

# Creation, History, and Future of the Contact Allergen Replacement Database (CARD)

James A. Yiannias, Ryan Miller, and Joseph M. Kist

THE CONTACT ALLERGEN REPLACEMENT DATABASE TEAM (Fig 1) is delighted to provide the American Contact Dermatitis Society with this review of the origin and future direction of the Contact Allergen Replacement Database (CARD) in celebration of the Society's twentieth anniversary. The following first-person narrative is that of the voice of the lead author (J.A.Y.).

## Personal History of CARD

My father itched for much of his life because he was atopic and because he had patch-test–confirmed contact dermatitis from lanolin alcohol. When I traveled from Arizona to Texas to visit my parents in the mid-1990s, my father expressed his frustration with his ongoing itch and rough red rash. I had recently graduated from my dermatology residency and felt reasonably comfortable with managing eczema, so I quizzed my father on which and how many skin care products he was using and on the frequency of their use. He was a well-educated man, so he made quite an effort to be attentive to allergen avoidance. By history, my father earned an “A plus” for his dermatologic routine. I empathized with his struggles and gently encouraged him to see his local dermatologist. After making a few playful remarks about their having “paid for a doctor,” my parents acknowledged that I probably was not the best physician to treat my father.

Later, when I went to use the bathroom, I engaged in a deeply entrenched but probably discourteous habit: I started reading the labels of all the skin care products on the counter, as I do in virtually any friend's or relative's bathroom. (I strongly encourage all our residents to do the

same.) Admittedly, I was looking to see if my father had slipped up despite his impressive declarations regarding allergen avoidance. I got revved up when I read the ingredients of his generic triamcinolone. It contained lanolin!

I scolded my father for not being more attentive in reading his skin care product labels. My father's manner was usually gentle, but he delivered a fiery charge on this occasion. “Dear God, man! Can't you just create a computer program to tell me what I *can* use, instead of coming home and scolding me for making the wrong choices? Take pity on us as patients because we need the help!”

Frankly, this seemed a sensible request, so I went back to Arizona and conveniently forgot my father's request for a few years. Over time, as I cared for my contact allergy patients, I realized that, despite my delivering what I thought was very good allergen avoidance education, they often continued to struggle. Most were familiar with their allergens but were overwhelmed by the task of avoiding those allergens in their skin care products. I often saw confusion on my patients' faces as I reviewed their need to avoid complexly named allergens such as methylchloroisothiazolinone or dimethylol dimethyl (DMDM) hydantoin. I sensed even greater concern from patients on the occasions when I also told them to avoid an allergen's cross-reactors. A favorite example is when an elderly patient from northern Arizona declared “you must surely be joking” after I told her to read product labels to avoid not only quaternium-15 and DMDM hydantoin but all formaldehyde releasers.

## Early Days of CARD 1.0 Design

By 1998, having cared for many contact allergy patients who were frustrated by the difficulty of avoiding skin care product allergens, and after reflecting on my father's suggestion to create a program that could help such patients, I began to search for software that could help patients. I was sure I could find a preexisting program that would let me enter a list of products and ingredients into a

*From Mayo Clinic College of Medicine, Rochester, MN; Mayo Clinic in Arizona, Scottsdale, AZ; and the University of Pennsylvania School of Medicine, Philadelphia, PA.*

*Reprints not available.*

DOI 10.2310/6620.2009.00010

© 2009 American Contact Dermatitis Society. All Rights Reserved.

DECKER<sub>X</sub>





**Figure 1.** The CARD team for 2009. From left to right: Ryan Miller; Janis Johnson, RN; James A. Yiannias, MD; Jenny Kevric, LPN; and Shelly Orona. Reprinted with permission.

database and that would then produce a list of products that were free of a given ingredient. Although a variety of database programs existed, I was unable to find one that was suitable “as is,” so I enrolled in a Microsoft Access database class and asked if I could learn by doing a project.

