Designation: D6355 – 07 (Reapproved 2017)

Standard Test Method for Human Repeat Insult Patch Testing of Medical Gloves[1]

This standard is issued under the fixed designation D6355; the number immediately following the designation indicates the year of original adoption or, in the case of revision, the year of last revision. A number in parentheses indicates the year of last reapproval. A superscript epsilon (ε) indicates an editorial change since the last revision or reapproval.

1. Scope

1.1 This test method is designed to evaluate the potential of glove materials under test to induce and elicit Type IV skin sensitization reactions (that is, allergic contact dermatitis) in humans.

1.2 This test method should be used by individuals experienced in or under the supervision of those experienced in the use of good clinical practice procedures.

1.3 During the performance of the Human Repeat Insult Patch Test (RIPT) for determining sensitization, investigators are confronted with skin responses that represent skin irritation (non-immunologic responses) or allergic contact dermatitis (ACD). The numerical scoring system for grading the intensity of both are similar and test facilities may vary in their scores that describe intensities of allergic and irritant skin responses. The hallmark of a mild allergic contact dermatitis is a sustained palpable erythematous reaction. Delayed-type allergic contact reactions from patch tests have intensity characteristics that favor scores of higher values for longer periods of time and typically do not produce a minimal score (score of 1, a just-perceptible erythema) for short durations (less than 48 h). It is the responsibility of the investigator to evaluate the scores in light of irritant reactions so that the responses are allergic in nature and not irritant. The investigator should denote a final score as either due to contact allergy or irritation. Paragraphs 9.5 – 9.5.5 describe a commonly used scoring system and discuss allergic and irritant responses in detail.

1.4 The Draize RIPT was published in 1944 as an attempt to decrease the frequency ACD.[2] The test techniques at that time were just being validated and this experimental design was largely empiric.[3] The principle of the test is as follows:

1.4.1 Multiple inductions of the study material at relatively non or low irritancy levels,

1.4.2 Approximately a two-week rest period, and

1.4.3 A standard diagnostic challenge of approximately 48 h and a delayed reading at approximately 96 h after patch application.

1.5 In the intervening years, with further experimentation added to this empiric approach, three additional principles have been learned:

1.5.1 Increasing the concentration of the study material,

1.5.2 Defining a no effect level (this is possible with only individual ingredients and not the final study material), and

1.5.3 The enhanced sensitivity and the use of occlusion (where occlusion would not ordinarily be present).

1.6 In 1945, Henderson and Riley[4] demonstrated that a test panel sample size of 30 000 subjects would have to be employed to ensure statistically that there would be no more than 0.1 % sensitization. If there are no allergic responses in a test panel of 200 subjects with exposures comparable to those of the population, then there could be as many as 1.5 allergic reactions per 100 users.

1.7 All medical devices must be safe and effective for their intended use. Since medical devices such as gloves come in contact with human tissue, they should be tested for biocompatibility in animals first. The human repeat insult patch test (RIPT) is one test that can be used to test rubber gloves for skin sensitization to chemicals used in the manufacture of gloves.

1.7.1 Since various forms of the RIPT exist, a single standardized test method that outlines the testing protocol, scoring system, and the criteria for skin sensitization should be developed.

1.8 *This standard does not purport to address all of the safety concerns, if any, associated with its use. It is the responsibility of the user of this standard to establish appropriate safety and health practices and determine the applicability of regulatory limitations prior to use.*

1.9 *This international standard was developed in accordance with internationally recognized principles on standardization established in the Decision on Principles for the*

[1] This test method is under the jurisdiction of ASTM Committee D11 on Rubber and Rubber-like Materials and is the direct responsibility of Subcommittee D11.40 on Consumer Rubber Products.

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[2] Draize, J.H., Woodward, G., and Calvery, H.O., "Methods for the Study of Irritation and Toxicity of Substances Applied Topically to the Skin and Mucous Membranes," *Journal of Pharmacology and Experimental Therapeutics*, Vol 83, 1944, pp. 377-390.

