International guidelines for the *in vivo* assessment of skin properties in non-clinical settings: Part 2. transepidermal water loss and skin hydration

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Background: There is an emerging perspective that it is not sufficient to just assess skin exposure to physical and chemical stressors in workplaces, but that it is also important to assess the condition, i.e. skin barrier function of the exposed skin at the time of exposure. The workplace environment, representing a non-clinical environment, can be highly variable and difficult to control, thereby presenting unique measurement challenges not typically encountered in clinical settings.
Methods: An expert working group convened a workshop as part of the 5th International Conference on Occupational and Environmental Exposure of Skin to Chemicals (OEESC) to develop basic guidelines and best practices (based on existing clinical guidelines, published data, and own experiences) for the *in vivo* measurement of transepidermal water loss (TEWL) and skin hydration in non-clinical settings with specific reference to the workplace as a worst-case scenario.

Results: Key elements of these guidelines are: (i) to minimize or recognize, to the extent feasible, the influences of relevant endogenous-, exogenous-, environmental- and measurement/instrumentation-related factors; (ii) to measure TEWL with a closed-chamber type instrument; (iii) report results as a difference or percent change (rather than absolute values); and (iv) accurately report any notable deviations from this guidelines.
Conclusion: It is anticipated that these guidelines will promote consistent data reporting, which will facilitate inter-comparison of study results.

Key words: skin hydration – transepidermal water loss – skin barrier – stratum corneum – guideline – non-clinical

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THE SKIN functions as a physical barrier preventing loss of body fluids and penetration of substances (chemicals) or infectious agents (1–3). This physical, permeability barrier resides primarily in the stratum corneum (SC) (4–6). Transepidermal water loss (TEWL) and skin hydration have been widely used as indices in evaluating skin barrier function (1, 4, 7–11). TEWL represents the diffusion of condensed water through the SC (7, 12), while skin hydration reflects the water content of the SC (4, 13). An altered skin barrier function is marked by an elevated TEWL and has been observed in a number of skin diseases (e.g. atopic dermatitis and psoriasis) and experimental perturbation studies (e.g. applications of solvents and detergents) (3, 11). Furthermore, elevated TEWL values in a disturbed skin barrier are frequently correlated with low hydration of the SC (3). Several lines of evidence suggest that a disturbed, compromised skin barrier may increase dermal absorption of chemicals and other large substances (e.g. particulate), which cannot penetrate the intact skin (14, 15).

In the workplace, damage to the skin and a compromised skin barrier due to physical and mechanical irritation and chemical insults commonly occur (14). Scrubbing, friction, or abrasion may partially or completely remove the SC and thus disrupt the skin barrier by exposing the viable and water-rich epidermis to the environment (14, 16). It is suggested that organic solvents increase skin permeability by extracting and altering the structure of intercellular lipids from the SC, while desmosomes may also be damaged (14). Surfactants (detergents) interact with skin lipids and proteins leading to disorganization of extracellular lipids, reducing corneocyte cohesion and decreasing skin hydration (14, 17). Occlusion created by prolonged wearing of protective clothing, most notably protective gloves, prevents evaporation of water leading to accumulation of water in intercellular spaces across the SC and swelling of corneocytes (1).

