DAKEWE达科为®

September 1, 2021
Shenzhen, China

Statement

Product Name: BioSci® Disposable Virus Sampling Tube

To Whom It May Concern:

We, **Shenzhen Dakewe Bio-engineering Co., Ltd.**, as the manufacturer of above product, hereby certify that:

1. The shelf life for above product is 18 months after the date of manufacture. The stability of above product was established using a real time stability study on a total of three lots, for the product stability report, please refer to ANNEX I - BIOSCI® DISPOSABLE VIRUS SAMPLING TUBE STABILITY RESEARCH DATA.
2. Our stability report have been reviewed by FDA EUA team and our extending shelf life and relabeling our product stock to reflect new shelf life have been approved by FDA EUA team. For the correspondence with FDA, please refer to ANNEX II - CORRESPONDENCE E-MAIL WITH FDA.

Sincerely:

Jiang Wei

Jiang Wei
Deputy General Manager
Shenzhen Dakewe Bio-engineering Co., Ltd.
Date: September 1, 2021

深圳市达科为生物工程有限公司 Shenzhen Dakewe Bio-engineering Co., Ltd.
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BIOSCI® DISPOSABLE VIRUS SAMPLING TUBE STABILITY RESEARCH DATA

Shenzhen Dakewe Bio-engineering Co., Ltd.

August, 2021

Catalogue

1. Summary

This study is to test the performance indicators under predetermined storage and transport conditions to evaluate whether BioSci® Disposable Virus Sampling Tube can meet the requirements of designed researches during the target validity period.

BioSci® Disposable Virus Sampling Tube contains Transport Medium and Disposable Swab(s). Since the shelf life of Disposable Swab has been confirmed to be 3 years, now we study and evaluate the stability of Transport Medium to determine the shelf life of BioSci® Disposable Virus Sampling Tube.

All the stability research experiments are summarized in this report and the specific data and conclusions are as follows.

2. Information

2.1 Lot Number

Transport Medium of BioSci® Disposable Virus Sampling Tube: TVTM2001, TVTM2002, TVTM2003

2.2 Calibrators and Quality Control Products

Positive strains for sterility testing:

Strain Name	Lot Number	Strain Code
Staphylococcus aureus	J03X20200327-2	CICC10145
Escherichia coli	D03X20200327-2	CICC10305

Strains used for bacteriostasis experiments:

Strain Name	Lot Number	Strain Code
Candida albicans	B03X20200327-2	CICC1965
Staphylococcus aureus	J03X20200327-2	CICC10145
Escherichia coli	D03X20200327-2	CICC10305

Organism used for the recovery of viruses, chlamydia, mycoplasma and ureaplasma：

Strain Name	Lot Number	Strain Code
Influenza A	70039566	ATCC® VR-1736
Chlamydia trachomatis	70040857	ATCC® VR-880
Mycoplasma pneumoniae	70030371	ATCC® 15531
Ureaplasma urealyticum	70027980	ATCC® 27618

2.3 Test Instruments

Fluorescence microscope

3. Experimental Methods

3.1 Experimental Design

3.1.1 Real-time stability

The product shall be stored at room temperature. And the designed shelf life is 18 months. The designed shelf life is based on the shelf life of COPAN's similar product No. 346C.

Store three batches of the product under the above conditions and test them at 0 days, 3 months, 6 months, 9 months, 12 months, 15 months, 18 months and 19 months. Performance tests throughout include appearance, pH, sterility test and bacteriostatic test. In the 19th month, the recovery of viruses, Chlamydia, Mycoplasma and Ureaplasma shall be tested, using BioSci transport medium within the validity period as a comparison.

3.1.2 Transport stability

Put the product within the validity period into the carton and store them at 40℃ for 28 days, and simulate drops and collisions once a day, and then test the product. This experiment design is based on the actual transportation situation.

Deal with three batches of the product in accordance with the above conditions and research on performance tests. Performance tests include appearance, pH, sterility test, bacteriostatic test and the recovery of viruses, chlamydia, mycoplasma and ureaplasma.

