PQS Target Product Profile (TPP)

WHO/PQS/E003/TPP05.1
Original: English
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TITLE: Humidity Control for Vaccine Refrigerators

TPP Reference:	E003/05.1
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Date of last revision:	New TPP

1. Need

Field testing and reports have highlighted adverse refrigerator conditions that impact immunization activities, related to excess humidity and condensation present in ILR and SDD vaccine refrigerators. High relative humidity levels (RH%) contribute to mold growth on compartment surfaces, primary storage containers (e.g. vials) and secondary cartons, presenting possible health risks to health staff and patients. These sustained, elevated humidity levels are noted to lead to the formation of condensation on cold surfaces, leading to 1) waterlogging and damage to vaccine vial labels and secondary cartons and 2) pooling of condensate within and outside the compartment.

One potential approach to address some of the issues caused by condensation and high humidity is to change vial labeling and secondary container materials from paper to a moisture resistant material. This approach, however, would not reduce condensation or mold growth inside the refrigerator. Therefore, controlling humidity – and thereby condensation – directly is the preferred approach for vaccine refrigerators.

WHO PQS proposes to introduce requirements for maximum operating compartment relative humidity levels, as described in this target product profiles (TPP). A vaccine refrigerator achieving acceptable relative humidity levels will be recognized as having "humidity control" via its WHO PQS catalog data page. Such definitions and classification will be ultimately incorporated into a revised set of ILR and SDD TPPs

to be published in 2021 for the purpose of specifying and testing humidity in vaccine storage compartments.

2. Normative references

Not applicable.

3. Terms and Definitions

The following terms are used to describe humidity conditions within vaccine storage compartments:

Ambient humidity: The relative humidity (%) of the chamber in which the appliance is being tested.
Compartment humidity: The relative humidity (%) of the vaccine compartment of the appliance.
Humidity control: A functional capability of a vaccine storage compartment, by which relative humidity levels are controlled such that limited or no condensation accumulates on compartment, vial or secondary carton surfaces and mold growth is inhibited.

4. Specification

The acceptability criteria for an appliance to be tested and rated as having humidity control are as follows:

Table 1: *Relative humidity acceptability criteria for storage compartments at ambient temperature and humidity levels*

Temperature Zone (ambient temperature)	**Ambient Humidity (RH%)**	**Acceptable Compartment Humidity (RH%)**
Hot (+43°C)	45-75%	55% or lower at +2-8°C

4.1 Laboratory Verification Protocol

Ambient test chamber conditions must be stabilized at the specified temperature and humidity at which the device is to be tested. A controlled surface area of water will be introduced to the compartment, along with a partial air exchange from a door/lid opening.

Compartment humidity will be evaluated 4 hours after the compartment door is closed. Relative humidity will be measured within the appliance compartment for 24 hours to ensure acceptable humidity control is present. The required humidity levels during testing will ensure that the appliance is able to evaporate an appropriate amount of water during use. This amount of water was determined based on testing and assumptions regarding realistic water introduction rates and possible water removal with known technologies.

See **Annex 1** for the working draft verification protocol.

4.2 Design of humidity mitigating controls

In order to minimize complexity and impacts on maintenance and risk of failures, efforts should be made by equipment manufacturers to meet the humidity control specification through approaches that minimize significant device design modifications, usability/functionality changes and additional components subject to degradation and maintenance. Any additional components introduced should only involve marginal increases in device energy consumption with preference for solutions requiring limited energy consumption.

Reason for change: Instances have occurred where cartons and vials in mains- and solar-powered refrigerators have been damaged by exposure to excessive moisture, i.e., humidity and condensation. This has resulted in the labels peeling off vials and mold growing on secondary cartons. According to the immunization policies in many countries, such vials and secondary cartons must immediately be discarded.

Therefore, such appliances with excessive condensation could cause a significant increase in vaccine wastage. This classification system will be utilized to evaluate, classify and communicate to customers the capabilities of appliances in mitigating adverse effects of humidity.

