

# Comparative metrology of the evaporimeter and the DermaLab<sup>®</sup> TEWL probe

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**Background/aims:** Transepidermal water loss (TEWL) measurements are one of the most frequently utilized of the non-invasive bioengineering techniques. Recently, Cortex Technology (Hadsund, Denmark) introduced the DermaLab<sup>®</sup> system, which can be equipped with a TEWL probe. It is based on the vapor pressure gradient estimation method of Nilsson and, thus, is quite similar to the Servo Med evaporimeter. In this paper, we compare these two commercial instruments under identical experimental conditions using both *in vitro* studies with physical standards as well as *in vivo* studies employing human volunteers.

**Methods:** Five different evaporimeters and four different DermaLab<sup>®</sup> main units equipped with one or two TEWL probes were configured in such a way that six freshly calibrated probes of each type could simultaneously be compared in an ambient environment with known relative humidity and temperature values. In follow-up experiments, each type of instrument was interfaced to a Pentium personal computer, and special data acquisition software was written so that changes in water loss rates could be monitored in real time. These follow-up studies included comparing water vapor transmission rates through various mem-

branes *in vitro* and a modified soap chamber test using the volar forearm of adult human volunteers *in vivo*.

**Conclusions:** Although we found very good agreement between the two instruments, our overall findings clearly demonstrate that the DermaLab<sup>®</sup> system with a TEWL probe is both more accurate and precise than the Servo Med evaporimeter when used under identical conditions. This is especially obvious when the comparisons between the two types of instruments are based on physical standards. The DermaLab<sup>®</sup> system with a TEWL probe was also found to be more sensitive and better able to resolve among detergents that differed in harshness. The superior performance of the DermaLab<sup>®</sup> system can be in part explained by the differences in the way the probes are calibrated by the factory.

**Key words:** computerized evaporimetry – transepidermal water loss (TEWL) – stratum corneum – barrier function – detergent damage

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IT IS GENERALLY appreciated that *in vivo* measurements of transepidermal water loss (TEWL) rates through human skin can be used to non-invasively monitor changes in stratum corneum barrier function. In normal, healthy skin, the barrier is quite effective and water loss rates are typically very low. If the barrier is not fully functional due to pathological processes or it is damaged by physical or chemical agents, there will be a corresponding increase in water loss rates that directly relates to the degree of impairment. Conversely, there will be a corresponding decrease in TEWL as the barrier is restored. This means that monitoring changes in TEWL over time not only allows one to evaluate therapeutic response to different treatments but can also be used to determine the effectiveness of various prophylactic strategies that could be used to prevent or lessen the injury in the first place. Thus, it is not surprising that there is con-

siderable literature dealing with TEWL measurements. Indeed, these methods were the very first to be reviewed by the Standardization Group of the European Society of Contact Dermatitis (1).

Over the years, a number of instrumental methods have been devised to measure TEWL (for general reviews, see 2–4). By far the most popular instrument has been the Servo Med evaporimeter (Kinna, Sweden), which is based on the vapor pressure gradient estimation method of Nilsson (5). The underlying principle is that there is a vapor pressure gradient close to the surface of the skin that is dependent upon the rate of water exchange through the skin. The probe consists of an open cylinder that is placed perpendicular on the skin site to be measured. Within this cylinder, there are sensors that are set at different fixed distances above the skin surface. At each point, the local relative humidity and temperature are mea-

sured by paired sensors and the vapor pressure at each point computed. The difference between the vapor pressure at these two points along the gradient is directly related to rate of evaporative water loss from that skin site.

Despite widespread use, comparative studies of how well this instrument performs are very few (see Table 1). In several studies (5–7), the comparisons were limited to a single instrument being evaluated against various physical standards in vitro. In cross comparisons where the evaporimeter was being evaluated against another instrument (8–12), a single instrument of each type was used to measure the biologic response to various perturbations of the stratum corneum, such as tape stripping in vivo. Although this does give some insight as to how well these different instruments correlate under actual use conditions, the uncertainty surrounding any biologic response measurement makes it difficult to rate how well each instrument is performing in terms of accuracy and reproducibility. Good correlation only tells you that the instruments agree, not that they are correct.

