Marking & Labelling Solutions

Ink Leachability: Keeping Ink on and out of the Bottle

Marking & Labelling Solutions

Continuous Inkjet Printing and HDPE Bottles have been married together since the inception of the CIJ technology. For nearly 40 years, there has been no question that when it's time to mark an HDPE bottle; the capabilities of an inkjet printer - fast dry time, legible code, and consistent print each and every time – are ideal for the HDPE substrate.

As PCI began executing their serialization strategy, which included helper codes2D datamatrix codes on round HDPE bottles, used for Aggregation- Ray Hook Sr. Manager, Global Serialization Services, recognized the need to validate that the inks being used for printing these helper codes weren't migrating through the bottles. Working in collaboration, PCI and Domino identified the key inks required and developed testing criteria to demonstrate compliance with industry leachability requirements.

The following White Paper details the research and results that has allowed Domino and PCI to confidently conclude that there is no ink migration of Domino inks through the walls of PCI's HDPE bottles.

The US Pharmacopeial Convention and USP 661.2

The US Pharmacopeial Convention, (USP) a scientific non-profit organization founded in 1820, sets specific standards for the identity, strength, quality, and purity of medicines, food ingredients, and dietary supplements manufactured, distributed and consumed worldwide. These standards carry with them the weight of enforcement by the FDA, and have become the standard in over 140 countries. The USP is a living, breathing organism comprised of scientists, practitioners, and regulators from across the world. This group has met every 5 years since its founding to discuss, vote on, and adopt resolutions that will continue to help secure the quality of the American drug supply. During the 2010-2015 revision cycle, the USP examined USP 661, Plastic Packaging Systems and Their Materials of Construction; specifically section USP 661.2 which dealt with Plastic Packaging Systems for Pharmaceutical Use.

USP 661.2 outlines how a plastic packaging system – which includes bags, bottles, cartridges, dry powder and metered-dose inhalers, nebulizers, prefillable syringes, vials, and bottles as packaging systems for capsules and tablets – is qualified to establish its suitability for use. Those criteria state that the package should not only protect the product and function properly, but also be compatible with the pharmaceutical product. The product ingredients cannot be adsorbed onto the surface, into the body, or migrate through the packaging system. In addition, the packaging system cannot release substances that then accumulate in the product in quantities sufficient to affect its stability. The packaging must be composed of materials that are safe for use with the pharmaceutical product (i.e., the packaging system does not release substances that then accumulate in the product in quantities that present a risk of toxicity, thereby compromising user safety).

Helper Codes bring USP 661.2 to PCI and Domino's Attention
The US Government passed the bill for patient safety, providing a system for affirming legitimate drug product and thereby discouraging counterfeiting and gray market activity. The first part of the DSCSA dealt with unit level Serialization, a compliance issue slated to be enforced on November 27, 2017 – 4 years after adoption of DQSA. The second portion of DSCSA – the Aggregation piece – is what piqued the interest of Ray Hook, Senior Manager of Global Serialization Services at PCI Pharma Services out of Rockford, IL.

PCI Pharma Services
PCI Pharma Services is a full service CMO and the global leader in contract pharmaceutical packaging, with seven facilities across its global supply chain supporting leading global pharmaceutical and biotech companies in providing lifesaving medicines ultimately destined to over 100 countries throughout the world. PCI has been a leader in Serialization efforts and have made substantial investments in equipment since DSCSA has passed in a conscious effort to prepare for the regulatory deadline. PCI has been actively serializing commercial products for both domestic and international markets for the past five years, with products destined for North America, Europe and emerging markets such as South Korea, Turkey, Brazil and China.

The introduction of high speed Serialization and online Aggregation creates unique challenges and complexities in the packaging process. As a provider of contract packaging services, PCI has the additional challenge of ensuring its assets and processes are agile, flexible and quickly deployable for many clients and configurations. It therefore demands a highly engineered system architecture across its global supply network.

Serialization requires that a unique identifier, a serialized code, be placed on every salable prescription drug product package. The process of Aggregation marries up serialized codes on individual salable packages with their mates in secondary and tertiary packaging for the purposes of traceability. For example, 24 cartons may be placed in a corrugated shipping container. Each of the 24 cartons will have a distinct serialized code, as well as that of the shipper itself. In turn, each shipper placed on a pallet will be subsequently married to the serial number of the pallet itself. Utilizing the principles of Aggregation, various partners within the supply chain such as the pharmaceutical company and distributor, wholesaler, and the pharmacy customer can affirm the contents of each pallet or case by the data configuration. Without the use of Aggregation, one is left to “infer” what is contained, or be left to physically open and investigate the contents to verify what is contained within.