[3] Shelanski, H. A., and Shelanski, M. V., "A New Technique of Human Patch Test," *Proc. Sci. Sect. Toilet Goods Assoc.* , Vol 19, 1953, pp. 46-49.

[4] Henderson, C. R., and Riley, E. C., "Certain Statistical Considerations in Patch Testing," *Journal of Investigative Dermatology* , Vol 6, 1945, pp. 227-232.

Development of International Standards, Guides and Recommendations issued by the World Trade Organization Technical Barriers to Trade (TBT) Committee.

2. Terminology

2.1 *Definitions:*

2.1.1 *allergen, n*—a substance capable of causing an allergic reaction.

2.1.2 *allergic contact dermatitis (ACD), n*— a Type IV delayed-in-time dermatitis that is caused by skin contact with a hapten that evokes a cell-mediated (delayed-type hyersensitivity) immune response.

2.1.3 *allergic contact dermatitis reaction, n*—an adverse immune response following exposure to chemical (non-protein) allergens.

2.1.4 *antigen, n*—any substance that provokes an immune response when introduced into the body.

2.1.5 *atopic dermatitis, n*—the most common form of chronic inflammatory dermatitis.

2.1.5.1 *Discussion*—Although immunologic mechanisms may play a role in producing this dermatitis, the role of any allergen in producing and sustaining this morphologically similar dermatitis is not proven or as clearly understood as classical allergic contact dermatitis.

2.1.6 *blister, n*—a vesicle containing serum.

2.1.7 *bullae, n*—synonymous with blister.

2.1.8 *cell-mediated immunity, n*—that portion of the immune system mediated by white blood cells called T-cells or T-lymphocytes.

2.1.9 *challenge test, n*—a medical procedure used to identify a substance to which a person is sensitive by deliberately re-exposing them to that substance in an attempt to reproduce the reaction.

2.1.10 *dermatitis, n*—inflammation of the skin evidenced by itching, redness, and various skin lesions.

2.1.11 *diagnostic patch tests, n*—a form of skin testing in which suspected allergens are applied to the skin, covered, and observed 48 to 96 h or more later to see if a reaction occurs.

2.1.11.1 *Discussion*—This test is often used to identify possible causes of allergic contact dermatitis.

2.1.12 *eczema, n*—synonymous with dermatitis.

2.1.13 *edema, n*—swelling caused by excessive infiltration of fluid into the skin.

2.1.14 *erythema, n*—synonymous with redness of the skin.

2.1.15 *immune response, n*—the activity of specialized cells or their products against antigens and allergens introduced to the body.

2.1.16 *immunize, v*—to render a patient immune from foreign substances.

2.1.17 *induration, n*—hardening of a tissue due to edema and cellular infiltration.

2.1.18 *inflammation, n*—a basic response of the body to injury, usually characterized by redness of the skin, warmth, swelling, and pain.

2.1.19 *irritation, n*—a chemically induced dermatosis without immunological involvement.

2.1.20 *mast cells, n*—tissue cells that contain packets of biochemicals responsible for the symptoms of allergy.

2.1.20.1 *Discussion*—When allergens attach to I_gE antibodies sitting on the surface of these cells, a signal is sent, causing them to release these biochemical mediators of allergy.

2.1.21 *mediators, n*—soluble products of immune cells that interact and/or activate other parts of the immune system.

2.1.22 *mild irritant control, n*—a substance that will produce a minimally perceptible dermatitis.

2.1.23 *neutral control, n*—a substance, such as water, that through clinical usage, has not been found to be an allergen.

2.1.24 *papules, n*—small, solid red elevations of the skin.

2.1.25 *predictive patch test, n*—a repeat insult patch test (RIPT) used as a toxicology test to determine the potential for ACD.

2.1.26 *sensitive, v*—to expose to an antigen, provoking an immune response so that on re-exposure to that antigen, a more advanced secondary response occurs. Synonymous with immunize.

