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Review

Cleaning and Other Control and Validation Strategies To Prevent Allergen Cross-Contact in Food-Processing Operations

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ABSTRACT

Food allergies affect an estimated 10 to 12 million people in the United States. Some of these individuals can develop life-threatening allergic reactions when exposed to allergenic proteins. At present, the only successful method to manage food allergies is to avoid foods containing allergens. Consumers with food allergies rely on food labels to disclose the presence of allergenic ingredients. However, undeclared allergens can be inadvertently introduced into a food via cross-contact during manufacturing. Although allergen removal through cleaning of shared equipment or processing lines has been identified as one of the critical points for effective allergen control, there is little published information on the effectiveness of cleaning procedures for removing allergenic materials from processing equipment. There also is no consensus on how to validate or verify the efficacy of cleaning procedures. The objectives of this review were (i) to study the incidence and cause of allergen cross-contact, (ii) to assess the science upon which the cleaning of food contact surfaces is based, (iii) to identify best practices for cleaning allergenic foods from food contact surfaces in wet and dry manufacturing environments, and (iv) to present best practices for validating and verifying the efficacy of allergen cleaning protocols.

Food allergies affect an estimated 10 to 12 million people in the United States: about 2% of adults and up to 6% of infants and children *(38, 41).* Each year, an estimated 30,000 individuals require emergency room treatment, and 150 to 200 individuals die because of allergic reactions to food *(35).* A food allergy is an abnormal reaction of the body's immune system to a protein in a food or ingredient *(40).* Some individuals exposed to a naturally occurring protein found in certain foods (typically by ingestion) produce the allergen-specific immunoglobulin (Ig) E antibodies. On subsequent exposure to the same protein, the offending protein cross-links two IgE molecules on the surface of a mast cell or basophil, which then leads to the release of mediators that trigger allergic symptoms. The physiological outcome of the allergic response may include skin irritations, gastrointestinal symptoms, nausea, and in severe cases, anaphylactic shock or even death *(45).*

More than 160 foods can cause allergic reactions *(19).* However, eight foods are thought to account for about 90% of all food allergic reactions in the United States. These eight most common allergenic foods are milk, eggs, fish, crustacean shellfish, tree nuts (e.g., almonds, pecans, and walnuts), peanuts, wheat, and soybeans *(46, 50).*

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Because prophylactic medical treatments (or fully effective postexposure treatments) do not exist for individuals with food allergies, strict avoidance of the allergy-causing food is currently the only means of avoiding a reaction. Consumers with food allergies depend on food labels that accurately declare the presence of allergenic ingredients. The Food Allergen Labeling and Consumer Protection Act (FALCPA) of 2004 requires food labels to clearly state when the food product or an ingredient in the food product is or contains one or more of the eight major allergenic foods (referred to as ''major food allergens'' in the FALCPA). A food ingredient may be exempt from FALCPA's labeling requirement if it is derived from highly refined oils or it has been part of a petition or notification process *(46).*

At present, there is no consensus on the minimum level of an allergenic protein or food that can cause a reaction in a sensitive consumer. Trace amounts of protein from allergenic foods have caused allergic reactions in some allergic individuals *(4, 11, 41).* As little as 1 to 3 mg of peanut, milk, or egg protein has elicited allergic reactions in the most sensitive individuals *(41).* According to a literature review conducted by the Threshold Working Group of the U.S. Food and Drug Administration FDA *(49),* the lowest observed adverse effect levels for proteins from the major allergenic foods were 0.13 to 1.0 mg of egg protein, 0.25

to 10 mg of peanut protein, 0.36 to 3.6 mg of milk protein, 0.02 to 7.5 mg of tree nut protein, 88 to 522 mg of soy protein, and 1 to 100 mg of fish protein. These results suggest that various allergenic proteins differ in their potential to elicit allergic reactions and that food allergic individuals differ in their sensitivity to these allergenic proteins.

Undeclared allergens can inadvertently appear in a product through a number of avenues, such as incorrect labeling (e.g., from changes in product formulation without commensurate label changes or inadvertent use of the wrong label or package), improper handling of rework, in-process and postprocess cross-contamination, and insufficient or ineffective equipment cleaning and/or sanitation procedures. Since the early 1990s, the food industry has devoted considerable resources to developing allergen control plans with the goal of preventing the unintended presence of allergens in food *(41).* Although allergen removal through cleaning of shared equipment or processing lines has been identified as one of the critical points for effective allergen control, there is little published information on the effectiveness of cleaning procedures for removing allergenic food materials from processing equipment. There also is no consensus on how to validate or verify the efficacy of cleaning procedures. The purposes of this review were (i) to study the incidence and cause of allergen cross-contact, (ii) to assess the science upon which cleaning food contact surfaces is based, (iii) to identify best practices for cleaning allergenic foods from food contact surfaces in wet and dry manufacturing environments, and (iv) to present best practices for validating and verifying the efficacy of allergen cleaning protocols.

METHODS

The information included in this review was obtained through an extensive review of the literature obtained by accessing PubMed and Food Science and Technology Abstracts databases. Key words that were used during the database searches were ''food allergen,'' ''cleaning,'' ''validation,'' ''verification,'' ''allergen control,'' ''allergen cross-contact,'' and combinations of these key words and phrases. Information on the use of allergen control during food manufacture also was obtained from the Food Products Association–Grocery Manufacturers Association, Ecolab, Inc., and the International Dairy Foods Association. The FDA web site was accessed to obtain information about the Food Allergen Partnership, the FALCPA of 2004, the Food Good Manufacturing Practices Modernization program, and the FDA's approach for establishing thresholds for the major food allergens. This review also contains expert recommendations on cleaning and validation from the authors, who are members of the National Center for Food Safety and Technology (NCFST) Allergen Task Force.

