Background:

This position paper was in response to an emerging regulatory situation in Italy relating to agricultural comingling arising during primary production. This paper will set out the current regulatory framework for the use of precautionaty labelling in Europe and industry best practices associated with this. The paper will also detail current clinicial perspectives relating to mustard allegy and ultimatly the approach used by Mondelez International to assess and manage allergens as part of their food safety programes. A full summary of the situation can be found in the appendix to the document and assocated PPT files.

Mondelez Situation:

Mondelez is using wheat flour made with 100% of Italian wheat (claim on the pack of several finished goods). Currently the packs of the main products are not labelled for mustard in contains (mandatory information) and/or cross contact (voluntary information). Capriata plant is using 6 suppliers of wheat products with Italian plants (and which use Italian wheat due to the claim).1 supplier produces wheat specialties with low impact in terms of quantity in recipe. They already announced the intention to label mustard, but they did not share any test result. 2 of suppliers of wheat flour already declared intention to label mustard and they shared positive results with PCR (qualitative test) and 1 with ELISA (quantitative test). 1 of the suppliers of wheat flour also declared the potential switch of label, but they also declared that all test results are negative. The remaining 2 of suppliers of wheat flour shared negative results of their monitoring program for mustard, but now they have some doubts because their customers found positive results on wheat flour delivered from their mills. We have no reported cases of reaction for mustard in consumer database at least in the last 3 years. There is a low / limited impact for raw material delivered to other Bakery plants (only wheat germ is produced in Italy and delivered to French plants).

In this assessment we specifically considered;

1. Prevalance of mustard allergy
2. Potentency[a] & severity[b] of mustard mediated reactions.
3. Threshold data for mustard protien
4. European regulatory framework for precautionary allergen labelling (PAL)
5. Analytical testing for mustard protiens
6. Conclusions.

[a]*amount needed to trigger response*

[b]*severity of immune mediated reaction (i.e. rashes, swelling, anaphylaxis etc)*

1. Reported consumer reaction data and industry recall data for mustard (EU)

According to the RASFF database in 2019 there were 194 notifications for allergens (up by 30%) Milk, gluten and soya are the most commonly reported allergens. Mustard accounted for 5% of notifications and the majority of these relate to labelling issues for undeclared mustard used as a deliberate ingredient. With the exception of the recalls in Italy (details below) there has been no market action in other EU member states relating to mustard cross-contamination, possibly due to the fact that precautionary allergen labelling is considered ‘voluntary’ within the regulatory framework of Food Information to Consumers

Regulation (1169/2011). From a RASSF notification perspective, not all allergen issues are harmonised in EU legislation. Sometimes, cross-contact of allergens are notified, occurring in foods due to cross-contamination e.g., from raw materials or on the same production lines as other products containing allergens. Such occurrence of allergen cross-contamination is not regulated at EU level.

In November 2021 Famila and A&O chains have reported**ly** recalled of some types of organic wholemeal pasta with the Natura Chiama Selex brand and Gragnano Igp pasta with the Saper di Sapori Selex brand due to the *"Presence of the mustard allergen* **".** These products are all sold in packs of 500 grams. In January 2022 COOP recalled a batch of COUS COUS 4 Cereals – organic – produced by Nuova Terra for the presence of undeclared mustard.

Prevalance of Mustard allergy in Europe

In 2019/2020 CODEX Committee for Food Labelling (CCFL) and CODEX Committee for Food Hygiene (CCFH) requested that WHO/FOA form an ad-hoc expert committee to inform CODEX on a number of topics related to food allergy and food allergens. This committee was composed of experts from academia, regulators, healthcare professionals and the food industry. The first meeting convened was to review the current list of priority allergens for management and labelling purposes[5] (Part 1: Review and validation of Codex priority allergen list through risk assessment). The conclusion of the expert group was that 'due to the lack of data on prevalence, severity and/or potency, or due to regional consumption of some foods, the Committee recommended that some of the allergens, such as buckwheat, celery, lupin, mustard, oats, soybean and tree nuts (Brazil nut, macadamia, pine nuts), should not be listed as global priority allergens but may be considered for inclusion on priority allergen lists in individual countries'

Prevalence Assessment for MUSTARD seeds (Sinapis alba, Brassica nigra, and Brassica juncea) within the risk prioritization matrix

Criterion: Prevalence is a proportion of a population at risk for allergic reactions to the specific food in question

Explanation: This criterion reflects if the allergen in question is responsible for a common food allergy of global importance, this criterion reflects degree to which the prevalence of the food in question is impactful on a global scale.

