliance on the anachronistic switch regulation procedure here is completely at odds with its modern approach to switches, which is to require the development and submission of data in the context of an NDA.

Moreover, even when it did promulgate switch regulations, FDA *never* did so over the objection of the sponsor of an NDA for a prescription version of the drug in question. We have reviewed the Federal Register notices for every switch regulation issued by FDA under the authority of section 503(b)(3), so far as we have been able to determine, and have not identified a single reference to an objection by an NDA holder.¹ In short, what FDA would propose to do by issuing a switch regulation without the sponsor's consent is unprecedented.

It also is unauthorized by section 503(b)(3). Congress intended that section to apply to drugs distributed by more than one company, not to the situation that would be presented in the typical switch of a single product or product line marketed by

¹See 20 Fed. Reg. 3499 (May 19, 1955); 20 Fed. Reg. 5635 (August 5, 1955); 20 Fed. Reg. 7166 (September 24, 1955); 20 Fed. Reg. 7927 (October 21, 1955); 20 Fed. Reg. 8189 (November 1, 1955); 21 Fed. Reg. 420 (January 20, 1956); 21 Fed. Reg. 768 (February 3, 1956); 21 Fed. Reg. 1417 (March 3, 1956); 21 Fed. Reg. 3247 (May 17, 1956); 21 Fed. Reg. 3672 (May 30, 1956); 21 Fed. Reg. 4341 (June 21, 1956); 21 Fed. Reg. 7698 (October 9, 1956); 21 Fed. Reg. 10275 (December 21, 1956); 22 Fed. Reg. 353 (January 17, 1957); 22 Fed. Reg. 2314 (April 6, 1957); 22 Fed. Reg. 3435 (May 16, 1957); 22 Fed. Reg. 4076 (June 11, 1957); 22 Fed. Reg. 6911 (August 28, 1957); 22 Fed. Reg. 8812 (November 1, 1957); 23 Fed. Reg. 324 (January 17, 1958); 23 Fed. Reg. 479 (January 24, 1958); 23 Fed. Reg. 8285 (October 28, 1958); 23 Fed. Reg. 10436 (December 30, 1958); 24 Fed. Reg. 2982 (April 18, 1959); 24 Fed. Reg. 5827 (July 22, 1959); 24 Fed. Reg. 6805 (August 21, 1959); 28 Fed. Reg. 7426 (July 20, 1963); 28 Fed. Reg. 9941 (September 13, 1963); 29 Fed. Reg. 18055 (December 19, 1964); 30 Fed. Reg. 13628 (October 27, 1965); 31 Fed. Reg. 9992 (July 22, 1966); 36 Fed. Reg. 824 (January 19, 1971).

one company under its own NDA or NDAs – hence the section authorizes the switch of “drugs” in the plural, rather than using the singular “drug” consistently used elsewhere in the FD&C Act.

The legislative history of both section 505(e) and section 503(b)(3) demonstrates that the particular requirements of section 505(e) supersede the general grant of rulemaking authority in section 503(b)(3). The FD&C Act as enacted in 1938 contained a simpler version of 505(e), which authorized FDA to suspend an NDA after notice and an opportunity for a hearing. At that time, and until 1962, the current NDA process did not exist; NDAs could become effective without affirmative approval by FDA. A manufacturer could legally market a “new drug” after obtaining an “effective” NDA, which only required a premarket notification that the drug was safe under the conditions suggested in the labeling. Thousands of other drugs entered the market as “old drugs,” without approved NDAs, based on informal FDA advice or on a self-determination of old-drug status without agency review of any sort.

Section 503(b)(3), enacted in 1951 as part of the Durham-Humphrey Amendment, was intended to address the flood of drugs on the market that had been subjected to differing levels of agency scrutiny, or none at all, often marketed by different companies with different labeling. The same drug might be marketed as a prescription drug by one company and an OTC drug by another, even for the same dosage and indication. The Durham-Humphrey Amendment gave FDA the authority to bring order to this chaotic situation by issuing regulations directed to an entire class of drug products marketed by different companies. See H.R. No. 700, 82d Cong., 1st Sess. 3 (1951).

