# REPORT ON THE TESTING OF TEVADAPTOR™(1) EFFICIENCY IN PREVENTING CYCLOPHOSPHAMIDE DRUG EMMISSION

March 5, 2016

**Prepared at the request and authorization of**

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(1)Tevadaptor is a Trade Mark of Teva Medical Ltd.

March 5, 2016

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Via Email Jred.massoomi@nmhs.org
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Dear Dr. Massoomi,

Per your request and authorization enclosed is the report on the experimental and analytical work regarding cyclophosphamide interaction with tevadaptor.

Very Truly Yours,

**American Analytics, Inc.**
Dr. Maria Echarte
Senior Chemist and
Environmental Scientist

**American Analytics, Inc.**
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## 1.0 EXECUTIVE SUMMARY

A series of experiments, designed to assess the ability of Tevadaptor™ (hereafter Tevadaptor) to prevent cyclophosphamide cytotoxic emissions from drug vials were performed. The original Tevadaptor experiment, performed by the manufacturer to prove the performance of the product, was replicated (Experiment A) in accordance to manufacturer's white paper. In addition, two modified types of experiments, with elements simulating realistic medical professionals' working conditions, at a shortened duration and lower temperature, were also performed (Experiments B and C). These conditions with lower temperature and shorter durations, were more favorable test condition for the adaptor.

All experiments showed cyclophosphamide emissions from Tevadaptor. The two experiments (B and C) showed higher emissions of the drug than Experiment A.

In summary, the results of the experiments demonstrate that the Tevadaptor with its "Toxi-Guard" charcoal matrix, its binding and retention capacity and 0.2 micron membrane did not contain or prevent emissions of cyclophosphamide during the testing of the device, in our experiments. As a result, the Tevadaptor system may not support compliance with 2004 NIOSH recommendations for handling hazardous drugs and may not properly protect health workers, as claimed by the manufacturer.

## 2.0 INTRODUCTION

According to its manufacturer, Tevadaptor, hereafter, the device, is equipped with "Toxi-Guard"™ activated charcoal drug binding matrix, and 0.2 micron hydrophobic

membrane. This device is designed to prevent the exposure of medical personnel and other health workers to cytotoxic drugs such as cyclophosphamide. The exposure may occur during handling, preparation, and administration of these drugs to patients (hereafter medical procedures). The potential exposure is from leaks, aerosols, vapors, and gases that may form and escape the drug vials during medical procedure. The experiments described in the report were designed to examine whether or not Tevadaptor prevents emissions of cyclophosphamide, a cytotoxic drug used in chemotherapy.

## 3.0 GOALS OF THE EXPERIMENTAL WORK

The goals of the experimental work described in this experiment were:

- Using cyclophosphamide and Tevadaptor replicate a demonstration experiment published by Tevadaptor (the Tevadaptor experiment) designed to prove the ability of the device to prevent emissions of cyclophosphamide as an example of a cytotoxic drugs
- Using cyclophosphamide, and Tevadaptor, perform additional two types of experiments simulating certain elements of actual device use routines in medical procedures and test the emissions, if any, from the device.

## 4.0 EXPERIMENTAL DESIGN

### 4.1 Replication of the Tevadaptor Experiment

These experiments dreplicated the experiment described by Tevadaptor (Ref 1, 2) to test the ability of the Tevadaptor transfer system to prevent the escape of hazardous

drug species. In general, dry nitrogen gas at a flow rate of 300ml/min were introduced to a cyclophosphamide vial equipped with Tevadaptor . Exhaust and emissions from the Tevadaptor were captured by a cold trap at -70 degrees C and analyzed.

These experiments were performed at 50 degrees C for 5 hours, with 500 mg and 1.0 gm cyclophosphamide in original manufacturer's vials. The details of these experiments are described in length in this report.

**4.2 Modification of the Tevadaptor Experiment: Shorter Time, Lower Temperature and 5ml of Drug Drawn Prior to Testing.**

The experimental design in this experiment was identical to the replicated Tevadaptor experiment with the following exceptions:

In these experiments, the system was put under lower stress as follows:

- The temperature was reduced from 50 degrees C to 23 degrees C (room temperature)
- The experimental time was reduced from 5 hours to 3 hours
- 5ml of drug were drawn simulating the work with multidose vials

All other conditions remained the same.

**4.3 Other Test**

Other tests include:

- Negative control: sampling of drug vial surfaces for cyclophosphamide residues at the commencement of the study.
- Positive control: identical to Tevadaptor test replication, but with a needle inserted into the vial instead vial adaptor of the Tevadaptor system.

The general experimental combinations are summarized in Table 4.1 below.

