In-situ analysis of the presence of a photoinitiator after curing

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Abstract

Over the past few years, regulatory reclassifications have continued to change how ink manufacturers world-wide formulate UV cured inks. Adding a chemical to the European Chemicals Agency (ECHA) **S**ubstances of **V**ery **H**igh **C**oncern (SVHC) list triggers changes in regulatory reporting. Manufacturers and importers of articles which contain the SVHC become legally required to notify customers/consumers if the concentration is greater than 0.1% w/w. In addition, ECHA must be notified if the total amount of SVHC imported into an EU country is greater than 1 metric ton/ year. While inclusion on the list is not a ban on use, it has this effect for ink manufacturers. For example, member companies of the European Printing Ink Association (EuPIA) agree to abide by the Exclusion Policy, which requires formulating inks away from the use of an SVHC. Additionally, brand owners may have similar requirements for packaging and printing inks. Under general exclusions for ink formulations, the Nestlé guidance states an SVHC "must not be used where suitable alternatives exist." In contrast to some European regulations, the USFDA does not explicitly regulate the contents of printing ink. However, the USFDA does regulate the food additives. Subsequently, it is the responsibility of the manufacturer of a food contact substance (FCS) to ensure the FCM is consistent with applicable authorizations and does not adulterate food.

Differing regulations between Europe and the US frequently lead to fit-for-use questions of ink formulations. We are commonly asked what substances are acceptable for use and what residual ink components are present in the matrix of the cured print. In response to previous customer questions and regulatory changes, INX has undertaken several studies to evaluate exposure of an SVHC during the manufacturing process. As an extension of previously completed work, the current study evaluates the presence of residual PI369 in a cured print and determine if that print contains levels of the residual SVHC above labeling requirements in the EU (0.1%).

Introduction

The previous study tested and evaluated the worker exposure to a photoinitiator after reclassification by the REACH committee of the European Chemicals Agency (ECHA) as a SVHC (Banke,TAGA, 2020). The photoinitiator, 2-Benzyl-2-(dimethylamino)-1-[4-(4-morpholinyl)phenyl]-1-butanone (PI 369; CAS119313-12-1; EC404-360-3), was reclassified from Repr. 2 H361 to Repr. 1B H360d, making exposure a concern for pregnant female workers. In a pressroom trial, PI369 exposure, in a location evaluated as worst-case, was less than 0.0003% of the no observed adverse effect level (NOAEL) (Banke, NPIRI, 2020).

UV curing occurs when photoinitiators absorb UV radiation, creating a radical to initiate cross-linking reactions (Bentayeb, 2013). Uncured UV components on printed packaging can undergo set-off—the unintentional transfer of print substances to packaging contents (Bradley, 2005). Migration studies are regularly conducted to quantify the printing ink components transferring into food simulants. However, migration of ink components into simulants addresses the question of how ***much*** transfers, not how much ***can*** transfer.

In a regulatory climate that is continually changing, reclassification of raw materials and chemicals frequently result in ink manufacturers need to reformulate or reevaluate ink systems. The European Packaging Ink Association (EuPIA) Exclusion Policy states that "substances and mixtures in stated hazard classes are excluded as raw materials for the manufacture of printing inks". With the regulatory space constantly in flux, the natural next step in analyzing PI exposure is to quantify the amount of PI left over after curing—the actual amount of PI that ***can*** transfer or is present in the case of an SVHC on labeling of a printed article. Typical worst-case calculations are based upon total amount of analyte in the formula compared to specific migration. It is well understood worst-case scenario calculations overestimate, at times grossly overestimate, the amount of an ink components migrating into food. From a manufacturing perspective, this results in ink formulators making formulation decisions and advising customers based on overestimated data. Quantifying residual PI further helps to refine the worst-case scenario calculations to account for analyte present that can migrate, allowing for more well-informed decision making when formulating inks.

