

U.S. Department of Labor Occupational Safety and Health Administration Directorate of Science, Technology and Medicine Office of Occupational Medicine

Potential for Sensitization and Possible Allergic Reaction To Natural Rubber Latex Gloves and other Natural Rubber Products

Safety and Health Information Bulletin

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Purpose

This safety and health information bulletin updates TIB 99-04-12 and informs field personnel, employees and employers about issues regarding sensitization and allergic reactions that have occurred in some individuals using natural rubber latex (NRL) products, particularly gloves, in the workplace setting. This bulletin can also provide information to personnel, especially health care staff, who use gloves as personal protective equipment or use other NRL products in their workplace.

Background

Natural rubber is utilized in a variety of products, including gloves, airways (*e.g.*, for intubation), airway masks, medication vial tops, anesthesia bags, various catheters, supplies for intravenous use, dental dams, balloons, and other items. ^{1,2,3} NRL glove use in the health care setting has risen dramatically since about 1987 due to increased awareness about the risk of contracting HIV, hepatitis B and C, and other infectious agents in the course of delivering health care to patients. ^{1,4} Thus, the frequency of exposure to NRL among health care and other employees has increased.

NRL products are also used to provide barrier protection from disinfectants and other chemicals and agents in health care and other environments. (NOTE: While NRL gloves provide an effective barrier for certain purposes, they are not universally suitable. The material properties and construction of a glove suitable for barrier protection must be determined in advance of use. Gloves appropriate

This Safety and Health Information Bulletin is **not** a standard or regulation, and it creates no new legal obligations. The Bulletin is advisory in nature, informational in content, and is intended to assist employers in providing a safe and healthful workplace. The Occupational Safety and Health Act requires employers to comply with safety and health standards as issued by either the Federal Occupational and Health Administration (OSHA) or an OSHA approved state plan. In addition, pursuant to Section 5(a)(1), the General Duty Clause of the Act, employers must provide their employees with a workplace free from recognized hazards likely to cause death or serious physical harm. Employers can be cited for violating the General Duty Clause if there is a recognized hazard and they do not take reasonable steps to prevent or abate the hazard. However, failure to implement any specific recommendations in this safety and health information bulletin is not, in itself, a violation of the General Duty Clause. Citations can only be based on standards, regulations, and the General Duty Clause.

for protection from the particular chemical or agent must be used). In some workplaces (*e.g.*, electronics, drug manufacturing, and food preparation), gloves are used to prevent contamination of products. NRL gloves have also appeared in some workplaces where there is a perceived need to protect employees from an exposure such as toll booths, post offices, and day care settings. Natural rubber-containing articles are manufactured in a variety of workplaces (*e.g.*, manufacturers of medical gloves, industrial gloves, balloons, rubber bands, boots and shoes, and many other products).

Health Issues

With more widespread use of NRL gloves after 1987 there was an increase in reported NRL sensitization and allergic reactions among patients and among employees, notably health care employees. In rare cases, these allergic reactions can be fatal. In addition to reports from the dermatology, allergy, and pulmonary literature of severe skin and respiratory symptoms, life threatening reactions associated with use of NRL products have been noted in pediatric patients with spina bifida who had repeated NRL exposure from numerous surgical procedures. 5,6,7 In addition, the U.S. Food and Drug Administration (FDA) received reports of numerous severe allergic reactions among NRL-allergic patients, including some deaths, associated with the use of NRL enema cuffs and gloves.8

NRL is found in a variety of plants but is mainly harvested from the rubber tree, Hevea brasiliensis. The tree's milky fluid (latex) contains variable amounts of proteins. These proteins, when present on a glove or adsorbed to glove powder, may be absorbed through the skin or inhaled. Many of these proteins have been characterized, with a number of them designated as allergens by the International Allergen Nomenclature Committee.9 Studies regarding these allergens are ongoing; some researchers have noted that up to 60 protein variations in NRL may be allergenic, or capable of causing sensitization in some individuals. 10,11,12 Some of these proteins, including some that are allergenic for some individuals, can be eliminated through the use of various processing techniques. A number of studies indicate that corn starch powder, often added to gloves to facilitate donning and removal, serves as a carrier for the allergenic proteins from the NRL. 2,3,13,14

In this document, "sensitization" or "sensitized" refers to the presence of an immunoglobulin (IgE) response to allergenic protein exposure. An individual may or may not show any symptoms of allergy, even though they are sensitized. "Allergic response" refers to a skin reaction in response to a

skin prick test. "Allergic reaction" refers to (1) local reactions such as a skin reaction in the area of exposure in response to wearing gloves or a glove challenge test, and (2) systemic reactions, which occur beyond the body areas of exposure and lead to various symptoms. This document refers to local or systemic allergic reactions that cause symptoms as "symptomatic."

