MEMORANDUM

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

DATE: July 20, 2007

TO: Participants at the Joint meeting between the Gastrointestinal Drugs Advisory Committee and Drug Safety and Risk Management Advisory Committee

FROM: FDA

SUBJECT: Errata to FDA Background document for the Tysabri (natalizumab) Advisory Committee on July 31, 2007

The Division of Gastrointestinal Products and the Office of Surveillance and Epidemiology provide the following corrections to the original background package submitted for the Tysabri (natalizumab) advisory committee meeting scheduled for July 31, 2007.

Errata sheet for FDA Briefing Package:

1. Table 69 on Page 86 of Tab 1 (FDA Clinical Review) entitled "Frequency of Serious Infections by Infection Type in Post-Marketing" should indicate in a footnote that of the four “Cases Mentioning PML” (suspect cases of PML), none was confirmed as PML by the Independent Adjudication Committee. (See the revised table below.)

Table 69. Frequency of Serious Infections by Infection Type in Post-Marketing

Type of infection	HCP Cases	Consumer Cases	Total Cases
Pneumonia	3	5	8
Urinary tract infection	4	1	5
Herpes meningitis / Encephalitis	2	0	2
Viral gastroenteritis	1	1	2
Infectious mononucleosis	1	0	1
Sepsis	1	0	1
Sinus infection	1	0	1
Pyelonephritis	1	0	1
Blister	1	0	1
Ovarian cyst	1	0	1
Cystitis	0	1	1
Gangrene	0	1	1
Infection	0	1	1
Herpes simplex	0	1	1
Ceullulitis	0	1	1
Total	**19**	**11**	**30**
Cases Mentioning PML	**4**	**0**	**4**

HCP: Health Care Provider
Of the four “Cases Mentioning PML” (suspect cases of PML), none were confirmed as PML by the Independent Adjudication Committee.

2. Table 79 on Page 102 of Tab 1 (FDA Clinical Review) entitled "Anti-TNF Therapy: Response, Dependence and Reason for Discontinuation” has an error in the second row, “Lost Response with Continued Treatment”, for the Placebo columns; YES 279 (31) and NO 81 (9) should be changed to YES 23 (13) and NO 44 (24). (See the corrected table below.)

Table 79. Anti-TNF Therapy: Response, Dependence, and Reason for Discontinuation – N (%)

Variable Statistics	Placebo (n=181)		Natalizumab (n=724)		Overall (n=905)	
	Yes	No	Yes	No	Yes	No
Responded to Initial Treatment	54 (30)	15 (8)	225 (31)	66 (9)	279 (31)	81 (9)
Lost Response with Continued Treatment	23 (13)	44 (24)	96 (13)	192 (27)	119 (13)	236 (26)
Became Dependent on Treatment	2 (1)	67 (37)	13 (2)	277 (38)	15 (2)	344 (38)
Discontinued Due to Adverse Events	13 (7)	56 (31)	50 (7)	240 (33)	63 (7)	296 (33)
Discontinued Due to Infusion Reaction*	9 (5)*	55 (30)	35 (5)*	212 (29)	44 (5)*	267 (30)

* "Discontinued Due to Infusion Reaction" categorized as "(NA)" for 5 (3), 44 (6), and 49 (5) subjects in the placebo, natalizumab, and overall groups, respectively, based on marking of "NA" category on Case Report Form for question "Discontinue due to Infusion Reaction".

(Values in table above are taken from Page 296 of the Study Report for Study CD301.)

3. In the reviews, Tab 1 (FDA Clinical Review) and Tab 2 (Office of Surveillance and Epidemiology Review), it was stated that the MS population to receive Tysabri should be those "unable to tolerate or with an inadequate response to other available MS therapies" and it was stated that the indication was revised to "relegate it [Tysabri] to a second-line therapy for relapsing-remitting MS." The indication in the current label states "…Tysabri is generally recommended for patients who have had an inadequate response to, or are unable to tolerate, alternative multiple sclerosis therapies." FDA would like to clarify to the reader that the MS indication for Tysabri was carefully written by FDA and the Sponsor to indicate that its use is *generally recommended* for patients who have had an inadequate response to, or are unable to tolerate, alternative multiple sclerosis therapies (e.g., as second- line therapy). However, the indication statement does not explicitly preclude the possibility of first-line therapy in some MS patients as part of the approved use. FDA recognizes that the health care provider needs to consider its use based on the unique circumstances of each patient.