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Final Report For Protocol Number: 02-11139-01 Certification of Pall Filters for use with Zymark TPWII and Zymark Multidose

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Certification of Pall Filters for use with Zymark TPWII and Zymark Multidose

1. PURPOSE

This document summarizes the results obtained after following Protocol No. 02-11139-01, "Certification of Pall Filters for use with Zymark TPWII and Zymark Multidose."

Lancaster Laboratories performed the certification of filters for Pall Life Sciences. The certification of the filters was executed according to the methods stated in Protocol No. 02-11139-01.

2. MATERIALS AND EQUIPMENT

The following filters were submitted to Lancaster Laboratories by Pall Life Sciences for certification for use with Zymark automated instrumentation.

1. AP-4527 Glass Pre-filter only
2. AP-4305 Glass over 0.2um GHP
3. AP-4557 Glass over 0.45um GHP
4. AP-4548 Glass over 0.45um Nylon
5. AP-4301 Glass over 0.45um PTFE
6. AP-4357 0.45um GHP
7. AP-4517 0.45um Nylon
8. AP-4520 0.2um PTFE
9. AP-4518 0.45um PTFE
10. AP-4587 0.45um IC (PES)
11. AP-4498 0.45um HT Tuffryn
12. AP-4190 0.8um Versapor

According to Protocol No. 02-11139-01, testing is also prescribed for filters AP-4364 0.2um GHP and AP-4437 0.2um Nylon. These filters were not tested because they were unavailable, and not submitted to Lancaster Laboratories for testing.

According to Section 2.3 of Protocol No. 02-11139-01, the PTFE filters, stated above, were not scheduled for the filtration of media by the Zymark Multidose. PTFE filters (hydrophobic) are not appropriate for the filtration of dissolution media.

The following equipment was used at Lancaster Laboratories for certification of filters for use with Zymark TPWII:

1. Zymark TPWII (Equip # 7273) w/ Controller (Equip # 8418) - Protocol Section 1.1-1.4
2. Zymark TPWII (Equip # 8417) w/ Controller (Equip # 8419) - Protocol Section 1.5
3. Analytical Balance – Mettler AT261 (Equip #5680)
4. 50g Calibration Weight (S/N 38143)

The following reagents were used at Lancaster Laboratories for certification of filters for use with Zymark TPWII:

1. Purified Water – Unit #7134
2. 2-Propanol – JT Baker/HPLC Solvent/Lot#X22H03

The following equipment was used at Lancaster Laboratories for certification of filters for use with Zymark Multidose:

1. Zymark Multidose Plus (S/N MD9927N4237) with Multifill (S/N MF9927N4178) attached to dissolution bath (ID MD002) which is a VanKel 7000.
2. Analytical Balance – Mettler AT261 (ID#8421) and Mettler AT250 (ID#4357)
3. Thermometer (digital) (ID# DT017/DP073 and ID# DT003/DP076)

The following reagents were used at Lancaster Laboratories for certification of filters for use with Zymark Multidose:

1. Purified Water – Unit #5139

3. EXPERIMENT

Each type of filter that was submitted to Lancaster Laboratories for automation certification on the Zymark TPWII was tested according to the following procedure. For each type of filter submitted, 9 filters were tested under the "Filter Holder" diagnostic. This diagnostic tested the following functions: filter dispensing, detection by the robot finger blocks, filter position in the filter holder, and filter discard. For each type of filter submitted, 8 filters were also tested by filtering a suitable solvent using an automated method on the TPWII. This

automated method was defined in Protocol No. 02-11139-01, using default TPWII filtration parameters. Filtration of such solvents was performed to test the performance of the filter when used in conjunction with the TPWII.

Each type of filter that was submitted to Lancaster Laboratories by automation certification on the Zymark Multidose was tested according to the following procedure. For each type of filter submitted, 6 filters were tested under the "Filter Holder" diagnostic. This diagnostic tested the following functions: filter dispensing, filter position in the filter holder, and filter discard. For each type of filter submitted, 24 filters were also tested by filtering purified water using an automated method on the Multidose. This automated method was defined in Protocol No. 02-11139-01. Filtration of purified water was performed to test the performance of the filter when used in conjunction with the Multidose.