CONTAMINATION OF FOOD PRODUCTS WITH ALLERGENS DURING FOOD MANUFACTURE

Cross-contact. Cross-contact is an on-going concern for food manufacturers and can occur at any stage during food production and storage (before final packaging). Cross-contact generally occurs through transfer of allergenic proteins during processing or handling, especially when multiple foods or ingredients are produced in the same facility or on the same processing line as are nonallergenic foods or foods containing other allergenic proteins *(11).* A variety of practices can result in cross-contact, including improper production sequencing on equipment, which carries allergenic proteins into the next product, inadequate cleaning of shared processing and/or packaging equipment between products, contamination of nonallergenic foods by airborne dust and aerosols of allergenic foods caused by static electricity and by use of compressed air to clean equipment, and the existence of crossover points on production machinery where allergenic ingredients or foods fall from one production line onto product on another production line *(8).* Cross-contact also can occur when foods are processed or cooked in water or oil previously used to process allergenic foods. Data from food recalls, retail surveys, and FDA plant inspections have been used to determine the types of foods most likely to contain undeclared allergenic foods, the conditions that result in allergen cross-contact, the methods commonly used to clean food processing lines and equipment, and the methods used to validate and verify the efficacy of a cleaning program *(43, 45–47, 51, 53).*

Food product recall data. The presence of undeclared allergenic foods has been a significant cause of product recalls *(41).* Of the more than 1,200 total food product recall actions between 1999 and 2002, 319 (about 25%) were due to the presence of one or more undeclared allergenic foods *(12).* Although incorrect labeling was the major cause (60%) of all recall actions occurring in fiscal year 1999, 18% of recall actions were attributed to equipment-related cross-contact *(47, 53).* The FDA *(51)* reviewed information gathered between 1999 and 2004 on 462 voluntary recalls involving undeclared allergenic foods and found that the most commonly recalled products were bakery, ice cream, and fishery products. Egg, milk, peanut, and tree nut ingredients were the allergenic foods most frequently associated with the recall actions.

FDA inspection findings. Between September 1999 and March 2000, the FDA in partnership with the Minnesota Department of Agriculture and the Wisconsin Department of Agriculture, Trade and Consumer Protection inspected 85 bakery product, ice cream, and candy manufacturers to study allergen labeling and control practices *(45).* The study was initiated in response to increased allergen-related recalls and concerns regarding cross-contact, resulting in undeclared allergenic residues. The study was focused on the use of peanuts and eggs in randomly selected small, medium, and large establishments. Products that were analyzed for the presence of allergenic food residues were (i) nonallergenic foods that were produced in sequence following products containing allergenic foods and (ii) nonallergenic foods produced after a change from a product containing an allergenic food where there was limited or no cleaning between the products.

Samples were collected from facilities with adverse audit findings; 73 samples were tested for undeclared peanut protein, and 45 samples were analyzed for undeclared egg protein. Five (11%) of the 45 bakery, ice cream, and candy

samples were positive (>10 ppm) for undeclared egg protein residue *(45)*. Some of the ice cream samples that tested positive for unlabeled egg were processed immediately following an egg-containing product on the same equipment, which may explain the presence of the egg protein residue. Eighteen (25%) of the 73 samples of ice cream, bakery, and candy food products were positive (>10 ppm) for undeclared peanut protein. In some candy production facilities, the equipment used to enrobe both nonpeanut and peanut-containing products was cleaned on only an annual basis, which may explain the presence of undeclared peanut residue. Inadequate cleaning of processing equipment (e.g., ice cream freezers, baking ovens, and transfer belts) may have been responsible for the presence of undeclared peanut residue in ice cream and bakery products. In general, investigators concluded that companies may introduce allergens into their products through inadequate cleaning of equipment during product changeover and from the use of inadequately cleaned utensils at various points in the production process. Only 4% of the establishments inspected utilized analytical testing to verify that cleaning and sanitation procedures were effective *(45)*.

A report *(51)* was submitted by the FDA to the Senate Committee on Health, Education, Labor and Pensions and to the House committee addressing issues relating to allergen cross-contact and advisory labeling. The report included findings from 1,470 allergen-focused inspections conducted during fiscal year 2002 and about 372 of these inspections conducted during the fiscal years 2003 and 2004. According to the report, 96% of the inspected facilities used one or more of the eight major allergenic foods as an ingredient. Based on information from FDA inspectors, an estimated 24 to 25% of facilities were likely to produce products tainted by cross-contact and thus contamination during manufacture. Allergenic protein residues on equipment were the most likely source of cross-contact contamination, followed by airborne food aerosols and particulates and buildup of food residue above the processing zone. Midsize companies (100 to 500 employees) were more likely to have airborne food aerosols and particulates as a source of cross-contact than either smaller or larger facilities. Larger facilities were somewhat more likely than midsized or small facilities to have product buildup on structural components above processing zones.

The results of the inspections provide some insight into current efforts being made to address the risks of food allergen cross-contact. The majority of food manufacturing facilities are aware of potential problems associated with improper handling and use of allergenic ingredients and foods in the food production environment. Larger facilities were more likely than smaller facilities to use practices and procedures designed to reduce the potential for cross-contact. This trend was seen across the food production spectrum from product development, materials receiving, equipment use, food processing and handling, and placement into the final package. However, all companies should continue to increase their awareness of the potential for cross-contact in food manufacturing by training all employees in the importance of allergen control and by developing a comprehensive allergen control program specific to each production facility.

Retail product surveys: Food Allergy Research and Resource Program. The Food Allergy Research and Resource Program (FARRP) sponsored two limited retail surveys of nondairy and kosher-pareve (free of milk, meat, and poultry) food products for undeclared casein residues *(18)* and of commercial ''egg-free'' pastas for egg residues *(17)*. Hefle and Lambrecht *(18)* conducted the milk allergen survey on products that should not contain milk, such as fruit juices, fruit juice bars, sorbets, dark chocolate, and kosher-pareve–labeled chocolate. Products were purchased from June 2002 through June 2003 and analyzed for casein content. These foods were selected because many dairy processors and chocolate manufacturers process nondairy products on the same processing equipment that is used for milk-containing products. Casein was not detected (<0.5 ppm) in about half of the 69 surveyed foods. When detected, the casein concentration ranged from 0.5 ppm to more than 12,000 ppm. Hefle and Lambrecht *(18)* also analyzed a variety of foods (whole wheat roll, tofu chocolate cheesecake, soy coffee drink, organic dark chocolate, dark chocolate, confectionery icing, apple-flavored energy bar, and dairy-free chocolate cupcake) suspected of causing allergic reactions in eight milk-sensitive individuals and found 5,500 to 44,500 ppm undeclared casein *(18)*.

In the egg allergen survey, 55% of the 22 samples of egg-free pastas tested positive (>1 ppm) for the presence of egg *(17)* at concentrations of 1 to >100,000 ppm.

Although the sources of dairy and egg contamination in the foods evaluated in the two FARRP surveys were not identified, improper formulation or inadequate cleaning of the manufacturing equipment may have been responsible for the contamination in some of the cases.

