DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 201023

REVISED WRITTEN REQUEST
AMENDMENT #1

Sanofi-aventis, U.S. LLC
500 Kendall Street, 5155-C3
Cambridge, MA 02142

Attention: Suzanne Thornton-Jones, Ph.D.
Director, Global Regulatory Affairs

Dear Dr. Thornton-Jones:

Please refer to your correspondence dated December 19, 2012, requesting changes to FDA's March 20, 2012, Written Request for pediatric studies for Jevtana® (cabazitaxel).

We have reviewed your proposed changes and are amending the below-listed sections of the Written Request. All other terms stated in our Written Request issued on March 20, 2012, remain the same. (Text added is underlined. Text deleted is strikethrough.)

- *Type of studies:*

  Phase 1-2: ~~A~~ The Phase 1~~-2~~ part is a dose-finding and safety ~~expansion~~ study of cabazitaxel monotherapy in pediatric patients with refractory solid tumors, including pharmacokinetics, with doses determined for all appropriate age groups. ~~Phase 2: A~~ This will be followed by a Phase 2 part ~~single arm study~~ to determine the response rates with and safety of cabazitaxel monotherapy in pediatric patients with recurrent or refractory high grade glioma or diffuse intrinsic pontine glioma. The Phase 2 part will be conducted at the dose determined by the Phase 1 portion of the study.

- *Indications(s) to be studied/ Objective of each study:*

  Phase 1~~-2~~ Part (dose escalation): Pediatric patients with metastatic or locally advanced solid tumors for whom no further effective therapy is available.

  Phase 2 Part (safety and activity): Pediatric patients with recurrent or refractory high grade glioma defined as WHO Grade III or Grade IV astrocytic or oligodendroglial tumor~~,~~ or recurrent or refractory diffuse intrinsic pontine glioma for whom no further effective therapy is available.

- *Patients to be Studied:*

  - *Age group in which studies will be performed*:

    Phase 1 ~~-~~ 2 Part (~~D~~dose escalation ~~part~~): ~~>~~5~~2~~ years and <~~12 years; > 12 and <~~ 18 years (with at least four children 2-4 years old treated at the recommended Phase 2 dose)

    Phase ~~1 -~~ 2 Part (~~S~~safety and activity~~expansion part~~): ≥2 years and ~~< 12 years (with at least four children 2 – 4 years old); ≥ 12 and~~ <18 years

    ~~Phase 2: ≥ 2 years and < 12 years; ≥ 12 years and ≤ 18 years~~

  - *Number of patients to be studied:*

    Phase 1 ~~-~~ 2 Part (dose escalation ~~part~~): ≥9 patients treated
    Phase ~~1 -~~ 2 Part (safety ~~expansion part~~and activity): ~~At least 10 treated patients age ≥ 2 and ≤ 18 years with at least 4 treated patients age 2- 4 years old Phase 2:~~ Use a Simon optimal two-stage design with 10 patients treated in the first stage. If >1 response is seen in the first 10 patients, treat an additional 19 patients (with at least four children 2-4 years old of the 29 patients to be studied).

    Phamacokinetics: At least 7 patients within each of the following specified age groups (2-6, 7-11 and 12-18 years old) must be evaluated. The number of patients may include patients from Part 1 and Part 2 of the study.

- *Study endpoints:*

  Primary Endpoint**:**
  Phase 1 ~~-~~ 2 Part (dose escalation): To estimate the maximum tolerated dose (MTD) and recommend a Phase 2 dose of cabazitaxel administered intravenously once every 21 days as a single agent in patients ~~> 5~~ ≥2 to <18 years of age.

  Phase 2 Part (safety and activity): To determine the objective response rate (complete and partial response) and the duration of response using the Macdonald criteria.

  Secondary Endpoints (will include, but not limited to the following):
  Phases 1 and 2:
  ~~Phase 1-2:~~
  - To characterize the safety and tolerability of cabazitaxel
  - To characterize the pharmacokinetics of cabazitaxel

  ~~Phase 2:~~
  - ~~To characterize the safety and tolerability of cabazitaxel~~
  - ~~To characterize the pharmacokinetics of cabazitaxel~~

- Data should be collected to analyze the objective response rate (complete and partial response) using the Response Assessment in Neuro-Oncology Working Group criteria (JCO 2010 28:1963).

