Received: 20 April 2024 | Revised: 14 July 2024 | Accepted: 12 September 2024

DOI: 10.1111/cod.14698

REVIEW

CONTACT DERMATITIS | WILEY

Allergic contact dermatitis caused by glucose sensors and insulin pumps: A full review

Part 1: Sensors and pumps, adverse cutaneous reactions, allergens, and diabetes devices causing allergic contact dermatitis

Anton de Groot[1] | Emma M. van Oers[2] | Norbertus A. Ipenburg[1] | Thomas Rustemeyer[1]

[1]Dermato-Allergology and Occupational Dermatology, Amsterdam University Medical Centers, Amsterdam, The Netherlands

[2]Amsterdam University Medical Centers, Amsterdam, The Netherlands

Correspondence
Anton de Groot, Dermato-Allergology and Occupational Dermatology Amsterdam, University Medical Centers, Meibergdreef 9 1105 AZ, Amsterdam, The Netherlands.
Email: antondegroot@planet.nl

Abstract

During the past 8 years, a large number of reports have appeared on allergic contact dermatitis to glucose sensors and insulin pumps in paediatric and adult patients with type 1 diabetes mellitus. Isobornyl acrylate in one particular sensor sensitised many hundreds of (published) individuals, and many other allergens were discovered in a large number of sensors and pumps. Diagnostic procedures with patch tests proved very complicated, as manufacturers showed a serious lack of cooperation with dermatologists in providing information on the ingredients of their products and samples for patch testing. This two-part article provides a full and detailed review of all aspects of the subject of allergic contact dermatitis to glucose sensors and insulin pumps. Part 1 begins with a general introduction to sensors and pumps, followed by the cutaneous adverse reactions that they have caused and a full account of the allergens in the diabetes devices. In addition, an overview of the glucose sensors and insulin pumps that have caused allergic contact dermatitis is presented. Part 2 presents all published case reports and case series, clinical features of allergic contact dermatitis to sensors and pumps, patch test procedures, differentiation from irritant dermatitis, management of allergic patients and (proposed) legislation.

KEYWORDS

allergic contact dermatitis, colophonium, contact allergy, continuous subcutaneous insulin infusion, diabetes medical device, diabetes mellitus, glucose monitoring, glucose sensor, insulin pump, isobornyl acrylate, *N*,*N*-dimethylacrylamide

1 | INTRODUCTION

Diabetes mellitus (DM) is a chronic metabolic disease characterised by elevated blood glucose levels. It is an increasingly prevalent disorder that causes significant morbidity and mortality and today represents one of the major public health problems globally.[1,2] In patients with DM, glycaemic control and its maintenance within the normal range are essential to avoid the onset of the multiple and potentially severe complications of the disease (e.g., hypoglycaemia) in the short and long term. In the past decade, the

development of high-tech devices such as insulin pumps, continuous glucose monitors (CGM) and flash glucose monitors (FGM) has revolutionised the treatment of DM, simplifying the life of patients both in the therapeutic and follow-up field.[1,3] Traditional self-monitoring of blood glucose levels using finger sticks has been replaced by continuous or flash glucose monitoring, and insulin pumps have eliminated the need for multiple daily insulin injections.[3,4] Compared with standard metered-dose insulin they have not only the benefits of reduced daily skin pricks, but also yield less fluctuation of glucose levels and fewer hypoglycaemic episodes. Moreover, these devices are associated with lower baseline haemoglobin A1c levels, they improve microvascular outcomes and have resulted in markedly improved quality of life for the patients.[1] Therefore, diabetes devices are rapidly being adopted by patients,[5] with up to 30% to 40% of individuals with type 1 diabetes (especially children and adolescents) and an increasing number of patients with type 2 diabetes using them.[1]

However, diabetes devices are associated with a number of cutaneous adverse events, including itch, irritant contact dermatitis, scars, wounds, infections, lipohypertrophy and -atrophy, and allergic contact dermatitis; detachment of the sensor or transmitter during sports or upon water contact may also occur.[3,6] A common feature of the sensors and pumps is that they are fixed on the skin for 3 to sometimes 14 days, for which the use of strong adhesives, which may contain acrylates, is necessary. Therefore, the emergence of cases of allergic contact dermatitis (ACD) could be and was anticipated.[7] However, it turned out worse. During 2017, after the wide adoption of the newly introduced FreeStyle Libre (FSL) glucose sensor, a worldwide epidemic of ACD was born.[4] What started with the discovery of isobornyl acrylate (IBOA) as an important contact allergen in FSL evolved into the detection of a multitude of sensors and insulin pumps causing ACD by a large number of allergens.

This article provides a full review of the literature on ACD to glucose sensors and insulin pumps. It discusses how the allergens were discovered, and presents all available data on culprit allergens and devices that have caused ACD, frequency and clinical features of allergic reactions, management of patients with ACD including secondary prevention, and diagnostic procedures. Relevant literature was identified in January–March 2024 by an electronic database search in PubMed/MEDLINE and Embase using as key words 'glucose sensor', 'insulin pump', 'insulin infusion set', and 'isobornyl acrylate' in combination with 'allergy' and 'allergic contact dermatitis'. In addition, the reference lists of retrieved articles were searched by hand to identify other relevant articles to be included.

This is not the first, but by far the most comprehensive and clear review article on the subject. Reviews have previously appeared in 2018,[6] 2019[2] (limited, mostly side effects of insulin and other antidiabetic drugs), 2020[8] (very limited, also other medical devices), 2020[4] (isobornyl acrylate), 2020[9] (limited review, in German), 2020[10] (isobornyl acrylate, limited review, practice-oriented), 2021,[1,5] 2022,[3,11] and 2023.[12]

2 | DIABETES DEVICES: GLUCOSE SENSORS AND INSULIN PUMPS

2.1 | Glucose sensors

Glucose sensors are devices implanted within the skin or subcutaneous tissue that transmit in vivo glucose readings to an external device. Glucose sensors were first approved by the Food and Drug Administration (FDA) in the USA in 1999, with newer generations marketing their extended durability.[1] There are 2 types of glucose monitoring systems: continuous glucose monitoring (CGM) (e.g., Dexcom and Enlite) and flash glucose monitoring (FGM), more appropriately but less often termed 'intermittently scanned continuous glucose monitoring'[13] (e.g., FreeStyle Libre and FreeStyle Libre 2). The first CGM system became available in 2005 and the first flash system (FSL) was introduced in 2014 in the European Union and (slightly different version) in the US in late 2017.[13] In both systems the glucose sensor measures the interstitial glucose levels. The sensor electrodes are inserted under the skin, with glucose values then being sent to the transmitter of the device. An adhesive patch, which has a perforated space for wire access, is used to fix the plastic sensor and transmitter to the skin.[11]

With CGM, tissue glucose monitoring is performed continuously, that is, every 5 min. Via Bluetooth, the values are transmitted to a reader, application on a smartphone, or pump, along with hypoglycaemia or hyperglycaemia alerts, which are particularly helpful at night or during sports activities.[1,5] A CGM system is generally worn on the abdominal skin, usually for up to 10 days. Thereafter, the sensor is removed with the plaster, and a new one is attached to a different skin area. CGM systems have undergone constant development. A CGM glucose sensor introduced in 2018 (Eversense) is implanted subcutaneously for 90 days (approved for up to 180 days in the European Union). The sensor is placed through a small incision and closed with Steri-Strips (3 M). Directly above the sensor, a transmitter is fixed on the skin with a double-sided adhesive patch that requires daily replacement to prevent any allergens migrating from other parts of the device from piling up in the adhesive.[1] A disadvantage of the earlier CGM monitors was that they required twice-daily calibration with fingerstick blood glucose testing.[14]

With flash glucose monitoring (FGM), the glucose values can only be accessed when the patient 'flashes', which means that the associated scanner is held in the immediate vicinity of the sensor. The FreeStyle Libre sensor 1 was a flash-type sensor, which had the advantage of a 2-week period remaining on the skin and—contrary to the CGM systems at that time[6]—of not requiring any calibration, thereby minimising fingersticks. Nowadays, nearly all glucose sensors perform CGM and need no calibration anymore.[15]

2.2 | Insulin pumps

Insulin pumps (also called insulin infusion pumps and continuous subcutaneous insulin infusion [CSII] sets), allow for continuous delivery of

short-acting insulin and thereby facilitate more precise blood glucose control, sometimes in conjunction with glucose monitors.[11] Insulin pumps are used especially by patients with type 1 diabetes mellitus, as they have a complete deficit of pancreatic β cells and require a replacement insulin therapy for life.[5] The first insulin pump, the Biostator (Miles Laboratory Inc., Elkhart, IN, USA), was invented in 1974 and had the size of a microwave oven.[1] Nowadays, commonly used insulin pumps are approximately the size of a deck of cards.

There are two types of insulin pumps: traditional insulin pumps (infusion sets) and 'tubeless' insulin pumps.

Traditional insulin pumps contain an insulin reservoir and pump, which is often worn at the waistline, tubing to deliver the insulin from the pump to the body, and an infusion set that connects the system to the patient's skin with adhesives. The infusion set includes a short plastic cannula that is inserted into the subcutaneous tissue through a metallic needle in its center, with either a mechanical inserter, or is inserted by hand. After insertion, the needle is retracted, and the cannula fixed with the adhesive to the skin remains in place. There are also some infusion sets with stainless steel needles. The infusion set is changed by the patient every 2–3 days, requiring cleansing of the area with alcohol/chlorhexidine.[1]

Tubeless insulin pumps (also called 'patch pumps' or 'pods') are 'all-in-one' devices that adhere to the skin directly overlying the site of cannula insertion. They remain fixed in place by an adhesive patch. The pump and insulin reservoir are attached directly to the adhesive patch; there is no tubing. These pumps are typically replaced every 3 days.[11] The first pump of this type was the Omnipod insulin pump, released in 2005 in the USA and 2010 in Europe. Patch pumps are more discrete than traditional pumps because they can be worn directly on the skin unattached to clothing.[1] Since the tube and connected pump is perceived as annoying, especially during the night, the tubeless insulin pump is becoming increasingly popular.[5]

2.3 | Glucose sensors and insulin pumps: trade names, types, and producer information

Glucose sensors discussed in this review for having caused ACD, having been analysed for the presence of allergens, or both, are shown in Table 1; for insulin pumps and insulin infusion sets see Table 2. Another diabetes device discussed in this article, not fitting into either category, is MiaoMiao (High Brilliant Health Technology, Shanghai, China [uncertain whether this is correct]; miaomiao.cool). This device is an add-on transmitter that converts the flash glucose monitoring system of FSL 1 and 2 into a continuous glucose monitoring system (CGM).[16] This device will be outdated soon: the more recent FSL 3 is a CGM.

3 | CUTANEOUS SIDE EFFECTS OF DIABETES DEVICES

Diabetes devices are associated with a number of cutaneous side effects, including itch, pain, burning, bruising, erythema, oedema,

TABLE 1 Glucose sensors discussed in this review.

Brand name	Type	Producer, address, website
Dexcom G4 Platinum™[a]	CGM	Dexcom, San Diego, CA, USA (dexcom.com)
Dexcom G5™[a]	CGM	Dexcom, San Diego, CA, USA (dexcom.com)
Dexcom G6™	CGM	Dexcom, San Diego, CA, USA (dexcom.com)
Dexcom G7™	CGM	Dexcom, San Diego, CA, USA (dexcom.com)
Enlite™	CGM	Medtronic, Northridge, CA, USA (medtronicdiabetes.com)
Eversense® XL	CGM	Ascensia Diabetes Care, Basel, Switzerland (ascensia-diabetes.ch)
FreeStyle Libre® 1[a]	FGM	Abbott diabetes care, Alameda, CA, USA (diabetescare.abbott)
FreeStyle Libre® 2	FGM	Abbott diabetes care, Alameda, CA, USA (diabetescare.abbott)
FreeStyle Navigator® II[a]	FGM	Abbott diabetes care, Alameda, CA, USA (diabetescare.abbott)
Guardian 4™	CGM	Medtronic, Northridge, CA, USA (medtronicdiabetes.com)
TouchCare® A6[a]	CGM	Medtrum Technologies, Shanghai, China (medtrum.com)

Abbreviations: CGM, continuous glucose monitor; FGM, flash glucose monitor.
[a]This specific device is not produced anymore; newer versions are (usually) available.

TABLE 2 Insulin pumps and insulin infusion sets discussed in this review.

Brand name	Type	Producer, address, website
Accu-chek® Insight Flex	Infusion set	Roche Diabetes Care, Basel, Switzerland (rochediabetes.com)
MiniMed™ Quick-set™	Infusion set	Medtronic, Northridge, CA, USA (medtronicdiabetes.com)
MiniMed™ Silhouette™	Infusion set	Medtronic, Northridge, CA, USA (medtronicdiabetes.com)
MiniMed™ Sure-T™	Infusion set	Medtronic, Northridge, CA, USA (medtronicdiabetes.com)
mylife™ YpsoPump Orbit®	Infusion set	Ypsomed AG, Burgdorf, Switzerland (ypsomed.com)
Omnipod®	Patch pump (pod)	Insulet Corporation, Acton, MA, USA (insulet.com)
Omnipod® DASH	Patch pump (pod)	Insulet Corporation, Acton, MA, USA (insulet.com)
TouchCare® A6[a]	Patch pump (pod)	Medtrum Technologies, Shanghai, China (medtrum.com)

[a]This specific device is not produced anymore; newer versions are available.

bleeding, hematoma and dermatitis, the latter sometimes resulting in post-inflammatory hyper- or hypopigmentation.[1,3,6,17–19] Dermatitis may be either irritant contact dermatitis (ICD) or ACD. ICD can be elicited by chemical irritants, physical irritation due to the repetitive removal of adhesive materials, moisture accumulation under the medical device, and a reaction to the plaster itself, which causes direct cutaneous injury. The presence of ICD may promote the development of ACD by diminishing the integrity of the skin barrier, thereby increasing the presentation of allergens to the skin's immune system.[20] The long application time of the devices, notably the sensors (6–14 days) and the presence of acrylates also favour sensitization and development of ACD.[21] Scars, wounds, infections, lipohypertrophy and lipoatrophy are side effects seen especially with insulin pumps.[2,3,6,18,19]

In studies investigating the nature and epidemiology of skin reactions to diabetes medical devices, the frequency of cutaneous adverse reactions has shown a wide range, presumably dependent on the study design and definition of cutaneous complications. In dermatological literature presenting cases of ACD, the results of some Danish studies are often cited, showing that such cutaneous reactions occur frequently.[22–25]

In the first study, performed in 2016 and 2017, 178 children and adolescents with type 1 diabetes (T1D) who had been treated with a sensor or pump for more than 4 weeks, were invited to participate in a study investigating previous or current skin reactions to their device(s).[25] 144 of 178 (80%) patients or their parents filled out an online questionnaire. Of 143 pump users, 89% had experienced dermatological complications *in the past*, the most frequent of which were itching (78%), (dry or wet) wounds (50%), and non-specific eczema (46%). Ninety of the 143 pump-users (63%) had at least 1 site with a *currently* visible dermatological condition that was related to the device: 26% eczema, 23% red/blue dots and 13% dry wounds. Of 83 patients using a sensor, 79% had experienced dermatological complications *in the past*, most frequently itching (70%), eczema (46%), and wounds (33%). 46% of sensor-users indicated a *current* dermatological complication at one or more locations, including eczema (36%) and dry wounds (11%). The patients rated sensor-related dermal issues as significantly worse than those associated with pumps. The authors concluded that dermatological complications can be a serious problem in treating paediatric and adolescent patients with diabetes medical devices.[25]

In a 5-month follow-up study from these investigators, 81% of 138 patients from the original study continued to have dermatological complications at follow-up. Patients perceiving dermatological complications as a greater problem were found to have lower health-related quality of life.[22]

In a similar online questionnaire study by the same authors among 118 adult patients, 117 were currently using a pump and 48 wore a sensor. Ninety-three of 117 pump users (79%) had *previously* experienced dermatological complications of their device(s) at some point; for the sensor users the percentage was 71. Itch was the most common symptom, whereas eczema and wounds were the most common complications in both groups. More than one-third of the patients *currently* had dermatological complications that were associated with using either the pump (34%) or the sensor (35%). The duration of the skin lesions had been more than a week for 60% of the reactions. Of these lesions, eczema was the most frequent, especially for users of sensors. The authors concluded that dermatological complications associated with using pumps or sensors are a significant problem for adult patients with T1D.[24]

In a 4-months follow-up study by the same investigators, even higher percentages of dermatological complications were found: 65% for pumps and 74% for sensors. In many individuals, the skin problems found in the original study had persisted. Again, itching was by far the most prevalent symptom, and eczema was reported by 17% of pump and 25% of sensor users. Within the previous 4 months, 42 (38%) of the 111 pump users had changed their pump earlier than recommended because of one or more skin problems. At the time of follow-up, 46% of the pump users and 37% of the patients using a sensor had visible skin problems. It was shown that the skin problems were associated with increased disease burden from diabetes-specific distress.[23]

Several other recent studies also found high frequencies of adverse cutaneous reactions to diabetes medical devices (currently or previously): 60%,[26] 51%,[27] 42%,[28] and 40%.[29] It should be realised that these studies are very difficult to compare because of (major) differences in study design.

Nineteen observational studies and intervention trials that have reported on cutaneous complications from glucose sensors up to January 14, 2019 have been assessed in a systematic review.[17] The cutaneous complication event rate was 0.13–0.15 for every week of wear-time, indicating one event every 8 weeks. Reported occurrence varied considerably between trials with higher rates when researchers inspected the site (1.4 events per week of wear time) than when patient reported adverse events (0.04 events per week of wear-time). The most common cutaneous reaction was erythema (55%), followed by itching/pruritus (11%) and induration (9%). The studies reported more adhesive or wear-associated cutaneous complications (80%) (e.g. erythema and itch) than direct insertion-related complications (20%) (e.g., bruising or bleeding). As to severity: 79% of cutaneous complications were rated as mild, 20% were moderate, and only 1.5% were severe. Data from observational studies indicated that more than 70% of participants have experienced cutaneous complications related to sensor used at some point, with itch, eczema, and insertion wounds as the most common. Few participants in these trials ceased the use of their sensor due to these complications.[17] The authors concluded that the incidence rate of reported cutaneous complications with sensor use is low. However, they also suggested that the incidence rate is likely an underestimate of the true real-world incidence. To support this possibility, the authors pointed at the 2 studies of Berg et al.[24,25]: 'the data from observational studies indicate a likely high prevalence of experiencing cutaneous complications'.[17]

The frequency of ACD in patients using sensors or pumps will be discussed in part 2 of this review article.