3.2 Protocol of test

3.2.1 Appearance

The package shall be complete without damage and liquid leakage. The appearance shall be neat and the characters and symbols shall be clear. The Transport Medium should be red and transparent liquid without obvious precipitation.

3.2.2 pH Value

Detect the pH value according *FiveEasyPlus™ FE28 pH meter SOP*. The pH of Transport Medium should be 7.3±0.2.

3.2.3 Sterility test

Perform sterility tests according to the General Principles 1101 - Sterility Test Method of the *Pharmacopoeia of the People's Republic of China* (2020 edition).

(1) Open the clean air conditioning in the microbiological testing laboratory and the ultraviolet lamp of the clean table for sterilization.

(2)Two parallel samples were taken for detection, and 1 mL of the test sample was sucked into FTM medium and TSB medium respectively.

(3)Take one tube of FTM medium and one tube of TSB medium without samples, label them as negative control group.

(4)Take two tubes of FTM media, the one inoculated with *Staphylococcus aureus* working bacteria solution, the other inoculated with *Escherichia coli* working bacteria solution; take three tubes of TSB media, one inoculated with *Staphylococcus aureus* working bacteria solution, one inoculated with *Escherichia coli* working bacteria solution, and one inoculated with *Candida albicans* working bacteria solution; labeled as positive control group.

(5)Results Judgements

a) After the 14-day culture, the positive control group should have bacterial growth, and the negative control group should be clarified. Otherwise, the result will be invalid.

b) All the test groups were clear or turbid, but confirmed aseptic growth, could judge that the test samples met the requirements.

c) If any tube in the experimental group of the test sample is turbid and the bacterial growth is confirmed, could judge that the test sample does not meet the requirements.

3.2.4 Bacteriostasis test

Perform bacteriostasis tests according to the General Principles 1121 - Bacteriostatic Efficacy Test Method of the *Pharmacopoeia of the People's Republic of China* (2020 edition).

(1) Take fresh cultures of *Escherichia coli, Staphylococcus aureus* and *Candida albicans*, dilute10-fold gradient in centrifuge tube with 0.9% sterile sodium chloride solution under aseptic conditions and marked

them well. Then take 10μl of bacterial liquid in diluted centrifuge tube to the corresponding plate for coating (TSA for *Escherichia coli* and *Staphylococcus aureus* and SDA for *Candida albicans*).The numbered centrifugal tubes were stored at 2~8℃, and the TSA spread plate was incubated at 36℃and the SDA spread plate at 25℃ for 24 hours. Counted the number of plate colonies, and the colony concentration of the corresponding dilution tube with the number of colonies ranging from 100 to 1000 was 10^4 to 10^5cfu/mL, and the colony concentration of the third dilution tube ranging from 10^7 to 10^8cfu/mL.

(2)Take the corresponding dilution tubes of *Escherichia coli, Staphylococcus aureus* and *Candida albicans* with the concentration of bacterial solution of 10^7-10^8 cfu/mL, and take 30ul into 3mL Transport Medium. In this way, 10^5-10^6 cfu bacteria are inoculated into each mL of Transport Medium. Make Two parallel control groups for each kind of bacteria and set up positive control group and negative control group (see table below). After inoculation, they are cultured for 24 hours in the dark at 20-25℃.

Strains Name	Parallel	Bacterial Fluid	Test Volume	Inoculated Bacterial
Staphylococcus aureus	1	10^7～10^8	3mL	30ul
	2	10^7～10^8	3mL	30ul
	Negative	/	3mL	30ul0.9%NaCl
	Positive	10^7～10^8	3mL 0.9%NaCl	30ul
Escherichia coli	1	10^7～10^8	3mL	30ul
	2	10^7～10^8	3mL	30ul
	Negative	/	3mL	30ul0.9%NaCl
	Positive	10^7～10^8	3mL 0.9%NaCl	30ul
Candida albicans	1	10^7～10^8	3mL	30ul
	2	10^7～10^8	3mL	30ul
	Negative	/	3mL	30ul0.9%NaCl
	Positive	10^7～10^8	3mL 0.9%NaCl	30ul

(3) After 24 hours of incubation, remove 1 mL of each sample into a culture dish and pour 15 mL to 20 mL TSA medium immediately into the culture dish. After the medium solidified, put it into a constant temperature incubator for culture at 30-35℃, and count after 24 hours of culture.