Ranges:

Decision on criterion for matrix

	Bin 0	Bin 1	Bin 2	Bin 3	Bin 4
Prevalence (decision for matrix)	Insufficient data to determine low or high	Very low	Low	Mixed	High

Score __1_____ [bin 1,2,3 or 4]

Very low: <0.5% in one region only OR <0.1% in all regions

Low: <0.5% in all regions

Mixed: >1% in one region AND 0.5-1.0% in at least one other region

High: >1% in at least 2 regions

Potentency[a] & severity[b] of mustard mediated reactions.

Due to a current lack of published clinical studies (also linked to geographical restricted prevalence) there is not wholly conclusive threshold data (minimum eliciting dose) from clinical feeding trials for mustard. For mustard it has been reported that the minimum eliciting dose for **mustard is 0.8mg[2]** protein. The VITAL 3.0 ED05 level established for mustard is **0.4mg mustard protein[3].**

From data provided from the MDLZ supplier of wheat flour (see PPT Mustard emerging Issue in Italy), the highest suspected reported concentration of mustard was 56mg/kg. If this was used in a finished product composed of 83% wheat flour – (main product in MDLZ Capriata plant is ORO with 83% of wheat flour), this would give a concentration of 46.48 mg/kg or 4.6mg/100g. Looking at the VITAL 3.0 dose distribution data this would potentially trigger reactions in 20% of mustard allergic individuals. From data provided by the MDLZ supplier of wheat flours the vast majority of wheat flour samples tested returned negative results for mustard (ELISA & PCR)

Reported Reactions to mustard included: angioedema, airway obstruction, urticaria, wheezing, vomiting immediately after exposure and swelling of the lips, airway obstruction or anaphylaxis requiring emergency hospital attention[2]. These symptoms are considered moderate to severe (Brown, 2004). The other Canadian report concerned a single case. A 50 year-old woman had a history of anaphylactic type reactions after exposure to mustard. This clinical history was supported by a positive SPT for mustard (Connors *et al*., 2006).

Regulatory Framework Europe – Precautionary Allergen Labelling (PAL)

Regulation (EU) No 1169/2011 of the European Parliament and of the Council. Under this framework PAL is a voluntary particular and as such it is down to individual food business operators to decide if PAL is used on food products.

***Article 36* Applicable requirements**

1.Where food information referred to in Articles 9 and 10 is provided on a voluntary basis, such information shall comply with the requirements laid down in Sections 2 and 3 of Chapter IV.

2.Food information provided on a voluntary basis shall meet the following requirements:

(a) it shall not mislead the consumer, as referred to in Article 7;

(b) it shall not be ambiguous or confusing for the consumer; and

(c) it shall, where appropriate, be based on the relevant scientific data.

3.**[F1**Regulations may be made**]** on the application of the requirements referred to in paragraph 2 of this Article to the following voluntary food information:

(a)information on the possible and unintentional presence in food of substances or products causing allergies or intolerances;

F4...

4.In order to ensure that consumers are appropriately informed, where voluntary food information is provided by food business operators on a divergent basis which might mislead or confuse the consumer, **[F5**regulations may**]** provide for additional cases of provision of voluntary food information to the ones referred to in paragraph 3 of this Article.

FAO/WHO Conclusions for the use of PAL based on Quantitative Risk Assessment

The second and third sessions of the FAO/WHO expert committee advising CODEX[5,6] addressed the following topics: 1) Review and establish threshold levels in foods of the priority allergens & 2) Review and establish precautionary labelling in foods of the priority allergens. The conclusions from the expert group were as follows.

1. They noted that the data reported in the publications of Remington, et al., (2020) and Houben, et al., (2020) were the most comprehensive and best described source available, both in terms of content and curation, with supportive peer-reviewed publications. Dose-distribution analysis methodology was similarly well-described within this dataset. The Committee reviewed the data sources for each priority allergen, taking into consideration both included publications and those which had been collated but excluded, and the extent and type of bias in the data. Characterising the hazard forms a critical component of risk assessment and considers both the numbers of people with the relevant allergy who will be affected by exposure to any given amount of allergen and the characteristics of any reaction that may occur. The first element is covered by dose distribution modelling, which is now well understood and developed. The second element is an evaluation of the likely health impact. A key factor that impacts the health of allergic individuals is reaction severity. Severity is a complex and multidimensional concept with an ill-defined relationship to dose; as such severity data suitable for modelling are limited. Two principal sources of data were reviewed: 1) evidence of anaphylactic reactions in clinical data at defined doses and 2) data on symptoms associated with reactions up to and including the ED01, ED05 and ED10 reported by Remington, et al. (2020) and Houben, et al. (2020). The latter indicated that all symptoms up to ED05 fell into a mild or moderate category, while analysis of clinical data indicated that up to 5% of reactions at both ED01 and ED05 could be classed as anaphylaxis, although none were severe, based on the World Allergy Organisation definition. Furthermore, the Committee noted the extreme rarity of fatal food anaphylaxis (1 per 100000 person-years in the allergic population) and observed that no fatal reactions had been observed following exposure to doses at or below those considered for RfD (i.e. the ED01 and the ED05). Considering both the proportion of individuals potentially affected and the severity characteristics of reactions at ED01 and ED05, including the absence of reports of

