DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
1431 Harbor Bay Parkway Alameda, CA 94502-7070 (510) 337-6700 Fax:(510) 337-6702 Industry Information: www.fda.gov/oc/industry	04/10/2013 - 04/26/2013* FEI NUMBER 1000523075

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED

TO: Taiyin Yang, Ph.D., Senior VP, Pharmaceutical Development & Manufacturing

FIRM NAME	STREET ADDRESS
Gilead Sciences, Inc.	333 Lakeside Drive
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Foster City, CA 94404-1147	Manufacturer

This document lists observations made by the FDA representative(s) during the inspection of your facility. They are inspectional observations, and do not represent a final Agency determination regarding your compliance. If you have an objection regarding an observation, or have implemented, or plan to implement, corrective action in response to an observation, you may discuss the objection or action with the FDA representative(s) during the inspection or submit this information to FDA at the address above. If you have any questions, please contact FDA at the phone number and address above.

DURING AN INSPECTION OF YOUR FIRM WE OBSERVED:

Observations pertaining to (b) (4) (b) (4) **and** (b) (4) (b) (4)

OBSERVATION 1

The accuracy, sensitivity, specificity, and reproducibility of test methods have not been established.

Specifically,

A. Your firm is utilizing test methods that have not been validated to support release and stability testing of drug substances (DS) and drug products (DP). There is no assurance that the data generated from these test methods are reliable. For example,

1. The following test methods were used to test (b) (4) (b) (4) drug product lots (b) (4), and drug substance lots (b) (4); as well as (b) (4) b) (4) drug product lots (b) (4), (b) (4), and drug substance lots (b) (4). These lots are referenced in (b) (4) (b) (4).

Description (for DP)	Test Method *no associated TM	Instrument	Effective date
ID, Assay and Impurities	STM-0015.00 (version 01 does not exist)	(b) (4)	3/8/2007
	STM-0015.02	(b) (4)	5/1/2008
	STM-0010.03	(b) (4)	2/3/2009
Dissolution	STM-0016.00	(b) (4)	3/9/2007
	STM-0016.01	(b) (4)	3/4/2011
	STM-0016.02	(b) (4)	4/29/2011
	STM-0016.03	(b) (4)	12/6/2011

SEE REVERSE OF THIS PAGE

EMPLOYEE(S) SIGNATURE
Carl Lee, Investigator
Kim Thomas Cruse, Chemist

DATE ISSUED
04/26/2013

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
1431 Harbor Bay Parkway Alameda, CA 94502-7070 (510) 337-6700 Fax:(510) 337-6702 Industry Information: www.fda.gov/oc/industry	04/10/2013 - 04/26/2013* FEI NUMBER 1000523075

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED

TO: Taiyin Yang, Ph.D., Senior VP, Pharmaceutical Development & Manufacturing

FIRM NAME	STREET ADDRESS
Gilead Sciences, Inc.	333 Lakeside Drive
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Foster City, CA 94404-1147	Manufacturer

Description (for DS)	Test Method *no associated TM	Instrument	Effective date
ID, Assay and Impurities	STM-0010.00	(b) (4)	3/9/2007
	STM-0010.01	(b) (4)	12/7/2010
	STM-0010.02	(b) (4)	2/9/2011
(b) (4) Purity	STM-1031.01	(b) (4)	1/22/2008
	STM-1031.02	(b) (4)	6/25/2008
	STM-1031.03	(b) (4)	6/21/2010

2. The following test methods were used to test (b) (4) ((b) (4) (b) (4) drug product lots (b) (4) and (b) (4), and drug substance lots (b) (4). These lots are referenced in (b) (4) (b) (4).

Description (for DP)	Test Method *no associated TM	Instrument	Effective date
ID, Assay and Impurities	STM-1155.04	(b) (4)	12/17/2009
Dissolution	STM-1828.01	(b) (4)	11/23/2009
	STM-1156.03	(b) (4), (b) (4)	12/14/2009

Description (for DS)	Test Method *no associated TM	Instrument	Effective date
ID, Assay and Impurities	STM-1108.03	(b) (4)	5/29/2009
	STM-1108.04	(b) (4)	12/17/2009
	STM-1108.05	(b) (4)	5/6/2010
(b) (4) Purity	STM-1920.01	(b) (4)	5/3/2010

B. Your firm is utilizing test methods that have not been adequately validated to support release and stability testing of clinical, registration, process validation batches of Elvitegravir drug product. There is no assurance the data generated from these test methods are reliable. For example,

