510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY TEMPLATE

A. 510(k) Number:

K042970

B. Purpose for Submission:

New collection and transport culture medium device (system)

C. Measurand:

N/A

D. Type of Test:

Non-propagating Transport Device with culture medium

E. Applicant:

Copan Diagnostics, Inc., 2175 Sampson Avenue, Suite 124, Corona, CA 92879

F. Proprietary and Established Names:

Proprietary Name: Copan Universal Transport Medium (UTM-RT) System; Common/Usual Name: Transport Culture Medium Devices; Classification Name: Transport Culture Medium Devices

G. Regulatory Information:

1. Regulation section:

   21 CFR 866.2390

2. Classification:

   I

3. Product code:

   JSM

4. Panel:

   Microbiology (83)

H. Intended Use:

1. Intended use(s):

   Copan Universal Transport Medium (UTM-RT) System is intended for the collection and transport of clinical specimens containing viruses, chlamydiae, mycoplasma or ureaplasma from the collection site to the testing laboratory.

2. Indication(s) for use:

   UTM-RT can be processed using standard clinical laboratory operating procedures and is indicated for transport and collection of viral, chlamydial, mycoplasma and ureaplasma culture.

3. Special conditions for use statement(s):

   Prescription use (Part 21 CFR 801 Subpart D)

4. Special instrument requirements:

   N/A

I. Device Description:

Copan Universal Transport Medium (UTM-RT) System is a transport culture medium intended for collection and transport of clinical specimens containing viruses, chlamydia, mycoplasma or ureaplasma from the collection site to the testing laboratory. Copan UTM-RT System includes a plastic screw-cap tube with conical bottom containing transport medium (1.5, 3, or 10 ml) and three 3 mm size glass beads. UTM-RT System tubes can be supplied alone, or in a kit with one of six possible collection swab options in a sterile peel pouch which facilitate the collection of specimens from various sites on a patient:

- One regular size plastic shaft swab with polyester fiber tip
- Two regular size plastic shaft swabs with polyester fiber tips
- One regular size plastic shaft swab and one Minitip plastic shaft swab pre-scored for easy breakage, both with polyester fiber tips
- One Minitip plastic shaft swab with polyester fiber tip pre-scored for easy breakage
- One Combo stainless steel wire-plastic shaft Minitip swab with polyester fiber tip
- One regular size plastic shaft swab and one Combo stainless stell wire-plastic shaft Minitip swab, both with polyester fiber tips.

Copan UTM-RT medium is stable at room temperature and consists of: Hank's balanced salt solution, bovine serum albumin, L-cysteine, gelatin, sucrose, L-glutamic acid, HEPES buffer, phenol red, sucrose, vancomycin, amphotericin B, and colistin. The medium is isotonic and non-toxic to mammalian host cells.

Tubes of Copan UTM-RT System medium can be used for transporting scrapings, vesicle aspirates, and small pieces of tissue and stool samples. UTM-RT can be processed using standard clinical laboratory operating procedures for viral, chlamydial, mycoplasma and ureaplasma culture.

The survival of viruses, chlamydiae, mycoplasma and ureaplasma depends on many factors including the type and concentration of the microorganism, duration of transport and storage temperature. For optimum sample viability, it should be transported directly to the laboratory and preferably cultured within 24 hours of collection. If immediate delivery is not possible, specimens should be refrigerated (2-8^{o}C); if freezing is required - snap-freeze in slurry of dry ice and acetone and place at -70^{o}C.

J. Substantial Equivalence Information:

1. Predicate device name(s):

   - Multi-Microbe Collection & Transport System, M4 Medium, MicroTest Inc.
   - MicroTest^{TM} Multi-Microbe Collection & Transport System, M4 Medium, REMEL - Apogent [Covered by the same 510(k) due to acquisition of MicroTest Inc. by REMEL-Apogent]

2. Predicate 510(k) number(s):

   K910526

3. Comparison with predicate:

   Copan Universal Transport Medium (UTM-RT) System products are substantially equivalent to the predicate transport medium devices. The Copan UTM-RT System product and the predicate devices are similar in design, intended use, and overall function.

   The Copan and predicate devices are single-use products intended for the collection and transport of clinical specimens containing viruses, chlamydiae, mycoplasma and ureaplasma. Both the Copan and predicate device(s) are offered in product configurations with medium supplied alone or in kit formats with medium and specimen collection swab options.