4 | ALLERGIC CONTACT DERMATITIS

4.1 | Introduction

Allergic contact dermatitis is the most frequently reported adverse cutaneous effect of diabetes medical devices. All sensors and pumps are fixed on the skin for 3 to sometimes 14 days, for which the use of strong adhesives, which may contain acrylates, is a necessity. Therefore, the emergence of cases of ACD to sensors was anticipated.[7] Indeed, in 2016 a first case was reported, a patient who had developed ACD from ethyl cyanoacrylate in the Dexcom G4 Platinum sensor.[30] At that time already, many patients who had used the very popular FreeStyle Libre sensor (FSL) presented to dermatologists with what appeared to be an allergic reaction to the adhesive patch of the sensor. A year later, Belgian and Swedish investigators had discovered isobornyl acrylate (IBOA) as an allergen in FSL by performing chemical analyses of acetone extracts of the sensor. They suspected (which was soon confirmed) that the adhesive patch itself was not the source of IBOA. Rather, it was suggested that IBOA had been released from a glue used to join the top and bottom part of the sensor, and subsequently migrated into the adhesive patch.[31] This landmark article presenting 15 allergic patients, 12 of who had positive patch tests to IBOA (of 13 tested) was the start of a long line of publications with case reports and (large) case series of patients with ACD from FSL, which has rightfully been termed a 'worldwide epidemic'.[4] Soon other diabetes devices also were found to contain IBOA and many publications on allergic reactions to various sensors and pumps with a large number of culprit allergens followed, up to the present time.[32] In this chapter, all aspects of ACD from diabetes medical devices are reviewed.

4.2 | The search for allergens that have caused allergic contact dermatitis

Patch testing is the diagnostic method used to establish contact allergy in patients suspected of ACD. Relevant contact allergy (identifying the allergen that has caused ACD or contributed to it, either at present or in the past) can be found only when the culprit allergen is present in the patch test materials, which are selected on the basis of the clinical picture, patient history, and a thorough investigation of contact materials in the patient's personal and occupational settings. Information on possible allergens in contact materials can often be obtained from product labelling (cosmetics, pharmaceuticals, and household products), material safety data sheets (industrial products), or from the manufacturer. However, when the first cases of suspected ACD to the relatively new glucose sensors used by patients with diabetes emerged, there was no information available on the composition of and possible allergens in the adhesive patches and the housings of these devices, as manufacturers do not need to disclose the chemical composition of their products.[33] In the first reported case of ACD to the Dexcom G4 Platinum sensor, the manufacturer provided the information upon the request from the investigators. Next, targeted testing identified ethyl cyanoacrylate as the culprit allergen, which was present in a glue that attached the sensor pod to the non-skin part of the adhesive.[30] However, when patients with possible ACD from the FSL sensor were seen in Belgium and Sweden, the investigators contacted the manufacturer in several countries and various affiliates and found that their requests for information on compounds used in the production of the sensor were 'very unfruitful'.[31]

How, then, was the culprit allergen in FSL identified? When, in Malmö, the first patient was seen with dermatitis corresponding to the contact area of FSL, a patch test was performed with an ultrasonic bath extract of the whole sensor. A positive reaction consistent with an allergic morphology was noted and 20 controls were negative. Thus, the diagnosis was ACD caused by the sensor, but what was the allergen?[31] The discovery of IBOA as the culprit allergen was apparently purely accidental: a paediatric patient in Antwerp, Belgium, with ACD from the sensor was tested by mistake with IBOA, which was not intended to be applied as part of the acrylate series, and this patient had positive reactions to IBOA.[4] Based on this new information, the investigators in Sweden analysed acetone extracts made from different parts of the sensor with gas chromatography–mass spectrometry (GC–MS) in a more targeted manner and found IBOA to be present in all samples.[31]

Since then, most chemicals present in glucose sensors and insulin pumps causing ACD, that were shown to be culprit allergens by patch testing, have been identified by GC–MS analyses of acetone, methanol or ethanol extracts from the devices.[34] That performing these time-consuming and costly analyses[35] has been a necessity is a direct result of the appalling lack of cooperation from manufacturers in providing ingredient information of their products (will further be discussed in part 2).[20,31,33,36–43] In only a few cases have manufacturers confirmed the presence of allergens that were identified by testing the baseline series (colophonium)[44,45] or an acrylate series (butyl acrylate) in their diabetes device products.[46]

In this paragraph, all analyses of extracts of glucose sensors and insulin pumps reported in literature related to the subject of ACD are summarised. Table S1 (which can be found in the Supporting Information) shows an alphabetical list of these allergens, specifying the devices in which they have been identified, mode of detection and references. In most studies, the amount of the chemicals has been quantified. These data is not shown here, as the results of the analyses are dependent on the mode of sample preparation (e.g., solvent used, time of incubation, use of ultrasonic bath or not) and many parameters with performing gas chromatography–mass spectrometry.[31] Thus, a proper assessment and evaluation of the amount of allergen identified can only be done in connection with the exact data of how sampling and analyses were performed. This falls outside the scope of this review and readers are advised to consult the original publications (shown).

An alphabetical list of devices with the allergens identified in them is shown in Table 3. A summary of chemical analyses which were *negative* for specific chemicals is provided in Tables S2 and S3, Supporting Information, both of which can be found in the Supporting Information. It should be realised that a negative test (allergen not identified) does not exclude the possibility that the chemical

TABLE 3 Glucose sensors and insulin pumps and the allergens identified in these diabetes devices.[a]

Glucose sensor/insulin pump	Allergen(s) identified in these devices	References
Accu-chek Insight Flex infusion set	Isobornyl acrylate (IBOA)	47
Dexcom G4 Platinum sensor	Ethyl cyanoacrylate	30,48,49
Dexcom G5 sensor	4,4′-Methylene diphenyl diisocyanate (MDI)	50
Dexcom G6 sensor	Isobornyl acrylate (IBOA)	21,51,52
	Methyl dehydroabietate	21
	2,2′-Methylenebis(6-*tert*-butyl-4-methylphenol) monoacrylate (MBPA) (from early 2020 on)	52,53
Dexcom G7 sensor	Colophonium related substances: hydrogenated resin acids and derivatives	32
	Dicyclohexylmethane-4,4′-diisocyanate (DMDI)	
	Isobornyl acrylate (IBOA)	
Enlite sensor	Butyl acrylate	46
	Colophonium (rosin)	45
	N,*N*-Dimethylacrylamide (DMAA)	54
	Isobornyl acrylate (IBOA)	54,55
	Methyl dehydroabietate	54
FreeStyle Libre 1 sensor	Butylated hydroxytoluene (BHT)	56
	2,4-di-*tert*-Butylphenol	56
	N,*N*-Dimethylacrylamide (DMAA)	57
	Isobornyl acrylate (IBOA)	15,20,31,47,55,57–59
	Isophorone diisocyanate (IPDI)	57
	Methyl dehydroabietate	60
	4,4′-Methylene diphenyl diisocyanate (MDI)	50
FreeStyle Libre 2 sensor	Butylated hydroxytoluene (BHT)	58
FreeStyle Navigator II sensor	Isobornyl acrylate (IBOA)	31
Guardian 4 sensor and adhesive	Isobornyl acrylate (IBOA)	60
	N,*N*-Dimethylacrylamide (DMAA)	60
Guardian 4 sensor (transmitter part)	1,6-Hexanediol diacrylate (HDDA)	60
MiniMed Silhouette infusion set	4,4′-Methylene diphenyl diisocyanate (MDI)	50
MiniMed Quick-set infusion set	Isobornyl acrylate (IBOA)	47,54
	4,4′-Methylene diphenyl diisocyanate (MDI)	50
Minimed Sure-T infusion set	Isobornyl acrylate (IBOA)	47
	4,4′-Methylene diphenyl diisocyanate (MDI)	50
mylife Ypsopump Orbit infusion set	Isobornyl acrylate (IBOA) Dicyclohexylmethane-4,4 diisocyanate (DMDI)	51
Omnipod insulin pump	Colophonium (rosin)	45
	N,*N*-Dimethylacrylamide (DMAA)	61
	Di(ethyleneglycol)ethyl ether acrylate (DEGEA)	61
	Dipropylene glycol diacrylate	61,62
	Isobornyl acrylate (IBOA)	20,40,61,63
	Tripropylene glycol diacrylate (TPGDA)	61
Omnipod DASH pump	Colophonium derivatives	32
TouchCare A6 sensor and pump	Colophonium (rosin)	44
	Ethyl cyanoacrylate	44
	Isobornyl acrylate (IBOA)	44
	Methyl dehydroabietate	44

[a]Only data for recent glucose sensors and insulin pumps (>2015).

TABLE 4 Chemicals in diabetes devices that have caused allergic contact dermatitis.

Chemical	Synonym/abbreviation	CAS number
1-Benzoylcyclohexanol	Hydroxycyclohexyl phenyl ketone	947-19-3
Butyl acrylate	BA	141-32-2
Butylated hydroxytoluene	BHT	128-37-0
2,4-di-*tert*-Butylphenol	2,4-DTBP	96-76-4
β-Carboxyethyl acrylate	2-Carboxyethyl acrylate	24615-84-7
Colophonium	Rosin; colophony	8050-09-7
Dicyclohexylmethane-4,4′-diisocyanate	Bis(4-isocyanatocyclohexyl)methane; DMDI; hydrogenated MDI	5124-30-1
N,*N*-Dimethylacrylamide	DMAA	2680-03-7
Dipropylene glycol diacrylate	DPGDA	57472-68-1
Epoxy resin		61788-97-4 (generic)
Ethyl cyanoacrylate	ECA	7085-85-0
1,6-Hexanediol diacrylate	HDDA	13048-33-4
Isobornyl acrylate	IBOA	5888-33-5
Isophorone diisocyanate	IPDI	4098-71-9
2,2′-Methylenebis(6-*tert*-butyl-4-methylphenol) monoacrylate	2-*tert*-Butyl-6-(3-*tert*-butyl-2-hydroxy-5-methylbenzyl)-4-methylphenyl acrylate; MBPA	61 167-58-6
Methyl methacrylate	MMA	80-62-6
Nickel		7440-02-0
2-Phenoxyethyl acrylate[a]	PEA	48145-04-6
Phenoxypoly(ethyleneoxy)ethyl acrylate	Phenol, ethoxylated, esters with acrylic acid; polyethylene glycol phenyl ether acrylate; PEEA	56641-05-5

[a]2-Phenoxyethyl acrylate was likely an allergen in cases of ACD to insulin pumps, but as yet unproven.

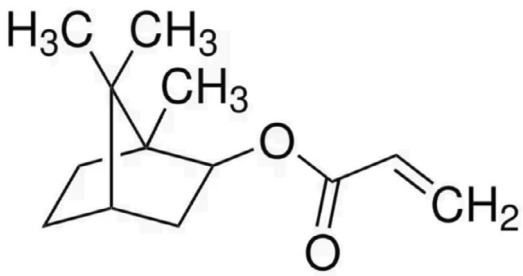
investigated is in fact present in the device under investigation, as the results of chemical analyses can depend on the protocol used for preparation of extracts and chemical analysis.

4.3 | The allergens that have caused allergic contact dermatitis

Up to now (April 25, 2024) 18 chemicals, of which 10 are acrylates, have caused ACD by their presence in glucose sensors, insulin pumps, or both; they are shown in Table 4. Some of these allergens are discussed in more detail in paragraphs 4.3.1–4.3.5. Paragraph 4.3.6 gives an overview of all allergens, the diabetes devices in which they were present and caused ACD, numbers of patients and all relevant literature references.

4.3.1 | Isobornyl acrylate

Isobornyl acrylate (IBOA) (CAS number 5888-33-5; EC number 227-561-6; molecular formula $C_{13}H_{20}O_2$; IUPAC name (1,7,7-trimethyl-2-bicyclo[2.2.1]heptanyl) prop-2-enoate; synonyms: acrylic acid, isobornyl ester; *exo*-1,7,7-trimethylbicyclo[2.2.1]hept-2-yl acrylate) (European Chemical Agency [ECHA] name)) is the isobornyl ester of acrylic acid. Its structural formula is shown below. The commonly used abbreviation for isobornyl acrylate is IBOA.



IBOA is an acrylate monomer that polymerises when exposed to sources of free radicals, such as UV-radiation. It is used in many plastic materials (used for valves, tubes lining and stoppers), adhesives, sealants, coatings, paints and inks. It has excellent adhesion properties, good chemical resistance, and low shrinkage, making it a popular choice for use in UV-curable coatings on various substrates such as plastics, metals, and wood. Another application is its use in pressure-sensitive sealants.[64]

IBOA was identified by chemical analyses in commercial cosmetic samples of alkyl glucosides, and was considered to be an impurity collected during the industrial process. The investigators suggested that

IBOA may play a role as hidden allergen, explaining some cases of allergic reactions to alkyl glucosides.[64] Other investigators could not identify IBOA in a foam dressing containing lauryl glucoside that had caused ACD nor in glucoside materials used for patch testing that gave positive reactions.[65] The original observation of IBOA in alkyl glucosides,[64] therefore, has not yet been confirmed.

Before 2017, only a few publications had reported on ACD from IBOA. In 1995, in Belgium, 2 women had developed ACD from an insulin infusion set caused by IBOA present in the UV-cured glue used to fix the needle into the plastic of the cannula (will be detailed in part 2).[66] In 2013, Dutch investigators described the case of a process operator in a factory producing glass fibres who had developed hand eczema.[67] His work involved painting glass fibres with UV-cured paint, printing the glass fibres, covering them with an acrylate coating, and cleaning the machines. Contact allergy to IBOA was established as the cause of his eczema, which was a component of both the glass fibre coating and the UV-cured ink he had contact with. The authors also tested 14 patients known to be allergic to (meth)acrylates with IBOA 0.3%, 0.1%, 0.033% and 0.01% in petrolatum, but none had a positive reaction to IBOA, suggesting that IBOA does not cross-react to other (meth)acrylates.[67] The same lack of cross-reactivity was observed in other studies (detailed in paragraph 4.3.1).[68]

IBOA was first highlighted as an important contact allergen in 2017, when investigators from Belgium and Sweden reported on 15 patients with type I diabetes mellitus who had severe ACD from the glucose sensor FreeStyle Libre (FSL), which had been in use since 2015.[31] Twelve of 13 patients patch tested with IBOA reacted positively to it: 11/12 to IBOA 0.1%, 10/12%–0.05%, and 9/13%–0.01%. Results of chemical analyses showed IBOA to be present in both the sensor housing (0.003%–0.3%, depending on the part from which the extracts were made) and in the adhesive patch (0.006%). The analyses indicated that the adhesive patch itself may not have been the actual source of IBOA. Rather, it was suspected that IBOA was released from a glue used to join the top and bottom part of the sensor, and that this acrylate subsequently migrated into other parts of the sensor including the adhesive.[31] This was later confirmed by the same investigators, at which time the manufacturer of the adhesive patch confirmed that no IBOA is used in the adhesive in contact with the skin or in the adhesive used to fix the patch to the sensor.[57,69] The investigators also convincingly showed that it was IBOA itself that caused the positive patch test reactions and not an impurity in the IBOA test material.[59]

Following this publication in 2017, many case series of patients with ACD caused by IBOA from the use of the FSL sensor were reported from Belgium (with very likely some overlap between two or more publications),[37,47,50,57,59,70,71] Sweden,[41,56,57] Germany,[15,72] Spain,[36,38] Finland,[39] Portugal[73] and Denmark[20] between 2018 and 2022. The number of patients was 4 or 5 in four studies[15,20,38,50] and 6–10 in six.[36,41,57,70,72,73] There were also studies with a large number of sensitised patients: 13,[56] 18,[47] 34,[37] 51[39] and 52.[59] The most important data of these case series will be presented in part 2. In addition, a large number of single (sometimes 2 patients) case reports of ACD from IBOA in FSL have been published.[36,40,54,69,74–92]

The sudden and explosive rise of IBOA as an allergen in diabetes devices made IBOA the 2020 American Contact Dermatitis Society Allergen of the year.[4]

IBOA was also identified by chemical analyses using gas chromatography–mass spectrometry (GC–MS) in the commonly used glucose sensors Enlite and Dexcom G6, the patch pump Omnipod and various other diabetic devices (Table S1, Supporting information). In most of these, IBOA has caused cases of ACD (paragraph 4.3.6), some from primary sensitization and others from elicitation in individuals who had previously become sensitised to IBOA, nearly always from the use of FSL. In the case of Omnipod (just as with the FSL sensor), IBOA was not used in the adhesive patch (confirmed by the manufacturer of the patch), but dissolved from the body of the pump and subsequently migrated into the adhesive part, thereby coming into contact with the skin and causing ACD.[15,63]

IBOA has been by far the most frequently identified culprit allergen in patients with ACD from diabetes devices, especially the FSL sensor. At least 330 cases have been published with large numbers of sensitised patients in individual studies. After being sensitised by IBOA from the use of FSL, many patients subsequently suffered ACD from other IBOA-containing diabetes devices, either from insulin pumps (e.g., References 40,44,56,69,89, glucose sensors,[36,75] or both. One individual later had an allergic reaction to a disposable blood pressure cuff, which was found to contain IBOA.[88]

According to the manufacturer, from July 31, 2020 on, IBOA was no longer present in newly produced FSL devices.[93]

IBOA is not only an allergen in diabetes devices. It has recently caused ACD from its presence in infusion sets for treating pulmonary hypertension with treprostinil[94] and in various glues, used to apply protective covers to smartwatches,[95] to fix UV-tempered-glass screen protectors on mobile phones[96] and to attach false nails.[97] A paediatric patient previously sensitised to IBOA by (unspecified) diabetes devices 2 years later developed dermatitis within hours of wearing a hospital wristband. GC–MS analysis of acetone extracts showed the presence of 38 ppm IBOA and of 2-phenoxyethyl acrylate (which could not be tested).[98] A role for IBOA in a case of ACD to ECG electrodes has been suggested but was not ascertained.[99]

As to patch testing, at first, when IBOA was tested at 0.1% (the usually advised test concentration for acrylates) and sometimes lower, 0.1% pet. was considered to be adequate for patch testing.[31] A patch test preparation containing 0.1% IBOA in petrolatum became commercially available mid-2019 from Chemotechnique (www.chemotechnique.se). Later, however, it was found that some patients who had negative reactions to IBOA 0.1% pet. did have positive patch tests to 0.3% pet., sometimes only at a late reading at D7.[20,21,44,52,56] Thus, it became clear that using 0.1% may have resulted in false-negative reactions, possibly explaining some negative reactions to IBOA observed in patients who suffered ACD from FSL. Adequate controls have been negative to IBOA 0.3% pet. and no late reactions suggestive of patch test sensitization have been reported.[56] Therefore, testing IBOA at 0.3% pet. may be preferable and a late reading at D7 or D8 is necessary when reactions are negative at D3 or D4.[44,56]

TABLE 5 Frequency of co-reactivity to SLM in patients sensitised to IBOA.

