

## Anti-Wrinkle

# Guidelines for Evaluation of Anti-Wrinkle Products

## Task Force Committee for Evaluation of Anti-Aging Function

### 1. Introduction

Consumers want cosmetics that are effective in preventing and improving wrinkles. The EU has a category of cosmetics called Anti-Wrinkle Products, and while the United States may not have such a category, it is possible to state temporary improvement of wrinkles as an efficacy claim on products labels. In Japan, however, it is not acceptable to use expressions related to wrinkles on product labels, other than as an effect of make-up.

In the EU, if efficacy data possessed meet the format of the Guidelines for the Evaluation of the Efficacy of Cosmetic Products issued by COLIPA (European Cosmetic, Toiletry and Perfumery Association) and can be submitted or disclosed in accordance with a request from the respective authority, then efficacy may be claimed for cosmetics in accordance with the level of the data.

To facilitate the work of the cosmetics industry in collecting data and the work of the supervising regulatory authority, a specialist working group called EEMCO (European Group for Efficacy Measurements on Cosmetics and Other Topical Products) was organized in 1994. EEMCO carries out scientific reviews of measurement procedures to evaluate the efficacy of cosmetics and regularly publishes reports in specialist journals. Among the procedures reported on are those for hydration,<sup>1)</sup> skin color,<sup>2)</sup> tensile functional properties of the skin,<sup>3)</sup> skin surface pH,<sup>4)</sup> and TEWL,<sup>5)</sup> as well as those for skin topography measurements<sup>6)</sup> including texture and wrinkles.

In Japan, while efficacy claims concerning wrinkles are not accepted for cosmetics or quasi-drugs as indicated above, through the development of active ingredients and innovation in formulation techniques, it is now possible to develop cosmetics that help to prevent and improve wrinkles. And though the regulations in this respect may differ from those of other countries, the ac-

tions of cosmetics on the market with respect to the skin differ very little and cosmetics from other countries are now readily available in Japan. In view of this, and in order to further promote globalization, there is a need to permit efficacy statements concerning the prevention and improvement of wrinkles in Japan. A prerequisite for achieving this purpose would be the verification of such efficacy by means of highly reliable scientific measurement procedures, as in the EU. Until now, each Japanese cosmetics company has carried out wrinkle-related evaluations using its own procedures. With a view to standardizing them, the Japan Cosmetic Industry Association set up an evaluation procedure task force committee in 1998. Over a period of some five years, the committee discussed varying definitions of wrinkles, conducted surveys concerning wrinkle-related measurement procedures and evaluation techniques, carried out measurements on wrinkles using various procedures, evaluated the improvement effect of the continuous use of cosmetics with respect to wrinkles, and prepared guidelines for evaluating anti-wrinkle effects. The results of these activities were reported in the Journal of the Japanese Cosmetic Science Society.<sup>7)–11)</sup> However, no great progress has been made since then.

Against this background, the Task Force Committee for Evaluation of Anti-Aging Function has further promoted the standardization of anti-wrinkle evaluation methods to facilitate the Ministry of Health, Labour and Welfare's acceptance of anti-wrinkle efficacy standards for cosmetics and quasi-drugs. In our study of measurement procedures, we have conducted detailed investigations of data produced by previous research, various experiments, literature surveys, and awareness surveys.<sup>12)</sup> In doing this, we have gone further than just recording the details of the procedures; we have also considered a very broad range of other aspects of measurement including selection of subjects, measurement environment, and efficacy judgment standards. As a re-

sult of those efforts, we have prepared guidelines for evaluating products that target crow's feet. We limited ourselves to crow's feet because consumers have a great interest in such wrinkles<sup>12)</sup> and because currently established evaluation methods also target them. However, in view of the tremendous advances being made in measurement techniques, we cannot assume that the methods mentioned here will always be the best for meeting current needs; thus, revision will be needed as and when appropriate.

## 2. Guidelines for Evaluation of Anti-Wrinkle Function—Cosmetics

### 2-1. Target Area and Recommended Subjects

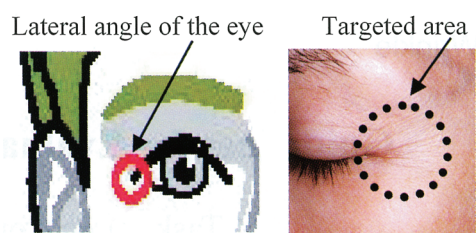
The corners of the eyes are the target area, and recommended subjects are healthy women or men with wrinkles ranging from grade 1 to 3 (Refer to Fig. 1. Standard Wrinkle Grades). Each subject is assigned at random to a treated group or a non-treated control group. There is no clear bias in wrinkle grade distribution, left-right distribution, or age distribution between the two groups. If the trial is to be conducted on both the left and right sides of the same person's face, the subject should have the same wrinkle grade on both sides. The product is applied to one side and the other side is left untreated according to a random design. When male subjects are included the male/female ratio should be similar in both groups.

Subjects with wrinkles due to illness or other special causes, as well as those employed by the testing organization and those coming under the following categories, should be eliminated:

- (1) Those with a past history of allergic reaction to cosmetics
- (2) Those undergoing hormone replacement therapy
- (3) Women who are pregnant or breast feeding
- (4) Those who have undergone beauty therapy that could affect the testing area
- (5) Others whose participation is deemed inappropriate by a doctor.

### 2-2. Testing Facility and Testing Environment

Testing is carried out under the supervision of a controller. As a rule, an organization should request testing to be done by an unrelated facility (either in Japan or another country). However, if the allocation of samples and target areas and the recruitment of subjects



Reference: The corner of the eye means the area of the lateral angle of the eye (the point where the upper and lower eyelids meet) and crow's feet wrinkles means linear furrows that go outwards from the lateral angle of the eye.

are entrusted to an unrelated facility and the details kept secret, the requesting organization may conduct the testing itself. When testing is conducted at an overseas testing facility, subjects skin attributes should conform to skin types III and IV (Fitzpatrick Classification). Visual evaluation, evaluation by means of objective instrument measurements, the taking of replicas, and photography should all be done in a room with a controlled environment in which conditions are kept constant (including temperature, humidity, and lighting). When testing is conducted at several facilities, it must be ascertained beforehand that no inter-facility or inter-tester deviations will arise.

### 2-3. Restrictions on Subjects

Subjects should be instructed that during the four weeks prior to testing and for the full duration of the testing period, they should refrain from receiving any specific skincare treatment (e.g. facial esthetics) that could affect the area of the face being tested, avoid activities in which there would be excessive exposure to UV radiation such as swimming, mountain climbing, sunbathing, and outdoor exercise, and not start taking any new supplements. If subjects regularly use sunscreen or skincare products, they must continue to use the same products throughout the testing period (topical cosmetic products or pharmaceutical preparations whose aim is wrinkle improvement are not permitted).

### 2-4. Test Samples and Their Application

For test samples, only the essential features of the preparations should be listed (e.g. cream, emulsion, etc.). Test samples should be applied in an appropriate amount by the method determined for the test until the

day before the final measurements (in the case of measurements made during the period of the test, however, the test sample should not be applied on measurement days). Records of the composition, manufacturing method, and date of manufacture should be kept for test samples so that follow-up investigations can be conducted as required.

## **2-5. Trial Period**

The period of any trial should be at least two weeks, which is considered the minimum period for verifying efficacy. This pertains irrespective of the season in which the trial is conducted.

## **2-6. Number of Subjects**

Preliminary testing will help determine the number of subjects to be included in the test; this number should be sufficient to allow effects to be detected. The number of subjects should be sufficient to permit statistical analysis of the results.

## **2-7. Trial Procedures**

### **2-7-1. Evaluation items**

- Visual evaluation
- Photography
- Measurement of wrinkles using instruments

Two-dimensional image analysis of replicas or three-dimensional analysis of replicas or *in vivo* three-dimensional analysis is selected.

- Evaluations are made just before and after the trial.
- Evaluations are also made during the testing period if necessary.
- From among the above evaluation procedures, conduct those necessary for “2-11 Overall Efficacy Judgment” (two-dimensional and three-dimensional analysis procedures).

### **2-7-2. Measurement conditions**

- Measurements should be made in a room that offers an environment with constant conditions (including temperature, humidity, and lighting), and the conditions should not be changed during the period of the trial. The desirable temperature range is 20–22 degrees Celsius and relative humidity between 45 and 55 percent.
- In order to avoid the influence of makeup on the measurements, each subject’s face should be washed with the same facial cleanser before entering the measurement room each time measure-

ments are conducted during the period of the trial; and the measurements should only be taken after an acclimatization period of at least 15 minutes after the subject enters the room.

- Each time measurements are taken, the position and orientation of the body should be the same as at the start of the trial. An effort should be made to ensure that measurements are taken at the same hour of the day each time.

