Novel Authentication Technology Using Molecular Tags as a PCID in Solid Oral Dosage Forms

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Introduction

A review, by The World Health Organization (WHO), of publications between 2007-2016 estimates that 10.5% of medicines are substandard or falsified and could account for loss of $30.5 billion of pharmaceutical sales in low- and middle-income countries.[1] Medicines impacted cover a wide range of treatment categories including oncology, contraceptives, antibiotics, vaccines and other life-saving medicines.[2] The FDA has issued guidance to address this issue by incorporating physical or chemical identifiers (PCID) into solid dosage forms.[3] Positive detection of the PCID can provide authentication and traceability to individual dosage forms. In this study, an Opadry® complete film coating system was used to carry a DNA-based molecular tag (SigNature®, Applied DNA Sciences, Inc., USA), as a PCID covert authentication platform. This DNA tag is considered as a "molecular bar code", enabling identification to the source, which could be a product type, or other meaningful attributes.

Methods

SigNature molecular tag was incorporated into samples of blue, gray and white pigmented Opadry film coating, then compared with untagged samples. Opadry powder samples were tested for the presence of the tag with SigNify® Reagent Mix and a SigNify® IF portable reader (Applied DNA Sciences, Inc., NY, USA) using real-time polymerase chain reaction (rt-PCR).

Tagged and untagged film coating samples were coated onto placebo tablets (10mm, bi-convex round), to a 3% weight gain using a Labcoat I (O'Hara Technologies, Inc., Ontario, Canada) with the processing conditions described in Table 1.

Table 1. Opadry Coating Process

Parameter	Opadry
Charge (kg)	1
Solids content (%w/w)	20
Spray rate (g/min)	8
Bed temp (°C)	45
Inlet ait temperature	64
Air flow (cfm/m^3/hr)	125 / 212
No. of guns	1
Gun type	VAU
Pan speed (rpm)	20
Atomization ait (psi / bar)	20 / 1.4
Pattern air (psi / bar)	20 / 1.4

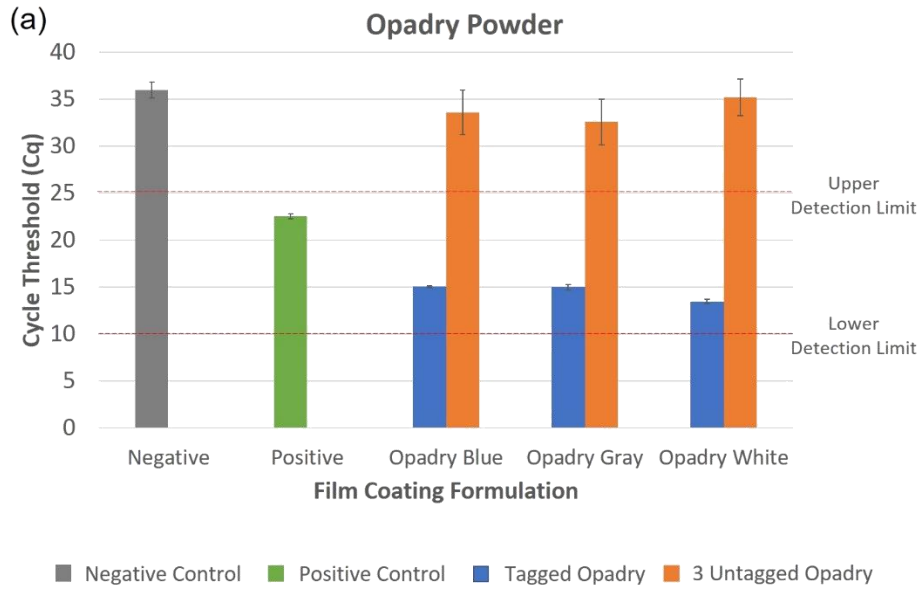
Samples of the film coated tablets were prepared and tested for the presence of the DNA tag, using the rt-PCR, as described above. Tablet appearance was compared analytically by measuring color difference using a DataColor600 reflection spectrophotometer (DataColor, Inc., USA), surface gloss using a Model 803A Surface Analysis System (TRICOR Systems, Inc., USA) and surface roughness using a PS50 Optical Profilometer (Nanovea, Inc., USA). Limit of CIELAB total color difference (DE) were defined as 2.5, 2.0 and 1.5 for blue, gray and white samples, respectively. The performance of

both tagged Opadry dry powder and film coated tablets under accelerated storage condition (40°C/75% RH) were also evaluated.

