

Is Allergy to Industrial Enzymes Used in Household Detergent Products Stable in The General Population?

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Abstract

It has long been recognized that industrial enzymes used in household detergent products can cause respiratory allergy, and therefore that occupational exposure must be carefully controlled. This is achieved by the extensive application of measures to control the airborne concentration, including encapsulation in inert casings, as well as the requirement for employees to wear personal protective equipment. In contrast, although their use in consumer products should always be subject to rigorous safety assessment, consumer exposure cannot be similarly controlled. Over a decade ago, data suggested consumer use did not lead to allergy (an asymptomatic frequency of 0.23% skin prick test positives was found). Since then, consumer use has increased and it is timely to revisit this matter. Given the difficulties of a general population survey, we interrogated data generated when employees begin work in detergent or enzyme manufacturing industries. Starters are assessed to provide baseline information on whether they already have enzyme-specific IgE. This medical screening showed that of 8289 new employees (6317 male / 1972 female), 18 individuals (16 male / 2 female) had positive tests for IgE to either protease (14 cases) and/or amylase (10 cases). This frequency of positive individuals, at 0.22%, is lower, but not significantly different ($p < 0.01$). Although this population is neither the same as that tested previously, nor a perfect surrogate for the general consumer population, it is concluded it demonstrates that current consumer use of laundry/cleaning products containing enzymes is generally safe and not a cause of respiratory allergy.

Keywords: IgE allergy; Enzymes; Detergents, Occupational allergy; Industrial hygiene; Occupational hygiene; Risk assessment, Consumer products

Introduction

A substantial spectrum of consumer cleaning products, including laundry detergents, contain a variety of enzymes (often proteases and amylases), not least because those enzymes are readily available and provide economically viable biodegradable cleaning functionality. Increasingly, they have been adopted also because they deliver product functionality such as lower wash temperatures, meaning substantially less energy is required

(<https://www.aise.eu/priorities/safe-sustainable-use/low-temperature-washing/>). These enzymes can be derived from bacteria, plants and/or fungi, and have a generally very safe toxicology profile [1], but notably they do have the ability to cause respiratory allergy given sufficient degree of exposure [1-6]. Consequently, it is necessary to limit inhalation exposure so that this risk to human health is properly managed. In the occupational setting, this can be achieved by manufacturers adhering to

the guidance regarding best practice promulgated by trade associations [7-12]. Evidence has already been presented that these guidelines (including engineering controls, air monitoring, safety training and regular health surveillance), which are recommended by and freely available from the detergent industry, when properly adhered to can ensure worker safety [13-15].

The occupational situation mentioned above is very different from the consumer use of enzyme-containing products. Accordingly, any company placing on the consumer market a product which contains enzymes has to consider the possibility that the intrinsic respiratory allergenic hazard of any enzyme content might translate into an adverse effect for consumers. This is achieved by carrying out a thorough risk assessment to ensure consumer safety and for which essential guidance is freely available [16-18]. This assessment has to include both intended and reasonably foreseeable misuse; product abuse is excluded. However, a key difference from the occupational setting is that consumers cannot be monitored regularly for adverse health effects in the way that is possible for a workforce (reviewed in [7,1]). Where chemicals (i.e. not proteins such as enzymes) in a consumer product give rise to allergic responses in the skin (contact allergy), dermatologists have ready access to a clinical process and a diagnostic tool, the patch test, that combined are central to identifying the clinically relevant culprit agent (reviewed in [19]). This contrasts somewhat with respiratory allergy, where establishing a cause effect relationship is harder, since provoking pulmonary responses diagnostically is almost always a complex matter, not least for obvious ethical reasons [20]. Furthermore, the clinical suspicion of such disease being caused by enzymes in consumers rarely arises even to the extent of leading to initial diagnostic procedures, such as skin prick testing. The consequence is that individual (and particularly non-occupational) patient data in the clinical literature is very scarce compared to the situation that is seen with contact allergy to chemicals.