### **2-7-3. Photography procedures**

Refer to Supplementary Guidelines: 1. Wrinkle Photography.

### **2-7-4. Procedures for instrument measurements**

Refer to Supplementary Guidelines: 2. Wrinkle Measurements.

### **2-7-5. Evaluation items and procedures**

#### **2-7-5-1. Visual evaluation**

Before and after the application of the test sample, an expert dermatologist or dermatologist with equivalent clinical experience should evaluate the wrinkle grade, or this may be done by a Trained Expert (researcher with expertise of wrinkles) under the supervision of a dermatologist. Evaluation is conducted in accordance with the following procedures.

- At the start of the trial, assign wrinkle grades according to the standard wrinkle grades in the photographs in Fig. 1.

At the time of each measurement, reference should be made to photographs taken at the start of the trial or the previous measurement, and a wrinkle grade score should be assigned based on the standard wrinkle grades in Fig. 1.

When wrinkle grades do not match the standard wrinkle grades in Fig. 1, a grade midway or one-quarter of the way between two grades may be assigned (e.g. 3.25, 3.5, or 3.75).

#### **2-7-5-2. Photographic evaluation**

An expert dermatologist or dermatologist with equivalent clinical experience should assign a wrinkle grade score to photographs based on the standard wrinkle grades before the start of the trial and at the time of each measurement, or this may be done by a Trained Expert (researcher with expertise of wrinkles) under the supervision of a dermatologist.

When wrinkle grades do not fit in with the standard wrinkle grades in the photographs, a grade midway or one-quarter of the way between two grades may be assigned (e.g. 3.25, 3.5, or 3.75).





Fig. 1. Standard Wrinkle Grades



### 2-7-5-3. Evaluation using instruments

Using two-dimensional image analysis of replicas with oblique illumination, three-dimensional analysis of replicas, or *in vivo* three-dimensional analysis, make wrinkle measurements before the beginning of the trial and at the established intervals throughout the trial and compute wrinkle analysis parameters.

### 2-8. Subject Questionnaires

Have subjects fill out questionnaires to check for problems with the use of samples and to ascertain usage and efficacy.

### 2-9. Adverse Events and Reactions

Adverse events are defined as various undesirable effects occurring during the period of the trial for which a causal relationship with the test sample cannot be established. Adverse reactions are defined as various undesirable manifestations occurring after a subject starts to use the test sample, for which a causal relationship with the sample cannot be ruled out and there is a reasonable possibility that the manifestations were caused by it.

In either case, a report describing the details of the onset and subsequent course of the undesirable effects, their degree of seriousness, and whether or not any measures were taken, the details of the measures taken, and the outcome of treatment should be made, and the doctors supervising the test should make a judgment of whether there is a causal relationship with the test sample or not.

### 2-10. Efficacy Analysis

Using appropriate statistical methods, compare changes over the course of the trial and afterward for all evaluation items in the group treated with the product and the non-treated group. In the following cases, data from subjects should be omitted from the analysis:

- (1) Infrequent or other improper use of the product
- (2) When adverse events occurring during the trial make continued participation impossible or adverse reactions occur
- (3) When there is concern about the reliability of data, for example in the case where medicines are being taken during the trial.

Efficacy is analyzed after eliminating data from subjects coming under the above categories and after a safety analysis is carried out for all subjects who used

the test sample.

### 2-11. Overall Judgment of Efficacy

A product is judged to have efficacy if, as a result of the efficacy analysis, there is a significant improvement in wrinkles ( $p < 0.05$ ) in the treated group as compared with the non-treated group using visual evaluation or photographic evaluation, or there are significant changes in analysis parameters in the treated group ( $p < 0.05$ ) as compared with the non-treated group.

### 2-12. Ethical Guidelines

Ethical considerations should be in accordance with the Ethical Guidelines for Clinical Research (Ministry of Health, Labour and Welfare Notification No. 225, 2003), dated 30 July 2003. It is necessary for testing to be approved by an ethics committee, and the informed written consent of subjects must be obtained. In order to protect personal information, adequate care must be taken in its filing and management.

## 3. Guidelines for Evaluation of Anti-Wrinkle Function—Quasi-Drugs

### 3-1. Target Area and Recommended Subjects

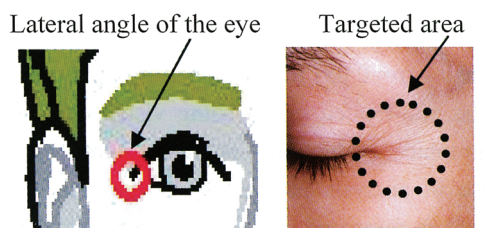
The corners of the eyes are the target area, and recommended subjects are healthy women or men with wrinkles ranging from grade 3 to 5 (Refer to Fig. 1. Standard Wrinkle Grades). Each subject is assigned at random to a treated group or a non-treated control group. There is no clear bias in wrinkle grade distribution, left-right distribution, or age distribution between the two groups. If the trial is to be conducted on both the left and right sides of the same person's face, the subject should have the same wrinkle grade on both sides. The product is applied to one side and the other side is left untreated according to a random design. When male subjects are included the male/female ratio should be similar in both groups.

Subjects with wrinkles due to illness or other special causes, as well as those employed by the testing organization and those coming under the following categories, should be eliminated:

- (1) Those with a past history of allergy to cosmetics
- (2) Those undergoing hormone replacement therapy
- (3) Women who are pregnant or breast feeding
- (4) Those who have undergone beauty therapy that

could affect the testing area

- (5) Others whose participation is deemed inappropriate by a doctor.



Reference: The corner of the eye means the area of the lateral angle of the eye (the point where the upper and lower eyelids meet) and crow's feet wrinkles means linear furrows that go outwards from the lateral angle of the eye.

### 3-2. Testing Facility and Testing Environment

Testing is carried out under the supervision of a controller according to a double-blind design. As a rule, an organization should request testing to be done by an unrelated facility (either in Japan or another country). However if the allocation of samples, application areas, and other aspects are entrusted to an unrelated facility and their details kept secret, the requesting organization may conduct the testing itself. When testing is conducted at an overseas testing organization, subjects skin attributes should conform to skin types III and IV (Fitzpatrick Classification). Visual evaluation, evaluation by means of objective instrument measurements, the taking of replicas, and photography should be done in a room with a controlled environment in which conditions are kept constant (including temperature, humidity, and lighting). When testing is conducted at several facilities, it must be ascertained beforehand that no inter-facility or inter-tester deviations will arise.

### 3-3. Restrictions on Subjects

Subjects should be instructed that during the four weeks prior to testing and for the full duration of the testing period, they should refrain from receiving any specific skincare treatment (e.g. facial esthetics) that could affect the area of the face being tested, avoid activities in which there would be excessive exposure to UV radiation such as swimming, mountain climbing, sunbathing, and outdoor exercise, and not start taking any new supplements. If subjects regularly use sunscreen or skincare products, they must continue to use

the same products throughout the testing period (topical cosmetic products or pharmaceutical preparations whose aim is wrinkle improvement are not permitted).

### 3-4. Test Samples and Their Application

For test samples, only the essential features of the preparations should be listed (e.g. cream, emulsion, etc.). Test samples should be applied in an appropriate amount by the method determined for the test until the day before the final measurements (in the case of measurements made during the period of the test, however, the test sample should not to be applied on measurement days). Records of the composition, manufacturing method, and date of manufacture should be kept for test samples so that follow-up investigations can be conducted as required.

### 3-5. Trial Period

The period of any trial should be at least two months, which is considered the minimum period for verifying efficacy. This pertains irrespective of the season in which the trial is conducted.

### 3-6. Number of Subjects

Based on preliminary testing, the number of subjects chosen should be large enough to allow effects to be detected. The number of subjects should be sufficient to permit statistical analysis of the results.

### 3-7. Trial Procedures

#### 3-7-1. Evaluation items

- Visual evaluation
- Photography
- Measurement of wrinkles using instruments

Two-dimensional image analysis of replicas or three-dimensional analysis of replicas or *in vivo* three-dimensional analysis is selected.

- Evaluations are made just before and after the trial.
- Evaluations are also made in the testing period if necessary.
- From among the above evaluation procedures, conduct those necessary for “3-11. Overall Efficacy Judgment” (two-dimensional and three-dimensional analysis procedures).

#### 3-7-2. Measurement conditions

- Measurements should be made in a room that offers an environment with constant conditions (including temperature, humidity, and lighting), and

the conditions should not be changed during the period of the trial. The desirable temperature range is 20–22 degrees Celsius and relative humidity between 45 and 55 percent.

- In order to avoid the influence of makeup on the measurements, each subject's face should be washed with the same facial cleanser before entering the measurement room each time measurements are conducted during the period of the trial; and the measurements should only be taken after an acclimatization period of at least 15 minutes after the subject enters the room.
- Each time measurements are taken, the position and orientation of the body should be the same as at the start of the trial. An effort should be made to ensure that measurements are taken at the same hour of the day each time.