The study of Pinnagoda et al. (13) is especially noteworthy because it utilized both in vitro and in vivo studies to compare the water loss rates obtained with four different evaporimeters run under the same controlled conditions. They found considerable variations, with one of the probes being distinctly out of range, and felt that the manufacturer's recommended calibration procedure needed to be improved.

Recently, Cortex Technology (Hadsund, Denmark) introduced the DermaLab<sup>®</sup> system that can be

equipped with a TEWL probe. It is based on the vapor pressure gradient estimation method of Nilsson (5) and thus is quite similar to the Servo Med evaporimeter. In this paper we compare these two commercial instruments under identical experimental conditions using both in vitro studies with physical standards as well as in vivo studies based on a typical application, namely, detergent damage.

## Material and Methods

### *Servo Med evaporimeter hardware and software specifications*

Five different evaporimeters (3 single probe EP1C's, 1 dual probe EP1D & 1 single probe EP2) were utilized in this study. Although the EP2 is a new version of the evaporimeter, there are very few differences between it and the older EP1. Indeed both share the same probe, which is the critical component. Thus, by running all five instruments side by side we could evaluate six probes simultaneously. All probes were taken out of inventory and had not been previously used. Each had certificates signed by Per-Anders Östby of Servo Med AB that indicated that they were recently calibrated by the factory. In the initial study, the relative humidity (RH) and partial pressure of the ambient environment were read from the metered display of the EP1's by activating the appropriate switch on the front panel. The highest degree of filtering (+10 and +20 buttons both activated) was used to give a representative value free of minor fluctuations (14, 15).

In follow-up studies, only the computerized EP2 utilizing software (16) created by cyberDERM, inc. (Media, PA, USA) was employed. These data acquisition programs utilized the data inputs sent to a Pentium personal computer (PC) via the parallel port from the DATASHUTTLE 12-bit analogue-to-digital (A/D) converter (Strawberry Tree, CA, USA) that is built-in to the EP2. In this manner, the computed water loss rate as well as the values for relative humidity and temperature of the upper and lower sensors on which it is based can be monitored in real time. The damper switch was left off so that the least damped signal was available for computer analysis.

### *DermaLab<sup>®</sup> with TEWL probe hardware and software specifications*

Four different DermaLab<sup>®</sup> main units (2 single probe units and 2 dual probe units) were utilized in this study. This allowed six probes to be evaluated simultaneously. All probes were recently calibrated by our group using "constant humidity" solutions that were prepared as saturated aqueous salt solutions of lith-

TABLE 1. Previous reports dealing with comparative performance studies of the Servo Med evaporimeter for measuring evaporative water loss rates

Reference	Compared against	Method utilized
Nilsson (5)	—	In vitro, calibration box
Wheldon & Monteith (6)	—	In vitro, Celgard WVTR
Schultz et al. (7)	Dermatest ventilated chamber	In vivo, SLS response
Blichmann & Serup (8)	—	In vitro, wet cotton pad In vivo, palm & forearm
Scott et al. (9)	Ventilated chamber method	In vivo, tape stripping n-hexadecane
Barel & Clarys (10, 11)	Tewameter	In vivo, tape stripping Occlusion Various skin sites
Rogiers (12)	Tewameter	In vivo, SLS response
Pinnagoda et al. (13)	Other evaporimeters	In vivo, forearm In vitro, Op-site WVTR

ium chloride and sodium chloride. These were housed in a temperature-stable environment with sufficient time for the water temperature, air temperature and humidity to all come into equilibrium before any electronic adjustments were made. In the initial study, the values of ambient RH and temperature were read from the liquid crystal display (LCD) of the various DermaLab<sup>®</sup> main units by electing "Environmental Check" from the menu. The slowest filter was used to give a representative value free of minor fluctuations (17).