Global brand owners manufacturing and packaging food need to consider packaging regulations in the country of origin as well as regulations in the country of destination. Lack of harmonization between countries and regulations leads to questions and ambiguity for packaging compliance. The US Food and Drug Administration (USFDA) regulates food safety by imposing suitable purity requirements for food stuffs, through Food, Drug and Cosmetic Act of 1958 (Keller and Heckman, 2019; Wagner, 2013). This regulation is the basis for food contact materials (FCM) which are considered food additives or indirect additives from migration into food stuff. While also requiring FCMs manufacturers to adhere to GMP, the EU regulates ink by assuring FCMs do not transfer components under normal or foreseeable conditions which could endanger human health or causes unacceptable changes to food composition (Keller and Heckman, **2019**; Regulation No 1935/2004).

Additional ambiguity stems from what manufacturers and printers would need to disclose when shipping finished, packaged goods internationally. Under current REACH guidelines, European Union (EU) or European Economic Area (EEA) suppliers are required to inform customers and consumers if the concentration of an SVHC is above 0.1% wt/wt. The current work provides clarity for FCMs which may be packaged in one country and shipped globally. By evaluating a cured ink for the residual PI present we can quantify the residual PI, relate that amount to total packaging, and develop a better worse-case scenario calculation. Knowing the residual content of the SVHC as a percentage of the total packaging, allows ink manufactures to provide data driven guidance to customers shipping good globally and importing goods into EU countries.

Methods

Print Conditions Two UV curable inks containing differing photoinitiators were printed on glass slides under the following conditions: 2 or 12 conventional UV lamp passes using 250 fpm line speed. The Air Motion Systems unit uses a standard medium pressure mercury vapor water cooled UV lamp. At 250 fpm, the instrument delivers 64 mJ/m^2.

The magenta ink has 3 photoinitiators and the cyan ink has 4 photoinitiators in the formula. Three photoinitiators reported in this study were chosen for the regulatory classifications; PI369 and PI907 are both SVHCs and PIITX is on the Nestle list.

Table 1. Percent photoinitiator in the two inks evaluated for residual content. Both UV ink formulas contained other photoinitiators, however this study focused on the two PIs classified as SVHCs and one excluded for use on the Nestlé Guidance.

	PI369 SVHC	**PI907 SVHC**	**PIITX Swiss Ordinance A Nestle Guidance Table 2**
Magenta	0	6%	2%
Cyan	2.2%	3.6%	0

Detection Method From the cured ink samples, ink was scrapped off of the glass slide and extracted with acetonitrile. The acetonitrile was filtered through a 0.2 micron syringe filter and then analyzed by LC/MS/MS using an Agilent 1290 coupled with an Agilent 6460 Triple Quadrupole Mass Spectrometer. The acetonitrile extract was removed and centrifuged to remove any fibers or particles from the filter. The supernatant was removed for analysis and put in an amber vial for storage in the refrigerator (4ºC).