(4)Result Judgements

a) Colonies in the positive control group grew normally, while in the negative control group grew without colonies, can judge that the experiment is effective.

b) When the experiment is effective, the number of colonies in the experimental group is less than that in the positive control group, can judge that the bacteriostatic efficacy meets the requirements, otherwise it does not meet the requirements.

3.2.5 Recovery of Viruses, Chlamydia, Mycoplasma and Ureaplasma

Influenza A, *Chlamydia trachomatis*, *Mycoplasma pneumoniae*, and *Ureaplasma urealyticum* were chosen for recovery study.

Neat stocks of the above microorganisms were prepared for testing. Two different dilutions of the neat stock suspensions were prepared and, from these, 100 µl were directly inoculated onto swabs in triplicate. The swabs were transferred into the Transport Medium and held at 4℃ for the required amount of time. At key time points following inoculation (0, 72 h), each sample was vortexed after which an aliquot of the suspension was inoculated into suitable culture media. Viability of viruses and chlamydiae was determined by shell vial assay followed by immunostaining and enumeration of fluorescent foci. The viability of mycoplasmas and ureaplasmas was determined using direct culture methods onto appropriate growth media followed by enumeration of colony forming units (CFU). Cultures were processed by standard laboratory techniques and examined following optimal incubation periods.

4. Performance Evaluation Data and Result

4.1 Real-time stability Studies

4.1.1 Appearance

a) The package is complete without damage and liquid leakage;

b) The appearance should be neat and the characters and symbols should be clear.

c) The Transport Medium should be red and transparent liquid without obvious precipitation.

Lot No.	0 months	3 months	6 months	9 months	12 months	15 months	18 months	19 months
TVTM2001	√	√	√	√	√	√	√	√
TVTM2002	√	√	√	√	√	√	√	√
TVTM2003	√	√	√	√	√	√	√	√

4.1.2 pH Value

Lot No.	pH (Repeat test 5 times)							
	0 months	3 months	6 months	9 months	12 months	15 months	18 months	19 months
TVTM2001	7.23	7.26	7.28	7.31	7.34	7.35	7.34	7.41
	7.23	7.24	7.27	7.31	7.34	7.31	7.37	7.35
	7.23	7.24	7.27	7.31	7.32	7.35	7.39	7.32
	7.23	7.24	7.27	7.32	7.35	7.32	7.40	7.39

	7.24	7.25	7.27	7.31	7.35	7.36	7.38	7.34
TVTM2002	7.26	7.28	7.31	7.34	7.36	7.36	7.39	7.34
	7.28	7.29	7.30	7.35	7.36	7.35	7.41	7.40
	7.27	7.28	7.31	7.32	7.38	7.38	7.35	7.41
	7.25	7.29	7.30	7.33	7.36	7.37	7.34	7.36
	7.26	7.27	7.31	7.34	7.36	7.35	7.31	7.38
TVTM2003	7.22	7.24	7.28	7.31	7.35	7.36	7.34	7.31
	7.22	7.24	7.26	7.29	7.35	7.36	7.34	7.39
	7.25	7.24	7.27	7.29	7.32	7.35	7.32	7.42
	7.22	7.24	7.26	7.31	7.35	7.34	7.38	7.34
	7.25	7.25	7.26	7.31	7.33	7.33	7.36	7.37

4.1.3 Sterility Validation

Lot No.	"-" means the test result is negative(sterile); "+" means the test result is positive(with bacterial growth)(2 duplicate tubes)															
	0 months		3 months		6 months		9 months		12 months		15 months		18 months		19 months	
	FTM	TSB	FTM	TSB	FTM	TSB	FTM	TSB	FTM	TSB	FTM	TSB	FTM	TSB	FTM	TSB
TVTM2001	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
TVTM2002	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
TVTM2003	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—