severe anaphylaxis, the Committee agreed that, for all priority allergens, the safety objective would be met by starting the definition of RfD at the ED05 (as evaluated using the data from Remington, et al. (2020) and Houben, et al. (2020). To make the application simpler, the Committee further simplified its recommendations by rounding the ED05 values down to one significant figure (with some exceptions for allergens with limited data). Those foods with close ED05 values were then grouped together and a single value derived for the RfD, further rounding down the value, if necessary. The resulting RfDs as mg of protein from the allergenic source are summarised in the table below.

Taking into consideration this recommendation the ED05[3] is 0.4mg mustard protein. Assuming portion size of 100g of baked good finished product this would be represented as 0.4mg/100g or 4mg/kg. Typically wheat flour is used in a baked good recipe at a level of 50% therefore this would increase the PAL labelling threshold to 8mg/kg. Protein content of mustard seeds = 26% therefore >31mg/kg whole mustard needed to exceed proposed CODEX ED05 threshold for PAL labelling

Analytical Methods – Mustard.

There are two main analytical methods to detect mustard proteins. 1 Commercial ELISA kits 2. DNA based detection methods based on polymerase chain reaction (PCR). The main issue with the ELISA method is that it cannot differentiate between different species of brassica (rape seed / canola / wild mustard – Charlock *Sinapsis Arvensis*) and therefore a positive result is not conclusive for the presence of black, brown or yellow mustard (Sinapis alba, Brassica nigra, and Brassica juncea). For PCR many methods are qualitative (positive / negative at the limit of detection of the test.) and detection is not a direct measure of mustard protein which makes quantification problematic and difficult to determine the actual food safety risk posed to consumers.

Wheat Processing

During the agricultural production of wheat, it is possible that other brassicas may grow amongst the crop or alongside the boarders of the field. There are some controls such as physical size exclusion used during the harvest which would eliminate a portion of the ad-mix but there is a chance that this could be milled with the wheat. As the quantitative analytical methods cannot differentiate between different species of brassica and PCR methods are qualitative its is impossible to evaluate the food safety risk.

Conclusions

Although mustard is a regulated allergen in Europe if used as a deliberate ingredient in foods, prevalence is relatively uncommon when compared to other allergenic ingredients. The situation with agricultural comingling is not a new issue and if it was significant, we would have expected to see many more reactions in the community. The vast majority of market action (recalls / withdrawals / notifications) is linked to where mustard is used as a deliberate ingredient and not declared on the label. Analytical data supplied by the Italian Millers association does show a small number of positive results, however due to analytical

limitations it is impossible to say if this is due to mustard species or other brassicas for which allergenicity has not been established.

Under the European regulatory framework set out in 1169/2011, the use of precautionary allergen labelling is voluntary and for the individual food business operator to decide. It does however stipulate that this must be based on a risk assessment and must not mislead the consumer.

The ambition of Mondelez allergen management programs is to maximize choice and minimize risk for the food allergic consumer and precautionary allergen labelling should be used as a last resort if there is a clear and demonstrable risk of cross-contamination. With all of these facts considered we will not be adding mustard PAL to our finished goods. We will however be monitoring the situation closely and working with our trade partners to see if there is new evidence which could cause us to reconsider and change our approach.

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6. Ad hoc Joint FAO/WHO Expert Consultation on Risk Assessment of Food Allergens Part 3: Review and establish precautionary labelling in foods of the priority allergens

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Appendices

WHY DO WE NEED TO REVIEW MUSTARD RISK IN ITALY?

There is an emerging issue in Italy due to presence of mustard in the supply chain of wheat grains

Italian association of millers highlighted the potential presence of mustard in wheat (hard and soft) - 40% of durum wheat samples and 15% of soft wheat samples have been found positive for mustard (Barilla) - and gave recommendation to the miller to add mustard in cross contact declaration.

Mustard cross contamination happens in the field due to presence of wild variety of mustard, and crop rotation practices.

Italian Authorities sent circular to the control organisms and food associations to highlight the need to label mustard if food operator cannot exclude presence of mustard from materials/ products. They reject approaches from other countries (e.g. Vital, Canadian position) based on risk assessment of FGs.

A further challenge is the availability of analytical method to detect and/or quantify mustard in wheat flour (PCR can detect at low level DNA – but not proteins – without quantification and ELISA can quantify proteins but there is cross reactivity with canola). Italian Authorities gave task to official laboratory to review methods and establish proper protocol for mustard check. Trade associations of food producer and millers will cooperate and support this review of analytical method (e.g. : samples).

