On Dose Authentication Using Molecular Taggants Applied in a Clear Film Coating

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Introduction

Counterfeiting of drugs is an escalating problem due to low risks for the criminal and high potential rewards. A recent report highlighted its continued growth despite the implementation of serialization attempting to secure the supply chain.[1] According to a review paper 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 cancer medicines, contraceptives, antibiotics, vaccines and other life-saving products.[3] The FDA has issued guidance to address this issue with the incorporation of physical or chemical identifiers (PCID) into solid dosage forms.[4] Positive detection of the PCID would help detect counterfeit products by providing authentication and traceability to individual dosage forms. In this study, a clear Opadry® complete film coating system containing a molecular taggant, as part of the SoteriaRx® on-dose authentication platform (a PCID technology), was applied to color coated acetaminophen tablets. The tagged tablets were investigated for authenticity and other performance attributes over 6 months of storage at accelerated ICH stability conditions.

Methods

Using a Labcoat I (O'Hara Technologies, Inc.) fully perforated coating pan, Opadry, Opadry II, or Opadry QX blue pigmented film coating systems, without the molecular taggant, were coated onto acetaminophen (APAP, 500 mg) tablets to a 3% weight gain (WG) to achieve color uniformity. A clear Opadry top-coat including the molecular taggant was added to a 1% WG. After coating, the tablets were stored in induction sealed 120 mL HDPE bottles with two desiccants at 40°C/75% RH conditions over 6 months.

Table 1. Opadry Coating Process Parameters

Parameter	Opadry	Opadry II	Opadry QX	Opadry Clear
Coating Pan Charge (Kg)	2.5	2.2	2.5	2.5
Dispersion Solids Content (%w/w)	15	20	30	8
Spray Rate (g/min)	20	20	20	12
Bed Temperature (°C)	45	45	39	45
Inlet Air Temperature (°C)	69	69	55	64
Air Flow (cfm/m3/hr)	175 / 297	175 / 297	175 / 297	175 / 297
Number of Spray Guns	1	1	1	1
Spray Gun Type	VAU	VAU	VAU	VAU
Pan speed (rpm)	18	18	18	18
Atomization air (psi / bar)	20 / 1.4	20 / 1.4	20 / 1.4	20 / 1.4
Pattern air (psi / bar)	20 / 1.4	20 / 1.4	20 / 1.4	20 / 1.4

Taggant detection was performed using a PCR portable reader based on a real time polymerase chain reaction.

Tablet color was measured analytically with a DataColor600 (DataColor, Inc.). The limit of CIELAB total color difference (DE) was defined as 2.5 for blue samples. Drug assay and drug dissolution were evaluated following USP monograph specifications.

Results

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

Name	Color Coating	Clear Coating Applied to 1% WG
Uncoated	No Coating	No Coating
White Untagged	Opadry White	No top-coat
Opadry + Tagged Clear	Opadry Blue	Opadry Clear (tagged)
Opadry II + Tagged Clear	Opadry II Blue	Opadry Clear (tagged)
Opadry QX + Tagged Clear	Opadry QX Blue	Opadry Clear (tagged)

Figure 1. Coated and Uncoated Tablets

(a) Uncoated

(b) White Tagged Opadry + Tagged Clear

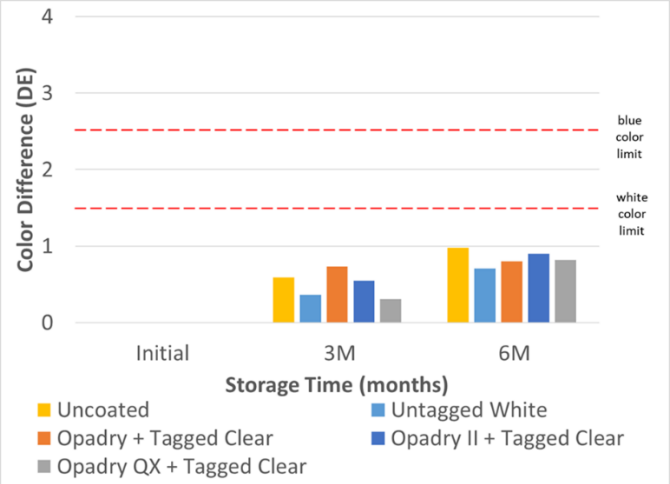
(c) Opadry + Tagged Clear

(d) Opadry II + Tagged Clear

(e) Opadry QX + Tagged Clear

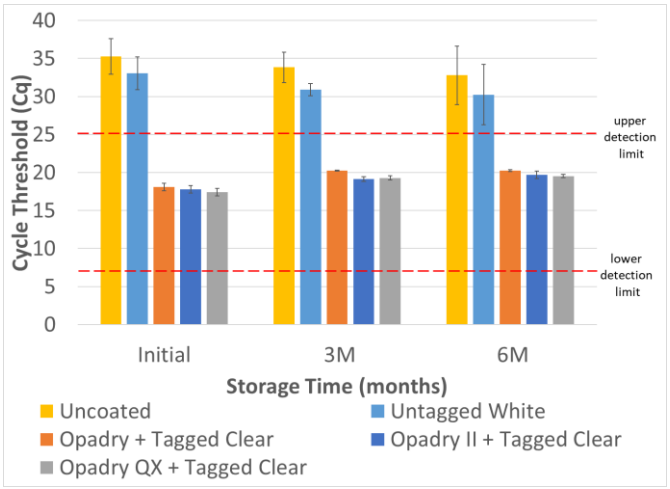
The coated tablets had an elegant finish with a uniform color distribution and an elegant glossy appearance as shown in Figure 1.