Thus, section 503(b)(3) contemplates switching *plural* “drugs” when the prescription requirement imposed on a class of drugs is “not necessary for the protection of the public health,” while section 505(e) addresses procedures relating to a *single* “drug,” subject to safety, effectiveness, and other standards and requirements imposed by the NDA licensing provisions in section 505(b)(1) of the FD&C Act. Notably, the 1951 Amendments did not repeal, amend, or otherwise mention section 505(e), presumably because Congress still intended that provision to address individual drug products approved through NDAs, and thus to require a hearing prior to the revocation of an approved NDA.

Eleven years later, the Drug Amendments of 1962 completely revamped the drug approval process to require premarket approval, and reaffirmed the adjudicative process for withdrawing the approval of an NDA under section 505(e). The Drug Amendments of 1962 required FDA to determine affirmatively that new products had demonstrated their effectiveness (by substantial evidence), and their safety, and required FDA to review all NDAs that were already effective to determine whether they met the effectiveness standard.

Given this chronology, it is clear that the current version of section 505(e), which is more recent than section 503(b)(3) and is aimed specifically at NDA-approved drug products, applies when FDA seeks to withdraw a single NDA that has already been approved by FDA. Therefore, in cases where FDA targets a single NDA-approved product or other small number of drugs subject to NDAs, the adjudicative process requirement of section 505(e) supersedes the generic notice and comment rulemaking requirements of section 503(b)(3). The two provisions are thus reconcilable

by recognizing FDA's rulemaking authority under section 503(b)(3), subject to certain restrictions imposed by section 505(e) and the general requirements of the Administrative Procedure Act ("APA") and procedural due process. See *Air North America v. Department of Transportation*, 937 F.2d 1427, 1436 (9th Cir. 1991) (holding that an agency must comply with the APA as well as with its governing statute); see also *W.C. v. Bowen*, 807 F.2d 1502, 1504 (9th Cir. 1987).²

B. A Hearing is Required by Principles of Administrative Law and Procedural Due Process.

Even if section 503(b)(3) somehow superseded the more specific requirements of section 505(e) and applied to this situation in the abstract, any proposed switch regulation would still be subject to the general requirements of the APA and related principles of administrative law and procedural due process. See *Air North America*, 937 F.2d at 1436 ("Even though the Department's revocation of AirNA's certificate complied with section 1371(r), the revocation is nevertheless invalid if the Department failed to comply with the requirements of the [APA]."). As further explained below, a hearing would still be required were FDA to propose a switch over the sponsor's objection because the switch amounts to an adjudication.

FDA obviously has both rulemaking authority and adjudicative authority. Yet simply because section 503(b)(3) permits the FDA to act by rulemaking to remove a

² The question of whether FDA must provide a hearing when it acts broadly across large classes would be unlikely to be presented in the switch context, because switch issues typically are considered with respect to only one or a small number of drugs at a time, and each drug would raise individual issues pertaining to whether it could be switched. Of course, whether only a few or many drugs are involved, FDA would be free to proceed through the switch regulation process if the sponsors did not object and there were sufficient data available to support the switch.

prescription designation in certain situations does not relieve the agency of its obligation to provide an adjudicative process when it is otherwise required. The switch of one or a small number of NDAs to OTC status amounts to the modification or withdrawal of a license, and triggers a right to a hearing. "Obviously, the [agency] cannot, merely by invoking its rulemaking authority, avoid the adjudicatory procedures required for granting and modifying individual licenses." *Committee for Effective Cellular Rules v. FCC*, 53 F.3d 1309, 1318 (D.C. Cir. 1995). See also *Aeronautical Radio, Inc. v. FCC*, 928 F.2d 428, 451 (D.C. Cir. 1991) (rejecting the granting of licenses without a hearing); *Air North America*, 937 F.2d at 1436 (holding that agency's compliance with its governing statute did not obviate compliance with the APA).

