



(51) International Patent Classification:

G01N 30/12 (2006.01) G01N 30/72 (2006.01)
G01N 30/46 (2006.01) G01N 30/00 (2006.01)
G01N 30/88 (2006.01) G01N 30/06 (2006.01)

(21) International Application Number:

PCT/EP2015/056023

(22) International Filing Date:

20 March 2015 (20.03.2015)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

14160980.0 20 March 2014 (20.03.2014) EP

(71) Applicant: **PHILIP MORRIS PRODUCTS S.A.**
[CH/CH]; Quai Jeanrenaud 3, CH-2000 Neuchâtel (CH).

(72) Inventor: **CRUDO, Jean-René**; Rue de la Dîme 4, CH-2072 Saint-Blaise (CH).

(74) Agent: **DOWLING, Ian**; Reddie & Grose LLP, 16 Theobalds Road, London Greater London WC1X 8PL (GB).

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY,

BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

Published:

- with international search report (Art. 21(3))
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))

(54) Title: IMPROVED METHOD AND APPARATUS FOR ANALYSIS OF VOLATILE COMPOUNDS

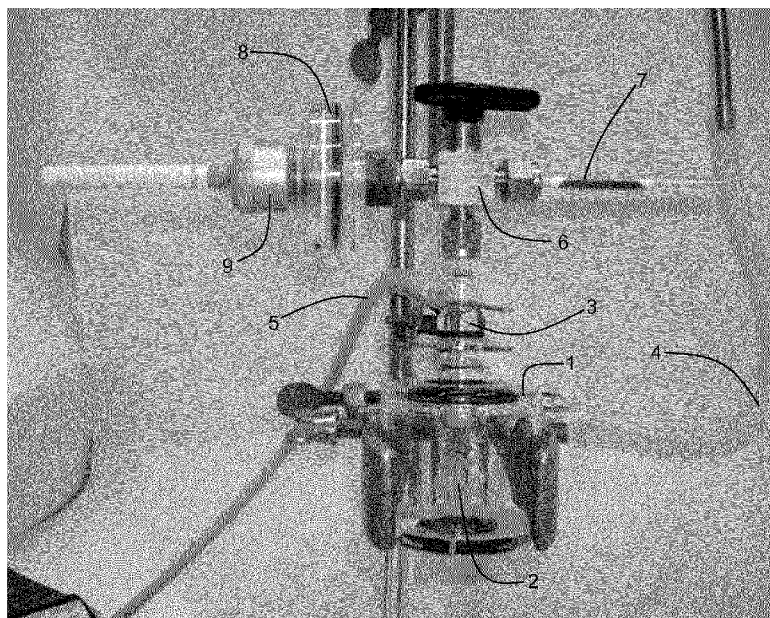


Figure 1

(57) Abstract: There is provided a system for capturing an aerosol from a smoking article, the system comprising a smoking article holder (9) for receiving a smoking article, a cooling mantle (1) and a vial (2) received within the cooling mantle (1). The system further comprises a nitrogen evacuation pipe (4) in fluid communication with the cooling mantle (1) for controlling a supply of liquid nitrogen to the cooling mantle (1), and a head connection (3) providing fluid communication between the smoking article and the vial (2). The system also comprises a puff generator and a pipe connection (5) connecting the puff generator to the head connection (3).

IMPROVED METHOD AND APPARATUS FOR ANALYSIS OF VOLATILE COMPOUNDS

The invention relates to an improved system for capturing an aerosol from a smoking article, a method for separating aerosol compounds, a gas chromatography-mass spectrometry (GC-MS) system, and a method of capturing an aerosol from a smoking article. Methods and systems according to the present invention are particularly useful for cigarette smoke characterization using a novel cold trap, dual gas chromatography columns and cryofocusing systems.

Cigarette smoke is a highly complex matrix which presents analytical difficulties for the analyst when having to perform compound identification by GC-MS (gas chromatography analysis coupled with mass spectrometric detection). Cigarette smoke is a complex matrix containing between 4000 and 5300 different identified compounds and is known to consist of two distinct parts: the particulate phase, which can be trapped using a glass fiber pad filter (as described in ISO 4387:2000 and ISO 22634:2008), and the volatile phase, which can be collected in sampling bags or by impingers containing a trapping solvent either at room temperature or cooled. Another trapping methodology has been described using a cryogenic instrument, with a liquid extraction after the smoking run. However, all these trapping methods have drawbacks: the glass fiber trap does not allow the collection of volatile compounds, and the trapping in sampling bags leads to rapid decomposition of unstable species, which requires time dependent handling in order to avoid significant analytical variations. And finally, all the described trapping methodologies using solvents result in sample dilution as well as a potential for chemical interactions between the trapped compounds and the solvent.

On the chromatographic side, the choice of column is an important factor because the samples can contain compounds that cover a wide range of volatility and polarity. Screening a diverse array of compounds can be challenging because the selected column is usually not optimal for the whole array, but rather is a compromise which can lead to unresolved chromatographic peaks.

It would therefore be desirable to provide novel systems and methods for trapping and analysing aerosols that overcome the above disadvantages with known systems and methods.

According to a first aspect of the present invention, there is provided a system for capturing an aerosol from a smoking article, the system comprising a smoking article holder for receiving a smoking article, a cooling mantel, and a vial received within the cooling mantel. The system further comprises a nitrogen evacuation pipe in fluid communication with the cooling mantel for controlling a supply of liquid nitrogen to the cooling mantel, and a head connection for providing fluid communication between the smoking article and the vial. The system also comprises a puff generator and a pipe connection connecting the puff generator to the head connection.

The system for capturing an aerosol from a smoking article according to the present invention uses a cryogenically cooled vial, which can advantageously eliminate the need to utilise a trapping solvent to capture the aerosol. Therefore, in preferred embodiments the interior of the vial is solvent-free. Eliminating a trapping solvent eliminates the risk of chemical reactions between trapped aerosol compounds and a trapping solvent. Eliminating a trapping solvent can also improve the potential of subsequent analytical techniques, such as GC-MS, to identify compounds that may otherwise be masked by a solvent peak.

At least one of the cooling mantel and the head connection may be formed from a material that can withstand the cryogenic temperature to which the vial is cooled. Preferably, both the cooling mantel and the head connection are formed from a material that can withstand the cryogenic temperature to which the vial is cooled.

Preferably, one or both of the cooling mantel and the head connection are formed from a material that can withstand temperatures of about -150 degrees Celsius. Preferably, the material is glass.

To facilitate condensation of the aerosol inside the cryogenically cooled vial, the vial is preferably formed from glass, wherein the internal geometry of the vial forms a Vigreux column. The Vigreux column structure advantageously increase flow turbulence and maximises contact between the internal surface of the vial and the aerosol.

In any of the embodiments described above, the system may further comprise an adsorption tube arranged for selective fluid communication with the glass head connection. In a preferred embodiment, the system further comprises a three-way valve arranged for fluid communication with a smoking article and in fluid communication with the adsorption tube and the head connection, wherein the three-way valve is switchable between a first position in which the head connection is in fluid communication with the smoking article and a second position in which the head connection is in fluid communication with the adsorption tube. This arrangement can advantageously prevent contamination of the aerosol captured in the vial by allowing the head connection to be selectively connected to the adsorption tube between puffs.

To allow the pressure within the system to equilibrate and to prevent backflush through the smoking article between puffs, the adsorption tube preferably comprises a first end in fluid communication with the three-way valve and a second end that is open and unconnected, the adsorption tube comprising an adsorbent positioned within the tube between the first and second ends. Between puffs the head connection can therefore be selectively connected to the adsorption tube via the three-way valve to allow the pressure within the vial and the head connection to equilibrate with the ambient air pressure. The adsorbent within the adsorption tube prevents contamination of the interior of the vial with gases or aerosols from ambient environment.