During several months in early 1998, I learned the basics of using Access 97 software (Microsoft Corporation, Redmond, WA) and built a rudimentary program for creating a “shopping list” without specified ingredients. For example, if I entered “quaternium-15,” the database would create a list of products that did not contain quaternium-15. However, the program acknowledged neither cross-reactors nor synonyms. This meant that a user who entered “quaternium-15” in the database would receive a flawed shopping list. Specifically, the list would be free of products that contained “quaternium-15” but would still include products that listed the ingredient as “quat-15” or “quaternium 15.” My father would certainly have still itched if he had been given a shopping list from this version of the database.

Indeed, the greatest challenge in CARD’s design was making the database recognize cross-reactions and synonyms. Programmatically, it was not feasible to have CARD recognize a cross-reaction versus a co-reaction versus a synonym. Thus, to identify and include all ingredients that would cause a patient to react, the term “allergen functional category” (AFC) was coined. An AFC includes all potential allergenic relationships (cross-reactions, co-reactions, and synonyms). Given my novice status as an Access user, CARD 1.0 was able to assign only one AFC to a given allergen (Table 1). Another limitation of CARD 1.0

**Table 1.** Sample Allergen Functional Categories in CARD Version 1.0

| <i>Skin Care Product Ingredient or Patch-Test Allergen</i> | <i>Allergen Functional Category</i> |
|------------------------------------------------------------|-------------------------------------|
| Fragrance                                                  | Fragrance/fragrance                 |
| Balsam of Peru                                             | Fragrance/fragrance                 |
| Orange oil                                                 | Fragrance/fragrance                 |
| <i>Aloe vera</i> leaf extract                              | Fragrance/fragrance                 |
| Quaternium-15                                              | Formaldehyde                        |
| Imidazolidinylurea                                         | Formaldehyde                        |
| Dimethylol dimethyl hydantoin                              | Formaldehyde                        |

was its inability to allow the end-user clinician to customize cross-reactions.

CARD’s design was based on the principle that skin care products would be entered along with all of their ingredients. I wanted to ensure that, if ingredient X was an unrecognized allergen in 1998 but was recognized to cause allergy in 2009, CARD could appropriately guide the patient. Also, CARD was programmed to not limit the number of allergens that could be entered. With these fundamentals in place, CARD 1.0 was put into clinical use at Mayo Clinic in the fall of 1998.

## Product Selection

Once the database was designed, I turned to the selection of products. Because CARD’s primary purpose was to guide patients away from their known allergens, I started with skin care products that were mostly free of common allergy-causing preservatives and fragrances. As CARD grew, a wider variety of skin care products (primarily from nationally prominent companies) was incorporated. Our development team also insisted (and continue to insist) that product information come directly from the manufacturer and not through other sources such as pharmacy or government Web sites. This minimizes data transfer errors or omissions and ensures that product formulas are up to date.

A recurrent obstacle on the path to a database with complete product ingredient lists was the reluctance or inability of some skin care product manufacturers to provide us with product information en masse. Thus, CARD’s product list was fairly limited in the early 2000s. As CARD has become better recognized, more companies have been willing to provide product information. Many companies now place product information on their Web sites, allowing broader product inclusion.

At times, clinicians and patients complain that CARD provides a limited number of products. CARD currently lists more than 3,000 active products. One of the most

common scenarios in which CARD recommends a limited number of products involves patients who have allergies to para-phenylenediamine (PPD) or glyceryl thioglycolate (GTG). There are alternatives to PPD and GTG; however, CARD excludes the alternatives by default because these alternatives may cross-react. The clinician can override this default by accessing CARD's "customize cross-reactors" page. Thus, the clinician must choose which specific alternative ingredients may be used by the patient. Examples of products that are not commonly found or easily obtained are hair colorants or permanents that are free of fragrance. The CARD team encourages to provide us with the names and ingredients of these challenging products if the information is obtained directly from the manufacturers.

Patients also express concerns with CARD's listing products that are discontinued. CARD purposely includes products with formulas that are up to 1 year old so that patients will know that they may continue to use products they have already purchased.

### Data Entry

When I first designed the *Access* database for CARD, I entered the products myself, and a list of about 300 products was manageable. Data entry for the original version of CARD was done one ingredient at a time; in version 2.0, all the ingredients of a given product can be entered in one step.

