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Protocols for leakage testing

A Microfluidics Association white paper.

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Content

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Introduction

This document is written to serve as a guideline for the testing of microfluidic devices, which are devices designed to manipulate fluids that are confined in a small volume. For instance, a channel with at least one dimension smaller than 1 mm is a microfluidic channel. Practically all designers and manufacturers of microfluidic devices check their devices for leakage. The aim of this document is to provide direction to microfluidic engineers and scientists about when and how to perform leakage testing, a failure mode that is commonly seen in microfluidic devices. In the context of this white paper, leakage is defined as an unintentional outward release of medium to the environment. It is the intention of this group to also create similar documents for internal leakage within or into the microfluidic system. Information about the science behind leakage testing is published elsewhere.[2]

As this document is created with the help from experts working on a diverse range of microfluidic products, it is expected to be applicable for a wide range of microfluidic products. Due to the small amount of medium leaking from these devices, it is more challenging to detect leakage and leakage rate from microfluidic devices compared to leakage from devices with larger internal volumes. These quantitative measurements (e.g., leakage volume, leakage rate) are essential for statistical process control, which is needed to safeguard product quality.

In this paper, we start by discussing the need for specifying leakage. The specification is also tied to the Failure Mode and Effect Analysis (FMEA) for a microfluidic device since the ability to accurately diagnose the leakage impacts the risk associated with the device failure. The FMEA is defined for various aspects of the product lifecycle, such as leakage during storage, transport, and usage of the product. The specifications need to be validated through standard test methods. Possible leakage test methods include visual inspection, liquid pressure drop, air pressure drop, burst pressure testing, loss (gain) of mass, and maximal operational pressure testing. An appropriate selection of these tests, or protocols, should be made during development and production of microfluidic devices. A flowchart to help in the selection of an appropriate protocol is presented as Figure 1. This flowchart considers key operational conditions such as the type of medium, internal pressure, and temperature, as well as safety considerations.

The diversity in microfluidics applications and technologies is too large for using a single all-encompassing test protocol. Rather, this white paper introduces a roadmap for engineers and scientists to follow for developing product specific leakage protocols. This document should not be construed as policy for evaluating microfluidic devices by any regulatory agency. However, it is the intention of the Microfluidics Association (MFA) to eventually translate contents within this white paper into a standard for leak testing specifically intended for microfluidic devices.

[2] Vania Silverio et al., Overcoming Technological Barriers in Microfluidics: Leakage Testing, in: Frontiers in Bioengineering and Biotechnology, 2022, under preparation

How to specify leakage?

To establish the specification for leakage of a microfluidic device, the designer should ask at least two critical questions:

- **Question 1:** Would a leak be dangerous to the user or pose a risk to the environment?
    - **Additional considerations:** If so, then the leakage specification may require a Threshold Limited Value, such as the one used for defining the concentration breathed in air for 5 consecutive eight-hour working days without harmful effects) or similar safety regulations.
- **Question 2:** What amount of leakage will have a negative influence on the performance of the device? This not only depends on the location of the leak (upstream or downstream the sensing area), but also on the function of the device and type of measurement.
    - **Additional considerations:** This depends on the location of the leak relative to the sensing area, as well as function of device and type of measurements. For devices where the measurement is based on reaching an equilibrium between the liquid to be tested and the sensor surface, a primary concern is that enough liquid is in the measurement chamber or flowing through it. With a reservoir of sufficient volume or enough sample, a small leak may be acceptable. The situation is different when the result of the measurement depends on the amount of liquid flowing over the sensor surface, in which case stricter specifications on the allowable leakage may be needed. A similar situation occurs if two different liquids are mixed, such as for a dilution. In that case, a leak can affect the mixing process or dilution ratio.

Malfunctioning risk analysis / FMEA for microfluidic devices

Given the commonality of leaks in microfluidic devices, and given risk features as one of the top most reasons for specifying leakage, a bottom-up approach that FMEA can offer may be most meaningful approach when developing a new device or changing a device design. Assuming that the leakage poses medium to high risk, a risk analysis can alleviate concerns with the risk or potentially eliminate it through design change/production improvement programs or a test/visual inspection mitigation strategy. An example risk analysis table is shown in Table 1. The elements in Table 1 are not expected to be all inclusive and are provided in the order in which they should be considered while developing a device. The identified actions may require further analysis or corrective and preventative actions especially if the risks are found to be unacceptable. The severity, probability and detection are represented by a number on the scale of 1:10, and the product of these numbers indicates the risk priority.