The practical effect is that whereas the risk assessment for the skin sensitizing chemicals that cause contact allergy in consumers has the benefit of clinical feedback (e.g. [21,22]), that situation is vanishingly rare for consumer respiratory allergy. Thus, for non-occupational respiratory allergy, particularly for proteins, including enzymes, one key source of evidence that safety assessment has been carried out adequately derives from a focused assessment of target groups of consumers (e.g. [23]). The second is the absence of clinical case reports and a third a consideration of the frequency of sensitization to enzymes that can be found in the general population (e.g. [24]). In the present work, we have endeavored to supplement the currently available evidence base in this third category and discuss those results in the context of the previously published datasets. In addition, it is also appropriate to ask whether the frequency that is now found has changed in the light of increasing use of enzymes in various industries and of enzyme-containing products by consumers (www.fortunebusinessinsights.com/industry-reports/enzymes-

[market-100595](http://www.fortunebusinessinsights.com/industry-reports/enzymes-market-100595)).

Methodological Approach

Five companies involved in the manufacture of enzymes on an industrial scale, or of consumer cleaning products which use those industrial enzymes agreed to participate. For each company involved in the preparation of this present publication, all new employees are always required to participate in a pre-placement health screening. Specific details may vary between the companies, but that screening process always includes a health questionnaire, including a focus on any history of respiratory allergies, a lung function test and an assessment for specific enzyme allergies either by a skin prick test or evaluation of serum IgE [7-14]. For this last-mentioned aspect, each company agreed to provide the results of the screening for pre-existing IgE-mediated sensitization to either a protease and/or an amylase, which would be the most abundantly used enzymes in consumer cleaning products. Data were harvested for new employees over the time period 2010-2020, and the data grouped by gender and age. The starting date of 2010 was chosen to avoid any overlap with a previous publication [23].

Results

For the five companies that participated, over the 10 year time period, a total of 8289 new employees were assessed. Table 1 presents the breakdown of this data. For legal reasons, as well as those of important medical confidentiality, it is not possible to give a greater level of detail, particularly including any personal individual information.

Table 1 presents the broad age groups of the employees screened, their gender split and the numbers found to be positive to either a protease and/or an amylase. In total, there were 24 positive reactions, but these occurred in only 18 individuals, with 6 proving to be positive to both enzyme categories. The frequency of positive reactions to either of the enzyme categories was fairly similar - for protease it was 0.17% and for amylase it was 0.12%. Although only males were protease positive pre-employment, the gender balance for amylase broadly reflected the overall balance of the test population. However, these numbers were regarded as too small to permit any meaningful statistical analysis.

As mentioned above, unfortunately it was not possible to interrogate in detail why at the start of a new employment, occasionally individuals deliver a positive IgE response to enzymes. However, one potential explanation could be that the new employee in question was transferring their existing skills from another enzyme manufacturer/user and who therefore had a previous history of occupational exposure. In addition, it was noted also that the positive findings occurred often in individuals that had a history of allergies to a range of common protein allergens, and/or who had been treated to alleviate allergy symptoms since childhood (but which cannot be detailed further here for medicolegal/confidentiality reasons). That having been

said, the primary conclusion from this data harvesting was that of the 8289 individuals, approximately no more than 1 in 600 had a positive reaction to a test for the presence of specific IgE to either a protease and/or an amylase class of enzyme.

Table 1: Results of pre-employment screening for protease/amylase IgE.

Employees pre-occupational data			
Year group	Number tested (M/F)	Protease positive (M/F)	Amylase positive (M/F)
< 30	4019 (3057 / 962)	2 (2/0)	3 (2/1)
30-39	2406 (1828 / 578)	6 (6/0)	6 (5/1)
40-49	1255 (939 / 316)	3 (3/0)	0 (0/0)
>50	609 (493 / 116)	3 (3/0)	1 (1/0)
In total	8289 (6317 / 1972)	14 (14 / 0)	10 (8 / 2)