Retail product surveys: Swiss products. From 1979 to 2005, European labeling regulations required that allergenic ingredients be declared on food labels only when these allergens constituted more than 25% of the final food product *(23)*. However, this standard did not provide the highly sensitive consumer with the information necessary to avoid undesirable allergic reactions *(10)*. Schäppi et al. *(36)* tested a range of products purchased in the Swiss marketplace for undeclared peanut allergens and found that in certain product categories (cereals, cereal bars, cookies, and various types of snacks) a high percentage of products contained peanut protein. Of 45 selected samples, 19 contained undeclared peanut protein exceeding 5 ppm. Sources of contamination identified by the producers of the products included (i) contaminated raw materials, (ii) common transport containers for peanuts and other foods or food ingredients, (iii) lack of separate production lines and equipment for peanut-containing and peanut-free foods, (iv) processing of peanut-free products immediately after peanut-containing products, (v) uncontrolled, inadequate, or improper rework management, and (vi) insufficient cleaning *(36)*.

In November 2005, a new food labeling regulation came into effect in the European Union *(42)*. According to the new legislation, only ingredients accounting for less

TABLE 1. *Components of an allergen control plan (ACP)*[a]

Basic components of ACP	Recommendations and comments
General	1) Form an allergen control team consisting of representatives from manufacturing, quality and regulatory affairs, research and development, engineering, sanitation, and food safety sectors. 2) Conduct a risk assessment to determine the choice of the specific allergen management procedures. 3) Develop an allergen map (allergen process flow diagram) to understand where allergenic ingredients and foods are in a plant and where they are introduced into the process. 4) Develop an ACP specific for each processing facility. 5) Review the ACP regularly and update when necessary.
Segregation of allergenic foods or ingredients during storage, handling, and processing	1) Store allergenic ingredients or products separately to prevent cross-contact. a) Use clean and closed containers. b) Separate storage areas for allergenic and nonallergenic ingredients and/or products. c) Use dedicated pallets and bins. d) Use clearly designated staging areas for allergenic foods and ingredients. 2) Identify allergenic ingredients by a mark or tag (or color code) and isolate them from nonallergenic products in storage. 3) When dedicated processing lines are in close proximity, build physical barriers to separate allergenic and nonallergenic production lines. 4) For production lines with crossover points, prevent allergenic foods from falling onto nonallergenic production lines. 5) Prevent spread of aerosols during processing.
Supplier control programs for ingredients and labels	1) Require ingredient suppliers to have a documented ACP. 2) Require letters from suppliers that guarantee that purchased ingredients are free of undeclared allergens. 3) Audit suppliers on a regular basis to assess the effectiveness of the ACP. 4) Require certificates of analysis from suppliers. 5) Conduct a supplier survey that includes: a) The ACP of the supplier. b) The range of allergenic products produced by the supplier. c) The allergen cleaning program. d) Allergen training records for the supplier. 6) Ensure that allergenic ingredients are shipped in clearly marked, sealed containers and that the containers are not damaged or broken.
Prevention of cross-contact during processing	1) Scheduling of processing runs. a) Schedule long runs of products containing allergenic ingredients to minimize changeovers. b) Segregate allergenic and nonallergenic product production areas, or if this is not possible process nonallergenic foods before allergenic products. c) Schedule sanitation immediately after production of foods containing allergenic ingredients. d) When product design permits, add allergenic ingredients as late in the process as possible. 2) Use of dedicated systems. a) Dedicate processing equipment and lines, if possible, to prevent allergen cross-contact. b) Dedicate tools, containers, and utensils and color code or clearly mark them. c) Minimize reuse of processing and/or cooking media (water or oil). d) Restrict personnel working on processing lines containing allergenic ingredients from working on nonallergenic production lines. 3) Control of rework and work in progress. a) Use color-coded tags to identify and record when reworked products with allergenic ingredients are produced, where they are stored, the products to which they are reworked into, and when these products are added back into the line. b) Use rework containing unique allergenic foods and/or ingredients only in the same formulation (e.g., ''like into like'' practice) 4) Maintain equipment to ensure that the systems are operating as designed. 5) Design traffic patterns and airflow in the production facility to prevent allergen cross-contact.
Product label review; label and packaging usage and control	1) Ensure that packaged foods regulated under the Federal Food, Drug, and Cosmetic Act that are labeled on or after 1 January 2006 comply with the FALCPA food allergen labeling requirements. 2) Ensure that product specification and formulation changes are reflected immediately on labels. 3) Discard out-of-date labels or packaging in a timely manner. 4) Implement proper inventory control procedures for packaging materials. 5) Implement proper packaging staging control procedures. 6) Educate line personnel on techniques for ensuring that product labels are switched appropriately at product changeover.

TABLE 1. *Continued*

Basic components of ACP	Recommendations and comments
Validated allergen cleaning program	1) Construct processing equipment and plant structure with good sanitary features including: a) Ease of cleaning and sanitizing. b) No dead spots that allow accumulation of food. c) Accessibility of equipment for inspection. 2) Parts of the allergen cleaning program to be developed: a) Sanitation standard operating procedures. i) Protocols are clearly written and easy to follow. ii) Define the scope (range of applications, equipment, and products) of the cleaning procedures. iii) Define who is responsible for the cleaning operations. iv) Include detailed cleaning instructions. b) Cleaning validation procedures. i) Protocols are clearly written and easy to follow. ii) Define the intention and scope of validation. iii) Describe the sampling procedures. iv) Define and describe the analytical procedures to be used. v) Define the final acceptance criteria. c) Cleaning verification procedures. i) Protocols are clearly written and easy to follow. ii) Define the intention and scope of verification procedures. iii) Describe the sampling procedures. iv) Define and describe the analytical procedures to be used. v) Define the acceptance criteria. 3) Validate the analytical procedures used to validate and verify cleaning efficacy by the end user. 4) Keep records for cleaning, validation, and verification. 5) Evaluate the allergen cleaning program periodically for effectiveness.
Training	1) Provide general training on allergen awareness and control for all employees at all levels of the company. 2) Provide specific training to employees depending on their job responsibilities.