Once FDA approves a new drug application under section 505, the manufacturer holds a license to produce and distribute the product subject to the restrictions imposed in the NDA. Courts generally recognize that the initial consideration of a licensing application is an adjudicative function. See *Hornsby v. Allen*, 326 F.2d 605, 608 (5th Cir. 1964) ("[W]hen a municipal or other governmental body grants a license it is an adjudication that the applicant has satisfactorily complied with the prescribed standards for the award of that license."). See also 5 U.S.C § 551 (6)-(8). Moreover, the FD&C Act clearly provides an adjudicative process for obtaining approval of an NDA, as section 505(d) mandates notice and opportunity for a hearing if FDA proposed to refuse to approve an NDA. 21 U.S.C. § 355(d).

It is also widely accepted that when an issuing agency considers the suspension, modification, or revocation of an already-approved license, a hearing must take place prior to an actual change in the status of the licensee. See *American*

Airlines, Inc. v. CAB, 359 F.2d 624, 631 (D.C. Cir. 1966). See also *Bowens v. North Carolina Dep't of Human Resources*, 710 F.2d 1015 (4th Cir. 1983); *Illinois v. NRC*, 591 F.2d 12 (7th Cir. 1979); *Gilliland v. FAA*, 48 F.3d 316 (8th Cir. 1995). The APA also generally requires an adjudicative procedure before the withdrawal of a license. See 5 U.S.C. § 558(c). In fact, "an amendment of licensing . . . under the [APA] . . . results in even more rigorous procedural requirements than apply to initial licensing." *American Airlines*, 359 F.2d at 631.

In addition to APA requirements, a proposed switch without the sponsor's consent would require a hearing based on the *Londoner* and *Bi-Metallic* guideposts and their progeny. These cases establish that a process is adjudicative in nature if it focuses on a particular set of facts or individuals directly affected by the action. *Bi-Metallic Inv. Co. v. State Bd. of Education*, 239 U.S. 441 (1915), and *Londoner v. Denver*, 210 U.S. 373 (1908), provide the classic illustration of the distinction between rulemaking and adjudication. In *Bi-Metallic*, a citizen of Denver demanded a hearing prior to the imposition of a city-wide property tax assessment. 239 U.S. at 445. The Court found that because of the general applicability of the tax, no single individual was entitled to an individual adjudicative process. *Id.* In *Londoner*, however, the city of Denver undertook municipal improvements and then levied a tax on certain taxpayers to pay for those improvements. 210 U.S. at 373. One of the taxpayers challenged the imposition of the tax without the benefit of a hearing. *Id.* The Court found that the taxpayers were entitled to a hearing because the city regulation imposed a burden on a few individuals rather than all citizens of the city. *Id.*

Londoner and *Bi-Metallic* “represent a recognized distinction in administrative law between proceedings for the purpose of promulgating policy-type rules or standards, on the one hand, and proceedings designed to adjudicate disputed facts in particular cases on the other.” *United States v. Florida E. Coast Railway Co.*, 410 U.S. 224, 245 (1973). Cases expanding on *Londoner* and *Bi-Metallic* have outlined several factors that establish whether an administrative body can proceed by rulemaking or must instead provide an adjudicative proceeding.

As the cases below illustrate, an agency may generally forgo an adjudicative proceeding only if the action it undertakes is applicable to a large and generalized group of parties, does not place a particular burden on an individual or a discrete group, does not require consideration of a particular set of facts, and, related to all of these, if it would be inefficient to proceed by adjudication. A proposed switch, over the objection of the NDA sponsor, fails to satisfy any of these requirements. Such a proposal would apply to just one drug manufacturer and one product (or a very small number of manufacturers and products), would impose a burden solely on the licensee, would require consideration of a particular set of facts – namely, the safety, effectiveness, and labeling of a drug product – and would alter a previous FDA decision made through adjudication. If FDA proceeded by rulemaking, it would amount to an “individual action . . . masquerading as a general rule.” *American Airlines*, 359 F.2d at 631; accord *Comm. for Effective Cellular Rules*, 53 F.3d at 1320. Thus, even if the general application of section 503(b)(3) permitted FDA to amend NDAs through rulemaking, the individualized facts in a particular case would demand an appropriate adjudicative proceeding.