Table 1. FMEA for Microfluidic Devices

	Topic	Potential Failure Mode	Effect / severity (S: 1-10)	Potential Causes / Mechanisms / probability (P: 1-10)	Test / visual inspection /observable Effect of Failure Detection (D: 1-10)	Risk priority number S*P*D	Improvement / prevention actions	Actions taken for further Investigation
Materials	General	Delamination	Leakage / 6	Corrosion / 5	Visual inspection / 5	150	Selection of appropriate materials, limit exposure time	
	Polymer devices	Delamination	Leakage / 6	Contaminati on/ 4	Visual inspection / 1	24	Clean room procedures	
	Glass/silicon devices	Delamination	Etc.					
	Glass devices	Cracks	Etc.					
Building blocks	Valve	Misalignment	Leakage					
	Reaction chamber							
	Channel							
Components	Connector	Etc.						
	Blister							
	Tube							
Process step	Interfacing	Too low of a flow speed in flow cell	Incorrect measurem ent results / 7	Deformed ferrule used / 2	Leakage test / 7	98	Visual inspection	Stricter procedures ferule purchase and reusage
Operational conditions	Worst case use							
	Storage							
	Transport							
	End of Life							
	Environment al							

The rating descriptions provided in Tables 2-4 below help determine the risk priority number that allows prioritization of which tasks are most critical to consider during the product development phase.

Table 2. Rating description for effect and its severity (S)

Value	Description	Criteria
1	Minor	It is not likely to have much of an impact and will most likely be ignored by the stakeholder.
2	Low	It is likely to cause some amount of uneasiness to the stakeholder.
3	Low	Stakeholder will suffer some discomfort due to a minor problem with performance.
4	Moderate	User is uncomfortable due to performance not up to the desired level.
5	Moderate	User is dissatisfied or there is a reduction in performance affecting the overall process
6	Moderate	Quality cost due to warranty and repairs or there is a significant loss in performance
7	High	User is highly dissatisfied due to failure in some important parts of the process. There is also the likelihood of many defects affecting overall productivity.
8	High	User is highly dissatisfied due to failure in ALL parts of the process. There is also the likelihood of many defects affecting overall productivity.
9	Very High	Process becomes unstable which may create safety issues for the operator and exceed standard acceptance criteria.
10	Very High	Leakage will create safety issues for the operator or others.

Table 3. Rating description causes or mechanisms and probability (P)

Value	Description	Failure Rate	Percent Defective	Criteria
1	Remote	< 1 out of 1.5 x10^6	<0.00007 %	Failure has never been seen in any relevant testing
2	Very Low	1 out of 1.5 x 10^5	0.0007 %	
3	Low	1 out of 1.5 x 10^4	0.007 %	Failure only seen once or twice in relevant scenarios
4	Unlikely	1 out of 2 x 10^3	0.05 %	
5	Moderate	1 out of 400	0.25 %	Failure potential has been noted in several relevant scenarios or tests. If procedures are followed, the failure potential is minimal.
6	Moderate	1 out of 100	1 %	
7	High	1 out of 20	5 %	Failure potential has been noted in many relevant tests/scenarios. In-process control may be required to avoid failure.
8	Very High	1 out of 8	12.5 %	
9	Very High	1 out of 3	33 %	Failure potential has been noted in many scenarios/tests. An active non-standard feedback control loop may be required.
10	Extremely High	>1 out of 2	50 %	Failure potential has been noted in most scenarios/tests. The process should be re-evaluated, and/or a redesign should be considered.