Description (for DP)	Test Method	Instrument	Effective date	Validation Deficiency(s)
ID, Assay and Impurities	STM-0015.04 (TM-166.00)	(b) (4)	11/15/2010	Did not meet recovery requirement for Assay
Dissolution	STM-0016.04 (TM-168.00)	(b) (4) (b) (4)	12/22/2011	The intermediate precision did not meet release specification of (b) (4)

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
1431 Harbor Bay Parkway Alameda, CA 94502-7070 (510) 337-6700 Fax:(510) 337-6702 Industry Information: www.fda.gov/oc/industry	04/10/2013 - 04/26/2013* FEI NUMBER 1000523075

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED

TO: Taiyin Yang, Ph.D., Senior VP, Pharmaceutical Development & Manufacturing

FIRM NAME	STREET ADDRESS
Gilead Sciences, Inc.	333 Lakeside Drive
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Foster City, CA 94404-1147	Manufacturer

C. Your test methods for the clinical and primary stability batches are not the same as the proposed commercial test methods because the analytical techniques and parameters are different between the methods. Your firm did not perform a bridging study to establish method comparability for the following test methods.

Type of Testing and Testing Time points	STM	Detection Parameters
(b) (4) Finished Product Assay- Clinical and Primary Stability batches Time points –different methods are being used at different time points to analyze the lots Stability time points –initial release (b) (4) months Stability time points (b) (4) months	ID, Assay and Degradation Method: STM-0015.00 *STM-0015.02 STM-0015.03 STM-0015.04 STM-0015.05	(b) (4) (b) (4)
(b) (4) Finished Product Dissolution- Clinical and Primary Stability batch. Time points –different methods are being used at different time points to analyze the lots Time points –initial release (b) (4) months Time points (b) (4) months	Drug Product Dissolution Method: STM-0016.00 (b) (4) STM-0016.01 STM-0016.02 STM-0016.03 STM-0016.04 (b) (4) STM-0016.05	(b) (4)

(b

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE Carl Lee, Investigator Kim Thomas Cruse, Chemist	DATE ISSUED 04/26/2013

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
1431 Harbor Bay Parkway Alameda, CA 94502-7070 (510) 337-6700 Fax:(510) 337-6702 Industry Information: www.fda.gov/oc/industry	04/10/2013 - 04/26/2013* FEI NUMBER 1000523075

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED

TO: Taiyin Yang, Ph.D., Senior VP, Pharmaceutical Development & Manufacturing

FIRM NAME	STREET ADDRESS
Gilead Sciences, Inc.	333 Lakeside Drive
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Foster City, CA 94404-1147	Manufacturer

Drug Substance Assay- Clinical and Primary Stability batch. Time points –different methods are being used at different time points to analyze the lots	ID, Assay and Impurities Method STM-0010.00 (b) (4) STM-0010.01 (b) (4) STM-0010.02 (b) (4) STM-0010.03 (b) (4) STM-0010-04 (b) (4) STM-2145.00 (b) (4) STM-2145.01 STM-2145.02 (b) (4) Purity STM-1031.01 (b) (4) STM-1031.02 (b) (4) STM-1031.03 (b) (4) STM-1031.04 (b) (4) STM-1031.05 (b) (4)	(b) (4) STM 00, (b) (4) (b) (4) (b) (4) STM 2145-00, 01 and 02- are different methods (b) (4) (b) (4) (b) (4) (b) (4)
(b) (4) Finished Product Assay- Clinical and Primary Stability batch. Time points –different methods are being used at different time points to analyze the lots	ID, Assay and Degradation Method: STM-1155.04 (b) (4) STM-2395.00 (b) (4) STM-2395.0 1 STM-2395.02	STM 1155.04 STM-2395.00, 01 and 02 are the same methods (b) (4)
Time points –different methods are being used at different time points to analyze the lots	Drug Product Dissolution Method: STM-1828.01 (b) (4) STM-1156.03 (b) (4) STM-1156.04 (b) (4) STM-1156.05 (b) (4)	(b) (4) (b) (4)

SEE REVERSE OF THIS PAGE

EMPLOYEE(S) SIGNATURE

Carl Lee, Investigator CL
Kim Thomas Cruse, Chemist

DATE ISSUED

04/26/2013

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
1431 Harbor Bay Parkway Alameda, CA 94502-7070 (510) 337-6700 Fax:(510) 337-6702 Industry Information: www.fda.gov/oc/industry	04/10/2013 - 04/26/2013* FEI NUMBER 1000523075