A limited number of studies have been published in which changes in skin barrier function in workplaces have been investigated. Coenraads et al. (18) measured skin vapor loss (SVL) from the skin of metal industry workers during exposure to water-soluble oils and mineral oil. Over the 12-week study, four workers exposed to mineral oil developed contact dermatitis, with a marked increase in SVL. The SVL of other 50 workers remained normal, although SVL levels in workers exposed to water-soluble oils were slightly but not significantly higher than that of the control group. Goh and Gan (19) measured changes in TEWL in newly employed machinists exposed to cutting oils. Smit et al. (20) measured TEWL in apprentice hairdressers and nurses and results implied that hairdressers had an increased risk of hand dermatitis at TEWL >15 $g/m^2/h$ in the hand, but the increased risk was not statistically significant. No relationship was observed for nurses. In a study conducted by Berndt et al. (21), the validity of skin bioengineering methods (including skin hydration and TEWL) as predictive measures for the development of hand eczema, was investigated in a follow-up study of metalworker trainees. They concluded that no single biophysical method can be considered as a valid screening test. However, a combination of short irritation tests and skin hydration permits identification of individuals at high risk for hand dermatitis with a high sensitivity, but with low specificity. Chou et al. (22) measured TEWL in rayon manufacturing workers exposed predominantly to carbon disulfide and sulfuric acid. Significant differences in basal TEWL levels between exposed Chinese workers and a control group were reported. Chou et al. (23) measured TEWL and skin hydration changes among manufacturing workers employed in ultra-low humidity. Both TEWL and skin hydration decreased within 2 weeks of exposure to ultra-low humidity. The maximum change in TEWL occurred after 0.5–1 month and for skin hydration after 2 weeks. In another study by Chou et al. (24), TEWL was measured in cement workers exposed to chromium. They reported a significant increase in TEWL for workers exposed to high levels of chromium. More recently, du Plessis et al. (25) measured TEWL and skin hydration in base metal refinery workers. Results indicated a significant decrease in skin hydration during an 8 h work shift, which recovered to baseline (before shift) levels at the end of the shift. A significant increase was reported between TEWL measured prior to and after the work shift. Changes in skin barrier function were most probably due to exposure to sulfuric acid used in the electrowinning (refining) of nickel. Furthermore, Kütting et al. (26) measured TEWL in metalworkers and reported a slightly but significantly lower TEWL in a group of workers using barrier cream after a 1 year follow-up. However, no other significant difference in TEWL were reported for other sub-groups investigating skin care, skin protection, or both. Most evident from these studies are: (i) the variation in ambient measurement conditions [e.g. temperature and relative humidity (RH)] under which skin barrier function was measured; (ii) the range of different anatomical positions (locations) that were measured; (iii) the frequent lack of information regarding the exact methodology of measurements (e.g. acclimatization time, calibration of instruments and number of measurements for each anatomical position); and (iv) the manner in which collected data were represented and interpreted.

Guidelines exist for the measurement of TEWL and skin hydration in highly controlled clinical settings (7, 27, 28); however, measurement conditions in non-clinical settings, such as workplaces, may be more variable as a result of numerous factors that are often beyond the control of

investigators. Workplaces represent 'worst-case' environments for *in vivo* measurement of skin properties. Hence, there is a need to develop guidelines on non-clinical (e.g. workplace) measurement of TEWL and skin hydration to establish best practices for data collection and reporting. In response to this need, an expert workshop was convened as part of the 5th International Conference on Occupational and Environmental Exposure of the Skin to Chemicals (OEESC) held in Toronto, Canada in June 2011. This paper presents a consensus summary of workshop participants to develop guidelines and best practices for measuring TEWL and skin hydration in non-clinical settings such as the workplace.

Instrumentation and Measurement Principles

Transepidermal water loss represents the outward permeation of condensed water through the SC by means of diffusion, but excludes other forms of water loss such as perspiration (7, 12). TEWL can be measured by using an open-chamber method or closed-chamber method and commercially available instruments are listed in Table 1. Open-chambers are open to the surrounding atmosphere and thus are easily influenced by external air convection and turbulence (29), which necessitates the use of a draft shield to reduce air convection. Closed-chamber methods are more recent designs in which the measuring chamber is enclosed from the surrounding atmosphere and measurements are thus not influenced by external air convection and turbulence (12, 30).

Transepidermal water loss can be calculated by measuring the water vapor pressure (VP) gradient at the skin surface, which is considered constant in the absence of external convection currents. In the open-chamber method, the VP gradient is calculated by measuring the difference in VP between two distinct points aligned perpendicularly to the skin surface. VP is calculated as the product of RH and saturated VP, which is dependent on temperature. Relative humidity is measured using capacitive sensors, while temperature is measured with fast thermistors all located in the cylindrical measuring chamber with open ends. One open end is placed on the skin, while the other acts as an exhaust to allow water vapor to escape to the atmosphere. (4, 9, 12). Measurement with these instruments is restricted to horizontal skin surfaces because of interference from natural air convection (12). However, continuous measurement of TEWL is possible and longer measurement times (approximately 30 s) are more commonly used.