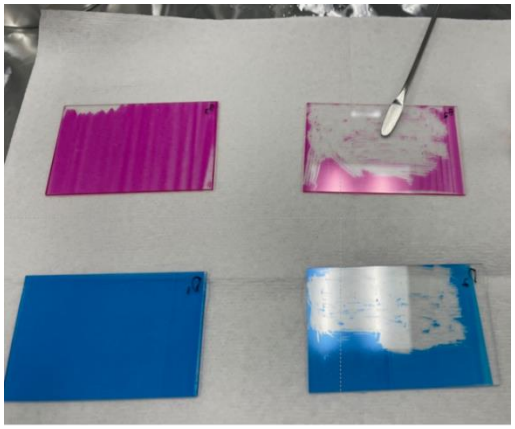

Plate Ink scraped off plate

Analysis and analyte quantitation was completed using a previously described method (Banke, 2020). Fresh calibration standards were prepared including an internal standard of thioxanthen-9-one. Standards were prepared and analyzed consistent with method validation principles (N>6, %RSD < 10% for all standard concentrations) Sample extracts were separated using a Restek Biphenyl LC Column (2.1 x 50 mm; 2.7 microm) on an Agilent 1290 HPLC. Photoinitiators and UV material were detected by multiple reaction monitoring (MRM) on an Agilent 6460 Triple Quadrupole Mass Spectrometry (MS/MS). For MRM, the instrument scans for the presence of a molecular ion, applies a voltage to fragment the ion into smaller parts. Positive identification by MRM occurs by detecting the transition of the molecular ion and fragments. MRM detection increases the sensitivity of detection and eliminates the influence of compound in the sample matrix which are not of interest. Separation and detection were previously optimized for this system (method modified from Gallart-Ayala, et al. 2011). Internal and external standards were employed to reduce the effect sample matrix and to quantify the analytes present.

Extraction vial

Sonicate, filter extract through 0.2-micron filter

Autosampler vial

All of the data reflects averages of 6 (N=6) extractions for each condition. Sample extract dilutions were optimized for the analysis (10X and 100X dilution). Extracts were analyzed by LC/MS/MS by multiple injections ($N \geq 5$) and data represents the average quantified amount over the dilutions. Error is reported as the standard error on the mean (± SEM).

Neat ink was extracted for PI content for recovery study (Average recovery = 103 ± 0.4%) . Student t-test and analysis of variance (ANOVA) applied where applicable.

Add autosampler vial, add internal standard, analyze by LC/MS/MS

Agilent 1290 HPLC
Agilent 6460 Triple Quadrupole Mass Spectrometer at INX R&D Analytical

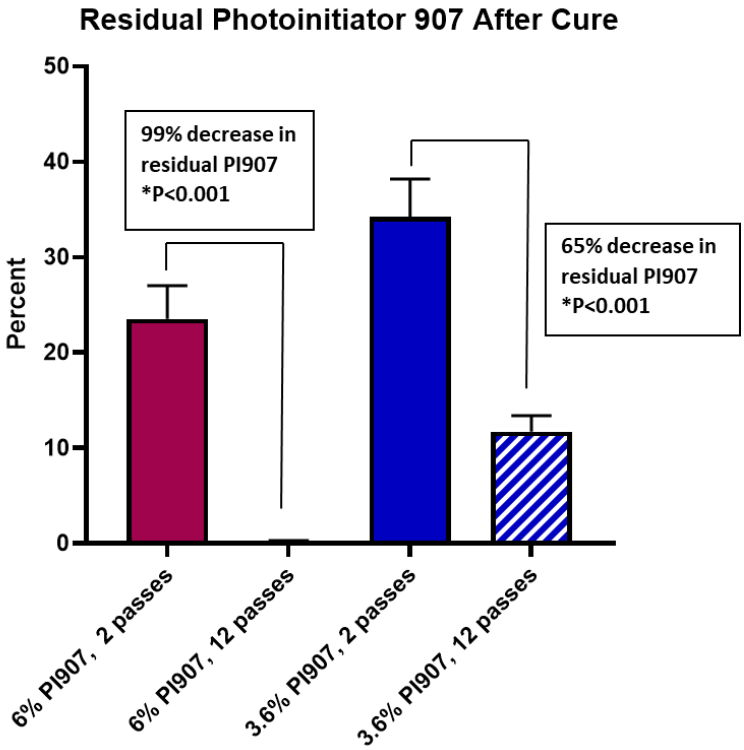

Figure 2. Residual photoinitiator, PI907, after cure. Data represents a percentage of total PI907 in the ink formula (6% PI907 Magenta wt/wt; 3.6% PI907 Cyan wt/wt). One-way Anova: *P<0.001.