At the Skin Study Center, we routinely use a dual probe DermaLab<sup>®</sup> system because it allows us to obtain simultaneous duplicate readings for each evaporative water loss measurement. In our follow-up studies, we limited ourselves to a single probe configuration so that we could have a setup similar to the Servo Med EP2, which can only be used as a single probe instrument. The DermaLab<sup>®</sup> main unit was interfaced via RS-232c cabling to the serial port of a Pentium PC using Windows-95 and data acquisition software by cyberDERM, inc. (Media, PA, USA). In continuous mode, the DermaLab<sup>®</sup> system will transmit data in the form of ASCII text at a rate of 4 lines per second. Each line provides not only the computed water loss rate but also the values for relative humidity and temperature of the upper and lower sensors on which it is based (18). The fastest filter was employed so that the least damped signal was available for computer analysis.

#### *Initial studies involving a side by side comparison of all units*

All of the Servo Med evaporimeters and DermaLab<sup>®</sup> units were placed in the same environmental chamber and allowed to warm up for 3 h. The 12 probes being simultaneously evaluated were placed side by side on a plexiglass holder with the sensors of each probe oriented parallel to the floor. The probes were placed as far away from the main unit as the cabling would allow (approximately 3 feet) and surrounded by a plexiglass shield to eliminate any artifacts due to operator movements. At 5 min intervals over the next hour, the RH and temperature or partial pressure values were recorded for each probe. Concurrent measurement of the room RH and temperature was also done using a certified thermohygrometer (OHMIC, Easton, MD, USA).

#### *Follow-up in vitro studies using reference standards*

A reference box was constructed using a closed chamber containing an open cell foam material that

was fully loaded with a standard amount of water. The upper lid had three openings that were covered with polymeric films that differed in water vapor transmission rates (WVTR) according to ASTM E 96-95 (19). Sufficient area was exposed so that the operator could simultaneously evaluate a single probe of a Servo Med evaporimeter with a single probe from a DermaLab<sup>®</sup> system. Each probe was clamped in place so that the different surfaces could be easily slipped into place under the paired probes. A series of measurements in which the evaporative water loss was sequentially determined on the low, medium and high WVTR films ten times in succession was performed using a fixed duration program that calculated the mean water loss rate in gm/m<sup>2</sup> h under steady-state conditions for 30 s. The individual values for each of the paired determinations was statistically evaluated using a linear regression model (20). In addition, the data were classified according to the three WVTR values and then compared for both accuracy and precision.

#### *Follow-up in vivo studies based on the modified soap chamber test*

This clinical study utilized the modified soap chamber test as described by Simion et al. (21). It involved 11 panelists who had their volar forearms exposed to 5% aqueous solutions of eight test products under occlusion for 24 h, as described. Transepidermal water loss rates were measured in duplicate at each site with both the Servo Med evaporimeter and the DermaLab<sup>®</sup> units using cyberDERM, inc. software to insure that steady-state conditions had been achieved (22). This was done immediately before patching and 2.5 h after the patches had been removed. The individual values for each of the paired determinations was statistically evaluated using a linear regression model (21). In addition, the net change from baseline was computed for each test product and the statistical significance of these differences evaluated using a repeated measures ANOVA and Tukey's protected *t*-test for cross comparisons.

Since this study involved human volunteers, the probes were not placed directly on the skin surface. Instead, a removable protective skin cover that was replaced for each panelist was employed. In the case of the Servo Med evaporimeter, we used the model #2107 protective cover with screen and grid that elevates the probe approximately 6 to 7 mm. In the case of the DermaLab<sup>®</sup> system, we used a disposable plastic disc that only elevates the probe approximately 0.25 mm.