Similarities		
Item	Device	Predicate
Intended Use	Collection and transport of clinical specimens containing viruses, chlamydiae, mycoplasma or ureaplasma	Same
Single-use Device	Yes	Yes
Medium Formulation	Hank's Balanced Salt Solution Bovine Serum Albumin L-cysteine Gelatin Sucrose L-glutamic acid HEPES buffer Vancomycin Amphotericin B Colistin Phenol red	Hank's Balanced Salt Solution Bovine Serum Albumin Gelatin Sucrose Glutamic acid HEPES buffer Vancomycin Amphotericin B Colistin Phenol red Cryoprotectants
pH	7.3 $\pm$ 0.2	7.3 $\pm$ 0.2
Storage Temperature	2 - 25^{o}C (refrigerated and room temperature)	2 - 8^{o}C (refrigerated)
Volume	1.5 ml; 3 ml; or 10 ml	3 ml
Glass Beads	3 x 3 mm	2 x 3 mm
Container	Plastic, conical bottom	Same
Product Configuration	Medium Tubes; Kit with Medium Tubes and Swab Options	Same
Swab Tip	Polyester	Dacron (Polyester)
Swab Shaft	Plastic; Stainless Steel - Plastic	Plastic; Stainless Steel
Shelf Life	12 months	12 months

Differences		
Item	Device	Predicate
Medium Formulation	Hank's Balanced Salt Solution Bovine Serum Albumin L-cysteine Gelatin Sucrose L-glutamic acid HEPES buffer Vancomycin Amphotericin B	Similar except: contains cryoprotectants does not contain L-cysteine

Differences		
Item	Device	Predicate
	Colistin Phenol red	
Storage Temperature	2 - 25°C (refrigerated and room temperature)	2 - 8°C (refrigerated)
Volume	1.5 ml and 10 ml, in addition to 3 ml	3 ml only
Glass Beads - Size	3 x 3 mm	2 x 3 mm
Swab Shaft	Plastic; Stainless Steel - Plastic	Plastic; Stainless Steel

K. Standard/Guidance Document Referenced (if applicable):

NCCLS document M40-A (ISBN 1-56238-520-8; ISSN 0273-3099) - Quality Control of Microbiological Transport Systems; Approved Standard

L. Test Principle:

N/A

M. Performance Characteristics (if/when applicable):

Following studies were conducted to evaluate the performance characteristics of the Copan Universal Transport Medium (UTM-RT) System:

- Recovery studies using Copan UTM-RT System and comparative product to determine the ability of the products to maintain viability of various strains of viruses, chlamydiae, mycoplasma and ureaplasma during storage and use.
- Stability testing on aged Copan UTM-RT products to support the 12-month expiration date.
- Viability studies were performed using Copan UTM-RT with a variety of viruses, chlamydiae, mycoplasma and ureaplasma. Swabs accompanying each transport system were directly inoculated in triplicate with 100µl of organism suspension. Swabs were then placed in their respective transport medium tubes and held for 0, 24 and 48 hours at either 4°C or room temperature (20-25°C). At the appropriate time interval, each swab was vortexed, removed from its transport medium tube, and aliquot of this suspension was inoculated into shell vials or into appropriate culture media. All cultures were processed by standard laboratory culture technique, and examined after a specified incubation time. Organism viability was determined by fluorescing foci counts for viruses and chlamydia strains and by CFU counts for mycoplasma and ureaplasma strains. Evaluated organisms: Adenovirus, Cytomegalovirus, Echovirus Type 30, Herpes Simplex Virus Type 1, Herpes Simplex Virus Type 2, Influenza A, Parainfluenza 3, Respiratory Syncytial Virus, Varicella Zoster Virus, Chlamydia pneumoniae, Chlamydia trachomatis, Mycoplasma hominis,

Mycoplasma pneumoniae and Ureaplasma urealyticum.

1. Analytical performance:

   a. Precision/Reproducibility:

   N/A

   b. Linearity/assay reportable range:

   Recovery:

   Recovery studies were performed on Copan UTM-RT System and predicate to determine maintenance of viability of various strains of viruses, chlamydiae, mycoplasma and ureaplasma during storage and use.

   The panel of organisms used in testing was chosen to reflect organisms normally encountered in typical microbiology lab; holding temperatures and time intervals for swab culturing reflect conditions encountered in routine clinical use.

