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ENSURING THE SAFETY AND QUALITY OF CONSUMER PRODUCTS WITH ADVANCED ANALYTICAL TECHNOLOGIES

INTRODUCTION

Analytical testing across the broad commercial range of consumer products is essential to ensure the safety of end users, support the continuous supply of quality offerings to the marketplace, protect a company's brand and reputation, and meet regulatory requirements. Product recalls and failures are costly. A company can suffer enormous tangible and intangible losses. The adoption of new analytical methods and technologies can enable companies to maximize the accuracy, cost-efficiency, and productivity of risk assessment and ongoing monitoring of product safety and quality.

Among the challenges consumer product companies face in ensuring ongoing product quality and safety is the shifting regulatory landscape. In some cases, regulatory requirements have become more stringent within industries such as pharmaceuticals or cosmetics. Other regulatory trends may relate to a specific chemical class or type of product or application. New scientific and medical findings on the health effects and potential toxicity of chemicals and materials used in consumer products or their packaging will continue to drive regulatory rules and guidelines to which manufacturers must adapt.

Additional challenges include the need to understand, test for, and monitor the potential effects of new types of compounds or polymers used in manufacturing consumer products. The increasing emphasis on the use of renewable resources and sustainably sourced materials and on substituting bio-based compounds for synthetic chemicals affects product and process design and contributes to the need for novel analytical approaches and techniques across the manufacturing workflow.

Applying state-of-the art analytical methods and technologies for testing and monitoring critical safety and quality parameters presents not only challenges, but also benefits. These may include reducing the risk of product failures and recalls; minimizing batch-to-batch variability; improving product stability, performance, and shelf-life; collecting data to inform method development, product improvements, or future product design/development; supporting patent or liability issues; and identifying product features that offer a competitive advantage.

This white paper highlights five different compound types commonly used in consumer products—biocides, disperse dyes, flame retardants, phthalates, and primary aromatic amines—and some of the analytical and regulatory challenges related to each. For each type of compound, a related application describes the use of novel liquid chromatography and mass spectrometry technologies to solve complex analyses.

BIOCIDES

Biocides play an important role in controlling microbial growth in a large variety of personal care products, cosmetics, and household products. Left unchecked, bacteria, viruses, and molds can contaminate virtually any material that provides a sufficient source of nutrients and moisture. The results may include not only potential negative health effects, but these microorganisms can also interfere with manufacturing processes, damage infrastructure, and spoil consumer goods.

Biocides added to consumer products are typically identified as disinfectants, preservatives, antifouling products, or pest control agents. They tend to be highly regulated. In the United States, regulatory responsibility for biocides is shared by the Environmental Protection Agency (EPA) and, for applications in cosmetics, food, and personal health care products, by the Food and Drug Administration (FDA). In the European Union, the Biocidal Products Regulation (EU No. 528/202) and the European Commission's Biocidal Products Directive (98/8/EC) provide regulatory control.

A rapid, and reproducible method was developed to separate, identify, and quantify six biocides within 3 minutes[1] using the ACQUITY® Ultra Performance Liquid Chromatography (UPLC®) System. UPLC technology utilizes sub-2 µm hybrid particle chemistries, allowing chromatographers to work at higher efficiencies with a wider range of linear velocities, flow rates, and back pressures – the result is faster analyses, lower cost per sample and better data quality.

The biocides analyzed were Kathon (containing 0.4% of (1a) 2-methyl-4-isothiazolin-3-one and 1.2% of (1b) 5-chloro-2-methyl-4-isothiazolin-3-one), (2) carbendazim, (3) 1,2 benzisothiazol-3-one, (4) 2-phenoxyethanol, (5) benzoic acid, and (6) methyl paraben. These are commonly found ingredients in a range of products including adhesives, paints and coatings, sealants, inks, wood and paper products, textiles and leather products, cosmetics, personal care products, laundry and dishwashing detergents, and household and industrial cleaners.