### **3–7–3. Photography procedures**

Refer to Supplementary Guidelines: 1. Wrinkle Photography.

### **3–7–4. Procedures for instrument measurements**

Refer to Supplementary Guidelines: 2. Wrinkle Measurements.

### **3–7–5. Evaluation items and procedures**

#### **3–7–5–1. Visual evaluation**

An expert dermatologist or dermatologist with equivalent clinical experience should evaluate the wrinkle grade, or this may be done by a Trained Expert (researcher with expertise of wrinkles) under the supervision of a dermatologist, before and after the period of application of the test sample. Evaluation is conducted in accordance with the following procedures:

- (1) At the start of the trial, assign wrinkle grades according to the standard wrinkle grades in the photographs in Fig. 1.
- (2) At the time of each measurement, assign wrinkle grades based on the standard wrinkle grades in Fig. 1 after referring to photographs taken at the start of the trial or the previous measurement.

When wrinkle grades do not fit in with the standard wrinkle grades in Fig. 1, a grade midway or one-quarter of the way between two grades may be assigned (e.g. 3.25, 3.5, or 3.75).

#### **3–7–5–2. Photographic evaluation**

An expert dermatologist or dermatologist with equivalent clinical experience should assign a wrinkle grade score to photographs based on the standard wrin-

kle grades in Fig. 1 before the start of the trial and at the time of each measurement, or this may be done by a Trained Expert (researcher with expertise of wrinkles) under the supervision of a dermatologist.

When wrinkle grades do not fit in with the standard wrinkle grades in Fig. 1, a grade midway or one-quarter of the way between two grades may be assigned (e.g. 3.25, 3.5 or 3.75).

### **3–7–5–3. Evaluation using instruments**

Using two-dimensional image analysis of replicas with oblique illumination, three-dimensional analysis of replicas, or *in vivo* three-dimensional analysis, conduct wrinkle measurements before the trial and at the time of each measurement and use them to compute wrinkle analysis parameters.

### **3–8. Subject Questionnaires**

Have subjects fill out questionnaires to check for problems with the use of samples and to ascertain usage and efficacy.

### **3–9. Adverse Effects and Events**

Adverse events are defined as various undesirable effects occurring during the period of the trial for which a causal relationship with the test sample cannot be established. Adverse reactions are defined as various undesirable manifestations occurring after a subject starts to use the test sample, for which a causal relationship with the sample cannot be ruled out and there is a reasonable possibility that the manifestations were caused by it.

In either case, a report describing the details of the onset and subsequent course of the undesirable effects, their degree of seriousness, and whether or not any measures were taken, the details of the measures taken, and the outcome of treatment should be made and the doctors supervising the test should make a judgment of whether there is a causal relationship with the test sample or not.

### **3–10. Efficacy Analysis**

Using appropriate statistical methods, compare changes over the course of the trial and afterward for all evaluation items in the group treated with the product and the non-treated group. In the following cases, data from subjects should be omitted from the analysis:

- (1) Infrequent or other improper use of the product
- (2) When adverse events occurring during the trial



make continued participation impossible or adverse reactions occur

- (3) When there is concern about the reliability of data, for example in the case where medicines are being taken during the trial.

Efficacy is analyzed after eliminating data from subjects coming under the above categories and after a

safety analysis is carried out for all subjects who used the test sample.

### 3-11. Overall Judgment of Efficacy

A product is judged to have efficacy if, as a result of the efficacy analysis, there is a significant improvement in wrinkles ( $p < 0.05$ ) in the treated group as compared

**Table 1.** Basis of Evaluating Anti-Wrinkle Effects of Cosmetics and Quasi-Drugs and Related Items

	Cosmetics	Quasi-drugs	Pharmaceuticals (for reference)
①Target wrinkle area	Corner of the eye	Corner of the eye	All areas with wrinkles, including the corner of the eye (including the area between the eyebrows, the nasolabial groove, etc.)
②Recommended subjects	Subjects with wrinkles of grade 1 to 3	Subjects with wrinkles of grade 3 to 5	No stipulation
③Function evaluation procedures	Single-blind test (The evaluator is unaware of which is the treated group and which is the non-treated group.)	Double-blind test	—
	Comparison between treated and non-treated group	Comparison between the group (or area) treated with the preparation containing the active ingredient and the group (or area) treated with the placebo preparation *In the case of area, comparison of the lateral angle of the eye on left and right sides for the same subject	—
④Evaluation items	<ul style="list-style-type: none"> <li>•Visual, photographic evaluations with reference to standard wrinkle grades</li> <li>•Two-dimensional or three-dimensional instrument analysis of replicas or <i>in vivo</i> three-dimensional analysis</li> </ul>	<ul style="list-style-type: none"> <li>•Visual, photographic evaluations with reference to standard wrinkle grades</li> <li>•Two-dimensional or three-dimensional instrument analysis of replicas or <i>in vivo</i> three-dimensional analysis</li> </ul>	—
⑤Basis of evaluating efficacy	Significant improvement in wrinkles observed in at least one of either instrument, visual, or photographic evaluation	Significant improvement in wrinkles observed in instrument evaluation as well as in either visual or photographic evaluation	—
⑥Trial period	At least two weeks	At least two months	No stipulation
⑦Efficacy claim	Makes less noticeable those wrinkles that are due to dryness	Improves wrinkles	Cures wrinkles
⑧Wrinkle improvement mechanism	Not required	Required (Excepting those products whose purpose is simply to moisturize the stratum corneum.)	Required

with the non-treated group using visual evaluation or photographic evaluation, or there are significant changes in analysis parameters in the treated group ( $p < 0.05$ ) as compared with the non-treated group.

### 3–12. Ethical Guidelines

Ethical considerations should be in accordance with the Ethical Guidelines for Clinical Research (Ministry of Health, Labour and Welfare Notification No. 225, 2003), dated 30 July 2003. It is necessary for testing to be approved by an ethics committee, and the informed written consent of subjects must be obtained. In order to protect personal information, adequate care must be taken in its filing and management.

### 4. Summing Up

These guidelines have been prepared by the Task Force Committee for Evaluation of Anti-Aging Function for the purpose of gaining approval for new anti-wrinkle-related efficacy claims in Japan. In drawing up the guidelines, we performed a survey of wrinkle measurement methods currently in use, a literature survey regarding the efficacy of anti-wrinkle preparations, and an analysis of wrinkle awareness surveys<sup>12</sup> targeting consumers, dermatologists, and pharmacology researchers. Based on the results, we studied evaluation standards and efficacy claims for two levels, one of them efficacy at the cosmetics level and the other efficacy at the quasi-drug level. Our conclusions are summarized in Table 1. We considered cosmetics that have a moisturizing action with respect to the stratum corneum and quasi-drugs to have different actions, and we determined the efficacy claims to be “Makes wrinkles due to dryness less noticeable” and “Improves wrinkles,” respectively. In addition, we prepared separate standards for judging the efficacy of these two product categories and, in the case of quasi-drugs, established an obligation to explain the mechanism of action for improvement of wrinkles. Table 1 expresses the basis of the guidelines.

With the constant advances that are being made in wrinkle measurement procedures, new ones will surely be developed. We also foresee that new bases for wrinkle improvement will be established and that the development of new active ingredients will speed up. As this happens, it may be necessary to change the efficacy claims in the guidelines from time to time and in such cases it will be necessary to conduct further study and

make the necessary revisions.

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## Supplementary Guidelines: 1. Wrinkle Photography

### 1. Introduction

These guidelines have been drawn up for the taking of photographs used in wrinkle evaluation and have the following objectives:

- (1) To achieve reproducibility in photography by minimizing the effect of the photography conditions on wrinkle photographs taken before trials, during trials, and upon their completion
- (2) To ensure that photographic images suitable for wrinkle evaluation can be obtained at the time of each observation
- (3) To provide pointers by which even persons with no particular specialist capability may take photographs of constant quality, which can be used extensively in objective wrinkle evaluation.

While these guidelines assume the taking of photographs using a camera, which has generally been the case up till now, if the above three objectives are fulfilled, other equipment may also be used. However, in that case, observance of the points in Item 2 below is also necessary.

### 2. Instructions for Photography

#### 2–1. Equipment

- Arrange lighting to minimize bright spots on skin surface as well as difference between light and dark.
- Arrange the position and angle of the camera in consideration of achieving uniformity and good focus in the area of the wrinkles being examined.
- The equipment conditions should be completely identical before and after the trial.

#### 2–2. Environment

- Use a room in which environmental conditions (temperature, humidity) can be kept constant.

#### 2–3. Subjects

- Take photographs after subjects have acclimatized to the environment in the room for photography (in conformance with the acclimatization period in Guidelines for Evaluation of Anti-Wrinkle Products). Acclimatization conditions should be constant.
- Fix the subject's face in position using a chin rest/head frame for this purpose.
- Instruct the subject to lightly close his/her eyes.