Timing for PQS Inclusion: 2020, i.e., effective starting in January 2021
PQS will release further guidance on the specifications and testing protocols to be used in evaluating humidity control during prequalification of new appliances. These specifications and protocols will go into effect and apply to all appliances tested from 1 January 2021 onwards.

Appliances not meeting humidity control specification will still be considered for prequalification in 2021, but equipment manufacturers are encouraged to develop solutions to solve the challenges faced by immunization programs as a result of condensation

Annex 1: DRAFT Vaccine refrigerator humidity control verification protocol (WHO/PQS/E003)

Test chamber conditions: steady temperature of +43°C ± 1°C and relative humidity of 65% ± 10%.

Appliance: power supply constantly on and providing power throughout the testing, already stabilized between +2-8°C

Compartment monitoring parameters: temperature and relative humidity

Dummy evaporative load:

A dummy evaporative load will be used in place of the dummy vaccine load for the humidity control test. General test conditions of the dummy vaccine load will apply to the dummy evaporative load.

Prepare a dummy evaporative load using open-top glass containers.

- The internal height of the container shall be at least 2.0 cm.
- Measure the surface area of the container opening in cm^2 (length x width for rectangular dishes, diameter x diameter x 0.785 for circular dishes). If the container has drafted walls, measure the length, width, and/or diameter at a height of 0.5 cm below the top rim.
- Select the number of containers required to build a dummy evaporative load whose surface area in cm^2 is equal to the measured vaccine net storage capacity in liters multiplied by six, ± 10%.
- Estimate the volume required to fill all the dummy evaporative load containers to within 0.5 cm of their tops. Fill a separate water storage container with at least that much water.
- *Test dummy load container size and water depth must be confirmed in final version of verification protocol.*

Pre-condition the dummy evaporative load and filled water storage containers at +8°C.

Fill the dummy evaporative load containers with conditioned water to within 0.5 cm from the top of each container and place in the appliance as follows so that they do not interfere with the sensor positions already established:

Front-opening appliances:

- Place the filled containers evenly on the shelves designated for vaccine storage.

Top-opening refrigerators:

- Place the filled containers evenly on the bottom of baskets supplied for vaccine storage.

- If baskets are not required to keep vaccine away from the base and walls of the appliance, place the filled containers evenly on the base of the appliance.

Humidity sensor:

- Follow the existing guidelines outlined for temperature sensor placement in Annex 1 of the E003/RF03 verification protocol.
- Place the humidity sensor at the same location as temperature sensor #19 (refer to Annex 2 of the E003/RF03 verification protocol). Humidity sensor location must be < 10 cm away from this temperature sensor.
- The humidity sensor must be accurate to ± 3% in the range of 25% to 75%.

Procedure:

1. Place relative humidity monitor in the vaccine compartment as described above.
2. Start recording humidity and temperature monitors at a rate of one measurement per minute.
3. Confirm that both the power supply and refrigerator are on, to remain on for the entire duration of the test.
4. After the refrigerator has run for the manufacturer-rated cool down time, open the lid or door of the appliance and start a 5-minute timer.
5. Load the appliance with pre-conditioned evaporative load as described above. Ensure that the water-pack freezing compartment (if present) is empty.
6. At the conclusion of the 5-minute period, close the lid or door of the appliance and let it run for 4 hours.
7. After this initial 4-hour period, continue recording temperature and relative humidity every minute for 24 hours. This will be the test period.

Acceptance criteria:

If the following acceptance criteria are met, the vaccine refrigerator will be recognized as having humidity control.

1. Stabilized internal temperatures maintained between +2°C and +8°C in the vaccine storage compartment and below -3°C in the water-pack freezing compartment (if present).
2. Average relative humidity at or below 55% for the duration of the 24-hour test period.
3. Relative humidity does not exceed 65% for the duration of the 24-hour test period.

Annex 2: Consolidated Industry Feedback & WHO PQS Responses

1. Industry feedback: The relative humidity in the test chamber must be fixed: either 75% or any other value but not between 45% and 75%.

