# On the release of a toxicant from PLA film filter on iQOS heat stick

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The difference of opinion and dispute between researchers from University of California and Philip Morris International R&D about formation of formaldehyde cyanohydrin, a highly toxic chemical in polylactide (PLA) film filter in iQOS device interested us from chemical point of view.

iQOS is an electrically-heated "heat-not burn" smoking system popular alternative to conventional cigarettes.

Figure 1. iQOS heat stick

In iQOS heat stick (Figure 1) the *first part* (the partition between the remaining filters and tobacco) does not allow harmful particles to penetrate. The *second part* is made from polylactide (a biodegradable polymer film made from sugar cane or starch). This section of the filter provides a comfortable level of "tobacco vapor" temperature released during the process of heating tobacco (up to 350˚C). The *third part* is the cellulose-acetate filter as in ordinary cigarettes. The *last element* in the filter system is the mouthpiece.

Researchers from University of California (Reverside, CA, USA) published an article [1], in which they have reported about potential danger of using poly(lactic acid) (PLA) film filter in iQOS. Containing in heatsticks, this thin polymer film plays the role of aerosol cooler to provide comfort temperature of inhaling. PLA with melting point 153-155$^0$C can melt during iQOS use predominantly in the section closest to the tobacco plug. The authors studied 3 mm cut out portion of the polymer-film (16.7%) closest to the tobacco plug by gas chromatography–mass spectrometry (GC–MS) using an Agilent 7890B GC coupled with a 5977A MSD. Evaluation of iQOS aerosols was performed using headspace analysis. Chromatographic separation was accomplished using an Agilent J&W HP-5ms Ultra Inert GC Column (30 mx0.25 mmx0.25 μm) and ultra-pure helium (>99.999% purity) as the carrier gas at a flow rate of 1.5 mL/min at 40°C

for 5 min, 45°C for 5 min, 90°C for 5 min, 130°C for 5 min, 135°C for 5 min, 165°C for 5 min, 190°C for 2 min at 10°C/min heating rate (Figure 2). They have reported about the release of an acute toxicant formaldehyde cyanohydrin starting from 90°C, according to the mass spectral matching (acceptance criteria >85%) towards the spectral library of National Institute of Standard and Technology (NIST).

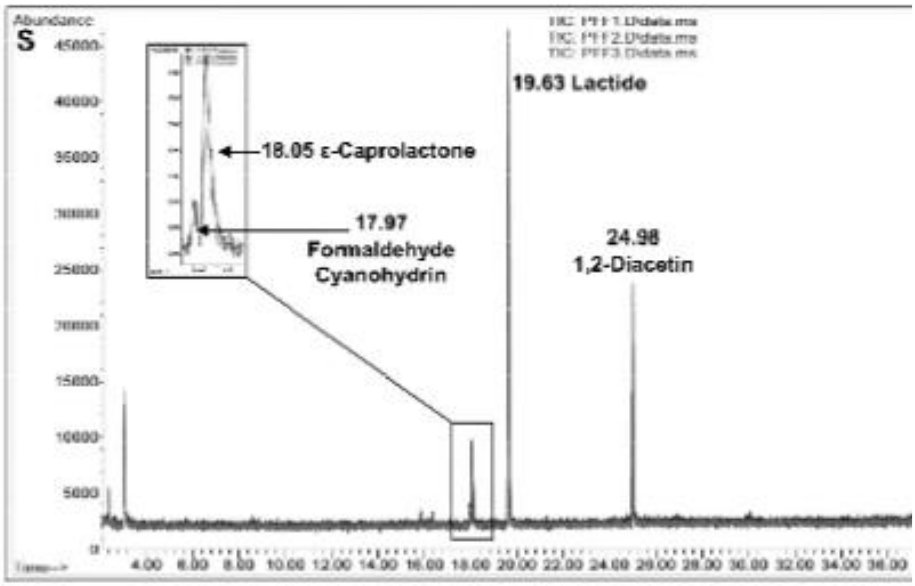


Figure 2. University of California, GC-MS spectrometry headspace analysis of cut out portion of unused PLA filter closest to tobacco plug after heating [1].

According to the authors GC–MS headspace analysis of cut out portion of unused PLA filter closest to tobacco plug after heating showed the presence of ε-caprolactone, lactide, 1,2-diacetin (plasticizer), and highly toxic formaldehyde cyanohydrin (Figure 2).

The authors of the article asserted that charring takes place in iQOS at heating referring to the article published by Auer *et al* [2] which showed the presence in iQOS systems volatile organic compounds, carbon dioxide, nitric oxide as well as polycyclic aromatic hydrocarbons, particularly high amount of acenaphthene, at temperatures less than 350°C (Table 1).

Table 1. Concentrations of volatile organic compounds in iQOS and conventional cigarettes [2].