#### 2–4. Other

Standard photographic items should be used for image correction to compensate for differences when taking photographs.

### 3. Procedures for Photography Using a Camera (recommended)

#### 3–1. Equipment

##### 3–1–1. Camera

A single-lens reflex digital camera is recommended for the camera body and a macro (or micro) lens (with a focusing distance equivalent to 60–105 mm in a 35 mm camera) is the recommended lens. A picture quality of 2.5 megapixels in a CCD of the APS film size (approx. 24×16 mm) should be sufficient (equivalent to a Nikon D1). As for the camera settings, the white balance should be set to a mode fitting the lighting conditions, for instance a mode for flash photography. The shutter speed and aperture settings should be such that the whole observation area around the lateral angle of the eye is in focus and this should be properly checked. Increasing the aperture setting will increase the size of the area in focus.

Regarding resolution, if a Nikon single-lens reflex digital camera is being used, the Fine mode/JPEG (1/4) compressed image setting will produce photographs adequate for evaluation purposes.

The camera should be positioned at an angle that



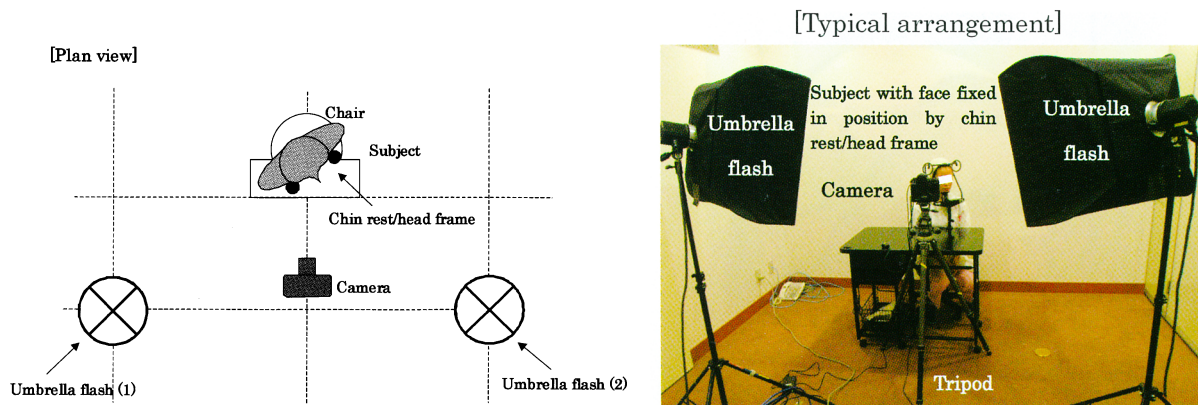


Fig. 1. Arrangement of Equipment for Wrinkle Photography

makes the wrinkle examination area at the lateral angle of the eye appear as a planar surface as far as possible, but fine adjustments will be needed for each subject. The camera height should be kept constant.

Images to be used in wrinkle evaluation should be printed in at least 2L size since this allows wrinkles to be clearly discerned. In order to ensure that images are all of uniform quality, they should not be printed out using a personal printer.

### 3-1-2. Lighting

To minimize the effect of bright spots on the skin, the use of an umbrella flash is recommended. A ring flash attached to the end of the lens may also be used. A disadvantage with umbrella flashes is the space needed and the trouble involved in setting them up. While the ring flash is more convenient, care needs to be taken since bright spots are easily produced on the skin.

The position of the umbrella flash should be determined so that it complements the camera settings and enables adequate exposure conditions to be achieved. It should also be positioned so that the light from the flash illuminating the area under observation comes from above to avoid bright spots on the skin. Refer to the typical arrangement of photographic equipment including umbrella flashes in Fig. 1.

### 3-2. Environment

A room in which temperature and humidity can be maintained at constant levels is recommended. The temperature and humidity should be the same as in the Guidelines for Evaluation of Anti-Wrinkle Products—a temperature range of 20–22 degrees Celsius and relative humidity between 45 and 55 percent—and these conditions should not change during the period of the trial.



Fig. 2. Chin Rest/Head Frame Made by Takei Scientific Instruments Co., Ltd.

### 3-3. Subjects

In order to minimize errors in angles, the face should be fixed in place using a chin rest/head frame such as the one in Fig. 2 made by Takei Scientific Instruments Co., Ltd., which is used for examining the eyes. This type of rest is very easy to use and Fig. 3 shows it in use. With certain other types of chin rest/head frame, however, it is necessary to ensure that the rest does not obscure the lateral angles of the eyes or other observation areas. Instruct subjects to gently close their eyes when taking photographs.

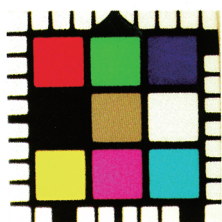
1. Photography range
2. Wrinkle evaluation range
3. Photography centered on the lateral angle of the eye (take several photographs if possible)

### 3-4. Concurrent Photography and the Image Correction Standard

For the purposes of color correction and scale correction, a photo scale and color chart are attached in the vicinity of the wrinkle observation area, for instance at the temple, so that they do not interfere with evaluation,



**Fig. 3.** Chin Rest/Head Frame in Use



**Fig. 4.** Image Correction Color Chart  
(CASMATCH, BEAR Medic Corporation)

and then the photograph is taken. A typical photo scale and color chart is shown in Fig. 4.

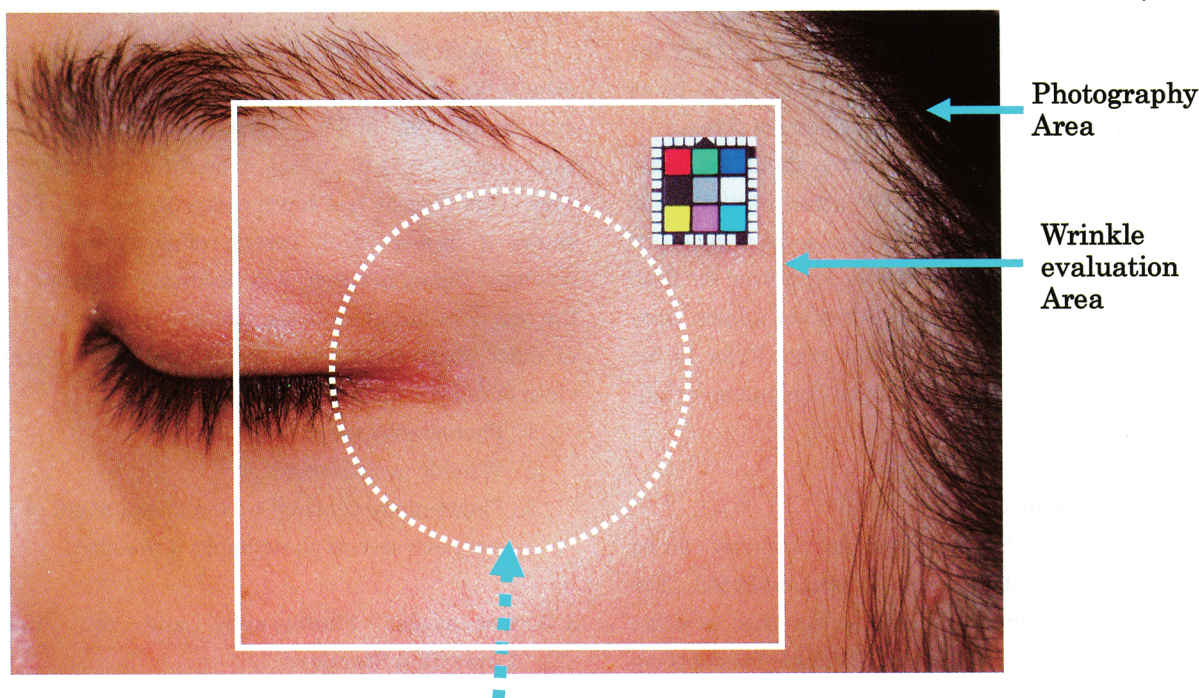
### 3-5. Range of Wrinkle Photography

It is recommended that the range of wrinkle photography be such that the subject cannot be identified from the photographic image, in consideration of portrait rights; also, the range should make the evaluation of crow's feet possible. For example, in Fig. 5, the range of photography is from the closed eyes to the sideburns, and the wrinkle evaluation range starts from a point no further than the middle of the eye.

### 4. Procedure of Wrinkle Photography

The following is a typical procedure for wrinkle photography:

- (1) Have the subject wash his or her face to remove makeup or any facial care products.
- (2) Have the subject enter the photography room (with constant temperature and humidity conditions) and allow the person to acclimatize for at least 15 minutes.
- (3) Attach a photo scale/color chart on the subject close to the wrinkle observation area.
- (4) Have the subject sit on the chair and put his/her



**Photography Centered on Lateral Angle of Eye**  
**(take several photographs if possible)**

**Fig. 5.** Wrinkle Photography Fields

chin on the chin rest of the head frame.