Two types of closed-chamber methods are available, namely a condenser chamber method and an unventilated-closed chamber method. With the unventilated-chamber method, the measuring cylinder is closed off at the top. When placed on the skin, water vapor from the skin collects in the chamber and with time the humidity in the chamber increases, slowly at first, and thereafter linearly. Flux density (amount of water diffusing through the SC per unit distance and time) is calculated from the change in RH and temperature over time (12). Due to the accumulation of water vapor and humidity in the chamber, these instruments must be purged after each measurement and cannot be used for continuous measurements (9, 12). Purging is controlled by the instrument and can take between 20 and 90 s but can be accelerated by waving the instrument through the air. Overall, the measurement time of unventilated-closed chamber instruments is very short (<10 s) (31). There are claims by

TABLE 1. *Commercially available TEWL measurement instruments in alphabetical order*

Instrument	Measurement principle	Manufacturer
Aquaflux	Condenser type closed-chamber	Biox Systems Ltd, London, United Kingdom
AS-CT1	Unventilated closed-chamber type	Asahi Biomed Company Ltd, Yokohama, Japan
DermaLab	Open-chamber type	Cortex Technology, Hadsund, Denmark
Evaporimeter EP1 and EP2	Open-chamber type	ServoMed, Stockholm, Sweden
H4300[*]	Unventilated closed-chamber type	Nikkiso-YSI, Tokyo, Japan
Tewameter TM210 and TM300	Open-chamber type	Courage & Khazaka, Cologne, Germany
VapoMeter SWL3	Unventilated closed-chamber type	Delfin Technologies, Kuopio, Finland

*No longer manufactured (31).

some manufacturers that measurement with closed-chamber type instruments is not affected by the probe angle, but several studies reported an angular dependence (32, 33).

With the condenser-chamber method, the small measurement cylinder is closed off at the top by a condenser. The temperature in the condenser is controlled below the freezing point of water, creating a humidity gradient that causes water diffusion away from the skin surface. The gradient is calculated from two humidity values with one located in the chamber wall and the other from the condenser. The condenser also removes incoming water vapor by condensing it to ice, thus making continuous measurements possible (12).

Skin hydration represents the water content of the SC and is measured indirectly. It is well known that the electrical properties of the skin are dependent on the water content of the SC (4, 13). If the skin is considered as a resistor in parallel with a capacitor in a simple electrical model, these two components (resistance and capacitance) contribute to the total impedance or electrical opposition to an alternating current (resistance) applied on the surface of the skin. Skin hydration is, therefore, measured as the total impedance applied to the skin or alternatively as electrical conductance (reciprocal of resistance) or capacitance (13, 34, 35). Commercially available instruments based on these measurement principles are listed in Table 2.

Factors Influencing TEWL and Skin Hydration Measurements

Endogenous-, exogenous-, and environmental-related factors that influence TEWL and skin hydration are summarized in Table 3. Experimental- and instrumentation-related factors may also influence measurements, but many of these factors can be controlled or minimized by using a well-developed measurement protocol

and are, therefore, addressed in later sections of the text.

Generally, baseline TEWL is independent of age among persons in their working years (36–38), although some studies suggest that TEWL values may be slightly lower in persons over 60 years old (39–41). Skin hydration, however, decreases slowly but steadily with age (34, 41).

There is insufficient evidence to conclude that gender affects TEWL (36, 42–44) and skin hydration (11, 34, 44).The influence of race/ethnicity on both TEWL and skin hydration is quite controversial (11, 52). Several studies demonstrate that no apparent difference exists in baseline TEWL between human races (43, 49, 50, 53, 54), whereas some other studies suggest racial differences in baseline TEWL (46–48) and skin hydration values (49–51). However, it should be noted that these results may be confounded by differences in anatomical positions measured and small numbers of participating subjects (85). Reed et al. (43) suggest that skin type according to the Fitzpatrick scale (a classification of skin phototypes to predict ease of tanning or sun burning), rather than race, explains differences in TEWL values measured.

Transepidermal water loss values vary among anatomical regions of the body, possibly due to factors such as the degree of vasculature in the underlying tissue, musculature in the limb, and skin tonicity. Among anatomical regions, TEWL values tend to be highest on the palm (40, 55, 57, 60). TEWL on the dominant forearm might be significantly higher than the non-dominant forearm (86, 87), although not all studies report such a difference (42, 65). Different TEWL values have also been reported at different sites on the same anatomical position. For example, on the volar forearm, TEWL is higher and more variable closest to the wrist and elbow (56, 65, 87). There are large variations in skin hydration across different anatomical areas (28, 41, 61), with higher values associated with the forehead

TABLE 2. *Commercially available skin hydration measurement instruments in alphabetical order*

