Brussels

GUIDANCE ON USE OF BBPA BRIEFING NOTES

1. Thank you BBPA and EBC

Over a period of 25 years, the BBPA has funded the development of briefing notes on sensitive food safety issues affecting the beer category. The objective of this proactive initiative is to avoid being caught unprepared if there is a food safety scare or incident that impacts beer. Protection of the beer category as a whole is the first line of defence in protecting individual brands.
The Brewers of Europe have introduced a similar initiative in developing Technical Information Sheets at European level. However, it is recognised that it will take several years before this initiative delivers comprehensive coverage of the food safety issues that could possibly affect beer or its ingredients. To address this, the feasibility of obtaining access to the BBPA/BRI briefing notes has been investigated. EBC acted as a conduit for the supply of the briefing notes from BBPA to The Brewers of Europe.

2. Distribution

2.1 BBPA briefing notes are made available to The Brewers of Europe members.

2.2 This availability is provided through a password protected part of The Brewers of Europe website.

2.3 Each The Brewers of Europe member is accountable for the control and use of the BBPA briefing note.

2.4 The National Member Associations will assist their members with the implementation and direction of the information to a specific application.

2.5 Wide-scale distribution of the BBPA briefing notes should not occur.

2.6 The Brewers of Europe Secretariat must be advised of the outcome of the application of the BBPA briefing note.

3. Responsibilities

Neither The Brewers of Europe, its constituent Communications, Task Issue Management Teams nor the Technical Information Sheet Supplier can be held responsible for any error or adverse outcome from the use of the BBPA briefing notes.

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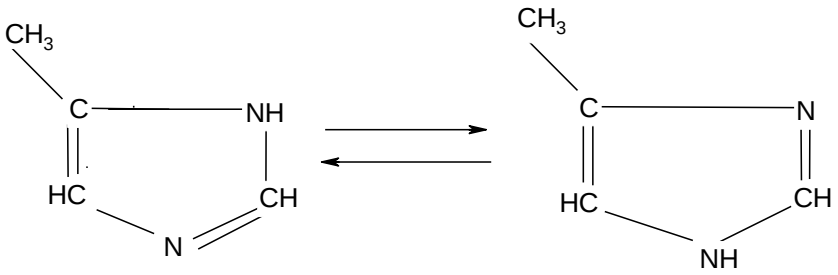
BBPA/BRI BRIEFING NOTE
No. 3.25 4-methyl imidazole

BACKGROUND BRIEF

- 4-methyl imidazole can be formed as a byproduct during the caramelization process, for example, during the manufacture of caramels.
- Caramel colourings are widely used in many countries to add colour to beer, to supplement that derived from malts and roasted cereals.
- Recent studies suggest that 4-methyl imidazole can cause cancer in animals.
- It is not known if it has the same effect in humans. However, many regulatory bodies across the world, including in the EU, have set a limit for the amount of 4-MI which can be present in caramel, as a precaution.
- All caramels used by BBPA members comply with these limits.

1. What is 4-methyl imidazole (4-MI)?

CAS No: 822-36-6
EINECS No: 212-497-3



4-Methylimidazole (4MI) is a chemical used in the manufacture of pharmaceuticals, photographic chemicals, dyes and pigments, cleaning and agricultural chemicals, and rubber. 4- and 2-methyl imidazole are also used in epoxyresins.

4-MI has been identified as a by-product of reactions between reducing sugars and ammonium groups (Maillard reactions), as in the manufacture of ammonia and sulphite-ammonia caramels (caramel classes III and IV) *(Moon and Shibamoto, 2011)*. Potentially, it can also be formed in the manufacture of speciality malts and in the roasting of coffee (see Section 2).

It has also been detected in mainstream and side stream tobacco smoke.

2. Sources of 4-MI in the brewing industry

The major source of 4-MI in beer is ammonia caramel (Caramel class III: E150c).Analysis of 5 ammonia caramels, using a method involving solid-phase extraction followed by LCMS, reported concentrations of 4-MI ranging from 85 – 188 mg/kg, with a mean of 139 *(Klejdus, 2006).*None of the samples exceeded the current EU limit for 4-MI in ammonia caramel, which is 250mg/kg.

Theoretically, traces of 4-MI could be formed during the manufacture of speciality malts and their extracts, since Maillard reactions also occur during these processes. However, there is no data to confirm whether or not detectable 4-MI does occur in these materials (See also section 4).

