

**FDA Authority To Require Risk Management Programs  
for Generic Versions of OxyContin®:  
Supplemental Points**

This memorandum supplements our previous White Paper which addressed the Food and Drug Administration's authority to require that firms submitting abbreviated new drug applications for controlled-release oxycodone hydrochloride products that list OxyContin® (oxycodone HCl controlled-release) Tablets as the reference listed drug develop and implement appropriate risk management programs ("RMP").

FDA's recent publication of a final rule on bar coding requirements for human drug products (69 Fed. Reg. 9120, February 26, 2004) reflects the agency's long-standing view that it has the legal authority to require drug manufacturers to implement appropriate risk management measures. Like virtually all risk management tools, the purpose of mandatory bar coding is to supplement truthful, complete and non-misleading labels and prescribing information with additional measures that are intended to enhance or supplement the communication and understanding of that information. As described by the agency in the preamble to the bar coding rule:

In brief, medication errors are a serious public health problem, and putting bar codes on drug products is expected to significantly reduce medication errors. . . . Bar codes can help reduce or detect potential medication errors by enabling health care professionals to check whether they are giving the right drug via the right dose and right route of administration to the right patient at the right time.

69 Fed. Reg. at 9121.

The objective of the rule is to enable the health care sector to utilize technological solutions to reduce preventable adverse drug events (ADEs) and acute hemolytic transfusion reactions (AHTRs) associated with medication errors and transfusion errors in hospitals.

69 Fed. Reg. at 9151-2, footnotes omitted.

Based on its conclusion that the potential benefits of virtually across-the-board bar coding outweigh the costs, the agency reiterated its legal authority in a manner that clearly also supports our view that the agency has ample legal authority to require drug product manufacturers to implement RMPs when the agency believes that such programs are warranted. As described by the agency in the final rule:

We believe we have the authority to impose a bar coding requirement for the efficient enforcement of various sections of the act. These include sections 201(n), 201(p), 501, 502, 503, 505, and 701(a) of the act . . . .

A bar coding requirement for drugs . . . would permit the efficient enforcement of the misbranding provision in section 502(a) and (f) of the act, as well as the safety and effectiveness provisions of sections 201(p) and 505 of the act. Bar coding is expected to significantly advance: (1) The provision of adequate directions for use to persons prescribing, dispensing, and administering the drug; (2) the provision of adequate warnings against use by patients where a drug's use may be dangerous to health; and (3) the prevention of unsafe use of prescription drugs.

Section 502(a) of the act prohibits false or misleading labeling of drugs. This prohibition includes, under section 201(n) of the act, failure to reveal material facts relating to potential consequences under customary conditions of use. Information in a database that could be readily accessed through the use of a bar code, such as the drug's strength, dosage form, route of administration, and active ingredient and drug interactions is material with respect to consequences which might result from use of the drug under such conditions of use. Because all of the drugs (prescription drugs and the subset of covered OTC drugs) covered by this final rule may be used in the hospital setting, such use in hospitals can be considered the "conditions of use as are customary or usual." Bar coding can be expected to reduce the incidence of the following types of medication errors:

- Administering the wrong dose to a patient;
- administering a drug to a patient who is known to be allergic;
- administering the wrong drug to a patient or administering a drug to the wrong patient;
- administering the drug at the wrong time; and
- missing or duplicating doses.

Because information accessed through use of the bar code will reveal material facts relating to potential consequences under customary conditions of use, the bar code requirements are justified under section 502(a) of the act.

Section 502(f) of the act requires drug labeling to have adequate directions for use, adequate warnings against use of a drug product by patients where its use may be dangerous to health, as well as adequate warnings against unsafe dosage or methods or duration of administration, in such manner and form, as necessary to protect users. The bar code would make it easier for the person administering the drug to have full access to all of the drug's labeling information, including directions for use, warnings, and contraindications. Moreover, because the bar code's information would go to the computer where it could be compared against the patient's drug regimen and medical record, the person administering the drug will be able to determine whether the right patient is receiving the right drug (including the right dose of that drug in the right route of administration) at the right time. The person administering the drug will also be able to avoid giving products to a patient who might be allergic to, or otherwise unable to take, a particular drug. Because the bar code will facilitate access to information including adequate directions for use and adequate warnings, the bar code requirements are justified under section 502(f) of the act.