Figure 2. Color Difference (DE) for Tagged and Untagged APAP Tablets Following Storage for 6 Months at 40°C/75% RH



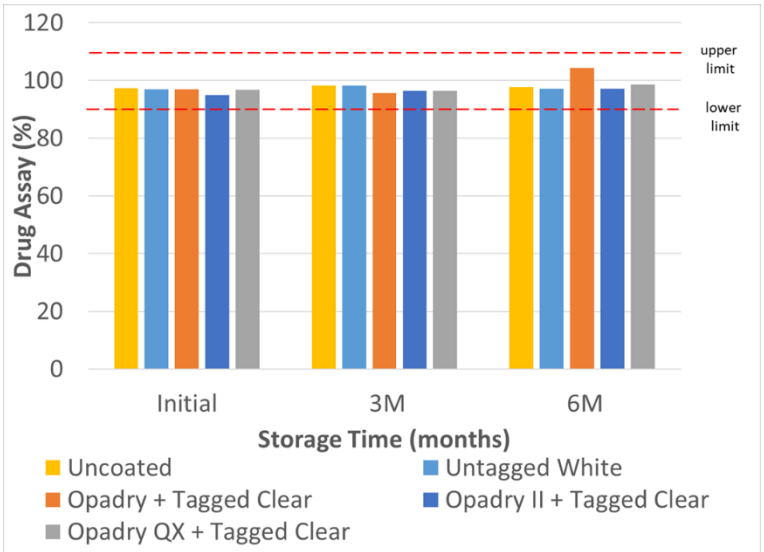
When placed on stability the tablet color was within specification and did not show any significant color change (Figure 2).

Figure 3. Cycle Threshold (Cq) for Tagged and Untagged APAP Tablets Following Storage for 6 Months at 40°C/75% RH



Coated and uncoated APAP samples were analyzed using real-time PCR and the resulting cycle threshold (Cq) is shown in Figure 3. A higher Cq value indicates more cycle time required to amplify the molecular taggant to reach the threshold level and therefore indicates a lower quantity of taggants. Any Cq value > 25 is considered non-detectable. The negative control and untagged Opadry provided a Cq >30 indicating no detection of the taggant. The molecular taggant was successfully detected through 6 months of storage at 40°C/75% RH.

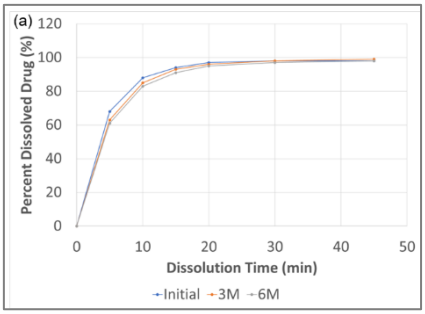
Figure 4. Drug Assay of Tagged and Untagged APAP Tablets Following Storage for 6 Months at 40°C/75% RH



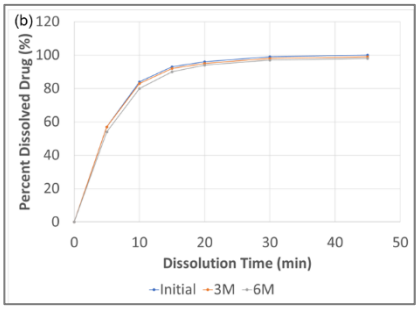
The drug assay for all tablets remained within USP specification of 90-110% of the label claim across all time points and was unaffected by the presence of a coating or by the presence of the DNA-based molecular taggant, as shown in Figure 4.

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

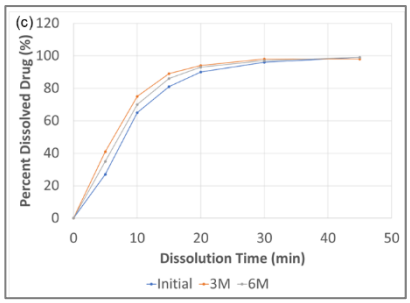
(a) Uncoated



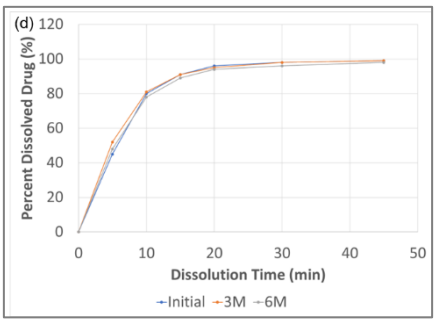
(b) White Untagged



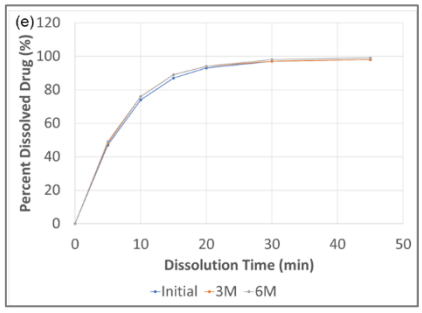
(c) Opadry + Tagged Clear



(d) Opadry II + Tagged Clear



(e) Opadry QX + Tagged Clear



The drug dissolution profile, as shown in Figures 5a to 5e, was consistent regardless of whether the tablets were tagged, coated, or stored at the stability conditions.

Conclusions

SoteriaRx on-dose authentication platform successfully applied a covert tag to acetaminophen tablets.

The tagged Opadry coatings were applied as a clear top-coat over the previously applied pigmented coating. The presence of the molecular taggant could not be visually detected, nor did it have any impact on tablet properties, such as color difference, drug assay, or drug dissolution testing at the initial time point or after storage.

The positive authentication results and the minimal impact on other testing capabilities indicated that the SoteriaRx is an excellent method for an on-dose PCID authentication technology platform.

References

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