To help ensure patients receive information about currently available products, products whose formulas have not been updated for 1 year are inactivated. The CARD administrative team searches manufacturers' Web sites in a "rolling" fashion so that information about each company's product line is updated annually. If the product information is not available online, the team contacts the manufacturer in writing and by telephone to obtain the information.

### Efficacy Assessment

After a few months of using CARD with a small number of products, my colleagues and I set out to determine whether or not it was truly a beneficial tool. A study assessing the efficacy of CARD showed no statistically significant difference in the control of dermatitis in patients who received traditional avoidance therapy (education from the clinician plus allergen avoidance handouts) versus patients who received CARD-facilitated education (education from the clinician, allergen avoidance handouts, plus a CARD shopping list).<sup>1</sup> However, we

were able to enroll only a small number of patients because the CARD shopping list had already become the standard of care at Mayo Clinic. After patients had read the study's informed-consent terms, many declined because participation delayed their obtaining a CARD printout. Of the patients who received the CARD shopping list, 91% reported CARD to be either somewhat helpful or very helpful in managing contact dermatitis. All the patients who did not receive the database printout said that it would have been helpful.

Joseph M. Kist worked with me to study the efficacy of this database. I remember fondly that, early in our collaboration, Dr. Kist looked me squarely in the eye and declared that the original name of the database, the Contact Allergen Avoidance Program (CAAP), just "had to go." He coined the name represented by the acronym CARD. (It's hard to deny that Dr. Kist has a penchant for words.)

The efficacy research study was accompanied by Mayo Clinic funding to allow expanded administrative support; the number of products in CARD thus increased to about 1,000 during the study.

The presentation of the CARD utility study findings at the March 2001 Annual Meeting of the American Contact Dermatitis Society (ACDS) spurred significant interest among the Society's members and leadership. Mayo Clinic proposed a collaboration with the ACDS to provide the Society's members access to CARD. With mentoring from former ACDS president James Marks and the support and guidance of ACDS administrator Cindy Froehlich, the Cosmetic, Toiletry and Fragrance Association (CTFA) agreed to financially support the ACDS so that it could make CARD available to ACDS members. These funds support the time necessary for acquisition of product ingredients, data entry, as well as assignment of all cross-reaction relationships. Now known as the Personal Care Products Council, it continues to provide support to the ACDS to allow CARD's ongoing product updates.

In 2006, the American Academy of Dermatology recognized CARD's value with the awarding of its Gold Triangle Award, given for CARD's excellence in design and content.

### Evolution of CARD and Technical History of Versions 1.1 and 2.0

The migration of CARD from a Microsoft *Access* database to the Web application it is today was the result of a dynamic collaboration of clinical and technical efforts. When the project was assigned in 2002 to Dave Lowicki of Mayo Clinic's department of software engineering, he used Microsoft's Active Server Pages (ASP) technology

(Microsoft Corporation) to develop the first Web user interface (UI) that was available to dermatologists. Because Microsoft Access is not designed for Internet use by multiple users, all of the original data in CARD needed to be ported to a new server (Microsoft's SQL Server [pronounced 'sequel server']) that would allow simultaneous use by a large number of clinicians.

Enabling clinicians to access CARD via the Internet was a big step in CARD's technical evolution, but the data entry and quality assurance processes were cumbersome, to say the least. Also, clinician users of CARD still could not alter its handling of cross-reactions.

In 2005, CARD was handed from Dave Lowicki to Ryan Miller, with the main goals of eliminating CARD's dependence on Access and providing a richer and more robust administrative UI. Additional goals were to allow clinicians to alter cross-reactor handling and to allow a given ingredient to belong to more than one AFC. For example, should a patient who is sensitive to fragrance mix be advised to use a product containing aloe? In the first iteration of CARD, the program would have excluded aloe from the shopping lists of patients who were allergic to fragrance mix (see Table 1). However, in the revised versions of CARD, aloe was reclassified to reflect the fact that aloe *may* elicit allergy in patients who are sensitive to fragrance mix. Specifically, aloe is now assigned to the "mandatory" AFC as a botanical but to the "optional" AFC as a fragrance (Table 2). Similarly, clinicians may specify whether a patient should avoid all formaldehyde releasers or only those to which the patient is patch test proven to be positive (see Table 2).