In addition to the misbranding provisions, the premarket approval provisions of the act authorize FDA to require that prescription drug labeling provide the practitioner with adequate information to permit safe and effective use of the drug product. Under section 505 of the act, we will approve a new drug application (NDA) only if the drug is shown to be safe and effective for its intended use under the conditions set forth in the drug's labeling. Bar coding would allow health care professionals to use bar code scanning equipment to verify that the right drug (in the right dose and right route of administration) is given to the right patient at the right time. Thus, bar coding will ensure the safe and effective use of drugs by reducing the number of medication errors in hospitals and other health care settings.

69 Fed. Reg. at 9147-8. Thus, FDA concludes that, despite the fact that a bar code itself conveys no additional information about the drug – indeed, even the encoded “content” of the bar code is simply a restatement of the NDC number of the

product – printing the code on the product label may be legally required because it has to potential to enhance the communication of required labeling information and other information about the safe and effective use of the drug.

This legal rationale applies even more strongly to risk management tools that are targeted at particular categories of drug products which are believed to pose specific additional known and potential risks. If the agency believes it has the legal authority to require bar coding across-the-board based on a risk management rationale, surely it has the authority to require risk management measures tailored specifically to the unique risks posed by specific products. Moreover, there is no basis to distinguish the bar coding requirements imposed under the new regulation from other risk management requirements that may be imposed on specific sub-categories of products outside of a “rulemaking” proceeding. As the agency states in the bar coding rule:

After the effective date of any final rule, if a product required by the final rule to bear a bar code does not have such a bar code, the product may be considered adulterated or misbranded under the act and would be subject to regulatory action. Our enforcement actions under the act include, but are not limited to, seizure, injunction, and prosecution, and violation may result in withdrawal of approval of a product’s marketing application.

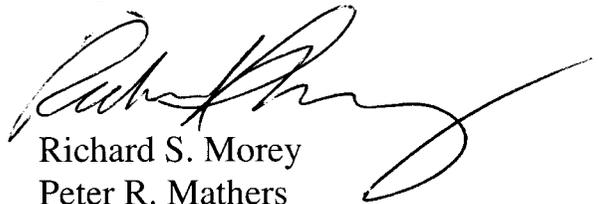
69 Fed. Reg. at 9148-9.

Significantly, the legal rationale adopted by the agency to underlay its bar coding requirement applies equally to applicants for NDA and ANDA approvals, and even applies to ANDA applicants where the label of the referenced listed drug does not carry a bar code. For example, under the transitional provisions announced in the February 26, 2004, notice, products marketed under ANDAs approved after the effective date of the regulations will need to include bar codes on their labels within 60 days of approval while currently-approved products, including the pioneer products on which those new ANDAs may be based, need not implement bar codes until as much as two years later. 69 Fed. Reg. at 9120 and 9146-7. Additionally, particularly in the case of OTC drugs, the possibility exists that products approved under ANDAs may be subject to the bar code requirements even if the underlying products with approved NDAs are not. This is because the bar code requirements for OTC drugs turn on whether the drugs are packaged, labeled, marketed, promoted or sold to hospitals. 21 C.F.R. § 201.25(b)(3), 69 Fed. Reg. at 9170. Thus, the requirements for placing bar codes

on OTC drugs turn on whether the product is positioned for sale to hospitals and not on whether the corresponding brand name product displays a bar code. (This same distinction would apply to a conventionally packaged prescription product which is the subject of an ANDA, but where the reference listed drug is packaged in a LDPE form, fill and seal container. *See* 21 C.F.R. § 201.25(b)(1)(F), 69 Fed. Reg. at 9170.)

For these reasons, we reiterate our belief that FDA currently has the legal authority to refrain from approving ANDAs for modified-release oxycodone products until the Agency is satisfied that the sponsors of those applications have developed and implemented appropriate RMPs.

Respectfully submitted,

A handwritten signature in black ink, appearing to read 'Richard S. Morey', with a long, sweeping flourish extending to the right.

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