Table 4. Rating description for detection (D)

Value	**Description**	**Failure Rates**	**Percent Defective**	**Criteria**
1	Remote	< 1 out of 1.5 $x10^6$	<0.00007 %	Failure has never been seen in any relevant testing
2	Very Low	1 out of 1.5 x 10^5	0.0007 %	
3	Low	1 out of 1.5 x 10^4	0.007 %	Failure only seen once or twice in relevant scenarios
4	unlikely	1 out of 2 x 10^3	0.05 %	
5	Moderate	1 out of 400	0.25 %	Failure potential has been noted in several relevant scenarios or tests. If procedures are followed the failure potential is minimal.
6	Moderate	1 out of 100	1 %	
7	High	1 out of 20	5 %	Failure potential has been noted in many relevant tests/scenarios. In-process control may be required to avoid failure.
8	Very High	1 out of 8	12.5 %	
9	Very High	1 out of 3	33 %	Failure potential has been noted in many scenarios/tests. An active non-standard feedback control loop may be required.
10	Extremely High	>1 out of 2	50 %	Failure potential has been noted in most scenarios/tests. The process should be re-evaluated, and/or redesign should be considered.

Commonly used microfluidic leakage tests

As mentioned previously there are several types of leakage testing possible that use either the operating liquid, or more sensitive methods of tracer gases. Such leak tests can also use both pressure and vacuum methods. The detailed discussion about commonly used leakage tests is outside the scope of this whitepaper and is covered elsewhere.[3]

Once the component or the final system containing several components has been developed, testing is required. Depending on the type of device and risk it poses to the user, this testing may include verification and validation studies at the system or component level.

There are many leakage tests possible, but not all of them are suitable to conduct at the typical microfluidics lab or manufacturing facility. This section gives some general comments on leakage testing followed by descriptions of commonly used microfluidic leakage tests.

General comments:

- As leakage is influenced by temperature, it is advisable to do the tests at the intended operational temperature.
- Testing outside the intended operating parameters/conditions could, in a useful way, accelerate the detection of failure or provide insight into potential failure modes.
- If the main cause of leakage of a certain design is based on too much pressure on a certain part of the device, using gas or liquid for testing will not make much difference. If the leakage is based on a tortuous small path through which liquid can flow if the pressure is high enough, using gas might show a problem that might not be detectable in real life situations when a liquid is used. On the other hand, it is known that certain liquids lead to faster de-lamination than others. This again demonstrates the importance of doing an FMEA and identifying potential fault modes.
- The tests discussed below will not elucidate any damage during use due to the interaction between the medium and the device. To test for failures like these, one should expose the device over a relevant period to the medium to be used before performing a new leakage test. This destructive test should be included in the product release program.
- Depending on the type of device, further leakage testing may be needed after subjecting the system to other stresses, such as shelf life, aging, transport, environmental conditions, mechanical stresses (e.g., shock, vibration), and electric, electromagnetic, and wireless interferences. Also, leakage testing should be performed under the worst-case operating conditions with a safety factor built in to account for unforeseen extreme operating conditions.

The list provided below is not all inclusive and the device developer may have to consider tests that best meet their needs.

Visual inspection for leakage

Probably the most common leakage test method is to check for visual signs of leakage, such as the observation of sweating (not due to condensation) or formation of droplets. This type of test can be done at the operational condition or at the justified worst-case condition while the liquid continues to flow through the device. This is labor intensive and time-consuming, and it may take time before

[3] Herbertson et al. Frontiers in Bioengineering and Biotechnology, 2022, under preparation

enough liquid has leaked to become visible. Also, if leakage rate is slower than evaporation it may not be visible. Further, it is a time-consuming process and can only be used with non-toxic or non-hazardous liquids. The device should be able to be reused, otherwise this becomes a destructive test and the device should be discarded after testing. Only relatively large leaks can be detected as the smallest optically detectable amount (by an unaided eye) is a droplet of a few µL. Using colored liquid, a liquid with a tracer, magnification, or wiping the outer surface with a dry cloth can increase the sensitivity of the observation. This test is not quantitative and only useful for detecting major processing design weaknesses. One advantage to visual observation is that the location of the leak can usually be determined. In addition, it can be easily implemented not only during product testing but also by the end user without much additional resources (e.g., microscopes).

Liquid pressure drop

Unexpected changes in pressure can be indicative of device leakage. To measure pressure drops associated with device leaks, a port is connected to a pressure source with a sensitive transducer. In this quantitative test, the amount of pressure applied to the system can be increased to 1.5 times the expected operational pressure to offer a safety factor. The device is disconnected from the pressure source and the pressure decay over time is monitored during the anticipated duration of use of the device.

