Performance and Stability of an On-Dosage Authentication Technology Using Molecular Tags on the Coated a Model Active

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Introduction

Counterfeiting of drugs is an escalating problem due to low risks for the criminal and high potential rewards. Despite the implementation of serialization to secure the supply chain, a recent report highlighted that the problem continues to grow.1 According to a review by the World Health Organization (WHO), an estimated 10 to 30% of medicines are substandard or falsified in low- and middle-income countries.2 These medicines cover a wide range of treatment categories including oncology medicines, contraceptives, antibiotics, vaccines, and other life-saving medicines.3 The FDA has issued new guidance to tackle this problem through the incorporation of physical or chemical identifiers (PCID) into solid dosage forms.4 Detection of the PCID would help prevent counterfeiting through fast authentication and traceability of individual dosage forms. In this study, a fully formulated Opadry®, Complete Film Coating System, incorporating a DNA-based PCID was applied to acetaminophen (APAP) tablets. The tagged tablets were evaluated for authenticity and other performance attributes during storage at ambient and accelerated conditions.

Methods

Opadry film coating samples with and without DNA-based molecular taggant were coated, using a Labcoat I fitted with a 15” fully perforated coating pan (O’Hara aTechnologies, Inc.), onto 500 mg APAP tablets following identical coating conditions, as described in Table 1. Pigmented Opadry coatings were applied to 3% WG to achieve color uniformity, while a clear Opadry was coated to a 1% WG over APAP tablets previously coated with a blue pigmented Opadry® II, High Performance Film Coating System. The samples evaluated in this study are described in Table 2. After coating, the tablets were stored in induction sealed 120 mL HDPE bottles with two desiccants at 30°C/65% RH through 12 months and 40°C/75% RH conditions over 6 months. Uncoated tablets were also stored under the same conditions as a control.

Table 1. Opadry Coating Process Parameters

Parameter	Opadry White or Pigmented	Opadry Clear
Coating Pan Charge (Kg)	2.5	2.5
Dispersion Solids Content (%w/w)	20	8
Spray Rate (g/min)	20	12
Bed Temperature (°C)	45	45
Inlet Air Temperature (°C)	69	64
Air Flow (cfm/m^3/hr)	175 / 297	175 / 297
Number of Spray Guns	1	1
Spray Gun Type	VAU	VAU
Pan speed (rpm)	18	18
Atomization air (psi / bar)	20 / 1.4	20 / 1.4
Pattern air (psi / bar)	20 / 1.4	20 / 1.4

Tablet color was measured analytically with a DataColor600 (DataColor, Inc.). The limit of CIELAB total color difference (DE) was defined as 2.5, 2.0, and 1.5 for blue, brown, and white samples, respectively.

DNA detection was performed using a PCR portable reader based on real-time polymerase chain reaction (rt-PCR). Drug assay and drug dissolution were evaluated following USP monograph specifications.

Table 2. Configuration of Tagged and Untagged Coatings Evaluated On Tablet Samples

Name	Pigment Coating Applied to 3% WG	Clear Coating Applied to 1% WG
Blue Tagged	Opadry Blue (tagged)	2.5
Brown Tagged	Opadry Brown (tagged)	
White Tagged	Opadry White (tagged)	
Clear Tagged	Opadry II Blue (untagged)	Opadry Clear (tagged)
White Untagged	Opadry White (untagged)	

Results

The coated tablets had an elegant finish with a uniform color distribution as shown in Figure 1. Comparison of white tagged (Figure 1c) and white untagged tablets (Figure 1e) exhibited no observable difference. Additionally, when placed on stability the tablet color was within specification and did not show any significant color change, as shown in Figure 2.

Figure 1. Opadry Coated and Uncoated Tablets. (a) Blue Tagged, (b) Brown Tagged, (c) White Tagged, (d) Clear Tagged over Opadry II Blue, (e) White Untagged and (f) Uncoated.

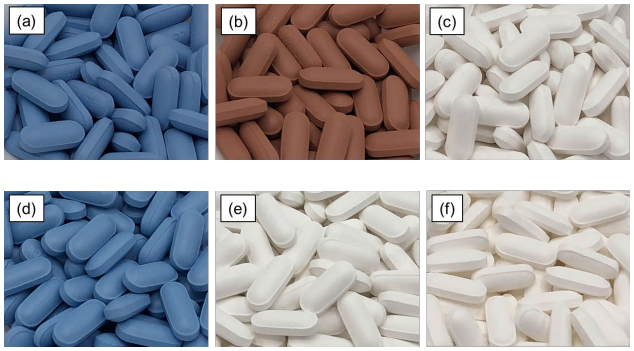


Figure 2. Color Difference (DE) for Tagged and Untagged APAP Tablets Over Stability Through 12 Months 30°C/65% RH or 6 Months 40°C/75% RH

