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January 16, 2001

Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Rm. 1061
Rockville, MD 20857

RE: Docket No. 00N-1682

Dear Sir or Madam,

I would like to take this opportunity to comment on "Agency Information Collection Activities; Proposed Collection; Comment Request; Radioactive Drug Research Committee" [Docket No. 00N-1682] published in the Federal Register Jan. 5, 2001, Vol 66, No. 4, pp 1137-1138.

I wish to focus my comments on one particular item: the reporting requirements on Form 2915 as required by 361.1(c)(3). Specifically, item # 6.b. on Form 2915 states "If this is a study summary submitted within the annual report, provide the radiation dose commitment to the whole body, the critical organ, and each organ specified in 21 CFR 361.1(b)(3)(i) received by *each* subject....."

Comment # 1. The term "radiation dose commitment to the whole body" is not clear. Historically, "whole body" dose was calculated by assuming homogenous distribution of the radioactive material throughout the entire body; however, for investigations "intended to obtain basic information regarding the metabolism (including kinetics, distribution, and localization) of a radioactively labeled drug or regarding human physiology, pathophysiology, or biochemistry...", the assumption of homogeneous distribution throughout the body is patently inappropriate. Reporting of "the absorbed dose to whole body" calculated in this way is absurd and totally useless. More appropriate calculations for body dose involve the summation of individual organ doses multiplied by organ weighting factors, such as the Effective Dose Equivalent (H_E) described in NCRP Report No. 93, 1987 or the Effective Dose (E) described in NCRP Report No.116, 1993. Reporting of Effective Dose Equivalent or Effective Dose is appropriate and should be specified.

Comment #2. The instructions and table headings require absorbed doses to be in units of "mR." It should be pointed out that mR (standing for milli-Roentgen) is a unit of exposure, not a unit of absorbed dose. Absorbed dose uses the unit of rad (traditional) or gray (SI). This error should be corrected.

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Comment #3. I believe that the reporting of sex and age of each patient over 18 years is unnecessary. Note that Item 6.f. of the form requests the "number of research subjects studied this reporting year under 18 years of age." For those subjects over 18 years, age is irrelevant for FDA review. Similarly, sex is irrelevant for FDA review. Therefore, I recommend that reporting requirements for sex of each subject and for age of each subject over 18 years of age be deleted.

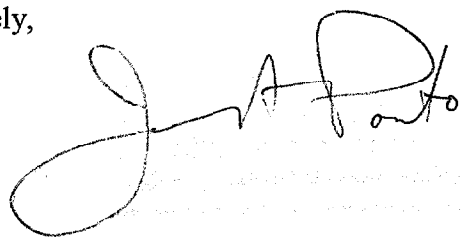
Comment #4. For most RDRC protocols, each subject will be administered the same amount of radioactivity and will receive the same nominal radiation absorbed doses; i.e, each subject is equivalently a *representative* subject. In this situation, re-stating, in the annual report, the identical numerical values for a representative subject again for each individual subject is wasteful of resources and is of no additional value. Furthermore, for subjects who are not representative, absorbed dose values are of relevance only if the absorbed dose to the body or to a specified organ is greater than that estimated for a representative subject. Therefore, I recommend that absorbed doses for individual subjects who are also representative subjects or absorbed doses for individual subjects which are less than those estimated for a representative subject be eliminated from the annual reporting requirements; i.e., listing absorbed doses would only be required for individual subjects who are not representative of the intended research subject population and who receive an absorbed dose to the body or a specified organ that exceeds that estimated for a representative subject.

Comment #5. I believe that the Estimated Annual Reporting Burden stated in Table 1 of the Federal Register notice for Form 1915 under-estimates the time required for completion of the form as currently exists. I estimate that the time expended to complete an annual summary on Form 2915 is approximately 10 hours (nearly 3 times longer than the 3.5 hours cited), largely due to irrelevant, duplicative listing of absorbed doses for each individual subject as described above. Elimination of this unnecessary reporting would reduce the time expended to complete the summary report back down to the original estimate of 3.5 hours.