[a] Summary of published information *(2, 4, 7, 8, 11, 15, 22, 24, 30, 41, 48, 52, 55)* on food ACP. Recommendations and comments were obtained from these sources and from the NCFST Allergen Task Force members.

than 5% of the formulation in any food product are exempted from food labeling. However, ingredients derived from commonly allergenic foods must be declared on the label, even if they account for <5% of the formulation *(42).*

Reuse of cooking and/or processing media. One possible mechanism by which allergen cross-contact can occur is through the reuse of cooking media such as water or frying oil. However, little information has been reported on allergen carryover from one processed food to another through reuse of these media. In the food industry, a single batch of oil commonly is used to fry a variety of food products. For example, some nut suppliers roast peanuts and multiple varieties of tree nuts in the same roaster *(24).*

Similarly, donuts that do not contain egg may be fried in oil used to process egg-containing donuts. Several incidences of allergic reactions have been attributed to foods prepared in shared frying oil in restaurants *(60).* However, there are no reported incidences of allergic reactions caused by processed foods prepared in reused oils *(41),* which suggests that only small amounts of allergenic protein from allergenic foods are transferred into the frying oil or that the allergenic proteins may be filtered or cleaned from the shared oils before these oils are used to fry nonallergenic foods.

In a project recently completed at the NCFST, researchers determined the level of peanut allergen transferred into oil during roasting of whole peanuts and subsequently transferred to whole tree nuts (almonds, cashews, and hazelnuts) roasted in the same oil *(26).* The highest amount of peanut protein detected in the roasting oil was approximately 300 mg/kg (ppm) of oil. Hazelnuts, cashews, and almonds roasted in the used oil contained peanut protein at up to 16 mg/kg (ppm). Thus, reuse of cooking or roasting oil can result in carryover of allergenic proteins. Oil contaminated with peanut protein was filtered through a cellulose filter with or without filtering aids, significantly reducing peanut allergen levels in both the oil and the subsequently roasted tree nuts *(26).* Additional research is needed to determine the possible allergen-related safety risks associated with the reuse of cooking media.

CONTROL AT PROCESSING PLANTS TO PREVENT CROSS-CONTACT

Approaches for controlling allergens. Two fundamental approaches have been used to control allergenic

foods in processing plants: dedication-harmonization and allergen management. Dedication-harmonization refers to design and operation of manufacturing plants or lines so that all products being produced either are allergen free or contain the same allergen(s). However, insufficient product volumes and the high cost of equipment and personnel have forced most companies to produce similar food products with dissimilar allergen content in the same manufacturing facilities and on the same production lines *(8, 39)*. Therefore, these companies must manage the variety of products produced in their plants or on their manufacturing lines to assure that the dissimilar allergen ingredients do not contaminate those products where such allergens are not desired.

Numerous articles have been written regarding approaches to management of allergens in processing plants *(2, 4, 7, 8, 11, 14, 20, 22, 24, 41, 52, 55)*. Table 1 outlines key components of an allergen control plan (ACP) and recommendations for implementing each components of the ACP. The FDA's Current Good Manufacturing Practices (CGMP) Modernization Working Group for Foods *(48)* issued a white paper in 2005 indicating that allergen control should be addressed in the modernization of the CGMP. The Working Group commented that each food processing establishment that produce foods containing any of the major allergenic foods should develop and adopt an ACP. The ACP should address six elements: training of processing and supervisory personnel, segregation of allergenic foods during storage and handling, use of validated cleaning procedures for food contact equipment, prevention of cross-contact during processing, product label review including label usage and control, and supplier control programs for ingredients and labels. The Working Group also suggested that food processors develop and maintain written sanitation procedures that define the scope, sanitation objective, management responsibility, monitoring, corrective action, and record keeping associated with sanitation procedures and recommended that sanitation procedures be developed for all food contact equipment and surfaces. Safety training for workers in food processing plants that manufacture foods containing any of the eight major allergenic foods should include information on the significance of food allergens, proper control of product labeling, and the prevention of allergen cross-contact *(48)*. It is essential that training be provided for both newly hired employees and temporary and seasonal workers.

Allergen cleaning and removal. Cleaning is considered a first line of defense against allergen cross-contact on shared processing lines. The importance of cleaning in allergen control is illustrated by studies in which inadequately cleaned equipment was considered responsible for causing several individuals to experience allergic reactions from milk- or peanut-contaminated foods *(29, 31, 59)*.

From 2002 to 2004, FDA inspectors *(51)* evaluated equipment cleaning practices used by food production facilities both in terms of control measures and efficacy checks. They found that 79 to 80% of facilities used one or more control measures associated with production equipment to prevent allergen cross-contact. Large facilities were more likely than small facilities to use cleaning protocols and production scheduling for allergen control. Of the facilities that attempted to control cross-contact via equipment, 33% used dedicated equipment, and 76% used shared equipment with cleaning protocols between manufacture of the food containing allergenic ingredients and manufacture of the product without allergenic ingredients.

In 2005, Institute of Food Technologists (IFT) researchers *(43)* assessed the state of manufacturing and labeling practices used by the food industry to manage food allergens. More than 94% of surveyed small, medium, and large food companies had ACPs and more than 77% of companies included cleaning and sanitation as part of their ACP.

The most powerful tool utilized by skilled sanitation experts to remove allergens from food processing equipment in a food manufacturing environment is water. In most instances, the decision of whether to use water is a function of the water activity of the food being produced at that process point. For example, water is typically used for cleaning at process points for wet mixes but is used less frequently for cleaning at points where the food has low water activity (e.g., after baking or spray drying). Facilities that process high-water-activity foods are designed to accommodate water and have equipment that can be disassembled and electronics wired to either withstand or be protected from moisture. The floors and walls of such facilities are designed with smooth surfaces to prevent microbial growth and adsorption of allergenic ingredients and to allow for easy and effective cleaning. These facilities also have floor drains for drainage of water after wet cleaning.

Conversely, the dry goods manufacturing environment may not be designed to accommodate water and may even be designed to be free of water to facilitate the manufacture of particular products. Introducing water into equipment and environments not designed to accommodate it may promote uncontrolled microbial growth, development of harborage sites for bacterial pathogens, and premature equipment failure. The problem for the dry goods manufacturer has been uncertainty regarding the effectiveness of dry cleaning methods for removing allergenic food residues from processing equipment. Some processing equipment used in dry facilities (e.g., chocolate enrobers and baking ovens) are not designed for easy access and cleaning *(41)*. To manage allergenic foods in dry goods plants and lines, food manufacturers must rethink traditional equipment design to increase equipment accessibility and cleanability. Balancing effective pathogen control against effective allergen control also is an important consideration.

