Editorial

The need to disclose the composition of medical devices at the European level.

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A medical device (MD) is any instrument, equipment, material, or product intended to be used in humans for medical purposes, the main action of which is not obtained by pharmacological or immunological means. Hence, there is a very large number of MDs, ranging from simple contact lenses and sticking plasters to sophisticated pacemakers. They are classified into 4 categories (I, IIa, IIb, III) according to their risk level, which is based on several criteria, including indications, invasiveness, duration of use (< 1 hour, ≤ 30 days, > 30 days), and implantability, but also the risk related to the patient. Although there is no doubt that medical devices have greatly contributed to improve the quality of clinical care, they are able to sensitize and provoke allergic contact dermatitis.

Recently, several cases of allergic contact dermatitis (ACD) caused by MD have been published, particularly from glucose sensors and insulin pumps. In the current issue, Hyri et al report on the incidence of ACD to glucose sensors in diabetes patients in southern Finland (1). The first case caused by an insulin pump was described in 1985 (2) and by a glucose sensor in 2016 (3), respectively. Since then, the number of cases has increased considerably, making ACD from glucose sensors a “hot topic” in this regard. During the last decade, several authors have highlighted isobornyl acrylate (IBOA) (4-6) and N,N-dimethylacrylamide (DMAA) (7) as potent allergens in the glucose sensor FreeStyle Libre, one of the most widely used sensors in Europe, and also in other parts of the world (8). Due to lack of communication with, and cooperation from, the manufacturers regarding the qualitative composition of the sensor, the presence of both allergens in Freestyle Libre could only be identified by investigative chromatographic techniques. Beside the ones identified, even other allergens might be present since not all patients reacting to this sensor are allergic to the substances hitherto identified.

Poor and non-transparent sharing of information by the manufacturers marketing MDs for diabetics was already pointed out by Heineman et al in 2015 concerning insulin pumps (9). Manufacturers continue to refuse collaboration and communication despite numerous requests from the medical society and the literature over the last three years, the most recent example concerning information obtained by the ANSM (Agence Nationale de Sécurité du medicament et des produits de santé) in France, in May 2019, who informed that Abbott had modified one component of the Freestyle Libre (Abbott Diabetes Care, Witney, Oxon, UK) glucose sensors. However, the provided information is of no help to the diabetic patient since precise information is lacking: are IBOA and/or DMAA still present? Which component has

been modified? This is still not known even when requesting information from the manufacturer.

Many authors have called attention to the need for full ingredient labelling of other MDs as well, for example, medical dressings and adhesives containing acrylic compounds (10), or foam wound dressings containing alkyl glucosides, well-known allergens in cosmetic products (11), for which no cooperation from the respective manufacturers could be obtained either. This information is crucial, also in the light of potential type-I hypersensitivity reactions, including anaphylaxis, as in the case of an alginate dressing (12). In fact, all medical specialties are concerned, other examples including, but not limited to, surgical glues containing cyanoacrylate (13), also described as causes of ACD in diabetic patients (14, 15), MDs used in cardiology, such as silicone in pacemakers (16), but also colophonium and herbal extracts in self-adhesive electrocardiography electrodes (17). The list of MDs causing ACD is much longer, extremely varied and ever-changing, making it impossible to establish an exhaustive and up-to-date list on this subject.

In order to ensure better protection of public health and patient safety, on April 5, 2017, two new regulations on medical devices (Regulation EU 2017/745) and in vitro diagnostic medical devices (Regulation EU 2017/746) were adopted. They entered into force on 25 May 2017 progressively replacing the existing directives, and will become fully applicable in May 2020 for medical devices and May 2022 for in vitro diagnostic medical devices (18). These regulations contain important changes to the current system to enable the sector to produce safer and more innovative devices and help address future challenges. The safety of the medical devices and in-vitro diagnostic medical devices shall be provided by a new Medical Device Coordination Group, composed of member state experts and chaired by the Commission, increased cooperation between member states in the field of vigilance and market surveillance, and a mandatory coordination assessment of multinational clinical investigations.

Regarding patient benefits, the new rules introduce:

- “better protection of public health and patient safety”, i.e., stricter pre-marketing control, particularly for high-risk devices (e.g., coloured contact lenses or equipment

for liposuction), strengthening of clinical evaluation and investigation, and stricter requirements on the use of hazardous substances.

- a comprehensive EU database on medical devices, a large part of it available for the public, such as a newly introduced summary of safety and performance for all Class III and implantable devices
- a new device identification system that will allow easier traceability of medical devices
- an "implant" card for patients containing information about implanted medical devices
- a robust financial mechanism to ensure patients are compensated in case they receive defective products.

However, the two new regulations have no benefit at all for the management of contact dermatitis (or other diseases) caused by ingredients present in medical devices, because they do not mention any need for information on the qualitative composition nor labelling on the packaging of medical devices! This is all the more important since, beyond glucose sensors, insulin pumps, adhesives, etc., there is an increasing trend of marketing topical preparations as medical devices in order to avoid both pharmaceutical and cosmetic regulations!

Lack of collaboration forces the medical centres to carry out physicochemical analyses themselves in order to identify the sensitizing culprits in medical devices (4, 6, 7, 14, 19) , which also creates a considerable cost for the society. Indeed, this information is essential, not only to identify potential allergens (or other culprits) once sensitization has occurred, but also to offer alternative and safer medical devices to the affected patients. In agreement with the numerous previous reports about allergic contact dermatitis from medical devices (1, 10, 20-22), we again urge the legislators to implement full ingredient declaration and labelling of all medical devices, as well to require full cooperation of manufacturers with the medical community in case – sometimes even severe - (skin) adverse reactions occur. Finally, it is noteworthy that cosmetic users are far better protected with full ingredient cosmetic labelling than patients, both adults and children, who suffer from various diseases and who need to use medical devices!

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