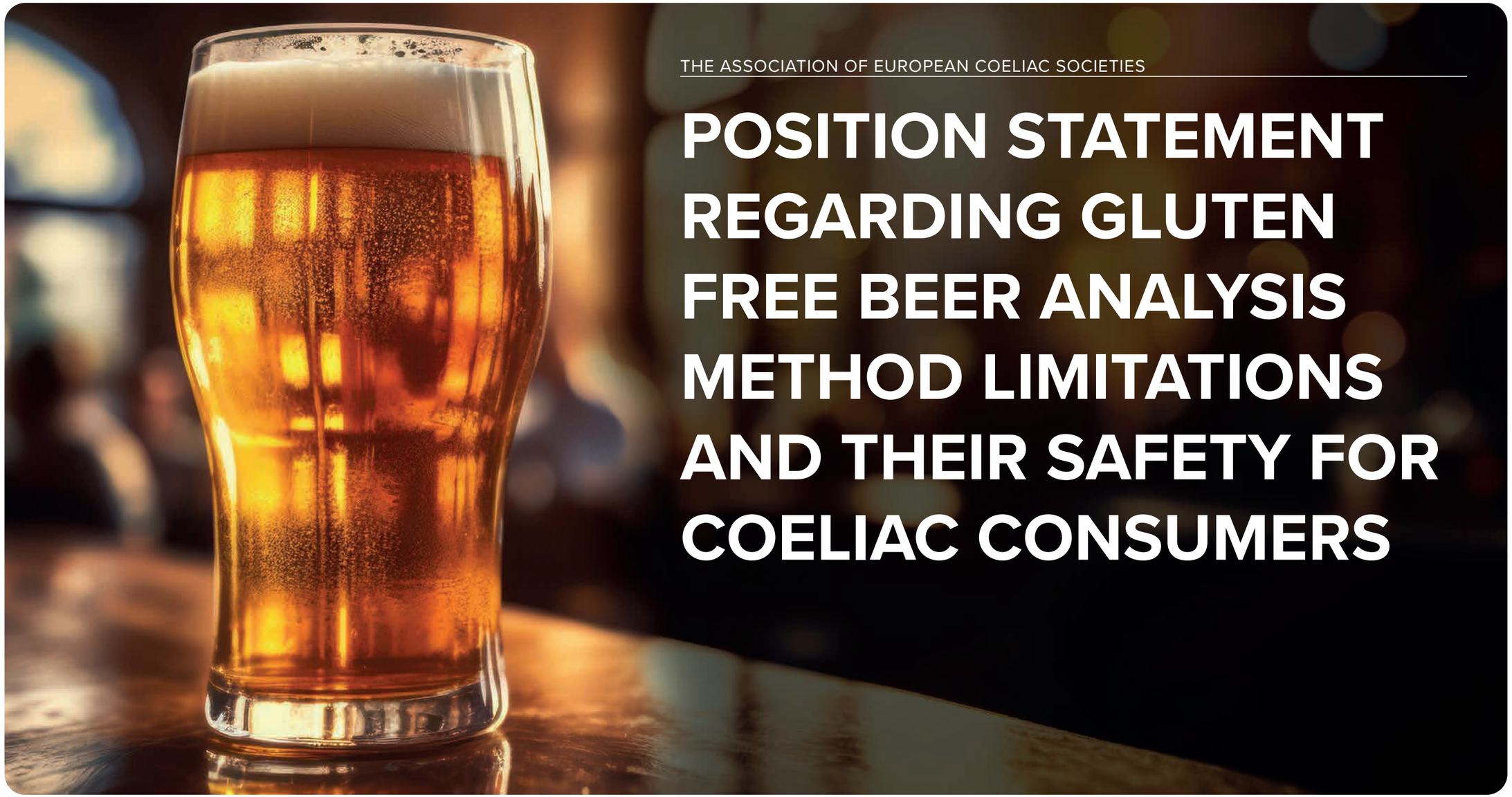


THE ASSOCIATION OF EUROPEAN COELIAC SOCIETIES

POSITION STATEMENT REGARDING GLUTEN FREE BEER ANALYSIS METHOD LIMITATIONS AND THEIR SAFETY FOR COELIAC CONSUMERS

AOECS
Association of European Coeliac Societies

POSITION PAPER

INTRODUCTION

Coeliac disease is an autoimmune disease caused by the ingestion of food containing gluten, which is a type of protein that can be found in cereal grains such as wheat, barley and rye.