- (5) Make fine adjustments to the position of the camera so that the area of wrinkle observation at the lateral angle of the eye is at the desired location on the camera screen (done for each subject).

- (6) Take several photographs, checking the focus each time, to avoid images being out of focus. Also check each image for overexposure and other problems.
- (7) Print photographs in a suitable size (e.g. 2L) and use them for evaluation.

## Supplementary Guidelines: 2. Wrinkle Measurements

### 1. Introduction

These guidelines were drawn up with the objective of standardizing wrinkle measurement procedures using instruments. From among the procedures developed up until now, we selected those having good reproducibility with regard to wrinkle topography data as well as the capability to achieve accurate measurements. The methods actually selected were the three listed below. They were selected with reference to Guidance on Wrinkle Evaluation Methods drawn up by the Japan Cosmetic Industry Association in 1998<sup>1)</sup> as well as based on the results of a survey of overseas contract testing organizations and one on instrument measurement conducted by members of the Task Force Committee for Evaluation of Anti-Aging Function.

- Two-dimensional analysis of skin surface replicas using oblique illumination
- Three-dimensional analysis of skin surface replicas
- In vivo* three-dimensional analysis (direct analysis not using replicas)

### 2. Analysis Methods with Replicas

Wrinkle topography measurements are made from replicas of wrinkle areas at the lateral angle of the eye and the results analyzed. This will be explained in detail below under three headings—Method of Taking Replicas, Two-Dimensional Analysis of Replicas with Oblique Illumination, and Three-Dimensional Analysis of Replicas.

#### 2-1. Method of Taking Replicas

##### 2-1-1. Replica materials

Among the recommended replica materials are SIL-FLO (Flexico, England) and EXAFINE (GC Co., Japan). These materials are capable of faithfully transferring the minute topography of the skin and their use

has been much reported on.

##### 2-1-2. Environmental conditions when taking replicas

Replicas are taken in an environment with constant temperature and humidity to which the subject has been adequately acclimatized. They are taken with the subject at rest in a seated position with the eyes lightly closed.

##### 2-1-3. Location of taking replicas

Take replicas from an area of at least 10×10 mm beginning at about 5 mm from the end of the eye (Refer to Fig. 1).

##### 2-1-4. Points to pay attention to when taking replicas

Attention should be paid to differences in physical properties, polymerization, and hardening times to ensure that the form of the wrinkles is accurately transferred to the replica. Attention should also be paid to the following:

- (1) Allow no bubbles to form in the replica agent when mixing
- (2) Remove the replica agent carefully once it has hardened.

### 2-2. Two-Dimensional Analysis of Replicas with Oblique Illumination

This method involves illuminating a replica of wrinkles from above at a fixed angle and perpendicular to the principal direction in which wrinkles are oriented and performing image analysis on the shadows produced using various parameters.<sup>2,3)</sup>

We will now describe the composition of equipment for this analysis technique and the principles involved.

#### 2-2-1. Composition of equipment

A typical input/analysis system using oblique illumination is shown in Fig. 2. It consists of the following three sections:



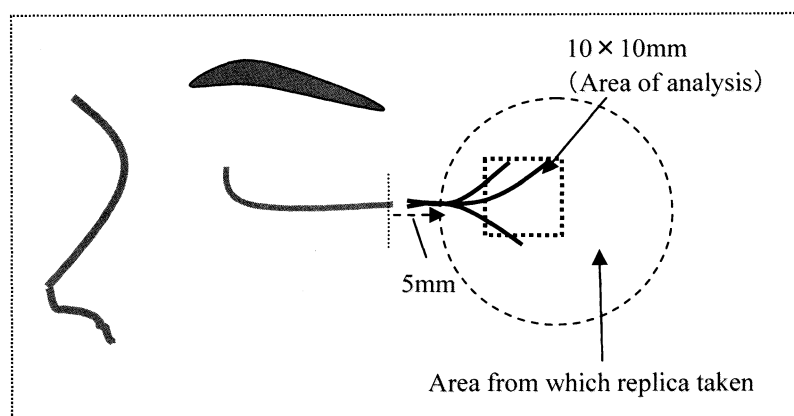


Fig. 1. Area from Which Replica Taken and Area of Analysis

### (1) Light projection section

The light projection section consists of a light-projecting device that illuminates the replica from a direction perpendicular to the orientation of the wrinkles at a fixed angle ( $20\text{--}30^\circ$ ) to the horizontal using the light from a halogen, xenon, or other type of lamp passed through an optical fiber, and a table to which the replica can be fixed.

### (2) Image input section

The image of the illuminated replica is magnified (around 30 times) using a stereoscopic microscope or other instrument. The image data is converted to digital signals by the CCD camera and then transmitted to the image analysis section.

### (3) Image analysis section

This consists of a specialized image analysis device or a personal computer equipped with image analysis software (Winroof-Pro, IPLab, Solution Systems, etc.).

### 2-2-2. Measurement principle

The shadow produced by the relief of the wrinkle replica (negative replica) when light from the projecting device is shone on it is isolated. Its area, width, and so forth are measured and from this wrinkle depth, area ratio and other parameters are calculated (Fig. 3).

### 2-2-3. Adjusting wrinkle position in two-dimensional analysis of replicas with oblique illumination

In evaluating the wrinkle-improving effect of samples or cosmetic materials, position adjustment is necessary in the analysis of the wrinkles transferred to replicas taken before and after the use of such cosmetic materials or samples. Two examples of this are: (i) the position of the replica is adjusted based on the features of the wrinkle itself, and (ii) the position of the area of analysis is adjusted based on the position of other landmarks such as moles. Image analysis software for position adjustment may be supplied as an accessory to the

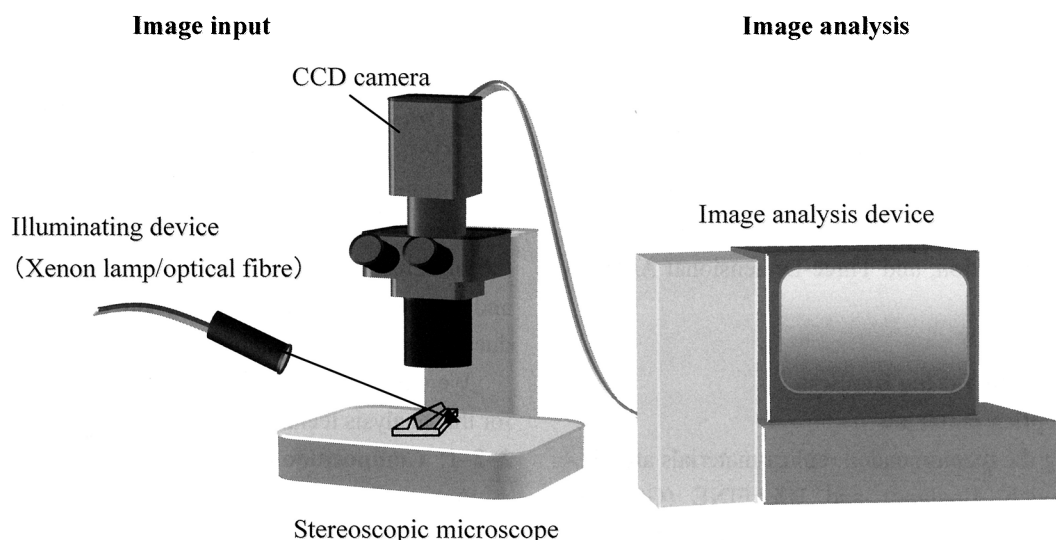


Fig. 2. Diagram of the Image Analysis System Using Oblique Illumination

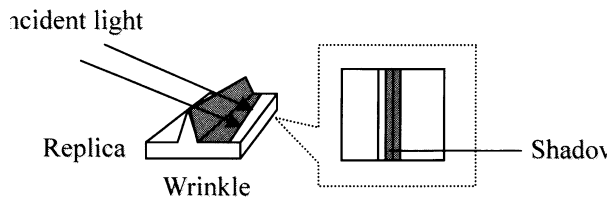


Fig. 3. Image Formed by Light Striking the Wrinkle Replica

image analysis device or self-developed.

#### 2-2-4. Wrinkle analysis procedures

Wrinkle analysis is conducted according to the following procedures:

##### (1) Binarization

The light from the lamp striking the replica produces a variety of shadows ranging from large dark shadows to thin, light shadows. Binarization is conducted to separate the large dark shadows that represent wrinkles. To do this, a brightness threshold is established, above which there is brightness and below which there is darkness, and all brightness values are converted to bright and dark. For instance, white could be 255 and black 0. This enables shadows to be separated since they would have a brightness level less than the threshold. Binarization facilitates subsequent analysis.