Table. Concentrations of 8 Volatile Organic Compounds, 16 Polycyclic Aromatic Hydrocarbons, 3 Inorganic Compounds, and Nicotine in Mainstream Aerosol and Temperature of the HNB IQOS Cigarette and Conventional Cigarettes

| Analyzed Compound | HNB Cigarette | | Conventional Cigarette | | Proportion of the Chemical in HNB and Conventional Cigarettes, % |
|---|---|---|---|---|---|
| | Amount, Mean (SD) | No. of Replications for Each Assay | Amount, Mean (SD) | No. of Replications for Each Assay | |
| Volatile organic compounds, µg per cigarette[a] | | | | | |
| Acetaldehyde | 133 (35) | 5 | 610[b] | 1 | 22 |
| Acetone | 12.0 (12.9) | 5 | 95.5 (13.5) | 2 | 13 |
| Acroleine | 0.9 (0.6) | 2 | 1.1 | 1 | 82 |
| Benzaldehyde | 1.2 (1.4) | 5 | 2.4 (2.6) | 2 | 50 |
| Crotonaldehyde | 0.7 (0.9) | 5 | 17.4 | 1 | 4 |
| Formaldehyde | 3.2 (2.7) | 5 | 4.3 (0.4) | 2 | 74 |
| Isovaleraldehyde | 3.5 (3.1) | 5 | 8.5 (10.8) | 2 | 41 |
| Propionaldehyde | 7.8 (4.3) | 5 | 29.6 (36.6) | 2 | 26 |
| Polycyclic aromatic hydrocarbons, ng per cigarette[c] | | | | | |
| Naphthalene | 1.6 (0.5) | 4 | 1105 (269) | 7 | 0.1 |
| Acenaphthylene | 1.9 (0.6) | 4 | 235 (39) | 7 | 0.8 |
| Acenaphthene | 145 (54) | 4 | 49 (9) | 7 | 295 |
| Fluorene | 1.5 (0.6) | 4 | 371 (56) | 7 | 0.4 |
| Anthracene | 0.3 (0.1) | 4 | 130 (18) | 7 | 0.2 |
| Phenanthrene | 2.0 (0.2) | 4 | 292 (44) | 7 | 0.7 |
| Fluoranthene | 7.3 (1.1) | 4 | 123 (18) | 7 | 6 |
| Pyrene | 6.4 (1.1) | 4 | 89 (15) | 7 | 7 |
| Benz[a]anthracene | 1.8 (0.4) | 4 | 33 (4.2) | 7 | 6 |
| Chrysene | 1.5 (0.3) | 4 | 48 (6.2) | 7 | 3 |
| Benzo[b]fluoranthene | 0.5 (0.2) | 4 | 24 (2.9) | 7 | 2 |
| Benzo[k]fluoranthene | 0.4 (0.2) | 4 | 4.3 (2.8) | 7 | 9 |
| Benzo[a]pyrene | 0.8 (0.1) | 4 | 20 (2.9) | 7 | 4 |
| Indeno[1,2,3-cd]pyrene | ND | 4 | NA | NA | NA |
| Benzo[ghi]perylene | ND | 4 | NA | NA | NA |
| Dibenzo[a,h]anthracene | ND | 4 | NA | NA | NA |
| Inorganics, ppm in the mainstream smoke[d] | | | | | |
| Carbon dioxide | 3057 (532) | 5 | >9000 | 3 | NA |
| Carbon monoxide | 328 (76) | 5 | >2000 | 3 | NA |
| Nitric oxide | 5.5 (1.5) | 5 | 89.4 (71.6) | 3 | 6 |
| Other measures | | | | | |
| Nicotine, µg per cigarette[a] | 301 (213) | 4 | 361 | 1 | 84 |
| Temperature, °C | 330 (10) | 2 | 684 (197) | 1 | NA |
| Puff total count | 12.6 (2.4) | 32 | 13.3 (3.1) | 6 | NA |

Abbreviations: HNB, heat-not-burn; NA, not analyzed; ND, not detected.

[a] We applied the methods described previously in Varlet et al[4] to analyze volatile organic compounds and nicotine.

[b] Because there was only 1 replication, no SD can be computed.

[c] We present values reported from Vu et al[5] for the ISO smoking regimen and for a mean of the 35 top-selling US cigarette brands.

[d] Carbon dioxide was measured with a Testo 535 (Testo), and carbon monoxide and nitric oxide were measured with a Pac 7000 that detected carbon monoxide (Draeger). The apparatus measured the smoke when it was released from the syringe pump.