Indeed, switching the terms of an individual approved NDA is the archetypical "particular" case requiring an individualized hearing. In *CAB v. Delta Airlines*, 367 U.S. 316 (1961), the Civil Aeronautics Board ("CAB") approved Delta's certificate of public convenience under the requirements of the Federal Aviation Act, and then sought to amend that certificate without notice or a hearing. *Id.* at 318. CAB then modified the certificate to bar Delta from maintaining its service to ten cities except for such service originating in Atlanta. *See id.* at 319-20. The Court held that, because of the specificity of the regulation, which was directed to a single carrier, Delta was entitled to a hearing prior to an amendment of its license. *See id.* at 331-32. *Londoner* and *Delta Airlines* are analytically similar to a scenario in which FDA would switch a sponsor's NDA by rule. All three purport to affect a single party (or discrete group) and would subject them to a particular burden. Indeed, an NDA drug switch is possibly an even stronger case, as the inquiry into the propriety of making a drug available OTC requires analysis of volumes of clinical data relevant to that product only.

By contrast, cases in which an agency action has been upheld as a rule exempt from hearing requirements, starting with *Bi-Metallic*, rely on the generalized nature of the action and its effect-- characteristics that are completely absent here. Although not dispositive, *Bi-Metallic* focused on the amount of people affected by the action. More recent cases have also undertaken this inquiry, and emphasized the necessity of an action's general applicability in upholding its enactment absent adjudicative procedures. *See, e.g., Air Line Pilots Ass'n, Int'l v. Quesada*, 276 F.2d 892 (2d Cir. 1960) (upholding a decision by FAA that prohibited pilots over sixty from flying for commercial airlines without providing affected pilots a hearing because it was

“directed to all the commercial airlines and to the more than 18,000 licensed commercial pilots”); *American Airlines*, 359 F.2d at 631 (upholding CAB’s “policy statement” declaring that only non-commercial, all-cargo planes could sell “blocked space” service because the regulation applied to all commercial carriers); *Florida E. Coast Railway Co.*, 410 U.S. at 245-46 (“Here, the incentive payments proposed by the Commission . . . were applicable across the board to all of the common carriers by railroad subject to the Interstate Commerce Act. No effort was made to single out any particular railroad for special consideration based on its own peculiar circumstances.”). As explained by the D.C. Circuit, “Where the agency is considering a general regulation, applicable to all carriers, or to all carriers within an appropriate class, then each carrier is protected by the fact that it cannot be disadvantaged except as the Board takes action against an entire class.” *American Airlines*, 359 F.2d at 631. A drug manufacturer obviously lacks such protection against an action taken against its previously approved NDA.

The use of informal rulemaking might be justified if the impact of the action does not fall disproportionately on particular individuals or parties. In *American Airlines*, the D.C. Circuit carefully distinguished between an actual administrative rule and a proceeding “that in form is couched as rulemaking, general in scope and prospective in operation, but in substance and effect is individual in impact and condemnatory in purpose.” 359 F.2d at 631. Thus, an adjudicative process is required “where an agency is considering an order against a particular carrier or carriers.” *Id.* Even if FDA purported to reclassify a class of drugs, if the impact fell disproportionately on one NDA holder, a hearing must be provided.

Courts also focus on the presence of factual questions in assessing whether a hearing is required.³ In *Quesada*, the court found that “no adjudicatory hearing is required where, as a result of generic rules that are otherwise procedurally and substantively valid, there is no contested issue.” 811 F.2d at 1585. See also *Upjohn v. FDA*, 811 F.2d 1583, 1585 (D.C. Cir. 1987) (finding no adjudicative hearing requirement where there is no contested issue). Similarly, an evidentiary hearing might not be required for modification of a particular license “when . . . a new *policy* is based upon the general characteristics of an industry.” *WBEN, Inc. v. U.S.*, 396 F.2d 601, 618 (2nd Cir. 1968) (emphasis added). By contrast, FDA’s decision to switch a drug from prescription to OTC status would be based almost entirely on characteristics of the particular drug product, and only remotely on the industry as a whole.