In any of the embodiments described above, the system may further comprise a filter

arranged for fluid communication with the smoking article, between the smoking article and the head connection. The filter can advantageously capture the particulate phase of the aerosol before the aerosol reaches the vial, such that the aerosol components captured within the vial are substantially only the volatile components of the aerosol. Preferably, the filter is formed from a material that does not comprise volatile compounds and does not generate volatile compounds during any subsequent heating process that may be used to release captured aerosol components from the filter for analysis. In preferred embodiments, the filter is a glass fiber filter.

The present invention also extends to a method for capturing an aerosol from a smoking article using a system according to the first aspect of the present invention, in accordance with any of the embodiments described above. Therefore, according to a second aspect of the present invention there is provided a method for capturing an aerosol from a smoking article, the method comprising providing a vial within a cooling mantle, providing a head connection in fluid communication with the vial, and providing a smoking article holder. The method also comprises providing a puff generator and a pipe connection connecting the puff generator to the head connection, optionally providing an adsorption tube arranged for selective fluid communication with the head connection, and providing a supply of liquid nitrogen to the cooling mantle to cool the vial. The method further comprises inserting a smoking article into the smoking article holder so that the smoking article is in fluid communication with the vial via the head connection and activating the smoking article to enable aerosol to be generated by the smoking article, and using the puff generator to generate a plurality of puffs on the activated smoking article, wherein each puff draws an aerosol from the smoking article into the vial via the head connection. In those embodiments in which the method comprises a step of providing an adsorption tube arranged for selective fluid communication with the head connection, the method may further comprise a step of selectively connecting the head connection to the adsorption tube between consecutive puffs to equilibrate the pressure inside the vial with the ambient air pressure.

As used herein, the term "activating the smoking article" is used to describe the process of effecting the release of an aerosol from the smoking article. The step of activating the smoking article may comprise at least one of a mechanical actuation of the smoking article and heating of the smoking article. In embodiments in which the smoking article is activated by heating, the heating may heat an aerosol-generating substrate. The heating may be effected by at least one of combustion of an aerosol-generating substrate, combustion of a combustible heat source, activation of a chemical heat source, activation of a heat-sink, activation of an electrically resistive heater, actuation of an inductive heater, and combinations thereof.

The method may further comprise a step of providing a filter in fluid communication with the smoking article, between the smoking article and the head connection, wherein each puff

generated by the puff generator draws the aerosol from the smoking article through the filter and into the vial. As described above with respect to the first aspect of the present invention, the filter is preferably formed from a material that does not comprise volatile compounds and does not generate volatile compounds during any subsequent heating process that may be used to release captured aerosol components from the filter for analysis. In preferred embodiments, the filter is a glass fiber filter.

The present invention also provides a novel system suitable for analysing aerosols, and in particular aerosols captured from smoking articles using the system according to the first aspect of the present invention. Therefore, according to a third aspect of the present invention there is provided a gas chromatography-mass spectrometry (GC-MS) system comprising first and second cryogenic traps, and first and second chromatographic columns. The first cryogenic trap is operable at a higher temperature than the second cryogenic trap, the first chromatographic column is preceded by the first cryogenic trap, and the second chromatographic column is preceded by the second cryogenic trap. The system further comprises at least two multiport valves arranged to control the flow through the GC-MS system.

By using two chromatographic columns, each preceded by a cryogenic trap operable at different temperatures, the system according to the third aspect of the present invention advantageously improves the chromatographic separation of aerosol component with different volatilities.

In particularly preferred embodiments, the system further comprises a mass spectrometer, wherein at least one of the multiport valves is configured to selectively provide fluid communication between each of the first and second chromatographic columns and the mass spectrometer.

Preferably, the polarity of the first chromatographic column is different from the polarity of the second chromatographic column. Using two chromatographic columns of different polarities also improves the chromatographic separation by allowing each chromatographic column to be adapted to different types of chemical compounds, which can significantly increase the total peak capacity of the analysis by selecting the chromatographic columns for their analytical specificity.

In any of the embodiments described above, at least one of the multiport valves is preferably switchable between a first configuration in which a flow outlet of the first chromatographic column is in fluid communication with a flow inlet of the second cryogenic trap, and a second configuration in which the second cryogenic trap is isolated and the flow outlet of the first chromatographic column is in fluid communication with a flow inlet of a mass spectrometer. This arrangement advantageously permits those aerosol components with a relatively high volatility to pass straight through the first chromatographic column from the first cryogenic trap and into the second cryogenic trap for subsequent release into the second

chromatographic column. Once the relatively high volatility components have passed into the second cryogenic trap, the second cryogenic trap can be isolated and the less volatile components of the aerosol can be sequentially released from the first chromatographic column and into the mass spectrometer for analysis by gradually increasing the temperature of the first chromatographic column.

The present invention also extends to a method for separating aerosol compounds using the system according to the third aspect of the present invention, in accordance with any of the embodiments described above. Therefore, according to a fourth aspect of the present invention there is provided a method for separating aerosol compounds comprising the steps of capturing semi-volatile aerosol compounds on a filter, capturing volatile aerosol compounds, and conveying the semi-volatile and volatile aerosol compounds via a head-space cold trap to a gas chromatography-mass spectrometry (GC-MS) system comprising first and second cryogenic traps and first and second chromatographic columns. The first cryogenic trap is at a higher temperature than the second cryogenic trap, the first chromatographic column is preceded by the first cryogenic trap and the second chromatographic column is preceded by the second cryogenic trap. The flow through the GC-MS system is controlled by at least two multiport valves.

Preferably, the filter is formed from a material that does not comprise volatile compounds other than those captured for analysis, and does not generate volatile compounds in addition to those captured for analysis during any heating process that may be used to convey the captured aerosol components from the filter to the GC-MS via the head-space cold trap. In preferred embodiments, the filter is a glass fiber filter.

Preferably, the polarity of the first chromatographic column is different from the polarity of the second chromatographic column.

In each aspect of the present invention, in accordance with any of the embodiments described above, the smoking article may be a filter cigarette or other smoking article in which a tobacco material that is combusted to form smoke. Therefore, in any of the embodiments described above, the smoking article may comprise a tobacco rod.

Alternatively, the smoking article may be an article in which a tobacco material or a nicotine-containing substrate is heated to form an aerosol, rather than combusted. In one type of heated smoking article, a tobacco material or a nicotine-containing substrate is heated by one or more electrical heating elements to produce an aerosol. In another type of heated smoking article, a tobacco material or a nicotine-containing substrate is heated by one or more inductive heating elements in combination with one or more susceptor materials. In another type of heated smoking article, an aerosol is produced by the transfer of heat from a combustible or chemical heat source or a heat-sink to a physically separate tobacco material or nicotine-containing substrate, which may be located within, around or downstream of the heat source.

The present invention further encompasses smoking articles in which a nicotine-containing aerosol is generated from a tobacco material, tobacco extract, or other nicotine source, without combustion, and in some cases without heating, for example through a chemical reaction.

The invention will now be further described, by way of example only, with reference to the accompanying figures in which:

Figure 1 shows a system for capturing an aerosol from a smoking article, in accordance with an embodiment of the first aspect of the present invention;

Figure 2 shows a cross-sectional view of the vial of the system of Figure 1;

Figure 3 shows a gas chromatography-mass spectrometry (GC-MS) system in accordance with an embodiment of the third aspect of the present invention;

Figure 4 shows a detailed cross-sectional view of one of the cryogenic traps of the system of the GC-MS system of Figure 3;

Figure 5 shows a chromatogram of mainstream smoke from a reference cigarette, the mainstream smoke captured using a trapping solvent and analysed using a single chromatographic column;

Figure 6 shows a chromatogram of mainstream smoke from a reference cigarette, the mainstream smoke captured using the system of Figure 1 and analysed after separation using the first chromatographic column of the system of Figure 3;

Figure 7 shows a chromatogram of mainstream smoke from a reference cigarette, the mainstream smoke captured using the system of Figure 1 and analysed after separation using the second chromatographic column of the system of Figure 3; and

Figure 8 shows an overlay of three chromatograms of the mainstream smoke of three identical reference cigarettes, each analysed separately using the systems of Figure 1 and 3 (second chromatographic column).