The principle of using inference is rife with concerns in high speed packaging operations and downstream warehousing and supply chain activities. Given the spirit of the DSCSA and the Serialization initiative, the integrity of both the physical packages as well as the Serialization data is paramount to ensuring a safe and effective supply chain.

PCI has taken a stance that inference would not be used and aggregation is the only trusted and reliable method to ensure 100% verification of all codes. Therefore, PCI demanded a solution across all its packaging processes that ensured a robust solution for Aggregation, while careful to not impact efficiency and OEE. This included packaging processes for many carton configurations, as well as high speed bottling. Bottling lines contain a multitude of challenges for aggregating including speed and throughput, material handling of irregular shapes, as well a line of sight – a critical concern given that each package must be verified using highly sophisticated online machine vision inspection.

While many packages had been serialized using laser or inkjet printing, serializing bottles presented a unique situation as there is not always a flat surface for laser printing. Therefore, for aggregating bottles into cases, PCI would need a ‘helper’ code printed on the cap or bottom of bottle in ink. This helper code provides an additional line of sight when executing verification and Aggregation activities in bundles and shipping containers.

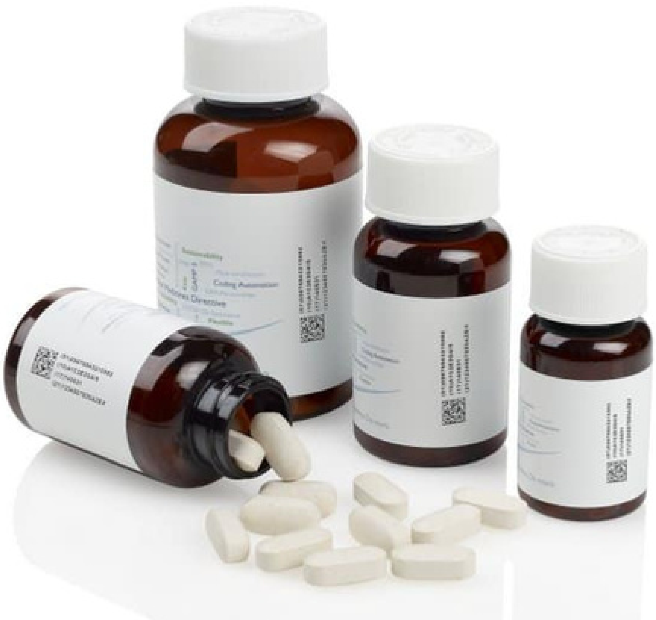
PCI approached Domino North America, their partner for marking and coding, and discussed the necessity to proactively establish that the High Density Polyethylene (HDPE) bottles in use, in conjunction with Domino's continuous inkjet printed helper codes, were going to meet the stringent requirements set forth by USP 661.2. Establishing compliance would ensure PCI's customers that their products would be packaged correctly and safely.

Establishing Testing Parameters

At the request of PCI, Domino North America began evaluating ink types appropriate for printing on HDPE bottles. PCI provided HDPE bottles with a very thin wall thickness of 0.015". These bottles would represent a worst-case scenario for wall thickness. Domino North America then commissioned the Domino Continuous Inkjet Leachables Study to confirm through scientific testing and analysis that the soluble constituents of the Domino Continuous Inkjet Fluids do not leach through the walls of the PCI specified HDPE bottles.

The study called for a 16x16 2D Datamatrix code to be printed using the following Domino ink types:

- 2BK106 Black Ink
- 2BK124 Black Ink for Plastics
- 1BK111 Black Ethanol Blend Ink
- 2CL158 Clear Fluorescent Low Transfer Fast Dry Ink



The Domino Sample Lab in Gurnee, IL used the Domino Ax350i continuous ink jet printer to print 40 bottles with these Domino inkjet fluids specifically selected for their ability to provide high quality, robust prints on HDPE bottles. The 40 bottles were then sent to Whitehouse Laboratories in Lebanon, NJ where they were evaluated against the guidelines set forth in USP 661.2

The testing protocol involved Whitehouse Laboratories preparing a C1 solution and a blank, and then performing physiochemical tests on the C1 solution including appearance, absorbance, acidity/alkalinity and total organic carbon (TOC). These tests are pass/fail by nature, so the PCI bottles and Domino marks had to be acceptable for each of the 4 criteria in the USP 661.2 tests with no exceptions.