Courts also have focused on efficiency in determining whether an agency may forgo a hearing. Thus, the Supreme Court has allowed an agency to address general licensing issues through the general rulemaking function where utilization of an adjudicative process would be needlessly inefficient. In *United States v. Storer Broadcasting Co.*, 351 U.S. 192 (1956), the Court addressed the permissibility of FCC amending its rule regarding the availability of additional broadcast licenses. FCC had issued a generally applicable rule by rulemaking despite a statutory requirement that an

³ Even if FDA believed that there were no disputed issues of material fact, it would still be required to follow its own regulations and provide a notice of opportunity for a hearing (NOOH). These regulations specify procedural protections for NDA holders and allow them an opportunity to identify factual issues. See 21 C.F.R. § 314.200. The agency cannot avoid the NOOH requirements simply by asserting through informal rulemaking that there are no factual issues to be resolved.

applicant be granted “a ‘full and fair hearing’ to determine whether additional licenses to the applicant would be in the public interest.” *Id.* at 200. In upholding the use of rulemaking, the Court highlighted the concern over inefficiency, reasoning that the FCC was not required “to waste time on applications that do not state a valid basis for a hearing.” *Id.* at 205. Notably, inefficiency concerns must give way to valid claims to a fact-based hearing. *See Air North America*, 937 F.2d at 1435 (noting no reason to follow *Storer* in *Delta Airlines*, where agency was not engaged in general rulemaking). Moreover, the concern for agency inefficiency basically encompasses the other factors courts consider – general versus particular applicability and burden, and whether a factual inquiry is necessary. There is no additional benefit to utilizing rulemaking proceedings here, where the determination whether to switch a particular manufacturer’s NDA would be completely fact-specific and would directly impact only the one manufacturer.

These general requirements of administrative law reflect the constitutional due process requirement that a person is entitled to adequate process prior to a decision affecting its interests. Due process analysis focuses on two questions. First, a person must have a cognizable due process right. *See, e.g., Ingraham v. Wright*, 430 U.S. 651 (1977); *Bliek v. Palmer*, 102 F.3d 1472 (8th Cir. 1997). If a due process right is present, a court will then consider what process is required to protect that interest. As discussed above, a NDA is a license to market a drug product. Government-issued licenses are commonly recognized as property rights. *See, e.g., Barry v. Barchi*, 443 U.S. 55 (1979) (government-issued license is a property interest). In determining what process is due, courts look to the familiar *Londoner* and *Bi-Metallic* framework. Thus, a

court will consider whether the party has been singled out for particularized treatment in analyzing whether a party has been denied due process by not receiving an adjudicative proceeding. In *Harris v. County of Riverside*, 904 F.2d 497 (9th Cir. 1990), the Ninth Circuit reasoned:

We find the present case to be more analogous to *Londoner* than *Bi-Metallic*. . . . Within the County's amendment process, however, the County specifically targeted Harris' property for a zoning change after notice had been published for the General Plan Amendment. . . . Under the facts of this case, the County's decision to alter its proposed General Plan Amendment specifically to rezone Harris' land constituted a decision which was distinct from, rather than a part of, approval of the General Plan Amendment. This decision, in contrast to approval of the General Plan Amendment, concerned a relatively small number of persons . . . rather than the entire population of the West Coachella Valley. . . . Moreover, this change 'exceptionally affected' Harris 'on an individual basis' by severely altering the permissible uses of Harris' land. . . . Because of its exceptional effect on Harris as a specific, identifiable individual, we believe that the County's decision to rezone Harris' land is the type of government action which is subject to procedural due process constraints.