It is beyond the scope of this review to fully discuss equipment design issues with respect to allergen control. However, some generalizations can be made. Food contact surfaces in processing and packaging equipment should be nonabsorbent, noncorrosive, nonreactive with the foods to be processed and packaged, and readily cleanable. The layout of new equipment should permit easy and rapid access to the interior for cleaning and sanitation. Existing equipment should be modified to make it accessible for cleaning

and for visual inspection and validation of cleaning protocols *(15)*.

The diversity of possible cleaning protocols is a reflection of the variety of physical properties of the allergenic foods and surfaces to be cleaned. Allergenic foods and ingredients may be in the form of solids, liquids, pastes, particulates, or powders. They can be suspended in water or fats and may be present in foods at low to high concentrations. Depending on the objective of a particular processing step, the equipment surface may be stainless steel or other metal, plastic, or cloth and may be textured or pervious. The finish and smoothness of the food contact surface and the surface condition (e.g., pitted, cracked, or scratched) also can vary. Overall, the nature of the allergenic protein, the food matrix, and the type of processing equipment will dictate appropriate cleaning protocols and the efficacy of the allergen cleaning protocol.

Allergen cleaning and removal: wet cleaning. Food soils vary in composition, and no single wet-cleaning protocol is ideal for all situations. Cleaning often must address the presence of complex films containing various combinations of food components, detergent components from previous cleanings, and insoluble hard-water salts. The solubility of these films depends on factors such as composition, age, dryness, and previous exposure to heat. The nature of the soil to be removed should be understood before choosing the optimum cleaning method.

Food soils on processing equipment can be categorized into four predominant types based on their macroconstituent makeup, i.e., carbohydrates, fats, minerals, or proteins; however, these soils typically are complex, containing a mixture of several components *(9, 37)*. In general, food proteins (including allergenic proteins) are the most difficult soils to remove, especially when they have been heat denatured and have adhered to food contact surfaces. Removal of protein films requires alkali-based (i.e., sodium or potassium hydroxide) detergents *(37)*. In many cases, these cleaners also contain oxidizing agents such as sodium hypochlorite, which help to solubilize the soil. Surfactants help to remove the insoluble soils by surface wetting and then dispersal by the cleaning solution. In situations where acidic detergent cleaners are needed to remove mineral deposits, the equipment must be cleaned first with an alkali detergent because acidic cleaners can cause protein soils to adhere to surfaces and become difficult to remove *(6, 9)*.

When the food or ingredient being processed is oil based, several oil flushes may be used to prerinse the equipment before water and detergents (preferably alkali detergents) are introduced. Without the oil flushes, the water-based detergents may extract out the oil from the food material but leave behind concentrated solid protein-containing materials *(22)*.

Wet-cleaning methods can be divided into four categories: (i) clean in place (CIP), where equipment requires minimal or no disassembly and the cleaning solution can be recirculated, (ii) clean out of place (COP), where equipment can be partially disassembled and cleaned in tanks, (iii) foam or gel cleaning, where the chemical is sprayed onto the equipment as a foam or gel that increases the contact time with the soil, and (iv) manual or hand cleaning, where equipment is fully disassembled and cleaned by hand. The choice of cleaning method depends on the characteristics of the foods that are processed on the line and the type of equipment being used. Four interrelated factors that affect the efficacy of the overall cleaning process are cleaning time, temperature of cleaning solution, composition of the cleaning fluid (detergent type and concentration), and mechanical force used to apply and agitate the cleaning fluid *(9)*. When possible, modern food plants use CIP systems to clean processing equipment. CIP systems are beneficial because cleaning is fully automated and can be applied consistently once procedures are validated *(41)*. Recycling of CIP solutions, especially the alkali detergent cleaner and final rinse water, is a common practice *(56, 61)*. The number of times solutions are reused depends on the nature of the product being processed, the quality of the prerinse, the quality of the CIP system itself, and the velocity with which the solution moves through the equipment *(5)*. For example, when the majority of the soil is removed during the prerinse, reuse of detergent solutions is more likely. When the soil load is heavy, reuse of the solution is not recommended, especially when allergens are a concern. When wash solutions are reused, the concentration of the detergent must be monitored. Each time the cleaning solution is reused, some active components will be depleted, so the concentration of these components in the cleaning formula should be tested so that the solution can be brought back to the desired concentration when necessary. This monitoring step is especially important when using chlorinated alkaline detergents because the chlorine concentration will decrease in the presence of organic soils. The chemicals in a CIP system are often reused many times until protein buildup in the solution becomes excessive. At present, little is known about allergenic protein carryover during reuse of cleaning solutions or whether such carryover presents a safety issue. Research is needed to determine how reuse of cleaning solutions affects the efficacy of cleaning and whether excessive protein buildup in cleaning solutions can result in recontamination of equipment surfaces with allergenic proteins.

For effective allergen cleaning, the factors that affect the efficacy of removal of allergenic foods from food contact surfaces must be identified. NCFST researchers studied wet-cleaning protocols for removing specific allergenic foods from a variety of food contact surfaces *(25, 27, 28)*. The efficacy of different cleaning protocols for removing hot milk soils, cold milk soils, and peanut butter soils from plates made of different food contact materials (stainless steel, Teflon, polyethylene, urethane, and polycarbonate) was measured. Plates were contaminated with a known amount of either peanut butter or milk and then washed with various types of cleaning agents or solutions (water, chlorinated alkali cleaner, and acid detergent cleaner) at different temperatures (ambient temperature, 62.8°C, and 73.8°C) for 30 min.