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED

TO: Taiyin Yang, Ph.D., Senior VP, Pharmaceutical Development & Manufacturing

FIRM NAME	STREET ADDRESS
Gilead Sciences, Inc.	333 Lakeside Drive
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Foster City, CA 94404-1147	Manufacturer

API Assay- Clinical and Primary Stability batches Time points –different methods are being used at different time points to analyze the lots	ID, Assay and Impurities Method STM-1108.03 (b) (4) STM-1108.04 (b) (4) STM-1108.05 (b) (4) STM-1108.06 (b) (4) STM-1108.07 (b) (4) (b) (4) Purity STM-1920.01 (b) (4) STM-1920.02 (b) (4) STM-1920.03 (b) (4)	(b) (4) (b) (4) ( )

OBSERVATION 2

The suitability of all testing methods is not verified under actual conditions of use.

Specifically,

A. Your firm did not verify the suitability of the following USP compendial methods for testing (b) (4) drug product and drug substance.

Description for DP	Test Method	Instrument	Effective date
(b) (4) (b) (4)	STM-0032.02	(b) (4)	7/27/2009
	STM-0032.03	(b) (4)	12/14/2010
(b) (4) (b) (4)	STM-1157.04	(b) (4)	3/24/2010

Description for DS	Test Method	Instrument	Effective date
(b) (4) (b) (4)	STM-0032.02	(b) (4)	7/27/2009
	STM-0032.03	(b) (4)	12/14/2010
	STM-0032.04	(b) (4)	8/24/2012

B. Your Stribild (b) (4) test method STM-1388.13, "Identification, Assay, and Degradation Product Content o(b) (4)

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE Carl Lee, Investigator Kim Thomas Cruse, Chemist	DATE ISSUED 04/26/2013

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
1431 Harbor Bay Parkway Alameda, CA 94502-7070 (510) 337-6700 Fax:(510) 337-6702 Industry Information: www.fda.gov/oc/industry	04/10/2013 - 04/26/2013* FEI NUMBER 1000523075

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED

TO: Taiyin Yang, Ph.D., Senior VP, Pharmaceutical Development & Manufacturing

FIRM NAME	STREET ADDRESS
Gilead Sciences, Inc.	333 Lakeside Drive
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Foster City, CA 94404-1147	Manufacturer

(b) (4) ", effective October 15, 2012, may not be suitable for accurately determining (b) (4) related impurities (b) (4)), and the unidentified degradant at (b) (4) because the (b) (4) at the (b) (4) as a (b) (4) and the (b) (4) degradant (b) (4) with (b) (4) .

OBSERVATION 3

The use of instruments not meeting established specifications was observed.

Specifically,

(b) (4) instrument #40537 was not qualified when it was used for (b) (4) analyses on (b) (4) primary stability batches (b) (4) . This instrument remains in use in the QC laboratory.

OBSERVATION 4

Laboratory records do not include complete data derived from all tests, examinations and assay necessary to assure compliance with established specifications and standards.

REPEAT OBSERVATION - FDA 483 dated July 11, 2012

Specifically,

A. There is no documentation or traceability to lot numbers, manufacture dates, re-test dates, weights and balance used to prepare the excipients in the placebo mixtures for determining the accuracy in the validation of STM-0015.04 (TM-166) and STM-2395.00 (TM-163.00) for both (b) (4) drug products.

B. Your firm performed method verification of STM-0032.04, a (b) (4) by (b) (4) (USP (b) (4)), for (b) (4) using the (b) (4) on or about 3/12/2013. Printouts in your data packet reveal (b) (4) results; however (b) (4) of the result sets are associated with sample (b) (4) for the (b) (4) (b) (4) verification and (b) (4) . There is no explanation in your records for this discrepancy.

C. Your firm performed method verification of STM-0032.04, a (b) (4) by (b) (4) (USP (b) (4), (b) (4) using the (b) (4) on or about 10/25/2012. The results of samples (b) (4) of (b) (4) runs (b) (4)) from these verification activities are missing from your laboratory records. There is no explanation of the missing data in your records.

D. Your firm performed stability testing of lots (b) (4) using STM-0032.03 on or about June 12, 2012. The results of samples (b) (4) for this analysis are missing from your data packet. There is no explanation of the missing data in your records.