## Appendix C: Comparison of *IQOS* HPHC Levels to the 3R4F Reference Cigarette and 31 Combusted Cigarettes on the U.S. market

Table 2. Aldehydes (formaldehyde, acetaldehyde, propionaldehyde, acrolein), acetone and hydrogen cyanide contents in iQOS, 3R4F Reference Cigarette and 31 Combusted Cigarettes of US brands [3]

| HPHC | Unit | 3R4F | | 31 US Brands | | MR0000059 | | | | | MR0000060 | | | | | MR0000061 | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | AVG (/cig) | AVG (/mg nicotine) | AVG (/cig) | AVG (/mg nicotine) | AVG (/cig) | AVG (/mg nicotine) | % Δ 3R4F* | % Δ US brands * | # of heatsticks equal 1 US brand* | AVG (/cig) | AVG (/mg nicotine) | % Δ 3R4F* | % Δ US brands * | # of heatsticks equal 1 US brand* | AVG (/cig) | AVG (/mg nicotine) | % Δ 3R4F* | % Δ US brands * | # of heatsticks equal 1 US brand* |
| Acetaldehyde | µg | 1637 | 899 | 1435 | 717.5 | 194 | 149 | ↓83.4 | ↓79.2 | 5 | 206 | 169 | ↓81.2 | ↓76.5 | 4 | 187 | 160 | ↓82.2 | ↓77.7 | 4 |
| Propionaldehyde | µg | 114 | 62.6 | | | 10.9 | 8.38 | ↓86.6 | | | 11.8 | 9.67 | ↓84.6 | | | 11.3 | 9.66 | ↓84.6 | | |
| Acetone | µg | 655 | 360 | | | 30.8 | 23.7 | ↓93.4 | | | 36 | 29.5 | ↓91.8 | | | 33.9 | 29.0 | ↓91.9 | | |
| Acrolein | µg | 157 | 86.3 | 158 | 79 | 8.25 | 6.35 | ↓92.6 | ↓92.0 | 12 | 9.26 | 7.59 | ↓91.2 | ↓90.4 | 10 | 8.49 | 7.26 | ↓91.6 | ↓90.8 | 11 |
| Formaldehyde | µg | 85.2 | 46.8 | 98.8 | 49.4 | 13.9 | 10.7 | ↓77.2 | ↓78.4 | 5 | 14.7 | 12.0 | ↓74.3 | ↓75.6 | 4 | 9.07 | 7.75 | ↓83.4 | ↓84.3 | 6 |
| Hydrogen cyanide (HCN) | µg | 346 | 190 | | | ND | ND | | | | ND | ND | | | | 2.94 | 2.51 | ↓98.7 | | |

MR0000059: *IQOS* system with *Marlboro HeatSticks*
MR0000060: *IQOS* system with *Marlboro Smooth Menthol HeatSticks*
MR0000061: *IQOS* system with *Marlboro Fresh Menthol HeatSticks*

ND – not detected
* comparison made using per mg nicotine values
Data Sources: NS308-H, NS309-H, and NS336-H in MR0000066 and SR1_Q08-A1_HPHC-MarketMap-Results.xls

From the FDA Briefing Document (Table 2, Fragment from Appendix C Table) it is seen that mean amount of aldehydes: formaldehyde, propionaldehyde and acrolein produced from tobacco pyrolisis in iQOS device insignificant in comparison with the amount of acetaldehyde (9.07, 14.7, 13.9 vs 187, 206, 194; Table 2) [3], and therefore formation of acetaldehyde cyanohydrin (2-hydroxy propionitrile) should be predominantly expected among all possible cyanohydrins. The cyanohydrins could be formed by interaction of corresponding aldehydes or ketons with hydrogen cyanide [4]:

$$RR'C{=}O + HCN \rightarrow RR'C(OH)CN$$

However the cyanohydrins were not detected and not listed in the table. Other possible reagent of this reaction hydrogen cyanide either was not detected in iQOS device or its content was insignificant. Since PLA doesn't contain nitrogen it can't be the source of this element to form nitrogen containing organic compounds, particularly cyanohydrins. Polycyclic aromatic hydrocarbons, particularly acenaphthene was also not detected and not listed in the FDA document.

Poly(lactic acid) or polylactide (PLA) is a biodegradable thermoplastic aliphatic polyester derived from renewable sources, such as corn, starch, sugarcane. PLA undergoes degradation during thermal processing, giving a rapid reduction of molecular weight due to depolymerization and intra-molecular transesterfication reactions leading to cyclic oligomers of lactic acid and lactide. However degradation processes through radical reactions proceed only for temperatures exceeding $250^0$C. Figure 3 presents TG weight losses of neat PLA (PLA/PBS 100/0) and blends with poly(butylene succinate)-PBA, which shows rather high thermal stability of neat PLA [5]