The efficacy of the cleaning protocols differed depending on the type of soil, the food contact surface, the tem-

TABLE 2. *Most common method and tests used for equipment cleaning validation and verification in order of decreasing frequency of use by food production companies*

Method or test	% companies using the method[a]	Available formats	Analyte	Limit of detection[b]	Uses	Advantages of method	Limitations of method
Visual inspection	100% of small companies; 90% of medium companies; 93% of large companies		Food residues	Depends on many factors, including type of food residue, nature of food contact surface, availability of adequate lighting, and visual acuity of inspector	Detects the presence of food residues on food contact surfaces, floors and walls of plant area, and structural areas and fixtures above processing zones	1. Rapid 2. No need for analytical equipment or laboratory 3. Good as first step in determining effectiveness of cleaning	1. Equipment must be accessible for inspection 2. Food soils must be visible 3. Negative findings must be validated with analytical methods (such as ELISA) 4. Results can be variable depending on visual acuity of inspector
ELISA	15% of small companies; 38% of medium companies; 52% of large companies	Quantitative or qualitative	Protein(s) from allergenic foods	Quantitative ELISA: peanut, 0.1–5 mg/kg (ppm); milk, 1–5 mg/kg; egg, 2–2.5 mg/kg; soy flour, 1–2 mg/kg; almond, 0.5–2.5 mg/kg; hazelnut, 0.5–2.5 mg/kg; wheat, 1.5–5 mg/kg; crustacean shellfish, 0.05 mg/kg Qualitative ELISA (peanut, milk, egg, soy, almond, wheat): <5 mg/kg	Quantitative ELISA: quantifies the amount of an allergenic food or a protein from an allergenic food in CIP rinse solutions, in foods, and on equipment surfaces Qualitative ELISA: determines the presence of allergenic foods or proteins from allergenic foods in CIP rinse solutions, in foods, and on equipment surfaces	1. Specific because it detects the presence of the allergenic food or allergenic protein(s) 2. Sensitive 3. Rapid (<3 h depending on specific test) 4. Quantitative ELISA kits for most of the major food allergens are available	1. Analyst must be trained to obtain reliable results 2. Laboratory with analytical equipment and supplies are often needed 3. Results of test can depend on the food matrix and degree or type of processing 4. Not available for all of the major allergenic foods 5. Sanitizers and detergents can interfere with tests

TABLE 2. *Continued*

Method or test	% companies using the method[a]	Available formats	Analyte	Limit of detection[b]	Uses	Advantages of method	Limitations of method
Total protein	0% of small companies; 0% of medium companies; 14% of large companies	Quantitative or qualitative	Total protein	≥0.5 μg protein/ml	Detects the presence of proteins in CIP rinse solutions and on equipment surfaces	1. Detects the presence of protein 2. Sensitive 3. Rapid (15 min to 2 h depending on specific test) 4. Some qualitative tests can be conducted in production area rather than lab 5. May be useful when an ELISA for specific allergenic food is not available	1. Does not specifically measure the presence or amount of allergenic food or allergenic proteins 2. Quantitative protein assays sometimes require laboratory equipment 3. Chemicals can interfere with tests
ATP	38% of small companies; 43% of medium companies; 44% of large companies	Regular ATP swab (hygiene or sanitation indicator) or sensitive ATP swab	ATP from both microbial sources and food	Information not available	Indicator of lack of adequate cleaning or sanitizing of food contact surfaces	1. Very rapid (<5 min) 2. Does not require lab or lab equipment 3. May be useful when an ELISA for specific allergenic foods is not available	1. Does not specifically measure the presence of allergenic food or allergenic protein 2. Use limited for wet-cleaned surfaces
Lateral flow devices	15% of small companies; 0% of medium companies; 15% of large companies		Specific protein or mixture of proteins from allergenic foods	Peanut, 5 mg/kg	Determining the presence of allergenic food or proteins from allergenic foods in CIP rinse solutions, in foods, and on equipment surfaces	1. Very rapid (<15 min) 2. Specific because it measures the presence of proteins from allergenic foods 3. Sensitive	1. Can be subject to "hook effect" when protein levels are high 2. Results of test can depend on the food matrix and degree or type of processing 3. Not available for all of the major allergenic foods 4. Sanitizers and detergents can interfere with test

[a] Percentage of surveyed large, medium, and small companies that reported using the method or test for equipment cleaning verification, according to Taylor et al. *(43)*.
[b] Limit of detection according to the manufacturer(s) of each method or test.

perature of the cleaning solution, and the concentration of the detergent in the cleaning solution. For example, water without chlorinated alkali cleaner was not effective at removing hot milk soil from stainless steel plates. Chlorinated alkali cleaner was able to remove all hot milk residues even when the detergent solution was at ambient temperature (20 to 23°C). In contrast, water alone at 62.8 and 73.8°C was effective at removing cold milk soils. Water alone at 62.8°C but not at ambient temperature was effective at removing peanut butter soils from most of the food contact surfaces studied. Both chlorinated alkali cleaner and acid detergent cleaner at 62.8°C, but neither at ambient temperature, were able to effectively remove all peanut butter residues from the food contact surfaces. These results indicate that food processors should evaluate the efficacy of cleaning protocols for each type of food soil, food contact surface, piece of equipment, and processing line, especially when processing allergenic foods.

Allergen cleaning and removal: dry cleaning. The challenges to removing allergenic foods from processing equipment and the surrounding environment without the use of water are substantial. The cleaning methods and tools used to dry clean equipment and environments are typically limited to vacuuming, sweeping, scraping, wiping with cloths or brushes, or using compressed air. According to the IFT report of allergen control practices in the food industry, these dry cleaning practices are used by a substantial number (>50%) of companies *(43).* Although compressed air may introduce significant hygienic challenges to surrounding areas because of formation of aerosols and airborne dusts, its use often is necessary to dislodge food residue from inaccessible areas of equipment and environments. According to the IFT report, 31, 81, and 84% of small, medium, and large companies, respectively, interviewed for the survey use compressed air to clean equipment and lines that have been in contact with allergen-containing ingredients and products *(43).* At present, the prevalence of cross-contact due to this cleaning practice is unknown. Compressed air should be used with discretion and only when no other cleaning options exist *(13).*

High-efficiency particulate air filtration vacuum systems have been developed to remove and contain dust and debris during dry cleaning of food plant areas such as food contact surfaces, ovens, and floors. These filtration systems are reported to filter collected material with particle sizes down to 0.3 μm at 99.97% efficiency *(33)* and are used by 24 to 64% of surveyed food manufacturing facilities *(43).* Central vacuum systems often are used for cleaning large areas, and smaller mobile units may be used in smaller operations or to clean localized areas *(13).* However, many plants still clean large areas with smaller vacuum systems because of allergen concerns associated with central systems.

Tools, such as brushes and dry cloths, frequently are used to clean food contact surfaces *(33).* According to the IFT report *(43),* more than 62% of companies use wiping or brushing to clean lines and equipment that have been in contact with allergenic ingredients and foods. When brushes are used, care should be taken to prevent dust generation and recontamination of neighboring surfaces. Brushes and all cleaning devices used to clean allergen-containing lines should be color coded and dedicated to prevent use on nonallergen equipment or lines and should be fabricated with nonporous materials to prevent the development and spread of contamination. Floors and walls of the production area should be visibly clean.