2.1.27 *study material, n*—a synthetic or natural polymer material used as a medical glove or as a part of a medical glove.

2.1.28 *vesicles, n*—small circumscribed fluid-filled elevations of the skin smaller than a blister.

3. Summary of Test Method

3.1 A general medical history of the study subjects should be taken and include information on dermatologic conditions and sensitivities to specific compounds. Studies conducted in accordance with this human RIPT protocol will employ a minimum of 200 study subjects. Prior to evaluating the material in a human RIPT, acceptable toxicology data should be obtained. The sensitization potential of the study material is evaluated in a test panel of a minimum group size of 200 subjects. The study panel should include men and women. The induction phase of the human RIPT includes 10 multiple 48-h (72-h on weekends) patches at the same site typically on the upper back with no rest between repatching except for scoring. The patch site is graded for skin responses prior to each subsequent patch application. In the event of any significant erythema, the site of patch application should be moved to another location to confirm the reaction. Following the completion of the induction phase, there is approximately a 21 day rest period to allow the development of latent sensitization. This is followed by two consecutive 48-h challenge patches applied to naive sites. Responses are evaluated after the removal of each consecutive 48-h patch application. A minimum of two delayed skin site gradings is required to differentiate irritation from sensitization reactions. If the results are equivocal, a second challenge, after the original challenge dermatitis has cleared, may be conducted to ensure that sensitization was not overlooked.

4. Significance and Use

4.1 This RIPT method assesses the potential of skin sensitization with a particular medical product by repeated topical applications to the skin of selected subjects. This is a procedure that has the potential to detect many, but not all, sensitzers. This requires multiple applications to induce a cell-mediated Type IV immune response sufficient to cause an allergic reaction.

4.2 In general, the sensitization procedure requires 10 multiple 48-h (72-h on weekends) applications of patches containing the study material over a three-week induction phase. Induction is followed by approximately a 21 day rest phase to allow the development of any latent sensitization. Study subjects are then challenged by the application of two consecutive 48-h patches of the study material to naive sites. Responses are evaluated and graded after the removal of each consecutive 48-h patch application.

4.3 Although this test method is a clinical method, it may be used as part of a risk analysis to determine the potential for Type IV allergic contact dermatitis.

4.4 This test method assumes that good clinical practices will be utilized, including adequate training of practitioners.

5. Interferences and Precautions

5.1 During the course of the study, the area of the study subjects where the patch is applied should not be bathed, showered, or washed. The patch area must stay dry. Wet patches can be a source of mild irritation reactions.

5.2 Caution: Patch testing can involve a certain risk to the subject due to sensitization or raising of the level of sensitivity to the study material.

6. Experimental Plan

6.1 *Subject Inclusion/Selection Criteria:*

6.1.1 Subjects ranging from 18 to 65 years.

6.1.2 Subjects who complete a medical/personal history form.

6.1.3 Subjects who have read, understood, and signed an informed consent agreement.

6.1.4 Subjects should include both male and female.

6.2 *Subject Exclusion/Rejection Criteria:*

6.2.1 Subjects with skin disease that, in the opinion of the investigator, could interfere with the evaluation.

6.2.2 Subjects taking medications that, in the opinion of the investigator, would interfere with the study.

6.2.3 Subjects with clinically significant psoriasis, eczema, or atopic dermatitis.

6.2.4 Subjects who are pregnant or become pregnant during the study.

6.2.5 Subjects with known sensitivity to natural rubber and rubber chemicals.

6.2.6 Subjects who have acquired a recent marked skin tanning or sunburn that, in the opinion of the investigator, would interfere with the study.

6.2.7 Subjects who have undergone any type of sensitization testing within the last thirty days.

6.2.8 Subjects who are lactating women.

6.2.9 Subjects exogenously or endogenously immunosuppressed.

6.3 *Study Group:*

6.3.1 *Sample Size*—A minimum of 200 subjects will complete the study.