- *Drug information:*

  - *Dosage form*- Cabazitaxel Injection in single use vial 60 mg/1.5 mL, supplied with diluent (5.7 mL)
  - *Route of administration*- Intravenous infusion
  - *Regimen*-
    Phase 1~~-2~~ Part (dose escalation~~-part~~): The starting dose of cabazitaxel will be 20 mg/m^2 administered intravenously on Day 1 of each 21 day cycle. If this dose is not tolerated, cabazitaxel 15 mg/m^2 will be administered intravenously using the same schedule. Doses below 15 mg/m^2 will not be given. If the 20 mg/m^2 dose is tolerated, additional dose levels of cabazitaxel will be explored using standard (3+3) dose escalation rules. The maximum Body Surface Area for the actual cabazitaxel dose calculation will be 2.1 m^2 for safety reasons. Following cycle 1, patients may receive additional cycles as clinically appropriate.

    ~~Phase 1-2 (safety expansion part): Patients will be treated at the maximum tolerated dose or recommended Phase 2 dose~~

    Phase 2 Part (safety and activity): The maximum tolerated dose or recommended Phase 2 dose, as determined in the Phase 1 study, will be administered intravenously on Day 1 of each 21 day cycle.

- *Statistical information, including power of study(ies) and statistical assessments:*

  Phase 1~~-2-~~ Part (dose escalation)~~Study~~: The maximum tolerated dose of cabazitaxel will be determined in pediatric patients (age ~~5~~2 – 18 years old) with advanced solid tumors using a 3+3 design. The minimum sample size required to identify the maximum tolerated dose is 9 patients. ~~A safety expansion phase at the maximum tolerated dose will be open to patients ≥ 2 and ≤ 18 years old with at~~ At least 4 patients should be treated at the MTD ~~being~~ in the younger age group (~~≥ 2 and < 5~~2-4 years old).

  Phase 2 ~~Study~~ Part (safety and activity): Patients will be treated at the recommended Phase 2 dose established in the Phase 1 study. The anti-tumor activity of cabazitaxel will be examined by employing a Simon optimal two-stage design. Ten patients will be accrued in the first stage. If only one or no patient experiences an objective response (partial or complete response based on the Macdonald criteria) in the first stage, the trial will be stopped for lack of efficacy. If 2 or more patients out of the first 10 patients achieve an objective response, then an additional 19 patients will be enrolled in the second stage. With a null hypothesis of a true response rate of 10%, the study is designed to have 80% power to detect a true response rate of 30% using a one-sided alpha level of 0.05. The response rate will be calculated as the percent of patients whose best confirmed response is a complete response or

partial response and a confidence interval for the response rate will be calculated. The median duration of response will be estimated for patients with an objective response.

For ease of reference, a complete copy of the Written Request, as amended, is attached to this letter.

Reports of the studies that meet the terms of the Written Request dated March 20, 2012, as amended by this letter, must be submitted to the Agency on or before September 30, 2016, in order to possibly qualify for pediatric exclusivity extension under Section 505A of the Act.

Submit reports of the studies as a supplement to an approved NDA with the proposed labeling changes you believe are warranted based on the data derived from these studies. When submitting the reports, clearly mark your submission **"SUBMISSION OF PEDIATRIC STUDY REPORTS – PEDIATRIC EXCLUSIVITY DETERMINATION REQUESTED"** in large font, bolded type at the beginning of the cover letter of the submission and include a copy of this letter. In addition, send a copy of the cover letter of your submission, via fax (240-276-9327) or messenger, to the Director, Office of Generic Drugs, HFD-600, Metro Park North IV, 7519 Standish Place, Rockville, MD 20855-2773.

If you wish to discuss any amendments to this Written Request, submit proposed changes and the reasons for the proposed changes to your application. Clearly mark submissions of proposed changes to this request **"PROPOSED CHANGES IN WRITTEN REQUEST FOR PEDIATRIC STUDIES"** in large font, bolded type at the beginning of the cover letter of the submission. We will notify you in writing if we agree to any changes to this Written Request.

If you have any questions, call Christy Cottrell, Regulatory Project Manager, at 301-796-4256.