In addition to the above concerns, gloves, including those made from NRL as well as some other materials, may contain chemical accelerators such as thiurams, carbamates, and benzothiazoles to which an employee may develop an allergic contact dermatitis. Antioxidants, biocides, soaps, and other chemicals used in the processing of NRL products may also contribute to this type of reaction.

Occupational Exposure Routes

The two major routes of occupational exposure are dermal contact and inhalation. Inhalational exposure can occur particularly when glove powder acts as a carrier for NRL protein, which becomes airborne when the gloves are donned, or removed. ^{2,3,13}

Allergenic proteins appear to be only a portion of the total protein content of NRL gloves. It has been noted that gloves with lower protein concentration caused fewer positive responses to skin prick tests than gloves with higher protein concentration; ¹⁵ also, higher total protein levels found on a glove generally have included high levels of NRL allergenic proteins. 16 However, several investigators have reported that glove NRL total protein content may not necessarily correlate with allergenic protein content, especially at lower protein levels. A number of workplace interventions have indicated that powder-free gloves with either lower total protein or lower allergenic protein content reduced risk of sensitization to allergenic NRL proteins or allergic reactions in persons already sensitized. ^{20,21,22,23,24} Importantly, most interventions have included the provision, and most investigators recommend, that only non-NRL gloves be used by those employees who are sensitized to or have exhibited allergic reactions to NRL proteins. ^{25,26}

The majority of health care employees are able to use NRL products to care for most patients. However, some employees may develop sensitivity to NRL upon repeated exposure. Variations exist in the reported prevalence of NRL allergy. This variation is probably due to different levels of exposure and methods of estimating NRL sensitization or allergy, as well as different study populations and sampling methods. The prevalence statistics in the studies mentioned below are based on seroprevalence, skin prick test positivity and/or allergic manifestations, and do not refer to the more serious anaphylactic response, which is rare but potentially life threatening in some individuals. In one example of an investigation of health care employees, a survey of active duty dental officers in the U.S. Army reported that the prevalence of allergic symptoms correlated with NRL use was 13.7%. ²⁷ An investigation of dental employees using NRL skin prick testing at two consecutive American Dental Association meetings in 1994 and 1995 revealed allergic responses in 9.1-9.7% of dental hygienists and assistants, although dentists showed a lower rate of 5.1-6.7%. A 2000 - 2002 study of dental hygienists using NRL skin prick testing found allergic response in 4.8% of those studied. 29 A study of 247 nurses recruited at a nurses' association meeting revealed that 6.9% responded to a natural rubber latex extract skin prick test, although the rate for positive skin prick test together with a history of symptoms associated with latex was somewhat less (5.7%). Another article concluded that 8.9% of 741 inpatient nurses were seropositive for anti-latex antibodies, an indication of sensitization.³¹ A study of 168 anesthesiologists and nurse anesthetists determined that 12.5% were sensitized (anti-latex IgE antibody positive), but only 2.4% had experienced allergic symptoms.³²

Several papers have also addressed sensitization or allergic response prevalence rates in the general population or in populations perceived to be surrogates for the general population. Examples include: (1) a study of volunteer blood donors which determined that 6.4% were seropositive for antilatex IgE antibodies, indicating sensitization to NRL;³³ and (2) a report that 6.7% of 996

ambulatory surgery patients were sensitized to NRL (IgE anti-latex antibodies).³⁴ In a review of a large number of prevalence studies in occupationally exposed groups, as well as in general populations in North America and Europe, 2.9% -12.1% of occupationally exposed groups, and under 2% of general population groups, reacted to skin prick testing, indicating allergic response to NRL.³⁵ A later analysis of prevalence studies found 6.9% to 7.8% of health care employees and 2.1% to 2.7% of the general population reactive to skin prick testing.³⁶

Health care employees particularly affected include operating room personnel, dental patient care staff, special-procedure and general-medical nurses, laboratory technicians, and hospital housekeeping personnel consistently exposed to NRL. NRL sensitization or allergic response or reaction has also been reported in greenhouse employees, hairdressers, doll manufacturing employees, and employees in a glove manufacturing plant.

