aids treatment activists coalition

Drug Development Committee

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October 13, 2003

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

Dear Sir or Madam:

The AIDS Treatment Activist Coalition (ATAC) is a national coalition of AIDS activists, many living with HIV/AIDS, working together to end the AIDS epidemic by advancing research on HIV/AIDS, its opportunistic infections and co-infection like hepatitis C virus, as well as broadening access to treatment. ATAC's Drug Development Committee (DDC) works with government, industry and academia to provide a community perspective to the development of new HIV drugs and the utilization of HIV therapies. We are writing to provide comments to the proposed amendments to 21 CFR Parts 310, 312, 314, 320, 600, 601, and 606.

We wish to express our dismay at a number of the changes proposed by the agency. Initially, we oppose the agency revoking the pediatric rule issued in December 2, 1998 (63 FR 66632), whereby sponsors are required to report specific information regarding pediatric populations. We believe it unconscionable for the agency to turn its back on this helpless population. Pediatric research, which has historically lagged far behind research in other populations, will undoubtedly make even less progress in the future if this requirement is revoked.

We are adamantly opposed to changing the term "adverse drug experience" as defined in Sections 310.305(b), 314.80(a) and 600.80(a) of FDA's existing post-marketing safety regulations with proposed Section 312.32(a), which would replace the term "associated with the use of the drug" with the term "suspected adverse drug reaction" (SADR); and rename "adverse experience" as "suspected adverse experience" in Section 600.80(a) and throughout the proposed regulations. To make our comments concise, but very much to the point, we can just imagine industry's marketing spin on the term "suspected". In this age of marketing frenzy on the part of industry from magazines to TV, etc., can you imagine the field day public relations departments will have with the patient community? We submit that "suspect" should only be used when describing industry's use of the proposed new term.

We are also extremely concerned with the new definition of "SADRs" in proposed Sections 310.305(a), 312.32(a), 314.80(a), and 600.80(a). The proposed definition for an SADR is "... there is a reasonable possibility that the product caused the response. In this definition, the phrase "a reasonable possibility" means that the relationship cannot be ruled out." The Federal Register notes that "the relationship cannot be ruled out" will be the controlling language for cases to be reported to the agency. We contend that if the relationship cannot be ruled out, it is clearly not "suspected." Further, the concept that "the relationship cannot be ruled out" is a much more strict standard for reporting adverse events than the more loosely defined current

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standard of "a reasonable possibility that the experience may have been caused by the drug" found in Section 313.32(a) of existing FDA pre-marketing reporting regulations. We believe that although "a reasonable possibility" may be potentially confusing, it greatly avoids the risk of under-reporting important safety events. The "reasonableness" standard has been employed in every facet of our nation's common law system since legal decisions were recorded in England and adopted by the United States in 1776.

From the perspective of a consumer, we firmly believe that changing the current definition as proposed will greatly enhance the safety risk to patients. Thus, we are opposed to the proposed changes and believe that in no event should the "reasonable possibility" standard be changed to include, "the relationship cannot be ruled out". For all the foregoing reasons, we are even more opposed to the definition only being "the relationship cannot be ruled out," omitting the "reasonable possibility" language completely. We believe that this alternative is even more dangerous to patient safety.

The proposed section on IND safety reports found in Section 314.80 does not seem to address adverse events that may be caused by one or more experimental agents. Differentiating between drugs to ascertain which drug in a multi-drug regimen is the probable cause of the adverse experience does not seem to be considered. We believe that this is a fatal flaw in this day of multi-drug experiments. We also wonder whether the new definition which mandates that the causal "relationship cannot be ruled out" will serve to completely preclude reporting such adverse events.

We fail to see how the proposed grading system of one (1) through four (4) will be applied to serious, non-serious, expected, and non-expected drug reactions in the New Drug Applications rules found in Section 314.80 and throughout the proposed regulations. We believe that it is imperative that the agency provide more guidance in this regard in ensure patient safety. Additionally, a patient report is not adequately described in this section and throughout. Patient reports are also treated as less than reliable. We fail to see the rationale for this apparent determination.

We are also vehemently opposed to the changes to the reporting requirement intervals proposed in Sections 314.80(c)(3)(i), (ii) and (iv) and 600.80(c)(3)(i) , (ii) and (iv).
Current agency reporting intervals require the submission of post-marketing periodic safety reports at quarterly intervals for three (3) years from the date of approval of the application in the United States. Thereafter, said reports are required annually. FDA is proposing revisions that would greatly reduce these reporting intervals. In cases where a marketed drug or biologic product has been approved on or after January 1, 1998, the agency is now proposing that reporting intervals should occur only semiannually; i.e., two (2) times per year for two (2) years after approval in the United States, annually for the next three (3) years, and every five (5) years thereafter.

Experience clearly shows that most adverse drug reactions are identified within the first few years of approval. Thus, we firmly believe if these relaxed regulations are promulgated as currently proposed by FDA, patient safety will be severely compromised by the very agency that is charged with protecting consumer safety in this regard.

In the current and proposed regulations set forth in Section 314.80(i) and(f) respectively, sponsors are required to maintain safety records for only ten (10) years. We believe that safety records should be maintained by sponsors for as long as a drug is marketed; and, that said sections should be amended accordingly.

Data from non-manufacturer initiated studies does not seem to be contemplated in the proposed regulations. Independent studies have been an important source of defining and confirming adverse events. How will safety reporting and requirements be regulated in these studies?

Moreover, race and age as adverse event factors do not seem to be contemplated. Gender seems to be unevenly recognized as a contributing factor, required in some reports, but not in others.

On the other hand, we applaud the agency for the new regulations that we believe will enhance patient safety and modernize its regulations. We are particularly pleased with a number of other proposed regulations, exemplified by the following:

The agency's acceptance of the concept of and its attempt to foster worldwide standardization of medical terminology, as well as regulatory definitions, reporting forms, documents and reporting requirements where patient safety is not compromised by the proposed regulation as previously indicated above.

Ensuring that adverse drug reactions will be reported to FDA if either the sponsor "OR" the investigator believes it is an adverse drug event.

Ensuring that safety information from both the sponsor's domestic and foreign study sites will be reported to the agency.

Ensuring documentation of worldwide exposure to a drug.

Ensuring that discordant data will also be reported to the agency regularly.

Ensuring that physician supervision will be present in a number of important instances.

Codifying the definitions and requirements regarding electronic communications.

Codifying "Guidance Documents" and deletion of redundant and variant sections.

We sincerely hope that these proposed regulations, especially the new term for and definition of an adverse drug experience and the new reporting requirement intervals will not be promulgated by the agency without the patient community having an opportunity to personally discuss these proposals with relevant agency personnel.

Please respond to Lynda Dee at 111 North Charles Street, Suite 500, Baltimore, MD 21201. Thank you for the opportunity to comment.

Very truly yours,

Lynda Dee, Co-Chair
ATAC DDC

cc: Health and Human Services Secretary Tommy Thompson
FDA Commissioner Mark McClellan
ATAC DDC