



DEPARTMENT OF HEALTH & HUMAN SERVICES

738 Food and Drug Administration
Rockville, MD 20857
JAN 28 P1:26

JAN 24 2002

C. Boyden Gray, Esq.
Wilmer, Cutler & Pickering
2445 M Street, N.W.
Washington, D.C. 20037

Re: Docket No. 01P-0586/CP1

Dear Mr. Gray:

This letter responds to your citizen petition, dated December 26, 2001, submitted on behalf of Bristol-Myers Squibb Company. You request the Commissioner of Food and Drugs to issue new regulations and/or amend existing regulations to implement section 11 of the Best Pharmaceuticals for Children Act (BPCA), Pub. L. 107-109.¹ To the extent you request that the Food and Drug Administration (FDA) issue regulations before implementing section 11, your petition is denied. To the extent you request FDA to issue regulations in the future as part of the continuing implementation process for this statutory provision, your petition is neither granted nor denied; the Agency has yet to make this decision.

Section 11 of the BPCA permits approval of abbreviated new drug applications (ANDAs) for drugs when pediatric labeling for the innovator drug product is protected by patent or exclusivity.² Section 11 also describes labeling FDA may require for the generic drug. Under this provision, FDA will determine what labeling is appropriate for generic drugs when the innovator's pediatric labeling has market protection. FDA will also specifically identify any pediatric contraindications, warnings, or precautions that may be necessary.

Your principal argument is that section 11 is not "self-executing," and, therefore, before FDA implements the statute, it must issue new or amended regulations. In addition, you contend that new or amended regulations are necessary before FDA can adequately protect children's health and protect innovator exclusivity. FDA disagrees with each of these contentions.

¹ A comment in opposition to your petition, dated January 10, 2002, and submitted on behalf of Watson Laboratories, was reviewed by the Agency.

² The exclusivity at issue in section 11 of the BPCA is 3-year exclusivity under section 505(j)(5)(D)(iii) & (iv) of the Federal Food, Drug, and Cosmetic Act (FFDCA) (3-year exclusivity).

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The BPCA Does Not Require FDA to Issue Regulations Before Implementing Section 11

The BPCA contains no language stating that regulations must be issued before section 11 may be implemented by FDA. Congress may provide that Agency action may be undertaken only by rulemaking under the Administrative Procedures Act. *See In re Bluewater Network*, 234 F.3d 1305 (D.C.Cir. 2000)(Coast Guard's failure to undertake any rulemaking mandated by Congress in the Oil Pollution Act of 1990 inconsistent with specific statutory requirement); *see also Becton, Dickinson & Co. v. FDA*, 448 F.Supp. 776 (N.D.N.Y.) *aff'd*, 589 F.2d 1175 (2nd Cir. 1978)(FDA must implement restricted device provisions through rulemaking). The BPCA, on the other hand, includes no requirement that FDA engage in rulemaking prior to implementing the statute. In the absence of express statutory language requiring rulemaking, government agencies possess broad discretion in deciding whether to proceed by general rulemaking or case-by-case adjudication. *NLRB v. Bell Aerospace*, 416 U.S. 267, 293-94 (1974); *SEC v. Chenery Corp.*, 332 U.S. 194, 203 (1947); *Cellnet Communication, Inc. v. FCC*, 965 F.2d 1106, 1111 (D.C. Cir. 1992)("an agency's refusal to initiate a rulemaking is evaluated with a deference so broad as to make the process akin to non-reviewability."). Courts have held that FDA may implement the ANDA approval provisions of the FFDCA through individual adjudication. *Teva Pharmaceuticals, USA, Inc. v. FDA*, 182 F.3d 1003, 1010 (D.C. Cir. 1999).

In the past, FDA has been successful in its approach to implementing pediatric legislation. Most of the BPCA is a reauthorization and expansion of the pediatric exclusivity established under the 1997 FDA Modernization Act (FDAMA). As a result of the FDAMA pediatric exclusivity, FDA has made technical and often complex assessments of (1) the adequacy of existing pediatric drug labeling, (2) the types of pediatric studies necessary to provide adequate pediatric labeling, and (3) the scope of both the pediatric study requirements and the resulting exclusivity. FDA began to implement pediatric exclusivity immediately after FDAMA was enacted in November 1997. FDA has implemented the FDAMA pediatric exclusivity provision solely through the use of guidance documents and has not issued implementing regulations.