MDLZ suppliers of wheat flour (and wheat products) are now dealing with unclarity about the topic, and even they had negative results, they received claims form customer for presence of mustard. Probably the consequence will be the request to label wheat flour for mustard in cross contact.

We have to decide approach : 1) <u>risk assessment on FGs</u> (supported by test program) OR 2) <u>labelling for</u> mustard (due to new information coming from suppliers).

- Risk assessment will require resources to execute analysis, it will add complexity to manage hold and release (material, product) in IM/EM plants and/or suppliers.
- Labelling will require changes in specifications, and project to change (gradually) packaging of FGs.
- Intermediate position (e.g. Statement, internet information) would be needed.
- IM and EM plants using Italian wheat flour are impacted by the issue (mainly Italian plants but some impact is expected also in other countries).
- We do not expect sampling from Authorities in the next future (until method validation will be not completed – approx. 6 months).
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Potential Longer-Term Implications

- **This issue can spread in other EU country and suppliers could raise the same concerns: there is ongoing discussion in Spain, and one of Viana supplier already asked to add mustard (and soya) to MDLZ specification.**
- **Approach of Authorities in the EU countries can be different (e.g. : some EU countries could accept risk assessment and set indicative value for FGs). How can we keep consistency of labelling across EU?**
- **Issue could impact also other Category (e.g. pasta used in Meals)**
- **Supplier could challenge MDLZ specification also for soya labelling (contamination from supply chain)**

Background of the issue

- **Irish contact for RASFF** notified that wheat grains admixture from Southern counties especially from Italy contains high level of mustard and soyabean.
- **September 2021** there was communication from Italian association of millers (Italmopa) to all members about potential contamination of durum and soft wheat by mustard in the wheat supply chain (from the field).
- **October 2021** this information has been shared with stakeholders (included Union Food, which is the association of bakery and pasta producers), and via suppliers, to the customers. The final recommendation from Italmopa to wheat flour producers was to label mustard in the wheat flour sold in the retail market and give information to B2B customer about occasional contamination of wheat by mustard.
- **October 2021** Union Food started conversations with Authorities and associated.
    - ❖ **During one of the first meeting Barilla** (who is biscuits but also pasta producer and owns several mills) shared the overall results of their report: more than 40% of durum wheat and 15% of soft wheat samples have been found positive for mustard. They shared their intention to label immediately pasta (durum wheat) with the warning for mustard by printing the information with ink jet in the shelf-life box on the pack. They also said that do not see urgency for biscuits and crackers (soft wheat).
    - ❖ **Additional complexity is coming from analytical method**, because today there is not a reliable protocol to quantify presence of mustard proteins (ELISA), and the different PCR techniques can give different results and, in any case, show only presence or absence of mustard (above LOD).
    - ❖ **The Authorities (Health Minister – Directorate General of Hygiene and Food Safety and Nutrition)** recommended to label mustard if producer cannot exclude presence in the product placed in the market. They won't support any risk assessment on finished product based on quantity of mustard proteins (e.g. Vital), and any epidemiological study of mustard allergy occurrence.
- **December 2021** The Health Minister – DGSAN sent a circular to Food Associations and local and central Authorities competent for control of foodstuffs. The circular confirms the need to label mustard if producer cannot exclude the presence and suggests the immediate and long terms measures to implement allergens labelling. In the same document the DGSAN took the commitment to set a study for the validation of the suitable method to be used for mustard analysis in food, in cooperation with Food Associations and food operators (with their contribution in terms of samples and funds).

<u>Mondelēz Situation</u>

- Mondelez is using wheat flour made with 100% of Italian wheat (claim on the pack of several finished goods).

- Currently the packs of the main products are not labelled for mustard in contains (mandatory information) and/or cross contact (voluntary information).
- Capriata plant is using 6 suppliers of wheat products with Italian plants (and which use Italian wheat due to the claim).
- 1 supplier produces wheat specialties with low impact in terms of quantity in recipe. They already announced the intention to label mustard, but they did not share any test result.
- 2 of suppliers of wheat flour already declared intention to label mustard and they shared positive results with PCR (qualitative test) and 1 with ELISA (quantitative test)
- 1 of supplier of wheat flour also declared the potential switch of label, but they also declared that all test results are negative.
- The remaining 2 of suppliers of wheat flour shared negative results of their monitoring program for mustard, but now they have some doubts because their customers found positive results on wheat flour delivered from their mills.
- We have no reported cases of reaction for mustard in consumer database at least in the last 3 years.
- Low / limited impact for raw material delivered to other Bakery plants (only wheat germ is produced in Italy and delivered to French plants).

Supplier Information – Mustard Contamination of Wheat Flour (see separate PowerPoint File – Mustard Immerging Issue in Italy)