Year and country	Number of patients positive to:		Strength of reaction to IBOA 0.1% pet.[a] and number and percentages of co-reactions to SLM:				References
	IBOA[b]	SLM (%)	IBOA +	IBOA ++	IBOA +++	IBOA 0.3%[c]	
2022 Denmark	7	3 (43%)	2/4 (50%)	1/1 (100%)		0/2 -	20
2021 Spain	8	5 (63%)	1/1 (100%)	3/3 (100%)	1/4 (25%)		36
2021 Belgium	14	7 (50%)	2/6 (33%)	4/6 (67%)	1/2 (50%)		47
2020 Portugal	8	1 (13%)					73
2020 Belgium	10	5 (50%)	1/4 (25%)	3/5 (60%)	1/1 (100%)		70
2020 Sweden	13	4 (31%)	0/2 (0%)	2/5 (40%)	2/4 (50%)	0/2 –	56
2020 Sweden	6	4 (67%)	1/1 (100%)	1/1 (100%)	2/2 (100%)	0/2 –	21
2019 Sweden	10	4 (40%)[d]		3/3 (100%)	1/1 (100%)		41
2019 Belgium, Sweden	3	2 (67%)			2/2 (100%)		54
2019 Belgium, Sweden	5	2 (40%)	0/1 (0%)	2/3 (67%)	0/1 (0%)		57
2019 Belgium	47	30 (64%)	5/14 (36%)	21/28 (75%)	4/5 (80%)		59
2019 Finland	4	2 (50%)					39
2017 Belgium, Sweden	11	5 (45%)	0/1 (0%)	4[d]/9 (44%)	1/1 (100%)		31

[a]Strength of positive patch test to IBOA at second reading (D3/D4).
[b]Includes only IBOA-positive patients who were also tested with the SLM in the European baseline series.
[c]Negative at 0.1%, positive only at 0.3% concentration (i.e. weaker allergy).
[d]A fifth patient had? + reactions to SLM at D2 and D4.

In the general patch test population, positive reactions to IBOA are infrequent, with 3 of 522 patients (0.57%) showing positive reactions in a study from a university hospital in Brussels, Belgium, performed between July 2019 and November 2020. All 3 had been sensitised by using diabetes devices.[100]

References for chemical analyses of IBOA in diabetes devices can be found in Table S1 (Supporting information), and for all reported allergic reactions in paragraph 4.3.6. Summaries of case series of ACD to IBOA will be provided in part 2. Summaries of case reports of allergic reactions to IBOA will also be shown in part 2 of this article.

Co-reactivities in patients allergic to isobornyl acrylate

Allergic contact dermatitis from IBOA, notably from its presence in the FreeStyle Libre sensor, has been reported in many case series, for example, References 31,37,39,47,59,71. It was soon observed that there was an overrepresentation of co-reactivities to the sesquiterpene lactone mix (SLM) in the European baseline series.[31] In addition, fairly frequent co-reactions to fragrance screening agents in the European baselines series (*Myroxylon pereirae* resin, fragrance mix 1, fragrance mix 2, colophonium, and Compositae-mix) and some individual fragrances, notably limonene and linalool hydroperoxides, were found.[47] Co-reactivities to other acrylates and methacrylates in patients sensitised to IBOA, however, appeared to be infrequent. These co-reactivities are detailed in the following paragraphs.

Sesquiterpene lactone mix. In a 2017 study from Belgium and Sweden, the researchers noted a striking co-reactivity to the sesquiterpene lactone mix (SLM) in patients sensitised to IBOA from the use of FSL.[31] In 11 patients with positive patch tests to IBOA, 5 (45%) also had positive reactions to the SLM, which is included in the European baseline series, and which contains equimolar concentrations of alantolactone (0.033%), costunolide (0.033%) and dehydrocostus lactone (0.033%). The relevance of these positive reactions to SLM could not be established and no explanation for the large number of positive SLM co-reactions was provided.[31] Since then, the association between IBOA and SLM has been confirmed in many other case series of IBOA-allergic individuals[20,21,36,39,41,47,54,56,57,59,70,73] and was also reported in single or dual case reports.[74,76,77,79,83,86,101]

Data on IBOA–SLM co-reactivity in case series are shown in Table 5. In 13 studies with a total of 146 IBOA-allergic patients (range per study 3–47, median 8), percentages of reactivity to SLM ranged from 13 to 67, median 50, mean 50.7. For comparison, in a 2019–2020 European study, of 8658 patients patch tested with the SLM 0.1% pet. in the baseline series, 71 (0.82%) had a positive reaction to this screening agent for Compositae-plants.[102] These data show an obvious and unmistakable overrepresentation of SLM allergy in IBOA-allergic individuals ($p < 0.001$, chi^2 test).

In 2019, in the largest study thus far, again from Belgium, 47 patients who had suffered ACD from FSL and who had positive patch tests to IBOA were tested with the European baseline series and 30 (64%) co-reacted to the SLM.[59] The authors discussed several potential mechanisms, the first option being cross-reactivity. The spatial structure of IBOA and those of the three sesquiterpene lactones (SLs) in the SLM (alantolactone, costunolide, dehydrocostus lactone) are completely different, so they are not likely to activate the same T cell receptor; therefore, cross-reactivity was considered to be quite

improbable. A second possibility proposed was that enzymatic or non-enzymatic reactions, such as autoxidation on air exposure, could result in modifications of the chemical IBOA structure. This could, in turn, induce the formation of a new metabolite that is able to cross-react with SLM components, the authors hypothesized.[59]

A third possible explanation was that co-sensitization results from the presence of sesquiterpenes in the FSL glucose sensor. Therefore, ethanolic extracts of the adhesive and the plastic covers from 2 FSL sensors were analysed with gas-chromatography–mass spectrometry (GC–MS). However, no alantolactone, costunolide or dehydrocostus lactone could be detected in the extracts of the different parts of the FSL sensor. Likewise, GC–MS failed to show any of these lactones to be present in the IBOA used for patch testing. Conversely, no IBOA was found in an SLM extract or in alantolactone, costunolide and dehydrocostus lactone solutions.[59] Thus, the authors concluded that positive patch test reactions to SLM in patients sensitised to IBOA are more likely to represent a cross-reaction than co-sensitization resulting from the presence of SLs in the sensor. However, it was postulated that it can never be completely excluded that small amounts of SLs might be present in the sensor, but not in sufficient quantity to cause a reaction.[59] Around the same time, the Abbott Diabetes Care Scientific Affairs Department informed other investigators that FSL does not contain sesquiterpene lactones.[39]

The authors attributed a possible role for the co-sensitization to camphene, which is a building block in the synthesis of IBOA and a substance found in plants containing sesquiterpene lactones. Camphene being an impurity in IBOA and SLM might explain the simultaneous positive reactions.[59] However, in a later Swedish study, 13 patients who had developed ACD from diabetes devices and who were allergic to IBOA, were patch tested with camphene 5% pet. and there were no positive reactions, making the camphene hypothesis unlikely.[56]

In 2022, Belgian researchers used the in vivo re-test model[103] to evaluate the possibility of cross-reactivity between IBOA and SLM.[76] This model is based on the assumption that, when a patient shows a positive patch test to a hapten (in this case IBOA), persisting allergen-specific T cells that reside in that particular part of the skin will provoke a faster and/or stronger reaction upon re-exposure to the same chemical, and also to a cross-reactive substance (in this case SLM). The authors investigated a patient who had developed ACD from FSL and who had positive patch test reactions to IBOA 0.1% and 0.3% and a? + reaction to the SLM on D3 and D7. Six weeks later, when all reactions had disappeared, patch tests with SLM 0.1% pet. were again applied onto the patient's skin: one of each on the two previously positive skin test sites of IBOA (0.1% and 0.3% pet.) on the right upper arm, and also one on the (control) left upper arm. Readings now showed, already on D2, a strong (++) reaction to both SLM 0.1% pet. patch tests at the sites of previous IBOA reactions, whereas on the left upper arm (control, normal skin) SLM 0.1% pet. again only gave a doubtful (?+) reaction on D3, diminishing at D7.[103]

Thus, the reaction to SLM 0.1% pet. upon re-testing was indeed much stronger at the previously positive patch test sites of IBOA as compared with the same patch test performed on normal (previously patch test uninvolved) skin. This suggests, according to the authors, that immunological cross-reactivity to SLs indeed occurs in patients primarily and strongly sensitised to IBOA.[76] As possible mechanism was suggested that IBOA, by rotating around single bonds, can form a 'conformer' displaying a chemical structure that closely mimics the α-methylene-γ-butyrolactone ring of sesquiterpene lactones. The ring structure allows cross-reactivity between different sesquiterpene lactones and, presumably, also between IBOA and SLM. The authors presented this as hypothesis as it is unknown whether (protein-bound) IBOA will effectively behave as such in front of the T cell receptor.[103] It would, however, also concur with observations that IBOA only rarely cross-reacts with other acrylates.[76]

According to these authors, several other observations also favour the cross-reaction hypothesis[76]:

1. concomitant sensitization to IBOA and SLM cannot be explained by concomitant exposure: analyses have not shown SLs to be present in the FSL sensor (the device most frequently responsible for IBOA-sensitization) nor in the IBOA patch test material. Conversely, no IBOA has been identified in the SLM[59];
2. positive patch test reactions to SLM in IBOA-sensitised patients often seem to lack relevance, potentially indicating nonrelevant cross-reactivity;
3. in many of these patients the patch test reactivity to IBOA is more pronounced than to SLM, suggesting that, in the event of cross-reactivity, IBOA acts as the primary (relevant) sensitizer, whereas SLM is only a secondary (possibly irrelevant) co-sensitizer.[47,76] Indeed, when the data of 7 of the larger data are taken together, of 60 patients allergic to IBOA and co-reacting to SLM, in 26 (43%) the SLM reaction was equal in strength to the IBOA-reaction and in 34 (57%) weaker; in not a single patient was the patch test to SLM stronger than to IBOA.[21,31,36,47,56,59,70]

We have made another observation that also supports the cross-reaction hypothesis, but which has gained little attention: patients with stronger reactions (++, +++) have a higher chance of co-reactivity to SLM than patients who have a + reaction to IBOA.[21] The relevant data are summarised in Table 5, where the reactivity to SLM is stratified according to the strength of the reaction to IBOA. In 12 studies, 34 patients had a + reaction to IBOA 0.1% pet. Of these 34, 12 (35%) co-reacted to SLM. Of 71 patients with a ++ reaction to IBOA, 45 (63%) co-reacted to SLM and for the +++ reactors to IBOA the percentage SLM co-reactivity was also 63 (15 positive to SLM in 24 IBOA-positive patients). The difference in SLM co-reactivity between IBOA reactors with a + strength reaction (35%) and ++ and also +++ reactions (63%) is statistically significant ($p = 0.005$, chi^2 test).

In addition, quite strikingly, of 6 patients who were negative to IBOA 0.1% but who did have a positive reaction to IBOA 0.3% (indicating the presence of a weak sensitization to IBOA), none had a positive reaction to SLM.

On the same note, whereas in a study from Denmark of 5 patients with a + or ++ reaction to IBOA 3 (60%) co-reacted to the SLM, of 4 additional patients who had a? + reaction to IBOA, not a single one

reacted to SLM.[20] We also found that, generally speaking, stronger reactions to IBOA also resulted in stronger reactions to SLM. Conversely, there has not been a single positive reaction to SLM in IBOA-negative patients in any of the studies reviewed for this article.

All data take together, it seems highly likely that the co-reactions to SLM in patients allergic to IBOA are the result of cross-reactivity; the mechanism behind this, however, is still unclear.

Fragrance markers and fragrances. In a study from Belgium, 11 patients with positive patch tests to IBOA were also tested with limonene hydroperoxides 0.3% and 0.2% pet. and with linalool hydroperoxides 0.5% and 1% pet. One or both fragrances were positive in 8 of the 11 (73%) patients with 6 reactions to limonene (55%) and 7 (64%) to linalool. However, the fragrance allergy was considered to be relevant in 3/8 (37%) only, which led the authors to suggest that other fragrance-containing materials might be of importance, e.g. industrially used adhesives.[47] In many other studies, co-reactivities of the fragrance markers in the baseline series (*Myroxylon pereirae* resin, fragrance mix 1, fragrance mix 2, and colophonium) were observed in patients sensitised to IBOA; the results are summarised in Table 6.

Taken all studies together, of 149 IBOA-patients, 32 (21.5%) co-reacted to *Myroxylon pereirae* resin. For comparison: in a large-scale multinational study, 1124 of 16 980 unselected patients suspected of contact dermatitis (6.6%) had a positive reaction to MP.[102] The difference is statistically significant ($p < 0.001$, chi^2 test). Similar differences were seen with fragrance mix 1 (13.8% co-reactions in 130 IBOA-positives, 6.8% in 16 928 unselected patients [$p = 0.002$]), colophonium (11.1% vs. 3.3% in 81 resp. 16 994 patients [$p < 0.001$]) and fragrance mix 2 (16.2% vs. 3.8% in 37 resp. 17 519 patients [$p < 0.001$]).

Thus, just as with the SL mix (paragraph 4.3.1), positive reactions to these 4 fragrance screening agents and probably also limonene hydroperoxides and linalool hydroperoxides[47] are significantly over-represented in patients sensitised to IBOA. An explanation is not readily available, with the possible exception of colophonium (−derivatives) in the diabetes devices' adhesives. It is not likely that these patients, many of who are children, have been heavily exposed to fragrances and fragrances products, which may indicate a lack of relevance for many of these reactions. However, limonene is present in certain types of colophonium and can also be added as tackifier to adhesive products. This may result in sensitization and overrepresentation of allergy to limonene in patients with allergic reactions to adhesive materials.[104]

Other acrylates and methacrylates. Most patients diagnosed with ACD from (meth)acrylates have multiple sensitizations to such chemicals when patch tested, although they have probably not been exposed to

TABLE 6 Frequency of co-reactivity to fragrance markers in patients sensitised to IBOA.[a]

Year and country	Number of IBOA-allergic patients, numbers with positive patch tests to fragrance markers and percentages (%)					References
	IBOA[b]	MP	FM 1	FM 2	Colophonium	
2022 Denmark	7	4 (57.1%)				20
2021 Spain	8	1 (12.5%)	1 (12.5%)	1 (12.5%)	2 (25%)	36
2021 Belgium	14	4 (28.6%)	3 (21.4%)			47
2021 Sweden	3	2 (66.7%)		1 (33.3%)	1 (33.3%)	52
2020 Portugal	8	1 (12.5%)	2 (25%)			73
2020 Belgium	10	1 (10%)	1 (10%)		1 (10%),	70
2020 Sweden	13	2 (15.4%)	1 (7.7%)	2 (15.4%)	1 (7.7%)	56
2020 Sweden	6	1 (16.7%)	1 (16.7%)			21
2019 Sweden	10	1 (10%)	1 (10%)	1 (10%)		41
2019 Belgium	47	8 (17.0%)	3 (6.4%)		4 (8.5%)	59
2019 Belgium, Sweden	3	1 (33.3%)	2 (66.7%)	1 (33.3%)		54
2019 Belgium, Sweden	5	2 (40%)				57
2018 France	4	2 (50%)				63
2017 Belgium, Sweden	11	2 (18.2%)	3 (27.3%)			31
Range percentages positive		10-66.7%	0-67%	0-33.3%	0-33.3%	
Median		17.6%	14.6%	15.4%	10%	
Mean		21.5%	13.8%	16.2%	11.1%	

Abbreviations: FM 1, Fragrance mix 1; FM 2: Fragrance mix 2; IBOA, isobornyl acrylate; MP, *Myroxylon pereirae* resin (balsam of Peru).
[a]Individual fragrances such as linalool and limonene hydroperoxides are not included in this table, as the total number of patients tested with it are usually not mentioned.
[b]Includes only IBOA-positive patients who were also tested with the European baseline series.

TABLE 7 Frequency of co-reactivity to (meth)acrylates in patients sensitised to IBOA.