By 2005, significant advancement in the Web programming industry allowed us to transfer all of CARD's functions to the Web. The challenge was that, in order to leverage the new technology, the existing application would need a fundamental rewriting. After hundreds of hours of discussion with Ryan Miller, primarily focused on

CARD programming logic, we were able to craft a new release in late 2006. This new version was written in ASP.NET 2.0 and used a SQL Server entirely as its data source. In other words, CARD was now fully a Web-based tool.

Since becoming fully Web based, both the user and the administrative interfaces of CARD have had incremental upgrades, such as the use of ASP.NET AJAX for dynamic controls, Web services, a "PDF generator" that allows users to save their shopping lists as PDF files, and the implementation of a Unique Patient Allergen Code (UPAC). Another big advantage of ASP.NET 2.0 is that the application can make use of newer versions of the .NET framework (eg, version 3.5 and beyond).

### Future of CARD

We are currently exploring an additional UI for patients. The functionality of CARD for patients would be restricted to the generation of an up-to-date shopping list for each patient. Programming that allows the clinician's cross-reaction preferences to be saved has been cost prohibitive; thus, if patient access were granted, the shopping lists would be based on CARD's default (safest) cross-reactions.

CARD's programming logic is applicable to more than skin care products. CARD could readily include other products, such as gloves or shoes. However, because of time resource restrictions and the limited availability of full ingredient listings for these products, such other products have not been added to CARD to date.

CARD could also be used in any country. The UI language could simply be changed to a given country's preferred language, and products available in that region could be entered.

The ACDS is exploring methods of sustaining CARD for years to come. Monthly Web conferences are held to teach physicians how to properly categorize skin care

**Table 2.** Sample Allergen Functional Categories in CARD Version 2.0

| Skin Care Product Ingredient or Patch-Test Allergen | Allergen Functional Category  |                  |
|-----------------------------------------------------|-------------------------------|------------------|
|                                                     | Mandatory                     | Optional         |
| Fragrance                                           | Fragrance/flavor              | Botanical        |
| Balsam of Peru                                      | Fragrance/flavor              | Botanical        |
| Orange oil                                          | Fragrance/flavor              | Botanical        |
| <i>Aloe vera</i> leaf extract                       | Botanical                     | Fragrance/flavor |
| Quaternium-15                                       | Quaternium-15                 | Formaldehyde     |
| Imidazolidinylurea                                  | Imidazolidinylurea            | Formaldehyde     |
| Dimethylol dimethyl hydantoin                       | Dimethylol dimethyl hydantoin | Formaldehyde     |

product function (eg, moisturizer versus sunscreen) and how to assign cross-reactions. Our hope is that several physicians will become CARD administrative “super-users.” To decrease the time needed to maintain CARD, we are exploring narrowing the number of products in CARD to about 1,000 core products that address the most typical skin care product allergies.

We continue to welcome manufacturer contact information (submitted to CARD@mayo.edu), especially so that we can expand choices for patients who are sensitive to allergens that are difficult to avoid (eg, patients allergic to fragrance *and* PPD or glyceryl thioglycolate). We are developing manufacturer direct entry of product information. Before becoming available on a patient’s shopping list, all of a manufacturer’s direct entries will be verified by the CARD administrative staff.

Having worked on CARD for more than a decade, I wonder how long it will be clinically relevant. In our lifetimes, will it be possible to program a person’s Langerhans’ cells and lymphocytes to not cause contact

dermatitis when the person is exposed to an allergen? If so, I suspect that clinicians and patients may look back fondly at “the old days,” when allergens actually needed to be avoided. Until then, CARD can help our patients successfully avoid their known allergens. As ACDS administrator Cindy Froehlich says, “With CARD, we have a winning hand.”

### Acknowledgments

We gratefully acknowledge that CARD’s success is due largely to the unwavering support the American Contact Dermatitis Society and the Personal Care Products Council have provided our team.

### Reference

1. Kist JM, el-Azhary RA, Hentz JG, Yiannias JA. The contact allergen replacement database and treatment of allergic contact dermatitis. *Arch Dermatol* 2004;140:1448–50.