Instrument	Measurement principle	Manufacturer
ASA-M2	Conductance	Asahi Biomed Company Ltd, Yokohama, Japan
Corneometer CM820 and 825	Capacitance	Courage & Khazaka, Cologne, Germany
Dermalab Moisture Unit	Impedance	Cortex Technology, Hadsund, Denmark
MoistureMeter SC	Capacitance	Delfin Technologies, Kuopio, Finland
Nova Dermal Phase Meter DPM 9003	Impedance	Nova Technology Corporation, Portsmouth, NH, USA
Skicon 200 and 200 EX	Conductance	ISBS Co Ltd, Hamamatsu, Japan

TABLE 3. *Influence of endogenous-, exogenous- and environmental- and measurement-related factors on the measurement of TEWL and skin hydration*

	TEWL		Skin hydration	
	Influence	References	Influence	References
Endogenous factors				
Age	Yes	(11, 39–41)	Yes	(11, 34, 41)
	No	(36–38)		
Gender	No	(11, 36, 42–45)	No	(11, 34, 44)
Ethnicity	Yes	(7, 46–48)	Yes	(49–51)
	Controversial	(11)	Controversial	(11, 16, 52)
	No	(43, 49, 50, 53, 54)		
Anatomical position	Yes	(7, 11, 38, 40, 48, 55–60)	Yes	(11, 28, 34, 41, 60, 61)
Skin temperature	Yes	(7, 9, 11)	Yes	(11)
Sweating	Yes	(9, 11, 62)	Yes	(11, 63)
Circadian rhythm	Yes	(11, 64–66)	Yes	(66)
			Controversial	(11)
	No	(58)	No	(64)
Skin health	Yes	(3, 59, 67–69)	Yes	(3)
Exogenous factors				
Skin washing and wet work	Yes	(70, 71)	Yes	(14, 71)
Solvents/Surfactants	Yes	(49, 50, 58, 72, 73)	Yes	(14)
Occlusion	Yes	(37, 57, 74, 75)	Yes	(1, 14)
			Controversial	(76)
Skin damage	Yes	(77, 78)	Yes	(74)
Caffeine (topical application)	Yes	(79)		
Smoking	Yes	(24, 80)	Yes	(81)
Environmental and measurement factors				
Air convection/movement	Yes	(9, 11)	Yes	(11)
Ambient temperature	Yes	(9, 11)	Yes	(11)
Relative humidity	Yes	(9, 11)	Yes	(11, 34, 61, 63)
Direct light	Yes	(9, 11)		
Season	Yes	(9, 11, 61, 82, 83)	Yes	(61, 84)
			Controversial	(11)

and palm of the hand, while lower values are associated with the abdomen, thigh, and lower leg (34). More recently, Kleesz et al. (60) reported the highest skin hydration levels for either occluded areas (e.g. axilla) or areas rich in eccrine glands (e.g. forehead), while the scalp measured the lowest levels. It appears as though there are no apparent differences between skin hydration of symmetrical sites of the body. As with TEWL, significant differences exist between skin hydration measured on proximal and distal parts of the volar forearm (34).

Sweating from thermal, emotional, and physical mechanisms increases TEWL and skin hydration values (62, 63), but can be controlled by allowing for adequate acclimatization of subjects to the measurement environment and performing measurements under specific conditions of ambient temperature and humidity (7, 27, 28).

Reports of time-dependent effects on TEWL and skin hydration are conflicting. Some reports suggest that circadian rhythmicity exists for forearm and facial TEWL (64, 66), while others report no diurnal variation in TEWL or a decrease in TEWL values during the day (58, 64). Yosipovitch et al. (64) reported no diurnal rhythms in skin hydration on the face and the forearm, whereas Le Fur et al. (66) reported a diurnal rhythm on the forearm.

Skin health influences TEWL and skin hydration, with TEWL values higher and skin hydration lower, for example, in atopic dermatitis in general (3), even when measured at uninvolved skin.

Exogenous factors influencing TEWL which have important implications for workplace measurement are skin washing and wet-work, use of topical products, exposure to chemicals (including frequency of exposure to solvents and detergents/surfactants), occlusion, and skin damage. Voegeli (71) reported that skin washing increased TEWL, while no significant changes in skin hydration occurred, although there was a tendency for hydration values to decrease with washing. Skin hydration may

increase following prolonged or frequent exposure to water (14). Skin cleansing using anionic surfactants, antimicrobial soaps, and moisturizing soaps increase TEWL values (36, 46, 57, 70, 88, 89), while use of cosmetic creams/lotions may lower TEWL values (30). Barrier creams are sometimes used in industry to protect skin from chemical exposures, however, use of these products may lower TEWL values (90, 91). Exposure to some organic solvents with or without subsequent irritation using sodium lauryl sulfate (SLS) may also increase TEWL values (49, 50, 73), while surfactants will decrease skin hydration (14). Changes in TEWL following exposure to SLS is dependent on the exposure dosage (high dose causes an increase in TEWL) and time of measurement following exposure (92). Occlusion without (37, 57) or with (49, 50) subsequent irritation using SLS causes transient increases in TEWL values. Occlusion as a result of wearing protective gloves leads to transient increases in TEWL and skin hydration (30 min after removal of gloves) (74) and may even lead to hyper-hydration of the SC (1, 14, 74, 75).