Year and country	Nr. pat. IBOA pos[a]	Nr. pat. (M)A pos. (%)	Positive (meth)acrylates and comments	References
2021 Spain	8	1 (13%)	HPMA, HDDA, HEA, bis-EMA, THFMA	36
2021 Belgium	14	2 (14%)	MMA, TREGDMA	47
2020 Portugal	8	0		73
2020 Belgium	10	2 (20%)	BA, EA, HEA	70
2020 Spain	5	1 (20%)	MMA	38
2020 Sweden	6	0	One reaction to ethyl cyanoacrylate, which is known *not* to cross-react to or from (meth)acrylates	21
2020 Sweden	13	1 (8%)	2-carboxyethyl acrylate	56
2019 Belgium, Sweden	3	0		54
2019 Germany	5	1 (20%)	HEA	15
2019 Belgium	48	14 (29%)	8 reactions to EA and 3?+ reactions to EA; see text for more data	59
2019 Finland	Max. 35	4 (min. 11%)	All had previously used nail cosmetics	39
2018 France	4	1 (25%)	HEA, EA, HEMA; previously used nail cosmetics without dermatitis	63
2017 Belgium, Sweden	9	1 (11%)	HPA	31

Abbreviations: BA, butyl acrylate; bis-EMA, 2,2-bis(4-[2-Methacryloxyethoxy]phenyl)propane; EA, Ethyl acrylate; EHA, etylhexyl acrylate; HDDA, 1,6-Hexanediol diacrylate; HEA, hydroxyethyl acrylate; HEMA, 2-hydroxyethyl methacrylate; HPA, hydroxypropyl acrylate; HPMA, 2-hydroxypropyl methacrylate; MMA, methyl methacrylate; THFMA, tetrahydrofurfuryl methacrylate; TREGDMA, triethylene glycol dimethacrylate.
[a]Includes only IBOA-positive patients who were also tested with a (meth)acrylate series.

all of the positive compounds. Most often, the finding of multiple positive reactions is explained as the result of cross-allergy. Indeed, it is generally acknowledged that primary sensitization to methacrylates may result in both methacrylate and acrylate cross-sensitization. Conversely, patients sensitised to acrylates may cross-react to other acrylates but are unlikely to show cross-sensitization to methacrylates.[105] IBOA appears to be an exception to the rule. Many authors have observed an absence of co-reactivity to other (meth)acrylates[21,54,73] or a low number of such reactions[31,36,38,39,47,56,70] in patients sensitised to IBOA. Also, in a number of cases where co-reactions were present, the patients had used acrylate-containing nail cosmetics acting as a possible source for these sensitizations.[39,63]

In a large study from Belgium, 48 patients with ACD from FSL and reacting to IBOA were tested with a (meth)acrylate series.[59] Only 14 (29%) had positive reactions to one or more other (meth)acrylates. In 12 of these individuals (86%), ethyl acrylate (EA) reacted positively; in 8/12 (67%) EA was the only positive reaction. In 2 EA-positives, there was only one other positive patch test, to triethylene glycol diacrylate and ethylhexyl acrylate, respectively. One EA-allergic patient co-reacted to 4 acrylates and one methacrylate. The last patient co-reacted to 6 acrylates and 3 methacrylates. It was not mentioned whether the 2 patients with multiple (meth)acrylate reactions, both women, had used nail cosmetics or had other sources of (meth)acrylate exposure. The authors did not discuss these results.[59]

The data on cross-reactivity to (meth)acrylates in other case series of patients allergic to IBOA are summarised in Table 7. In all studies, no or occasional co-reactions were observed and in such patients, mostly to a few (meth)acrylates only. Indeed, of the 168 IBOA-allergic patients presented in these studies, only 28 (17%) had one or more co-reactions.

These data provide a strong indication that IBOA has a very limited tendency for cross-reactions to other acrylates or methacrylates, notwithstanding the large share of positive reactions to ethyl acrylate in patients with co-sensitizations in one large study.[59] It has been suggested that the special branched structure of IBOA may prevent cross-reactivity to other acrylates.[70]

Concerning the reverse situation, IBOA cross-reacting from other (meth)acrylates: in previous studies no such co-reactions to IBOA have been observed in—at least 70—patients primarily sensitised to other (meth)acrylates.[67,76,106]

2-Phenoxyethyl acrylate. In a 2021 study from Belgium,[47] of 14 patients sensitised to IBOA from the use of the FSL sensor 9 (60%) co-reacted to 2-phenoxyethyl acrylate 0.1% pet. Analyses with gas chromatography–mass spectrometry (GC–MS) of acetone extracts of several brands of glucose sensors (incl. FSL) and insulin infusion sets ($n = 6$) failed to identify 2-phenoxyethyl acrylate (PEA) in any device. However, IBOA was found to be a contaminant of the in-house prepared PEA patch test preparation.[47]

Other (meth)acrylates. Four patients allergic to IBOA were patch tested with isobornyl methacrylate (IBOMA) 2% pet. and 2 (50%) had

positive reactions to IBOMA. These were considered to be cross-reactions to isobornyl acrylate.[47]

4.3.2 | Colophonium and colophonium derivatives

Colophonium (colophony, rosin) (CAS number 8050-09-7; EC-number 232-475-7) is the non-volatile residue left after distilling off the volatile oil from the oleoresin obtained from *Pinus palustris* and other species of *Pinaceae*. Colophonium is composed of about 90% resin acids (mainly abietic acid) and 10% neutral substances, of which the resin acids and their auto-oxidation products are the allergenic components. Colophonium and their derivatives (modified colophonium) may be used in adhesives, sticky tapes, hydrocolloid dressings, cosmetics, medical devices, paper products, printing inks, polishes, stringed instruments, paints, lacquers, soldering products and many other industrial and consumer applications. The substance is routinely tested at 20% pet. in the European Baseline series (EBS). Derivatives of colophonium may have a different allergenic potential from unmodified colophonium and some (e.g., abietic acid, hydroabietyl alcohol) may not always cross-react to colophonium tested in the EBS, possibly resulting in missed cases of sensitization to colophonium when the derivatives are not tested separately.[32,46,107,108] In 2019–2020, the frequency of positive patch test reactions to colophonium in 13 European countries ranged from 0.6% to 5.25% (median 3.6%), mean 3.3% (564 positives in 16 994 patients patch tested).[102]

ACD from colophonium or modified colophonium has been reported in patients using the Dexcom G7 sensor, Enlite sensor, the Omnipod pump, the Omnopid DASH[32] the FSL sensor and the TouchCare A6 pump and sensor. The allergenic materials were present in the adhesive patches as confirmed by the manufacturers of Enlite,[45] Omnipod[45] and TouchCare A6.[44] Colophonium (derivatives) have never been present in the adhesive patch of FSL (info from manufacturer).[39] The colophonium-derivative methyl dehydroabietate has been identified by gas chromatography–mass spectrometry (GC–MS) analyses of acetone extracts in Enlite (adhesive patch and housing),[54] FSL (housing)[74] and TouchCare A6 sensor and pump (adhesive patches and housings).[44] Colophonium-related substances, including hydrogenated resin acids and derivatives have been found in the Dexcom G7 sensor.[32]

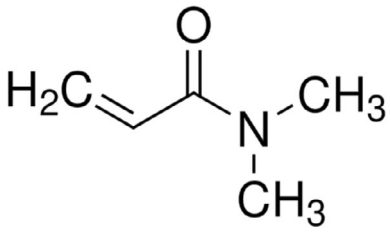
ACD from (modified) colophonium has been most frequently observed with the Enlite sensor ($n = 20$): a case series of (a maximum of) 6 patients,[46] a series of 5,[39] a series of 4[36] and 5 single case reports.[38,45,54,70,84] There are 3 single case reports of ACD from colophonium in the Omnipod pump,[44,45,77] 2 patients with ACD from modified colophonium in the FSL sensor[74] and in the Dexcom G7 sensor[32] and one case report each of TouchCare A6[44] and Omnipod DASH.[44] Most of these patients reacted to patch testing with colophonium 20% in the baseline series, sometimes accompanied by reactions to colophonium-derivatives.

In some patients, however, colophonium in the EBS was negative or? +, and the diagnosis of contact allergy to (modified) colophonium was based on positive patch test reactions to derivatives of colophonium. A patient with ACD from FSL had a doubtful reaction to colophonium but strongly positive patch tests to the derivatives methyl rosinate (methyl ester of rosin), methyl hydrogenated rosinate (hydrogenated rosin ester) and methyl dihydroabietate (hydrogenated methyl abietate).[74] Another patient with ACD from Enlite had a negative reaction to colophonium in the baseline series, but positive reactions to its derivative hydroabietyl alcohol (Abitol) and to a piece of the adhesive patch, known to contain modified colophonium.[39] A 3-year-old girl with ACD from Enlite was negative to colophonium, but positive to 'Enlite sensor', 'plastic support of sensor, grated' and modified colophonium (not specified).[36] In a woman aged 41 with ACD from Enlite, colophonium was positive at D2 but negative at D4. However, she did react to the derivative glyceryl rosinate and to the colophonium-containing adhesive patch.[54] A 9-year-old boy with ACD from Dexcom G7, which was found to contain colophonium-related substances including hydrogenated resin acids, did not react to colophonium 20% pet., had a weakly positive reaction to colophonium 60% in Softisan, but strong reactions to methyl hydrogenated rosinate and glyceryl hydrogenated rosinate.[32]

Summaries of case series and case reports of ACD to sensors and pumps/infusion sets caused by colophonium will be shown in part 2 of this article.

4.3.3 | *N,N*-Dimethylacrylamide

N,N-Dimethylacrylamide (CAS number 2680-03-7; EC number 220–237-5; molecular formula C_5H_9NO; IUPAC name *N,N*-dimethylprop-2-enamide; synonyms: 2-propenamide, *N,N*-dimethyl-; acrylamide, *N,N*-dimethyl-) is the acrylamide derivative that conforms to the structural formula shown below. The commonly used abbreviation for *N,N*-dimethylacrylamide is DMAA. It is used (like IBOA) as monomeric diluent in ultraviolet-curing adhesives.[57] It also has applications as (co-)polymer in coatings, synthetic fibres, and drug-releasing hydrogels.[39] DMAA is often used in combination with IBOA.[57]



In 2019, *N,N*-dimethylacrylamide (DMAA) was found to be an important sensitizer in the FreeStyle Libre sensor, in which DMAA had previously been identified by gas chromatography–mass spectrometry (GC–MS).[57] Of 7 patients suspected of ACD to FSL, all 7 had positive patch tests to DMAA 0.1% pet. and 6 of these also reacted to IBOA. Further analyses with GC–MS indicated the presence of DMAA in the sensor housing and IBOA in the sensor housing and the adhesive patch.

The authors considered it likely that IBOA and DMAA originated from an adhesive used to join the top and bottom parts of the plastic cover of the sensor. The high number of concomitant reactions to DMAA and IBOA was explained by simultaneous exposure to these substances during use of the sensor. Structural differences between the chemicals made cross-reactions between them unlikely.[57]

In Sweden, 4 more cases of ACD from DMAA in FSL were detected by testing with a medical device series containing DMAA 0.1% and 0.3% pet. One of these sensitizations was detected only by testing with 0.3% and a late reading at D7. It was advised to add the 0.3% pet. concentration of both DMAA and IBOA to a medical device test series and it was stressed that a reading on D7 is necessary.[56]

In Finland, one patient who had an allergic reaction to the Enlite sensor reacted positively to a patch test with DMAA 0.1% pet.[39]; the presence of DMAA in this sensor has been shown.[54] A patient from France who had ACD from the Omnipod insulin pump had positive patch tests to DMAA 0.1% and DPGDA. Chemical analyses showed DPGDA to be present in the adhesive and in the pump, but no DMAA.[62] Investigators from Sweden, however, identified (but not quantified) DMAA in an Omnipod device. One of their female patients with ACD from an Omnipod had positive patch tests to DMAA. It was uncertain whether she had been sensitised to DMAA in Omnipod (of which some batches contain DMAA and others not) or that she had previously been sensitised to DMAA from using FSL.[61]

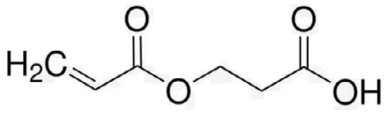
Before these publications of contact allergy to DMAA in diabetes devices, there appears to have been only one report of contact allergy to DMAA. This concerned a female worker at a factory assembling surgical needles, who had developed a blistering rash on the dorsa of her fingers and chin 2–3 months after a new adhesive had been introduced in the production process. Patch tests were positive to the adhesive 0.1% pet. and to 2 of its ingredients, DMAA (tested at 1% pet.) and tetrahydrofurfuryl acrylate (tested at 0.2% pet.).[109]

4.3.4 | Other acrylates

β-Carboxyethyl acrylate (2-Carboxyethyl acrylate)

β-Carboxyethyl acrylate (preferred name: 2-carboxyethyl acrylate; CAS number 24615-84-7; EC number 246-359-9; molecular formula $C_6H_8O_4$; IUPAC name 3-prop-2-enoyloxypropanoic acid; synonyms: 2-propenoic acid, 2-carboxyethyl ester) is the carboxyethyl ester of acrylic acid. Its structural formula is shown below.

2-Carboxyethyl acrylate is used in the preparation of DNase enzyme derivatives that act as potent preventative material of bacterial adhesion and biofilm formation in biomaterials. 2-Carboxyethyl acrylate is also used for the production of acrylic, vinyl acrylic, and styrene acrylic polymers, which are distinguished by their low glass transition temperatures (<30°C) as homopolymers. They are characterised by greater elasticity, as well as improved adhesion.[110] Its function in cosmetics is described as 'nail conditioning'.



Contact allergy to β-carboxyethyl acrylate has caused ACD from its presence in a glue used to fix the needle into the plastic of 3 insulin infusion sets in 2 patients from Belgium. Both women were also allergic to 3 other ingredients of the glue, IBOA, phenoxypoly(ethyleneoxy)ethyl acrylate and 1-hydroxycyclohexyl phenyl ketone (1-benzoylcyclohexanol).[66] Details will be presented in part 2.

In Poland, 40 of 80 workers of a plant manufacturing television (TV) receivers developed work-related eczema of the hands several weeks to months after the introduction of a new acrylic glue containing 25%–50% IBOA, 10%–25% acrylic acid, 10%–25% *N,N*-dimethylacrylamide and 2.5% β-carboxyethyl acrylate. When all 80 were patch tested, 12 had positive reactions to a total of 35 acrylates, most frequently TREGDA ($n = 10$) and DEGDA ($n = 9$). Three of the patients reacted to acrylates in the glue, all to β-carboxyethyl acrylate 0.1% pet., whereas none had positive reactions to IBOA 0.1% pet. Two of these 3 had chronic hand eczema, but the third had no skin lesions.[106]

In a series of 15 patients who had developed cutaneous reactions to FSL sensors and who were tested with a medical device series containing 2-carboxyethyl acrylate 0.1% pet., one individual reacted to IBOA, *N,N*-dimethylacrylamide (DMAA) and to 2-carboxyethyl acrylate. All 3 reactions were positive at D7 only. IBOA and DMAA are known to be present in FSL, but the presence of 2-carboxyethyl acrylate has not been confirmed and the significance of this sensitization, therefore, was unclear.[56]

Dipropylene glycol diacrylate

In 2022, Swedish investigators presented three patients who had developed ACD from dipropylene glycol diacrylate (DPGDA) in the Omnipod insulin pump.[61] All patients tested positive to 0.1% DPGDA in pet., two of them additionally to a 0.01% concentration and one had positive reactions to the adhesive patch of the pump and 2 acetone extracts. DPGDA was found in the extracts of the adhesive patches removed from the pump and from the Omnipod pumps themselves brought in by the patients, in estimated concentrations corresponding to a total amount of 1–10 μg in both the adhesive patches and in pumps.

An Omnipod pump from an earlier batch (expiry date September 2020) contained tripropylene glycol diacrylate, IBOA, *N,N*-dimethylacrylamide, di(ethyleneglycol)ethyl ether acrylate (DEGEA) but no DPGDA. One of the patients reacted positively to all of these allergens except DEGEA, which was not tested. It was concluded that the contents of Omnipod have changed over time and that, when ACD to medical devices is suspected, DPGDA 0.1% pet. should be tested. Further information will be provided in part 2. Soon thereafter, another patient with ACD from DPGDA was reported from France (details in part 2 of this article).[62]

Previously, occupational ACD to DPGDA in UV-cured paint had been reported in a 24-year-old male student, who worked temporarily in a paint factory on the canning of different types of paint.[111] Another worker in a paint factory developed a chemical burn from paint containing DPGDA on his working shoes, followed by active sensitization resulting in occupational ACD on the patient's dorsal feet.[112] Finally, a paint laboratory worker in Finland developed ACD from DPGDA in a UV-lacquer containing 34% DPGDA as shown by chemical analysis.[113]

Ethyl cyanoacrylate

Ethyl cyanoacrylate and other cyanoacrylates such as octyl cyanoacrylate are strong adhesives used for a variety of medical, industrial, and cosmetic applications. They are well-known causes of ACD, especially from their presence in cosmetic glues (for nails, hair- and eyelash extensions), anaerobic sealants and topical skin adhesives for wounds.[114–119] Ethyl cyanoacrylate present in the Dexcom G4 platinum glucose sensor caused ACD in 7 patients.[30,38,41,48,49,120] Summaries of these case reports will be shown in part 2 of this article.

Ethyl cyanoacrylate was found in extracts of both the adhesive part and the sensor part of the device, with approximate contents of 0.9 mg/cm^2 in the adhesive patch and 1.0 mg/cm^2 in the sensor.[49] Its presence in the device was confirmed by the manufacturer; ethyl cyanoacrylate-containing glue was used to attach the sensor pod to the adhesive non-skin part of the adhesive patch.[30,48,49] In response to numerous reports of intolerance to the Dexcom G4 Platinum, the company changed the manufacturing process by not using glues anymore but by attaching the sensor to the dermal patch using a thermic heat staking technique, thus avoiding the triggering intermediate adhesive layer.[57,121] Apparently, sensors produced after August 15, 2016 no longer contained ethyl cyanoacrylate.[48] The later versions (Dexcom G5 and G6) never contained ethyl cyanoacrylate.