PI907

Residual PI907, also an SVHC, differed slightly between the magenta and cyan inks, with 6% and 3.6% PI907 respectively. PI907 was the only photoinitiator quantified that was present in both inks. After 2 passes, 23% of PI907 (1.4 ± 0.4 mg PI369/gram ink) left in the cured magenta ink. After 2 passes, residual PI907 content decreases by 99% to 0.19% (0.1 ± 0.009 mg PI907 / g ink (Figure 2).

Residual PI907 content after 2 passes was 34% of the original PI content (12 ± 0.3 mg PI907/ gram ink) After 12 passes, the residual PI is 11% of the original content (11% of 3.6% PI in the formula; 4 ± 0.1 mg PI907/ gram ink).

Concentration in food based on the worst-case scenario calculation is 0.014 and 0.5 mg residual PI/kg food for magenta and cyan inks, respectively.

Results

PI369

After 2 conventional UV lamp passes using 250 fpm line speed, 13.4% of PI 369 (2.9 ± 0.5 mg PI369/gram ink) is left in the cured ink. After further curing, 12 passes, residual PI 369 content decreases by 88% to 0.3 ± 0.1 mg PI369 / g ink (Figure 1).

Using the EuPIA worst case scenario calculation for migration into food, the concentration of residual PI 369 in food would be 0.041 mg PI369/kg food after 12 passes.

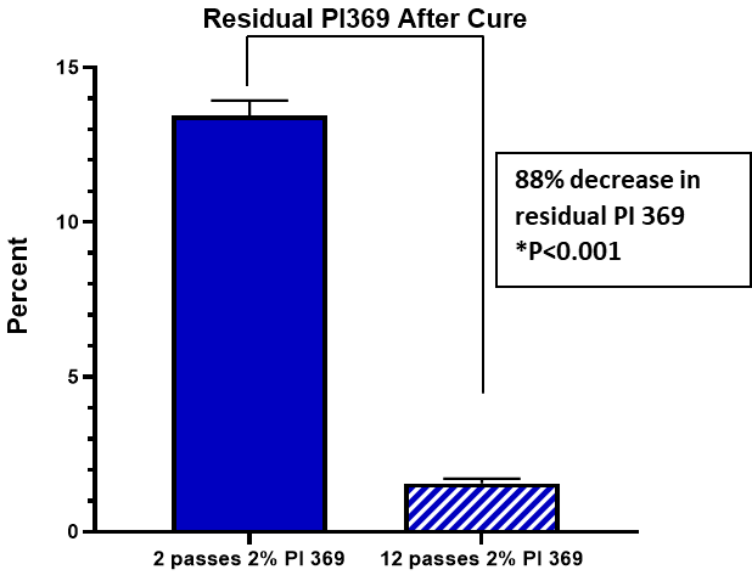

Figure 1. Residual photoinitiator, PI369, after cure. Data represents a percentage of total PI369 in the ink formula (2% PI369 wt/wt). T-test: *P<0.001.

PIITX

The residual PIITX content after 2 conventional passes is 56% (11 ± 0.3 mg residual PI / g ink) of the original amount, while only 1.7% (0.3 ± 0.02 mg residual PI / g ink) PIITX is left after 12 passes.

For PIITX, the worst-case scenario calculation in food is 0.04 mg residual PI/kg food.