Smoking and the consumption of caffeine through caffeinated beverages are common occurrences in most workplaces. Results from one study indicated significantly lower TEWL for non-smokers when compared with active smokers. No significant difference existed between TEWL of active and passives smokers (80). Wolf et al. (81) reported significantly lower skin moisture (hydration) in women smoking between 11 and 20 cigarettes per day. Brandner et al. (79) indicated a significant decrease in TEWL in male subjects when compared with females after topical application of caffeine.

Measurement Protocols for Non-Clinical Settings

The purpose of this protocol is to provide guidelines and best practices for measurement of TEWL and skin hydration in non-clinical settings by accounting for, and to the extent possible, minimizing or eliminating the influences of endogenous, exogenous, environmental, and measurement/instrumentation factors. Prior to performing any measurements, information on the purpose(s) of the study, risks and benefits of participation, and any other pertinent information should be clearly communicated to each study participant (worker). Informed consent must be obtained from each participant in accordance with the human subject policy of the institution(s) governing the study. Upon obtaining informed consent, precise instructions should be communicated to participants regarding acceptable hygiene practices (skin washing), the use of topical products (cosmetics, lotions, barrier creams, etc.) and ingestion of caffeinated beverages, or smoking prior to measurements (7, 79, 93).

Instruments and Supplies

Apart from a TEWL instrument and/or skin hydration measurement instrument as listed respectively in Tables 1 and 2, it is necessary to have an ambient thermometer and RH-meter. Measuring skin temperature with a skin thermometer prior to TEWL and skin hydration measurements is preferred. For TEWL measurements, it will indicate the temperature to which the TEWL probe should be heated to before making measurements. For skin hydration measurements, control of skin temperature and ambient room temperature is required to measure skin hydration at a single frequency (28).

For TEWL measurements, it is recommended that a closed-chamber type instrument be used in the workplace because this design is not influenced by air movement (12, 31), have short measuring times (<10 s) and some are small battery-operated devices making them easily portable. However, if an open-chamber TEWL instrument is to be used, a draft-shield is required to eliminate the effects of air movement on measurements.

Preparation, Handling, and Storage of Instruments

Depending on the instrument used, it should be turned on at least 15–30 min prior to taking measurements in the area in which actual measurements will be taken (9, 12, 27). If instruments are to be used intermittently during the day (work-shift), it should not be switched off between measurements (9). However, battery-operated instruments are designed to switch-off automatically after a few minutes of non-use. Differences between skin temperature and probe temperature may influence TEWL values (7), hence the use of probe heaters (provided by some manufacturers) is recommended. Prior to

and during measurements, the TEWL probe should always be handled with an insulated glove or other indirect means as holding the probe causes an increase in the temperature of the probe and subsequently influences TEWL readings (7, 12, 30).

For hygiene purposes, the probe head must be wiped with an alcohol-soaked tissue after completion of measurements on a study participant to prevent possible transfer of infections between participants. Another alternative is the use of shields, which are available from some manufacturers. Between uses, the instruments should be cleaned and stored in accordance with the manufacturer's instructions. In general, this implies cleaning of the instrument/probe with a soft tissue or an alcohol-soaked tissue to remove excessive dirt and storage in a clean dry place with temperature and RH resembling that of the usual environment when used.