6.3.2 *Clinical Sites:*

6.3.2.1 One clinical location with a minimum total sample size of 200 subjects.

6.3.2.2 The testing may be done in a single clinical location but avoiding extreme climatic conditions.

7. Institutional Review and Informed Consent

7.1 *Institutional Review*—The method for this study should be reviewed by an appropriate Institutional Review Board (IRB).

7.2 *Informed Consent*—An informed consent document should be obtained from each study subject prior to initiating the study.

8. Study Materials and Patch

8.1 The patch will be an adhesive bandage with a 2 by 2-cm or larger Webril pad (or equivalent) affixed.

8.2 All study materials should be applied in an amount proportionate to the size of the 2 by 2-cm or larger patch.

8.3 A Neutral Control patch will be a adhesive bandage with a 2 by 2-cm or larger Webril pad (or equivalent) wetted with 0.2 mL of distilled or deionized water.

8.4 The study glove material should be applied so that the inside glove surface is exposed to the skin of the test subject.

9. Study Design

9.1 The human RIPT is performed to determine the potential of the product for sensitization under conditions relative to anticipated consumer exposure.

9.2 *Patch Site:*

9.2.1 Patches should be applied to the upper back area, either to the right or left of the midline. (The arm may be used as an alternative patch site to the back area.)

9.2.2 The upper back, either to the right or left of the midline, is the most common site used for patch testing. This area has been preferred because of its larger, more uniform surface; it is more accommodating to multiple tests. For many volunteer subjects, testing at this site is less obtrusive. However, there are occasions when the upper arm or forearm may be the preferred site. There is no data that supports the superiority of one of these skin sites over another for inducing experimental sensitization.

9.3 *Study Description:*

9.3.1 *Induction Phase*—The induction phase of the RIPT includes 10 multiple 48-h (72-h on weekends) patches at a single site on the upper back with no rest between re-patching. The patch site is graded for skin reactions just prior to each application. The patch site is moved slightly in the event of significant erythema or irritation to confirm the reaction.

9.3.2 *Rest Period*—Following the induction phase, there is an approximately 21 day rest period to allow the development of any latent sensitization.

9.3.3 *Challenge Phase*—After the rest period, two consecutive 48-h challenge patches are applied to naive sites. Any reactions are scored 2 and 4 days after the initiation of the challenge phase. That is, the patch site is scored after the first patch is removed (48 h) and after the removal of the second 48-h patch (96 h). A minimum of two skin site gradings is required to aid in differentiating irritation from sensitization reactions. If the results are equivocal, a second challenge (rechallenge), after the original challenge dermatitis has cleared, may be conducted to ensure that sensitization was not overlooked.

9.3.4 *Rechallenge*—If a minimum of two skin reactions occurs during the challenge phase, a rechallenge may be necessary to distinguish irritation from sensitization and confirm the reaction. A patch is applied to a single naive skin location on the upper back or optionally duplicate naive patches are applied to two anatomical skin locations (for example, upper back and upper arm) when evidence of low grade sensitization or irritancy is apparent. Rechallenge patches are scored at patch removal (48 h) and at 96 h after patch application. A minimum of two skin gradings in the rechallenge phase are required to differentiate irritation from sensitization and to confirm the reaction.

9.4 *Study Flow Diagram of Human RIPT*—The standard test consists of an induction period of approximately 3.5 weeks, during which 10 patches are applied each Monday, Wednesday, and Friday. Each patch is left on for 48 h and then removed by the investigator. Scoring is performed immediately preceding the next patch application. The final 10 patches are applied on Monday of the fourth week and removed for final visual evaluation. Then, approximately 21 days after the last induction application (Monday of the seventh week), two consecutive 48-h challenge patches are applied at naive sites. The challenge patch is scored after the removal of each consecutive 48-h patch application. The timing of the scoring facilitates the identification of delayed and persistent responses, which are characteristic of allergic contact sensitivity. Subjects suspected of being sensitized may be rechallenged following the original challenge phase in the same manner as the original challenge if no clinical decision can be made. A delay period before rechallenge allows any skin reactions to subside, permitting better confirmation of the presence or absence of sensitization.