904 F.2d at 502-03. See also *Interport Pilot Agency, Inc. v. Sammis*, 14 F.3d 133, 143 (2nd Cir. 1994) (holding an action to be adjudicative when a decision is based on a determination of facts about the parties and their activities, businesses, and properties, and thus due process applies). Accordingly, a decision by FDA to alter the terms of an NDA holder's license to market a drug, over the holder's objections, without providing a hearing contravenes due process requirements and the *Londoner/Bi-Metallic* framework to which agency action must conform.

II. A Forced Switch Would Violate the NDA Holder's Proprietary Rights to Its Safety and Effectiveness Data.

Any switch necessarily is based in substantial part on the safety and effectiveness data in the original NDA that supported approval for prescription use.⁴ These data are proprietary to the NDA holder and cannot be used without its consent except in the limited circumstances permitted under the Hatch-Waxman Amendments and pursuant to the protections established by that law.

FDA could not legally approve an abbreviated new drug application (ANDA) to provide for OTC use of a listed drug that is limited to prescription use, because the labeling of the ANDA drug would not be the same as the labeling for the listed drug. 21 U.S.C. § 355(j)(4)(G). A supplement to the ANDA similarly could not be approved, because the labeling of the ANDA drug must remain the same as that of the listed drug even after approval; otherwise, the ANDA is subject to withdrawal. See 21 C.F.R. § 314.150((b)(10); 57 Fed. Reg. 17950, 17970 (April 28, 1992). Nor could FDA approve a switch through a section 505(b)(2) application by relying on the agency's prior finding of safety and effectiveness for the prescription drug, for reasons set forth in PhRMA's comments on FDA's draft guidance on section 505(b)(2) applications.⁵ Nor

⁴ It is theoretically possible that a switch might be supported by a full NDA submitted by a company other than the sponsor of the prescription NDA, including a full package of toxicology and clinical study reports establishing safety and effectiveness for OTC use without the need to reference the prescription NDA, but we are not aware of any case in which this has occurred and it seems highly unlikely. Moreover, even in the context of a full NDA to support a switch, FDA would need to respect the hearing rights of the holder of the prescription NDA and thus could not approve any switch application that would result in changing the status of the original drug without providing an opportunity for a hearing.

⁵ See comments submitted by PhRMA to Docket No. 99D-4809, April 3, 2000, at 3-4.

could FDA release the safety and effectiveness data in the prescription NDA, because these constitute confidential commercial information exempt from release under the Freedom of Information Act, and the NDA holder's opposition to switch presents "extraordinary circumstances" justifying withholding under the Hatch-Waxman Amendments.⁶ Moreover, any attempt to switch a drug through the ANDA or section 505(b)(2) process would have to recognize the exclusivity and patent protections established by the Hatch-Waxman Amendments.

Whether or not these protections have expired, FDA could not use the Hatch-Waxman process (either through an ANDA or a section 505(b)(2) application) to approve an OTC version of an approved prescription drug without first going through the hearing process described above to change the labeling of the NDA. Under the Durham-Humphrey Amendment, the same drug, at the same dose and for the same indication, cannot simultaneously be available on a prescription and nonprescription basis. Thus, under the Durham-Humphrey law, FDA would be barred from approving an application for OTC use of an approved prescription drug without addressing the prescription status of that drug – which would be subject to the NDA holder's section 505(e) hearing rights.⁷

⁶ See 5 U.S.C. § 552(b)(4); 21 U.S.C. § 355(l); 21 C.F.R. § 314.430.

⁷ This process would not be required to withdraw approvals of ANDAs for a prescription drug when the NDA holder seeks approval to switch the listed drug. ANDAs are required by law to have the same labeling as the listed drug and therefore approval of the ANDAs could be summarily withdrawn (without the need for any hearing process) upon approval of the switch for the listed drug, if the switch is protected by Hatch-Waxman exclusivity. If, on the other hand, the switch is not protected by exclusivity, then the ANDA applicants could supplement their applications to provide for OTC labeling and remain on the market. This is the process that FDA followed when Rogaine (topical minoxidil) was switched. See *Upjohn Co. v. Kessler*, 938 F. Supp. 439 (W.D. Mich. 1996).