Coeliac disease may affect up to 1.3 % of the global population. When it remains undiagnosed, coeliac disease can result in symptoms ranging from minor discomfort to life-threatening conditions like severe anaemia. Currently, the only known effective treatment is a strict, life-long, gluten-free diet.

The Association of European Coeliac Societies (AOECS) is a non-profit umbrella organisation comprised of national coeliac societies in Europe and worldwide.

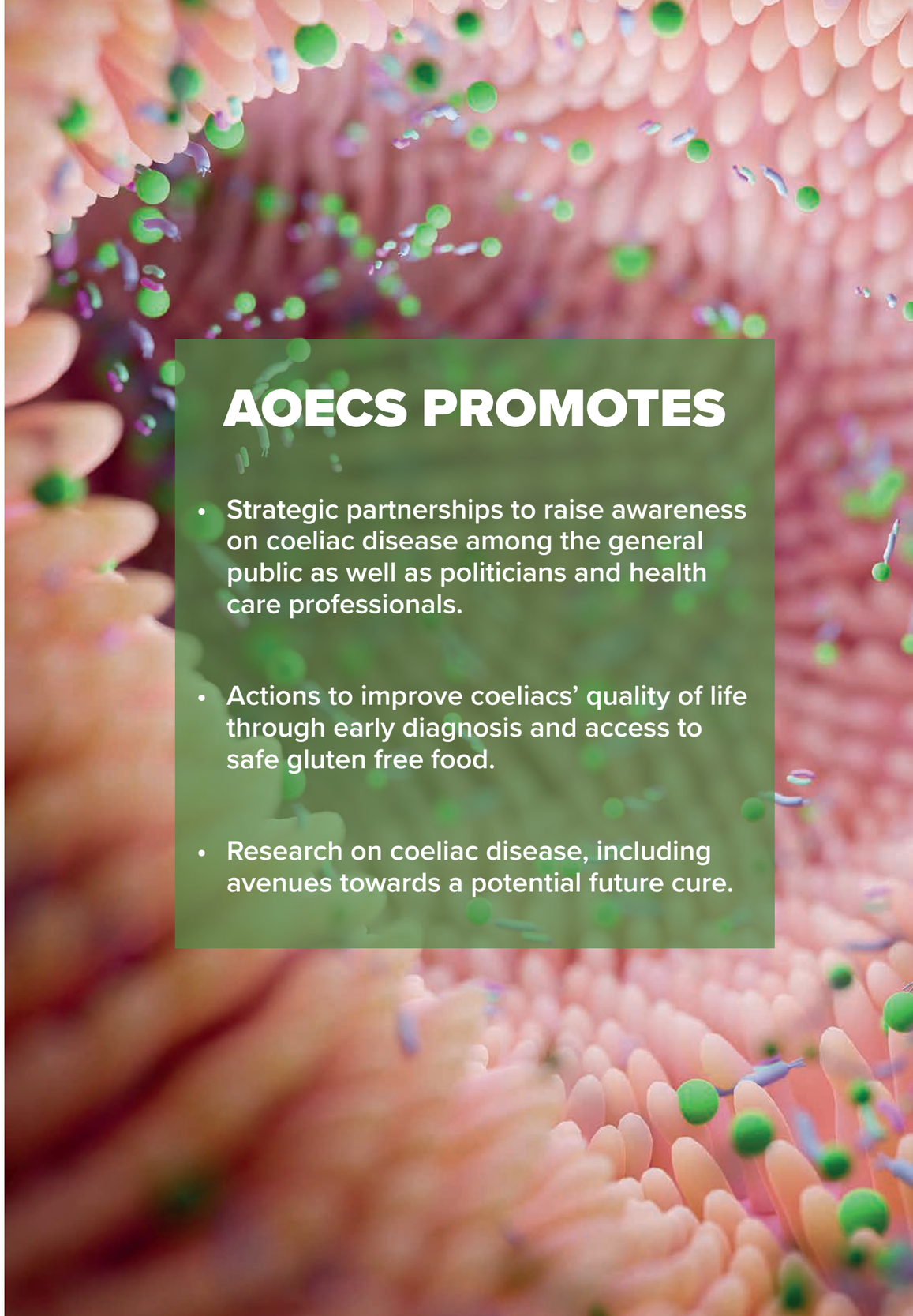
Together with its members, AOECS represents the voice of coeliac patients and their families in over 40 countries