3. Toxicity of 4-MI

4-MI is not currently listed by IARC as a carcinogen, although it has been selected for review *(IARC, 2011)*. In studies with rodents for the US Department of Health's National Toxicity Program, 4-MI was found to be a hepatic (liver) toxin. High doses were associated with increased incidence of leukaemias and cancers of the respiratory system *(Chan et al, 2008).* There was no consistent evidence of genotoxicity in these studies.

EFSA reviewed caramel in 2011, including the NTP studies *(EFSA, 2011).* They concluded that there was no evidence of genotoxicity and that the carcinogenic effects observed showed a clear threshold, with a No Observed Adverse Effects Level (NOAEL) of 80mg/kg body weight/day. EFSA considered that the group ADI of 300mg caramel/kg bodyweight /day (100 mg/kg body weight /day for ammonia caramel), together with the purity specifications, provided a sufficient margin of safety, but that it would be prudent to reduce levels of 4-MI in caramels as much as was feasible. There are no reports of 2-MI being found in caramels.

The toxicity of 4-MI contaminating ammonia caramel was considered by JECFA at their 15th meeting, when a temporary ADI of 0-100mg/kg body weight /day was introduced. At a subsequent meeting, limits were set for 4-MI in ammonia caramel. The most recent evaluation of ammonia caramel by JECFA, in 1987, took into account a number of long and short term studies using caramels with the new specifications. These suggested that the no-effect level for the health effect of greatest concern (a lymphocyte-depressing activity considered to be due to 2-acetyl-4-tetrahydroxy-butylimidazole - THI) was 20g/kg body weight /day. On the basis of this, an ADI of 0-200mg/kg body weight/day was set *(IPCS, 1987).* Carcinogenicity was not detected in these studies.

4. 4-MI in beers and other beverages

A range of soft drinks and dark beers available in Europe (dark lagers, stouts, Trappist beers and weissbeirs) were analysed for 4-MI using a GCMS method with a limit of detection of 0.6µg/litre and a limit of quantification of 2.2µg/litre *(Cunha et al, 2011).* Levels of 4-MI in dark beers ranged from 3 – 424 µg/litre, while those in soft drinks were higher, at 37 – 613 µg/litre. The highest levels were found in colas.

Substantially lower levels of 4-MI were reported by Klejdus et al *(2006),* using an LCMS method with solid phase extraction. The seven dark beers analysed (mostly from the Czech Republic) fell into two distinct groups: 4 beers contained 4-MI in the range 1.58 – 4.05 µg/litre (mean 3.28) whilst the other 3 beers were in the range 10 – 28 µg/litre (17.1). The authors suggested that the lower levels of 4-MI reflected the use of dark malts rather than caramel as a source of colour.

Details of reports for 4-MI in beers are shown in **Table 1.**

Significantly higher levels of 4-MI can be found in soft drinks, especially colas, and in coffee powder. In the case of soft drinks, the source is largely caramel, but with coffee it is probably formed during the roasting process.

There have been some suggestions that 4-MI could also occur in wines, but no analytical data is available. Caramel is not permitted as a colouring in wine in the EU, except for certain fortified wines such as sherry.

Table 1. 4-Methyl Imidazole in beers

Beverage type (no of samples)	Range [4-MI] µg/litre	Mean [4-MI] µg/litre	Data source	µg 4-MI / serving (330 ml)
Dark lagers (10)	<0.6 - 325	79	Cunha et al, 2011	26
Trappist ales (3)	20 - 424	198		65
Stouts (4)	18 - 142	80		26
Dark Weissbeir (3)	<0.6 - 3	1.4		0.46
Dark beers (7) **Samples 1- 4** **Samples 5 – 7** **All beers**	 1.58 – 4.05 10 - 28 1.6 - 28	 3.28 17.1 9.2	Klejdus et al, 2006	For a typical beer containing 9.2µg/litre, 330 ml would contain 3µg.