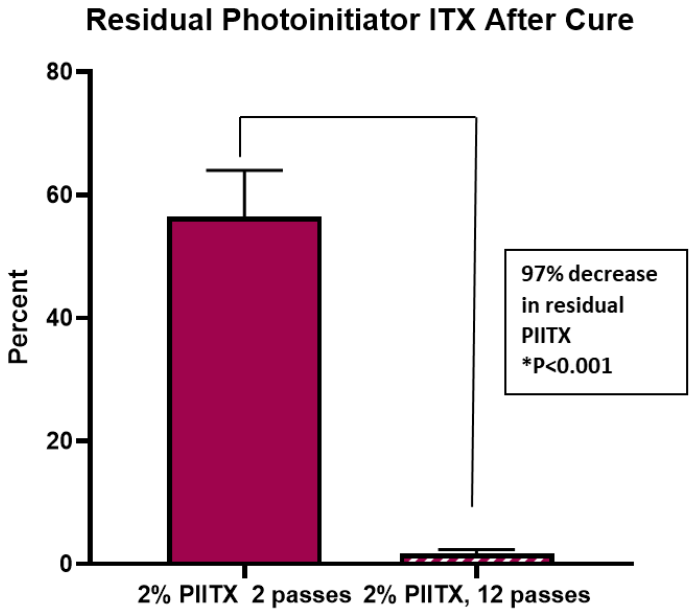

Figure 3. Residual photoinitiator, PIITX, after cure. Data represents a percentage of total PIITX in the ink formula (2% PIITX Magenta wt/wt). T-test: *P<0.001

Conclusion

In addition to providing clarity to exposure of UV/energy curable materials, previous work has provided a framework for quantifying exposure to UV materials in a real-world setting. The current work expands on the knowledge and by providing a method to quantify residual UV material and relate the quantified amount to total packaging weight.

Relating the residual PI content to packaging is dependent upon multiple factors. In the context of this work, we make several assumptions for ink coverage and film thickness. Ink coverage and thickness will vary depending on whether the color is a pantone color or a process color. Printing of a Pantone® color will result in a thicker coating closer to 2 g/ m^2 (offset) and 3 g/m^2 (flexo) coverage. A process color will be printed thinner than a Pantone® color. Additionally, when considering printing graphics, 100% coverage of the 4 base colors would result in a black print of 4 g/m^2. Per the EuPIA GMP Guidance, 2 g/m^2 coverage is used for calculating the mass of cured ink over the area of the packaging. While unrealistic in the final structure of a printed and packaged food, we assume one layer of film with thicknesses and weights as described in Table 2. Lastly, it is important to note the differences between the EU and USFDA food models. The EU Cube Model assumes that a 60 kg person comes in contact with 1 kg of packaged food which is in contact with 0.06 m^2 of packaging. While the USFDA assumes that in one day a person consumes 3 kg of packaged food, where 10 grams of food is in contact with 1 in^2 of packaging. Additionally, the USFDA uses consumption factors for each type of food stuff, however for the purposes of this work, this calculation is not considered here.

In all cases the residual amount of PI is less than 0.1% of the total packaging weight (Table 2). Even for the Cyan ink where the residual PI907 is 11% after cure, the mass of the PI as a percent of the total packaging is below 0.1%. However, from the EU Cube worst-case scenario calculation for concentration of PI in food, it is likely not migration studies and modeling is still needed.

Table 2. Packaging weight and thickness are widely available from vendors; three examples are reported below and used for reporting the percent of residual PI as a percent of the total package (ink + packaging). Italics denotes residual PI greater than 0.1%. (OPP: oriented polypropylene; IML: in mold label; GMP: good manufacturing practice)

		Total package weight ink + film	Cyan PI 369 12 passes	Cyan PI907 12 passes	Magenta PI907 12 passes	Magenta PIITX 12 passes
% Residual PI after 12 passes			1.56	11.70	0.19	1.71
% PI in formula			2.21	3.64	6	2
PET	106 g/ m^2 76.2 micron,	108 g / m^2	0.0006	0.0078	0.0002	0.0006
OPP white IML	33 g/ m^2 60 micron	35 g / m^2	0.0019	0.0243	0.0006	0.0019
OPP uncoated clear	27 g/ m^2 30 micron	29 g / m^2	0.0023	0.0288	0.0008	0.0023
EU Cube GMP Worst-Case Scenario Calculation Assuming 1 kg food/ 0.06 m^2 packaging mg residual PI/ kg food ppm			0.041	0.505	0.014	0.041
USFDA Model Calculation Assuming 10 g food/ in^2 packaging mg residual PI/ kg food ppm			0.044	0.543	0.0154	0.044

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