There are two ways of setting the threshold value—one assigns a different value depending on the status of the wrinkles transferred to the replica and the other always assigns a fixed value. More specifically, in the first case wrinkles are analyzed individually and the threshold value is varied depending on whether large or small wrinkles are being analyzed. In the second case, both large and small wrinkles are analyzed under the same conditions by keeping the threshold value constant. This depends on the idea the person conducting the measurements has with respect to initial settings.

In relation to the above, a method of correcting for unevenness in lightness has been reported. This involves detecting low frequency light prior to binarization using the Fourier transform and then eliminating it

by means of the inverse Fourier transform. Programs are available for carrying out such processing with the image analysis system described above.

##### (2) Calculation of wrinkle analysis parameters

The following parameters should be used in wrinkle analysis:

##### (A) Percentage of wrinkle area

The total area of the shadows is obtained for wrinkles in accordance with the principle shown in Fig. 3 and the percentage of this area of the analysis area (at least  $10 \times 10$  mm) is calculated, giving the percentage of wrinkle area.

##### (B) Wrinkle depth

Wrinkle depth is calculated from the area ( $s$ ) and length ( $l$ ) of the shadows produced by the wrinkle replica using the formula indicated in Fig. 4 below.

##### (B-i) Overall average wrinkle depth

Calculate the total of the depths of all wrinkles in the analysis area in accordance with Fig. 4 and compute the average.

##### (B-ii) Average largest wrinkle depth

The largest wrinkle is the wrinkle with the largest area of shadow in the area of analysis. The depth calculated in accordance with Fig. 4 is taken as the average largest wrinkle depth.

##### (B-iii) Maximum largest wrinkle depth

The maximum largest wrinkle depth is calculated from the maximum value of the breadth ( $d$ ; refer to Fig. 4) of the shadow of the largest wrinkle as defined in (B-ii) above using the following formula:

$$\text{Maximum largest wrinkle depth} = d \times \tan \theta$$

#### 2-2-5. Points to pay attention to in two-dimensional image analysis of replicas with oblique illumination

##### (1) Points to pay attention to concerning replicas

With the analysis system described above, any substantial curvature of a replica (replica distortion) due to facial contours or other causes will be a great source of interference and can make quantitative analysis difficult

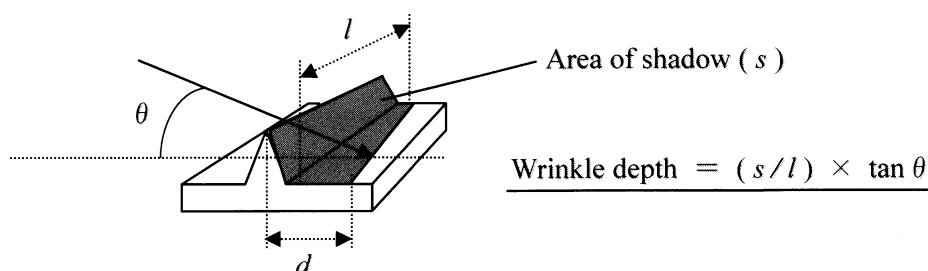


Fig. 4. Calculation of Wrinkle Depth from Projected Replica Image

to perform. In such cases, it is desirable to follow procedures that will minimize the effect of any bending in replicas. One way of doing this is to take a replica slightly bigger than the size of the analysis area and apply a supporting material (glass plate, etc.) to the reverse side. This enables replicas that have a flat baseline and minimal bending to be obtained.

- (2) Points to pay attention to when large and small wrinkles are present together

When there are both large and small wrinkles, the small ones may be obscured by the shadow of the large ones, meaning that the former will escape analysis. It is necessary to consider means of reducing this as much as possible such as illuminating the replica from different directions.

### 2-3. Three-Dimensional Analysis of Replicas

This method involves the analysis of data from three-dimensional measurements made on replicas taken of wrinkles at the lateral angle of the eye. Analysis conducted using three-dimensional measurement data affords higher accuracy than the two-dimensional image analysis using oblique illumination described in 2-2 above. The measuring instruments used should satisfy the following requirements:

- They should be able to make measurements over a measurement range of  $10 \times 10$  mm.
- The resolution along the X and Y axes should not be more than  $50 \mu\text{m}$  and the resolution along the z axis not more than  $5 \mu\text{m}$ .
- In wrinkle analysis, wrinkle position adjustment is required prior to and after applying a cosmetic preparation or quasi-drug. Therefore, when taking measurements, instruments should be capable of confirming the positions from which replicas are taken and of making comparisons.

We will now describe three procedures that use three-dimensional measuring instruments and satisfy the above requirements.

#### 2-3-1. Three-dimensional measurements with a laser confocal displacement meter

Using a laser displacement meter employing the confocal principle, three-dimensional measurement data is obtained by placing the measurement object on the XY stage and moving the stage backwards and forwards and left and right.

##### 2-3-1-1. Equipment composition

An actual system of this type is shown in Fig. 5.

The system consists mainly of the three following instruments:

- (1) Laser confocal displacement meter
- (2) XY stage and stage controller
- (3) Personal computer (PC) for controlling equipment.

#### 2-3-1-2. Principle of the laser confocal displacement meter

Fig. 6 shows the principle of the laser confocal displacement meter. The laser beam irradiated from a light source passes through the object lens, which moves rapidly up and down, based on the movement of the tuning fork, and focuses on the object. Next, the reflected light from the target object passes through a half mirror and a pinhole and reaches the light-receiving element. According to the confocal principle, when the laser beam focuses on the object, the reflected light is then concentrated at the pinhole, through which it enters the light-receiving element. By measuring the position of the tuning fork at that time, the distance to the object can be accurately measured.

#### 2-3-2. Three-dimensional measurements using the light sectioning method

This method of measurement involves the use of a three-dimensional digitizer adopting the light sectioning principle using a scanning slit laser.<sup>4),5)</sup> It greatly reduces measurement times over the system employing a laser confocal displacement meter described above. In the following, we describe the composition of equipment for this method and explain the principle of measurement.

##### 2-3-2-1. Equipment Composition

An actual system of this type is shown in Fig. 7. The system consists mainly of the following components:

- (1) Detector head
- (2) Scanner driver
- (3) Image encoder
- (4) PC for controlling equipment.

#### 2-3-2-2. Principle of the light sectioning measurement method

A slit laser is used to scan the whole surface of the measurement object and three-dimensional coordinates for surface contours are computed from the reflected light using the triangulation principle. In the following, we will explain the measurement principle in detail with reference to the schematic diagram in Fig. 8.

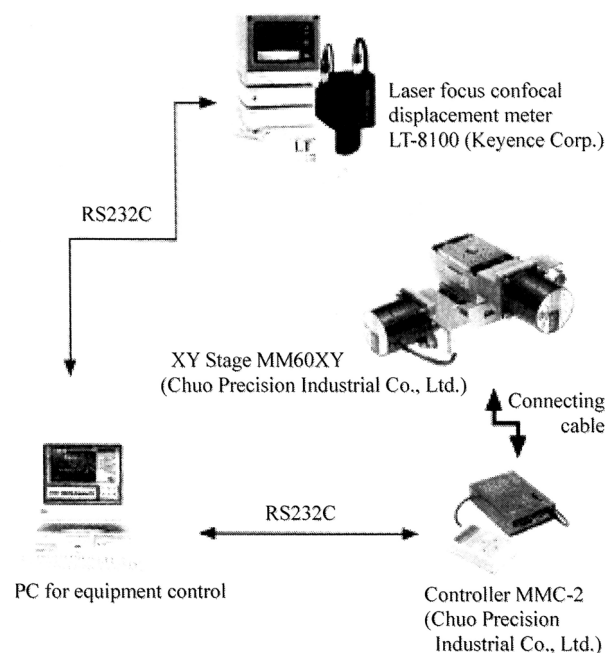
A beam from the slit laser scans the whole surface



of the replica and the projected image is captured by the CCD camera positioned above the measurement object. Using the projected image produced by the slit laser beam, the three-dimensional contours of the replica are computed according to the triangulation principle using the formula in Fig. 8.