In other words, whether FDA seeks to switch a drug through a switch regulation applicable to the NDA or by approving an ANDA or section 505(b)(2) application submitted by another manufacturer, it cannot do so in derogation of the hearing rights of the NDA holder.⁸

III. Forced Switches Would Represent Poor Public Health Policy.

The process of discovering and developing new medicines, and new uses for existing medicines, is expensive and time-consuming. It is undertaken principally through the investment of huge sums in research and development by private companies at their own initiative. This process serves the public well and has resulted in tremendous advances in the treatment and prevention of disease.

The sponsor of the NDA for prescription use has the most comprehensive and detailed knowledge of the drug and is in the best position to design, finance, and conduct additional studies necessary to evaluate the safety, effectiveness, and labeling of the drug for OTC use. Every recent switch has involved the development and submission of substantial amounts of data demonstrating that a switch candidate would be safe, effective, and properly labeled for OTC use. The data have been submitted almost universally in NDAs or supplements, which provide manufacturers the

⁸ Likewise, FDA could not rely on proprietary data in an NDA over the objection of the sponsor to determine that a prescription drug is generally recognized as safe and effective for OTC use. Such an approach also would be inconsistent with how FDA has regulated post-1962 drugs subject to NDAs, regardless of whether a switch is being considered. While the agency might consider whether it could determine that certain drugs were no longer "new drugs" after all of the patent and exclusivity periods had expired, that subject raises a number of policy questions that need not be considered here. It is enough in the present context to recognize that FDA lacks the statutory authority to switch a drug over the sponsor's objection through any process that does not recognize the sponsor's hearing rights and proprietary rights to its data.

opportunity to earn exclusivity rights established by Congress as an incentive to invest in the necessary research. See 21 U.S.C. § 355(j)(5)(D)(iii) and (iv). The prescription NDA holder is in the best position to take all of the relevant information into account and to decide when to initiate the switch process.

FDA would disrupt this system if it forced manufacturers to sell drugs for OTC use over their objection. Premature switches could put some members of the public at risk. Switches unsupported by adequate labeling studies similarly would result in suboptimal information and use on an OTC basis. Moreover, FDA would act arbitrarily and capriciously if it applied a lower standard to switches initiated by the agency itself or by third parties than it applies when the holder of the NDA seeks to switch its own drug. Forced switches also would alter revenue streams and expose manufacturers to different product liability risks from what they had planned for and on the basis of which they had made their research investments. These changes, in turn, would affect initial investment decisions in the drug development process, to the detriment of the public health.

The bottom line is that forced switches are being proposed by insurers that are merely seeking to shift costs away from their own drug benefit programs. They lack the data necessary to determine whether a switch is appropriate and are not proposing themselves to conduct the extensive studies needed to support any switch today. Rather, they are seeking to switch drugs based only on conclusory assertions, which FDA should reject.

There are good reasons to stick to the application process that has served FDA, industry, and consumers well for switches. It is the process most likely to

generate needed data and to ensure that only drugs that are actually safe for use without a prescription are released from the prescription requirement. A drug manufacturer is in the best position to know about the safety and effectiveness profiles of its products, and extensive prescription use often is essential to characterizing a drug's safety in actual use. The NDA process, initiated and carried through by the manufacturer, is best suited to determining whether a switch is appropriate for a particular drug product. Switches implemented through other processes could put the public at risk. In fact, the one time in which FDA did initiate a switch without the active support of the NDA holder – involving the bronchodilator metaproterenol – the agency quickly rescinded its decision after it received numerous adverse comments. See 48 Fed. Reg. 24925 (June 3, 1983).

There is no question that FDA plays an important role in the drug development process in general and in the switch process in particular. If the agency believes that a drug is an appropriate switch candidate, it should by all means consult with the NDA holder to determine whether there is interest in switch and, if there is, to develop a study program to support a switch application. Industry has a long history of working cooperatively with FDA in the drug development and approval process, and there is no reason why FDA cannot build on that history in this context as well. But forced switches would be unprecedented, would violate the rights of NDA holders, and would disserve the public.

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