Sincerely,

{See appended electronic signature page}

Richard Pazdur, M.D.
Director
Office of Hematology and Oncology Products
Center for Drug Evaluation and Research

ENCLOSURE(S):
Complete Copy of Written Request as Amended

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

WRITTEN REQUEST

NDA 201023

Sanofi-aventis, U.S. LLC
500 Kendall Street, 5155-C3
Cambridge, MA 02142

Attention: Suzanne Thornton-Jones, Ph.D.
Director, Global Regulatory Affairs

Dear Dr. Thornton-Jones:

Reference is made to your December 16, 2011, Proposed Pediatric Study Request for Jevtana® (cabazitaxel) that was submitted to IND (b) (4).

Brain tumors are the second most common pediatric cancer, after hematological malignancies, accounting for approximately 20% of all childhood cancers and gliomas are the most common type of childhood CNS tumor. Using the World Health Organization (WHO) classification criteria, gliomas are often classified into low grade (WHO Grade I and II) and high grade (WHO Grade III and IV) tumors. High grade glioma (HGG) represents about 8-10% of all pediatric CNS tumors. In pediatric oncology, HGGs include Grade III and IV anaplastic astrocytoma, anaplastic oligodendroglioma, oligoastrocytoma, anaplastic ependymoma, and glioblastoma. Diffuse intrinsic pontine gliomas (DIPG) are the most common pediatric brainstem cancers. Histologically, DIPG are usually high grade anaplastic astrocytomas or glioblastoma multiforme. According to the Central Brain Tumor Registry of the United States, the incidence of high-grade gliomas (any location) among patients <19 years of age was approximately 0.63 per 100,000 person years. Based on SEER 17 registries from 1995-2007, the 5-year relative survival rate is 34% for anaplastic astrocytoma and 19% for glioblastoma multiforme in patients 0-19 years of age.

Depending on the subtype, location and grade of the brain tumor, a combination of surgery, radiation therapy, and chemotherapy is often used in treating brain tumors in children greater than 3 years of age. Younger children do not normally receive radiotherapy because of the severe neurological sequelae. Surgery and radiation remain the cornerstones of treatment of HGG. Concomitant temozolomide and radiation are the standard treatment for adult patients with HGG, but this regimen has failed to demonstrate benefit in children. Although HGG consists of several tumor subtypes, each associated with a unique molecular profile, the treatment and prognosis do not differ significantly. Despite multimodality treatment, long term survival rates for HGGs remain poor. Most patients with HGGs will have tumor recurrence and will die of the disease within 3 years of the diagnosis. Given the tumor location, DIPG are

particularly difficult to treat and a majority of patients with DIPG tumors progress rapidly and die of the disease within one year of diagnosis.

Cabazitaxel is a microtubule inhibitor which binds to tubulin and promotes its assembly into microtubules while simultaneously inhibiting disassembly. This leads to the stabilization of microtubules, which results in the inhibition of mitotic and interphase cellular functions. Cabazitaxel is structurally similar to docetaxel; the hydroxyl groups present in docetaxel are replaced with methoxy groups in cabazitaxel. Cabazitaxel may offer a therapeutic benefit with improved disease outcome for patients with HGG, despite the disappointing anti-tumor activity of docetaxel and paclitaxel in previous clinical trials enrolling pediatric brain cancer patients. A limitation of paclitaxel and docetaxel for the treatment of HGG is the inability of these compounds to cross the blood-brain barrier (BBB). Based on nonclinical data, cabazitaxel may have the ability to cross the BBB, has potential anti-tumor activity in glioblastoma, and may be active in tumors that are both sensitive and insensitive to docetaxel.

To obtain needed pediatric information on cabazitaxel, the Food and Drug Administration (FDA) is hereby making a formal Written Request, pursuant to Section 505A of the Federal Food, Drug, and Cosmetic Act (the Act), as amended by the Food and Drug Administration Amendments Act of 2007, that you submit information from the studies described below.

- *Type of studies:*

  Phase 1-2: The Phase 1 part is a dose-finding and safety study of cabazitaxel monotherapy in pediatric patients with refractory solid tumors, including pharmacokinetics, with doses determined for all appropriate age groups. This will be followed by a Phase 2 part to determine the response rates with and safety of cabazitaxel monotherapy in pediatric patients with recurrent or refractory high grade glioma or diffuse intrinsic pontine glioma. The Phase 2 part will be conducted at the dose determined by the Phase 1 portion of the study.