Disposable (single-use) cloth or paper wipes saturated with water or alcohol have been used to clean food contact surfaces in areas where water is not compatible with the manufacturing environment. The advantage of these moistened wipes is that they localize water and minimize dust generation.

Nonallergenic foods or other inert dry materials (e.g., salt, flour, and starch) have been used to ''clean'' equipment in dry food manufacturing environments by purging (pushing through) the allergenic food from surfaces and equipment. An allergenic food such as wheat flour would be appropriate only when it is used to clean a line that processes wheat-containing products. Dry ice (solid CO_2) pellets, soda (sodium bicarbonate) blasters, and grit blasting also have been used for cleaning surfaces without water *(22).* The advantage of these methods is that they can be used to clean and remove most soils without damaging delicate surfaces. In most cases, the blasting techniques do not capture the soil removed from the surface, so additional steps are required to remove the soil from the manufacturing environment. The current lack of information regarding the effectiveness of dry cleaning methods for allergen removal indicates the need for more research in this area.

Validation and verification of allergen cleaning procedures. Validation of the cleaning protocol is an essential component of any effective allergen control program. Cleaning validation refers to the process of assuring that a defined cleaning procedure is able to effectively and reproducibly remove the allergenic food from the specific food processing line or equipment *(21).* Protocols to validate allergen cleaning efficacy provide the food manufacturer with feedback as to the effectiveness of the cleaning protocol and, very importantly, pinpoint areas of insufficient cleaning. Cleaning programs should be developed and validated before commercial manufacture of a product begins and any time changes are made to the manufacturing or cleaning process, such as reformulation of the food and modification of the process or equipment, scheduling times or sequences, or cleaning protocols; any of these changes can impact cleaning efficacy. Validation procedures may involve visual inspection of equipment surfaces, analysis of finished product and in-process materials, final rinse water, and diagnostic swab samples or a combination of these items. Confidence in the efficacy of the allergen cleaning protocol is increased when validation studies are performed several times each year.

Cleaning verification refers to the process of demonstrating that validated cleaning protocols have been properly performed once the commercial manufacture of a product begins. Methods used for cleaning verification (e.g., vi-

sual inspection and analysis of food contact surfaces, rinse water, or finished products) may be similar to those used for validation. However, critical cleaning parameters such as time, temperature, and cleaning solution concentration also must be monitored. At a minimum, equipment should be evaluated for cleanliness immediately after cleaning and before use, particularly when equipment is not used immediately after cleaning and there is a possibility of recontamination.

According to the IFT survey, more than 85% of interviewed companies validated their cleaning programs, and more than 71% conducted analytical testing to verify that the programs were effective *(43).* These figures are consistent with those in the FDA report *(51),* in which 83% of all facilities checked the effectiveness of their cleaning procedures. According to the IFT report *(43),* visual inspection was the most common verification method, followed by enzyme-linked immunosorbent assay (ELISA) and bioluminescence-ATP testing of samples regardless of the size of the manufacturing company or the food product category. Use of nonspecific protein detection and allergen-specific lateral flow devices for processing samples was limited *(43).* The FDA report *(51)* indicated that the most common methods used for cleaning verification were visual examination of the food contact surfaces (95% of facilities), chemical assays for allergens (5%), and other tests (6%). The most common methods for evaluating cleaning procedures for efficacy are described in Table 2.

Validation and verification of cleaning should start with a visual inspection of equipment (preferably in a dry state) to ensure that the surfaces are visibly clean. All portions of the equipment should be inspected to determine whether there is buildup of residual materials, especially in corners, on O-rings, and in other difficult-to-clean areas. Conveyor belts should be inspected for tears, scratches, or defects that may harbor food residue. The structural area and fixtures above the processing line also should be inspected to determine whether there is material buildup above the processing zones that could fall into the product *(52).* Floors and walls of the plant also should be visibly clean.

Although visual inspection is a valuable first step in establishing the effectiveness of a cleaning procedure, the technique has some major limitations for allergen control. There is little published evidence that the absence of visible residue corresponds to an allergen-free surface. However, it is generally assumed that presence of visible residues increases the likelihood that allergenic proteins are present. Visual remnants of allergenic food indicate failure of the allergen cleaning protocol and that additional cleaning is needed.

Visual inspection can be done only on equipment where food contact surfaces and areas of potential food product or ingredient accumulation are accessible for inspection and of sufficient visual contrast to the food being processed to enable observation of food residue. For example, it may be fairly easy to detect the presence of milk soils on stainless steel or darkly colored plastic or rubber surfaces but difficult to detect such soils on white plastic surfaces. The quality of the lighting also plays a vital role in visual detection of food soils. Visual inspection may be the only feasible verification tool in some situations because commercial detection tests may not be available for some allergens. Even in cases where equipment surfaces appear to be visibly clean, analytical methods must be used to verify the absence of allergenic food residues.

Analysis of the final rinse water, the samples of the first product from the manufacturing line, and intermediate (in-process) materials secured from points throughout the process immediately upon process startup can be used to validate and verify allergen cleaning efficacy. Swab samples often can be secured from equipment after allergen cleaning to provide an indication of the adequacy of the allergen cleaning protocol at that process point. The sampling plan should include swabbing equipment areas where significant buildup of food is known or expected to occur and areas that are particularly difficult to clean, such as seams, valves, O-ring seals, sampling ports, and porous and irregularly shaped surfaces. Care also should be taken to sample equipment that heats products during manufacture, because burned-on allergenic foods can be difficult to clean *(3).*

Swab sampling may be useful for determining the levels of allergenic food residues on equipment. However, there is no standardized method for obtaining swab samples. The swabbing process comprises several manual steps that are inherently subjective and vary from operator to operator. A standardized swabbing method is necessary for repeatable results regardless of who performs the swabbing. Factors that should be considered include the type of swab, the number of swabs per unit area, the amount of solvent (buffer or water) on each swab, the technique used to swab the area, the surface area sampled, and the procedures used to extract the analyte from the swab *(57).*