Table 4.1

General Experimental Conditions[1,2]

| Experiment Duration (minutes) | 180 minutes (3 hours) | 300 minutes (5 hours) |
|---|---|---|
| Vial Temperature | 23 degrees C | 50 degrees C |
| Vial Contents: cyclophosphamide | Experiment performed | Experiment performed |
| 500 mg | yes | yes |
| 1.0 gm | yes | yes |

[1] Include controls [2] Experimental details are presented in this report and Appendix 2

**4.4 Detailed Description of the Experiment Setup**

Please refer to Figure 1, Appendix 1, for following the description below. Specification for relevant items are listed in this report's Section 5.0, Materials and Methods.

- Compressed dry nitrogen gas supply is controlled by 2 stage regulator RG-1 and on/off valve V-1. V-1 is connected directly to the regulator.
- The gas flows though ¼ inch copper tubing 2 and 3 to mass flow controller RG-2.
- The gas flow is further controlled by middle valve V-2 into ¼ inch copper tubing 4.
- Copper tubing 4 is connected to the closed glass container "reactor" A or B with approximately ¼ inch medical infusion tubing, terminated with male Luer Lock connection.
- The flexible tubing, equipped with the male Luer Lock connection, is connected to the closed reactor through the female Luer Lock on the 3 1/2" long 19G spinal needle (N-1) inserted into the sealed reactor through a gas chromatography septum inside a compression filling at the top of the reactor, and then through tube (8) and the Tevadaptor septum, into the original drug vial CF.
- The vial (CF) containing cyclophosphamide solution is fitted with Tevadaptor and is suspended with a short silicone tube (8), (hereafter connector tube) from below the entrance point of the 19G needle.
- The cyclophosphamide powder originally in the vial was reconstituted with saline solution and dissolved by intensive manual shaking approximately 15 minutes long until powder fully dissolved, all according to manufacturer's recommendation.
- Syringe containing saline solution was used to fill the vial (CF) through Tevadaptor syringe adaptor.

- The Tevadaptor with drug vial is then connected to the above-mentioned short silicone tube (8) at its upper barbed part and was already connected below to the drug vial according to manufacturer specifications.
- The reactor is almost completely immersed (up to the access pipes) in a water bath kept at the experimental temperature ($t_H$) of 23 degrees C or 50 degrees C.
- The water bath temperature is continuously monitored by the thermometer according to the temperature (23 degrees C or 50 degrees C) assigned to the experimental run for the duration of the experiment.
- Needle NI is inserted half way into drug vial CF containing cyclophosphamide dissolved in saline solution, and the tip is well above the liquid level.
- The nitrogen gas flow at 300 ml per minute is introduced into the vial (CF) through needle N-1 and is mixed with the drug vapors and exits through the o.2 micron hydrophobic filter followed by Tevadaptor "Toxi-Guard" window and enters the reactor. The gas exits the reactor through silicone rubber tube (5) and flows into the cold trap, maintained at -70 degrees C.
- In the positive control experiment configuration, the Tevadapator was not used. Instead the vial adaptor, the original drug's vial's septum is penetrated by an additional 16G hypodermic needle to allow aerosols, vapors and gases to escape the drug vial (CF).
- Liquid, vapor, gases or aerosols are hereafter collectively identified as emissions.
- The emissions that may escape through the Tevadapator "Toxi-Guard's" charcoal and membrane equipped gas exchange window , or in control experiment can:

- Condense and/or deposit on the inside of the reactor walls
- Condense and/or deposit on the outer surface of the drug vial
- Condense and/or deposit on the inner wall of the silicone tubing (5)
- Flow through silicon tubing (5) and be captured by the cold trap (CT).

- The cold trap (CT) is immersed in a mixture of $CO_2$ ice and acetone, maintained at a temperature of -70 degrees C. the ice/acetone mix is contained in a Dewar vacuum flask (9).
- The temperature $t_c$ is monitored and maintained continuously at -70 degrees C.
- The emissions and moisture that were not trapped on the reactor walls or the inner wall of tubing (5) are now condensed and trapped in the cold trap (CF) at -70 degrees C.
- The gas effluent of the cold trap (CF) exit the trap into Rotometer R1.
- Calibrated Rotometer R1 is monitored continuously to ensure exit flow of 300 ml/min at atmospheric pressure at the Rotometer exit.
- The flow is adjustable to 300 ml/min at RG-1, V-1, RG-2, V-2 and V-3
- The whole experiment is performed in a chemical hood.
- At the completion of each experiment, all the following items are rinsed with 1:1 methanol $H_2O$ solution: The reactor inner walls, the outside of the drug vial, connecting tubing (8), the inner walls of connecting tubing (5), and all the inner parts of cold trap (CT). The vTevadaptor vial adaptor is excluded from rinsing. The rinsate is collected and preserved in glass vials with Teflon air compression cup (VOA vials) then the volume is measured. The vials with measured rinsate volumes are kept in the refrigerator at 4 degrees C pending chemical analysis.