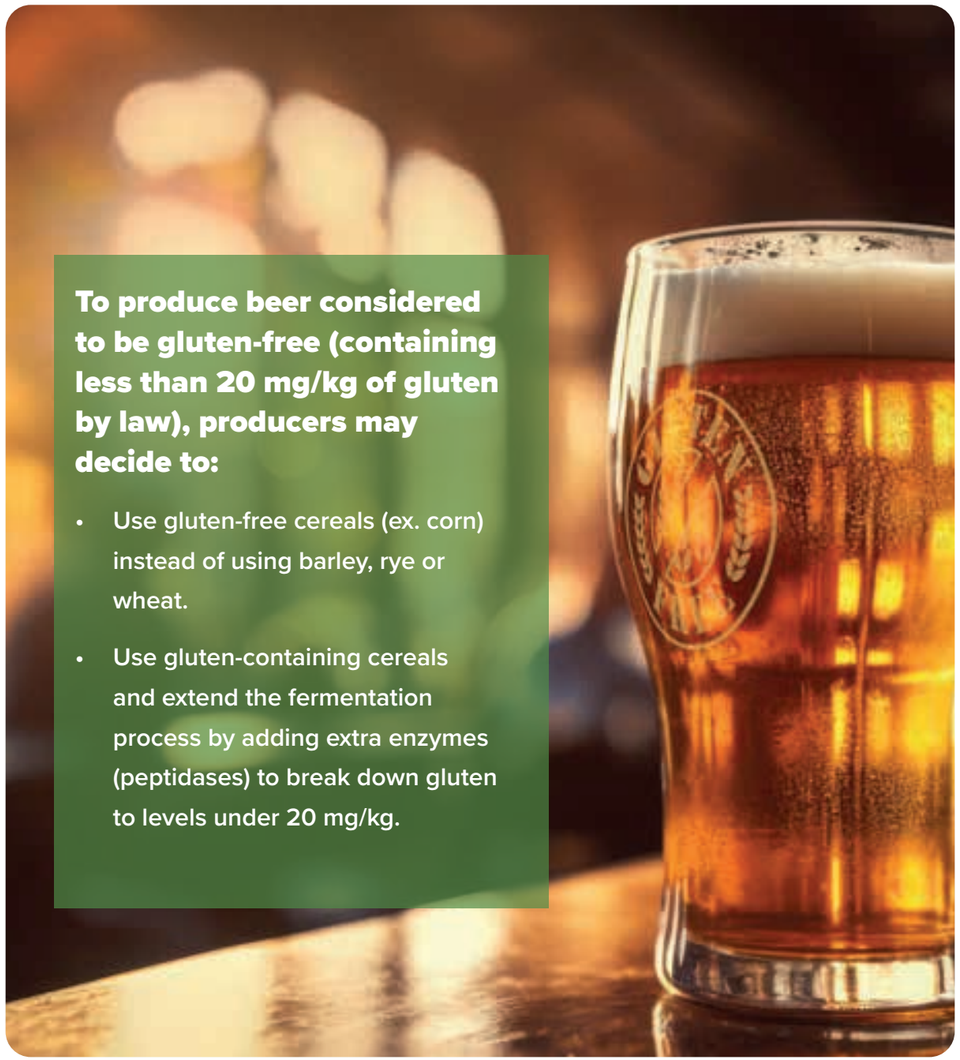
The AOECS owns the AOECS Standard for pre-packaged food products and the Crossed Grain Trademark, which is managed by its National Coeliac Societies in their respective countries.

Consequently, thousands of safe gluten-free food products are available on the market and easily recognisable by any consumer.

The AOECS Standard fully adheres to the Codex Alimentarius, which is the collection of standards and guidelines jointly established by FAO and WHO to protect consumer health.

AOECS is an observer member of the CODEX Commission, to advocate for coeliacs and ensure their specific concerns are taken into consideration.





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ABOUT BEER

Beer is generally produced from barley, a raw material that contains gluten. By definition, beer is a hydrolysed product, which means that its proteins have already been partially broken down, so digestion is easier. During hydrolysis, gluten prolamin molecules are broken down into smaller peptides by the addition of yeast and enzymes that breaks molecular bonds. This also makes gluten more difficult to detect.

The second option increases the hydrolysis process to create small enough peptides of the original gluten protein so that the final product becomes safe for people with coeliac disease to consume.

Currently, there is a legislative framework that outlines the special features of the hydrolysed products and the implications of their production and safety. These aspects are taken into consideration by coeliac patients and beer producers.