Pressure drop testing is a labor intensive and time-consuming process, but it allows manufacturers to test their devices with the liquid analyte of interest. Furthermore, the device should be suitable for reuse, otherwise this becomes a destructive test and the product cannot be used again. This test is more sensitive than visual inspection for leakage but may not be sensitive enough to detect slow, gradual leaks, as surface tension effects often prevent the escape of the liquids through the smaller leak sites. Thus, if there is a small leak, identifying the exact location of the leak might be difficult. Trapped air can also be problematic for detecting leakages when systems are filled with liquids. Air does weird things when trapped under pressure in devices.

Gas pressure drop

Pressure drop testing with gas is similar to the liquid pressure drop test with additional considerations and advantages. For example, when selecting a manometer, it is important to note that the internal volume of the test construction contributes to the sensitivity. One should minimize the internal volume of the system by using short sections of small diameter tubing to attach the pressure measurement instruments. Also, the connectors should have a small internal volume. To ensure that expansion/compression of the compliant components such as tubing do not falsely contribute to the test results, it is recommended that rigid stainless steel or PEEK/PFA (polyetheretherketone/perfluoroalkoxy) tubing are used. PEEK/PFA is probably sufficient under most pressures expected in microfluidics.

Non-destructive gas pressure drop testing is suitable for high volume production of parts/devices. With a sensitive manometer or pressure transducer, this testing with gas allows for the detection of even small leaks. These pressure drop tests are well established in larger gas/refrigerant systems. However, if there is a leak, finding its location might be difficult. Although it can be facilitated by using a bubble test. One disadvantage of this test might be that the relation between the leakage rate of air and the leakage rate of the intended medium must be known. In general, it is predicted that an air-based leakage test gives 51 times the amount of leaked medium compared to water, assuming the difference is governed by the difference in viscosity only, which might not be the case for leakage

through a long, narrow, tortuous path. Also, this method is less suitable when the device is comprised of compliant or permeable materials like PDMS (polydimethylsiloxane).

One should keep in mind that the leakage can be influenced by interactions between the materials of the construction and the medium used. For instance, delamination can occur when organic solvents act on interfaces. If that is the case, testing with the real-life medium would be needed. For ease of use and to prevent damaging the product, leakage tests should be done with dry air or an inert gas (e.g., nitrogen).

Leakage testing at higher pressures

Leakage tests only at the normal operating conditions may not be sufficient as they may not represent worst case scenarios or do not account for a factor of safety in design. Therefore for each leakage method, besides operating conditions, it may also be necessary to perform testing at higher pressures.

Burst pressure test

A burst test is a destructive test that is performed to determine the pressure at which a given component or system will "burst" or fail catastrophically. Burst pressure can be defined as the point at which a product fails due to a high internal pressure (i.e., the maximum pressure which the product can endure before it will break). Information about this failure point will ensure that a sufficient safety factor is applied during operation. It is important to consider burst pressure when designing any sort of system, especially for products where failure is not an option or when the device is used in high pressure applications. A burst test provides the margin between the maximum operating pressure in the field and the pressure when the product completely fails. For some applications, this safety factor is specified in applicable standards and/or regulations.

To establish the burst pressure, the device is pressurized slowly, either gradually or stepwise, until the device fails. A practical way of doing this may be to increase the pressure by steps equating to ¼ of the maximum pressure for which the device is supposed to be subjected. For instance, if the device is expected to work at a 200,000 Pa (2 bar) maximum, the incremental steps for determining burst pressure will be 50,000 Pa (0.5 bar). The time between two steps depends on the specified minimal leakage rate tolerated and the minimal detectable leak rate of the device / test system. A continuous pressure measurement allows one to determine the test duration and pressure applied to the system at the instant of device failure. As there may be significant variability in the burst pressure from one unit to another, this testing should be repeated on multiple samples to establish a meaningful safety factor. To ensure the safety of the operator, burst testing should only be performed in a containment chamber using appropriate personal protective equipment.

Maximal operational pressure test

Maximal operational pressure testing is a quality control method to ensure that a specific device unit or system functions properly before it leaves the manufacturing facility. Similarly, this type of test may be part of a repair or maintenance routine. Here, the device is pressurized for a period of time. Typically, this testing is performed at 2/3 of the expected burst pressure and the system is monitored for pressure decay. If the burst pressure is not known, an alternative might be testing at 1.5 times the expected maximum operational pressure during usage of the device.