1,6-Hexanediol diacrylate

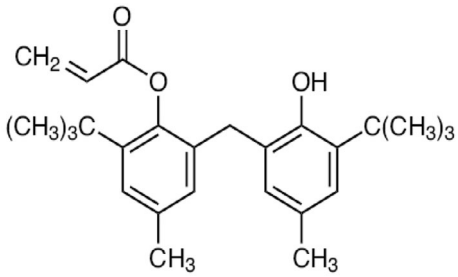
1,6-Hexanediol diacrylate (HDDA) is a difunctional acrylate ester monomer used in the manufacture of polymers. It is particularly useful in ultraviolet light-cured applications, including adhesives, sealants, alkyd coatings, elastomers, and photopolymers. In photo-cured inks, HDDA improves adhesion, hardness, abrasion and heat resistance.[122] HDDA was the cause of ACD in a patient who had used the Medtronic Guardian 4 sensor. This device consists of two parts—a sensor and a reusable transmitter. By gas chromatography–mass spectrometry (GC–MS), IBOA and *N,N*-dimethylacrylamide (DMAA), but no other acrylates, were observed in the extract of the sensor and in the extract of its adhesive patch. In the extract of the transmitter, however, 1,6-hexanediol diacrylate was identified in an estimated concentration of 5–10 ppm in 0.5 mL extract. The patient had positive patch tests to HDDA 0.1% pet. and 0.03%, 0.01%, 0.003% and 0.001% in acetone, the acetone extract and a large number of acrylates. The manufacturer confirmed the presence of HDDA in the transmitter, which was coated with a UV-cured lacquer containing HDDA.[123]

Cases of ACD to HDDA have (among others) been caused by its presence in a hospital wristband,[124] printing materials,[125] in ostomy pouch adhesives[126] and pipe relining resins.[127]

A lab worker in a paint factory was sensitised by accidental contact with pure HDDA[128] and a worker in the printing industry was also sensitised after a single accidental exposure.[125] Extensive contact with HDDA in UV-cured printing inks in a patient allergic to HDDA resulted in ACD progressing into erythema multiforme and later toxic epidermal necrolysis, which was confirmed by histopathology.[129]

2,2′-Methylenebis(6-tert-butyl-4-methylphenol) monoacrylate

2,2′-Methylenebis(6-*tert*-butyl-4-methylphenol) monoacrylate (CAS number 61167-58-6; EC number 262-634-6; molecular formula $C_{26}H_{34}O_3$; IUPAC name [2-*tert*-butyl-6-[(3-*tert*-butyl-2-hydroxy-5-methylphenyl)methyl]-4-methylphenyl] prop-2-enoate; synonyms: 2-*tert*-butyl-6-(3-*tert*-butyl-2-hydroxy-5-methylbenzyl)-4-methylphenyl acrylate; 2-(1,1-dimethylethyl)-6-[[3-(1,1-dimethylethyl)-2-hydroxy-5-methylphenyl]methyl]-4-methylphenyl acrylate [ECHA (European Chemical Agency) name]) is the acrylate that conforms to the structural formula shown below. The commonly used abbreviation for this chemical is MBPA.



MBPA is a heat and light stabiliser and an antioxidant used in a wide range of adhesive, plastic, and elastomer materials. This substance is an effective alkyl radical scavenger, which property is especially useful in processes at high temperatures and in low oxygen environments, such as during the initial mixing of adhesives.[52]

Contact allergy to MBPA was first reported by Swedish investigators in 2021.[52] They investigated 3 patients with suspected ACD to the Dexcom G6 sensor. Updated chemical analyses had shown the presence of a new acrylate in this sensor, 2,2′-methylenebis(6-*tert*-butyl-4-methylphenol) monoacrylate, which had not been observed in previous analyses of older Dexcom G6 sensors. When patch tested, all 3 were positive to MBPA 0.3% pet.[52] The manufacturer reported that the Dexcom G6 sensor had a new, stronger adhesive since October 2019[130] (not mentioning the presence of specific chemicals).

Shortly thereafter, another 4 patients with ACD from MBPA in Dexcom G6 were reported from Sweden[131] and 5 from Germany.[53] In the Swedish study, 2 of 4 sensitizations were identified only when MBPA was tested at 1.5% pet. (20 controls negative, no late-appearing reactions).[131] In the study performed by German investigators, MBPA was also identified in extracts of the sensor but not in

Dexcom G6 devices from 2018 and 2019. This confirmed the allergenic role of MPBA in the adhesive of the 2020 series of Dexcom, the composition of which had changed for better fixation to the skin.[53]

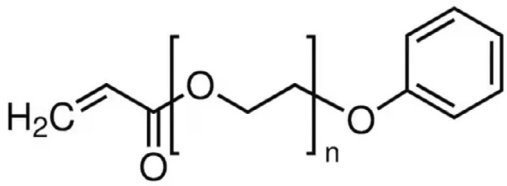
More detailed information on the patients allergic to MBPA in Dexcom G6 and investigations will be presented in part 2 of this article.

Methyl methacrylate

Contact allergy to methyl methacrylate present in the catheter of an insulin pump caused ACD in one woman in an early report from Italy.[132] Details will be presented in part 2.

Phenoxypoly(ethyleneoxy)ethyl acrylate

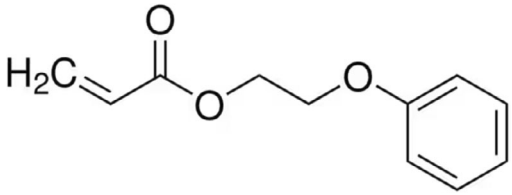
Phenoxypoly(ethyleneoxy)ethyl acrylate (CAS number 56641-05-5; EC number 500-133-9; molecular formula $(C_2H_4O)_nC_9H_8O_2$; IUPAC name not available; synonyms: phenol, ethoxylated, esters with acrylic acid; polyethylene glycol phenyl ether acrylate) is the acrylate that conforms to the structural formula shown below. The commonly used abbreviation for this chemical (mixture) is PEEA.



Contact allergy to phenoxypoly(ethyleneoxy)ethyl acrylate has caused ACD from its presence in a glue used to fix the needle into the plastic of 3 insulin infusion sets in 2 patients from Belgium. Both women were also allergic to 3 other ingredients of the glue, IBOA, 1-hydroxycyclohexyl phenyl ketone (1-benzoylcyclohexanol) and β-carboxyethyl acrylate.[66] Details will be presented in part 2 of this article. Six years later, in Finland, another patient also reacted to a glue in an insulin set, almost certainly the same glue as in the study from Belgium.[133] The patient reacted to 1 of the components of the glue, provided by the manufacturer, phenoxypoly(ethyleneoxy)ethyl acrylate (PEEA) 0.01% pet. By gas chromatography–mass spectrometry (GC–MS) analysis PEEA was found to contain around 10 phenoxyethoxyethyl acrylates of different chain length. These comprised 0.9% 2-phenoxyethyl acrylate, 13% phenoxy(mono)ethoxyethyl acrylate (which is also 2-phenoxyethyl acrylate) and 81% phenoxyethoxyethyl acrylate oligomers: 22% phenoxydiethoxyethyl acrylate, 21% phenoxytriethoxyethyl acrylate, and 38% phenoxypolyethoxyethyl acrylate.[133]

2-Phenoxyethyl acrylate

2-Phenoxyethyl acrylate (CAS number 48145-04-6; EC number 256-360-6; molecular formula $C_{11}H_{12}O_3$; IUPAC name 2-phenoxyethyl prop-2-enoate; synonyms: 2-propenoic acid, 2-phenoxyethyl ester; ethylene glycol phenyl ether acrylate; phenyl cellosolve acrylate) is the 2-phenoxyethyl ester of acrylic acid. Its structural formula is shown below. The commonly used abbreviation for 2-phenoxyethyl acrylate is PEA.



2-Phenoxyethyl acrylate (PEA) serves as a monomer in the synthesis of multifunctional polymers, which may have specific properties such as shape memory behaviour and responsiveness to external stimuli. It is also used to dilute low-molecular-weight compounds and adjust the viscosity of systems; in addition, PEA participates in light-curing processes, affecting the speed of polymerisation.[134]

There are no proven cases of ACD to diabetes devices caused by PEA. However, the substance phenoxypoly(ethyleneoxy)ethyl acrylate (PEEA), which has caused ACD in insulin pumps in 3 patients[66,133] contained nearly 14% 2-phenoxyethyl acrylate (paragraph 4.3.4). As it are the monomers in acrylates that are the usual allergens, it is likely that PEA was the sensitizer or one of the sensitizers in PEEA.

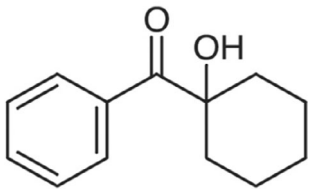
Co-reactivity to PEA in patients sensitised to IBOA was not the result of cross-allergy, but was caused by the contamination of the IBOA test substance with PEA[47] (paragraph 4.3.1.1.3). A patient who had become sensitised to dipropylene glycol diacrylate in the Omnipod pump co-reacted to many other acrylates including 2-phenoxyethyl acrylate 0.1% pet., which was probably a cross-reaction.[61]

PEA was, however, one of the allergens in a case of ACD to another medical device, a disposable blood pressure cuff, in a patient with diabetes. The other allergen was IBOA, to which the patient had previously become sensitised by the use of the FSL sensor. Both IBOA and PEA were identified in the cuff by gas chromatography–mass spectrometry (GC–MS).[88]

4.3.5 | Other culprit allergens

1-Benzoylcyclohexanol (1-hydroxycyclohexyl phenyl ketone)

1-Benzoylcyclohexanol (preferred name: 1-hydroxycyclohexyl phenyl ketone); CAS number 947-19-3; EC number 213-426-9; molecular formula $C_{13}H_{16}O_2$; IUPAC name (1-hydroxycyclohexyl)-phenylmethanone) is the ketone that conforms to the structural formula shown below. 1-Hydroxycyclohexyl phenyl ketone is used as photo-initiator in UV-radiation-curable technologies which are used in various applications and industry branches such as printing and packaging, coatings, furniture, flooring and adhesives.[135] Its function in cosmetics is described as 'binding'.



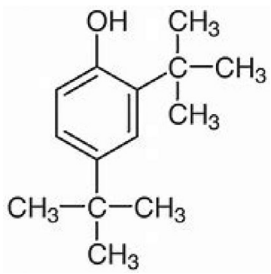
Contact allergy to 1-hydroxycyclohexyl phenyl ketone has caused ACD from its presence in a glue used to fix the needle into the plastic of 3 insulin infusion sets in 2 patients from Belgium. Both women were also allergic to 3 other ingredients of the glue, IBOA, phenoxypoly(ethyleneoxy)ethyl acrylate and β-carboxyethyl acrylate.[66] Details will be presented in part 2.

Butylated hydroxytoluene

Butylated hydroxytoluene (BHT) is an antioxidant used in food, cosmetics, metalworking fluids, pharmaceuticals, paints, glues, fillers, adhesives, plastic materials and many other products. It is a well-known, albeit not very frequent, cause of ACD, especially in cosmetics.[136] One patient allergic to the FSL sensor, who was patch test-negative to IBOA and *N*,*N*-dimethylacrylamide (DMAA) (the usual allergens in FSL) reacted to BHT 2% pet. and the structurally related chemical 2,4-di-*tert*-butylphenol (2,4-DTBP) 1% pet. Gas chromatography–mass spectrometry (GC–MS) analyses indicated the presence of both compounds in FSL. The authors suggested that a primary sensitization to BHT with a cross-allergy to 2,4-DTBP or vice versa could explain the simultaneous positive reactions.[56] However, as both chemicals are present in FSL, the allergy to BHT and 2,4-DTBP may also have been the result of concomitant sensitization.

*2,4-di-*tert*-Butylphenol*

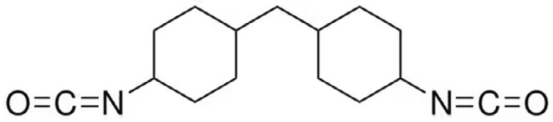
2,4-di-*tert*-Butylphenol (CAS number 96-76-4; EC number 202-532-0; molecular formula $C_{14}H_{22}O$; IUPAC name 2,4-di*tert*-butylphenol; synonyms: phenol, 2,4-di-*tert*-butyl-; 2,4-di-*tert*-butylhydroxybenzene) is the phenolic compound that conforms to the structural formula shown below. The commonly used abbreviation for this chemical is 2,4-DTBP.



2,4-di-*tert*-Butylphenol (2,4-DTBP) is used industrially as UV stabiliser and an antioxidant for hydrocarbon-based products ranging from petrochemicals to plastics. Illustrative of its usefulness, it prevents gumming in aviation fuels. It is also a natural product found in *Bacillus subtilis*, *Streptomyces parvulus*, and other organisms.[137] A PubMed search for contact allergy to this compound retrieved zero hits. One patient allergic to the FSL sensor, who was patch test-negative to IBOA and *N*,*N*-dimethylacrylamide (DMAA) (the usual allergens in FSL) reacted to 2,4-DTBP 1% pet. and to the structurally related chemical BHT 2% pet. Gas chromatography–mass spectrometry (GC–MS) analyses indicated the presence of both compounds in FSL. In another 60 patients with adverse skin reactions to medical devices patch tested with 2,4-DTBP no positive, doubtful, or irritant reactions were observed. The authors suggested that a primary sensitization to 2,4-DTBP with a cross-allergy to BHT or vice versa could explain the simultaneous positive reactions.[56] However, as both chemicals are present in FSL, the allergy to 2,4-DTBP and BHT may also have been caused by concomitant sensitization.

Dicyclohexylmethane-4,4′-diisocyanate

Dicyclohexylmethane-4,4′-diisocyanate (CAS number 5124-30-1; EC number 225-863-2; molecular formula $C_{15}H_{22}N_2O_2$; IUPAC name 1-isocyanato-4-[(4-isocyanatocyclohexyl)methyl]cyclohexane; synonyms: 4,4′-methylenedicyclohexyl diisocyanate; bis(4-isocyanatocyclohexyl) methane; 4,4′-diisocyanato-methylenedicyclohexane; 4,4′-methylenebis (cyclohexyl isocyanate); hydrogenated MDI) is the cycloaliphatic diisocyanate that conforms to the structural formula shown below. Commonly used abbreviations for dicyclohexylmethane-4,4′-diisocyanate are (4,4′)-DMDI (from dicyclohexylmethane-4,4′-diisocyanate) and (4,4′)-HMDI (from hydrogenated MDI).



Isocyanates are mainly used in the production of polyurethane resins, which can appear in a large variety of forms and products, including coatings for flooring, roofing, adhesives, sealants, flexible foams, rigid foams, elastomers and binders used in paint and lacquers.[138] Handling of isocyanates is a well-known occupational health hazard, mainly because of the adverse effects on the respiratory tract. In spite of the large numbers of workers exposed and the fact that isocyanates (including DMDI) have been found to be potent sensitizers in the guinea-pig maximisation test (GPMT),[138] relatively few reports on contact allergy to dicyclohexylmethane-4,4′-diisocyanate are found in the literature. In a company manufacturing medical equipment, 13 patients became sensitised to DMDI in a glue.[139] Single case reports have described sensitization to DMDI in a DMDI-charged cartridge to create resin-coated '3D labels',[140] and an industrial chemical product containing 40%–70% DMDI.[141] Older literature of allergic reaction to DMDI can be found in Reference 140.

An 8-year-old boy had ACD from IBOA, colophonium-derivatives and DMDI present in the Dexcom G7 sensor.[32] The same boy at age 6 had been reported because of problems while using the Dexcom G6 sensor and the mylife Ypsopump insulin pump.[51] He first developed

ACD to Dexcom G6 and a few months later to the pump. Patch testing revealed a strong sensitization to IBOA. At photographs taken on D7 no new reactions could be identified, but on D10 a new reaction was photographed which was interpreted to be DMDI 1% in pet. Acetone extracts made from both devices were analysed by gas chromatography–mass spectrometry (GC–MS) and IBOA was found in all four extracts. The GC–MS analyses also indicated the presence of DMDI in the extract made from the plastic part of the pump. It was considered likely that the ACD was caused by IBOA, but that DMDI-allergy may have contributed to the eczema caused by the mylife Ypso pump. The reaction to DMDI was noticed on D10. The authors acknowledged that this late-appearing patch test reaction may have indicated active sensitization. On the other hand, patch test reactions to isocyanates are known to sometimes appear late, also after the D7 reading in sensitised individuals. Unfortunately, the patient's guardian declined further investigation, so supplementary patch testing with DMDI to clarify this issue could not be performed.[51]

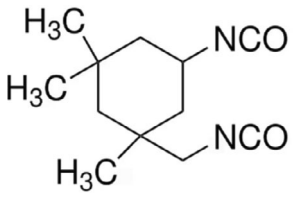
In another publication, one patient with ACD from a diabetes device (not specified) had a positive reaction to DMDI, but apparently it was not analysed whether the culprit device actually contained DMDI or other isocyanates.[142]

Epoxy resin

Contact allergy to epoxy resin used in an insulin pump to bind the tube (cannula) and the needle caused ACD in one patient reported in an early study from The Netherlands.[123] Details will be presented in part 2 of this article. Belgian investigators later stated that they had 2 similar cases of ACD from epoxy resin in the same insulin set on record.[66]

Isophorone diisocyanate

Isophorone diisocyanate (CAS number 4098-71-9; EC number 223-861-6; molecular formula $C_{12}H_{18}N_2O_2$; IUPAC name 5-isocyanato-1-(isocyanatomethyl)-1,3,3-trimethylcyclohexane; synonym: 3-isocyanatomethyl-3,5,5-trimethylcyclohexyl isocyanate) is the aliphatic diisocyanate that conforms to the structural formula shown below. Its commonly used abbreviation is IPDI. For general information on isocyanates see paragraph 4.3.5.



Contact allergy to isophorone diisocyanate appears to be very infrequent. In a retrospective study from the Finnish Institute of Occupational Health, over a period of nearly 13 years (1998–2010), only 9 patients were found to have had positive patch tests to IPDI, mostly related to hardeners for polyurethane paints.[143] In various other publications, positive patch test reactions to IPDI have been observed, but without data on specific exposure to this isocyanate (cited in Reference 144).

In a university hospital in Belgium, the patient files of 14 patients with suspected ACD from diabetes devices seen between November 2020 and March 2022 were reviewed.[50] Four patients who had previously developed ACD from FSL (and one also from the MiniMed Silhouette insulin pump) had shown positive patch tests to one or more allergens in the isocyanate series: three to 2,4-toluene diisocyanate (TDI) 2% pet., two to 4,4′-diaminodiphenylmethane (MDA) 0.5% pet., one to isophorone diisocyanate (IPDI) 1.0% pet. and one to polymeric methylene diphenyl diisocyanate (PMDI) 2.0% pet. The FSL sensors were found to contain 34 ppm MDI and 1.2 ppm IPDI and the MiniMed Silhouette insulin pump 0.1 ppm MDI. Thus, only the patient with a positive patch test reaction to IPDI had contact with the allergen to which he reacted, present the FSL sensor. The authors considered this reaction to IPDI to be relevant for the ACD previously caused by FSL in this patient.[50]

In an abstract from Sweden, two patients with ACD from a diabetes device (not specified) had a positive reaction to IPDI, but apparently it was not analysed whether the culprit device actually contained IPDI or other isocyanates.[142]

Nickel

Contact allergy to nickel present in the needle of their infusion sets caused severe localised ACD in two patients from Italy.[145,146] Details will be presented in part 2.