- The samples are analyzed by Agilent Triple Quad LCMS.
- All the experimental hardware that may come in contact with cyclophosphamide emissions are rinsed between experiments in the following manner:
    1. Rinse with 1:1 ratio LC grade methanol reagent: water
    2. Rinse thoroughly with hot tap water
    3. Soak in hot water/Alconox detergent mix for about an hour followed by brush scrubbing
    4. Triple rinse with hot tap water, followed by triple distilled water
    5. Dry with LC grade acetone
    6. Air dry

## 4.5 Type of Experiments

- All experiments included the use of Tevadaptor and a medication vial with 500mg or 1.0 gm cyclophosphamide
- The types of experiments are described in Table 4.5 below. The details of each experiment and controls are described in, Appendix 2.

Table 4.5
The Three Types of Tevadaptor Experiments

| Test ID | Type of Experiment | Medication Draw[(1)] Description | Duration (hrs) | Experimental Temperature (degrees C) |
|---|---|---|---|---|
| A | Replication of the Tevadaptor reported experiment (Ref 1, 2) | None | 5 | 50 |
| B | Modified with 5m drug withdrawal with bubble removal right after reconstitution, before insertion into reactor | Yes<br>Draw 4ml, inject 4ml back into the vial to remove air bubbles, then draw 5ml as final dose | 3 | 23 |
| C | Simulation of medical practice with syringe volume adjustment | Yes<br>A. perform bubble removal: draw 4ml, inject 4ml back<br>B. Perform dose correction: draw 6ml, inject 1ml back to correct the final dose to 5ml | 3 | 23 |

[(1))]Medication preparation and draw, and/or bubble removal, if any, is performed before the insertion of the cyclophosphamide vial into the reactor.

## 5.0 MATERIALS AND METHODS

Please refer to Figure 1 for item identifications. Items are listed in the order they appear in the process train illustrated in Figure 1

### 5.1 Materials

- Compressed dry nitrogen gas 99.99%: highest purity supplied by Proxair

- RG-1 and V-1 pressure regulator and shut off valve respectively: Matheson Gas Company
- Gas lines 2, 3 and part of 4: ¼ inch copper tubing certified clean of residues and VOCs.
- RG-2 pressure regulator with gage: column head pressure regulator used in Hewelett Packard (HP) gas chromatograph HP5890.
- V-2 regulating valve: HP19362-60575
- The end of tubing (4) connected to N-1: tubing portion of "secondary IV or transfer set" with universal spike and male Luer Lock connector. Braun ref V1921.
- N1: 3 ½ inch long 19G spinal needle with female Luer Lock
- N2: 16G hypodermic needle
- $t_1$ and $t_2$: thermometers with 0.1 degrees C accuracy
- septa at N1 entrance into the reactor: Restek GC septa product no. 27094, premium non-stick with centerguide
- reactor water bath: refrigerated and heated water bath for precise temperature control: MGW LAUDA Brinkman RM20, RMT
- water bath's water: Deionized laboratory water
- reactors A and B: glass vessels approximately 2"D x 6"H with removable lead, with pressure lock mechanism to prevent leaks.
- Tubing (8): silicone rubber tubing approximately ¼ inch idabout 1" long
- Tevadaptor/Onguard vial contained medication, 2018-03, Teva Medical Ltd., CE 0483, Lot MG408C15, reference 412111.

- Tevadaptor/Onguard syringe adaptor contained medication system, 2018-08, Teva Medical Ltd., CE 0483, Lot M6874H15, reference 412118.
- Two drug vial dosages: 500mg and 1 g containing cyclophosphamide powder (Baxter brand).

  500mg, lot/mfg/exp:560 339F/07.2015/0.7/2018

  1g, lot mfg/exp: 4K040G/11.2014/11.2017
- Cyclophosphamide diluent solution: 0.9% sodium chloride

  Injection USP, 100ml partially filled in 150ml PAB container, Rx only B/Braun Medical, Inc.
- Syringe used for filling drug vials: BD 60ml syringe
- Tubing 5 & 6: silicone rubber ¼ inch id
- Cold trap: glass vessel approximately 1.5 inch D x 12 inch long
- Dewar flask and container (9): approximately 7 inch x 13 inch, manufactured by Dilvac, G.B..
- Flow meter R-1: Dwyer Instruments, model RMA-12-SSV

**5.2 Materials**

- Cyclophosphamide and dilution liquid used were specified in Section 5.1 above.
- Cyclophosphamide analytical standard specifications:

Material: cyclophosphamide

Amount: 1g MW: 279.10

MFR: Toronto Research Chemicals, TRC 3 Brisbane Road, Toronto, Ontario, Canada M3J2J8

- compressed high purity nitrogen 99.99% and $CO_2$ ice: Praxair, North Hollywood, CA
- Dilution water: NERL reagent grade water, CAS 7732-18-5, exceeds CAP/LLSI specification for clinical laboratory reagent. Water (CLRW) and USP/NF purified water, Themo Scientific lot 766249
- Methanol: 4525K-1, Lot 155698, methanol HPLC grade, meets ACS specifications, 0.2 micron filtered, Fisher Chemicals.
- Acetone, A185K-4, Lot 156794, certified ACS, Fisher Chemicals

### 5.3 Analytical Methods

**Sample Preparation**
*Calibration stock solutions* Cyclophosphamide monohydrate powder (TRC's standard) was dissolved in 50% methanol-50% water solution, and the resulting mixture of 168 mg/L cyclophosphamide was further diluted 200-fold in the same solvent system to yield an 839 µg/L intermediate working standard stock. This stock was used to prepare the following final cyclophosphamide calibrator concentrations: 0, 0.839, 2.52, 4.20, 5.87, 8.39, 16.7, 25.2, 50.3, 83.9 µg/L.

**Equipment and Conditions**
Measurements were implemented on the Agilent 1200-series HPLC and 6410 triple-quadruple (QQQ) mass spectrometer, equipped with degasser and binary pump modules. Chromatographic separation was performed using a Kinetex C18 reversed phase column (150 × 2.1 mm, 100 Å core, 5 µm), preceded in-line by a UPLC biphenyl precolumn; (Phenomenex, Torrance, California). A gradient mobile phase system of acetonitrile and water with 0.1% formic acid was used for the chromatography at a steady flow rate of 0.4 mL/min. For each sample injection, the acetonitrile concentration was increased from 20 to 70% over 5 minutes, followed by a decrease back to 20% over 1 minute, and a final 4-minute step at 20% acetonitrile to ensure phase equilibration and eliminate carryover. Cyclophosphamide eluted at approximately 56% acetonitrile, with a typical retention time of 4.3 minutes.

**Mass Spectrometry**
The tandem mass spectrometry conditions were as follows: Source gas temperature 300 °C, at gas flow of 12 L/min, with nebulizer pressure of 50 PSI, and electrospray ionization capillary at 4000 V (positive polarity). Data was acquired using multiple-reaction monitoring (MRM), selecting for precursor in MS1, and monitoring for the

product ion in MS2. The cyclophosphamide transitions of 262.9→141.8 and 260.9→139.9 m/z were monitored with fragmentor setting value of 140V collision energy Value to of 20 V, and dwell time of 200 ms.

## 6.0 RESULTS

Table 1 presents the detailed experimental conditions of each experiment and the respective cyclophosphamide analytical results. The table also includes calculated cyclophosphamide mass emission rates, if any, captured by each experimental hardware component.

The detailed analytical results are presented in Table 2.

## 7.0 DISCUSSION

The results of the series of experiments reported herein show emissions of cyclophosphamide when Tevadaptor is used with cyclophosphamide drug vial.

The Tevadaptor experiment was performed at elevated temperature (50 degrees C) to increase drug volatility and for 5 hours. Experiment B and C were performed at 23 degrees C to simulate working conditions, and a shortened run time of 3 hours. Table 1, Appendix 2, summarizes the cumulative simple average cyclophosphamide mass emissions from Tevadaptor during each experiment in tests A, B, and C. The average emissions per experiment are presented graphically in Figure 2, Appendix 1.

The data suggests that the emission from experiments B and C are significantly higher than the cyclophosphamide emission detected in the replication of the Tevadaptor experiment. We believe that the higher emissions are due to the added elements taken from realistic use of the Tevadaptor in the simulated "real-life" working use conditions, versus the static use of the device in the Tevadaptor replicated experiment.

In summary, the results of the experiments demonstrate that the "Toxi-Guard" charcoal matrix and 0.2 micron membrane do not contain cyclophosphamide drug gases or vapors or aerosols during the use of the device, in our experiments. As a result, the Tevadaptor system may not 2004 NIOSH recommendations for handling hazardous drugs and may not properly protect health workers under all conditions.

## 8.0 CONCLUSIONS

8.1 The Tevadaptor experiment as described in Reference 1, 2, may have not taken into account emissions deposited on the reactor wall and inner walls of tubing connecting the reactor to the cold trap.