This quality control pressure test is a way to check for early life failures, which are failures that are unexpected and occur at the beginning of the product life cycle. These are different from the “normal” failures that occur after extended use of the product, perhaps due to chemical or mechanical wear.

This test can be used to inspect 100 % of outgoing devices or a selected number of devices (i.e., by sampling) and is often dictated by the quality systems processes that the manufacturer may have in place. In the case of higher pressures, testing is done with a liquid or in a containment chamber to ensure product and user safety. This method can also be used to condition a component or system before distribution.

Flowchart for selecting an appropriate leakage testing protocol

The number of leakage tests needed to demonstrate safety and performance depends on the product status and the protocol selected according to the flowchart in Figure 1 and the protocols in Table 5.The following flow chart helps one to decide which protocol to use.

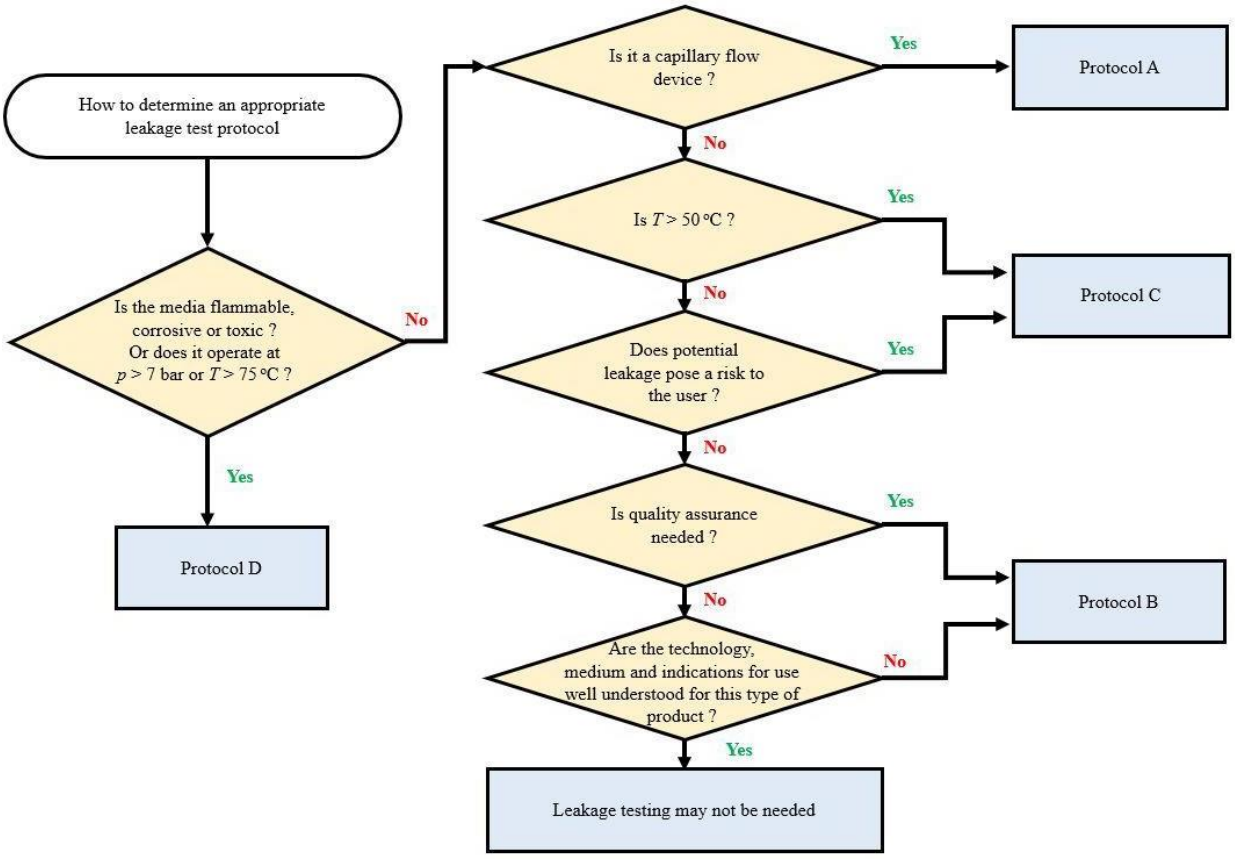

Figure 1. Protocol decision making flowchart. Note that the risk for each protocol will depend on the specific application and the specific fluid being used and would need to be independently assessed.