Calibration of Instruments

Only calibrated TEWL and hydration instruments should be used for measurements. There are two types of calibration that could be performed, namely manufacturer calibration and prior-to-use calibration (not applicable to all instruments). Manufacturer calibration requires that the instrument (and/or measurement probe) be sent to the manufacturer for calibration at specified intervals, which is determined by the manufacturer, usually once a year. When instruments are used very frequently, it is recommended, if practicable, that manufacturer calibration be done bi-annually or quarterly. Prior to use, calibration should be performed at regular intervals as specified by the manufacturer. The procedures of prior-to-use calibration may vary between manufacturers and should also be done in accordance with the instructions of the manufacturer. Due to the simplicity of some calibration procedures, calibration could easily be performed daily. As a measure of further quality control, and if practicable, prior-to-use calibrations could be verified after performing a set number of measurements on a specific day or in between two prior-to-use calibrations. For TEWL instruments, two flux calibration methods are currently in use, namely the more commonly used wet-cup method (for open and closed-chamber type instruments) and a new droplet method (for instruments

capable of recording continuous flux, but not unventilated closed-chamber type instruments). The reader is referred to Imhof et al. (12) for a more detailed description of these calibration procedures. For skin hydration instruments, a two-point (low and high value) calibration check should be performed prior to use and during periodic verifications of calibration.

Measurement of TEWL and/or Skin Hydration

Prior to measurement of TEWL and/or skin hydration, a study participant should be acclimatized to the measurement environment to avoid errors caused by environmental temperature or sweating. For clinical studies, EEMCO recommend an acclimatization period of least 15–30 min at an ambient temperature (20–22°C) and relative humidity (40–60%) prior to measuring TEWL (7, 27) and at least 20 min for skin hydration (28) to eliminate sweating. The anatomical position(s) to be measured should be exposed to ambient air for at least 10 min prior to measurement (28). In non-clinical settings such as the workplace, it may not always be feasible for a worker to leave their shift long enough to acclimatize for 20 min plus time for measurements. It should be noted that workers may be unwilling to have measurements performed on their own time (before, during or after a shift) because of personal reasons. An acclimatization period as long as practicably possible is recommended. In non-clinical settings such as workplaces, the environmental conditions recommended by EEMCO may not be readily achievable. In experiences gained from past workplace assessments, researchers may be provided a space for testing where there is little control over the ambient temperature, humidity and air movement. Hence, it is recommended that measurement conditions be controlled and characterized (reported) as far as reasonably practicable. Measurements during extreme conditions of cold, heat, or RH should be avoided.

Exogenous factors such as use of topical products, washing, occlusion, smoking and ingestion of caffeinated beverages may influence TEWL and skin hydration values. Ingestion of caffeinated beverages should be avoided 3 h prior to and during the work shift (93). Application of topical products in the intended measuring area

should be avoided 12 h prior to participation/measurement (94). In many workplaces, such as in healthcare sector, the food industry, and cosmetology where frequent (hand) washing or handling of topical products and lotions occur, this is not possible. The same applies to the use of barrier creams in the workplace. Therefore, the use of any topical product or lotion should be noted according to type used, frequency of application, and time of last application. In workplace studies, acute changes in TEWL and skin hydration during normal working procedures are of interest. Because of the acute effects of washing on TEWL and skin hydration (71), it is recommended that measurements be made before washing or application of topical products and lotions if feasible (e.g. before the start of the work shift and before the end of a shift). Many work tasks require wearing of highly occlusive personal protective clothing such as gloves and coverall suits made of numerous types of textiles and materials. As such, it is important to verify whether the worker (participant) wore protective clothing over an anatomical position and if so, to record information regarding the type of protective clothing, such as the frequency and duration of use, time between last use and measurement. Finally, unless the purpose of the study is to evaluate diseased skin, no measurement should be made on clinically inflamed skin or adjacent to such position. If the measurement position is compromised by disease or injury, a nearby position may be used instead. If a nearby position cannot be identified, the participant should rather be excluded from the study.

In clinical studies, the recommended anatomical position for TEWL and skin hydration measurement is the volar forearm away from the wrist (7, 28), although other anatomical positions have also been measured as well as differences between these anatomical positions. In the workplace, TEWL and skin hydration measurements should be made on anatomical positions relevant to the activities and tasks of workers. Even if another anatomical position is of interest, it is highly recommended to measure TEWL and skin hydration at the mid volar forearm as a standard reference. A complicating factor is the use of personal protective clothing and respirators, leaving in many instances the volar forearm occluded and only the neck and cheeks not occluded. In these instances, study goals must

be considered to determine the most appropriate anatomical positions to be measured, and if measured factors influencing values should be noted and considered when data are interpreted. For skin hydration measurements in particular, the presence of body hair may interfere with the contact between the sensor and the skin, which may influence measured values (28). Measurement on extremely hairy positions should be avoided, or alternatively, hair should be removed and the skin allowed to recover before measurements.