### 2-3-3. Three-dimensional measurement employing the fringe projection method

This method involves the projection of a pattern with parallel fringes onto the measurement object and observing the pattern from an angle that is different than the one of the projection. The projected pattern with parallel fringes is distorted by the unevenness of the measurement object's surface (Fig. 9), and analysis of the distorted patterns generates three-dimensional data. This method enables a measurement to be taken in



**Fig. 5.** Three-dimensional Measurement System Employing Laser Confocal Displacement Meter

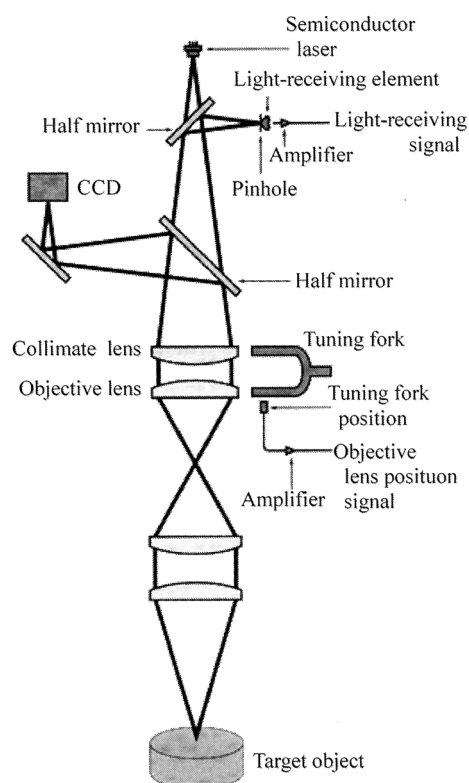
(Figs. 5 and 6 both taken from operation manual for Keyence LT8100 Laser Confocal Displacement Meter)

an even shorter time than that for optical triangulation. Typical systems using this technique for skin surface measurements are PRIMOS, made by the German company GFM, and dermaTOP-Blue, made by Breukmann, another German company. As both of these systems employ the same basic principle, we will explain a measurement taken with PRIMOS.

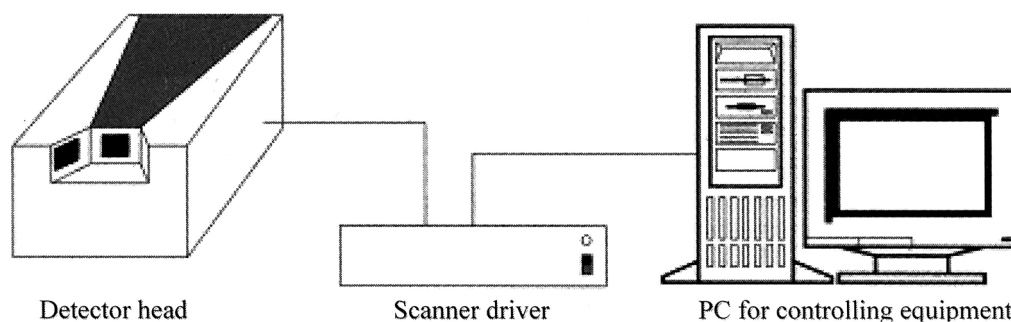
#### 2-3-3-1. Equipment composition

PRIMOS consists of the following:

- (1) Three-dimensional analysis unit (fringe projection device, CCD camera, etc.)
- (2) Personal computer system with a display for controlling the system



**Fig. 6.** Principle of Laser Confocal Displacement Meter.



**Fig. 7.** Schematic Diagram of the Three-Dimensional Measurement System Employing the Light Sectioning Method  
(Taken from the specification sheet for Hamano Engineering Co.'s VOXELAN HEV-50HS system.)

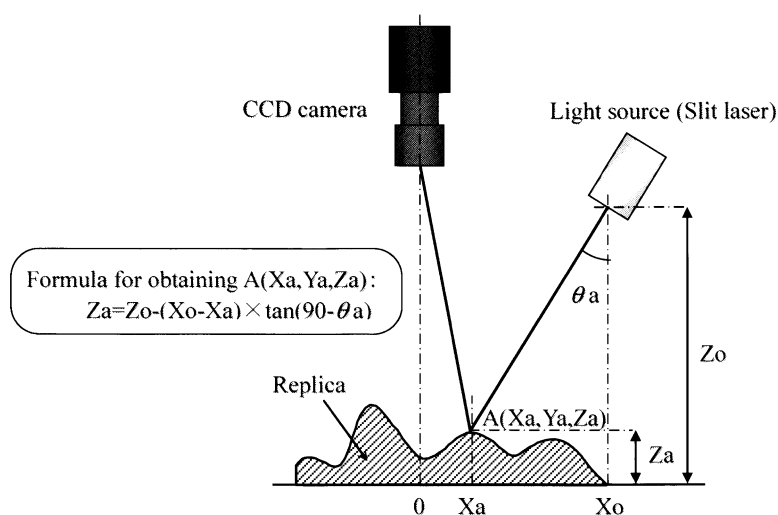


Fig. 8. Measurement Principle of the Light-Sectioning Method

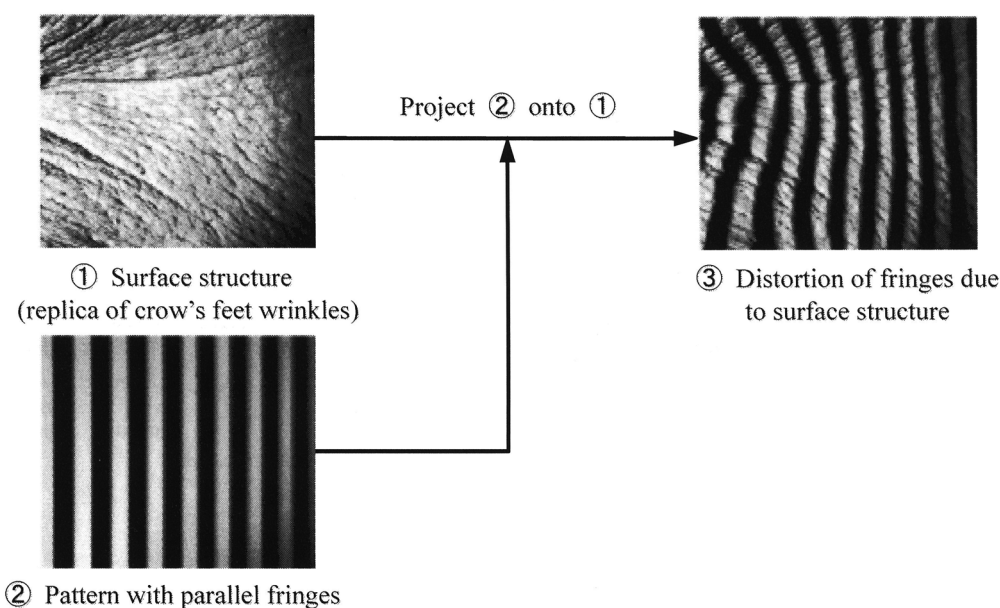


Fig. 9. Distortion Produced by Projecting a Pattern onto the Crow's Feet Replica  
 (Photographs from: Jaspers, et al.: XX1st IFSCC Congress, Berlin, 430-434, 2000)

(3) Measurement and analysis software (software provided with the PRIMOS system by GFM).

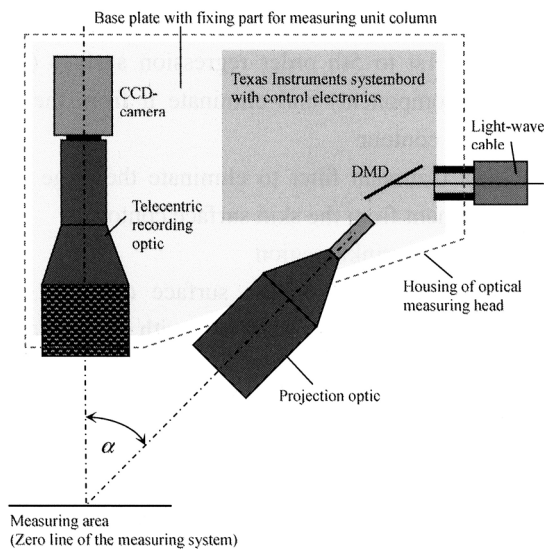
### 2-3-3-2. Principle of three-dimensional measurement using the fringe projection method

As shown in Fig. 10, a pattern with parallel fringes is projected onto the measurement object and the distortion produced in the patterns is recorded by a CCD camera placed at a different angle. If the surface of the measurement object is even, the original pattern will be observed, but if it is not, the pattern will be distorted (refer to Fig. 9). Analysis of the distortion produces three-dimensional data concerning the measurement object.<sup>6),7)</sup>

### 2-3-4. Wrinkle position adjustment in the three-dimensional analysis of wrinkles

In order to conduct accurate analysis of wrinkles before and after skin care treatment in clinical tests on cosmetics and quasi-drugs, wrinkle position adjustment is required. One method of doing this is by observing the overall image of the surface under measurement using a CCD camera and performing replica position adjustments using the wrinkles themselves or other features.

If the CCD camera does not have a function for position adjustment at the measurement location, this may be done by installing a lighting device that illuminates



**Fig. 10.** Optical System of PRIMOS

(Taken from the operation manual for the three-dimensional analysis system PRIMOS made by the German company GFM.)

the replica enabling an overall image to be observed. Illuminating wrinkles obliquely is convenient for position adjustment since this produces an image in which wrinkles are emphasized. Further, if three-dimensional data is collected over a wide field of view from replicas beforehand, through a comparison of the three-dimensional image of the wrinkles obtained from this data, position adjustment for the wrinkles in the area of examination may be conducted on this image.