The following protocols are for various types of applications (according to figure 1) as listed below:

- Protocol A: leakage testing of capillary devices.[4]
- Protocol B: leakage testing when Quality Assurance/control is needed.
- Protocol C: leakage testing for potentially medium risk situations.
- Protocol D: leakage testing for potentially high-risk situations.

Each of the protocols can then have multiple levels of tests both in different phases of the device development, and for various worst-case testing. Both are shown in Table 5 below. The leakage tests such visual leak test, water immersion bubble test, soap solution, pressure decay, vacuum

[4] Capillary flow exploits surface tension effects in high surface-to-volume structure for generation flow.

decay, tracer gas leak test etc can then be implemented for each of these protocols based on the desired sensitivity.

Table 5: Frequency of leakage tests to be performed

	Protocol	Leakage test	Burst pressure test	Maximum operating pressure test (@1.5 times the operating pressure)
Development phase	A	incidentally with the intended operating medium	-	-
	B	incidentally with the intended operating medium	incidentally with the intended operating medium or with air[5]	incidentally with air
	C	regularly with the intended operating medium	regularly with the intended operating medium	incidentally with air
	D	regularly with the intended operating medium	regularly with operating medium	100 % testing with air or helium
Production phase	A	sample test	-	-
	B	sample test		incidentally with air
	C	sample test		regularly with air
	D	100 % testing with air or helium	samples with air	100 % testing with air or helium

Leakage testing protocols should be developed based on the following considerations:

1. The results of malfunctioning risk analysis / FMEA should be considered. This might lead to a subdivision of protocol categories.
2. Time for which the device will be operational and the conditions during the lifetime of the device (i.e., considerations like fast diagnostic tests versus continuous processing, storage conditions, sterilization, and transport). These factors will determine if accelerated lifetime tests are needed.
3. Typically, one needs to estimate what constitutes the worst-case performance/design parameters for the device, and then perform testing at those conditions or using a 1.5 times safety factor for applied pressure.
4. For reusable devices, the influence of reuse or device wear should also be investigated.
5. The number of samples to be tested depends on the frequency of failure, the types of failure, and the consequences of failure for the user.
6. The leakage test duration should align with the intended duration of use of the product. To reduce the test duration, one could potentially assess the device at higher pressures or temperatures. If that is the case, one should investigate how these factors influence the leakage rate.
7. If the device is tested with air instead of a liquid, one should consider the following:
    a. What is the quantitative and qualitative relation between leakage of air and leakage of liquid regarding the specific device and conditions?

[5] Or nitrogen

   b. Testing with gases in microfluidic devices results in higher safety risks for the operator compared to testing with liquids. Therefore, more strict safety precautions are needed when using compressed gases.
8. Ad hoc installations with microfluidic components and devices connected by tubes should be checked before each experiment for safety and so as not to impact the leakage test results. This can be done by a pressure decay method on the test setup itself.
9. To accelerate the testing and achieve meaningful results, the distance between the pressure/liquid source and the product under investigation should be minimized as much as possible.
10. Temperature management. There are several aspects of this:
    a. What are the operational, sterilization and storage conditions and how do they affect the leakage behaviour of the device?
    b. The temperature may also change the internal volume of the device and the auxiliary components used for testing, thereby influencing the test results.
    c. Temperature control during testing is key to repeatability, temperature changes can cause the device to expand and deform, thus introducing leaks or changing leakage rates. Therefore, the temperature should be maintained at a constant value throughout the test.
    d. Temperature can be used to accelerate lifetime testing.
    e. Temperature treatment can be used to precondition the device.
11. One must consider the pressure drop between the manometer and the device under investigation. For example, if you apply 200,000 Pa (2 bars) but you have a pressure drop of 100,000 Pa (1 bar) in the system before the valve, you cannot say that your valve does not leak at 200,000 Pa (2 bars).
12. The test setup must be clearly defined and reported, taking into account the tubing dimensions, material properties like porosity, and deformability, as well as the connectors.
13. It can be decided that the device must be tested during a prolonged period or, for instance for reusable devices, during cycles of pressurizing / depressurizing.
14. It makes sense to test first for obvious failure points. These points can be identified by a Risk analysis / FMEA.
15. For a leak to appear, the test must be run for an appropriate amount of time. The time needed to test increases with decreasing pressure. Furthermore, the smaller the leak the longer it takes to detect. Therefore, one should think carefully before setting the leakage rate specifications.
16. For liquid leakage through a small capillary leak, it may be necessary to overpressure the system. One should keep this in mind when increasing the pressure to accelerate tests.
17. For liquid leakage testing, it is important to consider the interaction between the testing medium and the bonding interface. The device should be evaluated using liquids that simulate real use of the device.