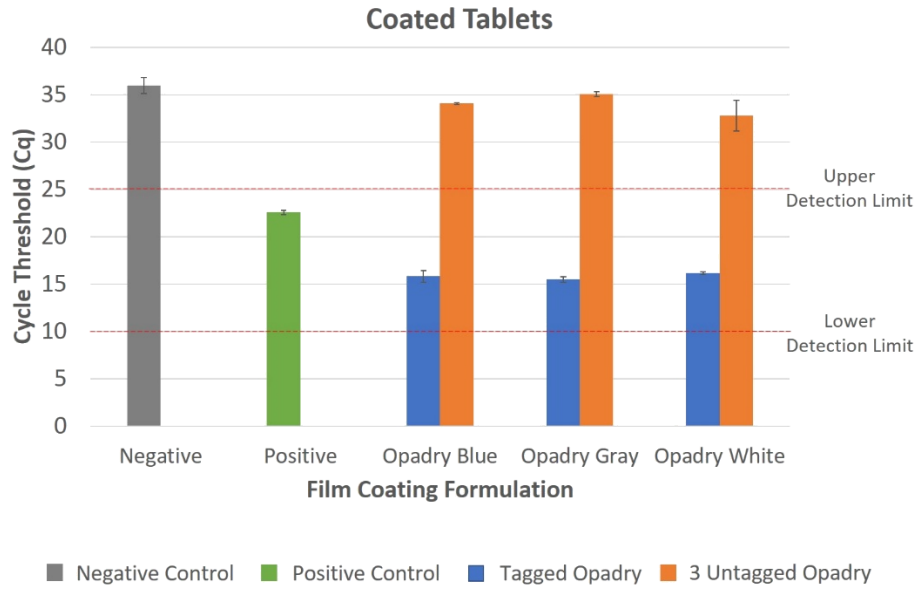
Results

Opadry samples were analyzed by rt-PCR and the resulting cycle threshold (Cq) was compared against negative and positive controls, as shown in Figure 1a. A higher Cq value indicates more cycle time needed to amplify DNA tag to threshold and therefore lower quantity of DNA present. In this study, any Cq value >25 were considered as non-detectable. The negative control and untagged Opadry samples, resulted in a Cq >30, indicating no detection of the tag. In comparison, the tagged Opadry samples and positive control had Cq values of 10-25 confirming presence of the tag.

Figure 1. Cycle Threshold (Cq) for (a) Opadry Powder and (b) Opadry Coated Tablets



(b)



Tablets coated with tagged and untagged Opadry were also tested by rt-PCR and indicated a similar trend. Untagged tablets and the negative control provided no detection (Cq values of greater than 30)

while tagged tablets and positive controls resulted in reliable detection, as shown in Figure 1b. Comparisons of coated tablets using appearance differentiation techniques: imaging, gloss, surface roughness, and color difference are shown in Figures 2-4 and Table 2, respectively. These appearance techniques were not capable of identifying significant differences between tagged and untagged tablets.

Figure 2. Comparison of Images for Tablets Coated with Tagged and Untagged Opadry