   This is because a fridge needs more cooling capacity when operating at 75% than at 45%, and so if one manufacturer tests at 45% and is successful, the same product might fail at 65%.

   PQS response: The humidity requirement of 45% to 75% contained in the draft for industry review was based on the current PQS E003/RF03-VP.3 general test conditions. The comment from industry is well noted, however. PQS intends to change the humidity test condition set point to a specific value; likely 65% RH, with a tolerance of ± 10%. The tolerance range of ± 10% is based on the comments from testing laboratory expertise that ± 5% for chamber control, and ± 5% for sensor accuracy are very reasonable.

2. Industry feedback: Regarding the procedure, we would like to mention that usually, when doing a temperature mapping (including for equipment), the three-dimensional coverage of the refrigerator volume should be considered; i.e. we recommend to verify at least 9 measurement points inside the refrigerator and 1 outside for the ambient temperature.

   We wish to recommend that PQS adapts the relevant specifications in such a way that a refrigerator manufacturer has to perform a temperature/humidity mapping per refrigerator model. This would show the cold/hot spot as well as a recommendation for placing the data logger, and would make the mapping report available to WHO customers.

   PQS response: Thank you for the feedback. The purpose of the proposed testing is to verify the ability of the refrigerator to remove moisture from the vaccine compartment. The amount of moisture removal identified should result in consistent relative humidity levels significantly below 100%. For this purpose, we have determined that measuring one humidity sample point is sufficient. Performing three-dimensional volume mapping would be a more comprehensive way to test and could be very informative. However, WHO PQS tries to balance the level of testing and cost burden with the need to ensure that equipment is appropriate for use in the intended situations and environments.

3. Industry feedback: I am interested to gain a better understanding of the observations of any further tests that have been carried out. Is it possible for you to share the thinking, for instance, behind the 4 hour grace period after door closed, and where you have observed RH55% at2 -8 °C and any other key metrics?

   PQS response: We performed several experiments with domestic refrigerators and PQS prequalified ice-lined refrigerators to determine the characteristics of moisture removal. The experiments involved placing different amounts of dummy evaporative load in the form of water-filled glass dishes. The main observations were:

a. The rate of evaporation in the refrigerator for a given surface area of water is inversely proportional to the relative humidity in the refrigerator. As such, high humidity levels inside the refrigerator yield low evaporation rates of any standing water. Refrigerators with insignificant moisture removal capability (e.g. ice-lined refrigerators) maintain high relative humidity (>90% observed).
b. For domestic refrigerators, the relative humidity in the refrigerator is directly proportional to the total rate of moisture removal. Put another way, as total water removal increases (from placing a larger evaporative load in the refrigerator for the test), so too does the internal relative humidity of the refrigerator.

These two observations outline the main motivation behind using a relative humidity approach for humidity control determination. If the refrigerator can maintain humidity significantly below 100% with an intentional evaporative load, it indicates the ability of the refrigerator to remove moisture from the vaccine compartment. The results from these experiments were used to determine a reasonable dummy evaporative load size for a desirable water removal rate while maintaining 55% R.H.

The 4-hour grace period at the beginning was included in order to minimize any effects due to air exchange during test setup. The very high humidity levels of the test chamber invariably will cause condensation during door opening. Since the test refrigerators will already have a dummy evaporative load, this 4-hour grace period will allow some time to "catch up" and remove the moisture due to air exchange condensation before the evaluation period begins.

4. Industry feedback: We have seen the need for dehumidification in regions that experience very high levels of humidity and we also have experience of regions that have no issue with humidity – I wonder if anyone has thought of making such a distinction as the additional feature of high levels of de-humidification will certainly add some cost – it might be helpful to give the purchasers a guide to when this feature would be appropriate since they may choose to not bear that extra cost.

   PQS response: The PQS working group is still discussing if humidity control will be a requirement of all refrigerators or an optional feature.