Figure 1 shows a system for capturing an aerosol from a smoking article, in accordance with an embodiment of the first aspect of the present invention. For the example described herein, the system was used to capture the aerosol from reference cigarettes 3R4F supplied by the University of Kentucky and conditioned according to the ISO 3402:1999 standard (at least 48 hours at 60 percent relative humidity and 22 degrees Celsius).

The system comprises a smoking article holder 9 into which each reference cigarette was inserted and lit with an electric lighter. Eight puffs were taken following the ISO 3308:2000 standard (one puff per minute, puff volume: 35 millilitres, puff duration: 2 seconds, puff shape: bell curve) using a puff generator. The system comprises two traps mounted sequentially and into which the cigarette smoke was collected. The first trap is a standard glass fiber filter 8 according to the ISO 3308:2000 standard and collects the particulate phase of the aerosol. The second trap is a custom made glass vial 2 cooled to a temperature of -150 degrees Celsius using a flow of liquid nitrogen regulated by an electronic controller and delivered through a

nitrogen evacuation pipe 4 connected to a glass cooling mantel 1 surrounding the glass vial 2. The glass vial 2 collects the volatile compounds of the cigarette smoke, representing the vapor phase.

As shown more clearly in Figure 2, the custom made glass vial 2 comprises a Vigreux column-like internal geometry in order to increase flow turbulence and to maximize contact between the vial surface and the aerosol. In this example, the external dimensions of the vial corresponded to the commercial model used for headspace analyses with the Turbomatrix 40 Trap (Perkin Elmer) headspace sampling device.

To prevent contamination from the laboratory, the system also comprises an adsorption tube 7 comprising a glass tube filled with activated charcoal, and a three-way switch valve 6, wherein the smoking article holder 9 and the glass fiber filter 8 are connected to a first valve port, the adsorption tube 7 is connected to a second valve port, and a glass head connection 3 is connected to a third valve port. The glass vial 2 and a pipe 5 connected to the puff generator are both connected to the glass head connection 3. During operation of the system, the three-way switch valve 6 was switched between puffs to let the pressure equilibrate and avoid any back flush through the glass fiber filter 8 and the cigarette.

At the end of the each smoking run with the reference cigarettes, the vial 2 was capped with a Teflon[®] cap. The glass fiber filter 8 contained in the filter holder was transferred into a separate standard headspace vial and capped with a Teflon[®] cap.

This trapping mode enabled the analysis of compounds with a large range of volatility without liquid extraction or dilution. The use of a headspace sampler gave the opportunity to sample the volatile and highly volatile compounds, without extracting the compounds with low volatility.

After trapping of the aerosol, a Turbomatrix 40 Trap headspace sampler was used to capture a fraction of the headspace volume onto a headspace trap prior to thermal desorption and injection into a chromatographic system via a heated transfer line. The headspace trap was loaded with three different sorbents: Tenax[®]GR, Carbotrap[®] and Carboxen[®]. This combination of sorbents was selected as no universal sorbent was adequate to trap and desorb the entire range of compounds of interest.

After each smoking run with a reference cigarette, the trapped semi-volatile (glass fiber filter 8 in standard headspace vial) and volatile (custom-made headspace vial 2) fractions were submitted for headspace extraction; the instrument conditions were optimized for each fraction to ensure the effective transfer of trapped smoke constituents. During the release phase, vapor pressure was controlled to influence both the diversity and quantity of compounds extracted, which required fine-tuning in order to avoid any segregation of compounds due to differing volatilities. The headspace volumes generated from each fraction were trapped concomitantly onto the same headspace trap, and the retained compounds were then released for injection

into a chromatographic system by thermal desorption at 210°C.

The chromatographic system used is shown in Figure 3, which shows a gas chromatography-mass spectrometry (GC-MS) system in accordance with an embodiment of the third aspect of the present invention. The particular GC-MS used in this example was a Perkin Elmer Clarus 500, modified by the addition of two cryogenic traps 20, 24 and two electronically actuated valves 30, 32 (4 ports gas valve, 300 psi, 1/16", N9302813, PerkinElmer, 8 ports gas valve, 300 psi, 1/16", N9302815, PerkinElmer), which were installed in the gas chromatography oven 18 to connect the two different chromatographic columns 22, 26 (1st column: Agilent DB-WAXetr, 30 m, 0.32 mm i.d., 1 µm; 2nd column: Agilent HP-PLOT/Q 30 m, 0.32 mm i.d., 20 µm). The two cryogenic traps 20, 24 enable the cryo-focusing of compounds at different temperatures to enable separate analysis of compounds having different volatilities. In this example, the first cryogenic trap 20 located before the first chromatographic column 22 (DB-WAXetr column) was cooled to a temperature of -80°C and the second cryogenic trap 24 located before the second chromatographic column 26 (HP-PLOT/Q column) was cooled to -120°C. The two switching valves 30, 32 were controlled by the GC-MS. These modifications in accordance with the third aspect of the present invention enabled a two-dimensional analysis of cigarette smoke fractions by gas chromatography coupled with mass spectrometry.

Figure 4 shows in more detail the construction of one of the cryogenic traps 20, 24. Each cryogenic trap 20, 24 comprises two metal cylinders 40, 42 separated by a layer of isolation material 44. The cryogenic traps 20, 24 can be cooled by liquid nitrogen that enters through a liquid nitrogen inlet 46 and exits the trap through a liquid nitrogen outlet 48.

Positioned within the centre of the cryogenic trap is a capillary tube comprising an inlet 50 through which the aerosol is admitted and an outlet 52 through which the aerosol leaves the cryogenic trap and enters the respective chromatographic column.

Each cryogenic trap also comprises a heating device 54 for heating the trapped aerosol to release the aerosol into the respective chromatographic column. Electrical connections 56 on the outside of the cryogenic trap connect to a type K thermocouple located inside the trap for measurement of the internal temperature.

Each cryogenic trap 20, 24 is located on the GC oven 18 in place of the classical injectors.

The analytical process was initiated by the operator by starting the sequence using the headspace autosampler 19. LabVIEW™ software then conveyed this start signal to the GC and to the cryogenic traps 20, 24 and was therefore used as a master controller for the analytical system. The two valves 30, 32 were controlled indirectly via the GC program sequence.

The first phase of the analytical process comprised introducing the sample and cryo-focusing of the sample using the cryogenic traps 20, 24. Following desorption of the headspace trap 19, which contained headspace constituents from both semi-volatile and volatile fraction

collections, eluted compounds were focused at -80°C in the first cryogenic trap 20 positioned in front of the first chromatographic column 22. Highly volatile compounds, which were not retained at this temperature, passed directly through the first chromatographic column 22. These were trapped by the second cryogenic trap 24 cooled at -120°C , located in front of the second chromatographic column 26, which was maintained at -120°C . These two different trapping temperatures led to a split of very volatile compounds from volatiles, so that each group of compounds could be selectively eluted on the two dedicated chromatographic columns 22, 26.

In the second phase of the analytical process, the volatile compounds in the first cryogenic trap 20 were released and eluted into the first chromatographic column 22. The first cryogenic trap 20 was rapidly heated to 200°C and a start signal was sent by the LabVIEW™ software to the GC-MS to start the chromatographic run. All compounds trapped in the first cryogenic trap 20 were released and introduced onto the first chromatographic column 22 (WAX column). Analytes with limited affinity for the first chromatographic column 22 eluted rapidly and were trapped in the second cryogenic trap 24. The remaining analytes continued to be separated on the first chromatographic column 22 (WAX column) by their different retention behaviours.