A 5 ppm mixture of the six biocides was separated using the ACQUITY UPLC system with a 3-minute linear gradient. Figure 1 shows an overlay of nine replicate injections of timed wavelength chromatograms obtained using the ACQUITY PDA detector and Empower® 3 Chromatography Data Software (CDS). Empower 3 is a compliance-ready CDS that simplifies the collection, processing, and reporting of chromatography test results. These results demonstrate the excellent reproducibility of the separation and the ability to clearly resolve the six compounds and the two active components of Kathon (1a and 1b).

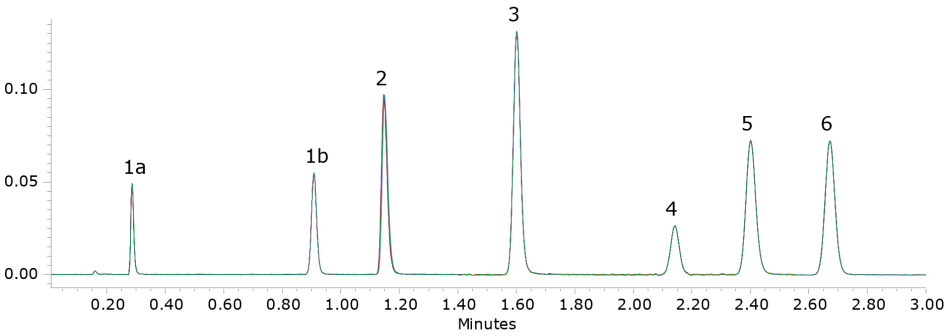

Figure 1. Overlay PDA timed wavelength chromatograms, retention time, and peak area of nine replicate injection of sample containing 1.25 ppm of 1a (2-methyl-4-isothazolin-3-one), 3.75 ppm of 1b (5-chloro-2-methyl-4-isothiazolin-3-one), and 5 ppm of 2-6: (0.00 min, 275 nm; 1.40 min, 225 nm; 2.55 min, 255 nm).

The advanced mathematical algorithms built into Empower 3 software created calibration curves based on the analysis of six concentration levels of each analyte. The residual sum of squares (R^2 values) of the calibration curves exceeded 0.9999, except for one, which was 0.9998. The amount of each biocide in the mixture quantified using UPLC/PDA data matched well with the actual values, indicating that this method can meet the regulatory demands for quantitative analysis of biocides.

Empower 3 software is able to create a PDA library from the pure component peaks in a user's chromatogram and to use this as the basis for subsequent sample analysis. Library matching and peak purity functions, which rely on Spectral Contrast™ theory for quantitative comparison of the shapes of UV spectra, help to confirm peak identities and provide assurance that spectrally distinct peaks are not co-eluting.

The automated library matching and quantification capabilities possible with PDA detection and Empower 3 software add confidence in peak confirmation that would not be possible using a single wavelength UV detector. ACQUITY UPLC PDA technology can accelerate the workflow for biocides analysis and enhance quality control, new product development, troubleshooting, and regulatory compliance in manufacturing cosmetics and personal care products.

DISPERSE DYES

Disperse dyes are synthetic, low molecular weight compounds that often contain azo or anthraquinone functional groups. Their most common use is in consumer products such as textiles, paper, and toys. Negative health effects linked to disperse dyes include an allergic response with prolonged skin exposure and the potential for azo groups to be converted to carcinogenic aromatic amines.[2]

DIN 54231 is a standard procedure developed for analyzing disperse dyes. An approach based on DIN 54231 was used to analyze nine disperse dyes using the ACQUITY Arc UHPLC System, XBridge® C_{18} Column and ACQUITY UPLC PDA and QDa® Detectors for dual UV and mass detection.[3] ACQUITY Arc™ is a dual-flow path liquid chromatography system capable of emulating both HPLC and UHPLC separations. The ACQUITY QDa is a novel mass detector that can be integrated into existing liquid chromatography configurations allowing any scientist to generate high-quality mass spectral data. The addition of mass detection allows for improved detection limits and provides more information for better characterization of potential impurity peaks.