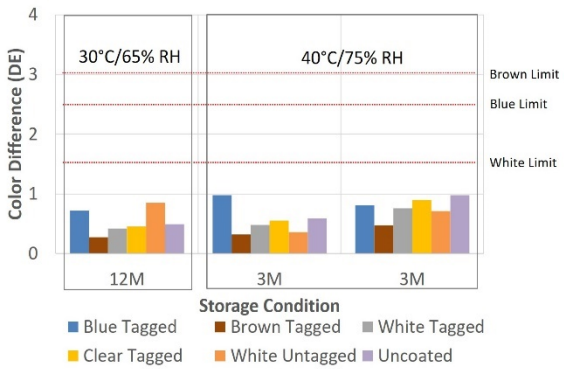


Figure 3. Cycle Threshold (Cq) for Tagged and Untagged APAP Tablets Stored for 12 Months at 30°C/65% RH or 6 Months 40°C/75% RH

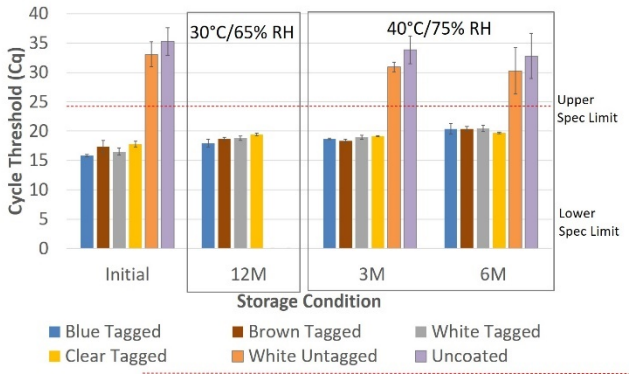


Figure 4. Drug Assay of Tagged and Untagged Tablets Stored for 12 Months 30°C/65% RH or 6 Months 40°C/75% RH

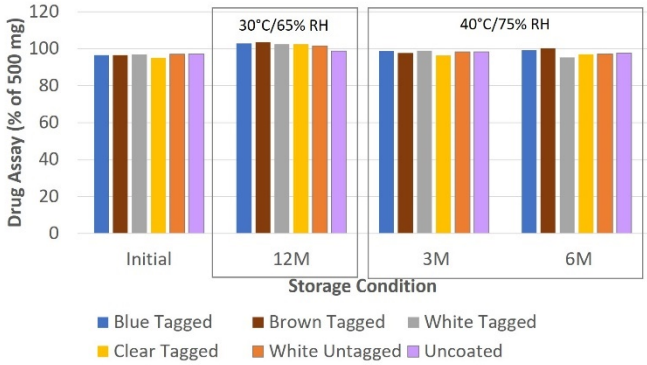
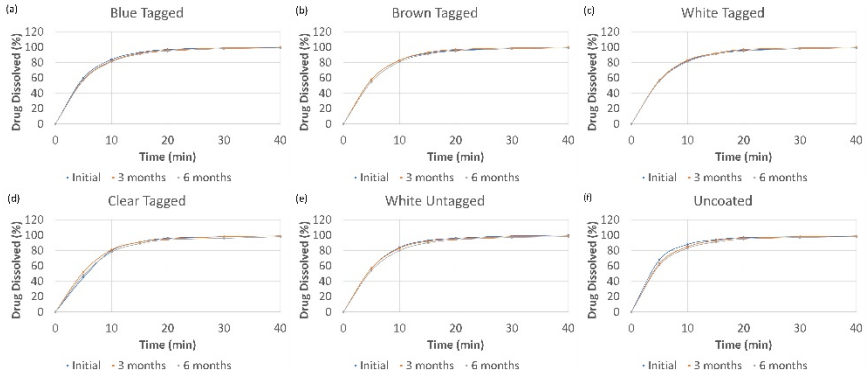


Figure 5. Drug Dissolution Profile of Tagged and Untagged Tablets Stored for 6 Months at 40°C/75% RH



Conclusions

Acetaminophen tablets were tagged with DNA-based molecular taggants available through the SoteriaRx® on-dose authentication platform from Colorcon. Tablets coated with an Opadry film coating containing the DNA-based molecular taggant were authenticated and differentiated from uncoated tablets or coated tablets without the taggant. Opadry coatings with taggant can be used in a pigmented system to provide brand differentiation through color, or as a clear coating applied on top of an existing untagged tablet film coating. The presence of the molecular taggant could not be detected by, nor did it have any impact on analytical techniques, such as color difference, drug assay, or drug dissolution testing at the initial time point or after storage at accelerated conditions. The ease of detection and minimal impact on

other performance criteria indicated that SoteriaRx is an excellent on-dosage PCID authentication technology.

References

1. It's time to stop murder by counterfeit medicine. April 2021
2. 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 April 2019
3. 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=1April 2019
4. 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 April 2019

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