4.3.6 | Summary of allergens causing allergic contact dermatitis

Table 8 provides an overview of all allergens in diabetes devices that have caused ACD, with the sensors or pumps in which they were present, numbers of patients with ACD reported and references.

4.3.7 | Allergic contact dermatitis from auxiliary products

Patients using diabetes devices may also apply other products at the device sites, which can sensitise the patient and induce ACD or worsen existing dermatitis caused by the sensor or pump. Cleansing products, including wipes, are used to remove adhesive material from the skin. Skin wipes containing (modified) colophonium are commonly used to clean and prime the skin during diabetes device changes.[77] Sensitization to this material may not only cause ACD, but can also result in intolerance to diabetes devices themselves, as some have been shown to contain colophonium or -derivatives (paragraph 4.3.2; Table S1, present in the Supporting information). Patients experiencing an allergic reaction from their diabetes device may, on their own instigation or on the advice of their physician or diabetes nurse, apply a (hydrocolloid) adhesive between the device and their skin to prevent the allergic skin reaction from emerging or to ameliorate the

TABLE 8 Summary of allergens, culprit products containing the allergen and causing ACD, numbers of patients and references.

Allergen	Culprit products containing the allergen and causing ACD	References and [Number of patients]
1-Benzoylcyclohexanol	Cliniset, Clini Soft, and Disetronic insulin pumps	66 [2]
Butyl acrylate	Enlite sensor	46 [1]
Butylated hydroxytoluene (BHT)	FreeStyle Libre 1 sensor	56 [1]
2,4-di-*tert*-Butylphenol (2,4-DTBP)	FreeStyle Libre 1 sensor	56 [1]
β-Carboxyethyl acrylate	See under 1-Benzoylcyclohexanol	66 [2]
Colophonium	Enlite sensor	36 [3], 38 [1], 39 [4], 45 [1], 46 [not specified, max. 6], 70 [1], 84 [1]
	Omnipod insulin pump	44 [1], 45 [1], 77 [1]
	TouchCare A6	44 [1]
Colophonium-derivatives[a]	Dexcom G7 sensor	32 [2]
	Enlite sensor	36 [1], 39 [1], 54 [1]
	FreeStyle Libre 1 sensor	74 [2][b]
	Omnipod DASH pump	32 [1]
Dicyclohexylmethane-4,4′-diisocyanate (DMDI)[c]	Dexcom G7 sensor	32 [1]
	mylife Ypsopump Orbit micro-infusion set [C]	51 [1]
N,*N*-Dimethylacrylamide (DMAA)	Enlite sensor	39 [1]
	FreeStyle Libre 1 sensor	56 [4], 57 [7]
	Omnipod insulin pump	62 [1]
Dipropylene glycol diacrylate	Omnipod insulin pump	61 [3], 62 [1]
Epoxy resin	Unspecified insulin pump	55 [2], 107 [2]
Ethyl cyanoacrylate	Dexcom G4 Platinum sensor	30 [1], 38 [1], 41 [1], 48 [1], 49 [2], 120 [1]
1,6-Hexanediol diacrylate (HDDA)	Guardian 4 sensor, transmitter part	60 [1]
Isobornyl acrylate (IBOA)	See under 1-Benzoylcyclohexanol	66 [2]
Isobornyl acrylate (IBOA)	FreeStyle Libre 1 sensor	15 [5], 21 [6], 31 [15], 36 [7], 37 [34], 38 [5], 39 [51], 40 [1], 41 [10], 44 [1], 46 [8], 56 [13], 54 [4], 57 [6], 47 [18], 59 [53], 63 [2], 50 [4], 69 [3], 70 [11], 71 [39], 72 [8], 73 [8], 76 [1], 77 [1], 78 [1], 79 [2], 80 [1], 81 (1], 82 [1], 83 [2], 84 [2], 85 [1], 90 [3], 91 [1], 92 [1], 144 [1]
	FreeStyle Navigator II sensor	31 [1]
	Dexcom G6 sensor	42 [1], 51 [1], 52 [3], 50 [1]
	Dexcom G7 sensor	32 [2]
	Enlite sensor	36 [2], 38 [2], 41 [1], 54 [4], 47 [2], 50 [1], 70 [2], 84 [1]
	Miao-Miao transmitter	16 [1]
	MiniMed Quick-set infusion set	54/70 [1], 47 [1], 101 [1]
	MiniMed Sure-T infusion set	54/70 [1], 70 [1], 101 [1]
	mylife Ypsopump Orbit infusion set	51 [1]
	Omnipod insulin pump	21 [3], 40 [1], 41 [5], 44 [1], 46 [1], 63 [4], 50 [1], 69 [1], 77 [1]
	TouchCare A6 sensor and insulin pump	44 [1]
Isophorone diisocyanate (IPDI)	FreeStyle Libre 1 sensor	50 [1]
2,2′-Methylenebis(6-*tert*-butyl-4-methylphenol) monoacrylate (MBPA)	Dexcom G6 sensor (new, from early 2020 on)	52 [3], 53 [5], 131 [4]
Methyl methacrylate	Insulin pump Set Per Micro-Infusione	132 [1]

(Continues)

TABLE 8 (Continued)

Allergen	Culprit products containing the allergen and causing ACD	References and [Number of patients]
Nickel	Insulin pump (Atrapid M.C. Medi)	145 [1]
	Insulin pump, not specified	146 [1]
Phenoxypoly(ethyleneoxy)-ethyl acrylate (PEEA)	Unspecified insulin pump	66 [2], 133 [1]
Tripropylene glycol diacrylate (TPGDA)	Omnipod	61 [1]

[a]Abietic acid,[74] Abitol (hydroabietyl alcohol),[32,39,74] hydrogenated methyl abietate (methyl dihydroabietate),[74] hydrogenated rosin ester (methyl hydrogenated rosinate),[43,74] methyl abietate,[74] methyl rosinate (methyl ester of rosin),[74] glyceryl hydrogenated rosinate.[32]
[b]The FSL housing was shown to contain methyl dehydroabietate; this is a related colophonium-derivate, but was itself not patch tested.
[c]DMDI was found in the plastic part of the pump; the patients had a positive reaction to DMDI at D10; it was uncertain whether this was a late reaction or patch test sensitization.

dermatitis (part 2). These products may all contain (potential) allergens. Some patients use local anaesthetic preparations such as EMLA® cream and plaster (containing lidocaine and prilocaine) to diminish pain and discomfort associated with the application of diabetes devices.[20]

Long-term application, prolonged contact time with the skin and existing damage to the skin from irritation, irritant dermatitis or ACD all increase the risk of becoming sensitised to such auxiliary products. Reported contact allergies are shown in the next paragraph. Unfortunately, with the exception of colophonium in Skin Tac wipes[77] and prilocaine in EMLA,[20] the culprit allergens have not been investigated and identified.

Case reports and case series

Of 15 children with ACD to diabetes devices, three had positive patch test reactions to Adhesive remover wipes from Smith and Nephew (a fourth had a? + reaction) and four had reactions to EMLA plaster ($n = 3$) or cream ($n = 1$). These 4 were tested with prilocaine and lidocaine and one had a + reaction to prilocaine.[20] Two children had positive reactions to the analgesic Tapin (one plaster, one cream), one to Duoderm (and another had a? + reaction, she also reacted to colophonium) and one appeared to be allergic to TENSO adhesive bandage. Whether these products had actually caused ACD or contributed to it and what the (potential) allergens were was not mentioned.[20]

One patient was allergic to colophonium in Skin Tac™ wipe.[11] A 56-year-old man with ACD from colophonium in the FSL sensor used Skin Tac wipes, which aggravated the dermatitis. Colophonium was one of the ingredients in the wipe.[74] A 9-year old boy who had ACD from ethyl cyanoacrylate in the Dexcom G4 Platinum sensor was also allergic to colophonium, which was present in the Skin Tac wipes he was using.[48]

A 12-year-old boy with ACD from FSL had positive reactions to IBOA (present in FSL) and to a piece of a hydrocolloid dressing (Duoderm Extra Mince), which he regularly placed between his diabetes device and the skin to prevent cutaneous reactions. Colophonium gave a doubtful reaction (?+) on D4, whereas three colophony-derivatives were positive (++). It was not discussed whether (modified) colophonium was an ingredient of the hydrocolloid, but the possibility was subtly suggested.[74]

A 7-year-old boy was suspected of ACD to a diabetes device (not specified); the rash persisted despite trialling different sensors and adhesive tapes. During the consultation, the patient's mother replaced the sensor demonstrating the process and techniques involved and it was noted that Tac adhesive barrier products were additionally being used to further secure the device. Patch tests were positive to hydroabietyl alcohol (a colophonium-derivative) and to Skin Tac adhesive barrier wipes, which contained partially hydrogenated rosin (colophonium) as the tackifying agent. Colophonium in the European baseline series was negative, as is often the case with patients sensitised to modified colophonium products (chapter 4.3.2).[147]

A 3-year-old girl with ACD from colophonium in the Enlite sensor had a positive patch test to an 'Overtape dressing' and a moisturising cream (no further data available).[36] An 18-year-old female patient had a positive patch test to 'isopropyl alcohol wipes' (++ on D4), but there were no other positive reactions.[36]

An 8-year-old boy had developed ACD from IBOA, DMDI (dicyclohexylmethane-4,4′-diisocyanate) and (derivatives of) colophonium in the Dexcom G7 sensor. He also had suffered ACD from Duoderm extra thin, used to protect the skin from contact with the sensor's adhesive patch. A patch test with the dressing 'as is' was positive, very likely due to the presence of modified colophonium in Duoderm extra thin. Details of this patient can be found in part 2 of this article.[32]

4.4 | The glucose sensors and insulin pumps that have caused allergic contact dermatitis: An overview

Fifteen insulin pumps (of which 4 were not specified), 6 sensors and one transmitter (Miao-Miao) have caused one or more cases of ACD. These devices are shown in Table 9 in alphabetical order; also specified are the culprit allergens contained in them, the number of patients in who ACD was elicited and the literature references. The FreeStyle Libre sensor has caused most cases of ACD and contained the largest number of culprit allergens (butylated hydroxytoluene, colophonium-derivatives, 2,4-di-

TABLE 9 Summary of diabetes devices that have caused allergic contact dermatitis, culprit allergens, number of patients and literature references.

Diabetes device	Culprit allergens	References and [Number of patients]
Cliniset insulin pump	1-Benzoylcyclohexanol	66 [2]
	β-Carboxyethyl acrylate	66 [2]
	Isobornyl acrylate (IBOA)	66 [2]
Clini Soft insulin pump	1-Benzoylcyclohexanol	66 [2]
	β-Carboxyethyl acrylate	66 [2]
	Isobornyl acrylate	66 [2]
Dexcom G4 Platinum sensor	Ethyl cyanoacrylate	30 [1], 38 [1], 41 [1], 48 [1], 49 [2], 120 [1]
Dexcom G6 sensor	Isobornyl acrylate (IBOA)	42 [1], 51 (1], 52 [3], 50 [1]
Dexcom G6 sensor (new, from early 2020 on)	2,2′-Methylenebis(6-*tert*-butyl-4-methylphenol) monoacrylate (MBPA)	52 [3], 53 [5], 131 [4]
Dexcom G7 sensor	Colophonium-derivatives	32 [2]
	Dicyclohexylmethane-4,4′-diisocyanate (DMDI)	32 [1]
	Isobornyl acrylate	32 [2]
Disetronic insulin pump	1-Benzoylcyclohexanol	66 [2]
	β-Carboxyethyl acrylate	66 [2]
	Isobornyl acrylate (IBOA)	66 [2]
Enlite sensor	Butyl acrylate	46 [1]
	Colophonium	36 [3], 38 [1], 39 [4], 45 [1], 46 [not specified, max. 6], 70 [1], 84 [1]
	Colophonium-derivatives	36 [1], 39 [1], 54 [1]
	N,*N*-Dimethylacrylamide (DMAA)	39 [1]
	Isobornyl acrylate (IBOA)	36 [2], 38 [2], 41 [1], 54 [4], 47 [2], 50 [1], 70 [2], 84 [1]
FreeStyle Libre 1 sensor	Butylated hydroxytoluene (BHT)	56 [1]
	2,4-di-*tert*-Butylphenol (2,4-DTBP)	56 [1]
	Colophonium-derivatives	74 [2]
	N,*N*-Dimethylacrylamide	56 [4], 57 [7]
	Isobornyl acrylate (IBOA)	15 [5], 21 [6], 31 [15], 36 [7], 37 [34], 38 [5], 39 [51], 40 [1], 41 [10], 44 [1], 46 [8], 56 [13], 54 [4], 57 [6], 47 [18], 59 [53], 63 [2], 50 [4], 69 [3], 70 [11], 71 [39], 72 [8], 73 [8], 76 [1], 77 [1], 78 [1], 79 [2], 80 [1], 81 (1], 82 [1], 83 [2], 84 [2], 85 [1],90 [3], 91 [1], 92 [1], 144 [1]
	Isophorone diisocyanate (IPDI)	50 [1]
FreeStyle Navigator II sensor	Isobornyl acrylate (IBOA)	31 [1]
Guardian 4 sensor, transmitter part	1,6-Hexanediol diacrylate (HDDA)	60 [1]
Insulin pump (Atrapid M.C. Medi)	Nickel	145 [1]
Insulin pump Set Per Micro-Infusione	Methyl methacrylate	132 [1]
Miao-Miao transmitter	Isobornyl acrylate (IBOA)	16 [1]
MiniMed Quick-set infusion set	Isobornyl acrylate (IBOA)	54/70 [1], 47 [1]
MiniMed Sure-T infusion set	Isobornyl acrylate (IBOA)	54/70 [1], 70 [1]
mylife Ypsopump Orbit infusion set	Dicyclohexylmethane-4,4′-diisocyanate (DMDI)	51 [1]
	Isobornyl acrylate (IBOA)	51 [1]

(Continues)

TABLE 9 (Continued)

Diabetes device	Culprit allergens	References and [Number of patients]
Omnipod insulin pump	Colophonium	44 [1], 45 [1], 77 [1]
	N,N-Dimethylacrylamide (DMAA)	62 [1]
	Dipropylene glycol diacrylate	61 [3], 62 [1]
	Isobornyl acrylate (IBOA)	21 [3], 40 [1], 41 [5], 44 [1], 46 [1], 63 [4], 50 [1], 69 [1], 77 [1]
Omnipod DASH pump	Colophonium-derivatives	32 [1]
TouchCare A6 sensor, pump	Colophonium	44 [1]
	Isobornyl acrylate (IBOA)	44 [1]
Unspecified insulin pump ($n = 4$)	Epoxy resin	66 [2], 123 [2]
	Nickel	146 [1]
	Phenoxypoly(ethyleneoxy)ethyl acrylate (PEEA)	66 [2], 133 [1]

tert-butylphenol, *N,N*-dimethylacrylamide, IBOA and isophorone diisocyanate), followed by the Enlite sensor and the Omnipod insulin pump with 4 allergens each.

AUTHOR CONTRIBUTIONS

Anton de Groot: Conceptualization; investigation; visualization; project administration; writing – original draft; writing – review and editing. **Emma M. van Oers:** Conceptualization; investigation; visualization; writing – original draft; writing – review and editing. **Norbertus A. Ipenburg:** Formal analysis; visualization; writing – review and editing. **Thomas Rustemeyer:** Supervision; writing – review and editing.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

ORCID

Anton de Groot https://orcid.org/0000-0002-6666-7292
Norbertus A. Ipenburg https://orcid.org/0000-0003-0679-4131
Thomas Rustemeyer https://orcid.org/0000-0001-7580-0684