The PDA chromatogram at 240 nm derived from the separation of a mixture of nine disperse dye standards (Figure 2, bottom) was compared to the Selected Ion Recording (SIR) channels from the QDa MS analysis, shown superimposed in Figure 2, top. It is clear that the addition of mass spectrometry significantly improved detection sensitivity for the dyes. In addition, focusing on peaks 4 and 5, coelution of these two disperse dyes would make accurate detection challenging using a UV detector alone and would require further chromatographic separation of the components, extending method development time. As the components of these two disperse dyes have different *m/z* ratios, the QDa mass detector was able to distinguish between them despite the coelution.

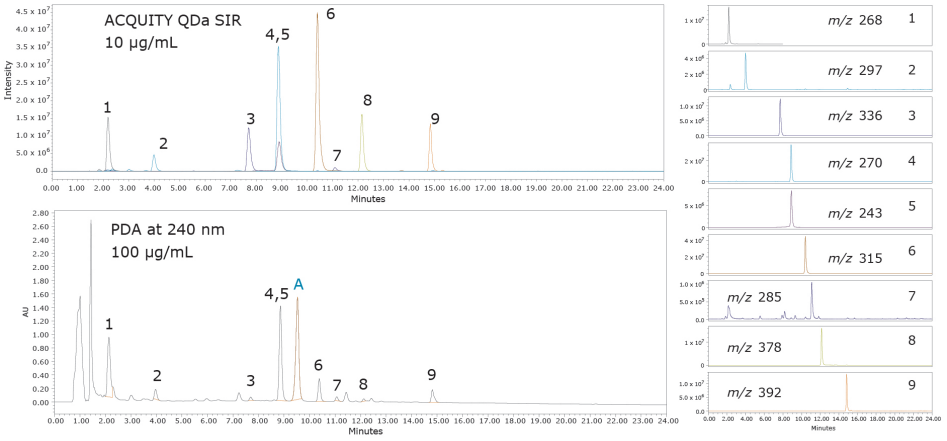

Figure 2. PDA chromatogram at 240 nm resulting from the separation of a mixture of nine disperse dye standards (bottom) and the superimposed SIR channels (top) using the DIN 54231 method. At right are the individual stacked SIR channel chromatograms (10 µg/mL, 5 µL injection).

Figure 3 takes a closer look at the peak labeled (A), representing an unknown component detected in the PDA data at retention time 9.5 minutes, but not present in the SIR channels because that specific *m/z* channel was not monitored

in the experimental method. Figure 3 shows the results of a separate experiment in which full scan QDa mass detection is performed simultaneously with PDA detection, revealing the mass spectra for all components of the mixture and a spectral peak for component A with *m/z* 267. The complementary information provided by PDA and QDa mass detection, combined with the analytical capabilities of Empower 3 CDS software, led to the determination that impurity A shared structural similarities with the disperse dye represented by peak 2 and originated from the individual authentic standard solution of this disperse dye.

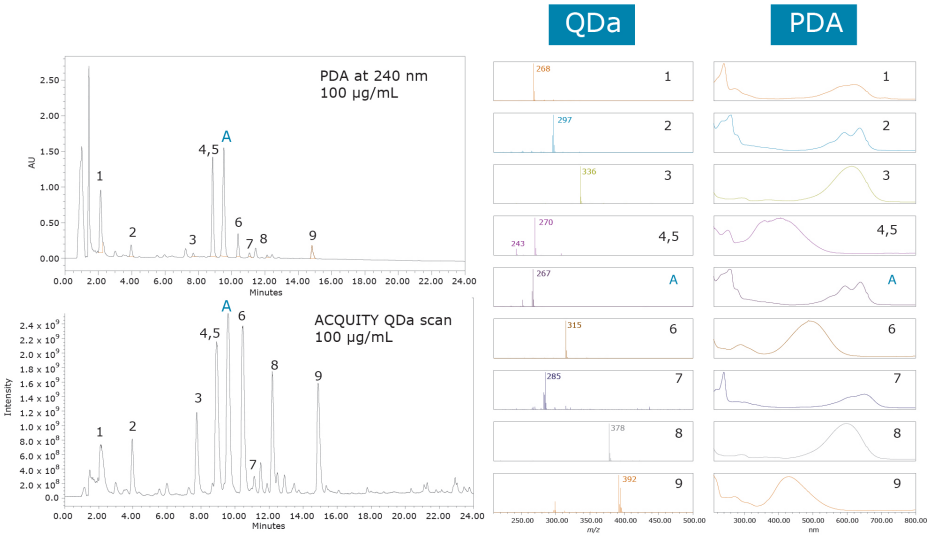

Figure 3. ACQUITY Arc PDA chromatograms (top) and QDa MS scan (bottom) from separation of nine disperse dye standards using DIN 54231 method. MS and UV spectra are shown at right.