- *Indications(s) to be studied/ Objective of each study:*

  Phase 1 Part (dose escalation): Pediatric patients with metastatic or locally advanced solid tumors for whom no further effective therapy is available.

  Phase 2 Part (safety and activity): Pediatric patients with recurrent or refractory high grade glioma defined as WHO Grade III or Grade IV astrocytic or oligodendroglial tumor or recurrent or refractory diffuse intrinsic pontine glioma for whom no further effective therapy is available.

- *Patients to be Studied:*

  - *Age group in which studies will be performed*:

    Phase 1 Part (dose escalation): $\geq$2 years and <18 years (with at least four children 2-4 years old treated at the recommended Phase 2 dose)

Phase 2 Part (safety and activity): ≥2 years and < 18 years

- *Number of patients to be studied:*

  Phase 1 Part (dose escalation): ≥9 patients treated

  Phase 2 Part (safety and activity): Use a Simon optimal two-stage design with 10 patients treated in the first stage. If >1 response is seen in the first 10 patients, treat an additional 19 patients (with at least four children 2-4 years old of the 29 patients to be studied).

  Phamacokinetics: At least 7 patients within each of the following specified age groups (2-6, 7-11 and 12-18 years old) must be evaluated. The number of patients may include patients from Part 1 and Part 2 of the study.

- *Study endpoints:*

  Primary Endpoint**:**
  Phase 1 Part (dose escalation): To estimate the maximum tolerated dose (MTD) and recommend a Phase 2 dose of cabazitaxel administered intravenously once every 21 days as a single agent in patients ≥2 to <18 years of age.

  Phase 2 Part (safety and activity): To determine the objective response rate (complete and partial response) and the duration of response using the Macdonald criteria.

  Secondary Endpoints (will include, but not limited to the following):
  Phase 1 and Phase 2:
  - To characterize the safety and tolerability of cabazitaxel
  - To characterize the pharmacokinetics of cabazitaxel
  - Data should be collected to analyze the objective response rate (complete and partial response) using the Response Assessment in Neuro-Oncology Working Group criteria (JCO 2010 28:1963).

  Pharmacokinetic Endpoints: Pharmacokinetic samples must be collected through approaches such as rich sampling or optimal sparse sampling in patients. Such data must then be appropriately analyzed using methods such as nonlinear mixed effects modeling or non-compartmental analysis. If appropriate, develop pharmacokinetic and pharmacodynamic (PK-PD) models to explore exposure-response relationships as measures of safety and activity.

- *Drug information:*

  - *Dosage form*- Cabazitaxel Injection in single use vial 60 mg/1.5 mL, supplied with diluent (5.7 mL)
  - *Route of administration*- Intravenous infusion

- *Regimen-*
  Phase 1 Part (dose escalation): The starting dose of cabazitaxel will be 20 mg/m^2 administered intravenously on Day 1 of each 21 day cycle. If this dose is not tolerated, cabazitaxel 15 mg/m^2 will be administered intravenously using the same schedule. Doses below 15 mg/m^2 will not be given. If the 20 mg/m^2 dose is tolerated, additional dose levels of cabazitaxel will be explored using standard (3+3) dose escalation rules. The maximum Body Surface Area for the actual cabazitaxel dose calculation will be 2.1 m^2 for safety reasons. Following cycle 1, patients may receive additional cycles as clinically appropriate.

  Phase 2 Part (safety and activity): The maximum tolerated dose or recommended Phase 2 dose, as determined in the Phase 1 study, will be administered intravenously on Day 1 of each 21 day cycle.

