aam
Association for Accessible Medicines

Biosimilars Council
A Division of the Association for Accessible Medicines

GRx+Biosims™

Generic + Biosimilar Medicines Conference

Emerging Technologies: How Can the Generic Industry Participate and Benefit?

Judy Murrah
Chief Information Officer, Applied DNA Sciences

Applied DNA Sciences

- Molecular taggants for authenticity and traceability
  - DMF filed; following FDA 2011 PCID Guidance; 3rd party affirmed GRAS
- Linear DNA CRO/CMO services in diagnostics and gene therapies
  - Linear DNA is bacteria-free, lowers risk
- ISO 9001:2015 Certification / ISO 17025:2005 Accreditation
- Over 125 issued patents and pending patent applications

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The Business Challenge:
Is Good Enough "Good Enough" Anymore??

Grow the bottom line…

- Low cost of goods
- Global supply chains
- Be the same but different
- Consumer confidence and loyalty

While fighting against…

- Counterfeit brand erosion
- Diversion eroding margins
- Internet competition
- Regulatory boundaries
- Media surround-sound (opioids, cost, wellness…)

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From Passive to Proactive

Labels, Inks, Holograms, etc.
Raman spectroscopy
Coatings
Tamper-evident

VERIFICATION

Serialization - Package
Blockchain - Package
PCID's – Package and SODF

INFORMATION: AUTHENTICATION TRACEABILITY

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Molecular Taggants: Emerging Technology for PCID

Guidance for Industry

Incorporation of Physical-Chemical Identifiers into Solid Oral Dosage Form Drug Products for Anticounterfeiting

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
October 2011
CMC

As appeared in October 2018 *Tablets & Capsules* Copyright CSC Publishing www.tabletscapsules.com

anti-counterfeiting

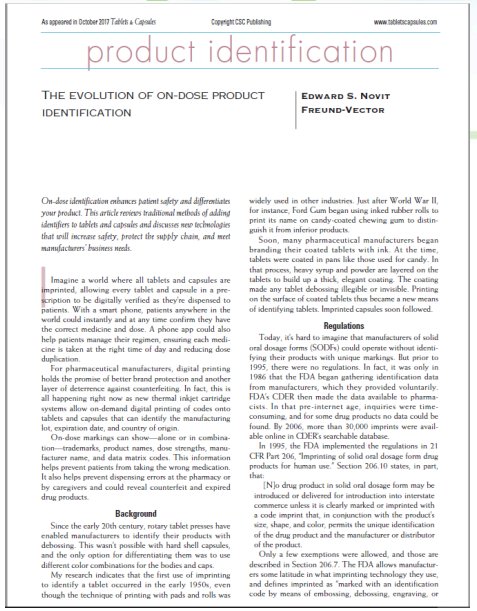
DNA MOLECULAR TAGGANTS: A HIDDEN KEY TO PHARMACEUTICAL PATIENT SAFETY

JUDY MURRAH
APPLIED DNA SCIENCES

Counterfeit drug products are a major problem for the pharmaceutical industry. This article discusses how DNA molecular taggants can help combat drug counterfeiting and improve the safety of the pharmaceutical supply chain.

The pharmaceutical industry has always been at the forefront of safety practices given the potentially dire consequences of a breach in product purity. Still, counterfeit drug products remain a growing problem [1]. Technologies that enable drug counterfeiting, adulteration, and diversion are becoming more accessible, accurate, and affordable, and online buying offers anonymous worldwide distribution. As it becomes easier to replicate the look and feel of a popular tablet or capsule and mimic the graphics and serialization on a package, the stakes have never been higher.

Tablets & Capsules, Oct. 2018



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product identification

THE EVOLUTION OF ON-DOSE PRODUCT IDENTIFICATION

EDWARD S. NOVIT
FREUND-VECTOR

On-dose identification enhances patient safety and differentiates your product. This article reviews traditional methods of adding identifiers to tablets and capsules and discusses new technologies that will increase safety, protect the supply chain, and meet manufacturers' business needs.

Imagine a world where all tablets and capsules are imprinted, allowing every tablet and capsule in a prescription to be digitally verified as they're dispensed to patients. With a smart phone, patients anywhere in the world could instantly and at any time confirm they have the correct medicine and dose. A phone app could also help patients manage their regimen, ensuring each medicine is taken at the right time of day and reducing dose duplication.

For pharmaceutical manufacturers, digital printing holds the promise of better brand protection and another layer of deterrence against counterfeiting. In fact, this is all happening right now as new thermal inkjet cartridge systems allow on-demand digital printing of codes onto tablets and capsules that can identify the manufacturing lot, expiration date, and country of origin.