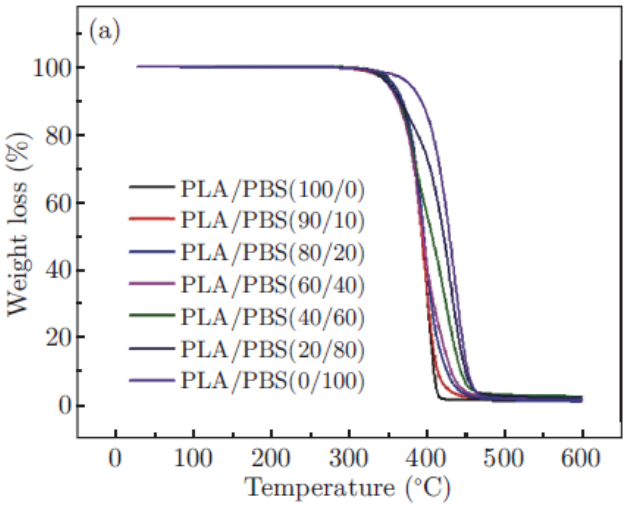


Figure 3. Thermo gravimetric curves of the neat PLA, PBS and PLA/PBS blends, heating rate 10±C/min [5].

To verify the hypothesis regarding formaldehyde cyanohydrin formation in iQOS system stated by the researchers from University of California Philip Morris International, R&D [6] repeated the analytical setup using headspace analysis coupled to gas chromatography high resolution mass spectrometry (HS-GC-HR-MS) (Figure 4).

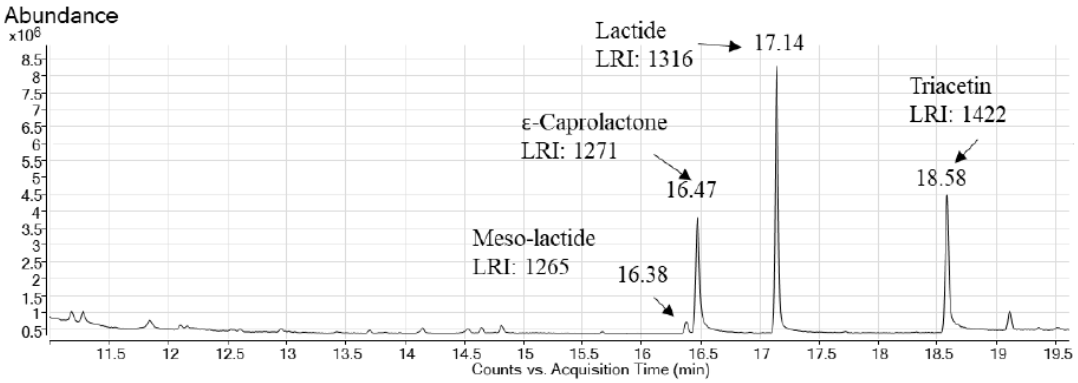


Figure 4. Philip Morris International R&D, GC-MS spectrometry headspace analysis of unused PLA filter [6].

Philip Morris International R&D showed:
• The difference in retention time of formaldehyde cyanohydrin obtained from the injection of the analytical grade reference standard (11.53 min) and the suspected compound observed in the PLA filter headspace analysis.
• No traces of formaldehyde cyanohydrin in the PLA filter chromatogram have been detected while searching for fragment ions obtained from the reference standard.
• The chemical identity of the suspected peak was confirmed as meso-lactide, a known condensation product of lactic acid.

**Conclusion**

Studying the arguments of both research teams we have come to the following conclusion:

- As was discussed above, polylactide can't be the source of formaldehyde cyanohydrins.
- Use of analytical grade reference standards in chromatographic studies is very important, which demonstrated researchers from Philip Morris International R&D.
- Thus, formaldehyde cyanohydrin absence in unused PLA filter after heating of the iQOS system is obvious.

**References**


1. Davis B, Williams M, Talbot P. "iQOS: evidence of pyrolysis and release of a toxicant from plastic." Tob. Control 2018; 0, 1-8.
2. Auer R, Concha-Lozano N, Jacot-Sadowski I, et al. Heat-not-burn tobacco cigarettes: smoke by any other name. JAMA Intern Med 2017;177:1050–2.
3. FDA Briefing Document: January 24-25, 2018TPSAC Meeting.
4. David T. Mowry. "The Preparation of Nitriles". Chem. Rev. 1948, **42** (2), p. 231.
5. E. Hassan, You Wei, He Jiao, Yu Muhuo. Dynamic Mechanical Properties and Thermal Stability of Poly(lactic acid) and Poly(butylene succinate) Blends Composites. Journal of Fiber Bioengineering and Informatics 6:1 (2013) pp.85-94.
6. A. Glabasnia, Ph. A. Guy, C.Goujon, S. Maeder. Analysis of Polylactic acid Filters, Response to the article entitled "iQOS: evidence of pyrolysis and release of a toxicant from plastic" by Davis B. et al., 2018. PMI Science, PMI R&D.