The addition of mass detection as a complementary analytical detection technique enhances confidence in compound detection and identification. Co-eluting components with different *m/z* ratios can be reliably analyzed using mass detection. The results also illustrate the power of mass detection for impurity analysis.

FLAME RETARDANTS

Flame retardants are an essential component of numerous types of consumer products, ranging from electronics to clothing and furniture. Brominated flame retardants (BFRs), which can decrease the likelihood and intensity of fires, are banned from use in certain types of electronic equipment. Legislation regulating the use of BFRs in consumer products and targeting toxic electronics-related waste includes the Restriction of Hazardous Substances (RoHS) Directive (202/95/EC) and the Waste Electrical and Electronic Equipment Director (WEEE, 2002/96/EU).[4,5]

An alternative to the conventional targeted approach to BFRs analysis, which relies on gas chromatography (GC)/MS using single ion recording (SIR) or multiple reaction monitoring (MRM) was developed using a Xevo® tandem (triple) quadrupole mass spectrometry system, Atmospheric Pressure GC (APGC) and MassLynx® Mass Spectrometry Software. APGC is a 'soft' ionization technique,

meaning less analyte fragmentation compared to electron impact (EI) ionization, which results in higher sensitivity and specificity.

A limitation of the traditional GC/MS approach is that by targeting specific BRFs it overlooks related compounds and matrix background. The new method takes advantage of the Xevo system's capability to collect MRM (MS/MS) and full scan MS data simultaneously using RADAR™ acquisition mode.[6] The ability to perform MRM and MS in parallel in a single acquisition allows the ability to calculate compound concentrations and detect unexpected contaminants in the background matrix that would not be detected using a targeted MRM screening method alone.

The case study presented shows the analysis of polybrominated diphenyl ethers (PBDEs) in a computer keyboard produced before legislation banning BFRs was enacted. The analysis was performed with two MRM transitions, selected for each degree of bromination, and an MS scan was acquired in parallel.

Figure 4 shows an overlaid trace of the MRM transitions (upper chromatogram), along with a BPI trace (lower chromatogram) of the MS scan data. The MS scan in Figure 4 is intense and very complex. The cluster/strip function within MassLynx was used to extract pairs of ions with a separation of 2 Da, which highlighted spectra with halogenated isotope patterns. The NIST08 mass spectral library was used to find spectra of compounds suspected to be in a sample of this nature.