   The decision is in part informed by the fact that although no bulk condensation may be visible in refrigerators in areas with low humidity, with no humidity control, conditions may still remain humid enough for long term mold growth and damage to packaging and labels. This may be especially true if moisture is introduced to the refrigerator compartment not only from the environment (door openings), but also from any moisture in the vaccine load. Transport via cold box can soak the cardboard secondary packaging and vial labels from ice-pack condensation, and in these cases humidity control will help to dry and prevent mold growth. Even if no condensation is visibly present, sustained periods of high humidity can lead to mold growth.

5. Industry feedback: Temperature of dummy load – stated as +8C. We suggest that you add a tolerance to this e.g. 8 °C +/- 0.5 °C as precise figures will be difficult to achieve.

   PQS response: The current PQS E003/RF03-VP.3 (the source of this language) has a general test condition for the environmental chambers of ± 1 °C. The general test conditions are currently not included in this TPP document but can be added if helpful.

6. Industry feedback: Humidity sensor <10cm from the temperature sensor – 10cm seems like quite a lot given the critical nature of linking humidity to temperature and the size of some of the smaller compartments so I would suggest that this is reduced to <4 cm – ideally both probes would be right next to each other.

   PQS response: This requirement is based on Figure Z2 from BS EN 62552:2013: Household refrigerating appliances — Characteristics and test methods. The temperature sensor in the PQS context is the brass billet used for temperature logging *per* PQS E003/RF03-VP.3. This should not be confused with any internal compensation of the humidity sensor itself.

   Regardless of this, given the manner in which the specification is currently written the exact temperature at the humidity sensor location is less critical as the relative humidity must stay below a threshold independent of temperature. Some hygrometer probes can be relatively large, so the tolerance will allow for a wide range of test equipment and mounting methods to be accommodated.

7. Industry feedback: We suggest that you clarify that the device should be provided with power during the testing (i.e. both the first 4 hours and the following 24-hour period).

   PQS response: Yes, we can add clarification of this in the testing protocol.

8. Industry feedback: Do you see an opportunity for manufacturers to undertake testing for this feature in their own labs? The prospect of having to go through the pain and cost of external testing is most unpalatable.

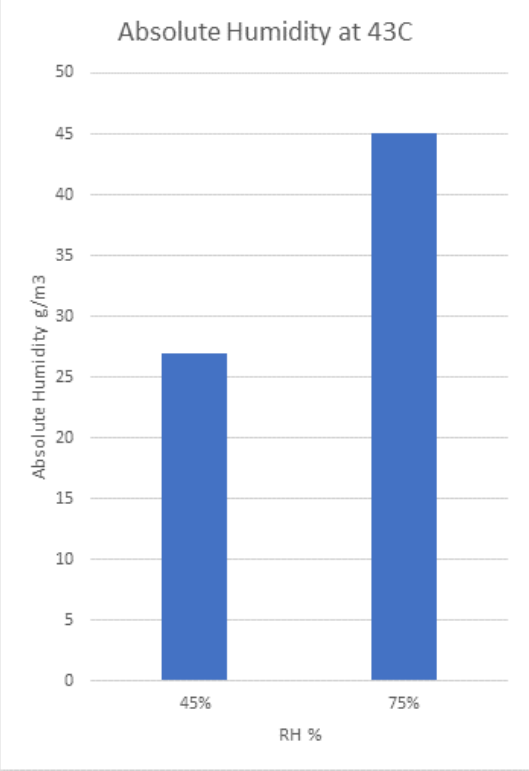
   PQS response: The PQS working group is still discussing if humidity control will require partial re-testing of currently prequalified refrigerators or if it will only apply to new applications. External testing is currently required for PQS prequalification, so we do not see this specific test as too much of an additional burden for new equipment submissions.

9. Industry feedback: It is important to link temperature with Relative Humidity since the amount of water in the air (the Absolute Humidity) is very different at different temperatures.

PQS response: The goal of testing is not to measure the amount water in the air (absolute humidity), but rather to evaluate the refrigerator's ability to remove moisture from the air. Ability to remove moisture from the vaccine compartment is demonstrated by maintaining relative humidity levels below a specified threshold. Without moisture removal capabilities, relative humidity values can reach high values (close to 100%) regardless of temperature, promoting mold growth and other issues.