Although the EU Food Safety Authority, EFSA, has not published any opinion or benchmark study regarding the analysis of hydrolysed gluten-free products, current scientific evidence and EU law support licensing and labelling beers made from barley or other cereals as gluten-free products. (EU Regulation 1169/2011, EU Regulation 828/2014).

Furthermore, the CODEX Commission (Codex Standard 118-1979) considers hydrolysed gluten-free products as being safe for consumption by people with coeliac disease.

Consequently, AOECS supports the verification of beer production and the labelling of the final product within its Crossed Grain Trademark Licensing System. However, it should be noted that the legislative framework is different worldwide, and patients and producers may encounter different situations outside the European Union.

IMPLICATIONS REGARDING THE ANALYTICAL METHOD

Beer producers cannot fully control hydrolysis, and so the resulting, broken-down fragments of gluten generated during the process may be different from one batch to another (H.G. Watson et al. 2018). The accurate analysis of gluten in beer is problematic, and brewers who wish to market gluten-free beers made from gluten-containing cereals such as barley or wheat must be sure that their products have been rigorously tested to ensure compliance with the legislation.

Some methods are more capable at detecting hydrolysed gluten than others. Current scientific evidence shows that hydrolysed gluten can be detected with the “R5 competitive ELISA method”, as recommended by the CODEX Commission. However, gluten molecules that are (partially or entirely) degraded into small peptide fragments during the fermentation or hydrolysis process are not detected by the “sandwich ELISA method”. Therefore, for fermented or hydrolysed products such as beer, syrup, baby food or soya sauce, the CODEX Committee recommends the use of the R5 competitive ELISA method, which can detect the changed version of the protein.

In the last few years, new approaches and studies regarding the sensitivity of the analytical methods for testing gluten in hydrolysed products have been published (K.A. Scherf et al. 2018, H.G. Watson et al. 2019; Fernández-Gil MdP, 2021), and novel proposals and methods to analyse gluten have been developed as an alternative to ELISA (A. Cebolla et al. 2018). AOECS and its member societies have actively followed this research.

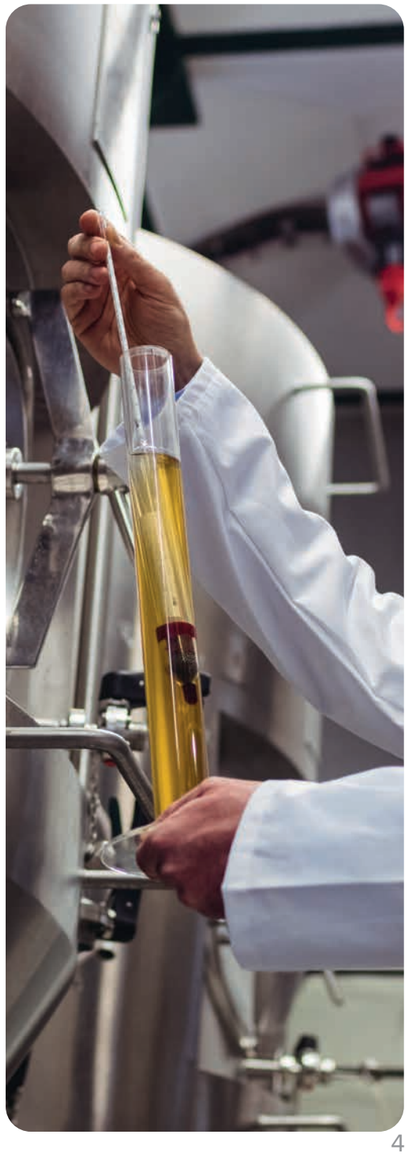
Most of these publications focus on beer as the main product of study, and some of them support the idea of possible limitations of the R5 competitive ELISA for the analysis of hydrolysed products. To this end, they explore the use of analytical methods that show more sensitivity, such as Liquid Chromatography-Mass Spectrometry (LC-MS) or LFIA, to quantify the number of immunogenic peptides in the final product with more precision (Liao, YS. Et al 2017, Ja Myun Yu et al. 2021, V. Segura et al. 2023). Although the approaches in these studies point to the effectiveness of their methods, it is important to keep in mind that they are not yet validated to quantify gluten in hydrolysed products (AOAC Official Methods of Analysis: 22nd Edition, 2023).

It must be noted that the reference material for testing hydrolysed gluten-free foods is also an important limitation. Further research is needed to accurately quantify gluten content in fermented-hydrolysed foods, as well as to define calibration standards for different fermentation processes, which can avoid false negative results. Establishing appropriate references that recognize the different protein and peptide profiles that may be present in final products will help ensure the accurate quantification of gluten. (Panda R. et al. 2019).