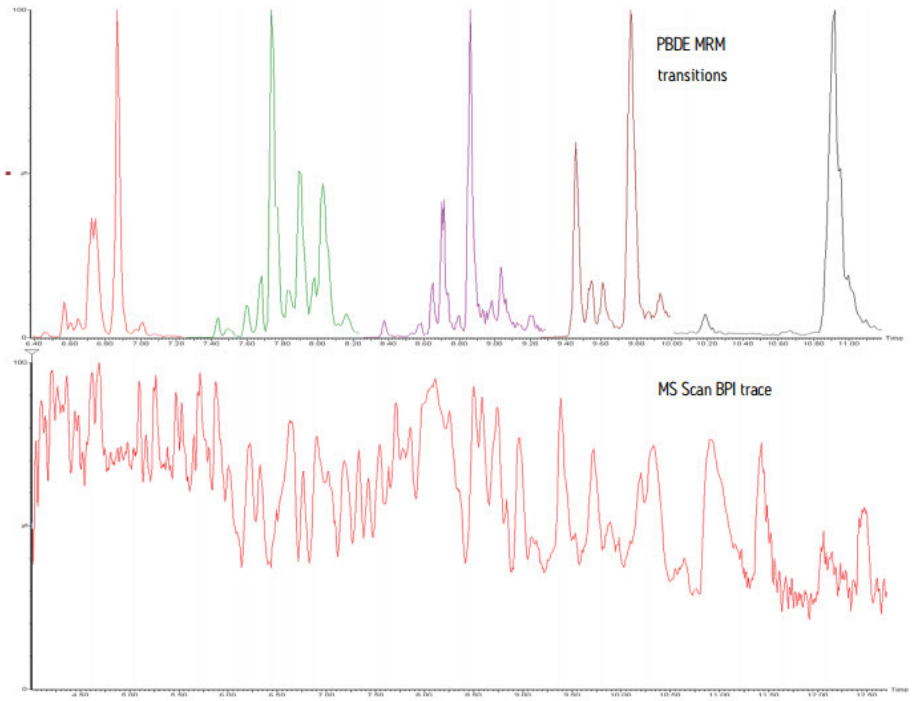

Figure 4. An overlaid trace of the MRM transitions (upper chromatogram) along with a BPI trace(lower chromatogram) of the MS scan data.

Figure 5 focuses on the spectrum of a peak acquired at 11.43 min, magnifying the molecular ion cluster. The figure also shows a comparison between the isotope cluster extracted from the peak and the theoretical isotope model of tribromophenoxyethane, which is the active ingredient in the commercial flame retardant Firemaster 680. These isotopic similarities combined with additional MS scan data for the fragment cluster indicating dissociation of the molecular ion support the tentative identification of the BRF compound.

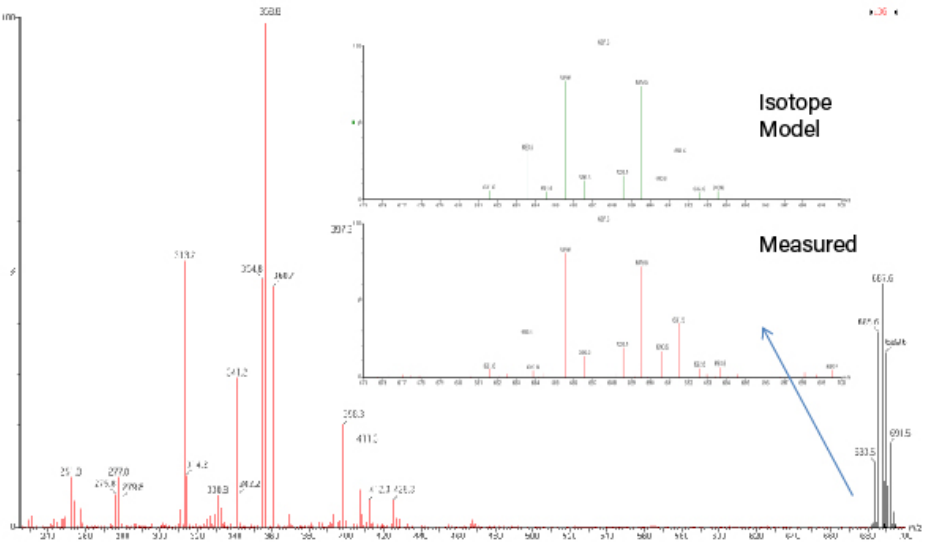

Figure 5. Mass spectrum of the peak at Rt-11.43 (molecular ion cluster magnified) and a comparison between the measured and theoretical isotope patterns.

While GC/MS using the Xevo/APGC System with RADAR functionality was able to accurately quantify the target compounds, the MS scan data made it possible to monitor components of the background matrix and identify other compounds as well. Using RADAR allows the system to alternate rapidly between MS and MS/MS modes without compromising performance or MRM data acquisition. As a result, a BFR compound not originally targeted was tentatively identified.

PHTHALATES AND PARABENS

Phthalates are esters of phthalic acid commonly used as plasticizers to increase flexibility, transparency, durability, and longevity of consumer products such as toys, electronics, clothes, flooring, wallpaper, and paints. They are also used as plasticizers, solubilizers, or denaturants in cosmetics and personal care products such as perfumes, nail polishes, and hair sprays. Parabens are esters of parahydroxybenzoic acid. Characteristics such as low volatility and high stability, and their antibacterial and antifungal properties have made them popular preservatives in cosmetics and personal care, pharmaceutical, food, and industrial products. Triclocarban is also present in many cosmetic and personal care products due to its antibacterial and antifungal properties.

