FEEDBACK

Investigation into the removal of challenge fluid from a membrane by steam sterilisation following aerosol integrity testing using VAL*AIR*DATA.

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Apr. '96 **No. F44**

SUMMARY

This test report shows that following integrity testing of a PTFE membrane with 20 times the concentration of aerosol used during a standard VALAIRDATA test, no detectable challenge fluid remains on the membrane after a single steam sterilisation.

The amount of challenge fluid used during the test is also shown to be around 1000 times less than that which the PTFE membrane sterile air cartridge (ZCHT-AZ) would be exposed to during a typical 7 day fermentation run, if a typical prefilter system was used prior to the sterile air cartridge.

INTRODUCTION

The principle of aerosol testing sterile air cartridges has been well received by customers because of the many practical advantages over liquid based integrity test methods. Of the many questions raised about the aerosol test, one which was being constantly voiced was that of challenge fluid remaining on the membrane of the cartridge following integrity testing. During the development stages of the VALAIRDATA work was carried out which demonstrated there was no increase in the differential pressure at the rated flow of the cartridge following repeated integrity testing and steam sterilisation. However, a number of customers now require further quantification of the amount of challenge fluid, if any, remaining on the membrane. The purpose of this test is to show that all the challenge fluid is removed following a standard steam sterilisation procedure of 121°C for 30 minutes.
A system was constructed as shown in Appendix 2. Various discs of PTFE were challenged in this rig to determine:-

METHOD

a) Background contamination of system (samples M1 and M2)

b) Actual challenge level presented to the discs of PTFE membrane (samples M6 and M7)

c) Once challenged the discs were then steam sterilised once at 121°C for 30 minutes

The contamination level for each of these was then determined using laser spectrometry, which can identify the specific absorbance characteristics of *Shell Ondina EI* challenge fluid (see Appendix 2 for absorbance characteristic).

A fuller description of the test method is available in a separate test report.
Determination of the calculation of results shown is given in Appendix 2.

RESULTS

Within the sensitivity of the test procedure (i.e. ≥2µg/ml) no challenge fluid was detected.

DISCUSSION

The challenge level used was between 662-782µg and this was 20 times higher per unit area of membrane than the normal test concentration.

As the background level was between 255-275µg, this shows that in comparison to the system the test adds little contamination (i.e. µg per test), and anything that is added is not detectable after steam sterilisation.

Most prefiltration in use today falls into three categories for oil removal based on the greatest allowable remaining oil content. These are:-

Quality Class ISO/DIS 8573.1	Oil (including vapour) mg/m^3
1	0.01
2	0.1
3	1.0
4	5
5	25

Taking the cleanest quality class with a maximum remaining oil content of 10µg/m^3 a 5" sterile air cartridge (e.g. ZCHT-AZ) would process approximately 8000m^3 of air during a typical 7 day fermentation with a total oil content of 80mg.

The amount of challenge fluid deposited during an integrity test is therefore negligible.

APPENDIX 1 - RESULTS

SYSTEM BACKGROUND OIL CONTENT (Condensate)

Sample ID	Description	Vol of Condensate (ml)	Test Vol (ml)	Solvent Vol (ml)	IR% Transmission I_0	I_1	I_2	I_3	Absorbance	Total Oil in Solvent µg/ml	Oil Content µg
M1	Unchallenged Upstream	60	50	25	98.43	80.71	82.36	86.14	0.211	9.19	275
	Unchallenged Downstream	45	45	25	99	93	91.61	94.11	0.0628	3.6	90
M2	Unchallenged Upstream	45	45	25	94.95	78	77.79	84.21	0.235	10.22	255
	Unchallenged Downstream	50	50	25	99.33	93.89	92.94	94.33	0.759	3.30	82

RESIDUAL OIL CONTENT ON PTFE MEMBRANE

Sample ID	Solvent Volume (ml)	I.R.% Transmission I0	I1	I2	I3	Absorbance	Oil Solvent µg
M3	25	Not Detectable				N/A	<2µg/ml
M4	25	Not Detectable				N/A	<2µg/ml
M5	25	Not Detectable				N/A	<2µg/ml
M1	25	Not Detectable				N/A	<2µg/ml
M2	25	Not Detectable				N/A	<2µg/ml