8.2 The Tevadaptor experiment (Ref 1) is static and does not simulate real medical procedure practice.

8.3 The results of this experiment with Tevadaptor demonstrate that the Toxi-Guard's charcoal matrix and the 0.2 micron membrane cannot effectively contain cyclophosphamide's aerosol vapors and gases. This problem may extend to other cyclotoxic drugs with the same properties.

8.4 It is not clear what is the binding capacity of the charcoal matrix and the 0.2 micron membrane and whether or not it is adequate for use with cytotoxic or other toxic drugs.

8.5 Our experiments simulating real medical procedure practice showed larger emissions than the replication of Tevadaptor experiment.

8.6 Tevadaptor could not contain cyclophosphamide in our experiment. Therefore, it may result in harmful exposure to medical professionals using the product.

8.7 The results of our experiment question the ability of Tevadaptor to support compliance with USP 797, ASHP, and 2004 NIOSH documentation for handling hazardous drugs.

## 9.0 DISCLAIMER

This report represents the results and analysis of the experiments with Tevadapator and cyclophosphamide, as described above.

## 10.0 REFERENCES

Reference 1: https://www.youtube.com/watch?v=9zMHBK8C-e4 link to Tevadaptor expaeriment clip

**Reference 2:** **White paper of the original Tevadaptor experiment**

# Minimizing Health Care Professional's Exposure to Hazardous Drug Species

Performed by ANALYST Research Laboratories, ISRAEL, February 2007


## Summary

Tevadaptor, a special device developed by Teva Medical Devices, to prevent the escape of hazardous drug species, including vapor, into the environment, was tested. Carboplatin, Etoposide, Cyclophosphamide and Doxorubicin HCl were used as the test compounds. Drug vials with attached Tevadaptor Vial Adaptor were connected to a system designed to capture any drug vapors leaking through Tevadaptor. Carboplatin, Etoposide, Cyclophosphamide, or Doxorubicin vapors escaping the adaptor were trapped at -70 C.

Sensitive LC/MS/MS methods were developed enabling the detection of Carboplatin, Etoposide, Cyclophosphamide, and Doxorubicin HCl at the nanogram (ng) level. The results showed that all

Tevadaptor units prevented analytes from escaping into the environment. When control TevadaptorTM units (devoid of filter system) were used, significant amounts of tested analytes were found.


## Objective

To test the ability of the Tevadaptor closed system to prevent the escape of hazardous drug species.

## Materials & Methods

Working standards of Carboplatin, Etoposide, Cyclophosphamide, and Doxorubicin HCl were prepared by dilution of a 100 pg/ml stock solution in methanol. The final calibration curve for all analytes contained 1, 2, 5, 10, 20 and 50 ng/ml in diluent (1:1 methanol:HPLC grade water).

The experimental set up included an original vial sealed with a rubber septum (supplied by the sponsor) containing the test material (Carboplatin, Cyclophosphamide, Etoposide or Doxorubicin HCl) with attached Tevadaptor Vial Adaptor. The vial - Tevadaptor assembly was placed in a 100 ml glass bottle and sealed with another rubber septum. A needle was introduced through both the bottle and the Tevadaptor septa, in a manner allowing an external stream of nitrogen to flow through the Tevadaptor into the vial, back to the bottle and from there through a second needle out into the collecting trap. The 100 ml glass bottle was kept in a water bath at 50°C in order to increase vapor pressure, and the collecting trap was immersed in a mixture of acetone and dry ice at -70°C.

Analyte vapors were collected at a stream of nitrogen of about 300 ml/min for 5 hours (-90L of nitrogen). At the end of the collecting time, the trapped analyte was dissolved in 10 mL of diluent (1:1 methanol:HPLC grade water) and analyzed by the LC/MS/MS method. The test was performed in one replicate (one control Tevadaptor unit, devoid of filters and one Tevadaptor unit) for Carboplatin, Etoposide, and Doxorubicin, and 12 replicates and 2 controls for Cyclophosphamide.

A recovery test was executed, employing the same vapor collection system using Naphthalene as a marker (because of its relatively high vapor-pressure). The test results demonstrated 90-100% recovery.

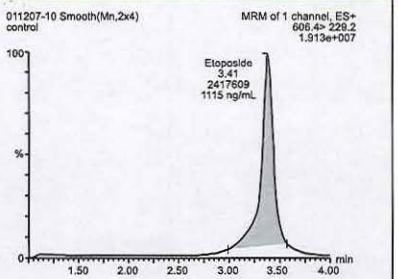
## Conclusion

Tevadaptor prevents hazardous drugs species, including vapor, from escaping into the environment.