The thresholds set in the current TPP are based on the assumption that the fridge must remain between +2C and +8C during the testing. The quoted RH requirements keep the RH at acceptable levels within that temperature range. Agreed, it would be more exact to calculate absolute humidity at each time point based on the temperature measurements. However, to ease testing burden, lower complexity of the written requirements and protocol and make calculations simple or non-existent, the tests as written should function to guarantee acceptable water removal and humidity control rates and balance with these other priorities.

10. Industry feedback: Take the test chamber for instance – text currently states 45% to 75% RH at 43 °C.



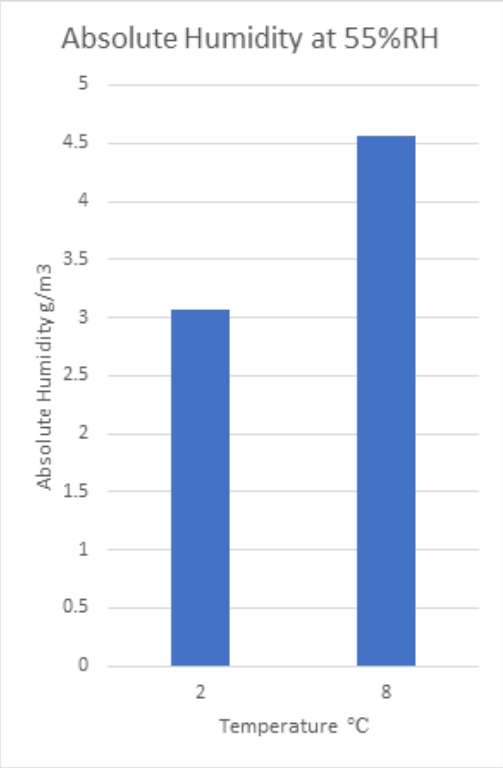
Actual water content is 40% higher at RH75% at 43 °C.

PQS response: Chamber humidity set point will be redefined (see comments above).

However, we do not anticipate the ambient chamber humidity to play a defining role in the compartment performance (assuming the door seals well) since there is only one door opening at the beginning of the test. A majority of the moisture added to the

system will be from the water dishes placed inside, not from the air exchange to the chamber.

11. Industry feedback: In the refrigerator compartment:



Actual water content is 33% higher at 8 °C.

So, at its extreme you may expect a 73% difference in dehumidification.

I can't think of much you might do with fixing the issue in the compartment except for adjusting the acceptable humidity to reflect the Absolute Humidity i.e. even it out so that the acceptable RH is relative to the average storage temperature on a sliding scale so 55% at 8 °C or 82% at 2 °C (same Absolute humidity of 4.5g/m3). This could be done but it requires some relatively complicated calculations.

PQS response: As noted above, the way the testing is set up currently attempts to acknowledge these differences, and defines acceptable humidity in the worst-case scenario to pass the testing (8 °C, 55%R.H.) with a safety margin. If manufacturers are able to achieve better performance (e.g. 2 °C 55%R.H.) that is acceptable as well. This does mean that some fridges may have to more effectively control humidity in the case that the set point tends more toward 2 °C as opposed to other equipment that tends more toward 8 °C. But both cases should control humidity acceptably in order to avoid mold growth, packaging damage and label damage. As noted above, we have specifically chosen not to define absolute humidity for simplicity (to avoid the complicated calculations).

12. Industry feedback: Regarding the manufacturer perspective on the ability to comply with proposed TPP requirements in the future; this is slightly more tricky since we don't have good data on the specific test conditions, nor have we had the chance to measure the impact on the product pricing. Certainly, this is considerable additional work and investment with unknown outcomes that is laying on top of years of previous heavy investment that has yet to bear fruit. Technically, my instinct is that the general principles of operation can be met – the bigger question is does any of this make sense commercially…

    PQS response: Thank you for sharing these concerns. The PQS working group continually discusses potential implications of additional investment and impact for manufacturers to comply with requirements. Please feel free to provide more feedback like this in the future.