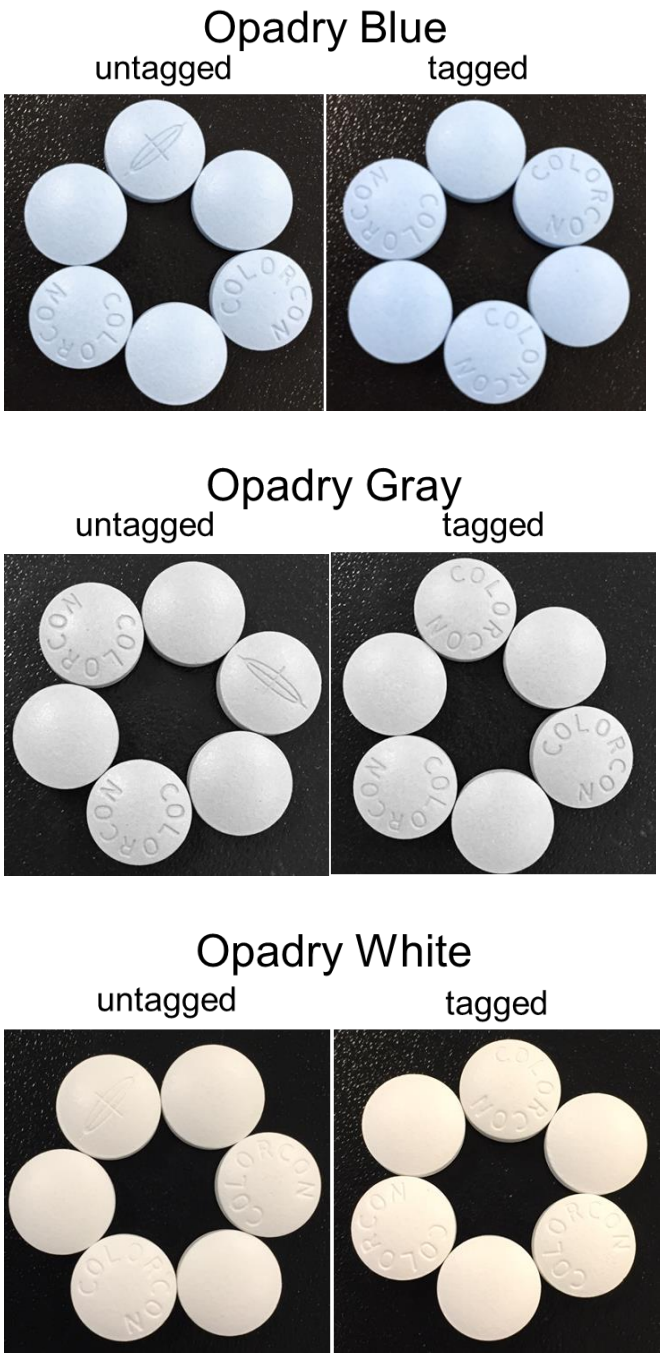


Figure 3. Comparison of Gloss for Tablets Coated with Tagged and Untagged Opadry

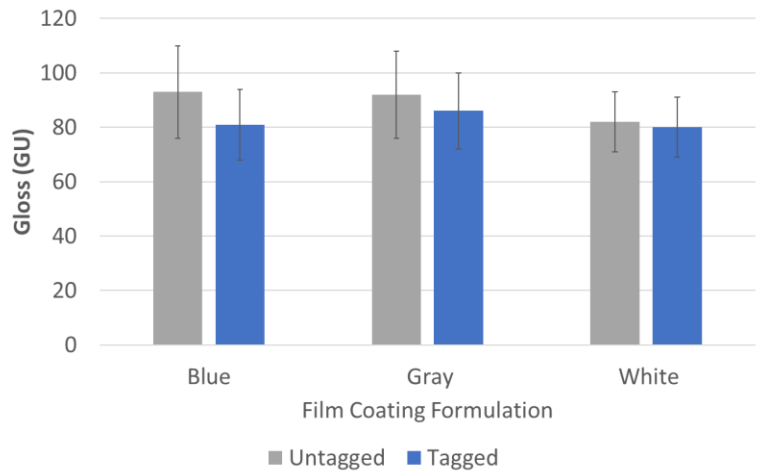


Figure 4. Comparison of Surface Roughness of Tablets Coated with Tagged and Untagged Opadry