In the third phase of the analytical process, the semi volatile compounds retained in the first chromatographic column 22 were analysed. The first valve 30 was switched (by the GC-MS) to isolate the second cryogenic trap 24 (maintained at -120°C) and the second chromatographic column 26 (PLOT Q column). This switching of the first valve 30 connected the exit of the first chromatographic column 30 (WAXetr column) to the mass spectrometer, connected to the outlet 21 of the GC oven 18, and enabled the analysis of the semi-volatile compounds remaining in the first chromatographic column 22. A first heat cycle of a dedicated double heat cycle GC oven temperature program was used with the following parameters: initial temperature: 41°C during 5 minutes, followed by a temperature increase at a rate of $5^{\circ}\text{C}/\text{minute}$, up to 250°C .

In the fourth phase of the analytical process, the volatile compounds captured in the second cryogenic trap 24 were released and analysed. After chromatographic analysis of the semi-volatile compounds using the first chromatographic column 22 (WAX column, 30 minutes run time), the GC oven 18 was cooled to 60°C using CO_2 to speed the process. For the release of the volatiles captured in the second cryogenic trap 24, the first valve 30 was switched to isolate the first chromatographic column 22 (WAX column) and the second valve 32 was switched back to direct the carrier gas through the second cryogenic trap 24, the second chromatographic column 26 (PLOT Q column) and into the mass spectrometer. The volatile compounds were introduced onto the second chromatographic column 26 (PLOT Q column) by rapidly heating the second cryogenic trap 24 to 150°C and chromatographically separated using

the second heat cycle of the GC oven temperature program with the following parameters: 60°C during 7.2 minutes, followed by a temperature increase at a rate of 7 °C/minute, up to 250°C, final temperature maintained during 9 minutes.

At the end of the analysis, the first valve 30 was switched again to allow the carrier gas to pass through both chromatographic columns 22, 26 and therefore flush the system. This step was done with the GC oven 18 heated to its maximal temperature, and to ready the first valve 30 for the next analytical run.

Data acquisition in scan mode was initiated 15 minutes after the start of each run, since no meaningful data was generated during the trapping phase for the second cryogenic trap 24. A second pause in acquisition was also made between 46.8 minutes and 54 minutes, during the cooling phase of the GC oven 18 before the second temperature gradient started.

To compare the described analytical process using the systems and methods according to the present invention with a classical analysis, the reference cigarette 3R4F (supplied by University of Kentucky) was conditioned according to ISO 3402:1999 standard and smoked using the ISO smoking regime (as described in ISO 3308:2000 standard, 1 puff per minute, puff duration: 2s, puff volume 35ml, puff profile: bell shape). The particulate phase of the smoke of ten cigarettes was trapped using a glass fiber filter and the gas phase was bubbled through cooled (-78°C) ethyl acetate in three small impingers (10ml per impinger) mounted in series. The glass fiber filter was extracted together with the solvent contained in the impingers and was analyzed by conventional gas chromatography analysis (one micro-liter of sample was injected on-column in a DB-FFAP column, 30 m, 0.25 mm i.d., 0.25 µm) coupled with mass spectrometric detection in scan mode.

Figure 5 shows a typical total ion chromatogram for the classical analysis of the reference cigarettes. As shown in Figure 5, one disadvantage of the classical analysis technique concerns the solvent, which prevents the detection of co-eluting compounds (volatile compounds) that elute at the same time as the solvent. Another issue with the classical analysis technique is compound co-elution, that is, concurrent elution of compounds from the sample, which leads to uncertainty during the process of peak identification.

However, using the systems and methods according to the present invention it is possible to overcome these disadvantages of the classical analytical technique. Specifically, the system according to the present invention comprises two dedicated chromatographic columns each selected specifically for each group of compounds' volatility. Using this set-up, the chromatogram shown in Figure 6 shows the semi-volatile compounds eluted first on the first chromatographic column 22 (DB-WAXetr column) and Figure 7 shows the chromatogram for the volatile compounds eluted second on the second chromatographic column 26 (HP-PLOT/Q column). As described above, the split between semi-volatile and volatile compounds was handled using the two specific chromatographic columns with dedicated oven programs, which

provided an improvement in the chromatography results.

When comparing the classical analysis technique with the systems and methods according to the present invention a clear improvement in selectivity is apparent when using the analytical process according to the present invention. In the chromatograms obtained using the systems and methods according to the present invention the peaks are properly resolved and they can therefore be identified with improved certainty. In addition, the second chromatogram shown in Figure 7 (starting at approx 53 minutes) allows the identification of numerous volatile compounds which are masked by the solvent peak when using conventional trapping and GC-MS analysis. Figure 7 demonstrates, for example, that compounds such as chloromethane, HCN, acetaldehyde, ethanol, acetonitrile, propionaldehyde and acetone were clearly separated when using the systems and methods according to the present invention.

Furthermore, the sensitivity of the technique according to the present invention allows the accurate analysis of cigarette mainstream smoke from a single cigarette, therefore reducing the number of cigarettes required, while increasing the level of information gained. The automation of the analytical process according to the present invention ensured reproducible retention times across several different runs, as shown in Figure 8, which displays overlaid chromatograms for very volatile compounds eluted through the second chromatographic column 26 (PLOT Q column). The same behavior was observed on the first chromatographic column 22 (WAXetr column). This reproducibility allows the creation of custom libraries to improve identification certainty.

The systems and methods according to the present invention can therefore facilitate the characterization of cigarette smoke in an efficient and simple way. The novel trapping system according to the first aspect of the present invention provides an improvement compared to classical liquid trapping, due to the absence of solvent, which reduces the sample preparation, prevents any chemical interaction between solvent and compounds of interest, and allows determination of chemical species which are usually masked by the solvent peak. In addition, sample preparation according to the present invention can be performed without dilution of the analytes from the aerosol, therefore the analysis can be performed on a single cigarette. The improved sensitivity and resolution provided by systems and methods according to the present invention enable a better and more comprehensive characterization of cigarette mainstream smoke.

Claims

1. A system for capturing an aerosol from a smoking article, the system comprising:
a smoking article holder for receiving a smoking article;
5 a cooling mantel;
a vial received within the cooling mantel;
a nitrogen evacuation pipe in fluid communication with the glass cooling mantel for
controlling a supply of liquid nitrogen to the glass cooling mantel;
a head connection for providing fluid communication between the smoking article and the
10 vial; and
a puff generator and a pipe connection connecting the puff generator to the head
connection.
2. A system according to claim 1, wherein at least one of the cooling mantel and the head
15 connection is formed from glass.
3. A system according to claim 1 or 2, wherein the vial is formed from glass and wherein the
internal geometry of the vial forms a Vigreux column.
- 20 4. A system according to claim 1, 2 or 3, wherein the interior of the vial is solvent-free.
5. A system according to any preceding claim, further comprising an adsorption tube
arranged for selective fluid communication with the head connection.
- 25 6. A system according to claim 5, further comprising a three-way valve arranged for fluid
communication with a smoking article and in fluid communication with the adsorption tube and
the head connection, wherein the three-way valve is switchable between a first position in which
the head connection is in fluid communication with the smoking article and a second position in
which the head connection is in fluid communication with the adsorption tube.
30
7. A system according to claim 6, wherein the adsorption tube comprises a first end in fluid
communication with the three-way valve and a second end that is open and unconnected, the
adsorption tube comprising an adsorbent positioned within the tube between the first and
second ends.
35

8. A system according to any preceding claim, further comprising a glass fiber filter arranged for fluid communication with a smoking article, between the smoking article and the head connection.

5 9. A method for separating aerosol compounds comprising the steps of:
capturing semi-volatile aerosol compounds on a glass fiber filter;
capturing volatile aerosol compounds; and
conveying the semi-volatile and volatile aerosol compounds via a head-space cold trap to
a gas chromatography-mass spectrometry (GC-MS) system comprising first and second
10 cryogenic traps and first and second chromatographic columns, wherein the first cryogenic trap
is at a higher temperature than the second cryogenic trap, wherein the first chromatographic
column is preceded by the first cryogenic trap and the second chromatographic column is
preceded by the second cryogenic trap, and wherein the flow through the GC-MS system is
controlled by at least two multiport valves.