Types of Reactions

Use of natural rubber products may result in reactions that fall into the following three categories (See also Types of Reactions table):

- (1) irritant contact dermatitis;
- (2) type IV delayed hypersensitivity (also called allergic contact dermatitis); and
- (3) type I immediate hypersensitivity (also called IgE/histamine mediated allergy).

These categories include reactions that vary from localized redness and rash; to nasal, sinus, and eye symptoms; to asthmatic manifestations, including cough, wheeze, shortness of breath, and chest tightness; to in some cases, severe systemic reactions with swelling of the face, lips, and airways that may progress rapidly to shock and, potentially, death.

When gloves are associated with skin lesions, the most common reaction is irritant contact dermatitis. Irritant contact dermatitis may be due to direct

irritation from gloves or glove powder or may be due to other causes, such as irritation from soaps or detergents, other chemicals, or incomplete hand drying. Irritant contact dermatitis presents as dried, cracked, split skin. Although irritant contact dermatitis is not an allergic reaction, the breaking of the intact skin barrier due to these lesions may afford a pathway for NRL proteins to gain access, and thus promote development of sensitization. In addition, irritant contact dermatitis lesions disrupt the barrier function that intact skin provides to inhibit passage of various chemicals and pathogens.

The second type of reaction that may be associated with glove use is allergic contact dermatitis (also known as type IV delayed hypersensitivity or allergic contact sensitivity). When glove use has been associated with this reaction, the majority of cases appear to be due to the chemicals used in processing NRL or other glove materials; a small percentage of these reactions have been reported to be due to NRL. The allergic contact dermatitis has an appearance similar to the typical poison ivy reaction, with blistering, itching, crusting, oozing lesions. Also, like poison ivy, this dermatitis appears 24-72 hours after the use of gloves or exposure to other sources of chemical sensitizers.

The third and potentially most serious type of reaction sometimes associated with glove use is a true IgE/histamine-mediated allergy (also called immediate or type I hypersensitivity) to allergenic glove protein [in the case of NRL allergy, to allergenic NRL protein(s)]. This type of reaction can involve local or systemic symptoms. Localized reactions occur at the site of exposure. For example, contact urticaria (hives), appearing in the area where contact occurred, is a localized reaction. Allergic rhino conjunctivitis and asthma following exposure to airborne allergen are localized reactions. Generalized reactions are those occurring at sites in the body distant from the site of exposure. For example, rhinitis or asthma after a skin exposure (or hives at a site other than where the exposure occurred) is a generalized reaction. The presence of allergic manifestations to allergenic NRL protein indicates an increased risk for anaphylaxis, a rare but severe reaction experienced by some individuals who have developed an allergy to certain allergenic proteins (*e.g.*, those present in NRL, some foods). A type I reaction can occur within seconds to minutes of exposure to the allergen (in the case of NRL, to allergenic natural rubber proteins), either by touching a product with the allergen (*e.g.*, gloves) or by inhaling the allergen (*e.g.*, powder to which natural rubber proteins from gloves have adsorbed). When such a reaction begins in highly sensitive individuals, it can progress rapidly from swelling of the lips and airways to shortness of breath, and may progress to shock and death, sometimes within minutes.

Any of these allergic signs and symptoms may be the first indication of development of sensitization. Sensitized employees with exposure to allergenic NRL proteins can develop allergic reactions such as skin (contact urticaria) and/or respiratory symptoms. A number of studies indicate that individuals with NRL allergy are more likely than NRL non-allergic persons to be atopic (individuals with an increased susceptibility for IgE response to common allergens, with symptoms such as asthma, eczema, or allergic rhinitis), 30,47,48 or that atopic individuals have an increased risk for developing sensitization to allergenic NRL proteins. 48 Once symptomatic NRL allergic responses occur, allergic individuals have continued to experience symptoms on exposure to allergenic NRL proteins. These symptoms have included life-threatening reactions, not only on exposure to allergenic NRL proteins in the workplace, but also upon receiving or accompanying a family member receiving health care services at inpatient as well as office-based settings. In addition, such reactions have occurred on exposure to consumer goods such as balloons, condoms, and other products. Symptoms have also occurred in some persons from exposure to certain plants or foods (e.g., bananas, kiwi, avocados, and chestnuts) with proteins that are cross-reactive with NRL allergenic proteins, and allergic symptoms have been reported by NRL allergic persons from eating foods handled by food service employees wearing NRL gloves. Moreover, some affected individuals continue to experience asthmatic