The European Union's Cosmetic Directive 1223/2009 bans or restricts the use of phthalates, parabens, and triclocarban due to concerns over their negative

health effects and potential health risks.[7] The concerns for phthalates related to their effects on the reproductive system and their link to increased cancer risk. Evidence has associated parabens with allergenic contact dermatitis and rosacea and suggested that they may be carcinogenic and potential endocrine disrupters. Triclocarban, too, has been linked to potential hormone and endocrine disruption and may contribute to the development of antibiotic resistance among bacteria.

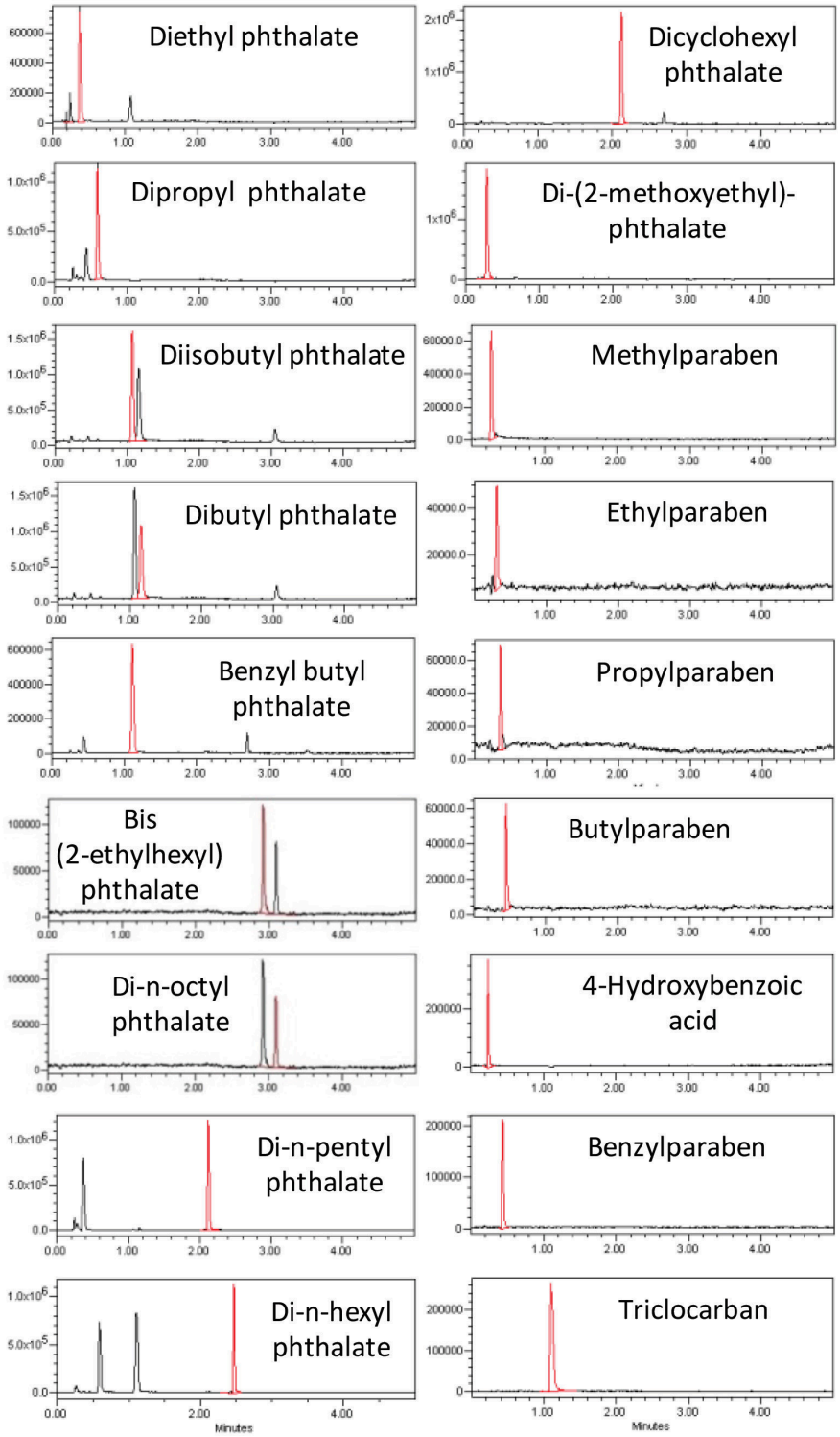

Figure 6. SIR chromatograms for phthalates, parabens, and triblocarban in a mixed 1.0 µg /mL calibration standard.

Given the rising consumer demand for products free of potentially harmful compounds, manufacturers are increasingly developing cosmetics and personal care products that do not contain phthalates, parabens, and triclocarban. A cost-effective and reliable method for identifying and quantifying these compounds was developed using the ACQUITY UPLC H-Class System, QDa Detector and Empower 3 CDS. The method provides improved sample throughput, shorter run times, reduced solvent usage, and enhanced sensitivity and selectivity compared to existing approaches.[8]

In the method described, separation of the sample was performed using reversed phase UPLC with a BEH C_{18} column, flow rate of 0.6 mL/min, and run time of 5 min. The MS analysis on the QDa detector with electron spray ionization (ESI) in both positive and negative modes and carefully selected SIR parameters was intended to cover all of the phthalates and parabens, as well as triclocarban, in the sample mixture (Figure 6). Optimization of the mobile phases and gradient eluting conditions aimed to ensure the separation of isomeric phthalate compounds without compromising sample throughput.

The 5-minute UPLC method described here is more than 7 times faster than existing HPLC and GC methods and uses more than 90% less solvent than available HPLC methods. It offers a fast and cost-effective approach for accurate and reproducible quantification based on mass detection during method development and routine analysis.