15 10. A method according to claim 9, wherein the polarity of the first chromatographic column is
different from the polarity of the second chromatographic column.

20 11. A method according to claim 9 or 10, wherein the steps of capturing the semi-volatile and
volatile aerosol compounds comprise capturing the semi-volatile and volatile aerosol
compounds from a smoking article comprising a tobacco or nicotine-containing substrate.

25 12. A gas chromatography-mass spectrometry (GC-MS) system comprising:
first and second cryogenic traps;
first and second chromatographic columns, wherein the first cryogenic trap is operable at
a higher temperature than the second cryogenic trap, wherein the first chromatographic column
is preceded by the first cryogenic trap and the second chromatographic column is preceded by
the second cryogenic trap; and
at least two multiport valves arranged to control the flow through the GC-MS system.

30 13. A GC-MS system according to claim 12, wherein the polarity of the first chromatographic
column is different from the polarity of the second chromatographic column.

35 14. A GC-MS system according to claim 12 or 13, wherein at least one of the multiport valves
is switchable between a first configuration in which a flow outlet of the first chromatographic
column is in fluid communication with a flow inlet of the second cryogenic trap, and a second

configuration in which the second cryogenic trap is isolated and the flow outlet of the first chromatographic column is in fluid communication with a flow inlet of a mass spectrometer.

15. A method for capturing an aerosol from a smoking article, the method comprising:

5 providing a vial within a cooling mantel;

providing a head connection in fluid communication with the vial;

providing a smoking article holder;

providing a puff generator and a pipe connection connecting the puff generator to the head connection;

10 optionally, providing an adsorption tube arranged for selective fluid communication with the head connection;

providing a supply of liquid nitrogen to the cooling mantel to cool the vial;

inserting a smoking article into the smoking article holder so that the smoking article is in fluid communication with the vial via the head connection and activating the smoking article;

15 using the puff generator to generate a plurality of puffs on the activated smoking article, wherein each puff draws an aerosol from the smoking article into the vial via the head connection; and

optionally, selectively connecting the head connection to the adsorption tube between consecutive puffs to equilibrate the pressure inside the vial with the ambient air pressure.

20 16. A method according to claim 15, further comprising a step of providing a glass fiber filter in fluid communication with the smoking article, between the smoking article holder and the head connection, wherein each puff generated by the puff generator draws the aerosol from the smoking article through the glass fiber filter and into the vial.