- *Known Drug Safety concerns and monitoring:* In adult patients treated with cabazitaxel, the most common (≥10%) grade 1-4 adverse reactions were anemia, leukopenia, neutropenia, thrombocytopenia, diarrhea, fatigue, nausea, vomiting, constipation, asthenia, abdominal pain, hematuria, back pain, anorexia, peripheral neuropathy, pyrexia, dyspnea, dysgeusia, cough, arthralgia, and alopecia. The most common (≥5%) grade 3-4 adverse reactions were neutropenia, leukopenia, anemia, febrile neutropenia, diarrhea, fatigue, and asthenia. Deaths due to causes other than disease progression within 30 days of last study drug dose were reported in 18 (5%) of cabazitaxel-treated patients. The most common fatal adverse reactions were infections (n=5) and renal failure (n=4). The majority (4 of 5 patients) of fatal infection-related adverse reactions occurred after a single dose of cabazitaxel. Other fatal adverse reactions in cabazitaxel-treated patients included ventricular fibrillation, cerebral hemorrhage, and dyspnea.

- *Extraordinary results:* In the course of conducting these studies, you may discover evidence to indicate that there are unexpected safety concerns, unexpected findings of benefit in a smaller sample size, or other unexpected results. In the event of such findings, there may be a need to deviate from the requirements of this Written Request. If you believe this is the case, you must contact the Agency to seek an amendment. It is solely within the Agency's discretion to decide whether it is appropriate to issue an amendment.

- *Statistical information, including power of study(ies) and statistical assessments:*

  Phase 1 Part (dose escalation): The maximum tolerated dose of cabazitaxel will be determined in pediatric patients (age 2-18 years old) with advanced solid tumors using a 3+3 design. The minimum sample size required to identify the maximum tolerated dose is 9 patients. At least 4 patients should be treated at the MTD in the younger age group (2-4 years old).

  Phase 2 Part (safety and activity): Patients will be treated at the recommended Phase 2 dose established in the Phase 1 study. The anti-tumor activity of cabazitaxel will be examined by employing a Simon optimal two-stage design. Ten patients will be accrued in the first stage. If only one or no patient experiences an objective response (partial or complete response

based on the Macdonald criteria) in the first stage, the trial will be stopped for lack of efficacy. If 2 or more patients out of the first 10 patients achieve an objective response, then an additional 19 patients will be enrolled in the second stage. With a null hypothesis of a true response rate of 10%, the study is designed to have 80% power to detect a true response rate of 30% using a one-sided alpha level of 0.05. The response rate will be calculated as the percent of patients whose best confirmed response is a complete response or partial response and a confidence interval for the response rate will be calculated. The median duration of response will be estimated for patients with an objective response.

- *Labeling that may result from the study(ies)*: You must submit proposed pediatric labeling to incorporate the findings of the study(ies). Under section 505A(j) of the Act, regardless of whether the study(ies) demonstrate that cabazitaxel is safe and effective, or whether such study results are inconclusive in the studied pediatric population(s) or subpopulation(s), the labeling must include information about the results of the study(ies). Under section 505A(k)(2) of the Act, you must distribute to physicians and other health care providers at least annually (or more frequently if FDA determines that it would be beneficial to the public health), information regarding such labeling changes that are approved as a result of the study(ies).

- *Format and types of reports to be submitted*: You must submit full study reports (which have not been previously submitted to the Agency) that address the issues outlined in this request, with full analysis, assessment, and interpretation. In addition, the reports must include information on the representation of pediatric patients of ethnic and racial minorities. All pediatric patients enrolled in the study(ies) should be categorized using one of the following designations for race: American Indian or Alaska Native, Asian, Black or African American, Native Hawaiian or other Pacific Islander or White. For ethnicity, you should use one of the following designations: Hispanic/Latino or Not Hispanic/Latino. If you choose to use other categories, you should obtain agency agreement.

  Under section 505A(d)(2)(B) of the Act, when you submit the study reports, you must submit all postmarketing adverse event reports regarding this drug that are available to you at that time. All post-market reports that would be reportable under section 21 CFR 314.80 should include adverse events occurring in an adult or a pediatric patient. In general, the format of the post-market adverse event report should follow the model for a periodic safety update report described in the Guidance for Industry E2C Clinical Safety Data Management: Periodic Safety Update Reports for Marketed Drugs and the Guidance addendum. You are encouraged to contact the reviewing Division for further guidance.