4. RESULTS

4.1 Zymark TPWII Filter Dispensing

The results are summarized in Table 1.

Table 1.

Filter Type	Observation 1	Observation 2	Observation 3
AP-4527 Glass Pre-filter only	9 of 9 pass	9 of 9 pass	9 of 9 pass
AP-4305 Glass over 0.2um GHP	9 of 9 pass	9 of 9 pass	9 of 9 pass
AP-4557 Glass over 0.45um GHP	9 of 9 pass	9 of 9 pass*	9 of 9 pass
AP-4548 Glass over 0.45um Nylon	9 of 9 pass	9 of 9 pass*	9 of 9 pass
AP-4301 Glass over 0.45um PTFE	9 of 9 pass	9 of 9 pass	9 of 9 pass
AP-4357 0.45um GHP	9 of 9 pass	9 of 9 pass	9 of 9 pass
AP-4517 0.45um Nylon	9 of 9 pass	9 of 9 pass	9 of 9 pass
AP-4520 0.2um PTFE	9 of 9 pass	9 of 9 pass	9 of 9 pass
AP-4518 0.45um PTFE	9 of 9 pass	9 of 9 pass*	9 of 9 pass
AP-4587 0.45um IC (PES)	9 of 9 pass	9 of 9 pass	9 of 9 pass
AP-4498 0.45um HT Tuffryn	9 of 9 pass	9 of 9 pass	9 of 9 pass
AP-4190 0.8um Versapor	9 of 9 pass	9 of 9 pass	9 of 9 pass

Observation 1 = The filters are dispensed from the filter turret without jamming.

Observation 2 = The filters are dispensed down the filter ramp properly.

Observation 3 = The filters are sensed by the filter dispenser potentiometer when in the pickup position.

* For the above noted filters/observations, 1 out of the 9 filters tested came down the filter dispensing ramp and was positioned slightly out of alignment at the end of the ramp (in the filter pick-up position). Therefore the sensor did not detect this filter. The filter turret continued to turn, dispensing a second filter. This second filter bumped the first filter into the correct filter pick-up position, which was then detected by the sensor. This first filter was picked up correctly by the finger block and the "Filter Holder" diagnostic continued without interruption. The second filter then moved down into the filter pick-up position and was detected by the sensor. The filter dispensing process was not interrupted, and the TPWII continued to function without error. Therefore this observation was not noted as a failure.

4.2 Zymark TPWII Detection of the Filter by the Robot Finger Blocks

The results are summarized in Table 2.

Table 2.

Filter Type	Observation 4	Observation 5	Observation 6
AP-4527 Glass Pre-filter only	9 of 9 pass	9 of 9 pass	9 of 9 pass
AP-4305 Glass over 0.2um GHP	9 of 9 pass	9 of 9 pass	9 of 9 pass
AP-4557 Glass over 0.45um GHP	9 of 9 pass	9 of 9 pass	9 of 9 pass
AP-4548 Glass over 0.45um Nylon	9 of 9 pass	9 of 9 pass	9 of 9 pass
AP-4301 Glass over 0.45um PTFE	9 of 9 pass	9 of 9 pass	9 of 9 pass
AP-4357 0.45um GHP	9 of 9 pass	9 of 9 pass	9 of 9 pass
AP-4517 0.45um Nylon	9 of 9 pass	9 of 9 pass	9 of 9 pass
AP-4520 0.2um PTFE	9 of 9 pass	9 of 9 pass	9 of 9 pass
AP-4518 0.45um PTFE	9 of 9 pass	9 of 9 pass	9 of 9 pass
AP-4587 0.45um IC (PES)	9 of 9 pass	9 of 9 pass	9 of 9 pass
AP-4498 0.45um HT Tuffryn	9 of 9 pass	9 of 9 pass	9 of 9 pass
AP-4190 0.8um Versapor	9 of 9 pass	9 of 9 pass	9 of 9 pass

Observation 4 = The robot finger blocks pick up the filter from the filter pick-up position.

Observation 5 = The robot finger blocks correctly position the filter in the filter holder.