25

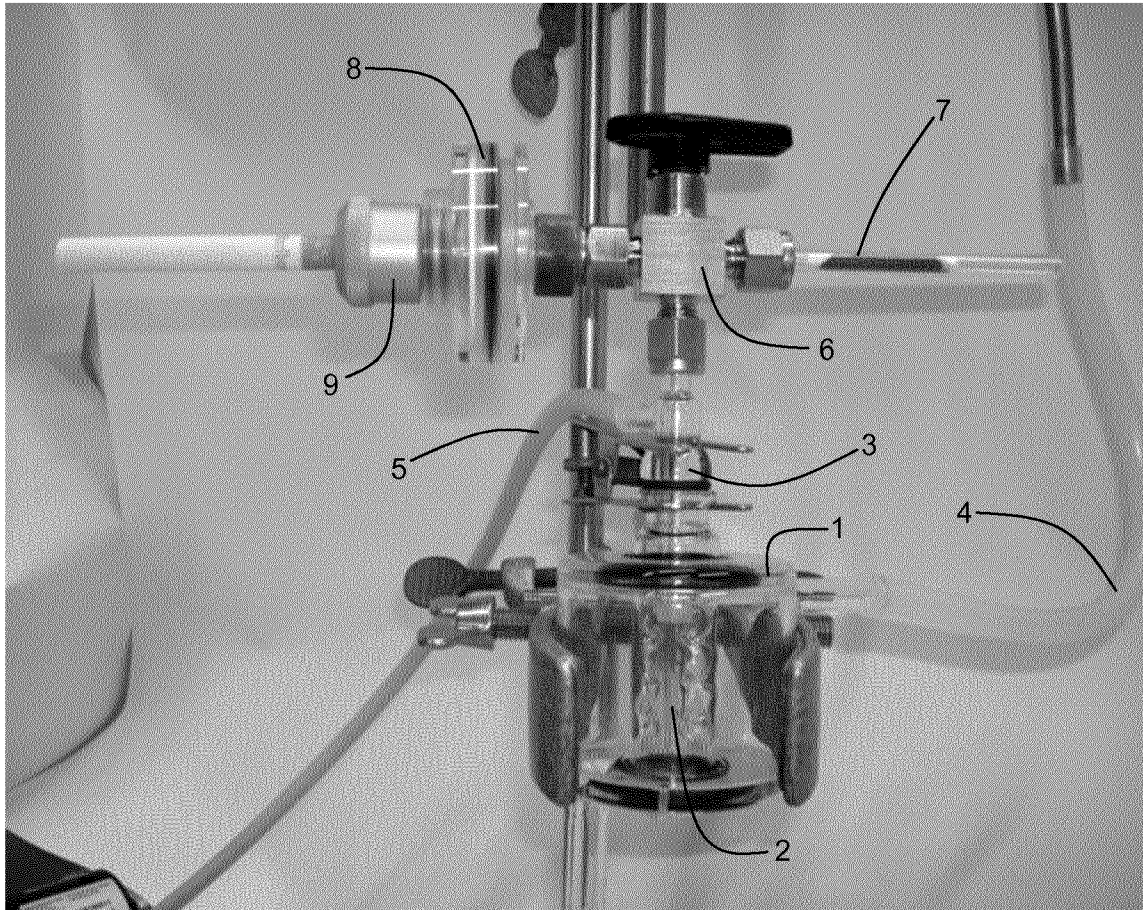


Figure 1

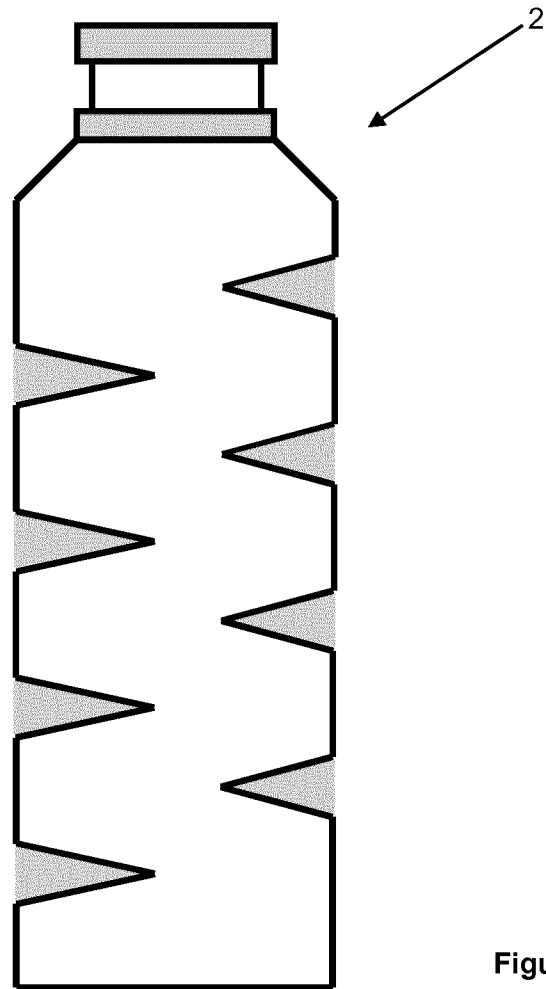


Figure 2

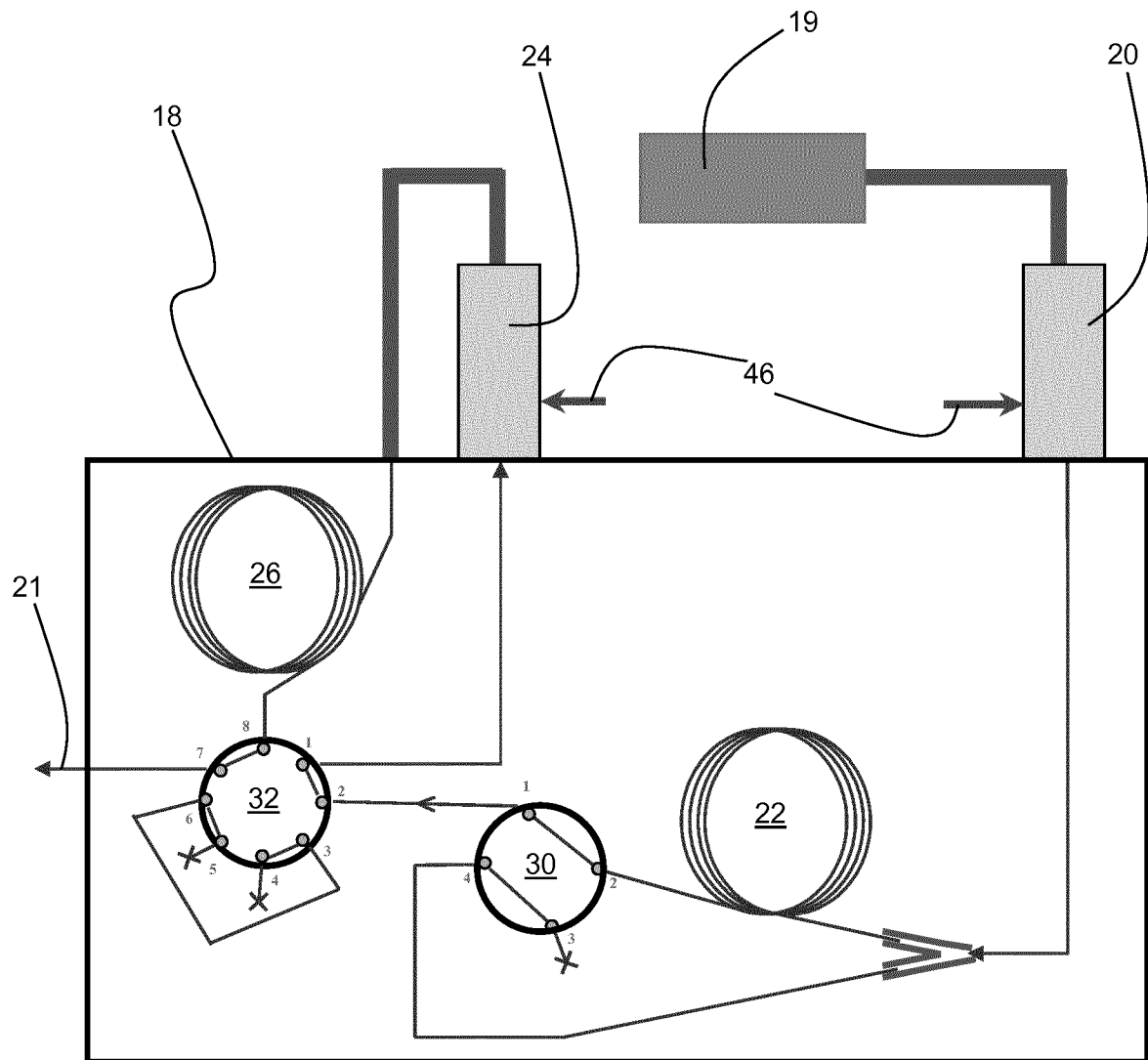