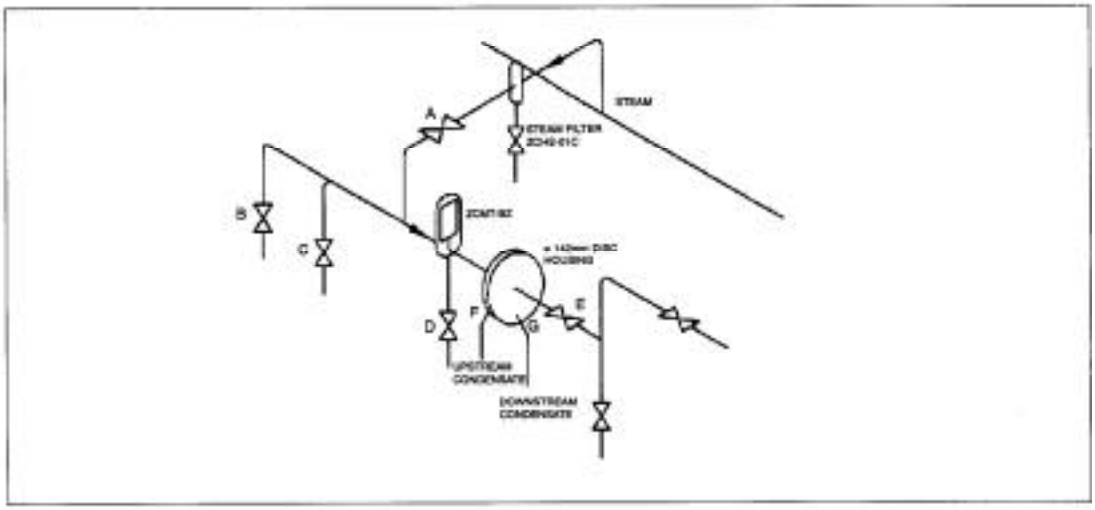
DETERMINATION OF AEROSOL CHALLENGE LEVEL

Sample ID	Solvent Volume	I.R.% Transmission I0	I1	I2	I3	Absorbance	Oil Solvent µg
M6	25	100	65.3	43.89	66.6	31.37	782
M7	25	100	72.5	51.5	72.5	26.49	662

APPENDIX 2

1) Challenge Rig Diagram
2) Calculation of Oil Content
3) Absorbance Characteristic Shell Ondina EI

STERILISATION PROCEDURE



START- Closed A, B, C, D & E
Cracked Open F & G

1) Open valves C & D fully.
2) Open valve A. Condensate drains from C & D.
3) When free steam exits, close C & D to cracked position.
4) The pressure then increases to 1 bar with the upstreamand downstream condensate of the disc under test draining into clean duran bottles.
5) Steam for 30 minutes @ 121°C.

Note: Between each test the empty rig is steamed for 10 minutes.

CALCULATION OF OIL CONTENT

The oil content is determined by taking the absorbance level at the three specific wavelengths as a faction of the 100% transmission and dividing this by the oil coefficient.

The oil coefficient for Shell Ondina is 0.023 and is determined by obtaining traces at various dilutions of oil/solvent beginning with 0.1 grammes/100ml of solvent.

The formula is as follows:- $\text{Absorbance} = \ln_{10} \frac{I_0^3}{I_1 \times I_2 \times I_3}$

Where I_0 is the base line absorbance, I_1, I_2 and I_3 are the absorbance at the specific wavelengths.

The oil content is then calculated by:- $\frac{\text{Absorbance}}{\text{Oil Coefficient}}$

Which gives a result in μg/ml of solvent used to extract the oil from the sample.

Example 1 - Residual Oil on PTFE Discs

From graph M6 PTFE:

I_0 = 100%
I_1 = 65.3%
I_2 = 66.6%
I_3 = 43.89%

The absorbance is given by:- $\ln_{10} \frac{(I_0^3)}{(I_1 \times I_2 \times I_3)}$

Absorbance = $\ln_{10} \frac{(100^3)}{(66.6 \times 65.3 \times 43.89)}$

= 0.719

The amount of oil in μg/ml is given by:- $\frac{\text{Absorbance}}{\text{Oil Coefficient}} = \frac{0.719}{0.023} = 31.26 \mu g/ml$

The sample disc was placed in 25ml of solvent therefore the total amount of oil deposited onthe disc was 25 x 31/26 = 781μg.

Example 2 - Residual Oil in Condensate

From graph M2 upstream:

I_0 = 94.95%
I_1 = 76.00%
I_2 = 77.79%
I_3 = 84.21%

$\ln_{10} = \frac{I_0^3}{I_1 \times I_2 \times I_3}$ $\ln_{10} \frac{94.95^3}{76 \times 77 \times 79 \times 84.21}$

= <u>0.235</u>

Oil Content in Solvent = $\frac{0.235}{0.023} = 10.22 \mu g/ml$

Total Condensate Collected = 45ml

Test Volume = 45ml

Therefore Total Oil in Condensate = $\frac{45 \times 25 \times 10.22}{45}$

= <u>255μg</u>

ABSORBANCE CHARACTERISTICS OF SHELL ONDINA EL