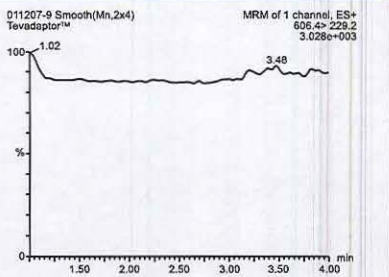
TEVADAPTOR®
When Safety and Simplicity Click

| Tested analyte | Amount of tested analytes in control samples (ng) | Amount of tested analytes in Tevadaptor samples (ng) |
|---|---|---|
| Etoposide | 11.50 | Not detected |
| Doxorubicin HCl | 460 | Not detected |
| Carboplatin | 53 | Not detected |
| Cyclophosphamide | 28-32 | Not detected |

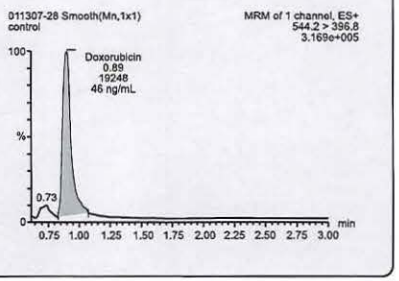
Etoposide Control Sample



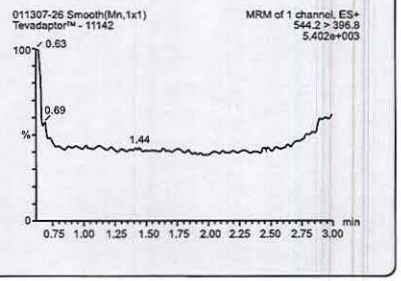

Etoposide Tevadaptor Sample




Doxorubicin Control Sample




Doxorubicin HCl Tevadaptor Sample

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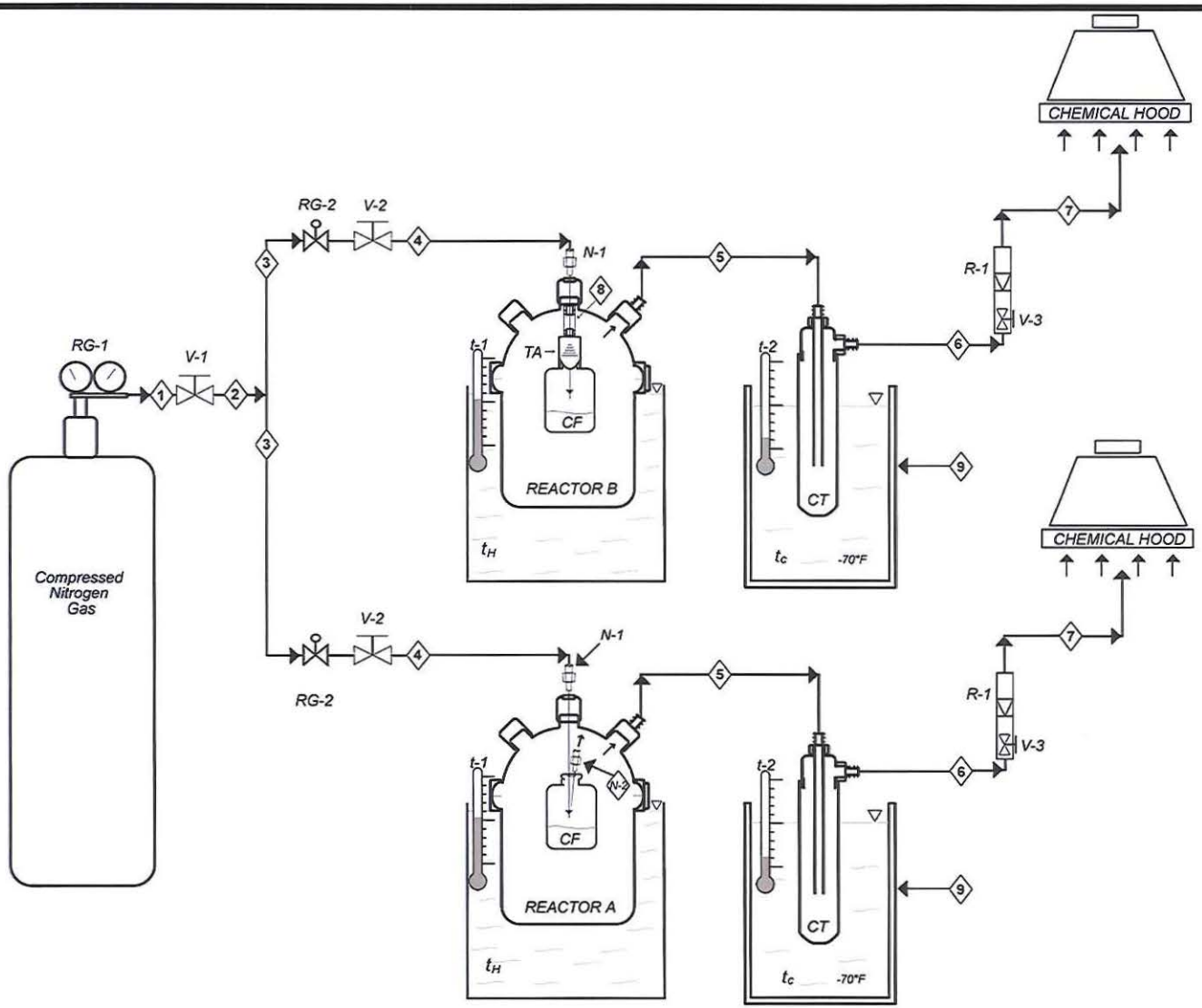
## APPENDIX 1: Figures