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	DATE ISSUED
	Carl Lee, Investigator Kim Thomas Cruse, Chemist	04/26/2013

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
1431 Harbor Bay Parkway Alameda, CA 94502-7070 (510) 337-6700 Fax:(510) 337-6702 Industry Information: www.fda.gov/oc/industry	04/10/2013 - 04/26/2013* FEI NUMBER 1000523075

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED

TO: Taiyin Yang, Ph.D., Senior VP, Pharmaceutical Development & Manufacturing

FIRM NAME	STREET ADDRESS
Gilead Sciences, Inc.	333 Lakeside Drive
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Foster City, CA 94404-1147	Manufacturer

Observations pertaining to commercial drug product operations

OBSERVATION 5

Control procedures are not established which validate the performance of those manufacturing processes that may be responsible for causing variability in the characteristics of in-process material and the drug product.

Specifically,

Your bulk hold studies for final powder blends, core tablets and film-coated tablets were not validated with representative samples. Your firm did not present additional study data to justify the use of these sampling plans in the following bulk hold studies.

Product	Protocol	Final Report	Sampling Location	Sample Size (per container)
(b) (4) (b) (4) (b) (4)	(b) (4)		not specified	(b) (4)
(b) (4) (b) (4)			(b) (4)	
Viread 300 mg tablets			not specified	
Viread Oral Powder			(b) (4) (b) (4)	Various sample sizes for different test attributes
Stribild			(b) (4)	(b) (4)
Truvada			not specified	

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
1431 Harbor Bay Parkway Alameda, CA 94502-7070 (510) 337-6700 Fax:(510) 337-6702 Industry Information: www.fda.gov/oc/industry	04/10/2013 - 04/26/2013* FEI NUMBER 1000523075

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED

TO: Taiyin Yang, Ph.D., Senior VP, Pharmaceutical Development & Manufacturing

FIRM NAME	STREET ADDRESS
Gilead Sciences, Inc.	333 Lakeside Drive
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Foster City, CA 94404-1147	Manufacturer

Atripla	(b) (4)	not specified	(b) (4)
Latairis 5mg tablets*		not specified	
Latairis 5mg tablets*		(b) (4)	
Complera		(b) (4)	

* Performed under two study protocols: (b) (4) studied 5mg and 10mg tablets in (b) (4) batch size; (b) (4) studied 5mg in (b) (4) batch size.

Further, a review of 4 of 4 deviation reports on powder blends exceeding hold time of (b) (4) calendar days revealed that they were closed because the powder blends didn't exceed the validated hold times, which were established in the above studies and were greater than (b) (4) calendar days.

A. GO-OPR-1384, a deviation of the (b) (4) days holding period for the (b) (4) (b) (4) batch (b) (4) was closed with justification from bulk hold study (b) (4) Complera tablet lot (b) (4) was manufactured with (b) (4) (b) (4) batch (b) (4) and released by QA.

B. GO-OPR-1141, a deviation of the (b) (4) days holding period for the (b) (4) (b) (4) batch (b) (4) was closed with justification from bulk hold study (b) (4) Atripla (Access) tablet lots (b) (4) were manufactured with (b) (4) (b) (4) batch (b) (4) and released by QA.

C. GO-OPR-1515, a deviation of the (b) (4) days holding period for the (b) (4) (b) (4) batch (b) (4) was closed with justification from bulk hold study (b) (4) Atripla tablet lot (b) (4) was manufactured with (b) (4) (b) (4) batch (b) (4) and released by QA.

D. GO-OPR-1945, a deviation of the (b) (4) days holding period for the (b) (4) (b) (4) batch (b) (4) was closed with justification from bulk hold study (b) (4) . Atripla tablet lots (b) (4) was manufactured with (b) (4) (b) (4) batch (b) (4) and released by QA.

OBSERVATION 6

The establishment of test procedures including any changes thereto, are not reviewed and approved by the quality control unit.

Specifically, your test method procedures, also known as Standard Test Methods (STM), and related changes are not approved by your quality assurance unit (QA). Standard Test Methods are used by QC analysts to perform release and

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
1431 Harbor Bay Parkway Alameda, CA 94502-7070 (510) 337-6700 Fax:(510) 337-6702 Industry Information: www.fda.gov/oc/industry	04/10/2013 - 04/26/2013* FEI NUMBER 1000523075

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED

TO: Taiyin Yang, Ph.D., Senior VP, Pharmaceutical Development & Manufacturing

FIRM NAME	STREET ADDRESS
Gilead Sciences, Inc.	333 Lakeside Drive
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Foster City, CA 94404-1147	Manufacturer

stability testing of clinical and commercial APIs and drug products.

