

Request to Revise Tables Email, November 3, 2014 - GARDASIL 9

From: Montague, Laura
To: alison_fisher@merck.com
Cc: Khurana, Bharat
Subject: 125508 IR #19 - Request to revise tables
Date: Monday, November 03, 2014 4:41:18 PM

Dear Alison,

In our email to you on 10-31-14, we indicated that we would be asking that Merck revise some tables previously submitted to STN125508/0 so that they do not include data collected at clinical sites V503-002----(b)(3)(b)(4)(b)(7)----. In item #1 below is the list of the tables that we would like you to revise. Item #2 is a list of tables that we request that you correct, as they appear to contain incorrect data.

1. Please provide re-analyses excluding the two (b)(3)(b)(4)(b)(7) sites of the data presented in the following tables, and indicate in the tables which numbers are changed:

A. V503-002 CSR

- 1 Subject characteristics at baseline: STN 125508/0, 5.3.5.1.p002_CSR, Table 10-4 (p135-138).
- 2 Subject disposition: STN 125508/0, 5.3.5.1.p002_CSR, Table 10-1 (p114-5).
- 3 Non-inferiority comparison GMT: STN 125508/0, Module 5.3.5.1.p002_CSR, Tables 11-5 and 11-6 (p 203-6)
- 4 Lot consistency GMT: STN 125508/0, Module 5.3.5.1.p002_CSR, Table 11-9 (p 213-215)
- 5 Non-inferiority comparison seroconversion rates: STN 125508/0, Module 5.3.5.1.p002_CSR, Tables 11-7 & 11-8 (p 207-10).
- 6 Lot consistency seroconversion rates: STN 125508/0, Module 5.3.5.1.p002_CSR, Table 11-10 (p 216-220)
- 7 Injection-site reactions: Table 12-8 (p258-261) and Table 12-9 (p262), SNT 125508/0 Module 5.3.5.1.p002-CSR
- 8 Systemic reactions: STN 125508/0, Module 5.3.5.1.p002, CSR Table 12-12 (p265-266).
- 9 Vaccine -related systemic reactions: STN 125508/0, Module 5.3.5.1.p002, CSR Table 12-20 (p279-280).
- 10 SAEs: STN 125508/0, Module 5.3.5.1.p002, CSR, Table 12-21 (282-296)

B. ISE

- 11 Subject characteristics: STN 125508/0_Module 2.7.3, Table 2.7.3: 58-60 (p228-230).
- 12 Subject disposition: STN 125508/0_Module 2.7.3, Table 2.7.3: 52-54 (p216-217).

13 Immunogenicity: STN 125508/0, Module 2.7.3_Table 2.7.3-hpvdiseases: 77, 78 and 79 (p257-264)

14 Subgroup analyses: STN125508/0_Module 2.7.3_Table 2.7.3-hpvdiseases: 81 (p280-281), Table 2.7.3-hpvdiseases: 82 (p282-283), Table 2.7.3-hpvdiseases: 85 (p286-287), Table 2.7.3-hpvdiseases: 86 (p288-289), Table 2.7.3-hpvdiseases: 87 (p290-291), and Table 2.7.3-hpvdiseases: 88 (p292-293).

15 Antibody responses by status of contraceptive use: STN 125508/0_Module 2.7.3_Table 2.7.3-hpvdiseases:128 (p389)

16 Antibody responses by status of immunosuppressant use: STN 125508/0_Module 2.7.3_Table 2.7.3-hpvdiseases:129 (p391)

C. ISS

17 Demographics: STN125508/0_Module 2.7.4_Table 2.7.4: 8 and Table 2.7.4: 9 (p64-65)

18 Systemic reactions: STN 125508/0_Module 2.7.4_Table 2.7.4: 17 (p80-81)

19 Vaccine related systemic AE: STN125508/0_Module 2.7.4_Appendices 2.7.4: 47 (p524-525) and Appendices 2.7.4:66 (p569-573)

20 Temperatures: STN125508/0_Module 2.7.4_Table 2.7.4: 19 (p83), _ Appendixes 2.7.4: 38-40 (p399-401).

21 Injection-site reactions: STN125508/0_Module 2.7.4_Appendices 2.7.4: 44-45 (p519-521) and Appendices 2.7.4:63-64 (p562-565)

22 Solicited AE by intensity: STN125508/0_Module 2.7.4_Table 2.7.4: 15-16 (p77-78),_ Appendixes 2.7.4: 28-33 (p365-370).

23 Solicited AE by race and ethnicity: STN125508/0_Appendix 2.7.4: 81 (p605), Appendix 2.7.4: 88 (p614), Appendix 2.7.4: 95 (p622), Appendix 2.7.4: 102 (p631), Appendix 2.7.4: 109 (p639), Appendix 2.7.4: 116 (p647), Appendix 2.7.4: 123 (p656), Appendix 2.7.4: 130 (p670-671), Appendix 2.7.4: 137 (p686), Appendix 2.7.4: 144 (p697), Appendix 2.7.4: 151 (p709) and Appendix 2.7.4: 158 (p721).

24 Systemic AE by SOC: STN125508/0_Appendix 2.7.4: 84 (p609-10), Appendix 2.7.4:91 (p617-8), Appendix 2.7.4: 98 (p626-7), Appendix 2.7.4: 105 (p634-5), Appendix 2.7.4: 112 (p642-3) , Appendix 2.7.4: 119 (p651-2), Appendix 2.7.4: 126 (p663-7), Appendix 2.7.4: 133 (p677-682), Appendix 2.7.4: 140 (p690-3), Appendix 2.7.4: 147 (p701-5), Appendix 2.7.4: 154 (p713-7) and Appendix 2.7.4: 161 (p726-730).

25 Pregnancy outcomes: STN 125508/0_Model 2.7.4, Table 2.7.4: 41 (p150) and Appendix 2.7.4: 233 (p881-2).

26 Pregnancy outcome by concept dates: STN 125508/0_Model 2.7.4, Appendix 2.7.4:241 (p908-9) and Appendix 2.7.4: 242 (p910-911).

D. Post Original Submission

27 Spontaneous abortions: STN 125508/0.13 (Module 1.11.3) and STN 125508/0.25 (Module 1.11.3)

2. The data presented in the columns of Efficacy (9vHPV vs. placebo) appear to be incorrect in Tables 11-25, -26, -27 and -28 (p380, 382, 384 and 386, Cervical, vulvar and vaginal disease), and Tables 11-31 and -32 (p391-2, Procedures) under STN 125508/0_Module 5.3.5.1.p001_CSR. Please provide the tables with correct numbers and also indicate in the tables which numbers are changed.

When you respond to this information request, we ask that you provide the tables in the order listed in this email, and include the request number – for example 1C21. Further,

we request that you submit the revised tables as a response to information request in module 1.11. If you have any questions, please contact Dr. Bharat Khurana or me.

Thank you,

Laura Montague

Regulatory Project Manager

FDA/OMPT/CBER/OVRR

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