In summary, I believe that several requirements for completion of Form 2915 are irrelevant, wasteful, or incorrect. I recommend that FDA consult with one or more external experts (e.g., practicing nuclear medicine, nuclear pharmacists, radiation safety officers, etc.) in order to appropriately revise this form.

Thank you for your consideration of this comments.

Sincerely,



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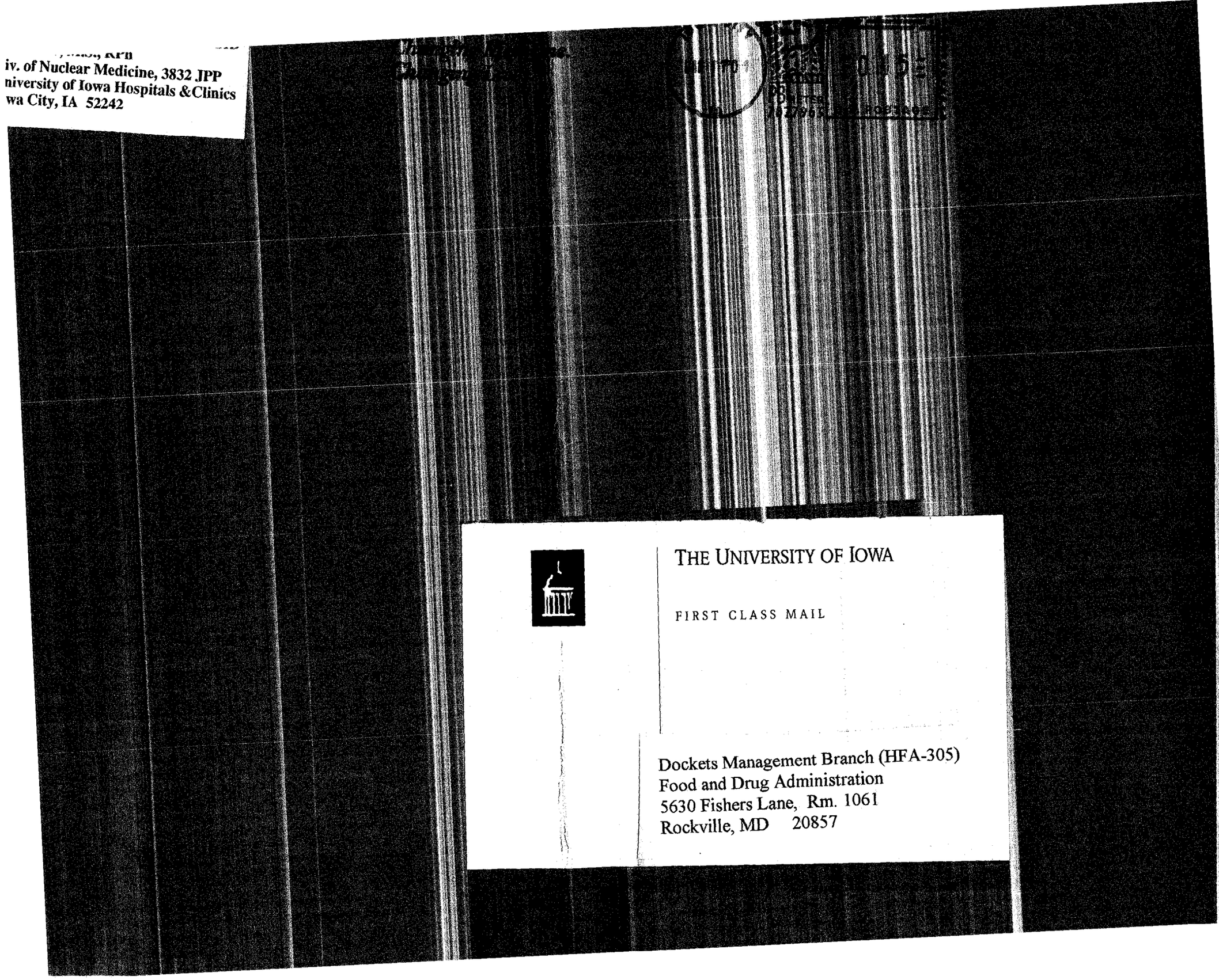

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