TABLE 2. Accuracy and precision of the relative humidity readings obtained with the Servo Med evaporimeter and DermaLab<sup>®</sup> with TEWL probes from a side by side comparison involving multiple units and probes of each type

Evaporimeter probe combo	% RH reading	DermaLab <sup>®</sup> probe combo	% RH reading
1	30.9±0.8	1	34.5±1.0
2	29.8±0.6	2	33.3±0.8
3	35.7±0.9	3a	34.2±0.6
4a	40.8±1.1	3b	34.1±0.8
4b	33.8±0.9	4a	35.2±0.6
5	36.2±1.0	4b	34.1±0.6
Mean	34.55	Mean	34.22
SD	3.98	SD	0.63
% CV	11.51	% CV	1.84

SD=standard deviation; CV=coefficient of variation.

TABLE 3. Accuracy and precision of the partial pressure readings obtained from the Servo Med evaporimeter and the temperature readings obtained from the DermaLab<sup>®</sup> with TEWL probes from a side by side comparison involving multiple units and probes of each type

Evaporimeter probe combo	Partial pressure	DermaLab <sup>®</sup> probe combo	Temperature
1	6.5±0.8	1	23.8±0.6
2	5.4±0.7	2	24.3±0.4
3	6.4±0.8	3a	23.9±0.4
4a	7.5±1.0	3b	24.1±0.4
4b	6.5±0.8	4a	23.1±0.4
5	6.5±0.9	4b	23.2±0.3
Mean	6.65	Mean	23.72
SD	0.81	SD	0.49
% CV	12.21	% CV	2.07

SD=standard deviation; CV=coefficient of variation.

## Results

### Initial studies involving a side by side comparison of all units

With the various evaporimeter and DermaLab<sup>®</sup> instruments that were available to us, we were able to simultaneously record the relative humidity values of six probes of each type. As shown in Table 2, the average values obtained for both sets of probes were not only in excellent agreement with each other but also matched the relative humidity value obtained with the certified thermohygrometer for these ambient conditions of 34% relative humidity. In both cases, the standard deviations associated with each probe were very small and clearly indicated that reproducibility of successive measurements with any individual probe of either manufacturer was quite high.

Upon closer inspection of the data, it became readily apparent that there is considerably more variation

among the probes of the Servo Med evaporimeter compared to those of the Cortex Technology DermaLab<sup>®</sup>. Indeed, despite being freshly calibrated by the factory, several of the probes appeared to be beyond the permissible range of accuracy ( $\pm 15\%$  or  $2 \text{ gm/m}^2 \text{ h}$ ) specified by the factory (15). In striking contrast, the coefficient for all of the TEWL probes for the DermaLab<sup>®</sup> was less than 2%, which means that they were well matched and could be considered interchangeable (23).

In addition to the relative humidity values, we were able to measure either the partial pressure or the temperature of the ambient room conditions with the Servo Med evaporimeter or DermaLab<sup>®</sup>, respectively. These results are summarized in Table 3.

Although not directly comparable, the spread in the partial pressure data of the Servo Med probes is much greater than that seen in the temperature data of the DermaLab<sup>®</sup> probes, suggesting that the Servo Med evaporimeter may be less reliable. Since concurrent measurement using a National Institute of Standards and Testing (NIST) certified thermohygrometer indicated the room temperature was  $23.5^\circ\text{C}$ , we knew that the DermaLab<sup>®</sup> readings were very accurate. According to the Clausius-Clapeyron equation, the water vapor pressure at 34% RH and  $23.5^\circ\text{C}$  should be  $7.34$ . This means that the Servo Med probes that gave an average value of 6.65 were considerably less accurate in this regard. When expressed in terms of temperature the observed error associated with the Servo Med evaporimeter was approximately  $1.5^\circ\text{C}$  lower than that expected from the standard reference value. Ad-