Final comments

This whitepaper is only a first step towards developing leakage test protocols. During the creation of this whitepaper, we formulated the following questions:

- What is the minimal amount of liquid that can be detected by visual inspection? Can this detection limit be improved by markers etc.?
- What is the minimal amount of gas leakage that can be detected by bubble testing? Can this detection limit be improved?
- How accurate can one test for leakage with the method of comparing in and out going flow?
- How accurate can one test for leakage with gas- and liquid pressure drop testing?
- How does temperature influence these tests? How do things like gas inclusion etc. impact liquid leakage tests? I.e., what are the fault modes of leakage testing.
- In the end, we would like to have a table comparing test methods that are applicable for microfluidics. It should address like accuracy, sensitivity, ease of use, application area etc. etc.
- What is the quantitative and qualitative relation between the leakage of gas and liquid in microfluidic devices? Otherwise formulated: the relation between flows of liquid and gas in small channels and through pinholes.
- Is it possible to accelerate the detection of leakage testing (for instance pressure of temperature)?
- Is it possible to make detailed leakage test protocols out of the experiments done in MFMET? This could include recommendations for equipment to be used.
- Can we expand the microfluidics FMEA?
- Can we expand this whitepaper to cover also internal leakage testing?

We would recommend more research to answer these questions.

Appendix I: Case Studies of leakage tests and fault modes that cause leakage

This Appendix describes some common case studies that microfluidic device developers may encounter. The specific information about the test laboratories (i.e., foundries), and the manufacturer's products were anonymized to protect the privacy, the intellectual properties, and the agreements between the parties.

Case 1: Checking for leaks in a flow cell designed and produced by a foundry.

Let us take up an example of a foundry that does only incidental leakage testing during development to assess the quality of the design for a device developer. They rely on process control during production to confirm the leak tightness of the new devices. However, a customer asked for routine testing during production.

The device to be tested is designed to be used in real life at 200,000 Pa (2 bar) for a 15 min duration, during which time the device should not lose more than 1 % of the aqueous liquid from inside the cell. The internal volume of the cell is 2 mm^3. They want to test during the development phase to check the design, and they want to test samples taken during production to check that particular process. A hundred percent (100 %) testing is seen as unnecessary, as they have strict process control protocols for the production. The test is not overly time-consuming.

They discovered that they could not use the DIN EN 1779 that uses non-destructive leak testing procedure, since this protocol was developed for leakage testing of much larger devices (i.e., gas tanks, etc.) and therefore is more applicable for much larger leakage volumes.

During the development phase the foundry fills some of the devices with liquid, pressurizes them and checks for pressure decay over a certain period. As they do not want to do destructive testing during production, they decided to do the testing of samples during production with air, accepting that this test does not correspond to a real-life situation.

They made their own testing setup. As the internal volume of the test construction contributes to the sensitivity of the test with air, they use a barometer with a small internal volume of 7.5 µL (7.5 mm^3) and short tubing with small cross sections. To ensure that expansion / compression do not contribute to the results, stainless steel tubes were used.

Issues that they see as critical (leakage fault modes) are:

1. Bonding defects caused by contamination or out-of-specification bonding conditions. Especially, heterogeneous bonding is critical.
2. Typical sources of contamination leading to leakage include particles, surface corrosion or scratches, and fingerprints (i.e., problems that can be minimized by stricter adherence to protocols).

The foundry then reports the findings to the device developer. The device developer upon finding that the extent of the leakage would impact device performance starts considering design changes to mitigate this issue.