Results and Conclusion
The test results from Whitehouse Laboratories show that the PCI HDPE samples marked with Domino 2BK106, 2BK124, 1BK111, and 2CL158 fluids PASSED all tests in accordance with USP 661.2, and that the ingredients of the Domino ink do not migrate through the bottle. Specifications of each test performance can be found in the Appendix.

PCI has always been able to partner with preferred vendors to provide innovative technologies, flexible solutions, and an integrated supply network supporting lifesaving medicines. Through their partnership with Domino, PCI can confidently report to their customers that all printing being done on their HDPE bottles is completely safe for their consumers and fully in compliance with the regulations set forth in USP 661.2. PCI's customers have come to expect a high level of confidence in their packages and Domino has consistently provided support to continue that reputation of quality.

Whitehouse Laboratories
A Division of AMRI

Report of Analysis (Revised)

Client: Domino Amjet
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Gurnee, IL 60046

Phone: (224) 545-2165
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Lab Tracking #: 45291
Received On: 2/10/2017
Analysis Dates: 2/21/2017; 3/21/2017
Report Date: 2/23/2017
Revised Date: 3/24/2017
P.O. Number: 21897

Sample ID: Bottles with four ink types – 2BK106 Black Ink, 2BK124 Black Ink for Plastics, 1BK111 Black Ethanol Blend Ink, and 2CL158 Clear Fluorescent Low Transfer Fast Dry Ink

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Test Method: USP 39 / NF 34 Supplement 2 <661.2> Plastic Packaging Systems for Pharmaceutical Use – Physicochemical Tests

Reference Standard: Not Applicable

Test Result: See pages 2 – 7

Attachments: None

Comments: The sample meets USP 39 / NF 34 Supplement 2 requirements for the tests conducted. Report revised to include test results for Bottles 2 – 6. All additional samples meet USP 39 / NF 34 Supplement 2 requirements.

Laboratory Management Approval,
Date: 3/24/2017
Justine Young
Associate Director of Container Qualification

Quality Assurance Data Review,
Christine Paisker Date: 3/24/2017
Christine Paisker
Quality Assurance Manager

TEST RESULTS

USP <661.2> PHYSICOCHEMICAL TESTS

Bottle # 1:

Appearance

Result: *Solution C1* was clear and colorless.

Specification: *Solution C1* is clear and colorless.

Absorbance

Result: The maximum absorbance was 0.01.

Specification: The absorbance is NMT 0.20.

Total Organic Carbon

Result: The difference in TOC concentrations between *Solution C1* and a *suitable blank* was 1 mg/L.

Specification: The difference in TOC concentrations between *Solution C1* and a *suitable blank* is NMT 8 mg/L.

Acidity or Alkalinity

Result: The solution was *colorless* after the addition of phenolphthalein solution, *pink* after the addition of 0.01 N sodium hydroxide, and *orange-red* after the addition of 0.01 N hydrochloric acid and 0.1 mL of methyl red solution.

Specification: The solution is *colorless* after the addition of phenolphthalein solution, *pink* after the addition of 0.01 N sodium hydroxide, and *orange-red or red* after the addition of 0.01 N hydrochloric acid and 0.1 mL of methyl red solution.

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Test Results Continued onto Page 3…

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Test Results Continued from Page 2…

TEST RESULTS

USP <661.2> PHYSICOCHEMICAL TESTS

Bottle # 2:

Appearance

Result: *Solution C1* was clear and colorless.

Specification: *Solution C1* is clear and colorless.

Absorbance

Result: The maximum absorbance was 0.07.

Specification: The absorbance is NMT 0.20.

Total Organic Carbon

Result: The difference in TOC concentrations between *Solution C1* and a *suitable blank* was 1 mg/L.

Specification: The difference in TOC concentrations between *Solution C1* and a *suitable blank* is NMT 8 mg/L.

Acidity or Alkalinity

Result: The solution was *colorless* after the addition of phenolphthalein solution, *pink* after the addition of 0.01 N sodium hydroxide, and *orange-red* after the addition of 0.01 N hydrochloric acid and 0.1 mL of methyl red solution.

Specification: The solution is *colorless* after the addition of phenolphthalein solution, *pink* after the addition of 0.01 N sodium hydroxide, and *orange-red or red* after the addition of 0.01 N hydrochloric acid and 0.1 mL of methyl red solution.

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Test Results Continued onto Page 4…

QAU Review: CP 3/24/2017

Test Results Continued from Page 3…

TEST RESULTS

USP <661.2> PHYSICOCHEMICAL TESTS

Bottle # 3:

Appearance

Result: *Solution C1* was clear and colorless.

