

Bonnie J. Goldmann, M.D.
Vice President
Regulatory Affairs

Merck & Co., Inc.
West Point PA 19486
Fax 484 344 2516
Tel 484 344 2383
215 652 5000

3663 '02 FEB 27 P3:14

February 26, 2002

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



**RE: Docket No. 01D-0435
Draft Guidance on Electronic Common Technical Document Specification**

Merck & Co., Inc, is a leading worldwide, human health product company. Merck's research has produced many of the most important pharmaceutical products on the market today.

Merck has participated with health authorities and industry scientists from around the globe in the harmonization of regulatory standards under the auspices of the International Conference on Harmonization (ICH). Merck continues to support the objectives of ICH: to identify and correct unnecessary redundancies and time-consuming inefficiencies in development of pharmaceutical and biological products caused by incompatible regulatory schemes.

In the course of bringing Merck's product candidates through developmental testing and clinical trials to the market, Merck has filed numerous original and supplemental New Drug Applications (NDAs) and Biological License Applications (BLAs). Merck typically prepares a single Worldwide Marketing Application (WMA) which is filed electronically and, less often, filed on paper, in most countries in the world, simultaneously. Therefore, we are very interested in this *Draft Guidance on Electronic Common Technical Document (eCTD) Specification* (hereafter referred to as *The Draft Guidance on eCTD*) and well qualified to comment on it.

In general, the document is well written and the comments we offer may provide clarification of some gray areas.

- Within Appendix 3, the File Organization Module (page 3-11, CTD Numbering Scheme), Items 3.2.S.2.2, 3.2.S.2.3, 3.2.S.2.5 and 3.2.S.2.6 indicate that sponsors should use a single PDF file for NCEs and multiple PDF files for biotech products. It is not clear why the number of PDF files should differ for biotech products. What would these multiple PDF files contain and how should they be named?
- There is inconsistency between the organization of some toxicology information described in Module 4 of *The Draft Guidance on eCTD* versus that stated in the *Guidance for Industry, M4S The CTD for Safety*. Specifically, *The Draft Guidance on eCTD* lists "Local Tolerance" and "Other Toxicity" within Appendix 3, as Sections 4.2.4 and 4.2.5

01D-0435

C. 3

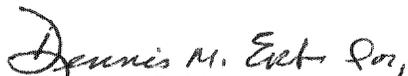
(pages 3-24 and 3-25, respectively). In contrast, the *Guidance for Industry, M4S The CTD for Safety* lists these items as subsections under Section 4.2.3, Toxicity, as subsections 4.2.3.6 and 4.2.3.7. Similar guidance for industry in the European Union on this same topic, known as the *EU Notice to Applicants*, describes placement of the same toxicology information as in *The Draft Guidance on eCTD*. Since ICH consensus has been valiantly pursued to harmonize the organization of all information in the CTD, we must conclude that this *lack* of harmonization in the *Guidance for Industry, M4S The CTD for Safety* is an oversight. Therefore, the structure proposed in *The Draft Guidance on eCTD* will be followed unless further clarification or guidance is provided.

- Appendix 3 (pages 3-33, Module 5.3.7) refers to Case Report Forms (CRFs) and Individual Patient Listings, without specific instructions about the Case Report Forms. CRFs are not routinely provided for *all* patients; they are provided for patients who have died during the study, for patients who discontinued participation or for specific patients as requested by FDA staff. Therefore, we will assume that this reference simply means that *if* CRFs are submitted, they will be included in this appendix, unless this is clarified further.

Also, in Module 5.3.7 Study 1, it is not clear whether or not the terms, *Document / Data set*, refer to both Case Report Forms as well as to Individual Patient Listings and clarification of these terms would be very useful.

We welcome the opportunity to comment on this Draft Guidance and to meet with you to discuss these issues.

Sincerely,


Bonnie J. Goldmann, M.D.

GB

FEDEX USA Airbill
Express

FedEx Tracking Number

833143251760

From ZIP

0200

Recipient

1 From

Date

2/26/02

Sender's Name

Bonnie Goldmann

Phone

484 344-2383

Company

Merck & Co

Address

5 Sentry Parkway East

City

Blue Bell

State

PA

ZIP

19422

Dept./Floor/Suite/Room

2 Your Internal Billing Reference

57834 7746 040

3 To

Recipient's Name

Dockets Management Branch (HFA-305)

Phone

Company

Food & Drug Admin.

Address

5630 Fishers Lane

To "HOLD" at FedEx location, print FedEx address.

We cannot deliver to P.O. boxes or P.O. ZIP codes.

Address

Room 1061

City

Rockville

State

MD

ZIP

20852

Dept./Floor/Suite/Room



4a Express Package Service

FedEx Priority Overnight
Next business morning

FedEx Standard Overnight
Next business afternoon

FedEx First Overnight
Earliest next business morning delivery to select locations

FedEx 2Day
Second business day

FedEx Express Saver
Third business day

4b Express Freight Service

FedEx 1Day Freight*
Next business day

FedEx 2Day Freight
Second business day

FedEx 3Day Freight
Third business day

* Call for Confirmation:

5 Packaging

FedEx Envelope*

FedEx Pak*
Includes FedEx Small Pak, FedEx Large Pak, and FedEx Sturdy Pak

Other

6 Special Handling

SATURDAY Delivery
Available only for FedEx Priority Overnight and FedEx 2Day to select ZIP codes

HOLD Weekday at FedEx Location
Not available for FedEx First Overnight

HOLD Saturday at FedEx Location
Available only for FedEx Priority Overnight and FedEx 2Day to select locations

Does this shipment contain dangerous goods?
One box must be checked.

No

Yes
As per attached Shipper's Declaration

Yes
Shipper's Declaration not required

Dry Ice
Dry Ice, 9, UN 1845

Dangerous Goods (including Dry Ice) cannot be shipped in FedEx packaging.

Cargo Aircraft Only

7 Payment Bill to:

Enter FedEx Acct. No. or Credit Card No. below.

Sender
Acct. No. in Section 1 will be billed.

Recipient

Third Party

Credit Card

Obtain Recip. Acct. No.

Cash/Check

Total Packages

Total Weight

Total Declared Value*

Total Charges

1

\$

.00

Credit Card Auth.

*Our liability is limited to \$100 unless you declare a higher value. See back for details.

8 Release Signature

Sign to authorize delivery without obtaining signature.

By signing you authorize us to deliver this shipment without obtaining a signature and agree to indemnify and hold us harmless from any resulting claims.
Questions? Visit our Web site at fedex.com or call 1.800.Go.FedEx® 800.463.3333.
Rev. Date 10/01 • Part #157612 • ©1994-2001 FedEx • PRINTED IN U.S.A. GBPE 12/01

446