Figure 3

4 / 8

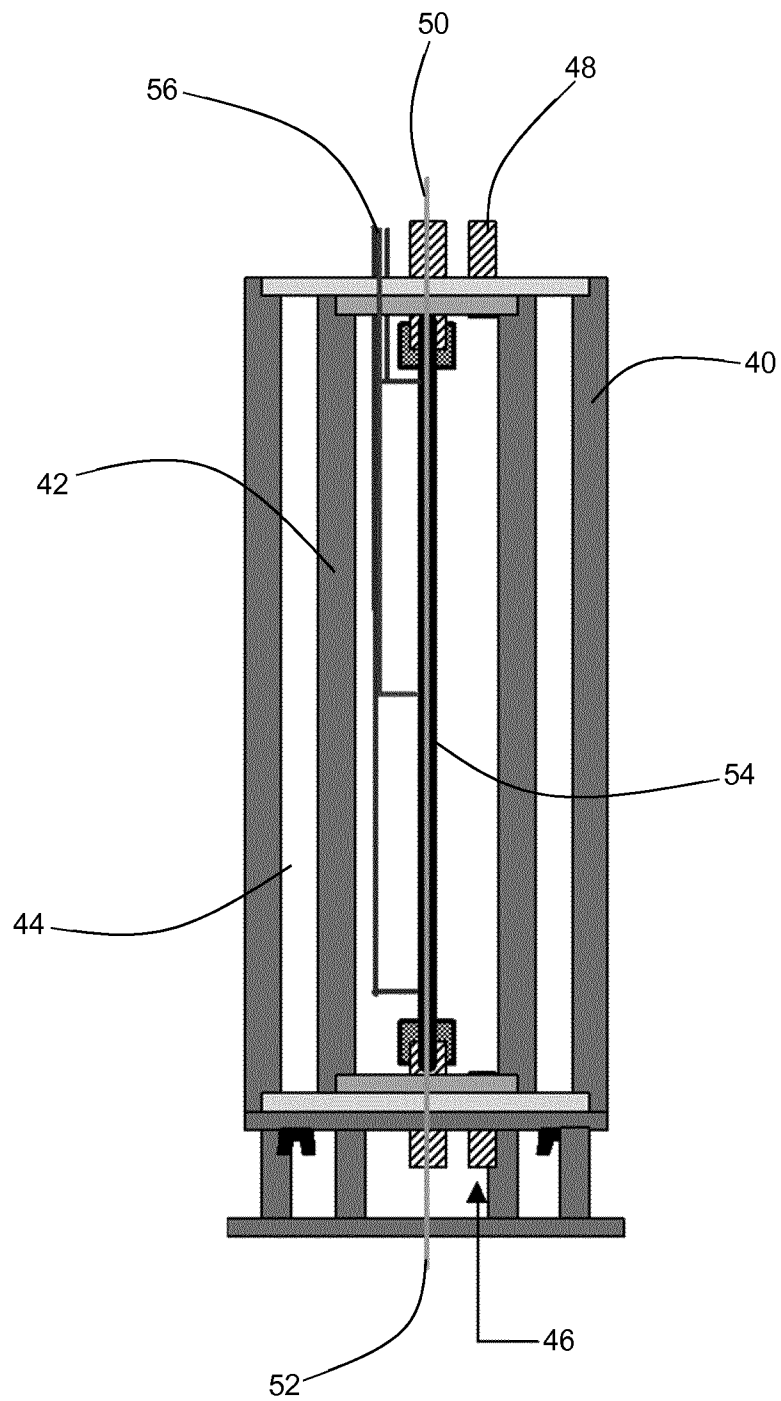


Figure 4

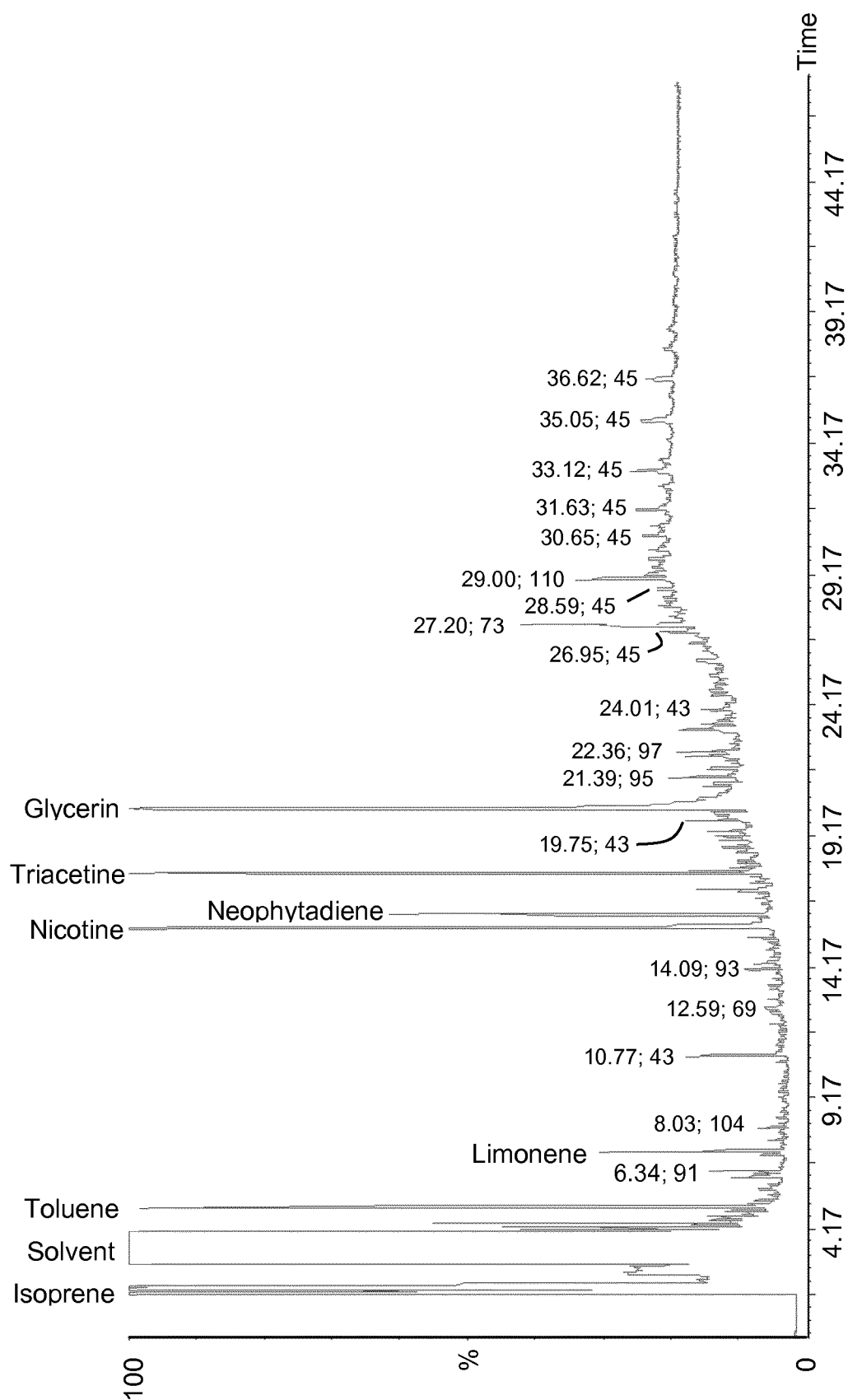
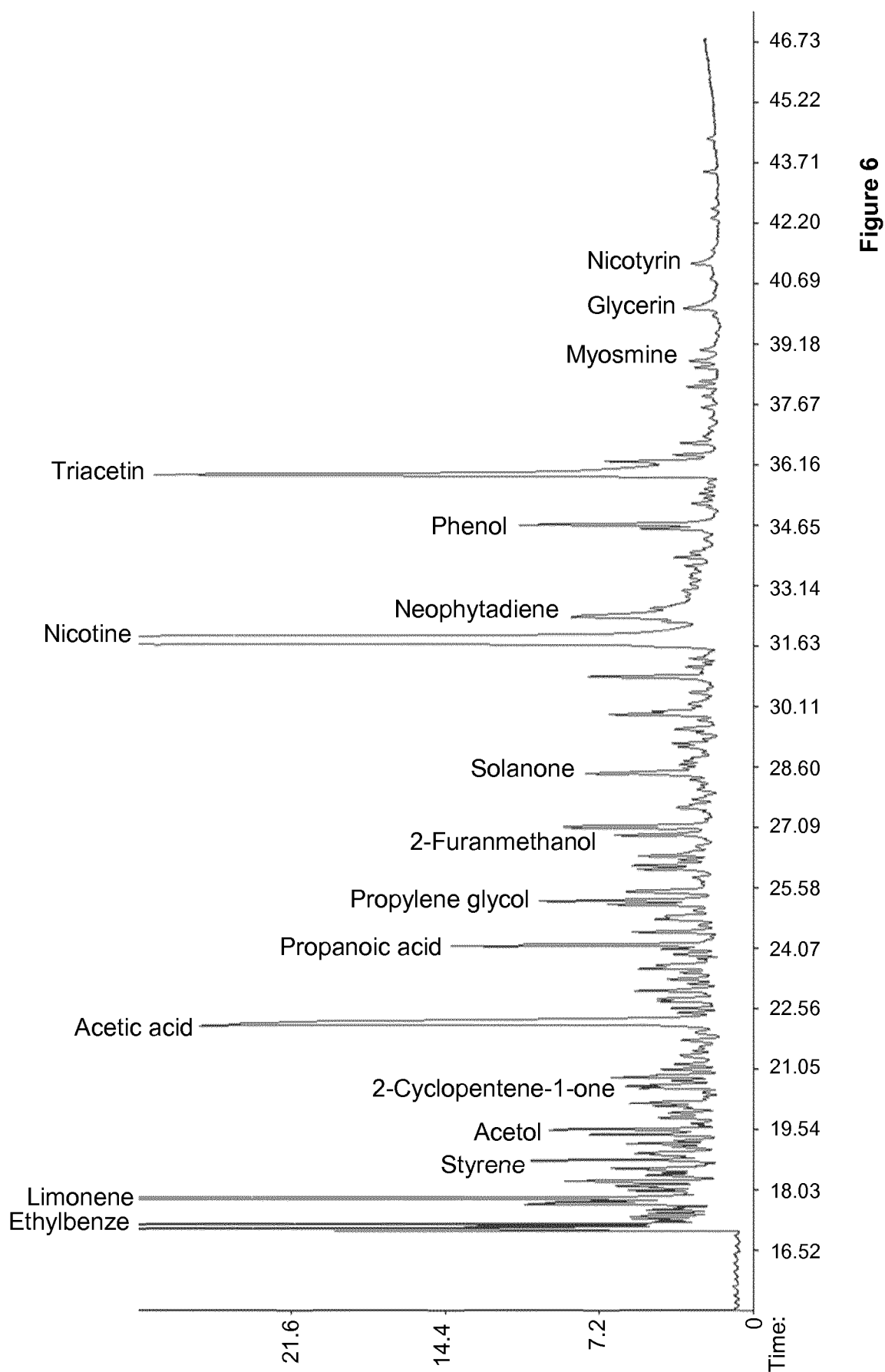