symptoms even without known contact with NRL; long-term treatment with steroids or other medications may be necessary for managing symptoms in these cases. Therefore, development of symptomatic allergic responses to allergenic NRL proteins in an individual may have lifestyle implications beyond the workplace.

Recommended Strategies - Risk Reduction

It is of primary importance that barrier protection be used when hands would otherwise contact infectious materials or hazardous chemicals. OSHA's Bloodborne Pathogens Standard (29 CFR 1910.1030) requires that gloves be worn when it is reasonably anticipated that hand contact may occur with blood, other potentially infectious materials,

Types of Reactions

Types of Reaction	Symptoms/Signs	Cause	Prevention/Management
(1) Irritant Contact Dermatitis	Itchy, red, inflamed, scaling, dry and cracked skin	Direct skin irritation by gloves, powder, soaps/detergents, incomplete hand drying	Obtain medical diagnosis, dematology consultation, avoid irritant product, assure glove material provides proper barrier; consider alternative gloves/products, cotton liners
(2) Allergic Contact Dermatitis (Type IV delayed hypersensitivity or allergic contact sensitivity)	Itchy, red, inflamed, scaling, dry and cracked blistering (similar to poison ivy reaction); 24-72 hrs. after contact	Accelerators (e.g. thiurams, carbamates, benzothiazoles) processing chemicals (e.g., biocides, antioxidants) NRL Consider penetration of glove barrier by chemicals	Obtain medical diagnosis, dermatology consultation; identify chemical. Consider use of glove liners such as cotton. Use alternative glove material without chemical. Assure glove material is suitable for intended use (proper barrier)
(3) NRL Allergy – IgE mediated (Type 1 immediate hypersensitivity)		NRL proteins; direct contact / breathing NRL proteins including glove powder containing NRL proteins, from powdered NRL gloves/environment	For (3)(a), (3)(b), and (3)(c): Obtain medical diagnosis, allergy consultation; substitute non-NRL gloves and other non-NRL products for affected worker Eliminate exposure to glove powder –
(3)(a) Localized contact urticaria	Hives in area of contact with NRL	Wearing NRL gloves or other direct contact with NRL allergenic proteins	use of reduced allergen, powder free gloves or non-NRL gloves for coworkers (assure glove material provides a proper barrier)
(3)(b) Other Allergic Manifestation	Allergic rhinitis, allergic conjunctivitis, asthma	Exposure to aerosolized NRL allergenic protein. Key role - glove powder	Clean NRL-containing powder from environment Consider NRL safe environment
(3)(c) Generalized Reaction	Manifesting as: generalized urticaria, asthma, upper respiratory symptoms, and/or flushing, rapid pulse, falling blood pressure, weakness. Can progress to anaphylactic shock	Exposure to NRL allergenic proteins by any one of several routes	

mucous membranes, non-intact skin, or contaminated items or surfaces, as well as when performing vascular access procedures [except as specified in paragraph (d)(3)(ix)(D)]. When gloves are being worn to protect against bloodborne pathogens, the standard requires that employers provide readily accessible alternatives (e.g., glove liners) for employees who are allergic to the gloves normally provided. NRL is a glove material that has been used in the health care environment for barrier protection for a number of years. In response to reported NRL allergy in some patients and health care employees, measures have been recommended to reduce the risk of reactions to allergenic NRL proteins in employees.