4.1.4 Bacteriostasis Validation

Strain A: *Staphylococcus aureus*

Strain B: *Escherichia coli*

Strain C: *Candida albicans*

Lot No.	"-" means that the test result is negative(completely inhibited); "√" means that the test result meets the requirements, but not completely inhibited; "×" means that the test result does not meet the requirements.																							
	0 months			3 months			6 months			9 months			12 months			15 months			18 months			19 months		
	A	B	C	A	B	C	A	B	C	A	B	C	A	B	C	A	B	C	A	B	C	A	B	C
TVTM2001	-	-	√	-	-	√	-	-	√	-	-	√	-	-	√	-	-	√	-	-	√	-	-	√
	-	-	√	-	-	√	-	-	√	-	-	√	-	-	√	-	-	√	-	-	√	-	-	√

TVTM2002	-	-	√	-	-	√	-	-	√	-	-	√	-	-	√	-	-	√	-	-	√	-	-	√
	-	-	√	-	-	√	-	-	√	-	-	√	-	-	√	-	-	√	-	-	√	-	-	√
TVTM2003	-	-	√	-	-	√	-	-	√	-	-	√	-	-	√	-	-	√	-	-	√	-	-	√
	-	-	√	-	-	√	-	-	√	-	-	√	-	-	√	-	-	√	-	-	√	-	-	√

4.1.5 Recovery of Viruses, Chlamydia, Mycoplasma and Ureaplasma

In the 19th month, the recovery of viruses, Chlamydia, Mycoplasma and Ureaplasma shall be tested, using BioSci transport medium within the validity period as a comparison.

Organism	Dilution of Neat Stock	Storage Time (h)	Incubation Time Prior to Reading	Mean Viability of Test Organism: Foci or CFU Counts with SD	
				BioSci-1*	BioSci-2*
Influenza A (ATCC® VR-1736)	1:10	0	24 hours	342±56	353±67
		72		101±38	132±41
	1:100	0		108±46	101±43
		72		70±32	62±40
Chlamydia trachomatis (ATCC® VR-880)	1:10	0	48 hours	263±55	274±47
		72		200±48	217±51
	1:100	0		91±32	83±24
		72		77±12	72±18
Mycoplasma pneumoniae (ATCC® 15331)	1:500	0	6 days	352±96	349±71
		72		204±47	218±33
	1:1000	0		183±62	196±51
		72		151±23	163±30
Ureaplasma urealyticum (ATCC® 27618)	1:500	0	6 days	432±101	410±94
		72		294±81	278±77
	1:1000	0		203±56	209±71
		72		98±40	104±37

*: BioSci-1 means BioSci Transport Medium stored for 19 months; BioSci-2 means BioSci Transport Medium within the validity period.

4.1.6 Result

The real-time stability test results have been completed completely, the results show that the performance of the products store at room temperature after 19 months met the design requirements.

4.2 Transport Stability Studies

4.2.1 Appearance

a) The package is complete without damage and liquid leakage;

b) The appearance should be neat and the characters and symbols should be clear.

c) The Transport Medium should be red and transparent liquid without obvious precipitation.

Lot No.	40℃	
	0 Day	28 Days
TVTM2001	√	√
TVTM2002	√	√
TVTM2003	√	√

4.2.2 pH Value

Lot No.	pH (Repeatedly test 5 times) at 40℃	
	0 Day	28 Days
TVTM2001	7.23	7.37
	7.23	7.36
	7.23	7.33
	7.23	7.34
	7.24	7.34
TVTM2002	7.26	7.32
	7.28	7.37
	7.27	7.35
	7.25	7.36
	7.26	7.37
TVTM2003	7.22	7.36
	7.22	7.35
	7.25	7.36
	7.22	7.35
	7.25	7.33

4.2.3 Sterility Validation

Lot No.	"-" means the test result is negative(sterile); "+" means the test result is positive(with bacterial growth)(2 duplicate tubes)			
	0 Day		40℃ 28 Days	
	FTM	TSB	FTM	TSB
TVTM2001	—	—	—	—
	—	—	—	—
TVTM2002	—	—	—	—
	—	—	—	—
TVTM2003	—	—	—	—
	—	—	—	—