9.4.1 *Timing of Patch Application:*

Induction Phase (10 × 48 h Patch Applications)				Rest Period	Challenge Phase (2 × 48 h Patches)	
Wk 1	Wk 2	Wk 3	Wk 4	Wks 5-6	Wk 7	Wk 8
M W F	M W F	M W F	M	(No Patch)	M	W

9.4.1.1 *Induction Phase*—The skin is scored at a single skin site for visual characteristics just prior to reapplication of each 48-h (72-h on weekends) patch.

9.4.1.2 *Challenge Phase*—The skin is scored at a single naive site for visual and palpatory characteristics after the removal of each consecutive 48-h patch application.

9.4.1.3 *Rechallenge Phase*—The skin is scored at a single skin site for visual and palpatory characteristics at 48 h and 96 h after patch application.

9.5 *Scoring of Reactions:*

9.5.1 Numerical scoring assigns a value to the intensity of patch test responses and does not qualify a reaction immunologically. The language used to describe intensities of reactions uses the core terminology that describes all primary skin lesions. The irritant and allergic reactions often overlap morphologically when both are midway in their intensity ranges and their respective durations. They can be characteristic in their extremes or when they exhibit certain morphologic hallmarks known to be characteristic of either the allergic or irritant response. Delayed-type allergic contact reactions from patch tests have intensity characteristics that favor scores of higher values for longer periods of time and typically do not produce a minimal score (a just-perceptible erythema) for short durations (less than 48 h). The pattern of an irritant patch test area may not always be continuous or confluent. Skewed or puddled patterns consisting of either macules, papules, or follicular lesions are commonplace. Irritancy frequently produces an abrupt or well marginated response from an “all or none” injury. By contrast, allergic responses are test site confluent and may “creep” beyond what was thought to be the test area. Instead of an “all or none response,” allergic dermatitis has a “long threshold,” a subtle or fading cutoff. The response rapidly becomes a sustained confluency of swelling with or without papules or vesicles. Knowledge of the test site’s behavior beyond a 48-h challenge is essential.

9.5.2 In the human RIPT, study materials can evoke responses in both the induction and elicitation phases of the test that represent irritation or allergy, or sometimes both. Unless a subject has an unknown preexisting allergy to the study material, scores in the first one week of the induction period are due to irritation. Scores in the third week of the induction can possibly represent the early development of contact allergy, particularly if they are strong and not in keeping with the scores recorded in the earlier weeks. The challenge phase requires that investigators are familiar with the classic expressions of both allergy and irritation. The challenge period requires taking skin readings beyond the time of final removal of the first application of the study material (greater than 48 h) in order to appreciate the morphological difference over time. Products with irritant scores scattered among all the panelists during the induction are particularly difficult to evaluate at the challenge phase. The investigator should denote a final challenge scores as either due to contact allergy or irritation.

9.5.3 *Scoring Allergic Contact Dermatitis:*

9.5.3.1 A true positive allergic (sensitization) reaction indicates that the subject has been exposed and has become sensitized to the study material. The challenge of a naive skin site, the delayed skin reaction, and the rechallenge protocol all maximize the sensitivity and reliability of the clinical method.

9.5.3.2 A positive allergic skin test reaction is typically characterized by erythema and edema, and may also be accompanied by papules or vesiculation, or both, in the challenge phase of the study. Strong reactions may spread beyond the patch site. A positive sensitization reaction is

expected to be delayed, persist for several days, and should often worsen over time. Sensitization typically peaks at 48 to 96 h after patch challenge application, and subsequently subsides. The reaction usually increases in strength with time, and is often greater at 96 h then at 48 h. Any questionable reaction to the study material during the challenge phase may be followed up by a rechallenge patch study for confirmation.