PRIMARY AROMATIC AMINES

Large amounts of primary aromatic amines (PAAs) have been broadly used as a chemical feedstock in the manufacturing of a variety of commodity products, such as pharmaceuticals, pesticides, explosives, epoxy polymers, rubber, aromatic polyurethane products, and azo dyes. Yet they are considered to be highly toxic and carcinogenic, which has led to legislation worldwide regulating their use. An example is the European Union's Cosmetic Directive 1223/2009, which prohibits the use of PAAs in cosmetic products.[7]

As these compounds remain a commonly used chemical feedstock, but their presence in final products is highly regulated, manufacturers require efficient, robust, and cost-effective methods for monitoring and quantifying the levels of PAAs during production. PAAs may persist or be produced as a result of incomplete reactions, impurities, or the formation of by-products or degradation products. Manufacturers that use PAAs have relied on various analytical methods such as the following: GC/MS preceded by ion-pair extraction with bis-2-ethyl phosphate and followed by derivatization with isobutyl choroformate; UPLC following solid phase extraction (SPE) with cation-exchange cartridges; or reduction by liquid phase sorbent trapping followed by thermal desorption GC/MS analysis.

A new analytical method using the ACQUITY UPLC H-Class system, QDa detector, and Empower 3 Software provides improved sensitivity and selectivity, faster run times and reduced solvent usage, which lowers costs and increases sample throughput.[9]

This fast and robust method was able to separate 30 PAAs in the 10-min run time. Peak tracking and identification of co-eluting peaks are simpler using mass detection. The use of mass detection compared to UV detection contributed to faster method development. Figure 7 illustrates this based on the identification of co-eluting peaks for two PAAs with similar optimum wavelengths. Samples of shampoo, blush, and eye shadow to which selected PAAs were added at various levels were analyzed using the method described. Resulting SIR chromatograms shown in Figure 8 demonstrate the utility of this approach.