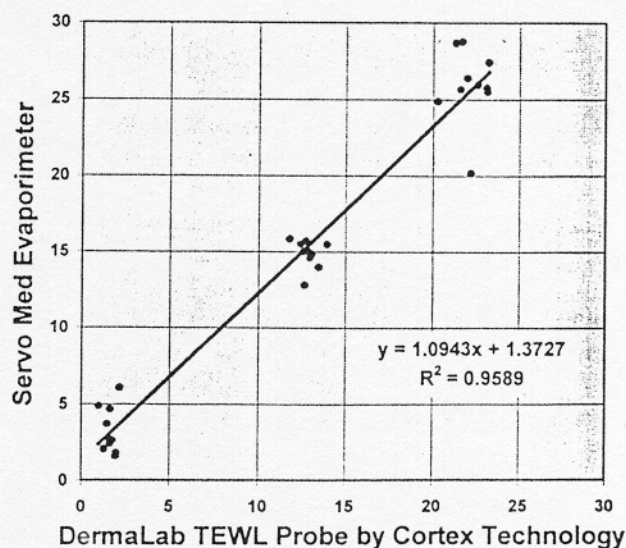


Fig. 1. Comparative metrology of EWL measurements.



ditional studies with other combinations of probes and evaporimeters, including the EP1C and EP1D, gave similar results.

#### Follow-up in vitro studies using reference standards

In order to assess the reproducibility of both instruments, comparative measurements were made of the evaporative water loss rates through three different membranes with known water vapor transmission rates. Figure 1 shows that there was excellent agreement between the Servo Med evaporimeter and the DermaLab® TEWL probe in this regard with the plot showing the expected clustering about three points representing the membranes of low, medium and high permissivity. It can also be seen from Fig. 1 that the DermaLab® values tended to be less than the corresponding value obtained with the Servo Med evaporimeter. This is also obvious in the data summarized in Table 4. Note that for each of the three different types of membranes, the coefficient of variation was always higher for the Servo Med evaporimeter, which means the reproducibility was better with the Der-

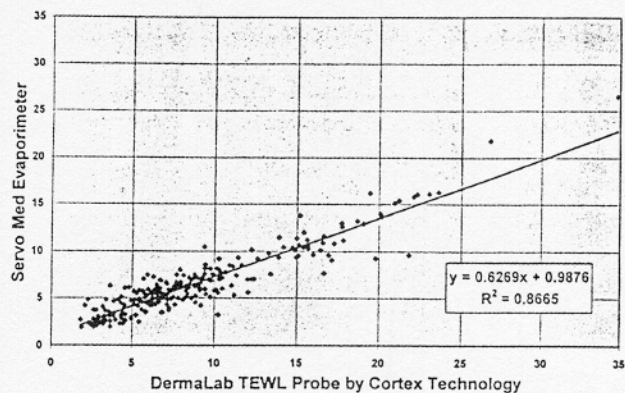


Fig. 2. Comparative metrology of TEWL measurements based on modified soap chamber test results.

maLab® TEWL probe.

#### Follow-up in vivo studies based on the modified soap chamber test

In order to assess the sensitivity of both instruments under actual use conditions involving human volunteers, transepidermal water loss measurements were taken before and after exposing the skin surface to detergent solutions that differed in harshness. Figure 2 shows that there was excellent agreement between the Servo Med evaporimeter and the DermaLab® TEWL probe over the wide range of values obtained in this clinical study. Please note that the degree of correlation was less than that seen in the in vitro study. This is most likely a reflection of the increased noise inherent in measurements obtained from human volunteers.

It is also important to note that in this comparison the Servo Med evaporimeter values tended to be lower than the corresponding value obtained with the DermaLab® system. Most likely this was due to the use of the protective covers, which place the Servo Med probe further from the skin surface and reduce the observed values, as discussed by Pinnagoda et al. (1, 14).

These data, as summarized in Table 5, also show that the DermaLab® TEWL probe is more sensitive than the Servo Med evaporimeter and resolves product differences better. This is especially true in the lower ranges where the DermaLab® system clearly distinguishes Codes E & G from B & C while the Servo Med evaporimeter fails to do so. In every cross comparison using a repeated measures ANOVA and Tukey's protected *t*-test, the degree of significance given by the DermaLab® system exceeded that obtained with the Servo Med evaporimeter.