Observation 6 = The robot finger blocks pick up the filter from the filter holder, delivering the filter to the waste can.

4.3 Zymark TPWII Filter Position in the Filter Holder

The results are summarized in Table 3.

Table 3.

Filter Type	Observation 7	Observation 8	Observation 9	Observation 10
AP-4527 Glass Pre-filter only	9 of 9 pass	9 of 9 pass	9 of 9 pass	9 of 9 pass
AP-4305 Glass over 0.2um GHP	9 of 9 pass	9 of 9 pass	9 of 9 pass	9 of 9 pass
AP-4557 Glass over 0.45um GHP	9 of 9 pass	9 of 9 pass	9 of 9 pass	9 of 9 pass
AP-4548 Glass over 0.45um Nylon	9 of 9 pass	9 of 9 pass	9 of 9 pass	9 of 9 pass
AP-4301 Glass over 0.45um PTFE	9 of 9 pass	9 of 9 pass	9 of 9 pass	9 of 9 pass
AP-4357 0.45um GHP	9 of 9 pass	9 of 9 pass	9 of 9 pass	9 of 9 pass
AP-4517 0.45um Nylon	9 of 9 pass	9 of 9 pass	9 of 9 pass	9 of 9 pass
AP-4520 0.2um PTFE	9 of 9 pass	9 of 9 pass	9 of 9 pass	9 of 9 pass
AP-4518 0.45um PTFE	9 of 9 pass	9 of 9 pass	9 of 9 pass	9 of 9 pass
AP-4587 0.45um IC (PES)	9 of 9 pass	9 of 9 pass	9 of 9 pass	9 of 9 pass
AP-4498 0.45um HT Tuffryn	9 of 9 pass	9 of 9 pass	9 of 9 pass	9 of 9 pass
AP-4190 0.8um Versapor	9 of 9 pass	9 of 9 pass	9 of 9 pass	9 of 9 pass

Observation 7 = The filter is correctly positioned in the filter holder.

Observation 8 = The filter properly fits into the luer fittings of the filter holder.

Observation 9 = Once the filter holder is closed onto the filter, the measured potential is 0.28-0.70, as measured by the "Filter Holder" diagnostic.

Observation 10 = Once the potential is measured, the filter holder opens properly to release the filter.

4.4 Zymark TPWII Filter Discard

The results are summarized in Table 4.

Table 4.

Filter Type	Observation 11	Observation 12
AP-4527 Glass Pre-filter only	9 of 9 pass	9 of 9 pass
AP-4305 Glass over 0.2um GHP	9 of 9 pass	9 of 9 pass
AP-4557 Glass over 0.45um GHP	9 of 9 pass	9 of 9 pass
AP-4548 Glass over 0.45um Nylon	9 of 9 pass	9 of 9 pass
AP-4301 Glass over 0.45um PTFE	9 of 9 pass	9 of 9 pass
AP-4357 0.45um GHP	9 of 9 pass	9 of 9 pass
AP-4517 0.45um Nylon	9 of 9 pass	9 of 9 pass
AP-4520 0.2um PTFE	9 of 9 pass	9 of 9 pass
AP-4518 0.45um PTFE	9 of 9 pass	9 of 9 pass
AP-4587 0.45um IC (PES)	9 of 9 pass	9 of 9 pass
AP-4498 0.45um HT Tuffryn	9 of 9 pass	9 of 9 pass
AP-4190 0.8um Versapor	9 of 9 pass	9 of 9 pass

Observation 11 = Once the filter holder opens to release the filter, the robot finger picks up the filter.

Observation 12 = The robot arm then delivers the filters into the filter waste container.

4.5 Zymark TPWII Filtration of Solvents

The results are summarized in Table 5.

Table 5.