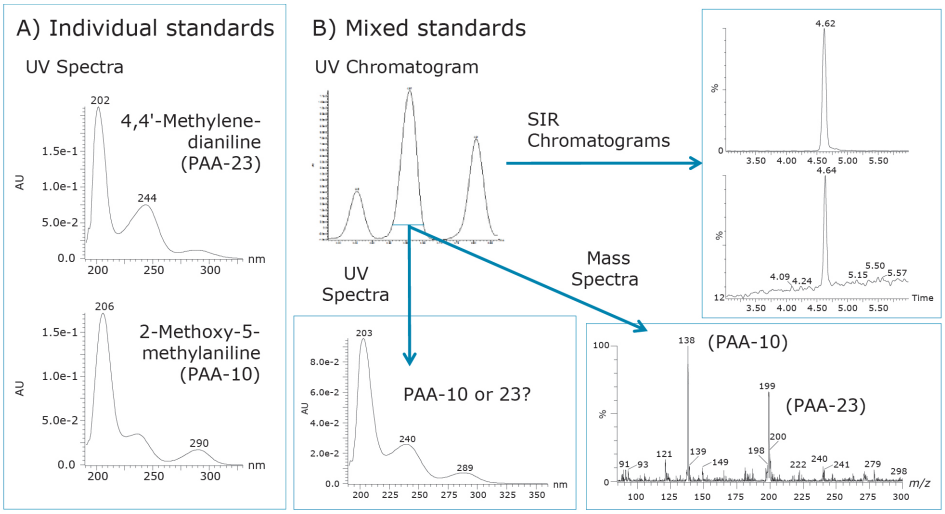

Figure 7. Comparison of UV versus mass detection for the identification of co-eluting peaks during method development for two PAAs (4,4'-methylene-dianiline and 2-methoxy-5-methylaniline). A: UV spectra from individual standards; B: UV and mass spectra, and SIR chromatograms from mixed standards.

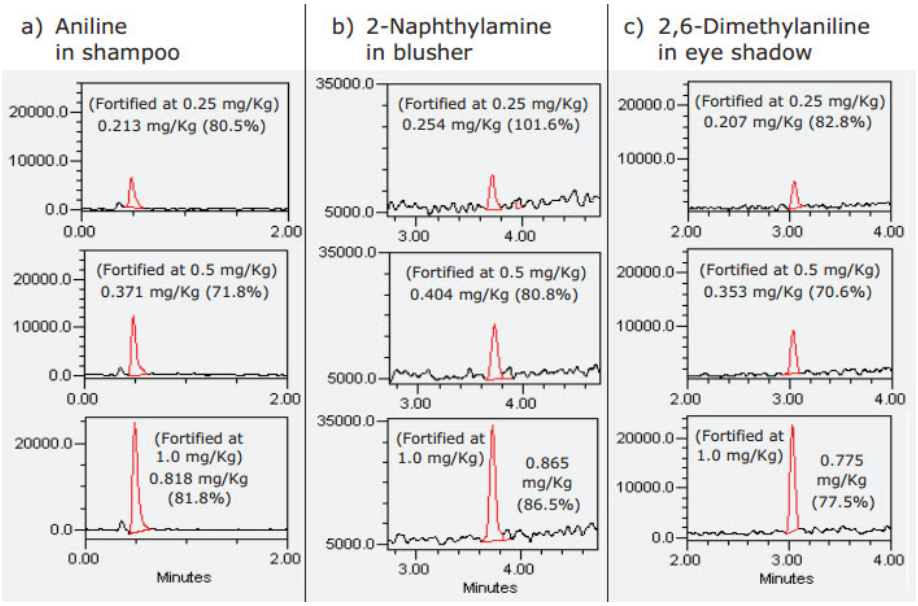

Figure 8. SIR chromatograms for selected PAAs in shampoo (a), blush (b), and eye shadow (c).

SUMMARY

The analytical testing of consumer products is a critical step towards ensuring the safety of end users, maintaining product quality, and protecting a company's brand. Manufacturers and their contract testing laboratories must have the ability to optimize throughput, maximize uptime, and readily characterize a wide range of complex samples—all while meeting national and international standards for permissible levels of target chemical compounds. Examples shown in this white paper illustrate how the latest technological advancements in column chemistries, chromatography, mass spectrometry, and data management software, can assist these organizations in reducing analysis times, consolidating methods, lowering laboratory operating costs, and achieving regulatory compliance.

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1155 Sixteenth Street, NW,
Washington, DC 20036

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