   Test organisms:
   - Viruses:
     - Adenovirus
     - Cytomegalovirus (CMV)
     - Echovirus Type 30 (Echo 30)
     - Herpes Simplex Virus Type 1 (HSV1)
     - HSV2
     - Influenza A
     - Parainfluenza Type 3
     - Respiratory Syncytial Virus (RSV)
     - Varicella Zoster Virus (VZV)
   - Chlamydiae:
     - Chlamydia pneumoniae Strain CM-1
     - Chlamydia trachomatis Type 1 Strain UW-12/UR
   - Mycoplasma:
     - Mycoplasma hominis
     - Mycoplasma pneumoniae
   - Ureaplasma:
     - Ureaplasma urealyticum

   Virus inoculum was prepared using standard clinical laboratory procedures for viral culture; harvested viral cells were combined into a new tube labeled as Neat Virus Stock Suspension (NVSS). Quantitation was performed using a series of 2- or 10-fold dilutions of each NVSS. 200µl of each NVSS dilution inoculated into shell vial cell cultures, incubated specified time, coverslips were removed and stained using either Direct Immunofluorescent Antibody (FDA) or Indirect Immunofluorescent

Antibody (IFA) staining for particular virus species. The number of infectious virus particles per 200 µl was established for each NVSS by counting the number of fluorescent foci of infected cells on coverslip monolayers visualized and illuminated using appropriate fluorescent microscope (protocols and results of comparative evaluation using viruses are given in Appendices E-1 through E-9, and E-15 of the submission).

Comparative viability study: The Copan UTM-RT System and predicate system were challenged with 2 dilutions of each NVSS, determined in quantitative assay (described above) for each virus. Two empirically chosen dilutions were close to the dilution of the NVSS that demonstrated infectivity in ~50% of the cells in quantitative assay; therefore, there was sufficient viral load at the beginning to measure decline of viral viability over holding time. 100 µl of each chosen NVSS dilution was dosed on a swab tip and immediately placed in Copan or predicate transport medium. This was done in triplicate for each dilution, each holding time point (0, 24, 48, 72, and 96 hours), and both RT (20-25^{o}C) and 4^{o}C.
Holding time up to 96 hours was set up to determine the extent of endpoint viability for both Copan and the predicate systems. Viability data beyond 48 hours is maintained on file, but is not reported in Package Insert.

Chlamydiae evaluation: Test strains (ATCC reference strains) were inoculated and grown in an appropriate cell line using standard clinical laboratory operating procedures for chlamydial culture. After 72 hours incubation, chlamydial cultures were detected and confirmed using a specific fluorescent staining technique; harvested and combined into a new tube labeled as Neat Chlamydia Stock Suspension (NCSS). Quantitation was performed using a series of 10-fold dilutions of each NCSS. Then 200µl of each 10-fold NCSS dilution was inoculated into shell vial cell cultures, incubated at specified times, coverslips were removed and stained using organism specific fluorescent antibody staining technique. The number of infectious Chlamydia particles per 200 µl was established for each NCSS by counting the number of infected cells with fluorescing cytoplasmic inclusions on coverslip monolayers, visualized and illuminated using appropriate fluorescent microscope.

Comparative viability study with different chlamydial cultures: The Copan UTM-RT System and the predicate system were challenged with 2 dilutions of each NCSS, determined in the quantitative assay (described above); there was sufficient chlamydia organism load at the start of each experiment to measure decline of viral viability over holding time. Then 100 µl of each chosen NCSS dilution was dosed on a swab tip and immediately placed in Copan or the predicate transport medium. This was done in triplicate for each dilution, each holding time point (0, 24, 48, 72, and 96 hours), and both RT (20-25^{o}C) and 4^{o}C.
Holding time up to 96 hours was set up to determine the extent of endpoint viability for both Copan and the predicate systems. Viability data beyond 48 hours is maintained on file, but is not reported in the Package Insert.

Mycoplasma and **Ureaplasma** evaluation: Fresh lyophilized preparations of each test organism (ATCC reference strains) were propagated using specified broth culture media and incubation conditions as described in the manufacturer's PI. Neat organism suspensions were labeled either Neat Mycoplasma Stock Suspension (NMSS) or Neat Ureaplasma Stock Suspension (NUSS). Comparative viability studies were performed using a neat (undiluted) and 10^{-1} or 10^{-2} diluted new broth suspensions.

Comparative viability study: The Copan UTM-RT System and predicate system were challenged with 2 dilutions of each NMSS and NUSS. 100 µl of NMSS and NUSS and 10^{-1} or 10^{-2} dilution were dosed on each swab tip and immediately places in Copan or predicate transport medium. This was done in triplicate for each dilution, each holding time point (0, 24, 48, 72, and 96 hours), and both RT (20-25^{o}C) and 4^{o}C. Results were analyzed by counting colony forming units (CFU) on each test plate under appropriate microscope.
Holding time up to 96 hours was set up to determine the extent of endpoint viability for both Copan and predicate systems. Viability data beyond 48 hours is maintained on file, but is not reported in Package Insert.

c. Traceability, Stability, Expected values (controls, calibrators, or methods):

Stability:

Stability testing was performed on aged Copan UTM-RT products to support the 12-month expiration date.

