Roche

October 27, 2003

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Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852

Re: Docket No. 2003D-0367: Draft Guidance for Industry: Providing Regulatory Submissions in Electronic Format--Human Pharmaceutical Applications and Related Submissions

Dear Sir or Madam:

Thank you for the opportunity to comment on FDA's draft Guidance for Industry on Providing Regulatory Submissions in Electronic Format--Human Pharmaceutical Applications and Related Submissions (Docket No. 2003D-0367).

Roche has the following general comments regarding this draft guidance document:

1. We recommend that FDA continue their collaboration with ICH in the further development of this and future FDA eCTD guidances to ensure globally harmonized standards for the facilitation of efficient global submissions.
2. The draft guidance no longer specifies a size limit to eCTD files. We would like to clarify if FDA will now accept files of any size.
3. We recognize the tremendous value of initiating the electronic submission process at the original IND stage. As such, we recommend that FDA create a guidance document providing guidance on submission of INDs in eCTD format. The existing guidance documents do not provide sufficient detail to guide industry through this process.
4. Could FDA please provide clarity on how electronic IND submissions will link dynamically with subsequent NDA eCTD submissions.

Roche herein provides the following specific comments on this draft guidance:

1. **Lines 144-145:**
   Please clarify what is meant by the term "initial submission of an application". We are unsure if INDs are included as there is currently no guidance addressing eCTD INDs. If an "initial submission" includes INDs and NDAs/BLAs, we recommend that the language be revised as follows: *" We believe it is most beneficial to begin your eCTD-based submissions with the initial submission of an application (i.e., IND or NDA/BLA).".*

2. **Lines 155-159:**
   The guidance document does not specifically address the situation where an original submission was provided as an e-sub. In this situation should a supplement to the application be submitted in e-sub format or in eCTD format?

3. **Lines 410-413:**
   Due to the large size of the labeling samples, sometimes it is not possible to provide them in their actual size. Please provide an alternative mechanism for submitting these samples. We recommend providing the samples as close to the actual size as possible with a reference to the actual size. We have encountered the same issue with submission of the actual color. Sometimes

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there are small variations in the color viewed on screen. Please address in the guidance the degree of color difference that would be acceptable and specify any potential alternatives for submission (e.g., submission of the labeling samples in paper copy so the color may be verified).

4. **Line 554-560:**
   Please provide the definitions of data tabulations and data listings. Are data tabulations the patient profiles?

5. **Lines 616-665 and 684-694:**
   Please clarify the location of the CRF and dataset folders. Is FDA requesting that the CRF and dataset folders be located in Module 5 using the same structure as outlined in the guidance for industry *Regulatory Submissions in Electronic Format – General Considerations* or should the CRF and dataset folders be located inside the study number folder?

6. **Line 719:**
   Please reiterate the *util* folder location found in line 337 in this section of the guidance document.

7. **Lines723-725:**
   Please provide clarification on the location of the us-rerional.xml location. Lines 349-351 indicate that us-regional.xml should be located in a folder named *us* in the folder *m1*, whereas lines 723-725 indicate that regional.xml should be located in the folder named *dtd*. Please clarify the location for this regional file. If they are different files please define the contents of these files in the guidance document.

Thank you for your consideration of these comments. Please do not hesitate to contact the undersigned should you have any questions.

Sincerely,

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HLR No. 2003-3162