### 2-3-5. Wrinkle analysis procedure

The procedure for wrinkle analysis is as follows:

#### (1) Replica distortion correction

Replica distortion correction is conducted because the replica's three-dimensional contour includes the overall inclination of the replica and bending in it. Some typical methods of replica distortion correction are as follows:

- Reconstitution through the elimination of low frequencies, (large wave component) by means of Fourier transform/inverse Fourier transform
- Obtain 1st to 5th order regression surface (large wave component) and eliminate it from the replica contour
- Use a Gaussian filter to eliminate the large wave component from the replica contour.

#### (2) Isolate the wrinkle region

After correcting the replica contour, set a threshold height and isolate areas with heights above this as the wrinkle zone. The standard used for setting the thresh-

old is usually the minimum depth of the wrinkles under evaluation.

#### (3) Calculation of wrinkle analysis parameters

The following parameters should be used in wrinkle analysis:

##### (i) Percentage wrinkle area

The percentage wrinkle area is taken as the percentage of the measurement field area occupied by the wrinkles that have been isolated from the corrected replica contour.

##### (ii) Overall average wrinkle depth

The overall average wrinkle depth is taken as the average depth of the wrinkles in the measurement field.

##### (iii) Average maximum wrinkle depth

The overall average wrinkle depth is taken as the average depth of the wrinkles with the greatest volume (or area) among wrinkles in the measurement field.

##### (iv) Maximum largest wrinkle depth

The maximum largest wrinkle depth is taken as the maximum depth of the wrinkles with the greatest volume (or area) among wrinkles in the measurement field.

##### (v) Total wrinkle volume

The total wrinkle volume is taken as the sum of the volumes of the individual wrinkles in the measurement field.

(vi) ISO standard surface roughness parameters (e.g.  $R_a$ ,  $R_z$ ,  $R_y$ ).<sup>8)-10)</sup>

- Arithmetic mean deviation of profile ( $R_a$ ):

Arithmetic mean of absolute ordinate values within the sampling length.

- Ten-point height of irregularities ( $R_z$ ):

Average value of the absolute height of the five highest peaks and the depth of the five deepest valleys within the sampling length.

- Maximum height of the profile ( $R_y$ ):

Sum of the largest profile peak height and the largest profile valley depth within the sampling length.

### 3. In Vivo Three-Dimensional Analysis

This technique involves the three-dimensional analysis of wrinkles at the lateral angle of the eye directly *in vivo*, without the use of replicas. Various parameters are derived from the three-dimensional measurements obtained and used in the analysis. One problem in making direct *in vivo* measurements is that the body cannot be kept completely still. Also, even if the area of measurement can be kept still using a stereotac-

tic face device, the measurement still needs to be taken in a very short time due to the influence of pulses and minute body movements. Three-dimensional measurement employing the projection of stripe patterns is one means of achieving this, and PRIMOS and dermaTOP-Blue, which were described in 2-3-3, are two systems capable of such measurement that are available on the market. They enable measurements to be made in less than one second.

### 3-1. Three-Dimensional Measurement Using Stripe Patterns Projection (Refer to 2-3-3)

#### 3-1-1. Equipment composition

Refer to 2-3-3-1.

#### 3-1-2. Measurement principle

Refer to 2-3-3-2.

### 3-2. Wrinkle Position Adjustment During *In Vivo* Three-Dimensional Analysis

In this type of analysis, too, wrinkle position adjustment is required before and after the use of a cosmetic or quasi-drug product. However, in contrast to the case of using replicas, perfect position adjustment when making measurements is not possible due to the difficulty of meeting the measurement conditions (facial angles, etc.) even if a stereotactic face device is used. Position adjustment is therefore performed using software for this purpose (measurement software supplied with the PRIMOS system incorporates a position adjustment function) and three-dimensional data is obtained before and after skin care treatment. However, there has to be three-dimensional data for before and after use for the identical location in the measurement field or it will not be possible to conduct position adjustment or analysis, so it is necessary to conduct a certain amount of position adjustment at the time of measurement.

### 3-3. Wrinkle Analysis Procedure

The procedure for wrinkle analysis is as follows:

#### (1) Skin surface contour correction

Skin surface contour correction is conducted prior to wrinkle analysis because the three-dimensional skin surface contour includes the overall inclination of the face and bending. Some typical methods of contour correction are as follows:

- Reconstitution through the elimination of low frequencies (large wave component) by means of

Fourier transform/inverse Fourier transform

- Obtain 1st to 5th order regression surface (large wave component) and eliminate it from the skin surface contour
- Use a Gaussian filter to eliminate the large wave component from the skin surface contour.

#### (2) Isolate wrinkle region

After correcting the skin surface contour, set a threshold height and isolate areas with heights above this as the wrinkle zone. The standard used for setting the threshold is usually the minimum depth of the wrinkles under evaluation.

#### (3) Calculation of wrinkle analysis parameters

Refer to 2-3-5.

### 3-4. Points to Pay Attention to During *In Vivo* Three-Dimensional Analysis

From a comparison of the results of three-dimensional analysis of the same location by the *in vivo* and replica methods, it was found that in the case of the former, it was difficult to measure wrinkle depth when the absolute depth was 40–50  $\mu\text{m}$  or less (data from the study conducted by the committee members) due to pulsatory motion or body movement. However, from the findings of a survey that was conducted separately, it has been observed that the minimum depth of topography that can be recognized as a wrinkle is more than 100  $\mu\text{m}$ , and therefore it is thought that this would not really pose a major problem in actual measurements.

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## Whitening

# Guidelines for Evaluation of Quasi-Drug Whitening Products for New Efficacy Claims

## Task Force Committee for Evaluation of Whitening Function

### 1. Introduction

Dark spots and freckles are frequently cited as pigmentation and skin-color problems in surveys on skin trouble. Reflecting this concern about their skin, consumers have high expectations of cosmetic products that promise a whitening effect, and the market for such products is very large.

Under Japan's Pharmaceutical Affairs Law, whitening cosmetics are classified as quasi-drug products and are allowed to make only two possible efficacy claims: "prevents pigmented spots and freckles due to sun exposure," or "prevents pigmented spots and freckles by inhibiting melanin formation."<sup>1)</sup> Only preventive effects can be claimed, and only those two. However, consumers expect more than mere prevention; they also want whitening cosmetics that will improve pigmented spots and freckles that have already formed. The Task Force Committee for Evaluation of Whitening Function (hereinafter the "Committee"), which is part of the Cosmetic Science Society's Committee for Studying Evaluation Methods for Cosmetic Functions, conducted a survey that found that consumers wanted whitening products that would facilitate the "disappearance of pigmented spots and freckles" and the "lightening of pigmented spots and freckles."<sup>2)</sup>

With the tremendous advances that have been made in science and technology, we have accumulated much knowledge concerning the mechanism for the formation of melanin and the control of melanin synthesis. Tremendous progress has also been made in evaluation technologies pertaining to the skin, including those for evaluating the condition of the skin surface and those for measuring skin color. Because of these advances, it is getting easier to analyze the efficacy claims of whitening cosmetics. In fact, a number of trials have reported on their efforts to evaluate the ability of such cosmetics to improve pigmentation.<sup>3)–26)</sup>

Against this background, the Committee carried out a project to study the drafting of Guidelines for Evaluation of Quasi-Drug Whitening Products for New Efficacy Claims, as its contribution to the realization of evidence-based claims by cosmetics in this field. Because it is important to create proper methods for obtaining the evidence needed to effectively evaluate new indications, the goal of the Committee was that the guidelines and their content should ensure that testing is conducted in an appropriate manner. This was achieved through literature and questionnaire surveys. The Committee was able to make a far-ranging study of the selection of subjects, standards for judging efficacy, and various other aspects, and to determine the individual items of the guidelines from the results. At the end of this report, we discuss the Committee's proposed efficacy claim.

Of course, as we continue to see tremendous advances in science and technology, some aspects of these guidelines may no longer be appropriate in the future. In such cases, it will be necessary to make revisions. We would also like to mention that the purpose of these guidelines is to provide basic guidance on evaluation procedures. Therefore, it will be necessary to draw up a protocol of detailed procedures for each type of testing that is conducted.

### 2. Guidelines for Evaluation of Quasi-Drug Whitening Products for New Efficacy Claims

#### 2–1. Qualified Pigmentation Symptoms and Subjects for Testing

Subjects are healthy women and men having superficial pigmentation symptoms (chloasma, lentigo senilis, ephelides, post-inflammation pigmentation (including sunburn), etc.). Those having Ota's nevus and other serious pigmentation symptoms are excluded as subjects.

Subjects are excluded under the following circum-