OBSERVATION 7

The written stability testing program is not followed.

REPEAT OBSERVATION - FDA 483 dated July 11, 2012

Specifically,

Stability testing is not performed in accordance with FCSOP-0081.08, Stability Testing of Active Pharmaceutical Ingredients and Drug Products, effective December 13, 2012. Your procedure requires stability testing to commence within (b) (4) calendar days from the sample pull date, and evaluate each deviation for potential impact.

A. As of April 19, 2013, fifty-five (55) drug product and API samples pulled in January 2013 to March 2013 have not had all of the required testing begin within (b) (4) calendar days from the sample pull date.

B. Stability testing is not performed timely and there is no documentation of an evaluation of each deviation for impact. For example:
   1. Samples at the (b) (4) month time point for Stribild lot (b) (4) were assay on April 2, 2013, about (b) (4) days after the sample was pulled on February 8, 2013.
   2. Samples at the (b) (4) month time point for Truvada lot (b) (4) were tested for dissolution on April 12, 2013, about (b) (4) days after the sample was pulled on February 18, 2013.

OBSERVATION 8

Written records of major equipment use are not included in individual equipment logs.

Specifically, your quality control laboratory do not maintain individual equipment usage logs for your balances and pH meters. These equipments were used in the test methods that are referenced in (b) (4) (b) (4) and (b) (4)(b) (4) : STM.0015.04 (TM-166.00), STM-0016 (TM-168.00), STM-0032, and STM-1157. Furthermore, balance weighing tapes do not consistently show the date, time and balance identification and or number.

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	DATE ISSUED
	Carl Lee, Investigator CL Kim Thomas Cruse, Chemist	04/26/2013

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
1431 Harbor Bay Parkway Alameda, CA 94502-7070 (510) 337-6700 Fax:(510) 337-6702 Industry Information: www.fda.gov/oc/industry	04/10/2013 - 04/26/2013* FEI NUMBER 1000523075

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED

TO: Taiyin Yang, Ph.D., Senior VP, Pharmaceutical Development & Manufacturing

FIRM NAME	STREET ADDRESS
Gilead Sciences, Inc.	333 Lakeside Drive
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Foster City, CA 94404-1147	Manufacturer

OBSERVATION 9

Laboratory controls do not include the establishment of scientifically sound and appropriate test procedures designed to assure that components, in-process materials, and labeling conform to appropriate standards of identity, strength, quality and purity.

Specifically,

A. The cleaning methods for your (b) (4) and (b) (4) instruments are not validated. We observed carry-over and artifact peaks in the chromatograms of the blank solutions for Atripla lot (b) (4), (b) (4) month at (b) (4), that your firm attributed to residual active ingredient(s) that were left over from previous analyses.

B. All laboratory worksheets (QC forms), logbooks and chromatography instrument usage logs used to record raw data for sample analyses and instrument calibrations and usages are not issued and controlled by your Quality Assurance unit to assure the reliability and integrity of the data.

For example:

1. There is no written procedure to control the use of laboratory worksheets and logbooks. The worksheets and logbooks are not inventoried, secured, or accounted for. Management has no knowledge of the total number of laboratory notebooks in circulation (used and unused).

2. Your analysts can issue laboratory worksheets and logbooks by themselves, and print blank worksheets without oversight from QC and QA. Laboratory logbooks are kept in unsecured cabinets and unused worksheets were observed on analysts' desks.

3. Form logbook #20 shows several examples where the date and time reflects that two different worksheets were printed for the same test; your firm cannot account for the unused (cross-out) worksheets.

4. The Legal department log for tracking some of the logbooks contain white-outs (b) (4)) and cross-outs of notebook numbers (b) (4)) without documenting the reasons of the changes. The log also contains pasting from a different log sheet over the current log sheet (5550-5554).

*** DATES OF INSPECTION:**
04/10/2013(Wed), 04/11/2013(Thu), 04/12/2013(Fri), 04/15/2013(Mon), 04/16/2013(Tue), 04/17/2013(Wed), 04/18/2013(Thu), 04/19/2013(Fri), 04/22/2013(Mon), 04/24/2013(Wed), 04/26/2013(Fri)

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	DATE ISSUED
	Carl Lee, Investigator Kim Thomas Cruse, Chemist	04/26/2013