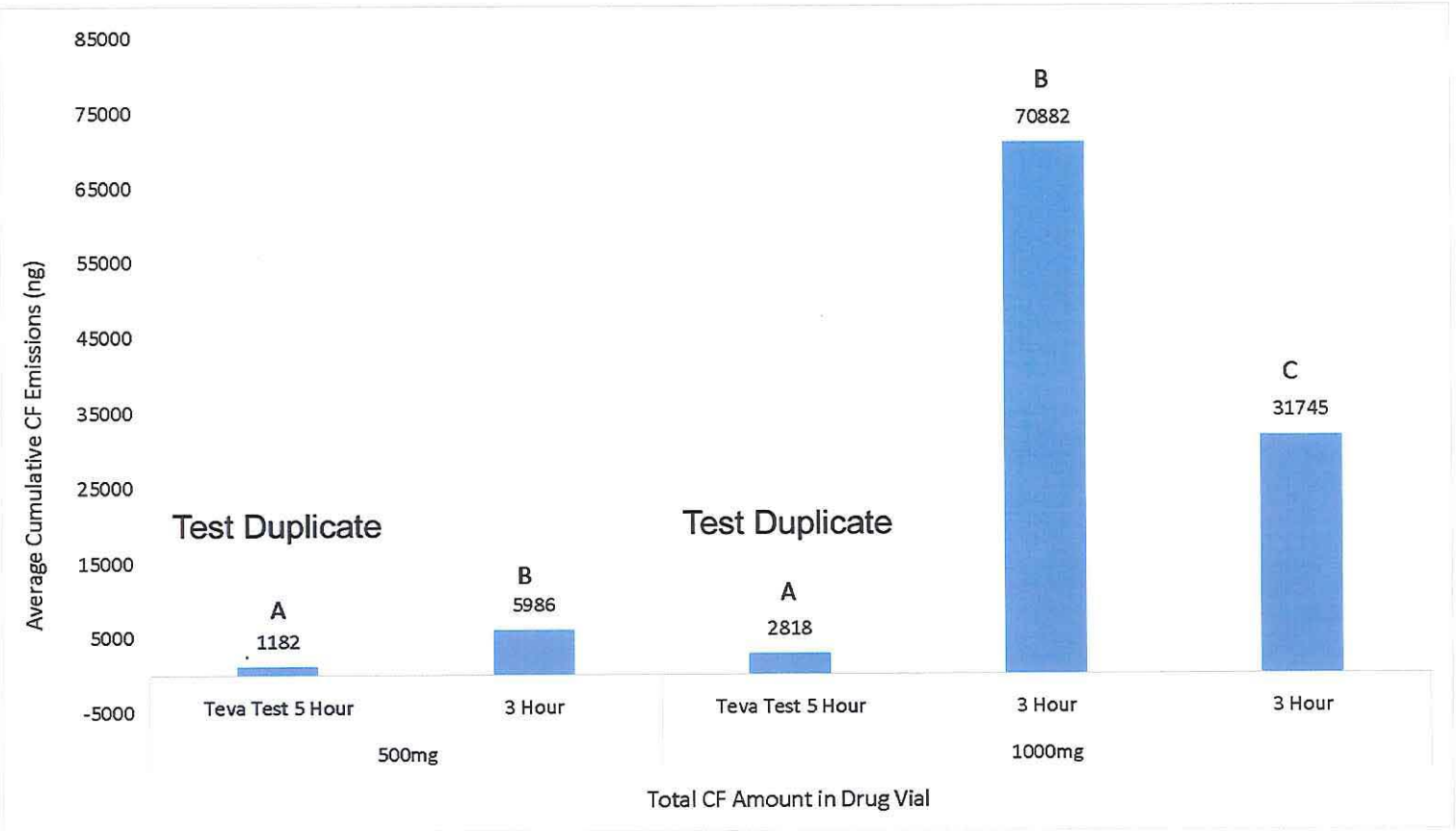

**American Analytics, Inc.**
9765 Eton Avenue, Chatsworth, CA 91311
Tel: 818-998-5547, Fax: 818-998-7285

**Schematic Experimental process diagram used for testing Tevadaptor with Cyclophosphamine contained in standard medication vial**