AOECS concludes that all methods currently under examination have limitations and uncertainties. This is supported by the Prolamin Working Group (PWG), a multidisciplinary group of experts founded in 1985 to coordinate research on gluten analysis in food and their clinical implications for coeliac patients and other gluten-related disorders.

The PWG published a 2021 position paper that stated, “More scientific studies are needed to better understand MS-detection of residual gluten in beer and other fermented foods and also to ensure that the R5 competitive ELISA picks up each peptide fragment it should”. The position highlights the need to further explore the use of LC-MS and its results, while also acknowledging that the high cost of this method makes it difficult to implement.

AOECS collaborates closely with the PWG and encourages it to promote further research on utilizing alternative methods—such as LC-MC, G12 competitive ELISA, or a combination of different antibodies like multiplex ELISA (Panda R. et al., 2017)—in an impartial manner. It is essential to remember that food analytical methods have a defined scope to determine whether the amount of a compound, in this case gluten, is present below or above a threshold set by legislation in a final product.



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IMPLICATIONS FOR THE HEALTH OF THE COELIAC COMMUNITY

The consumption of any alcoholic drink must always be in moderation, even if it is gluten-free.

Even well-managed coeliac disease with a strong adherence to the gluten-free diet implies an exposure to gluten, mostly inadvertently. This uncontrolled exposure to small amounts of gluten can trigger the autoimmune response, and it becomes necessary to study the immunogenicity of remaining peptides (Syage et al. 2018).

Clinical implications, as well as the evaluation of the immunogenicity of gluten-derived peptides, can only be evaluated by clinical studies.

Current studies do not have enough in vivo models to clearly define the effects caused by the consumption of remaining peptides on coeliac patients. Only some small in vitro experiments have been published. Most of the studies carried out at this point put the scope on the analytical method for gluten detection, the chemical composition of the peptides or the immunogenicity of the different peptide fragments. However, **none** consider the direct implications of the immunogenic activity of the remaining peptides on patients with coeliac disease.

Therefore, more clinical studies are needed. All clinical approaches need to be set up with care, and overcome all possible ethical objections, as participation in the study could be harmful for the patients involved. From AOECS, we encourage researchers to promote clinical studies from “a beer non-consumption approach” to align with the “no harm” ethical principle for clinical trials with humans.

CONCLUSIONS

- Beers are usually brewed from a cereal that is a source of gluten and which, according to EU law, may contain detectable traces of gluten below the 20 mg/kg limit that allows it to be labelled as gluten-free.

- At this point, there is limited evidence to say that the official method of analysis recommended by CODEX, R5 competitive ELISA, cannot effectively quantify gluten in hydrolysed products, or to conclude that gluten-free beers are unsafe for coeliacs. (Note: R5 competitive ELISA, Codex standard 118-1979 has not been revised since 2008. However, first action status was granted by AOAC in 2015.)

- The potential immunogenicity and inflammatory effects of the detected fragments can only be evaluated by clinical studies, as there are currently no validated in vitro models to assess the effects of the remaining peptides on individuals with coeliac disease.

- Although LC-MS/MS is more sensitive than the R5 competitive ELISA, it has not yet been validated to reliably quantify the amount of gluten in beer, so it is not yet an approved method for the detection of gluten. Furthermore, it is too expensive and too demanding in terms of time and skills for the manufacturers to implement it in their routine.

- New methods for the analysis of hydrolysed products must be studied. Exploring alternative analysis methods is important for food safety, not only in relation to gluten-free beer, but also in relation to other hydrolysed products that are consumed by coeliacs and so, must be added to the scope of research. AOECS encourages researchers from independent parties, such as the Prolamin Working Group, PWG, to carry out further studies.

- The lack of appropriate calibrants that reflect the protein/peptide profiles is another line of study to be further explored. It is necessary to distinguish between the profiles to define appropriate calibration standards and quantify them properly.

- AOECS encourages researchers from the International Society for the Study of Celiac Disease, ISSCD, to set up a clinical study from a non-consumption/elimination approach.

- Regulations for hydrolysed products don't need to be modified until more studies are done and there is more evidence related to such products. As the umbrella organization representing coeliac patients, AOECS remains vigilant of the situation, and encourages the authorities to act accordingly.

- AOECS supports its Member Societies to continue licensing gluten-free beer by following the AOECS Standard and analysing the product with the R5 competitive ELISA, until alternative methods that can better detect trace gluten are recognised by CODEX.