Filter Type	Solvent	Obs 13	Obs 14	Obs 15	Obs 16
AP-4527 Glass Pre-filter only	Water	8 of 8 pass	8 of 8 pass	8 of 8 pass	8 of 8 pass
AP-4305 Glass over 0.2um GHP	Water	8 of 8 pass	8 of 8 pass	8 of 8 pass	8 of 8 pass
AP-4557 Glass over 0.45um GHP	Water	8 of 8 pass	8 of 8 pass	8 of 8 pass	8 of 8 pass
AP-4548 Glass over 0.45um Nylon	Water	8 of 8 pass	8 of 8 pass	8 of 8 pass	8 of 8 pass
AP-4301 Glass over 0.45um PTFE	2-Propanol:Water (60:40)	8 of 8 pass	5 of 8 pass*	5 of 8 pass*	8 of 8 pass
AP-4357 0.45um GHP	Water	8 of 8 pass	8 of 8 pass	8 of 8 pass	8 of 8 pass
AP-4517 0.45um Nylon	Water	8 of 8 pass	8 of 8 pass	8 of 8 pass	8 of 8 pass
AP-4520 0.2um PTFE	2-Propanol:Water (60:40)	8 of 8 pass	7 of 8 pass*	7 of 8 pass*	8 of 8 pass
AP-4518 0.45um PTFE	2-Propanol:Water (60:40)	8 of 8 pass	8 of 8 pass	8 of 8 pass	8 of 8 pass
AP-4587 0.45um IC (PES)	Water	8 of 8 pass	8 of 8 pass	8 of 8 pass	8 of 8 pass
AP-4498 0.45um HT Tuffryn	Water	8 of 8 pass	8 of 8 pass	8 of 8 pass	8 of 8 pass
AP-4190 0.8um Versapor	Water	8 of 8 pass	8 of 8 pass	8 of 8 pass	8 of 8 pass

Obs 13 = The filter fits into the filter holder properly. Leaking of solvent around the luer holder is not evident.

Obs 14 = At least 80% of the requested volume of filtrate is collected.

* Obs15 = There are no recorded "filter abort" errors as a result of excessive backpressure.

Obs 16 = Filters are successfully dispensed, positioned in the filter holder, and discarded.

* For the above noted filters/observations, the filters did not meet the specific requirements as stated in Observation 14 and Observation 15. Although these filters did not meet the requirements as specifically defined, they are *not* considered as failures. A "filter abort" error is present because 80% of the requested volume of filtrate was not collected. Refer to table below for the actual amount of filtrate collected for these filters with a "filter abort" error. The analyst observed as each filter was tested, and no excessive backpressure or leaking

was evident. This error is likely present due to solvent retention by the filter or by non-optimized TPWII syringe flow rates – both of these factors would be optimized when a project-specific TPWII method is developed. However, in this case, default TPWII filtration parameters were used. Failure to meet the specific requirements of Observation 14 and Observation 15 are considered a function of the TPWII methodology that was used, and *not* a deficiency of the filter. Therefore, these filters are considered suitable for use with the Zymark TPWII workstation.

Table 6. Actual amount of filtrate collected for filters with “filter abort” errors.

Filter Type	% collected of the requested 3mL
AP-4301 Glass over 0.45um PTFE	78%, 78%, 79%
AP-4520 0.2um PTFE	78%

4.6 Zymark Multidose Filter Dispensing / Filter Discard

Results are summarized in table 7.

Table 7.

Filter Type	Obs 1	Obs 2	Obs 3	Obs 4	Obs 5	Obs 6
AP 4527 GxF Glass	6 of 6	6 of 6	6 of 6	6 of 6	6 of 6	6 of 6
AP-4305 GxF/0.2um GHP	6 of 6	6 of 6	6 of 6	6 of 6	6 of 6	6 of 6
AP-4557 GxF/0.45um GHP	6 of 6	6 of 6	6 of 6	6 of 6	6 of 6	6 of 6
AP-4548 GxF/0.45um Nylon	6 of 6	6 of 6	6 of 6	6 of 6	6 of 6	6 of 6
AP-4357 0.45um GHP	6 of 6	6 of 6	6 of 6	6 of 6	6 of 6	6 of 6
AP-4517 0.45um Nylon	6 of 6	6 of 6	6 of 6	6 of 6	6 of 6	6 of 6
AP-4587 0.45um Supor (PES)	6 of 6	6 of 6	6 of 6	6 of 6	6 of 6	6 of 6
AP-4498 0.45um HT Tuffryn	6 of 6	6 of 6	6 of 6	6 of 6	6 of 6	6 of 6
AP-4190 0.8um Versapor	6 of 6	6 of 6	6 of 6	6 of 6	6 of 6	6 of 6

Observation 1: Filters are dispensed from the turret without jamming.