| Drawn by: | DATE: | PROJECT: | FIGURE |
|---|---|---|---|
| J.R, M.U | 2016-03-03 | TEVADAPTOR | 1 |

## Figure 2

## Graphical Representation of Test Summary Results



## APPENDIX 2: Tables

## Table 1

Cumulative Cyclophosphammide Mass Emission Rates from Tevadaptor During Experimental Tests A, B, and C

| | Emissions (ng) | Number of Samples | Average (Emissions / Samples) | Number of Experiments | Average (Emissions / Experiments) |
|---|---|---|---|---|---|
| 500mg 5hrs (test A) | 3545 | 9 | 394 | 3 | 1182 |
| 500mg 3hrs (test B ) | 35915 | 18 | 1995 | 6 | 5986 |
| 1g 5hr (A test)*** | 11271 | 12 | 939 | 4 | 2818 |
| 1g 3hr (B test) | 141763 | 6 | 23627 | 2 | 70882 |
| 1g 3hr (C test) | 190470 | 18 | 10582 | 6 | 31745 |

*** bubble removal and non bubble removal combined

**Test A:** Teva test replication, shaker, 50°C bath, 5 hours, whithout draw.
**Test B:** 23° C, 3 hours, shaker, draw 5ml + bubble removal.
**Test C:** 23° C, 3 hours, shaker, withdrawal of 5ml drug after 6 ml drawal than correct to 5ml (Dose correction) + bubble removal (4ml)

Table 2: Experimental Conditions and Final Results of 23 Experiments with Tevadaptor Used on Cyclophosphamide medication Vials

| Test # | Original Tevadaptor test replication | Duration (hours) | Bath temperature | Modification of original test | Contamination on vial and inside reactor glass container (nanogram) | Contamination inside tube (nanogram) | Contamination in cold trap (nanogram) |
|---|---|---|---|---|---|---|---|
| 1 | Yes (type A) | 5 | 50°C | - | 1144 | 13 | 77 |
| 2 | Yes (type A) | 5 | 50°C | - | 1924 | 50 | 62 |
| 3 | Yes (type A) | 5 | 50°C | - | 3069 | <1 | <1 |
| 4 | Yes (type A) | 5 | 50°C | - | 481 | 259 | 151 |
| 5 | Yes (type A) | 5 | 50°C | - | 4428 | 56 | 334 |
| 6 | Yes (type A) | 5 | 50°C | - | 2238 | 53 | 202 |
| 7 | Yes (type A) | 5 | 50°C | - | <1 | 128 | 147 |
| 8 | Modified | 3 | 23°C | Draw 5ml type B | 18468 | 130 | 37 |
| 9 | Modified | 3 | 23°C | Draw 5ml type B | 316 | <1 | <1 |
| 10 | Modified | 3 | 23°C | Draw 5ml type B | 5760 | 9 | 43 |
| 11 | Modified | 3 | 23°C | Draw 5ml type B | 135792 | 115 | 44 |
| 12 | Modified | 3 | 23°C | Draw 5ml type B | 551 | <1 | 42 |
| 13 | Modified | 3 | 23°C | Draw 5ml type B | 9776 | 31 | 38 |
| 14 | Modified | 3 | 23°C | Draw 5ml type B | 2707 | 19 | <1 |
| 15 | Modified | 3 | 23°C | Draw 5ml type B | 3763 | 39 | <1 |
| 16 | Modified | 3 | 23°C | Draw 5ml type C | 5460 | 9 | 31 |
| 17 | Modified | 3 | 23°C | Draw 5ml type C | 8624 | 11228 | 38 |
| 18 | Modified | 3 | 23°C | Draw 5ml type C | 47656 | 17 | 2436 |
| 19 | Modified | 3 | 23°C | Draw 5ml type C | 110022 | 206 | 977 |
| 20 | Modified | 3 | 23°C | Draw 5ml type C | 833 | 19 | 410 |
| 21 | Modified | 3 | 23°C | Draw 5ml type C | 2402 | 30 | 73 |
| 22 | Positive control | 5 | 50°C | Needle instead vial adaptor | 35946 | 59 | 562 |
| 23 | Negative control | NA | NA | Sample all vials | <1 | | |

Type A replication of original test

Type B modification of original test: draw 4ml, push 4ml back do discard bubbles, pull 5ml.

Type C modification of original test: draw 4ml, push 4ml back do discard bubbles, pull 6ml, push 1ml to correct the final dose to 5ml.