Although a horizontal probe angle is of particular importance when using an open-chamber type TEWL probe, it is suggested that all TEWL measurements be performed on horizontal skin surfaces irrespective of the type of instrument used (12). When measuring the cheek or neck, the study participant must lie down, if possible, or adjust his body position to ensure a horizontal measurement area. For open-chamber type TEWL probes variations in pressure between the probe head and surface of the skin may alter TEWL values as a result of changes in the distance between skin and sensors (9, 29). Closed-chamber type TEWL instruments have minimal sensitivity to contact pressure, but timing of skin contact is of more importance as ambient temperature and RH is measured shortly before skin contact is made. For both types of TEWL instruments, adequate (light) constant pressure should be applied on the probe/instrument to ensure sufficient contact between the instrument/probe and skin surface (12). Skin hydration probes are equipped with a spring mechanism, which ensures application of adequate contact pressure before a measurement can be made (34). Measurements should be recorded when a stable signal is achieved. Because of differences in TEWL and skin hydration instruments, a measurement should be considered stable when it meets the criteria as defined by the manufacturer. It is also recommended that all TEWL and skin hydration measurements be made by the same person to reduce variability. The number of TEWL and skin hydration measurements made per anatomical position is highly variable in published clinical studies. It is recommended that three sequential measurements be made on the same anatomical position and the results averaged. A waiting time of 5 s between sequential skin hydration measurements on the same

anatomical position is recommended by one manufacturer (95). Furthermore, it is recommended that all measurements be made on a given anatomical position before moving to the next position. If repeat measures will be made on a specific anatomical position (e.g. before shift and after shift), both sets of measurements must be recorded at the same position to reduce errors. One can ensure that the same anatomical position is measured each time, by photographing the measurement location and using the photograph as a reference for future measurements, marking the skin adjacent to the measurement position with a non-toxic ink, and/or using a template. For hygienic purposes and to get rid of possible contaminants, the skin hydration probe should be wiped with an alcohol cloth between study participants, but not in between performing measurements on the same participant.

Interpretation of TEWL and Skin Hydration Measurements

Transepidermal water loss and skin hydration values are influenced by factors as summarized in Table 3, but there is also a lack of consensus regarding the reference values for normal and/or diseased skin. This is highlighted for example by differences between the manufacturer (95) and three studies (34, 96, 97) interpreting skin hydration values for the same instrument. As such, it is recommended that results for a given anatomical position be reported and compared as a relative (or percent) change in TEWL and/or skin hydration values. To illustrate, if the aim of a study is to assess acute changes in barrier function caused by exposure, then quantifying the difference in TEWL and/or skin hydration relative to the before shift (baseline) for a worker would be appropriate. If the aim of a study is to assess chronic changes caused by exposure or disease, then expressing the difference in TEWL and/or skin hydration between a worker and control subject as a percentage is preferred over absolute values.

TEWL and skin hydration results at a given anatomical position should be expressed as the arithmetic mean and standard deviation of the mean. If the aim of a study warrants use of a control group, the volunteers should be matched to workers as reasonably as possible with respect to relevant endogenous, exogenous, and environmental factors and measurements made in a similar environment with the same instruments.

Data Reporting

To ensure meaningful communication of results, a basic data set should be collected and reported with study results. In addition to notable deviations from the guidelines in this protocol, the following information must be reported (see Appendix A for a checklist to facilitate collection of pertinent information):

1 Endogenous factors

  a The anatomical position(s) and exact site(s) of TEWL and/or skin hydration and a rationale for the choice of site(s).

  b Skin health at time of measurements. For measurements on hands and wrists, health can be documented and assessed using, for example, a validated teledermatology toolkit for standardized hand photographs in non-clinical settings (98). Furthermore, the inclusion of a skin symptoms questionnaire for current symptoms might be advisable.

  c Time of day when measurements were performed. Note that if TEWL and/or skin hydration is to be quantified on different days for the same study participant, to the extent feasible, measurements should be made at the same time of day to minimize any possible effects of circadian rhythms.

2 Exogenous factors

  a Hygiene (washing) practices prior to measurement, including conformance or deviations from instructions given to study participants.

  b Use of any topical products, including conformance or deviations from instructions given to study participants. Note also if skin was dry wiped before measurement because of use of topical products.

  c Exposure to chemicals or mechanical damage to the skin as a result of work.

  d Use of any personal protective clothing or other materials that might have caused occlusion of the skin, including the type of covering, frequency, and duration of use, and time since last use.

e Ingestion of caffeinated beverages or smoking prior to measurement.