Verification of cleanliness often is performed using analytical methods. Immunoassays such as the ELISA have played a major role in validating allergen cleaning procedures. These assays, which can be purchased from a variety of manufacturers, are able to detect most (egg, milk, peanut, soy, some tree nuts, shrimp, wheat) of the eight major allergenic foods. Quantitative ELISAs, which are used to measure allergen concentrations in finished foods or in-process materials, typically have detection limits of 1 to 3 ppm *(41).* In general, the presence of allergenic food in the finished product or in-process materials indicates a failure in the design or execution of the allergen cleaning protocol. Qualitative ELISAs are used to detect the presence of allergens on swabbed equipment surfaces or in rinse water. Although the presence of an allergenic food in swab samples or rinse water indicates that the allergen cleaning protocol or its execution requires revision, it does not necessarily indicate the presence of the allergenic protein in the finished product. The transfer of allergenic protein from equipment surfaces to foods is a complex process that depends on many factors, including the adhesion properties of the protein to the surface, the abrasiveness of the subsequently processed food, the composition of the food contact surface, the temperature of processing, the concentration of the allergenic protein, and the properties of the al-

lergenic protein (e.g., physical form and solubility in the subsequent food being processed).

Although ELISAs generally are considered accurate, reliable, and rapid methods for detecting the presence of allergenic foods on equipment and in finished products, they have drawbacks. Because detection by ELISA is achieved through binding of target protein(s) and antibodies, any changes in the binding properties (immunoreactivity) of the target proteins will influence assay results. Thermal processing, hydrolysis, and exposure to oxidizing chemicals (hypochlorite) can affect the solubility and immunoreactivity of proteins *(5, 14, 44, 54).* Consequently, the ELISA may not detect residues of allergenic foods on equipment surfaces or in finished foods that have received thermal or hydrolysis treatment or on equipment that has been exposed to cleaning or sanitizing agents. The composition of the food matrix (oil versus water-based) also may affect extraction efficacy and consequently ELISA detection of the target proteins. There is a need to define appropriate sampling protocols, validate ELISA methodologies, and develop and identify reference materials for the major allergenic foods *(58).* Work is underway at the NCFST to characterize changes in the structure of allergenic proteins due to thermal processing and chemical treatments and to correlate these changes with changes in the detection of these proteins by ELISAs.

ELISA kit manufacturers have developed lateral flow formats (dipsticks) for several of their ELISA kits. Such tests are inexpensive and rapid (analysis time of $\leq$5 min) and can be used on site (in the plant) rather than just in the laboratory *(58).* However, on-site tests must be conducted by appropriately trained plant personnel.

Other methods also are being used by the food industry to validate and verify the effectiveness of cleaning programs. Some of these tests are based on detection of ATP or total protein and are faster and less expensive than ELISA methods but do not directly measure the presence of a particular allergenic food or protein. The ATP tests detect both microbial ATP and that associated with residual foods and, therefore, can be used only to verify the effectiveness of wet-cleaning procedures. Researchers at the NCFST and FARRP working with milk in solution that had been dried onto a stainless steel surface found that conventional ATP tests may lack the sensitivity of ELISA systems *(34).* However, a sensitive ATP test had sensitivity similar to that of an ELISA for milk in solution and in the form of a dried residue on stainless steel plates *(34).* In contrast, ELISAs were more sensitive for detecting egg in solutions than was the sensitive ATP test *(1).* However, when egg was dried on stainless steel surfaces, the sensitive ATP and ELISA had similar sensitivities *(1).* These studies indicate that sensitive ATP tests may be useful for validating wet-cleaning procedures. Research is underway at the NCFST to determine the conditions under which sensitive ATP and total protein tests can be used to verify cleaning protocols. Site-specific validation is needed before these methods can be used with confidence.

An ideal method for validating cleaning procedures would be rapid, automated, and performed in situ. Pharmaceutical manufacturers, who must be able to confirm that equipment is cleaned before it is used, are studying the use of spectroscopic methods for in situ cleaning validation. Recent work on mid-infrared spectroscopy has resulted in the development of a fiber optic–based spectrometer capable of direct spectroscopic surface analysis using a grazing-angle reflectance sampling head *(16, 32, 44).* Reported assessments of the device *(16)* have indicated low detection limits for surface contamination (0.05 $\mu g/cm^2$ for some active pharmaceutical ingredients). Kocaoglu-Vurma et al. *(30)* found that mid-infrared spectroscopy could be used to detect the presence of whole milk soils on different stainless steel surfaces. Further research is needed to determine whether this technique could be used to validate cleaning in a food manufacturing setting.

Development of an allergen cleaning program. Once the steps of the cleaning process and the validation and verification procedures are identified and optimized, the entire process should be fully documented and incorporated into an allergen cleaning program *(3).* This program consists of three parts: sanitation standard operating procedures (SSOPs), validation procedures, and verification procedures. The SSOPs should be as detailed as possible and should include (i) a description of the range of application for the procedures, equipment, and products, (ii) identification of who is responsible for performing the cleaning operations, and (iii) a detailed description of the cleaning procedure(s). The validation and verification procedures should (i) define the intention and scope of cleaning validation and verification, (ii) provide a detailed description of the sampling techniques and requirements and the specific analytical procedures to be used, and (iii) define the final acceptance criteria for cleaning validation and verification. Accurate written records should be maintained for cleaning, validation, and verification. The cleaning program should be reviewed periodically to ensure its effectiveness.

RESEARCH NEEDS

Considerable progress has been made in the past decade by the food industry in controlling allergens in food processing facilities. Despite this progress, undeclared (unlabeled) allergens still can inadvertently appear in food products due to cross-contact during manufacture and inadequate cleaning of shared processing and/or packaging equipment. In general, there is no agreement on which cleaning procedures are most effective for removing allergens from processing equipment or on how to validate the efficacy of cleaning procedures. Specifically, research is needed to identify cleaning protocols (wet and dry) that remove different allergen-containing soils (e.g., milk, egg, soy, and peanut) from a variety of food contact surfaces (e.g., stainless steel, plastics, cloth, and rubber). More information also is needed about the efficacy of CIP solution reuse and whether the reuse of processing and/or cooking media such as oils and water results in contamination of subsequently processed food products. Other areas where research is needed are characterization of the effects of thermal processing and cleaning agents on ELISA detection of

allergenic residues in foods and on food contact surfaces, definition of appropriate sampling protocols, validation of ELISA methods, and development of reference materials for the major allergenic foods. Comparisons of immunochemical allergen-specific methods and nonspecific methods (e.g., ATP and total protein) for determining cleaning efficacy also are needed.

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