Primary prevention involves reducing potential development of allergy by reducing exposure to NRL allergenic proteins for all employees. Food service employees, for example, use gloves as a barrier to infectious agents that may be present on their hands, and alternative gloves are available for food handler use. Alternative materials are appropriate for employees engaged in tasks such as gardening activities. Gloves made of NRL as well as alternative materials have been cleared for marketing as medical gloves by the FDA and can be used effectively for barrier protection against bloodborne pathogens. ^{49,50} General administrative procedures* that a facility can follow to reduce employee exposure to NRL proteins include:

(1) If selecting NRL gloves for employee use, designating NRL as a choice only in those situations requiring protection from infectious agents; (2) If selecting NRL gloves, choosing those that have lower allergenic protein content. Selecting

powder-free gloves affords the additional benefit of reducing response to environmental exposure; and (3) Providing alternative suitable non-NRL gloves as choices for employee use (and as required by OSHA's bloodborne pathogens standard [29 CFR 1910.1030, paragraph (d)(3)(iii)] for employees who are allergic to NRL gloves).

Use of powder-free gloves has been shown to reduce the dissemination of NRL proteins into the environment and decrease the likelihood of reactions by both the inhalation and dermal routes. 2,14,23,51 Appropriate work practices when wearing handprotective equipment, including NRL gloves, include avoidance of contact with other body areas such as the eyes or face. Handwashing after glove removal is required by OSHA's Bloodborne Pathogens Standard [paragraph (d)(2)(v)] and helps to minimize powder and/or NRL remaining in contact with the skin. Thorough clean-up of any residual powder in the workplace using HEPA vacuums for porous surfaces and either HEPA vacuums or wet methods for nonporous surfaces will decrease employees' exposure as well.

Since the reason for wearing gloves is to provide barrier protection from hazardous substances, substitute materials must maintain an adequate barrier protection and be appropriate for the hazard. At a minimum, gloves made from NRL or other materials and used for a medical purpose should be labeled as medical gloves. Such gloves must meet the FDA criteria for marketing, manufacturing, and testing of medical gloves.

One institution has reported that a coordinated effort to identify NRL sensitized individuals and reduce the

^{*}The American Academy of Allergy, Asthma, and Immunology and the American College of Allergy, Asthma, and Immunology (ACAAI) issued a joint statement on July 21, 1997, which advises that latex glove purchase and use should consist of only low-allergen, powder-free latex gloves. The National Institute for Occupational Safety and Health (NIOSH) also recommends that if latex gloves are chosen, provide and use reduced protein, powder-free gloves.³⁷ A 1998 Guideline for infection control in health care personnel, consisting of consensus recommendations of the Hospital Infection Control Practices Advisory Committee (HICPAC) to the CDC, included several recommendations regarding latex hypersensitivity, but did not include advice about use of powder-free gloves throughout an institution and made no recommendation for institution-wide substitution of non-latex products in health care facilities to prevent sensitization to latex (Am J Infection Control 1998;26:339).

use of "high allergenic" natural rubber latex gloves substantially reduced aeroallergen levels and costs.⁴ Another study reported that some NRL allergic employees have been able to work wearing nonlatex gloves when their coworkers wore powderfree latex gloves.⁵² Several publications have reported on the benefits of a facility-wide use of only lower protein, powder-free gloves (with already sensitized employees using non-latex gloves). These benefits include a decrease in cases of occupational asthma⁵³ and other clinical latex allergy symptoms, 54 and a decrease in latex allergic response confirmed by skin-prick test. 22,55 The Department of Veterans Affairs mandated a restricted use of latex gloves by hospital employees in July of 1998, and a prevalence study done during 1999-2001 found sensitization documented by IgE response in only 36 of 1,959 hospital employees (1.8%). A teaching hospital, which converted to low-protein, powder-free gloves, reported that costs related to missed workdays and workers compensation claims were reduced. This reduction suggested an overall financial benefit from this approach.²² Another institution studied several facilities, demonstrating that regardless of size, reduced disability and costs could be obtained by replacing NRL exam gloves with gloves of alternate material.³

FDA requires labeling statements for medical devices that contain natural rubber and prohibits the use of the word "hypoallergenic" to describe such products.⁸ NRL gloves with a reduced level of chemical accelerators were once called "hypoallergenic"; however, they must now be labeled to eliminate confusion associated with the former "hypoallergenic" claim and to provide more specific information to the user. Some NRL gloves and other devices produced before the effective date of the FDA regulation (September 30, 1998) may not carry the NRL labeling or may be labeled "hypoallergenic". If such products are found in a facility, these items should not be presumed to be NRL-free; these gloves may still contain the NRL allergenic proteins to which NRL sensitized employees can react. It is important to note that these FDA regulations do not apply to non-medical

devices, including utility gloves or food handling gloves.