REFERENCES

1. Hartsough EM, Hylwa SA. Wearable woes: allergens in diabetic devices. *Dermatitis*. 2021;32(1):19-31. doi:10.1097/DER.0000000000000673
2. Jedlowski PM, Te CH, Segal RJ, Fazel MT. Cutaneous adverse effects of diabetes mellitus medications and medical devices: a review. *Am J Clin Dermatol*. 2019;20(1):97-114. doi:10.1007/s40257-018-0400-7
3. Cameli N, Silvestri M, Mariano M, Messina C, Nisticò SP, Cristaudo A. Allergic contact dermatitis, an important skin reaction in diabetes device users: a systematic review. *Dermatitis*. 2022;33(2):110-115. doi:10.1097/DER.0000000000000861
4. Aerts O, Herman A, Mowitz M, Bruze M, Goossens A. Isobornyl acrylate. *Dermatitis*. 2020;31(1):4-12. doi:10.1097/DER.0000000000000549
5. Kamann S, Wagner N, Oppel E. Modern diabetes devices for continuous blood sugar measuring: limitations due to contact allergies. *J Dtsch Dermatol Ges*. 2021;19(12):1715-1721. doi:10.1111/ddg.14621
6. Herman A, de Montjoye L, Tromme I, Goossens A, Baeck M. Allergic contact dermatitis caused by medical devices for diabetes patients: a review. *Contact Dermatitis*. 2018;79(6):331-335. doi:10.1111/cod.13120
7. Heinemann L, Kamann S. Adhesives used for diabetes medical devices: a neglected risk with serious consequences? *J Diabetes Sci Technol*. 2016;10(6):1211-1215. doi:10.1177/1932296816662949
8. Khatsenko K, Khin Y, Maibach H. Allergic contact dermatitis to components of wearable adhesive health devices. *Dermatitis*. 2020;31(5):283-286. doi:10.1097/DER.0000000000000575
9. Wagner N, Kamann S, Oppel E. Kontaktallergie auf Glukosemesssysteme und Insulinpumpen [Contact allergy due to insulin pumps and glucose sensor systems]. *Hautarzt*. 2020;71(3) German:205-210. doi:10.1007/s00105-019-04533-x
10. Nath N, Reeder M, Atwater AR. Isobornyl acrylate and diabetic devices steal the show for the 2020 American contact dermatitis society allergen of the year. *Cutis*. 2020;105(6):283-285.
11. Bembry R, Brys AK, Atwater AR. Medical device contact allergy: glucose monitors and insulin pumps. *Curr Derm Rep*. 2022;11:13-20. doi:10.1007/s13671-021-00352-3
12. Cichoń M, Trzeciak M, Sokołowska-Wojdyło M, Nowicki RJ. Contact dermatitis to diabetes medical devices. *Int J Mol Sci*. 2023;24(13):10697. doi:10.3390/ijms241310697
13. van den Hove J, Jacobs MC, Tennstedt D, Lachapelle JM. Allergic contact dermatitis from acrylates in insulin pump infusion sets. *Contact Dermatitis*. 1996;35(2):108. doi:10.1111/j.1600-0536.1996.tb02305.x
14. Adolfsson P, Parkin CG, Thomas A, Krinelke LG. Selecting the appropriate continuous glucose monitoring system—a practical approach. *Eur Endocrinol*. 2018;14(1):24-29. doi:10.17925/EE.2018.14.1.24
15. Oppel E, Kamann S, Reichl FX, Högg C. The Dexcom glucose monitoring system—an isobornyl acrylate-free alternative for diabetic patients. *Contact Dermatitis*. 2019;81(1):32-36. doi:10.1111/cod.13248
16. Gatica-Ortega ME, Pastor-Nieto MA, Torres-Aranda R, Luna-Bastante L, Pérez-Hortet C. Contact dermatitis from MiaoMiao (an add-on transmitter to FreeStyle libre flash glucose monitoring system). *Contact Dermatitis*. 2021;85(1):92-94. doi:10.1111/cod.13788
17. Asarani NAM, Reynolds AN, Boucher SE, de Bock M, Wheeler BJ. Cutaneous complications with continuous or flash glucose

monitoring use: systematic review of trials and observational studies. *J Diabetes Sci Technol*. 2020;14(2):328-337. doi:10.1177/1932296819870849
18. Burgmann J, Biester T, Grothaus J, Kordonouri O, Ott H. Pediatric diabetes and skin disease (PeDiSkin): a cross-sectional study in 369 children, adolescents and young adults with type 1 diabetes. *Pediatr Diabetes*. 2020;21(8):1556-1565. doi:10.1111/pedi.13130
19. Messer LH, Berget C, Beatson C, Polsky S, Forlenza GP. Preserving skin integrity with chronic device use in diabetes. *Diabetes Technol Ther*. 2018;20(S2):S254-S264. doi:10.1089/dia.2018.0080
20. Alves da Silva C, Bregnhøj A, Mowitz M, Bruze M, Andersen KE, Sommerlund M. Contact dermatitis in children caused by diabetes devices. *Contact Dermatitis*. 2022;87(5):406-413. doi:10.1111/cod.14166
21. Svedman C, Bruze M, Antelmi A, et al. Continuous glucose monitoring systems give contact dermatitis in children and adults despite efforts of providing less 'allergy-prone' devices: investigation and advice hampered by insufficient material for optimized patch test investigations. *J Eur Acad Dermatol Venereol*. 2021;35(3):730-737. doi:10.1111/jdv.16981
22. Weng AT, Zachariae C, Christensen KB, Svensson J, Berg AK. Five-month follow-up shows no improvement in dermatological complications in children with type 1 diabetes using continuous glucose monitoring systems and insulin pumps. *J Diabetes Sci Technol*. 2021;15(2):317-323. doi:10.1177/1932296819882425
23. Christensen MO, Berg AK, Rytter K, et al. Skin problems due to treatment with technology are associated with increased disease burden among adults with type 1 diabetes. *Diabetes Technol Ther*. 2019;21(4):215-221. doi:10.1089/dia.2019.0007
24. Berg AK, Nørgaard K, Thyssen JP, et al. Skin problems associated with insulin pumps and sensors in adults with type 1 diabetes: a cross-sectional study. *Diabetes Technol Ther*. 2018;20(7):475-482. doi:10.1089/dia.2018.0088
25. Berg AK, Olsen BS, Thyssen JP, et al. High frequencies of dermatological complications in children using insulin pumps or sensors. *Pediatr Diabetes*. 2018;19(4):733-740. doi:10.1111/pedi.12652
26. Rigo RS, Levin LE, Belsito DV, Garzon MC, Gandica R, Williams KM. Cutaneous reactions to continuous glucose monitoring and continuous subcutaneous insulin infusion devices in type 1 diabetes mellitus. *J Diabetes Sci Technol*. 2021;15(4):786-791. doi:10.1177/1932296820918894
27. Lombardo F, Passanisi S, Tinti D, Messina MF, Salzano G, Rabbone I. High frequency of dermatological complications in children and adolescents with type 1 diabetes: a web-based survey. *J Diabetes Sci Technol*. 2021;15(6):1377-1381. doi:10.1177/1932296820947072
28. Al Hayek AA, Robert AA, Al Dawish MA. Skin-related complications among adolescents with type 1 diabetes using insulin pump therapy. *Clin Med Insights Endocrinol Diabetes*. 2018;11:1179551418798794. doi:10.1177/1179551418798794
29. Jick SS, Oleske DM, Persson R, Zamudio J, Facheris MF. Epidemiology of skin event rates among users of pumps for the subcutaneous administration of drugs for chronic conditions. *Curr Med Res Opin*. 2021;37(9):1563-1571. doi:10.1080/03007995.2021.1953971
30. Schwensen JF, Friis UF, Zachariae C, Johansen JD. Sensitization to cyanoacrylates caused by prolonged exposure to a glucose sensor set in a diabetic child. *Contact Dermatitis*. 2016;74(2):124-125. doi:10.1111/cod.12503
31. Herman A, Aerts O, Baeck M, et al. Allergic contact dermatitis caused by isobornyl acrylate in Freestyle® libre, a newly introduced glucose sensor. *Contact Dermatitis*. 2017;77(6):367-373. doi:10.1111/cod.12866
32. Mowitz M, Hosseini S, Siemund I, Ulriksdotter J, Svedman C. Allergic contact dermatitis caused by the Dexcom G7 glucose sensor. *Contact Dermatitis*. 2024;90(5):495-500. doi:10.1111/cod.14514
33. Herman A, Uter W, Rustemeyer T, et al. Position statement: the need for EU legislation to require disclosure and labelling of the composition of medical devices. *J Eur Acad Dermatol Venereol*. 2021;35(7):1444-1448. doi:10.1111/jdv.17238
34. Ulriksdotter J, Mowitz M, Svedman C, Bruze M. Patch testing and diagnosis when suspecting allergic contact dermatitis from medical devices. *Contact Dermatitis*. 2020;83(4):333-335. doi:10.1111/cod.13650
35. Mowitz M, Ulriksdotter J, Bruze M, Svedman C. In response to the letter to the editor on minimizing adverse skin reactions to wearable continuous glucose monitoring sensors. *J Diabetes Sci Technol*. 2021;15(4):978-979. doi:10.1177/19322968211008241
36. Gatica-Ortega ME, Mowitz M, Pastor-Nieto MA, et al. Contact dermatitis from glucose sensors in Spain: a multicentric approach. *Contact Dermatitis*. 2021;85(5):554-562. doi:10.1111/cod.13924
37. Herman A, de Montjoye L, Baeck M. Adverse cutaneous reaction to diabetic glucose sensors and insulin pumps: irritant contact dermatitis or allergic contact dermatitis? *Contact Dermatitis*. 2020;83:25-30. doi:10.1111/cod.1352930
38. Vidal-Albareda C, Yelmo-Valverde R, Solórzano-Zepeda C, Rodríguez-Muñoz N, de la Hoz-Caballer B, González de Olano D. Prevalence of contact dermatitis to glucose sensors in pediatric population and the main allergens involved. *Contact Dermatitis*. 2020;83(1):47-49. doi:10.1111/cod.13511
39. Hyry HSI, Liippo JP, Virtanen HM. Allergic contact dermatitis caused by glucose sensors in type 1 diabetes patients. *Contact Dermatitis*. 2019;81(3):161-166. doi:10.1111/cod.13337
40. Oppel E, Högg C, Summer B, Ruëff F, Reichl FX, Kamann S. Isobornyl acrylate contained in the insulin patch pump OmniPod as the cause of severe allergic contact dermatitis. *Contact Dermatitis*. 2018;79(3):178-180. doi:10.1111/cod.13017
41. Mowitz M, Fornander L, Hosseiny S, Ryberg K, Bruze M. Patch testing with isobornyl acrylate in 16 Swedish patients with contact dermatitis from glucose sensors and/or insulin pumps. *Acta Derm Venereol*. 2019;99(13):1286-1287. doi:10.2340/00015555-3256
42. Cichoń M, Myśliwiec M, Trzeciak M. Role of acrylates in the development of contact dermatitis in diabetic patients–a polish dermatology tertiary centre experience. *Contact Dermatitis*. 2024;90(2):126-133. doi:10.1111/cod.14436
43. Aerts O, Herman A, Bruze M, Goossens A, Mowitz M. FreeStyle libre: contact irritation versus contact allergy. *Lancet*. 2017;390(10103):1644. doi:10.1016/S0140-6736(17)32142-6
44. Hamnerius N, Mowitz M. Intense skin reaction to a new glucose monitoring and insulin pump system. *Contact Dermatitis*. 2020;83(6):524-527. doi:10.1111/cod.13663
45. Passanisi S, Lombardo F, Barbalace A, et al. Allergic contact dermatitis and diabetes medical devices: 2 clinical cases. *Contact Dermatitis*. 2018;79(2):115-117. doi:10.1111/cod.13012
46. Ahrensbøll-Friis U, Simonsen AB, Zachariae C, Thyssen JP, Johansen JD. Contact dermatitis caused by glucose sensors, insulin pumps, and tapes: results from a 5-year period. *Contact Dermatitis*. 2021;84(2):75-81. doi:10.1111/cod.13664
47. Dendooven E, Foubert K, Goossens A, et al. Concomitant positive patch test reactions in FreeStyle-allergic patients sensitized to isobornyl acrylate. *Contact Dermatitis*. 2021;84(3):166-174. doi:10.1111/cod.13706
48. Aschenbeck KA, Hylwa SA. A diabetic's allergy: ethyl cyanoacrylate in glucose sensor adhesive. *Dermatitis*. 2017;28(4):289-291. doi:10.1097/DER.0000000000000281
49. Peeters C, Herman A, Goossens A, Bruze M, Mowitz M, Baeck M. Allergic contact dermatitis caused by 2-ethyl cyanoacrylate contained in glucose sensor sets in two diabetic adults. *Contact Dermatitis*. 2017;77(6):426-429. doi:10.1111/cod.12873
50. Dendooven E, Foubert K, Naessens T, Pieters L, Lambert J, Aerts O. Isocyanates may contribute to allergic contact dermatitis from

diabetes devices and wound dressings. *Contact Dermatitis*. 2022; 87(5):414-419. doi:10.1111/cod.14187
51. Enberg J, Hamnerius N, Mowitz M. Allergic contact dermatitis caused by a new insulin pump system containing isobornyl acrylate. *Contact Dermatitis*. 2023;88(4):326-328. doi:10.1111/cod.14274
52. Svedman C, Ulriksdotter J, Lejding T, Bruze M, Mowitz M. Changes in adhesive ingredients in continuous glucose monitoring systems may induce new contact allergy pattern. *Contact Dermatitis*. 2021; 84(6):439-446. doi:10.1111/cod.13781
53. Oppel E, Högg C, Oschmann A, Summer B, Kamann S. Contact allergy to the Dexcom G6 glucose monitoring system—role of 2,2′-methylenebis(6-*tert*-butyl-4-methylphenol) monoacrylate in the new adhesive. *Contact Dermatitis*. 2022;87(3):258-264. doi:10.1111/cod.14141
54. Herman A, Baeck M, de Montjoye L, et al. Allergic contact dermatitis caused by isobornyl acrylate in the Enlite glucose sensor and the paradigm MiniMed quick-set insulin infusion set. *Contact Dermatitis*. 2019;81(6):432-437. doi:10.1111/cod.13374
55. Kamann S, Oppel E, Liu F, Reichl FX, Heinemann L, Högg C. Evaluation of isobornyl acrylate content in medical devices for diabetes treatment. *Diabetes Technol Ther*. 2019;21(10):533-537. doi:10.1089/dia.2019.0163
56. Ulriksdotter J, Svedman C, Bruze M, et al. Contact dermatitis caused by glucose sensors—15 adult patients tested with a medical device patch test series. *Contact Dermatitis*. 2020;83(4):301-309. doi:10.1111/cod.13649
57. Mowitz M, Herman A, Baeck M, et al. *N,N*-dimethylacrylamide—a new sensitizer in the FreeStyle Libre glucose sensor. *Contact Dermatitis*. 2019;81(1):27-31. doi:10.1111/cod.13243
58. Oppel E, Kamann S, Heinemann L, Klein A, Reichl FX, Högg C. Freestyle libre 2: the new isobornyl acrylate free generation. *Contact Dermatitis*. 2020;83(5):429-431. doi:10.1111/cod.13638
59. Herman A, Mowitz M, Aerts O, et al. Unexpected positive patch test reactions to sesquiterpene lactones in patients sensitized to the glucose sensor FreeStyle libre. *Contact Dermatitis*. 2019;81(5):354-367. doi:10.1111/cod.13330
60. Persad S, Lejding T, Svedman C, Mowitz M. The missing link: allergic contact dermatitis caused by 1,6-hexanediol diacrylate in a glucose sensor transmitter. *Contact Dermatitis*. 2023;89(4):303-305. doi:10.1111/cod.14385
61. Ulriksdotter J, Svedman C, Bruze M, Mowitz M. Allergic contact dermatitis caused by dipropylene glycol diacrylate in the Omnipod® insulin pump. *Br J Dermatol*. 2022;186(2):334-340. doi:10.1111/bjd.20751
62. Raison-Peyron N, Mowitz M, Dereure O, Svedman C. Allergic contact dermatitis in a patient after five years of use of Omnipod insulin pump. *J Diabetes Sci Technol*. 2022;16(5):1342-1343. doi:10.1177/19322968221110578
63. Raison-Peyron N, Mowitz M, Bonardel N, Aerts O, Bruze M. Allergic contact dermatitis caused by isobornyl acrylate in OmniPod, an innovative tubeless insulin pump. *Contact Dermatitis*. 2018;79(2):76-80. doi:10.1111/cod.12995
64. Foti C, Romita P, Rigano L, et al. Isobornyl acrylate: an impurity in alkyl glucosides. *Cutan Ocul Toxicol*. 2016;35(2):115-119. doi:10.3109/15569527.2015.1055495
65. Kerre S, Strobbe T, Naessens T, Theunis M, Foubert K, Aerts O. Alkyl glucosides: newly identified allergens in foam wound dressings. *Contact Dermatitis*. 2018;79(3):191-193. doi:10.1111/cod.13026
66. Busschots AM, Meuleman V, Poesen N, Dooms-Goossens A. Contact allergy to components of glue in insulin pump infusion sets. *Contact Dermatitis*. 1995;33(3):205-206. doi:10.1111/j.1600-0536.1995.tb00554.x
67. Christoffers WA, Coenraads PJ, Schuttelaar ML. Two decades of occupational (meth)acrylate patch test results and focus on isobornyl acrylate. *Contact Dermatitis*. 2013;69(2):86-92. doi:10.1111/cod.12023
68. Aalto-Korte K, Alanko K, Kuuliala O, Jolanki R. Occupational methacrylate and acrylate allergy from glues. *Contact Dermatitis*. 2008; 58(6):340-346. doi:10.1111/j.1600-0536.2008.01333.x
69. Kamann S, Aerts O, Heinemann L. Further evidence of severe allergic contact dermatitis from isobornyl acrylate while using a continuous glucose monitoring system. *J Diabetes Sci Technol*. 2018;12(3):630-633. doi:10.1177/1932296818762946
70. Herman A, Darrigade AS, de Montjoye L, Baeck M. Contact dermatitis caused by glucose sensors in diabetic children. *Contact Dermatitis*. 2020;82(2):105-111. doi:10.1111/cod.13429
71. Pyl J, Dendooven E, Van Eekelen I, den Brinker M, et al. Prevalence and prevention of contact dermatitis caused by FreeStyle libre: a monocentric experience. *Diabetes Care*. 2020;43(4):918-920. doi:10.2337/dc19-1354
72. Kamann S, Heinemann L, Oppel E. Usage of hydrocolloid-based plasters in patients who have developed allergic contact dermatitis to isobornyl acrylate while using continuous glucose monitoring systems. *J Diabetes Sci Technol*. 2020;14(3):582-585. doi:10.1177/1932296819876964
73. Queirós CS, Alexandre MI, Garrido PM, Correia TE, Filipe PL. Allergic contact dermatitis to IBOA in FreeStyle libre: experience from a tertiary care Portuguese hospital. *Contact Dermatitis*. 2020;83(2):154-157. doi:10.1111/cod.13578
74. Aerts O, Dendooven E, Raison-Peyron N. Sensitization to modified colophonium in glucose sensors: another problem for diabetes patients. *Contact Dermatitis*. 2022;87(6):553-555. doi:10.1111/cod.14213
75. Teufel-Schäfer U, Huhn C, Müller S, Müller C, Grünert SC. Severe allergic contact dermatitis to two different continuous glucose monitoring devices in a patient with glycogen storage disease type 9b. *Pediatr Dermatol*. 2021;38(5):1302-1304. doi:10.1111/pde.14767
76. Dendooven E, Dirinck E, Foubert K, Aerts O. "Re-testing" suggests that cosensitizations to isobornyl acrylate and sesquiterpene lactones may be due to cross-reactivity. *Contact Dermatitis*. 2022; 86(1):57-59. doi:10.1111/cod.13972
77. Huang C, DeKoven J. An unexpected source of glucose monitor-associated allergic contact dermatitis. *Contact Dermatitis*. 2021;85:235-236. doi:10.1111/cod.13815
78. Herman A, de Montjoye L, Marot L, Baeck M. Induction of leukoderma following allergic contact dermatitis to FreeStyle libre. *Contact Dermatitis*. 2019;81(6):456-458. doi:10.1111/cod.13360
79. Jáuregui I, Sánchez J, Segurola A, Galán C, Seras Y, Gamboa PM. Allergic contact dermatitis by isobornyl acrylate in glucose monitoring devices: report of two cases. *Contact Dermatitis*. 2019;81(3):219-220. doi:10.1111/cod.13349
80. Shinkawa E, Washio K, Tatsuoka S, Fukunaga A, Sakaguchi K, Nishigori C. A case of contact dermatitis caused by isobornyl acrylate in FreeStyle libre: the usefulness of film-forming agents. *Contact Dermatitis*. 2019;81(1):56-57. doi:10.1111/cod.13239
81. Corazza M, Scuderi V, Musmeci D, Foti C, Romita P, Borghi A. Allergic contact dermatitis caused by isobornyl acrylate in a young diabetic patient using a continuous glucose monitoring system (Freestyle libre). *Contact Dermatitis*. 2018;79(5):320-321. doi:10.1111/cod.13075
82. Kamann S, Oppel E. Hydrocolloid blister plaster decreases allergic contact dermatitis caused by Freestyle libre and isobornyl acrylate. *Contact Dermatitis*. 2019;81(5):380-381. doi:10.1111/cod.13329
83. Joyanes Romo JB, Borja Segade JM, Moreno Lozano L, et al. Contact dermatitis caused by glucose sensors: more than allergy to isobornyl acrylate. *J Invest Allergol Clin Immunol*. 2022;32(3):232-233. doi:10.18176/jiaci.0739
84. Ng KL, Nixon RL, Grills C, Tam MM. Solution using Stomahesive® wafers for allergic contact dermatitis caused by isobornyl acrylate in