Recovery stability:
Representative organisms used: CMV, HSV2, RSV, *Chlamydia pneumoniae*, and *Mycoplasma pneumoniae*. Test organisms (purchased from ATCC, or another manufacturer - *Mycoplasma pneumoniae*) were inoculated and grown in appropriate tissue cell lines or culture medium using standard clinical laboratory operating procedures for culture. NVSS, NCSS, and NMSS were prepared as in recovery studies above.

Three lots of Copan UTM-RT at the expiration point (12 months after manufacture date) and one lot just 1 month after manufacture date were each challenged with one concentration made from NVSS, NCSS, and NMSS. Then 100 µl of the appropriate concentration of each organism was dosed on each swab tip and immediately placed in Copan transport medium accompanying the swab tip used. This was done in triplicate for each test organism at each holding time point (0, 24, 48, 72, and 96 hours), and both at RT (20-25^{o}C) and 4^{o}C. Results were analyzed as above.
Holding time up to 96 hours was set up to determine the extent of endpoint viability for Copan system for viruses, *Chlamydia pneumoniae*, and *Mycoplasma pneumoniae*. Copan recommends that specimens for viruses, chlamydia, or mycoplasma culture should be transported and cultured within 24 hours after sample collection and placement in UTM-RT medium. The acceptance criteria - the recovery of tested

organisms after 48 hours holding time at both temperatures tested, at 12 and 1 months post-manufacture date - were met for all lots tested.

pH stability:
The pH of the test has been determined as an indicator of product stability, and was tested within 1 month, at 6 and 12 months after manufacture date, on 3 representative lots of UTM-RT medium stored under recommended temperature conditions. At specific time intervals, 10 pieces from each of the 3 lots were removed from storage and medium inside the tube tested using pH meter. For all products, pH was tested within the target pH value 7.3 ± 0.2 .

Visual Examination:
The visual appearance was evaluated on 3 representative lots, to detect any color change, turbidity or precipitation of the medium, within 1 month, after 6 and 12 months of manufacturing date, and was acceptable for all inspected tubes.

Cytotoxicity:

Cytotoxicity testing using an MRC5 cell line, performed on 3 representative medium lots within 1 and at 12 months after manufacturing, resulted in the UTM-RT testing non-toxic for all products tested at each of the time points.

Antibiotic stability:
The activity of antimicrobial agents in UTM-RT medium was evaluated on 3 representative lots of fresh tubes (within 48 hors of manufacturing), and 3 representative lots of 12 month old tubes; all products tested gave acceptable results .

d. Detection limit:

N/A

e. Analytical specificity:

Interference - contamination testing:
Protocol for contamination check for aseptic medium filling performed on UTM-RT medium tubes is provided. 1% of each of 3 lots was examined for turbidity or microbial growth in Thioglycolate and Triptone Soy Broth; if combined number of positives is $\leq$3%, the lot is accepted; if 4-5% tubes are re-incubated additional 4 days, re-checked 7^{th} day, if number unchanged - lot is accepted. If the number of positive is $\geq$6%, the lot is rejected. All lots tested were accepted.

f. Assay cut-off:

N/A

Quality Control:

All lot numbers of the UTM-RT medium are tested for microbial contamination, toxicity to host cells and the ability to maintain viability of desired agents. Procedures for quality control of UTM-RT transport medium and virus culture media are described in publications by the American Society for Microbiology:

- Gleaves et al, 1994, Cumitech 15A, Laboratory Diagnosis of Viral Infections, ASM, Washington, DC
- Warford et al, 1999, Cumitech 19A, Laboratory Diagnosis of Chlamydia trachomatis Infections, ASM, Washington, DC
- Isenberg, 2004, Clinical Microbiology Procedures Handbook, 2nd ed., ASM, Washington, DC

And by NCCLS:

- NCCLS, 2003, Quality Control of Microbiological Transport Systems, Approved Standard M40-A
- NCCLS, 2004, Viral Culture, Proposed Standard M41.

If aberrant quality control results are noted, patient results should not be reported.

2. Comparison studies:

   a. Method comparison with predicate device:

   Refer to comparative recovery studies described in 1.b. above.

   b. Matrix comparison:

   N/A

3. Clinical studies:

   a. Clinical Sensitivity:

   N/A

   b. Clinical specificity:

   N/A

   c. Other clinical supportive data (when a. and b. are not applicable):

   N/A

4. Clinical cut-off**:**

   N/A

5. Expected values/Reference range:

   N/A

N. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

O. Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.