Table 2. 4-Methyl Imidazole in other beverages

Beverage type (number of samples)	Range 4-MI µg/kg or litre	Mean 4-MI µg/kg or litre	Data source	µg 4-MI / serving
COFFEES (results expressed per kg coffee powder)				
Ground coffee	390 - 2050	920	Klejdus et al, 2006	
Instant coffee	570 - 730	650		For a typical serving using 5g coffee powder, 1 mug would contain 3.25µg 4-MI
All coffee	410 - 2050	867		
SOFT DRINKS (µg/litre as drunk)				
Branded colas (13)	214 - 416	288	Cunha et al, 2011	A typical 330ml serving would contain 111µg 4-MI
Generic colas (8)	255 - 613	385		
Energy drinks (8)	<0.6 - 37	5.2		A typical 250ml serving would contain 1.3µg 4-MI
Carbonated guarana (1)	438	438		A typical 250ml serving would contain 110µg 4-MI
Non-carbonated flavoured drinks (6)	<0.6 - 71	26		
Colas (5)	300 - 360	332	Moon & Shibamoto, 2011	A typical 330ml serving would contain 110µg 4-MI

5. Daily intake of 4-MI

Cunha et al *(2011),* using published consumption data, estimated that the maximum consumer exposure to 4-MI from soft drinks would be 2.3 µg/kg body weight/day in Europe and 5.7 µg/litre in the US.

It is more difficult to estimate likely exposure to 4-MI from beer drinking using currently available data, because the reported concentrations in beer vary widely between the different publications. Using Cunha's data for the 4-MI content of dark beers, consumption of half a litre of a dark beer containing the maximum level of 4-MI found (424µg/litre, in a Trappist beer) would equate to an exposure of 3.5 µg/kg body weight/day for a 60 kg person. This is similar to that delivered by half a litre of cola. Using Klejdus's data, consumption of half a litre of a dark beer containing the maximum level of 4-MI would equate to an exposure of 0.23 µg/kg body weight/day for a 60 kg person.

Consumption of lager or pale ale is unlikely to contribute a significant amount of 4-MI to the diet.

6. EU Legislation

In the EU, ammonia caramels may not contain more than 250 mg 4-MI/kg caramel, expressed on an equivalent colour basis (that is, where the caramel has a colour intensity standardised to 0.1a.u) *(EC, 1995).* This limit is currently being reviewed following the EFSA recommendation that 4-MI levels in caramel should be reduced as much as was feasible *(EFSA, 2011)*.

Ammonia caramel is an allowed colouring material for beer in the EU under Directive 94/36/EC *(EC, 1994),* which is implemented in the UK by the food additives legislation *(UK, 2009).* There are no restrictions upon the amount which may be used – that is, it may be used in accordance with Good Manufacturing Practice *(quantum satis).*

Directive 94/36/EC is currently being replaced by Regulation 1333/2008 *(EC, 2008)* which covers colours, sweeteners and miscellaneous additives. This regulation establishes a Community list of additives which are authorised for use in the EU. It is expected that most colours currently permitted will be transferred to this regulation, but some changes may be introduced. Until the Community lists are completed, colourings which are approved under Directive 94/36/EC may still be used.

7. Legislation outside Europe

Caramel is approved for use in beer in many other countries, including Australia, Canada, New Zealand and the USA. As in the EU, no limitations are placed on the amount of caramel which can be used in beer. Some, but not all, regulatory bodies have set limits for the 4-MI content of ammonia caramel.

In the USA, caramel is one several food colourings which are exempt from certification *(US, 2009)*. Purity criteria are set for heavy metals only, no limits are set for 4-MI. However, the Office of Environmental Health Hazard Assessment (OEHHA) of California has added 4-MI to the list of chemicals known to the state to cause cancer for purposes of the Safe Drinking Water and Toxic Enforcement Act of 1986 (Proposition 65) *(OEHHA, 2010a).* The No Significant Risk Level specified under this act is 16 µg/day *(OEHHA, 2012).*

The Food Chemicals Codex, in its latest (fifth) edition, sets a limit of 0.025% for 4-MI in caramel *(FCC, 2003).*

At their 55th meeting in 2000, the WHO/FAO's Joint Expert Group on Food Additives (JECFA) set a limit of 300mg/kg (200mg/kg on an equivalent colour basis) for 4-MI in ammonia caramel *(JECFA, 2006).*

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Update history.

Date	Changes
Feb 2011	Note created
April 2011	Comments from BBPA's BQSP incorporated. EFSA review of caramel included
January 2012	Updated NSRL of 25 ug/day in Prop. 65