glucose monitoring sensors. *Australas J Dermatol*. 2022;63(1):e56-e59. doi:10.1111/ajd.13675
85. Mine Y, Urakami T, Matsuura D. Allergic contact dermatitis caused by isobornyl acrylate when using the FreeStyle® libre. *J Diabetes Investig*. 2019;10(5):1382-1384. doi:10.1111/jdi.13023
86. Tramontana M, Hansel K, Bianchi L, Agostinelli D, Stingeni L. Allergic contact dermatitis caused by a glucose monitoring system: an emerging side-effect of diabetes medical devices. *J Eur Acad Dermatol Venereol*. 2020;34(5):e223-e225. doi:10.1111/jdv.16178
87. DeKoven JG, Shear NH. Cutaneous contact allergy to a glucose monitor. *CMAJ*. 2020;192(11):E286. doi:10.1503/cmaj.191216
88. Renaudin H, Darrigade AS, Dendooven E, Foubert K, Aerts O, Milpied B. Allergic contact dermatitis from a disposable blood pressure cuff containing isobornyl acrylate and 2-phenoxyethyl acrylate. *Contact Dermatitis*. 2021;84(6):462-464. doi:10.1111/cod.13761
89. Klein A, Kamann S, Högg C, Oppel EM. Kontaktallergie auf kontinuierliche Glukosemesssysteme und insulin-patch-Pumpen [Contact allergy to continuous glucose monitoring systems and insulin patch pumps]. *Hautarzt*. 2020;71(Suppl 1):41-43. German. doi: 10.1007/s00105-020-04623-1
90. Wagner N, Elsbergen L, Feustel J. Isobornyl acrylate-contact allergen in continuous glucose sensor system. *Allergy: Eur J All Clin Immunol*. 2019;74(Suppl):502. (Abstract). doi:10.1111/all.13961
91. Fitzgerald M, Wakelin S, Bruze M. A sticky situation for diabetes: allergic contact dermatitis to isobornyl acrylate in continuous glucose-monitoring devices. *Br J Dermatol*. 2019;181(Suppl.1):158 (Abstract).
92. Bulteel C, Huygens S, Gilissen L, Goossens A. Isobornyl acrylate in glucose sensors causes allergic contact dermatitis in children. *Pediat Dermatol*. 2018;35(Suppl.2):S22 (Poster).
93. Seibold A. Minimizing adverse skin reactions to wearable continuous glucose monitoring sensors in patients with diabetes. *J Diabetes Sci Technol*. 2021;15(3):713-714. (Letter to the editor). doi:10.1177/1932296820984763
94. Malinauskiene L, Šlekyte G, Mowitz M, Isaksson M, Zablockis R. Allergic contact dermatitis caused by isobornyl acrylate in two patients treated for idiopathic pulmonary arterial hypertension. *Contact Dermatitis*. 2020;83(2):170-171. doi:10.1111/cod.13617
95. Otero-Alonso A, Rodríguez-Vázquez V, López-Pesado I, Fernández-Redondo V. Smartwatch protective cover's glue: a new nonoccupational acrylate allergy. *Contact Dermatitis*. 2020;83(2):159-161. doi:10.1111/cod.13586
96. Amat-Samaranch V, Garcia-Melendo C, Tubau C, Puig L, Serra-Baldrich E. Occupational allergic contact dermatitis to Isobornyl acrylate present in cell phone screen protectors. *Contact Dermatitis*. 2021;84(5):352-354. doi:10.1111/cod.13747
97. Baek P, Adler BL. Allergic contact dermatitis to isobornyl acrylate in a home nail glue. *Contact Dermatitis*. 2024;91(1):64-66. doi:10.1111/cod.14541
98. Samaran Q, Raison-Peyron N, Dereure O, Svedman C, Dahlin J. Allergic contact dermatitis to isobornyl acrylate in a hospital wristband. *Contact Dermatitis*. 2024;91(1):62-64. doi:10.1111/cod.14539
99. Corazza M, Mantovani L, Zedde P, Forconi R, Scuderi V, Borghi A. A case of allergic contact dermatitis to (meth)acrylates in electrocardiogram electrodes. *Contact Dermatitis*. 2020;83(2):152-154. doi:10.1111/cod.13570
100. Herman A, Baeck M. Sensitization to isobornyl acrylate in a tertiary Belgian hospital. *Contact Dermatitis*. 2021;85(1):105-106. doi:10.1111/cod.1379714
101. Cichoń M, Sokołowska-Wojdyło M, Trzeciak M. Allergic contact dermatitis elicited by insulin infusion sets: first case reported in Poland. *Contact Dermatitis*. 2023;88(5):404-406. doi:10.1111/cod.14281
102. Uter W, Wilkinson SM, Aerts O, et al. ESSCA and EBS ESCD working groups, and the GEIDAC. Patch test results with the European baseline series, 2019/20–joint European results of the ESSCA and the EBS working groups of the ESCD, and the GEIDAC. *Contact Dermatitis*. 2022;87(4):343-355. doi:10.1111/cod.14170
103. Rustemeyer T, de Groot J, von Blomberg BM, Bruynzeel DP, Frosch PJ, Scheper RJ. Assessment of contact allergen cross-reactivity by retesting. *Exp Dermatol*. 2002;11(3):257-265. doi:10.1034/j.1600-0625.2001.110309.x
104. Dendooven E, Foubert K, Naessens T, et al. Allergic contact dermatitis from ("hypoallergenic") adhesives containing D-limonene. *Contact Dermatitis*. 2022;86(2):113-119. doi:10.1111/cod.14008
105. de Groot AC, Rustemeyer T. 2-hydroxyethyl methacrylate (HEMA): a clinical review of contact allergy and allergic contact dermatitis. Part 2. Cross- and co-sensitization, other skin reactions to HEMA, position of HEMA among (meth)acrylates, sensitivity as screening agent, presence of HEMA in commercial products and practical information on patch test procedures. *Contact Dermatitis*. 2024;90(1):1-16. doi:10.1111/cod.14430
106. Kiec-Swierczynska M, Krecisz B, Swierczynska-Machura D, Zaremba J. An epidemic of occupational contact dermatitis from an acrylic glue. *Contact Dermatitis*. 2005;52(3):121-125. doi:10.1111/j.0105-1873.2005.00527.x
107. Andersen KE, White IR, Goossens A. Allergens from the European baseline series. In: Johansen JD, Frosch PJ, Lepoittevin J-P, eds. *Contact Dermatitis*. Vol Chapter 31. 5th ed. Springer-Verlag; 2011:545-590.
108. Downs AM, Sansom JE. Colophony allergy: a review. *Contact Dermatitis*. 1999;41(6):305-310. doi:10.1111/j.1600-0536.1999.tb06178.x
109. Moffitt DL, Sansom JE. Occupational allergic contact dermatitis from tetrahydrofurfuryl acrylate in a medical-device adhesive. *Contact Dermatitis*. 2001;45(1):54. doi:10.1034/j.1600-0536.2001.045001054.x
110. Chemical Book. Accessed June 22, 2024. https://www.chemicalbook.com/ProductChemicalPropertiesCB8481270_EN.htm.
111. Estlander T, Jolanki R, Kanerva L. Occupational allergic contact dermatitis from UV-cured lacquer containing dipropylene glycol diacrylate. *Contact Dermatitis*. 1998;39(1):36. doi:10.1111/j.1600-0536.1998.tb05814.x
112. Isaksson M, Zimerson E. Risks and possibilities in patch testing with contaminated personal objects: usefulness of thin-layer chromatograms in a patient with acrylate contact allergy from a chemical burn. *Contact Dermatitis*. 2007;57(2):84-88. doi:10.1111/j.1600-0536.2007.01156.x
113. Aalto-Korte K, Henriks-Eckerman ML, Kuuliala O, Jolanki R. Occupational methacrylate and acrylate allergy—cross-reactions and possible screening allergens. *Contact Dermatitis*. 2010;63(6):301-312. doi:10.1111/j.1600-0536.2010.01760.x
114. Asai C, Inomata N, Sato M, et al. Allergic contact dermatitis due to the liquid skin adhesive Dermabond® predominantly occurs after the first exposure. *Contact Dermatitis*. 2021;84(2):103-108. doi:10.1111/cod.13700
115. Symanzik C, Weinert P, Babić Ž, et al. Allergic contact dermatitis caused by 2-hydroxyethyl methacrylate and ethyl cyanoacrylate contained in cosmetic glues among hairdressers and beauticians who perform nail treatments and eyelash extension as well as hair extension applications: a systematic review. *Contact Dermatitis*. 2022;86(6):480-492. doi:10.1111/cod.14056
116. Gonçalo M, Pinho A, Agner T, et al. Allergic contact dermatitis caused by nail acrylates in Europe: an EECDRG study. *Contact Dermatitis*. 2018;78(4):254-260. doi:10.1111/cod.12942
117. Sato M, Inomata N, Aihara M. A case of contact dermatitis syndrome caused by Dermabond®, followed by contact dermatitis caused by false eyelash glue and Aron alpha® glue: possibility of cross-reactions among cyanoacrylates. *Contact Dermatitis*. 2017;77(6):414-415. doi:10.1111/cod.12823

118. Cook KA, White AA, Shaw DW. Patch testing ingredients of dermabond and other cyanoacrylate-containing adhesives. *Dermatitis*. 2019;30(5):314-322. doi:10.1097/DER.0000000000000514
119. Bruze M, Björkner B, Lepoittevin JP. Occupational allergic contact dermatitis from ethyl cyanoacrylate. *Contact Dermatitis*. 1995;32(3):156-159. doi:10.1111/j.1600-0536.1995.tb00806.x
120. Lowe A, D'Souza N, Hughes J. A rarely reported contact allergy to ethyl cyanoacrylates in a continuous glucose sensor monitoring device in a child with diabetes, with a successful management outcome. *Brit J Dermatol*. 2017;177(Suppl. 1):173.
121. Gisin V, Chan A, Welsh JB. Manufacturing process changes and reduced skin irritations of an adhesive patch used for continuous glucose monitoring devices. *J Diabetes Sci Technol*. 2018;12(3):725-726. doi:10.1177/1932296817738076
122. Wikipedia. Accessed June 26, 2024. https://en.wikipedia.org/wiki/1,6-Hexanediol_diacrylate.
123. Boom BW, van Driel LM. Allergic contact dermatitis to epoxy resin in infusion sets of an insulin pump. *Contact Dermatitis*. 1985;12(5):280. doi:10.1111/j.1600-0536.1985.tb01137.x
124. van Amerongen CCA, Dahlin J, Isaksson M, Schuttelaar MLA. Allergic contact dermatitis caused by 1,6-hexanediol diacrylate in a hospital wristband. *Contact Dermatitis*. 2019;81(6):446-449. doi:10.1111/cod.13378
125. Morgan VA, Fewings JM. 1,6-hexanediol diacrylate: a rapid and potent sensitizer in the printing industry. *Australas J Dermatol*. 2000;41(3):190-192. doi:10.1046/j.1440-0960.2000.00429.x
126. Siemund I, Dahlin J, Mowitz M, Hamnerius N, Svedman C. Allergic contact dermatitis due to 1,6-hexanediol diacrylate in ostomy patients. *Contact Dermatitis*. 2024;90(5):501-506. doi:10.1111/cod.14516
127. Lejding T, Antelmi A, Dahlin J. Pipe relining: not only epoxy resins. Two cases of occupational contact allergy to acrylates. *Contact Dermatitis*. 2023;88(1):71-72. doi:10.1111/cod.14222
128. Botella-Estrada R, Mora E, de la Cuadra D. Hexanediol diacrylate sensitization after accidental occupational exposure. *Contact Dermatitis*. 1992;26:50-51. doi:10.1111/j.1600-0536.1992.tb00870.x
129. Ido T, Kiyohara T, Takahashi H, Yamaguchi Y, Tani D, Kumakiri M. Toxic epidermal necrolysis following allergic contact dermatitis caused by occupational exposure to ultraviolet-cured inks. *Acta Derm Venereol*. 2012;92(3):313-315. doi:10.2340/00015555-1255
130. Dexcom Inc. Field safety notice | Dexcom G6 sensor. FAS-SD-20-003. Advice from Manufacturer, December. 2020.
131. Mowitz M, Lejding T, Ulriksdotter J, Antelmi A, Bruze M, Svedman C. Further evidence of allergic contact dermatitis caused by 2,2′-methylenebis(6-*tert*-butyl-4-methylphenol) monoacrylate, a new sensitizer in the Dexcom G6 glucose sensor. *Dermatitis*. 2022;33(4):287-292. doi:10.1097/DER.0000000000000767
132. Saccabusi S, Boatto G, Asproni B, Pau A. Sensitization to methyl methacrylate in the plastic catheter of an insulin pump infusion set. *Contact Dermatitis*. 2001;45(1):47-48. doi:10.1034/j.1600-0536.2001.045001047.x
133. Jolanki R, Kanerva L, Estlander T, Henriks-Eckerman ML, Suhonen R. Allergic contact dermatitis from phenoxyethoxy ethylacrylates in optical fiber coating, and glue in an insulin pump set. *Contact Dermatitis*. 2001;45(1):36-37. doi:10.1034/j.1600-0536.2001.045001036.x
134. Chemical Book. Accessed June 26, 2024. https://www.chemicalbook.com/ProductChemicalPropertiesCB1113666_EN.htm.
135. Chemical Book. Accessed June 26, 2024. https://www.chemicalbook.com/CASEN_947-19-3.htm.
136. De Groot AC. Chapter 2.52: BHT. *Monographs in Contact Allergy Volume I. Non-fragrance allergens in Cosmetics (Part I)*. CRC Press Taylor and Francis Group; 2018:150-154.
137. National Library of Medicine. PubChem. 2,4-Di-tert-butylphenol. Accessed June 26, 2024 https://pubchem.ncbi.nlm.nih.gov/compound/7311
138. Hamada H, Bruze M, Zimerson E, Isaksson M, Engfeldt M. Sensitization and cross-reactivity patterns of contact allergy to diisocyanates and corresponding amines: investigation of diphenylmethane-4,4′-diisocyanate, diphenylmethane-4,4′-diamine, dicyclohexylmethane-4,4′-diisocyanate, and dicylohexylmethane-4,4′-diamine. *Contact Dermatitis*. 2017;77(4):231-241. doi:10.1111/cod.12809
139. Frick M, Björkner B, Hamnerius N, Zimerson E. Allergic contact dermatitis from dicyclohexylmethane-4,4′-diisocyanate. *Contact Dermatitis*. 2003;48(6):305-309. doi:10.1034/j.1600-0536.2003.00123.x
140. Kerre S. Allergic contact dermatitis to DMDI in an office application. *Contact Dermatitis*. 2008;58(5):313-314. doi:10.1111/j.1600-0536.2007.01290.x
141. Donovan JC, Kudla I, DeKoven JG. Rapid development of allergic contact dermatitis from dicyclohexylmethane-4,4′-diisocyanate. *Dermatitis*. 2009;20(4):214-217.
142. Mowitz M, Antelmi A, Bruze M, Ulriksdotter J, Svedman C. Isocyanate contact allergies in patients with contact dermatitis from glucose sensors and insulin pumps. *Contact Dermatitis*. 2022;86(Suppl.1):8-9. doi:10.1111/cod.14095
143. Aalto-Korte K, Suuronen K, Kuuliala O, Henriks-Eckerman ML, Jolanki R. Occupational contact allergy to monomeric isocyanates. *Contact Dermatitis*. 2012;67(2):78-88. doi:10.1111/j.1600-0536.2011.02049.x
144. Caldeira LE, Fernandes NP, Neto M, et al. A case of contact dermatitis caused by isobornyl acrylate in a glucose monitoring sensor. Allergy: Eur J all. *Clin Immunol*. 2020;75(Suppl 109):444-445. (Abstract).
145. Romaguera C, Grimalt F, Vilaplana J. Nickel dermatitis from an infusion needle. *Contact Dermatitis*. 1985;12(3):181-182. doi:10.1111/j.1600-0536.1985.tb01098.x
146. Corazza M, Maranini C, Aleotti A, Virgili A. Nickel contact dermatitis due to the needle of an infusion pump, confirmed by microanalysis. *Contact Dermatitis*. 1998;39(3):144. doi:10.1111/j.1600-0536.1998.tb05875.x
147. Passby L, Thompson D. Barriers to improvement: the role of tackifying agents in persisting continuous glucose monitoring-associated allergic contact dermatitis. *Brit J Dermatol*. 2022;187(suppl.1):136 (Abstract).

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

How to cite this article: de Groot A, van Oers EM, Ipenburg NA, Rustemeyer T. Allergic contact dermatitis caused by glucose sensors and insulin pumps: A full review. *Contact Dermatitis*. 2025;92(2):87-112. doi:10.1111/cod.14698