Specification: *Solution C1* is clear and colorless.

Absorbance

Result: The maximum absorbance was 0.00.

Specification: The absorbance is NMT 0.20.

Total Organic Carbon

Result: The difference in TOC concentrations between *Solution C1* and a *suitable blank* was 1 mg/L.

Specification: The difference in TOC concentrations between *Solution C1* and a *suitable blank* is NMT 8 mg/L.

Acidity or Alkalinity

Result: The solution was *colorless* after the addition of phenolphthalein solution, *pink* after the addition of 0.01 N sodium hydroxide, and *orange-red* after the addition of 0.01 N hydrochloric acid and 0.1 mL of methyl red solution.

Specification: The solution is *colorless* after the addition of phenolphthalein solution, *pink* after the addition of 0.01 N sodium hydroxide, and *orange-red or red* after the addition of 0.01 N hydrochloric acid and 0.1 mL of methyl red solution.

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Test Results Continued onto Page 5…

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Test Results Continued from Page 5...

TEST RESULTS

USP <661.2> PHYSICOCHEMICAL TESTS

Bottle # 5:

Appearance

Result: *Solution C1* was clear and colorless.

Specification: *Solution C1* is clear and colorless.

Absorbance

Result: The maximum absorbance was 0.01.

Specification: The absorbance is NMT 0.20.

Total Organic Carbon

Result: The difference in TOC concentrations between *Solution C1* and a *suitable blank* was 1 mg/L.

Specification: The difference in TOC concentrations between *Solution C1* and a *suitable blank* is NMT 8 mg/L.

Acidity or Alkalinity

Result: The solution was *colorless* after the addition of phenolphthalein solution, *pink* after the addition of 0.01 N sodium hydroxide, and *orange-red* after the addition of 0.01 N hydrochloric acid and 0.1 mL of methyl red solution.

Specification: The solution is *colorless* after the addition of phenolphthalein solution, *pink* after the addition of 0.01 N sodium hydroxide, and *orange-red or red* after the addition of 0.01 N hydrochloric acid and 0.1 mL of methyl red solution.

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Test Results Continued onto Page 7...

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Test Results Continued from Page 5…

TEST RESULTS

USP <661.2> PHYSICOCHEMICAL TESTS

Bottle # 5:

Appearance

Result: *Solution C1* was clear and colorless.

Specification: *Solution C1* is clear and colorless.

Absorbance

Result: The maximum absorbance was 0.01.

Specification: The absorbance is NMT 0.20.

Total Organic Carbon

Result: The difference in TOC concentrations between *Solution C1* and a *suitable blank* was 1 mg/L.

Specification: The difference in TOC concentrations between *Solution C1* and a *suitable blank* is NMT 8 mg/L.

Acidity or Alkalinity

Result: The solution was *colorless* after the addition of phenolphthalein solution, *pink* after the addition of 0.01 N sodium hydroxide, and *orange-red* after the addition of 0.01 N hydrochloric acid and 0.1 mL of methyl red solution.

Specification: The solution is *colorless* after the addition of phenolphthalein solution, *pink* after the addition of 0.01 N sodium hydroxide, and *orange-red or red* after the addition of 0.01 N hydrochloric acid and 0.1 mL of methyl red solution.

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Test Results Continued onto Page 7…

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Test Results Continued from Page 4…

TEST RESULTS

USP <661.2> PHYSICOCHEMICAL TESTS

Bottle # 4:

Appearance

Result: *Solution C1* was clear and colorless.

Specification: *Solution C1* is clear and colorless.

Absorbance

Result: The maximum absorbance was 0.01.

Specification: The absorbance is NMT 0.20.

Total Organic Carbon

Result: The difference in TOC concentrations between *Solution C1* and a *suitable blank* was 1 mg/L.

Specification: The difference in TOC concentrations between *Solution C1* and a *suitable blank* is NMT 8 mg/L.

Acidity or Alkalinity

Result: The solution was *colorless* after the addition of phenolphthalein solution, *pink* after the addition of 0.01 N sodium hydroxide, and *orange-red* after the addition of 0.01 N hydrochloric acid and 0.1 mL of methyl red solution.

Specification: The solution is *colorless* after the addition of phenolphthalein solution, *pink* after the addition of 0.01 N sodium hydroxide, and *orange-red or red* after the addition of 0.01 N hydrochloric acid and 0.1 mL of methyl red solution.

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Test Results Continued onto Page 6…

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Chat To Our Expert Team For More

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