TABLE 4. Reproducibility of the Servo Med evaporimeter and DermaLab® with TEWL probe based on 10 successive readings of the water vapor transmission rates (WVTR) obtained from three different membranes using a single probe instrument of each type in a paired fashion

WVTR	Servo Med evaporimeter			DermaLab® TEWL probe		
	Mean	SD	% CV	Mean	SD	% CV
Low	3.2	1.5	46.8	1.7	0.3	20.7
Medium	14.9	0.9	6.2	12.8	0.6	4.5
High	25.9	2.4	9.3	22.1	0.9	4.3

SD=standard deviation; CV=coefficient of variation.

TABLE 5. Comparative metrology of TEWL measurements based on the results of a modified soap chamber test

Code	DermaLab® TEWL probe		Servo Med evaporimeter	
	Mean±SD	Class	Mean±SD	Class
E	1.4±1.3	I	1.0±1.1	I
G	2.0±1.6	I	1.4±1.1	I
B	3.7±1.6	II	2.0±1.6	I
C	4.2±1.8	II	2.1±1.8	I
A	7.7±2.4	III	4.6±1.8	II
H	8.2±3.3	III	4.4±2.4	II
D	9.3±3.4	III	5.8±3.5	II
J	12.7±3.7	IV	8.1±3.6	III

SD=standard deviation.

## Conclusion

In this series of comparative metrology studies, we were able to simultaneously evaluate the accuracy, reproducibility and sensitivity of the Servo Med evaporimeter and the DermaLab<sup>®</sup> system with TEWL probe under identical conditions of use. It is quite clear that if one is only concerned with the reproducibility of measurements obtained with a single probe used successively, then both types of instruments will be judged to perform exceptionally well. It is only when one begins to cross compare different units and/or probes that the discrepancies become readily apparent. Although the problems we observed with the Servo Med evaporimeter were less than those reported by Pinnagoda et al. (13), they were nevertheless very bothersome. In contrast to the manufacturer's claims, we found that the Servo Med probes were not truly interchangeable, even when dealing with fresh probes that had just been calibrated by the factory.

We are not the first to criticize the manner in which the probes are calibrated by Servo Med. Pinnagoda et al. (13) previously commented that the factory method was inadequate. As detailed in the EP1 handbook (15), the factory recommended method is a three point calibration based on saturated aqueous salt solutions of lithium chloride, magnesium nitrate and potassium sulfate. After the sensors have come into equilibrium with the vapor phase above the appropriate salt, a trim potentiometer is used to adjust the electronic circuit of the lower sensor to give the proper RH value on the front panel meter. Another trim potentiometer is then used to adjust the output of the upper sensor circuit until a water exchange (WE) rate of zero is shown. This is repeated with the other two salts as well as redoing the first until the upper and lower sensors are zeroed for all three reference solutions. One problem with this approach is that the digital meter reads RH only to the nearest unit and WE to the nearest tenth. Thus, there is considerable uncertainty in these critical adjustments.

It is also important to realize that Nilsson's method is based on the vapor pressure gradient, which means the sensors must be properly calibrated for temperature as well. Unfortunately, the recommended method makes no provision for this with the Servo Med evaporimeter. This may explain the error in partial pressure measurements we uncovered during our studies.

In striking contrast, the computerized DermaLab<sup>®</sup> system outputs are such that a direct and simultaneous readout of the relative humidity and temperature readings of the upper and lower sensors are read-

ily available. During calibration, which involves two saturated salt solutions (lithium chloride and sodium chloride), trim potentiometers are used to set the appropriate RH and temperature values for each standard. Before leaving the factory, each of the main units is adjusted to a common reference standard as the default setting, so that the probes can be freely exchanged.

