CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

202123Orig1s000

STATISTICAL REVIEW(S)

STATISTICS FILING CHECKLIST FOR A NEW NDA/BLA

NDA Number: 202123 **Applicant: Gilead** **Stamp Date: 02-10-11**

SN 0012, SDN 0013

Drug Name: Emtricitabine/Rilpivirin/ Tenofovir Disoproxil Fumarate (Truvada®/TMC278) (FTC/RPV/TDF) Tablet

NDA/BLA Type: Priority Review

On **initial** overview of the NDA/BLA application for RTF:

	Content Parameter	Yes	No	NA	Comments
1	Index is sufficient to locate necessary reports, tables, data, etc.	X			Data was already submitted for NDA 202022
2	ISS, ISE, and complete study reports are available (including original protocols, subsequent amendments, etc.)	X			Original protocols and amendments were already submitted for NDA 202022
3	Safety and efficacy were investigated for gender, racial, and geriatric subgroups investigated.			X	Already submitted for NDA 202022
4	Data sets in EDR are accessible and conform to applicable guidances (e.g., existence of define.pdf file for data sets).			X	Already submitted for NDA 202022

NB: The applicant was issued a refuse to file letter for the initial NDA submission on 10-19-10. None of the RTF issues pertained to statistics. Gilead noted that it was instructed by the DAVP not to resubmit information previously submitted to this NDA, so the original filing checklist from January 2011 for the 10-19-10 submission of NDA 202123/0001 is still applicable since new items submitted for NDA 202123/0012 were not required for the statistical review.

IS THE STATISTICAL SECTION OF THE APPLICATION FILEABLE? _Yes_

If the NDA/BLA is not fileable from the statistical perspective, state the reasons and provide comments to be sent to the Applicant.

Please identify and list any potential review issues to be forwarded to the Applicant for the 74-day letter.

STATISTICS FILING CHECKLIST FOR A NEW NDA/BLA

Content Parameter (possible review concerns for 74-day letter)	Yes	No	NA	Comment
Designs utilized are appropriate for the indications requested.	X			
Endpoints and methods of analysis are specified in the protocols/statistical analysis plans.	X			
Interim analyses (if present) were pre-specified in the protocol and appropriate adjustments in significance level made. DSMB meeting minutes and data are available.		X		[a] See footnote below
Appropriate references for novel statistical methodology (if present) are included.			X	
Safety data organized to permit analyses across clinical trials in the NDA/BLA.	X			
Investigation of effect of dropouts on statistical analyses as described by applicant appears adequate.	X			

[a] DSMB sent sponsor review committee the interim analysis results and treatment codes (letters only) due to higher than expected discontinuation rate due to virologic failures in the TMC278 treatment arm.

Brief summary of controlled clinical trials
The following table contains information on the relevant trials contained in the submission.

Study number	Design	Treatment arms/Sample size	Primary endpoint/Analysis	Sponsor's findings
TMC278-TiDP6-209	**Randomized, db trial**	**TMC278 vs. EFV / approx 345 patients per treatment arm, all with FTC/TDF bkgd regimen**	**Virologic Responders (% < 50 copies/mL) at Week 48 using TLOVR algorithm**	**TMC278 non-inferior to EFV**
TMC278-TiDP6-215	**Randomized, db trial**	**TMC278 vs. EFV / approx 200 of 340 patients per treatment arm had bkgd FTC/TDF regimen**	**Virologic Responders (% < 50 copies/mL) at Week 48 using TLOVR algorithm**	**TMC278 non-inferior to EFV**

STATISTICS FILING CHECKLIST FOR A NEW NDA/BLA

Fraser Smith	March 2011
Reviewing Statistician	Date
Guoxing Soon	March 2011
Supervisor/Team Leader	Date

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/s/

FRASER B SMITH
03/09/2011

GUOXING SOON
03/18/2011

STATISTICS FILING CHECKLIST FOR A NEW NDA/BLA

NDA Number: 202123 / 0001 **Applicant: Gilead** **Stamp Date: 10-19-10**

Drug Name: Rilpivirin / TMC278 **NDA/BLA Type: Priority Review**

On **initial** overview of the NDA/BLA application for RTF:

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4	Data sets in EDR are accessible and conform to applicable guidances (e.g., existence of define.pdf file for data sets).			X	Already submitted for NDA 202022

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Interim analyses (if present) were pre-specified in the protocol and appropriate adjustments in significance level made. DSMB meeting minutes and data are available.		X		[a] See footnote below
Appropriate references for novel statistical methodology (if present) are included.			X	
Safety data organized to permit analyses across clinical trials in the NDA/BLA.	X			
Investigation of effect of dropouts on statistical analyses as described by applicant appears adequate.	X			

STATISTICS FILING CHECKLIST FOR A NEW NDA/BLA

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Fraser Smith — January 2011
Reviewing Statistician — Date

Guoxing Soon — January 2011
Supervisor/Team Leader — Date

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/s/

FRASER B SMITH
01/07/2011

GUOXING SOON
01/20/2011