3 Environmental factors

a Calendar date, season, and time of TEWL and skin hydration measurements.
b Average outdoor ambient temperature and RH.
c Ambient workplace temperature and RH.

4 Experimental and measurement/instrumentation factors

a The type of instrument/probe according to model and manufacturer.
b Equilibration time of TEWL instrument and/or hydration instrument in measurement environment.
c Calibration (manufacturer and prior to use, if applicable) of TEWL instrument and/or skin hydration instrument.
d Frequency with which the skin hydration probe calibration was verified during the study.
e Acclimatization conditions of study participants prior to measurements, including duration, ambient temperature, and RH in measurement area.
f How the instrument was applied to the skin surface, including handling of the TEWL probe and time to achieve a stable measurement in accordance with the manufacturer instructions.
g The number of measurements per anatomical position and lag time between measurements.

Summary

The skin, as the body's largest organ, is continuously exposed in the workplace to a variety of physical stressors and chemical contaminants capable of affecting the skin barrier. As such, there is an emerging perspective that it is not sufficient to just assess exposure to a stressor or chemical contaminant of concern, it is also important to understand the condition of the skin, i.e. the barrier function, at the time of exposure. A consensus summary of guidelines and best practices for measurement of TEWL and skin hydration in non-clinical settings, with emphasis on the workplace as a worst-case scenario, is presented. Key points of this guidelines are: (i) to minimize, to the extent feasible, the influences of endogenous-, exogenous-, environmental-, and instrument measurement/instrument-related factors; (ii) to measure TEWL with a closed-chamber type instrument because this design is not influenced by air movement, uses short measuring times, and some of these instruments are small battery-operated devices making them easily portable; (iii) to report results of TEWL and skin hydration measurements as a difference or percent change (rather than absolute values); and (iv) to accurately report notable deviations from this guidelines and all factors listed in the data reporting checklist. The intention of these guidelines is to provide consistency in non-clinical measurement and reporting of TEWL and/or skin hydration data, which is essential for comparison of different study results.

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Appendix A

The following checklist is provided to assist researchers with collection of critical variables for non-clinical measurement of TEWL, skin hydration, and skin surface pH [refer to Stefaniak et al. (99)]. Any other notable deviations from the guidance in these protocols should also be recorded.

	Yes	No	N/A

Environmental factors

1. Were the following recorded during the study?
    a. Season(s) during which measurements were made
    b. Typical average outdoor seasonal temperature and humidity levels
    c. Date(s) and time(s) of day of measurements

Endogenous factors

2. Were the following recorded for each participant during each work shift?
    a. Anatomical position(s) and exact measurement site(s)
    b. Health of the skin at the measurement site(s) assessed by a qualified person

Exogenous factors

3. Were the following recorded for each participant during each work shift?
    a. Time since last smoking
    b. Exposure to workplace stressor, including levels of exposure
    c. Deviations from protocol with regard to washing
        i. Whether measurement site was washed prior to measurement
        ii. Number of times the measurement site was washed
        iii. Elapsed time between the last washing event and the measurement
    d. Deviations from protocol with regard to use of any topical products
        i. Information on type of product (form, composition, manufacturer)
        ii. Whether the product was used on the measurement site
        iii. Number of times the product was applied to measurement site
        iv. Whether a dry wipe was used to remove product from skin prior to measurement
        v. Elapsed time between the last application of product and the measurement
    e. Use of occlusive coverings (protective garments, clothing)
        i. Information on type of occlusive covering
        ii. Whether the occlusive covering was used on the measurement site
        iii. Number of times the covering was used on the measurement site
        iv. Duration over which covering was on the measurement site
        v. Elapsed time between last removal of the covering the measurement

Experimental and measurement/ instrumental factors

4. Were the following recorded during the study?
    a. Equilibration time of the instrument in the measurement environment
    b. Calibration of the instrument including standards used
    c. Frequency of calibration verification
    d. Acclimatization conditions in room where measurements were made
        i. duration spent by study volunteers in room
        ii. temperature and relative humidity of room
    e. Temperature and humidity of the workplace
    f. Method used to apply the instrument probe to the skin surface
        i. contact angle
        ii. time to achieve a stable measurement
    g. Number of measurements per anatomical position and measurement site
    h. Lag time between measurements
        i. Whether measurement repeats were taken adjacently to each other or sequentially at exactly the same measurement site

N/A = not applicable.