Case 2: A company wants to check the design of a new product, improve it, and guarantee the quality during the production

A company does a FMEA before the first product is created. An important part of the FMEA is making a detailed specification and discussing this with experts, who have experience with similar devices or components. This is to identify potential quality issues and adapt the design where necessary.

At the top of their list of potential problems causing leakage is bonding. They see process control at the supplier's site as very important, even essential, but not sufficient. So, they test several samples during the development phase of a new product. They also determined that this quality control would need to be integrated for the entirety of the product's life cycle. After production release, they will still test samples coming from the production line on a routine basis. This test will consist of letting fluid flow through the device for a longer period and comparing the amount of fluid introduced to the system with the amount of fluid at the outlet. As variables, they evaluate the device using different types of liquid over a range of pressures and temperatures. They vary them during the test according to the real-life operating conditions that may occur. In that case, they can also identify leakage problems caused by long-time effects of the interaction of the liquid with the materials used, such as corrosion. Varying pressure and temperature will bring to light issues like creep and wear. They will use the results to identify potential weak areas in the design and critical steps in production, using the results for improvement of design and processing. Over time the number of samples tested will decrease, but never completely disappear. In time, they transfer these process control tests to the supplier for continued monitoring.

Case 3 An OEM producing devices that are being used for gases, sometimes toxic or flammable, at higher pressures.

A manufacturer tests all their devices for leaks with helium under vacuum before and after final delivery. They do all the tests with helium although their devices are meant to be used with liquids in real life. Generally, the manufacturer tests at 1.5 times the working pressure. For safety reasons, these tests and burst pressure tests are done in a steel containment chamber. According to them, when testing with helium they might be overdoing what is needed for some applications, especially when the device to be tested is used with liquids but using helium for leak testing is common practice in their field.

Issues that they found as critical (leakage fault modes) are:

1. To prevent leaks the company would use O-rings but found they determined re-use of the O-ring, i.e., disconnecting and reconnecting may have prompted leaks because of scratches and wear on the surface of the O-rings.
   During the design process one must carefully check the compatibility of a material with other materials used in the construction. One must also check if the total finalized product can withstand the pressure, as opposed to evaluating components individually.
2. The manufacturer also tried using CO_2 as an alternate for helium but determined that it might cause problems when used above the critical temperature.

Case 4: An installation containing microfluidic components and devices connected by tubes

Here we take up an example not of a specific product or company, but rather a situation where a device developer may use a multi-component system. In these kinds of setups, leakages are a common problem due to the connectors used. It is therefore strongly recommended to test the installation's leak tightness before starting the experiments or running the process. The easiest way to do it is to pressurize the installation with air and check for a pressure decay over time. If there is a leak, finding the precise compromised location might be difficult.

Critical leakage fault modes for such multi-component systems are:

1. For reservoirs, common problems are
   1.1 forgetting to use the O-ring,
   1.2 O-ring gets porous over time.
2. For connectors, common problems are:
   2.1 Tightening them too fast or not fast enough may to leakage.
   2.2 Fluidic force on the sidewall of the gasket.
   2.3 Cold flow of seal material or wear.
   2.4 Chemical wear of connector sealing.
   2.5 Mechanical wear of connector sealing.
   2.6 Mechanical fracture connector.

Appendix II: Definition of used terms[6]

- Burst pressure: a burst test is a destructive test to determine the pressure at which a given component will "burst" or fail catastrophically.
- Containment chamber: a device for isolating an object from its surroundings using a solid barrier. Its purpose is to protect the operator against debris from explosion of a pressurized device.
- Destructive test: technique in which the application is made to fail under extreme conditions to test the robustness of the application and to find the point of failure.
- Failure mode: refers to how and why a device, equipment, or machine can fail.
- Failure Mode and Effect Analysis (FMEA): a step-by-step approach for identifying all possible failures in a design, a manufacturing or assembly process, or a product or service.
- Intended operational pressure: the pressure at which the device and medium are exposed to during operation.
- Internal leakage: contained leakage of medium from one part of the device to another.
- Leakage: unintentional release of medium from the device to the environment.
- Maximal operational pressure: the maximum operational pressure the device should be exposed to during product testing. Above this value, the supplier cannot confirm correct performance of the device and safety of the operator.

[6] As agreed by the attendees of the MFA workshops.