4.2.4 Bacteriostasis Validation

Strain A : *Staphylococcus aureus*

Strain B : *Escherichia coli*

Strain A : *Candida albicans*

Lot No.	"-" means that the test result is negative(completely inhibited); "√" means that the test result meets the requirements, but not completely inhibited; "×" means that the test result does not meet the requirements.					
	0 Day			40℃ 28 Days		
	A	B	C	A	B	C
TVTM2001	-	-	√	-	-	√
	-	-	√	-	-	√
TVTM2002	-	-	√	-	-	√
	-	-	√	-	-	√
TVTM2003	-	-	√	-	-	√
	-	-	√	-	-	√

4.2.5 Recovery of Viruses, Chlamydia, Mycoplasma and Ureaplasma

Organism	Dilution of	Storage Time	Incubation Time	Mean Viability of Test Organism:

	Neat Stock	(h)	Prior to Reading	Foci or CFU Counts with SD	
				0 Day	40℃ 28 Days
Influenza A (ATCC® VR-1736)	1:10	0	24 hours	360±61	352±74
		72		111±42	103±31
	1:100	0		109±46	117±51
		72		76±24	70±27
Chlamydia trachomatis (ATCC® VR-880)	1:10	0	48 hours	261±67	243±54
		72		208±61	196±53
	1:100	0		97±27	92±31
		72		68±21	61±19
Mycoplasma pneumoniae (ATCC® 15331)	1:500	0	6 days	357±99	346±89
		72		214±51	207±43
	1:1000	0		176±67	182±59
		72		140±34	138±31
Ureaplasma urealyticum (ATCC® 27618)	1:500	0	6 days	421±106	437±97
		72		267±83	229±76
	1:1000	0		200±56	193±67
		72		87±46	80±37

4.2.6 Result

The transport stability test results showed that the performance of the products stored at 40℃ after 28 days, simulated drops and collisions once a day, met the design requirements.

5. Conclusion

The conclusions of the stability studies are as follows:

1) The real-time stability studies were completed within 19 months, and the product appearance, pH value, sterility, bacteriostasis validation, recovery of viruses, chlamydia, mycoplasma and ureaplasma all met the requirements.

2) In transport stability studies, the product is subjected to multiple collisions and drops when placed in the transportation package at 40℃ for 28 days, and the product appearance, pH value, sterility, bacteriostasis validation, recovery of viruses, chlamydia, mycoplasma and ureaplasma all met the requirements.

To sum up, through the stability studies on the Transport Medium, the shelf life and storage conditions of BioSci® Disposable Virus Sampling Tube produced by Shenzhen Dakewe Bio-engineering Co., Ltd. were

obtained as follows:

Storage and transport at room temperature, valid for 18 months.

RE: Re:RE: [EXTERNAL] Some questions about extending the shelf life of notified VTM

From:CDRH-EUA-Templates<COVID19DX@fda.hhs.gov>
TIme:Friday, Aug 20, 2021 6:05 AM
To:黄恩琪<huang_enqi@dakewe.com>
CC:Goodwin, David<David.Goodwin@fda.hhs.gov>; Leung, Lisa<Lisa.Leung@fda.hhs.gov>; GEN2000968@docs.fda.gov<GEN2000968@docs.fda.gov>

Dear Huang,

I am sorry for taking time to reply. I was on vacation last week and am just catching up.

Thank you for providing your stability report with data for your 18 month shelf-life claim.

You may relabel your VTM stock to reflect the 18 month shelf life.

No further documentation is necessary at this time.

Yours,

Grainne

Grainne Tobin

Policy Analyst, Division of Program Operations and Management

OHT7: Office of *In Vitro* Diagnostics and Radiological Health

Office of Product Evaluation and Quality

CDRH/ Food and Drug Administration

From: Huang Enqi <huang_enqi@dakewe.com>
Sent: Wednesday, August 18, 2021 3:19 AM
To: CDRH-EUA-Templates <COVID19DX@fda.hhs.gov>
Cc: Goodwin, David <David.Goodwin@fda.hhs.gov>; Leung, Lisa <Lisa.Leung@fda.hhs.gov>; GEN2000968@docs.fda.gov
Subject: Re:RE: [EXTERNAL] Some questions about extending the shelf life of notified VTM

Dear Grainne,

Sorry a lot for bothering you again. May I know if there are any other documentation needed? Our US clients urgently need our VTM with 18-month shelf life. In order to proceed with production as soon as possible to meet the client's needs, could you please help us to push the reviewing process?