Recommended Employee Evaluation and Management

The procedures outlined above may not be sufficient to protect all individuals who have already developed allergic symptoms on exposure to NRL allergenic proteins. Health care facilities should develop policies and procedures for reducing the risk of allergic reactions to NRL allergenic proteins in the workplace. The American College of Allergy, Asthma, and Immunology has suggested that "safe zones" (areas in which non-NRL products are used and NRL allergenic proteins have been removed from the environment) may be needed to protect those employees who are already sensitized to NRL allergenic proteins.⁵

Prudent risk reduction strategy involves an initial survey and assessment, with a coordinated effort to identify and catalogue all NRL products used in the workplace. An ongoing program, involving close coordination with resource and materials management staff, should be established to monitor the NRL content of incoming products so that management staff can be prepared to choose appropriate products for offering non-NRL alternatives/low allergen content products to control NRL allergenic protein exposure, as well as for creating NRL safe zones. The contribution of glove powder to allergenic protein levels in the workplace environment should also be considered and use of non-powdered gloves addressed. Mechanisms should be in place for reporting, evaluating, and managing cases of employees who experience allergic symptoms related to exposure to NRL allergenic proteins.

It is not possible, at present, to determine which employees will become sensitized or symptomatic on exposure to NRL allergenic proteins. Moreover, the extent of an individual employee's reaction, or the length of time required for such allergic reactions to develop in a sensitized employee, cannot be ascertained.³ Finally, it is not possible, at present, to

predict which individuals will progress from sensitization or from local contact urticaria to more dangerous allergic reactions, nor when this progression may occur.^{2,3} Laboratory and clinical evidence indicates that an association exists between allergy to some natural rubber proteins and allergy to some proteins in certain foods and plants (e.g., avocado, banana, kiwi, chestnut)^{58,59} and some aeroallergens (e.g., pollens, grasses). 60,61 A history of multiple surgeries has also been reported to be a risk factor for NRL allergy.^{2,5} In some institutions, periodic screening questionnaires for NRL allergic symptoms in employees with current or past history of significant NRL exposure (e.g., surgical personnel) have been useful for ascertaining reaction rates and managing those individuals experiencing reactions.^{3,5} Questionnaires and diagnostic testing have been determined to provide useful information as part of exposure control in a hospital occupational health program.²² A medical evaluation of hand dermatitis by a physician experienced in dermatologic diagnoses is essential for taking preventive steps and assuring effective therapeutic measures. Evaluation of signs/symptoms consistent with allergic responses to some NRL proteins should be accomplished under the direction of a physician with expertise in NRL allergy, with additional medical testing and treatment made available if indicated.

Provision of NRL-free procedure trays and crash carts for treatment of natural rubber allergic individuals has been recommended. Although the fundamentals of emergency response (*i.e.*, assuring an open airway, breathing, and circulation) remain of primary importance should an employee develop symptoms (including those caused by allergy to some NRL proteins) requiring resuscitation, the emergency needs of NRL-allergic individuals should be anticipated in the workplace, including provision of immediate access to non-natural rubber latex containing equipment needed for successful treatment.

Information Availability

Investigation continues into various aspects of NRL sensitization and allergic response; our understanding of these issues continues to evolve.

Meanwhile, employers and employees need to be aware of the present state of knowledge regarding sensitization and allergic reaction to some NRL proteins and how to address these issues.

Employees should be advised of symptoms that are consistent with allergic reactions as well as primary and secondary preventive measures for decreasing the risk of (1) development of sensitization to NRL proteins and (2) symptomatic responses in employees who are sensitized.

NIOSH published a 1997 Alert titled *Preventing Allergic Reactions to Natural Rubber Latex in the Workplace* (NIOSH publication number 97-135). NIOSH can be reached by calling 1-800-35-NIOSH (800-356-4674), or through the Internet http://www.cdc.gov/niosh/homepage.html.

OSHA field staff and consultation personnel should be aware of the potential for sensitization and possible allergic reaction to some NRL proteins among some individuals in workplaces where NRL products such as gloves are used.

Edwin G. Foulke, Jr. Assistant Secretary Occupational Safety and Health Administration

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