9.5.3.3 An occurrence of sensitization-like reactions in the early part of the induction phase may be indicative of preexisting sensitization to the study material. Subjects found to be pre-sensitized should be recorded as such and withdrawn from the study.

9.5.3.4 Irritation reactions are nonallergic inflammatory reactions of the skin that become red but are delimited to the application area of the study material. Typically there is no papule and vesicle formation. Irritant reactions generally weaken with time and disappear in a day or two. There can occur, however, irritant skin reactions that are indistinguishable from allergic responses. Weak or minimal irritation reactions may occur both during the induction and challenge phases of the study.

9.5.4 *Grading Skin Reactions:*

9.5.4.1 A basic grading scale that adequately categorizes the kinds of reactions encountered is used. Many grading scales have been used. The language used here to describe the intensities of reactions uses the core terminology that describes all primary skin lesions. The basic numerical score assigns an erythema value to the intensity of patch test response but does not qualify a reaction immunologically. A letter score of "E," "P," "V," or "B" accompanying the numeric score denotes the additional presence of edema, papules, vesicles, or bullae, respectively, and adds a value of 0.5 each to the basic numeric score. A positive allergic skin test reaction is typically characterized by a palpable erythema (erythema and edema), and may also be accompanied by papules or vesiculation, or both, in the challenge phase of the study.

9.5.4.2 *Basic Numeric Score Values:*

Basic Score	Description
0	No visible reaction
0.5	Doubtful or negligible erythema reaction
1.0	Mild or just-perceptible macular erythema reaction in a speckled/follicular, patchy or confluent pattern (slight pinking)
2.0	Moderate erythema reaction in a confluent pattern (definite redness)
3.0	Strong or brisk erythema reaction that may spread beyond the test site (intense redness)

9.5.4.3 *Supplementary Letter Score Values to be Added to the Basic Numeric Score:*

Letter Score	Numeric Score	Description
E	0.5	Edema
P	0.5	Papules
V	0.5	Vesicles
B	0.5	Bullae

9.5.4.4 The basic numeric and letter scores are totaled. A palpable erythema with a total score of 1.5 or greater and characterized by both erythema and edema in the naive patch site of the challenge phase is usually indicative of an allergic response as long as it persists for two scoring intervals at least 24 h apart. The persistence or enhancement of reaction, or both, with time is characteristic of sensitization, while improvement is more typical of irritation. The interpretation of this grading system presumes that the study material does not produce excessive irritation.

9.5.4.5 If the results are equivocal, a second challenge, after the original challenge dermatitis has cleared, may be conducted to ensure that sensitization was not overlooked. Equivocal skin sensitization at the naive patch site of the challenge may also be compared with a Neutral Control patch to help determine if the reactions are clinically insignificant. It is the responsibility of the investigator to evaluate the scores in light of irritant reactions so that the responses are allergic in nature and not irritant. The investigator should denote a final score as either due to contact allergy or irritation.

9.5.5 *Interpretation of Sensitivity Scoring:*

9.5.5.1 *Examples 1 and 2*—The minimal scores of just perceptible erythema reaction are not indicative of sensitization in these examples. A rechallenge could be used to help confirm the lack of sensitization. Upon rechallenge, the absence of sensitization (erythema and edema) was confirmed. In cases of true sensitization, responses with visual characteristics of allergy such as erythema and edema should develop at the challenge sites and persist through two delayed scorings at least 24 h apart.