- AOECS Member Societies continuously work to build confidence among coeliac patients in managing risk, which is critical in many aspects of coeliac disease. AOECS and its member societies aim to avoid unnecessary fear and help coeliac patients to make informed decisions by verifying products against AOECS Standards and making these products easily recognisable by the Crossed Grain Symbol licenced to the brand.

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ABOUT AOECS

AOECS is an independent, non-profit organization. Since 1988, we have been dedicated to improving the lives of people affected by coeliac disease. AOECS represents 39 European national coeliac member societies and five affiliated coeliac organizations from outside of Europe.

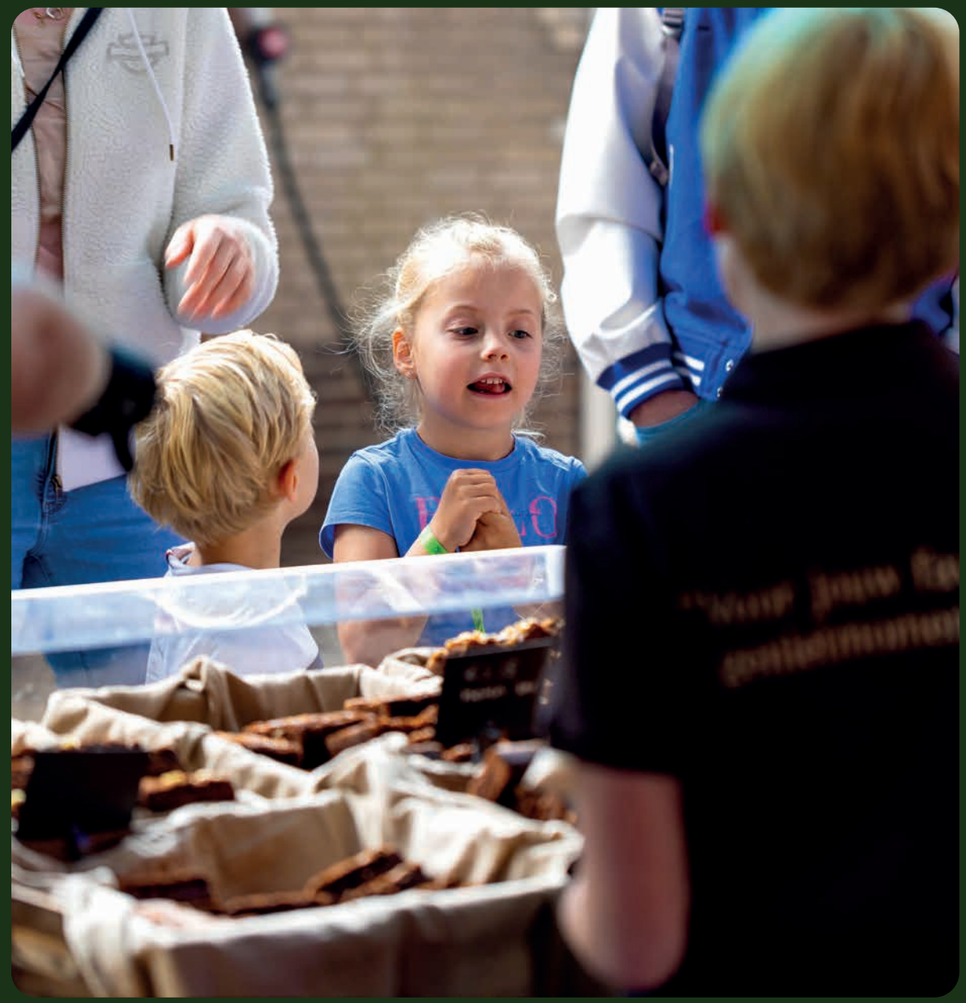
Coeliac disease (also spelled celiac disease) is an autoimmune disorder in which cereals containing gluten trigger an inflammatory reaction in the small intestine.

It is estimated that around 100 million people worldwide suffer from coeliac disease. However, only about 25% of them have received a diagnosis; the rest are either unaware of their condition or suffer from various related ailments.

If left untreated, the disease can lead to a severely reduced quality of life and symptoms such as infertility, osteoporosis and chronic fatigue.

As of today, the only known cure for coeliac disease is a lifelong, strict gluten-free diet.

Read more on www.aoecs.org



Young girl overwhelmed by the selection at a gluten-free festival in the Netherlands.

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