Discussion

The reality that certain enzymes possess an important intrinsic hazard, the potential to cause sensitization of the respiratory tract, has been recognized for several decades [1-15]. Furthermore, when occupational exposure occurs to a sufficient degree, not only can that sensitization be detected, but clinical symptoms appear (e.g. [2-6]). This speaks clearly to the necessity for exposure control, workforce education and health monitoring, in effect constant vigilance [13]. However, despite the hazard, enzymes (primarily proteases, amylases and lipases) have been used widely in a range of consumer products, most notably in household detergent products [25]. In such situations, a rigorous safety assessment is required, for which various sources of guidance are available [16-18,26]. Further publications have also detailed examples of product safety assessment customized to the specific product intended to be placed on the consumer market [23,24,27-34]. By their nature, these types of safety evaluation have to be carried out prior to the placement of a product on the consumer market. Where consumer safety cannot be assured, the product is not permitted to progress to the marketplace (e.g. [28,29]). Where marketing is allowed to proceed, the ultimate reassurance that the safety evaluation was correct comes from a long history of safe consumer use. To date, the authors are not aware of any evidence that unsafe products have been placed on the consumer market. Indeed, household detergent products containing enzymes have been placed on the consumer market for over half a century, where the risk of allergic reactions developing in skin through their use has been shown to be low [35,36].

A critical analysis concluded that although transcutaneous sensitisation to proteins can occur (typically through compromised) skin, in practice such skin contact with enzymes used in laundry and cleaning products does not pose a significant risk of allergic disease [35-37]. A literature search indicates also that such marketing has not been accompanied by any significant evidence of consumer respiratory allergy to their enzyme content:

use of the terms “consumer”, “enzyme” and “respiratory allergy” on PubMed (dated generated 56 hits of which only four, all from the first half of the 1970s, actually discuss potential cases of consumer allergy [38-41]. It was in this period that the allergenic potency of enzymes became more fully understood, and led to mitigation of the risk, for example by the development of new and safer enzyme products in which the enzyme protein has been encapsulated and thereby cannot released into the surrounding air, or, since the mid-1980s, by enzymes being supplied in liquid form which are used in fully enclosed systems (pipes, vessels) at manufacturing sites.

As an alternative to searching for individual cases, other workers have considered to what extent specific IgE to enzymes could be detected in the wider population. An early study suggested, rather surprisingly, that sensitization to a protease was already present prior to the introduction of enzymes into the market, with 15 of 301 people tested being reported to be positive [42]. However, the lack of any correlation between skin prick tests and radio allergosorbent results must cast considerable doubt on the reliability of this work. Furthermore, it was carried out largely on a topics and asthma sufferers, with only 20/301 being described as healthy volunteers. Nevertheless, it does serve as a reminder that undirected (i.e. not clinically motivated) assessments invite the complication of irrelevant false positives. Accordingly, it is reassuring that in a later, much larger study, involving 15,765 participants, only 37 positive results (0.23%) were found to be skin prick test positive to a range of enzymes used in household detergent products (proteases, amylases and lipases) [23]. It is even more reassuring that the large majority of these positives arose in the period up to the mid-1970s, after which the frequency of positive reactions fell to 0.13%. This result is wholly consistent with the argument that the risk of sensitization became properly controlled for consumers during the 1970s. At that time, the authors noted that their 14 positives post-1977 were not linked to exposure to laundry products, nor did the individuals have any clinical symptoms [23].

Conclusion

Given these experiences, in our present work we asked the question whether, since the 2010 publication, the situation with consumers had changed. As was partly the case in the 2010 work, we elected to harvest pre-employment screening data. From a total of 8289 individuals, 18 subjects (0.22%) were found to have positive reactions to tests for either a protease or an amylase. This is slightly lower than the overall rate from 2010, but is just a little higher than the rate previously found once the early data had been set aside. However, the values are not significantly different ($p < 0.01$), suggesting that there is in reality no directional trend in the background frequency of IgE positivity to enzymes in the general population. Consequently, it is concluded that, to date, the present usage of selected industrial enzymes in consumer cleaning products continues to be associated with an absence of respiratory allergy in the users. This conclusion also demonstrates that rigorous adherence to industry guidelines remains an essential contributor to both occupational and consumer safety [7-12], [16-18].

Conflicts of Interest

DB received equal financial support from A.I.S.E. and AMFEP for the preparation of this review. All other authors are paid employees of their respective companies and organizations.

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