Example 1	Induction Phase										Challenge Phase	
Applications:	1	2	3	4	5	6	7	8	9	10	48 h	96 h
Score:	1	1	1	0	0	0	0	0	0	0	0	1
Rechallenge:											0	0
Total Score:	1	1	1	0	0	0	0	0	0	0	0	1

Example 2	Induction Phase										Challenge Phase	
Applications:	1	2	3	4	5	6	7	8	9	10	48 h	96 h
Score:	0	1	0	0	0	OP	OP	0	OV	0	1	0
Rechallenge:											1	0
Total Score:	0	1	0	0	0	0.5	0.5	0	0.5	0	1	0

9.5.5.2 *Examples 3 and 4*—The induction scores show questionable reactions. A confirmatory rechallenge may be necessary even though the responses during the later part of the induction and challenge phase are not stronger than those earlier. Upon rechallenge, the absence of sensitization (erythema and edema) was confirmed since there was no delayed appearance of increased intensity of response. In cases of true sensitization, responses with palpable erythema (erythema and edema) should develop at the challenge sites and persist through two delayed scorings at least 24 h apart.

Example 3	Induction Phase										Challenge Phase	
Applications:	1	2	3	4	5	6	7	8	9	10	48 h	96 h
Score:	0	1	1	1	1	0	0	0	0	0	1	0
Rechallenge:											0	0
Total Score:	0	1	1	1	1	0	0	0	0	0	1	0

Example 4	Induction Phase										Challenge Phase	
Applications:	1	2	3	4	5	6	7	8	9	10	48 h	96 h
Score:	1	1	1	1	1	1	1	0	0	0	1P	0
Rechallenge:											1	0
Total Score:	1	1	1	1	1	1	1	0	0	0	1.5	0

9.5.5.3 *Example 5*—The induction and challenge scores are representative of allergic contact sensitization. A confirmatory rechallenge is not necessary since the responses during the later part of the induction and challenge phase have the visual characteristics of allergy such as erythema and edema, and are

stronger than those earlier. In cases of true sensitization, responses with palable erythema (erythema and edema) should develop at the challenge sites and persist through two delayed scorings at least 24 h apart.

Example 5	Induction Phase										Challenge Phase	
Applications:	1	2	3	4	5	6	7	8	9	10	48 h	96 h
Score:	0	0	0	1	1	0	1	2E	3E	3E	2E	3E
Rechallenge:											n/a	n/a
Total Score:	0	0	0	1	1	0	1	2.5	3.5	3.5	2.5	3.5

9.5.5.4 *Example 6*—The challenge scores as representative of allergic contact sensitization. A confirmatory rechallenge is not necessary since the responses during the later part of the challenge phase have the visual characteristics of allergy such as erythema and edema, and are stronger than those earlier. In cases of true sensitization, responses with palpable erythema (erythema and edema) should develop at the challenge sites and persist through two delayed scorings at least 24 h apart.

Example 6	Induction Phase										Challenge Phase	
Applications:	1	2	3	4	5	6	7	8	9	10	48 h	96 h
Score:	0	0	0	0	0	0	0	0	0	0	1P	3E
Rechallenge:											n/a	n/a
Total Score:	0	0	0	0	0	0	0	0	0	0	1.5	3.5

10. Report

10.1 *Reporting of Data*—Case report forms will be designed so that each study subject is identified by a subject number and the study material/product description.

10.2 *Study Monitoring*—The sponsor may visit the investigator and inspect any documentation associated with the study.

10.3 *Adverse Reactions*—If any unusual reactions occur during the study, it is understood that the investigator may stop application of the study material if the subject's condition so indicates.

10.4 *Final Report*—At the conclusion of the study, the sponsor will receive a report that includes:

10.4.1 A general summary,

10.4.2 A description of the clinical method,

10.4.3 Identification of study materials,

10.4.4 A description of the scoring system for grading reactions,

10.4.5 The alphanumeric scores indicating induction and challenge exposures and times,

10.4.6 The number of study subjects found to be presensitized and withdrawn from the study.

10.4.7 The number, age, gender, and ethnicity of the study subjects, and

10.4.8 The interpretation of the outcome as either due to contact allergy or irritation, and a discussion of the results.

11. Keywords

11.1 ACD; allergic contact dermatitis; allergy; dermatitis; Draize; glove; latex; natural rubber latex; repeat insult patch test; RIPT; rubber; sensitization; synthetic rubber

RELATED MATERIAL

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