Figure 5



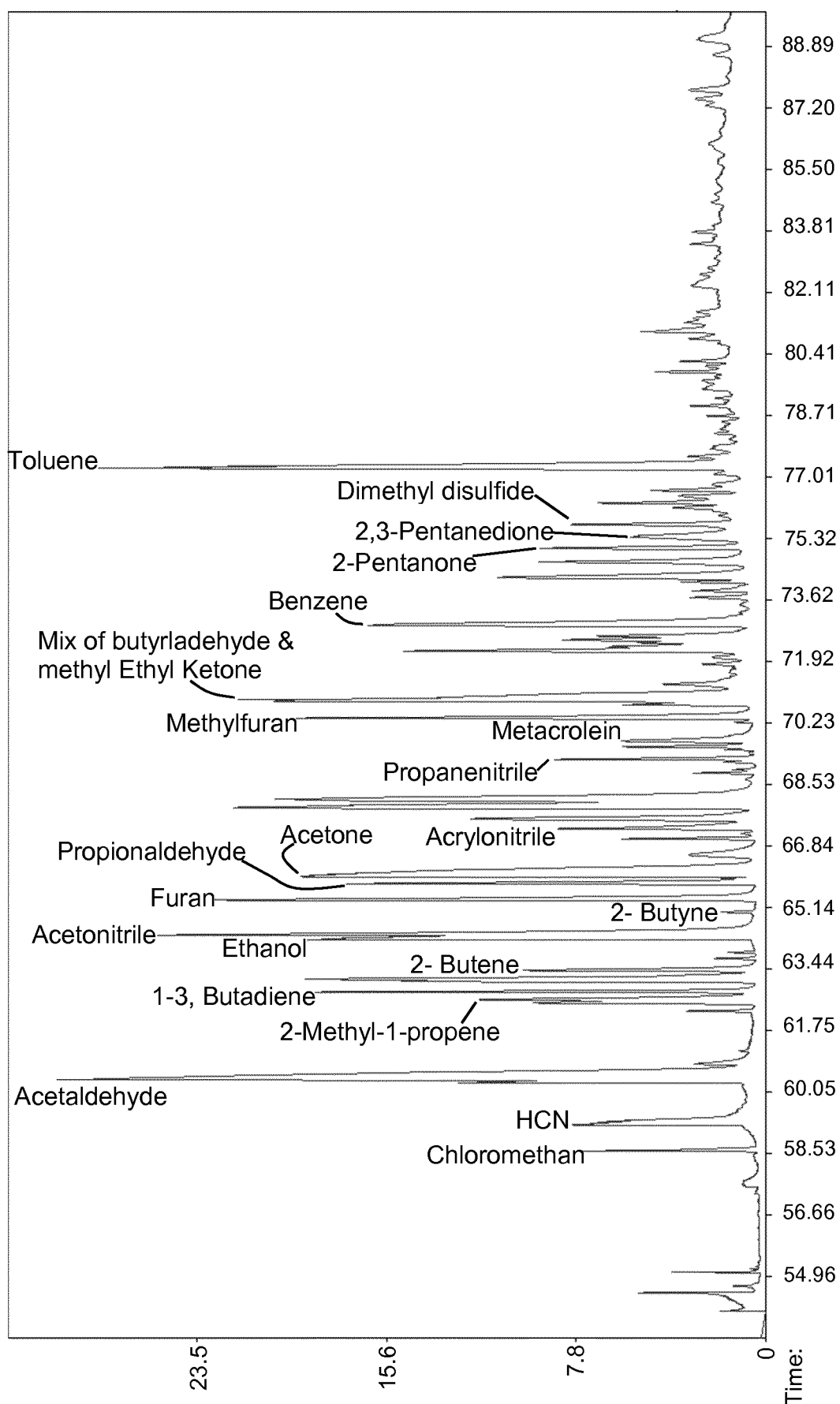


Figure 7

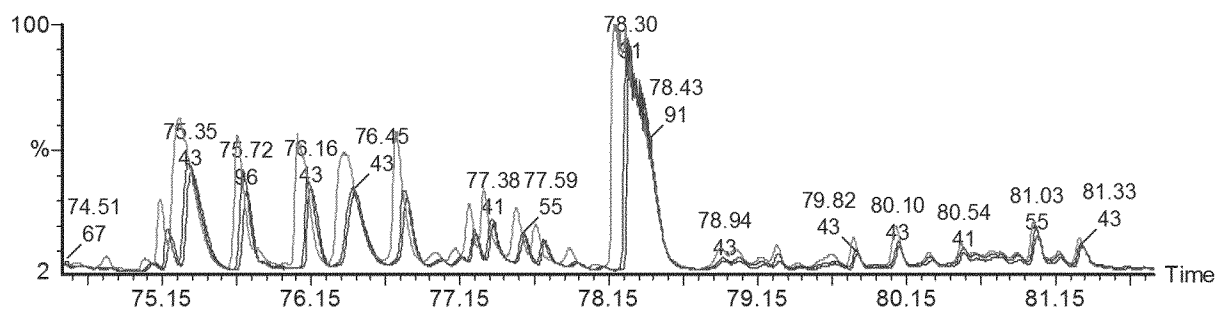


Figure 8

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2015/056023

A. CLASSIFICATION OF SUBJECT MATTER

INV. G01N30/12 G01N30/46 G01N30/88
ADD. G01N30/72 G01N30/00 G01N30/06

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

EPO-Internal, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	PLATA N ET AL: "Aerosols sampling using a new cryogenic instrument", JOURNAL OF AEROSOL SCIENCE, PERGAMON, AMSTERDAM, NL, vol. 37, no. 12, 1 December 2006 (2006-12-01), pages 1871-1875, XP028071018, ISSN: 0021-8502, DOI: 10.1016/J.JAEROSCI.2006.07.003 [retrieved on 2006-12-01]	1,4,15
Y	the whole document ----- -/--	2,8,16



Further documents are listed in the continuation of Box C.



See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search

12 August 2015

Date of mailing of the international search report

31/08/2015

Name and mailing address of the ISA/

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040,
Fax: (+31-70) 340-3016

Authorized officer

Dedman, Emma

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2015/056023

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	ANDREWS STEVEN S ET AL: "A liquid nitrogen immersion cryostat for optical measurements", REVIEW OF SCIENTIFIC INSTRUMENTS, AIP, MELVILLE, NY, US, vol. 71, no. 9, 1 September 2000 (2000-09-01), pages 3567-3569, XP012038524, ISSN: 0034-6748, DOI: 10.1063/1.1287343 abstract -----	2
Y	CN 102 636 374 A (CHINA TOBACCO GUANGDONG IND CO) 15 August 2012 (2012-08-15) figure 1 -----	8,16
A		1-7,15
A	CHARLES ET AL: "Composition and emissions of VOCs in main- and side-stream smoke of research cigarettes", ATMOSPHERIC ENVIRONMENT, PERGAMON, GB, vol. 41, no. 26, 19 July 2007 (2007-07-19), pages 5371-5384, XP022153053, ISSN: 1352-2310, DOI: 10.1016/J.ATMOENV.2007.02.020 page 5373, column 2, last paragraph - page 5374, column 1, last paragraph -----	5-7
X	KROCK K A ET AL: "RECENT ADVANCES IN MULTIDIMENSIONAL GAS CHROMATOGRAPHY", TRAC, TRENDS IN ANALYTICAL CHEMISTRY, ELSEVIER, AMSTERDAM, NL, vol. 13, no. 1, 1 January 1994 (1994-01-01), pages 13-17, XP000417702, ISSN: 0165-9936, DOI: 10.1016/0165-9936(94)85054-2 figure 1 -----	12,13
A		9-11,14
X	WO 97/14957 A1 (THERMEDICS DETECTION INC [US]) 24 April 1997 (1997-04-24) figures 11-14 page 12, line 1 - line 2 page 12, line 12 - line 14 page 15, line 22 - page 17, line 8 -----	12-14
A		9-11
A	CN 102 288 698 A (SHANGHAI TOBACCO GROUP CO LTD) 21 December 2011 (2011-12-21) abstract -----	1,15

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP2015/056023

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☒ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of additional fees.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
- ☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- ☒ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-8, 15, 16

apparatus and associated method for capturing an aerosol
from a smoking article

2. claims: 9-14

GC-MS apparatus and associated method for separating
semi-volatile and volatile aerosol compounds

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/EP2015/056023

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
CN 102636374	A	15-08-2012	NONE	

WO 9714957	A1	24-04-1997	DE 69637079 T2	24-01-2008
			EP 0876607 A1	11-11-1998
			US 5808178 A	15-09-1998
			WO 9714957 A1	24-04-1997

CN 102288698	A	21-12-2011	NONE	