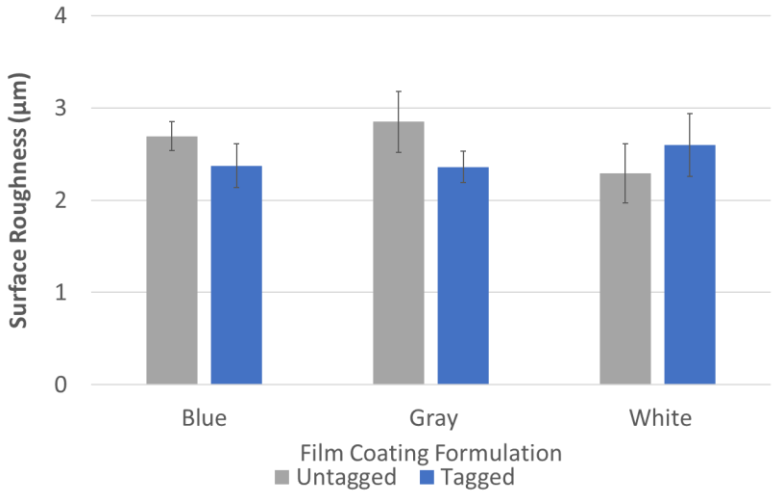
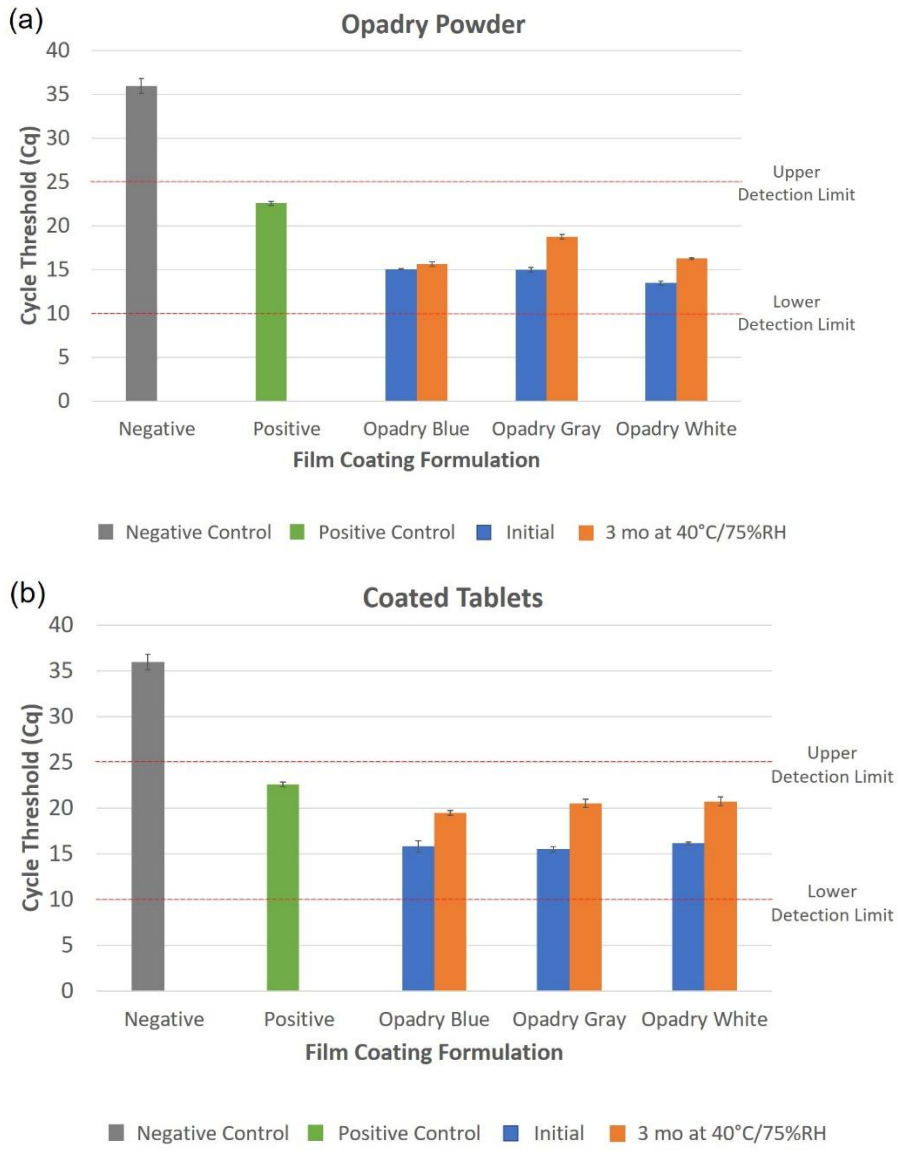


Table 2. Comparison of Color Difference of Tablets Coated with Tagged and Untagged Opadry

	Opadry Blue		Opadry Gray		Opadry White	
Parameter	**Untagged**	**Tagged**	**Untagged**	**Tagged**	**Untagged**	**Tagged**
Color Difference (DE)	Standard	0.16	Standard	0.43	Standard	0.47

Figure 5. Impact of Storage at 40°C/75% RH for 3 months on Cycle Threshold (Cq) for (a) Opadry Powder and (b) Opadry Coated Tablets



Conclusions

The SigNature molecular tag was successfully incorporated into an Opadry film coating as a covert PCID. This is an approach to uniquely identify tablets and capsules, and through authentication, protect against substandard and falsified medicines. The presence of tag could not be detected by appearance or common analytical methods; however, detection was confirmed by rt-PCR when used in conjunction with the matching SigNify Reagent Mix. Tagged samples of Opadry powder and coated tablets were differentiated from the untagged versions, indicating an excellent method for an on-tablet PCID authentication technology platform.

References

1. A Study on the Public Health and Socioeconomic Impact of Substandard and Falsified Medical Products. https://www.who.int/medicines/regulation/ssffc/publications/Layout-SEstudy-WEB.pdf?ua=1 accessed April 2019
2. WHO Global Surveillance and Monitoring System for Substandard and Falsified Medical Products. https://www.who.int/medicines/regulation/ssffc/publications/GSMS_Report_layout.pdf?ua=1 accessed April 2019
3. Guidance for Industry - Incorporation of Physical-Chemical Identifiers into Solid Oral Dosage Form Drug Products for Anticounterfeiting. https://www.fda.gov/downloads/drugs/guidances/ucm171575.pdf accessed April 2019

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