  Although not currently required, we request that study data be submitted electronically according to the Study Data Tabulation (SDTM) standard published by the Clinical Data Interchange Standards Consortium (CDISC) provided in the document "Study Data Specifications," which is posted on the http://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/ElectronicSubmissions/UCM199759.pdf and referenced in the FDA Guidance for Industry, *Providing Regulatory Submissions in Electronic Format - Human Pharmaceutical*

Product Applications and Related Submissions Using the eCTD Specifications at http://www.fda.gov/RegulatoryInformation/Guidances/ucm126959.htm

- *Timeframe for submitting reports of the study(ies):* Reports of the above studies must be submitted to the Agency on or before September 30, 2016. Please keep in mind that pediatric exclusivity attaches only to existing patent protection or exclusivity that would otherwise expire nine (9) months or more after pediatric exclusivity is granted, and FDA has 180 days from the date that the study reports are submitted to make a pediatric exclusivity determination. Therefore, to ensure that a particular patent or exclusivity is eligible for pediatric exclusivity to attach, you are advised to submit the reports of the studies at least 15 months (9 months plus 6 months/180 days for determination) before such patent or exclusivity is otherwise due to expire.

- *Response to Written Request:* Under section 505A(d)(2)(A)(i), within 180 days of receipt of this Written Request you must notify the Agency whether or not you agree to the Written Request. If you agree to the request, you must indicate when the pediatric studies will be initiated. If you do not agree to the request, you must indicate why you are declining to conduct the study(ies). If you decline on the grounds that it is not possible to develop the appropriate pediatric formulation, you must submit to us the reasons it cannot be developed.

  Furthermore, if you agree to conduct the study(ies), but have not submitted the study reports on or before the date specified in the Written Request, the Agency may utilize the process discussed in section 505A(n) of the Act.

Submit protocols for the above study(ies) to an investigational new drug application (IND) and clearly mark your submission "**PEDIATRIC PROTOCOL SUBMITTED FOR PEDIATRIC EXCLUSIVITY STUDY**" in large font, bolded type at the beginning of the cover letter of the submission.

Reports of the study(ies) must be submitted as a new drug application (NDA) or as a supplement to your approved NDA with the proposed labeling changes you believe are warranted based on the data derived from these studies. When submitting the reports, please clearly mark your submission "**SUBMISSION OF PEDIATRIC STUDY REPORTS - PEDIATRIC EXCLUSIVITY DETERMINATION REQUESTED**" in large font, bolded type at the beginning of the cover letter of the submission and include a copy of this letter. Please also send a copy of the cover letter of your submission to the Director, Office of Generic Drugs, HFD-600, Metro Park North IV, 7519 Standish Place, Rockville, MD 20855-2773. If you wish to fax it, the fax number is 240-276-9327.

In accordance with section 505A(k)(1) of the Act, *Dissemination of Pediatric Information*, FDA must make available to the public the medical, statistical, and clinical pharmacology reviews of the pediatric studies conducted in response to this Written Request within 210 days of submission of your study report(s). These reviews will be posted regardless of the following circumstances:

1. the type of response to the Written Request (i.e. complete or partial response);
2. the status of the application (i.e. withdrawn after the supplement has been filed or pending);
3. the action taken (i.e. approval, complete response); or
4. the exclusivity determination (i.e. granted or denied).

FDA will post the medical, statistical, and clinical pharmacology reviews on the FDA website at http://www.fda.gov/Drugs/DevelopmentApprovalProcess/DevelopmentResources/UCM049872.

If you wish to discuss any amendments to this Written Request, please submit proposed changes and the reasons for the proposed changes to your application. Submissions of proposed changes to this request should be clearly marked "**PROPOSED CHANGES IN WRITTEN REQUEST FOR PEDIATRIC STUDIES**" in large font, bolded type at the beginning of the cover letter of the submission. You will be notified in writing if any changes to this Written Request are agreed upon by the Agency.

Please note that, if your trial is considered an "applicable clinical trial" under section 402(j)(1)(A)(i) of the Public Health Service Act (PHS Act), you are required to comply with the provisions of section 402(j) of the PHS Act with regard to registration of your trial and submission of trial results. Additional information on submission of such information can be found at www.ClinicalTrials.gov.

If you have any questions, call Christy Cottrell, Regulatory Project Manager, at (301) 796-4256.

Sincerely,

{See appended electronic signature page}

Richard Pazdur, M.D.
Director
Office of Hematology and Oncology Products
Center for Drug Evaluation and Research

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

RICHARD PAZDUR
05/08/2013