GPhA
Generic Pharmaceutical Association

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

RE: Docket No. 00N-1484
Safety Reporting Requirements for Human Drug and Biological Products;
Proposed Rule

Comments of the Generic Pharmaceutical Association

Dear Sir or Madam:

The Generic Pharmaceutical Association (GPhA) appreciates the opportunity to comment on the above referenced Draft Guidance for this important class of drug products. GPhA represents 98% of generic drug manufacturers whose drugs are dispensed for over half of all prescriptions filled in the United States, but representing less than 10% of all drug expenditures. GPhA is the united voice of the generic drug industry and is committed to patient health and safety, and strongly supports any measures that will improve our health care system. GPHA would like to thank the Agency for this opportunity to provide feedback on the proposed rule in an effort to improve the safety of human drug and biological products.

GPhA believes that our comments are consistent with the Agency's efforts to work toward global harmonization of safety reporting requirements and to achieve more effective and efficient safety reporting system, and therefore is in general agreement with the tenets of the proposed rule. However, certain proposals do not appear to be consistent with the Agency's efforts to harmonize with other regulatory authorities in regard to drug safety reporting requirements and develop a more efficient and responsive process. As described below, certain proposed requirements appear to create significant new regulatory burdens without adding any apparent benefit to consumers or health care practitioners. Based on these concerns, specific comments are provided below.

00N-1484

1. III.A.3. Serious SADR, Nonserious SADR, and SADR With Unknown Outcome

It is recommended that the proposed reporting requirements for "SADR with unknown outcome" to be deleted from the reporting paradigm. This new term/category is unrecognized by ICH definitions/guidelines and will potentially convert a substantial number of non-serious cases into this new category and result in a heavy volume of follow-up activities. This approach appears to conflict with the goals of the Agency to streamline the process for non-serious reports and focus efforts on diligent investigation of serious reports.

2. III.A.8. Medication Error

It recommended that reporting requirements for "actual medication error" and "potential medication error" be removed from the proposed reporting requirements. These terms are again inconsistent with ICH guidance and also with the efforts for global harmonization.

GPhA applauds the Agency's efforts to focus on the health impacts of medications errors, however the underlying cause is typically related to factors outside the control of pharmaceutical manufacturers. GPhA recommends that the Agency reconsider its proposal regarding medication error reports and direct activities towards those components of the healthcare system that may have more direct involvement in the healthcare professional-patient-institution linkages. As noted, active monitoring of medication errors and resolution of their causes is an important activity. GPhA would welcome working with the Agency to assess how the pharmaceutical industry can assist in this effort in an effective and efficient manner.

3. III.A.9. Company Core Data Sheet

The labeling for a product approved as an ANDA is required by law to be the same as the approved labeling for the NDA reference product. Information on the safe use of an approved generic drug product, including information describing Precautions, Adverse Events, Warnings, etc., represents expected adverse events of the product and essentially constitutes the core data sheet and core safety information. ANDA applicants should be exempted from the proposed rule requiring the preparation and use of Company Core Data Sheets and Company Core Safety Information and rely on the approved labeling as the primary source of product information.

4. III.A.10, Data Lock Point and International Birth Date

Please clarify data lock point and international date for products with multiple active moieties with different approval dates.

5. Table 6 – Proposed Postmarketing Expedited Safety Reports

GPhA agrees that if there was a medication error involved with a suspected adverse event, it should be captured in the individual case report and submitted based on the seriousness/expectedness of the adverse event. However, it is requested that non-ICH required reports and timeframes, such as 45 calendar day and 30 calendar day reports, be removed as a requirement for medication errors and SADRs with unknown outcome for the reasons stated above. Industry is required to perform an active query for these expedited reports in an effort to obtain a full data set and clear documentation of such activities with individual case files, there does not seem to be any additional value in submitting these negative results (which simply says there was no additional information available after so many attempts) as 30-day follow up reports.

6. III.D.4. Always Expedited Reports

GPhA agrees with the Agency's assessment that certain medically significant events should be subject to an always expedited report regardless of expectedness. However, we would like to point out that it is not uncommon for laypersons to report some of these listed serious diagnoses with described symptoms/manifestations that are clearly inconsistent with the given diagnoses or reaction, or that are manifestly misunderstood by the lay reporter. GPhA recommends that the regulations permit such initial reports to be omitted from the 'always expedited' category if a health care professional determines the initial report to be unsubstantiated upon investigation.

7. III.D.5 Medication Errors

See comment number 2 above.

8. III.D.6. Follow-up Reports

See comment number 5 above.

9. III.D.8. Scientific Literature

The proposed rules and current draft guidance for industry do not distinguish requirements of literature report submission between companies holding applications for generic (ANDA) products and those for reference drug products (mostly NDAs but can also include ANDAs. The firm holding application for a particular reference drug product should be the designated responsible party for active literature search and submission of appropriate literature report for that particular product. This approach will eliminate the potential for voluminous duplication of effort by industry and FDA.

10. III.E.1.h. and III.F.4. Contact Person

The proposed rule would require a licensed physician be responsible for the content of post marketing safety reports submitted to the FDA. This responsibility should not be limited to a licensed physician. The proposed rule should be consistent with the principle embodied in the regulations that a person engaged in an activity should have the education, training and experience, or any combination thereof, to enable that person to perform the assigned function (qualified healthcare professionals i.e.; nurses, pharmacists, physician assistants, etc.).

11. III.E.2.g. Safety Studies

For the same reasons provided in comment number nine above, the reporting requirements for safety studies should be limited to holders of reference drug products.

12. III.E.2.k.vii Medication errors

See comment number 2 above.

13. III.E.5.a. Reporting Intervals

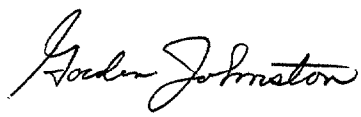
In efforts to harmonize with ICH guidelines, we agree with the proposed schedule of submitting PSUR to the Agency as semiannual reporting for 2 years after U.S. approval, annual for the next 3 years, and every 5 years thereafter. These reporting periods encompass substantial post-approval experience with the particular drug product as well as an established body of evidence in regard to the safe use of the drug product. Therefore, the additional proposed reporting requirements, (i.e. 7.5 years, 12.5 years, etc.) which are inconsistent with ICH guidelines, appear to provide little opportunity for generation of new information related to the drug. In addition, the proposed rule imposes another reporting requirement for all products: semiannual submission of individual case safety reports for ALL products, indefinitely. We believe that this is an unnecessary requirement, which is not expected to provide information that is genuinely useful for patient safety. Again, we request that the Agency reconsider this additional requirement of semiannual submission. Alternatively, these individual case safety reports can be included in PSUR and follow the same schedule.

14. III.F.5. Computer-Generated Facsimile of FDA Form 3500A or VAERS Form

We request that the Agency "grandfather" the use of previously approved versions of FDA Form 3500A and not subject them to requirements specified in this section of the proposed rule.

Thank you for your consideration of these comments.

Respectfully submitted,



Gordon Johnston
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