Looking forward to hearing from you.

Yours sincerely,

Huang Enqi | Regulatory Affairs Specialist

Shenzhen Dakewe Bio-engineering Co., Ltd.

Room 702-703, Building No.1 Shenzhen Biomedicine Innovations Industrial Park No.14 Jinhui Road, Kengzi Street Pingshan District, Shenzhen, China

E-mail: Huang_enqi@dakewe.com

---------- Original ----------

From: "黄恩琪"<huang_enqi@dakewe.com>;

Date: Thu, Aug 12, 2021 10:07 PM

To: "CDRH-EUA-Templates"<COVID19DX@fda.hhs.gov>;

Cc: "Goodwin, David"<David.Goodwin@fda.hhs.gov>; "Leung, Lisa"<Lisa.Leung@fda.hhs.gov>; "GEN2000968@docs.fda.gov"<GEN2000968@docs.fda.gov>;

Subject: Re:RE: [EXTERNAL] Some questions about extending the shelf life of notified VTM

Dear Grainne,

I hope you are fine and safe. Sorry for my late reply, the stability report of our VTM is attached for your reference. If there are any questions or if there are any other documentation needed, please feel free to contact me.

Thanks a lot for your patience and cooperation!

Yours sincerely,

Huang Enqi | Regulatory Affairs Specialist

Shenzhen Dakewe Bio-engineering Co., Ltd.

Room 702-703, Building No.1 Shenzhen Biomedicine Innovations Industrial Park No.14 Jinhui Road, Kengzi Street Pingshan District, Shenzhen, China

E-mail: Huang_enqi@dakewe.com

---------- Original ----------

From: "CDRH-EUA-Templates"<COVID19DX@fda.hhs.gov>;

Date: Sat, Aug 7, 2021 06:15 AM

To: "黄恩琪"<huang_enqi@dakewe.com>;

Cc: "Goodwin, David"<David.Goodwin@fda.hhs.gov>; "Leung, Lisa"<Lisa.Leung@fda.hhs.gov>; "GEN2000968@docs.fda.gov"<GEN2000968@docs.fda.gov>;

Subject: RE: [EXTERNAL] Some questions about extending the shelf life of notified VTM

Dear Huang,

I apologize for my slow response to your question. Could you please provide a copy of your revised shelf-life report.

Yours,

Grainne

Grainne Tobin

Policy Analyst, Division of Program Operations and Management

OHT7: Office of *In Vitro* Diagnostics and Radiological Health

Office of Product Evaluation and Quality

CDRH/ Food and Drug Administration

From: Huang Enqi <huang_enqi@dakewe.com>
Sent: Wednesday, July 28, 2021 4:52 AM
To: CDRH-EUA-Templates <COVID19DX@fda.hhs.gov>; CDRH-EUA-Templates <COVID19DX@fda.hhs.gov>
Subject: [EXTERNAL] Some questions about extending the shelf life of notified VTM

Dear Sir/Madam,

We, Shenzhen Dakewe Bio-engineering Co., Ltd., is one of manufacturers that have properly completed the VTM notification process, and now we have some questions:

1. If we **have finished the shelf life evaluation** of our VTM and we **want to extend the product shelf life**, are we required to **notify FDA** and **update the stability evaluation report to FDA**?

2. For the **VTM in stock**, if we want to **extend the 'expiry by'**(eg. change the 'expiry by' from 2021-09-01 to 2021-12-01) **by relabelling them**, is this relabelling acceptable?

Could you please answer these questions for us? It would be greatly appreciated to hearing from you!

Yours sincerely,

Huang Enqi | Regulatory Affairs Specialist

Shenzhen Dakewe Bio-engineering Co., Ltd.

Room 702-703, Building No.1 Shenzhen Biomedicine Innovations Industrial Park No.14 Jinhui Road, Kengzi Street Pingshan District, Shenzhen, China

E-mail: Huang_enqi@dakewe.com