At first glance, it would seem that a three point calibration would be better than a two point calibration, especially since the reference standards are in the same form, namely saturated aqueous salt solutions that generate a constant humidity in the air space above the solution. As reviewed by Brownawell (23) only lithium chloride and sodium chloride, which are used to calibrate the DermaLab<sup>®</sup> TEWL probe, are considered to be a "good choice". Potassium sulfate, which is used to calibrate the Servo Med evaporimeter, is greatly affected by traces of other salts, requiring that the glassware used to prepare said solutions be scrupulously cleaned. Magnesium nitrate, which is the other salt used by Servo Med, is especially problematic because of its high temperature coefficient. Compounding this problem is the fact that because air has much less thermal mass than the water/salt solution, it can be at a different temperature from the liquid. This will cause a considerable error in the observed RH reading. This is not a problem with the DermaLab<sup>®</sup> TEWL probe since its sensors directly read the temperature of the vapor phase.

Although the results obtained with Cortex Technology's DermaLab<sup>®</sup> system with TEWL probe and the Servo Med evaporimeter are well correlated, the two instruments are not equivalent in performance. In the *in vitro* study based on WVTR measurements, the coefficient of variation for each of the three different types of membranes was always higher for the Servo Med evaporimeter, which means the reproducibility is better with the DermaLab<sup>®</sup> TEWL probe. In the *in vivo* study, we found that the DermaLab<sup>®</sup> system with TEWL probe was also more sensitive than the Servo Med evaporimeter in resolving differences in detergent solutions of varying harshness, which related to the degree the stratum corneum barrier was disrupted.

The *in vitro* and *in vivo* comparative studies also illustrate quite nicely the dramatic impact the protective covers can have on the readings obtained with the Servo Med evaporimeter. In the *in vitro* studies where both types of instruments were directly placed on the membranes being measured, the DermaLab<sup>®</sup> system tended to give lower values than the Servo Med EP2. In the *in vivo* studies that required protec-



tive covers to be used when taking measurements from human volunteers, the relationship was reversed. In the case of the DermaLab<sup>®</sup> system with TEWL probe, the insertion of the disposable plastic cover only resulted in the sensors being moved 0.25 mm farther away from the skin surface. This has very little effect on the observed TEWL readings. In striking contrast, the use of the model #2107 protective cover with the Servo Med evaporimeter caused its sensors to be moved approximately 6 to 7 mm farther away from the skin surface. This will decrease the observed readings since the sensors are now located in a region where the gradient is less steep.

Although this is less of a problem with the thinner model #2106 protective cover, it is not recommended for human studies. We concur, as it has been our experience especially in short-term moisturizer studies, that contamination with creams and ointments is likely to occur since the treated surface can touch the lower sensor if the probe is held too firmly against the skin. We have found that product transfer can also be a problem with the stainless steel mesh grid that rests on the skin surface when the model #2107 protective cover is used. This problem is easily overcome by replacing the protective covers between measurements from different test sites. Unfortunately the protective covers for the Servo Med evaporimeter are very expensive, and this requires a considerable outlay of funds to do properly. Such problems do not exist with the disposable plastic covers used with the DermaLab<sup>®</sup> system with TEWL probe, as a thin bar prevents the skin from entering the probe cylinder – eliminating the possibility of the lower sensor becoming contaminated.

We have considerable experience with evaporative water loss measurements. Indeed, we have been using various models of the Servo Med evaporimeter for more than 20 years. The EP2 evolved from the computerized system (24) we designed some 10 years ago. For the last 6 months, we have had the opportunity to use the DermaLab<sup>®</sup> system with TEWL probe in a wide variety of applications. We feel very strongly that Cortex Technology's DermaLab<sup>®</sup> system, especially one with dual TEWL probes, should be the preferred way of making these types of measurements due to the enhanced reproducibility and sensitivity that can easily be achieved with this approach. We have also come to appreciate that monitoring the temperature readings of the upper and lower sensors is essential in critical measurements. This is in keeping with the observations made for those investigators who have used the Tewameter (10–12). Such studies are not possible with the Servo Med evaporimeter

since there are no provisions for obtaining temperature readings from this instrument.

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