FDA's implementation of the FDAMA pediatric exclusivity was challenged by the generic drug industry on the grounds that the guidance was a legislative rule that should have been issued through notice and comment rulemaking. The court cited the test in *American Mining Congress v. Mine Safety & Health Admin.*, 995 F.2d 1106, 1112 (D.C.Cir. 1993), which requires initial assessment of "whether in the absence of the rule there would not be an adequate basis for ... agency action." *National Pharmaceutical Alliance v. Henney*, 47 F. Supp. 2d 37, 41 (D.D.C. 1999). As the court observed, "the statute [FDAMA] on its face provides all the 'legislative basis' that is necessary for the agency's action." *Id.* Such is the case with the BPCA as well.

The statements of Representatives Tauzin and Jackson-Lee (cited in your petition at p.9) are no substitute for express statutory language requiring a rulemaking. It is well established that reliance on statements made during floor debates should be avoided. *Garcia v. United States*, 469 U.S. 70, 76 (1984). Representatives Tauzin and Jackson-Lee's statements cannot impose upon FDA a requirement for rulemaking that is absent from the statute.

Regulations Are Not Necessary Before FDA Can Adequately Protect Children's Health and Protect Innovator Exclusivity

The task before FDA in implementing section 11 is to ensure that labeling for ANDAs adequately protects pediatric health and is consistent with marketing exclusivity for the innovator. FDA already has considerable experience in labeling generic drug products for safe and effective use, as well as experience ensuring that approved generic drug product labeling does not impinge on 3-year exclusivity rights. The Agency regularly reviews ANDA labeling under 21 CFR 314.127(a)(7). That regulation permits approval of ANDAs without protected innovator labeling (i.e., when the absence of the protected labeling does not render the drug product less safe or effective for the remaining nonprotected conditions of use). Moreover, since issuing the pediatric labeling regulations at 21 CFR 201.57 in 1994, the Agency has devoted substantial resources to review and approval of pediatric labeling. FDA has developed additional expertise in this area with the 1997 passage of the FDAMA pediatric exclusivity provisions. Although section 11 represents a new approach to labeling drugs with respect to pediatric use, its implementation will involve the scientific and medical expertise and judgment FDA regularly exercises.

Finally, FDA understands your concern that innovators' 3-year exclusivity be respected during the implementation process. FDA has been implementing the 3-year exclusivity provisions of the Drug Price Competition and Patent Term Restoration Act since its passage in 1984, and the Agency is therefore confident in its ability to respect innovator exclusivity. One provision in section 11 permits the Secretary to require in generic drug labeling "a statement of any appropriate pediatric contraindications, warnings, or precautions that the Secretary considers necessary." FDA has long stated that the submission of studies supporting the addition of new "risk information" to a product's labeling does not make the new drug application (NDA) eligible for exclusivity. *See* 54 FR 28,872, 28,899 (July 10, 1989); *see also* 59 FR 50,338, 50,356-57 (October 3, 1994) (NDA holders "have no valid interest in precluding [risk] information from the labeling of other products."). Although it is possible that the interaction of this limitation on exclusivity and the new labeling provision may raise complicated issues regarding the use of information protected by exclusivity, FDA is confident it can implement section 11 at this point without issuing new regulations.

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Conclusion

FDA has reviewed the arguments raised in your petition and has concluded that the BPCA does not require FDA to engage in a rulemaking before implementing section 11. Moreover, FDA is confident it has the technical expertise and experience necessary to adequately protect both pediatric health and any 3-year exclusivity earned by innovator Companies. To the extent you request that FDA issue regulations before implementing section 11, your petition is denied. To the extent you request that FDA issue regulations in the future as part of the continuing implementation process for this statutory provision, the petition is neither granted nor denied; the Agency has yet to make this decision.

Sincerely yours,

A handwritten signature in cursive script, appearing to read "John Marshall" or similar, with a date "10/7" written below it.

Dennis E. Baker
Associate Commissioner
for Regulatory Affairs