Observation 2: Filters are dispensed down the filter ramp properly.

Observation 3: Used filter pushed to the next position and end filter is discarded.

Observation 4: Filter changing happens 6 successive times.

Observation 5: Filter is correctly positioned in the filter holder.

Observation 6: Filter properly fits into the luer fittings on the filter holder.

4.7 Zymark Multidose Filter Position in the Filter Holder

See observations 5 and 6 in table 7. Position observed as part of the filter dispensing/ filter discard test.

4.8 Zymark Multidose Filtration of Media

The Zymark Multidose was set up with purified water in the auxillary tank. The method was set to dispense 1000mL of the media (heated to 37C) into each of 6 vessels. The multidose was programmed to take samples at 10, 20, 30, and 60 minutes, flushing 15mL through the filters and collecting 1mL of sample. The program specified using one filter for each pull for a total of 24 filters for the entire method. The multidose was programmed to use 12mL per minutes as the flow rate. The one mL sample was dispensed into previously weighed HPLC vials and the volume dispensed was determined by weighing the filled vials and determining the volume by the density (previously determined on the purified water media). The events of the method can be reviewed in the Output1.dat file that is printed for each run on each filter.

The data and observations for each filter is summarized in table 8.

Table 8.

Filter Type	Obs 1	Obs 2	Obs 3	Obs 4
AP 4527 GxF Glass	24 of 24	24 of 24 See NB28693/75	24 of 24	24 of 24
AP-4305 GxF/0.2um GHP	24 of 24	24 of 24 See NB28693/76	24 of 24	24 of 24
AP-4557 GxF/0.45um GHP	24 of 24	24 of 24 See NB28693/77	24 of 24	24 of 24
AP-4548 GxF/0.45um Nylon	24 of 24	24 of 24 See NB28693/79	24 of 24	24 of 24
AP-4357 0.45um GHP	24 of 24	24 of 24 See NB28693/80	24 of 24	24 of 24
AP-4517 0.45um Nylon	24 of 24	24 of 24 See NB28693/81	24 of 24	24 of 24
AP-4587 0.45um Supor (PES)	24 of 24	24 of 24 See NB28693/82	24 of 24	24 of 24

AP-4498 0.45um HT Tuffryn	24 of 24	24 of 24 See NB28693/78	24 of 24	24 of 24
AP-4190 0.8um Versapor	24 of 24	24 of 24 See NB28693/83	24 of 24	24 of 24

Observation 1: filters fit into the filter holder properly and no leaking is evident.

Observation 2: sample collected $\pm 25\%$ of the target volume of 1mL.

Observation 3: there are no "filter abort" errors as a result of excessive back pressure.

Observation 4: filters are successfully dispensed, positioned in the filter holder and discarded.

5. DEVIATIONS

For deviations relating to TPWII testing, refer to observations noted in Sections 4.1 and 4.5 of this document. Although the observations deviated slightly from the requirements as stated in Protocol No. 02-11139-01, the filters that were tested are suitable for use with the Zymark TPWII.

No deviations from the expected and recorded results are noted for the Zymark Multidose filter testing.

6. CONCLUSION

Any deviations noted within this document have negligible impact on the functionality or compatibility of the filter for use with Zymark automated systems. All other testing meets the requirements stated in Protocol No. 02-11139-01. Results indicate that the Pall filters that were tested are suitable for use in conjunction with Zymark TPWII and Zymark Multidose equipment.

DOCUMENTATION

Zymark TPWII "Filter Holder" Diagnostic (Protocol Sections 1.1-1.4)

Notebook 33364 pp. 18-21

Zymark TPWII Filtration of Solvents (Protocol Sections 1.5)

Notebook 33364 pp. 18, 22-25

Zymark Multidose "Filter Holder" Diagnostic (Protocol Sections 2.1-2.2)

Notebook 28693 pp. 73-74

Zymark Multidose Filtration of Media (Protocol Sections 2.3)

Notebook 28693 pp. 74-83