On-dose markings can show—alone or in combination—trademarks, product names, dose strengths, manufacturer name, and data matrix codes. This information helps prevent patients from taking the wrong medication. It also helps prevent dispensing errors at the pharmacy or by caregivers and could reveal counterfeit and expired drug products.

Background

Since the early 20th century, rotary tablet presses have enabled manufacturers to identify their products with debossing. This wasn't possible with hard shell capsules, and the only option for differentiating them was to use different color combinations for the bodies and caps.

My research indicates that the first use of imprinting to identify a tablet occurred in the early 1950s, even though the technique of printing with pads and rolls was widely used in other industries. Just after World War II, for instance, Ford Gum began using inked rubber rolls to print its name on candy-coated chewing gum to distinguish it from inferior products.

Soon, many pharmaceutical manufacturers began branding their coated tablets with ink. At the time, tablets were coated in pans like those used for candy. In that process, heavy syrup and powder are layered on the tablets to build up a thick, elegant coating. The coating made any tablet debossing illegible or invisible. Printing on the surface of coated tablets thus became a new means of identifying tablets. Imprinted capsules soon followed.

Regulations

Today, it's hard to imagine that manufacturers of solid oral dosage forms (SODFs) could operate without identifying their products with unique markings. But prior to 1995, there were no regulations. In fact, it was only in 1986 that the FDA began gathering identification data from manufacturers, which they provided voluntarily. FDA's CDER then made the data available to pharmacists. In that pre-internet age, inquiries were time-consuming, and for some drug products no data could be found. By 2006, more than 30,000 imprints were available online in CDER's searchable database.

In 1995, the FDA implemented the regulations in 21 CFR Part 206, "Imprinting of solid oral dosage form drug products for human use." Section 206.10 states, in part, that:

> [N]o drug product in solid oral dosage form may be introduced or delivered for introduction into interstate commerce unless it is clearly marked or imprinted with a code imprint that, in conjunction with the product's size, shape, and color, permits the unique identification of the drug product and the manufacturer or distributor of the product.

Only a few exemptions were allowed, and those are described in Section 206.7. The FDA allows manufacturers some latitude in what imprinting technology they use, and defines imprinted as "marked with an identification code by means of embossing, debossing, engraving, or

Tablets & Capsules, Oct. 2017

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How it’s made

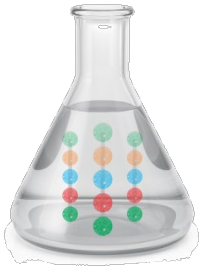
What’s the Claim?

Identify manufacturer?
Identify content?
Identify production line?
Identify year?

Assign Molecular Tag Or Family from Library

- “Information-carrying molecular bar code”
- One-time small-scale or repeat large scale

Formulate with Carrier at parts per billion / trillion



Ingredients

Coating

Packaging

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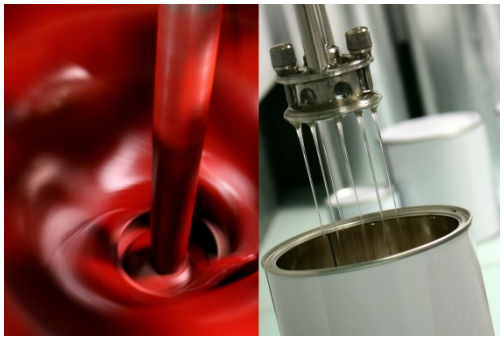
How it’s applied

Spray Drying

Inks and Varnishes



Continuous Inkjet

Seamless to the manufacturing process

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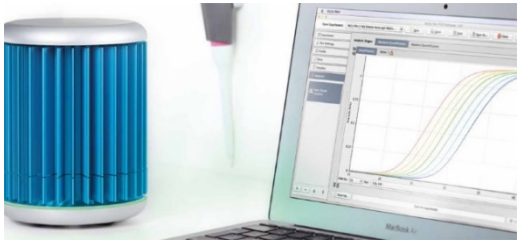
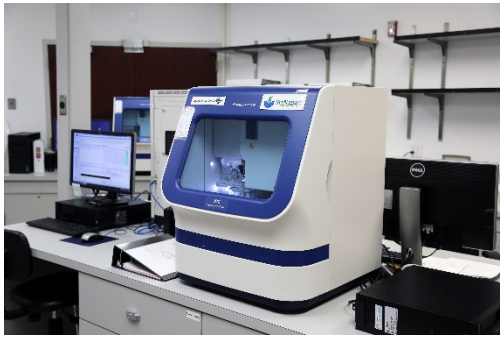
TEST

How it’s tested

Mobile / Handheld
qPCR



Portable
qPCR



Laboratory
DNA qPCR, CE, Sequencing

- Known samples: Quality control of Manufacturing process
- Unknown samples: Authentication of suspect goods

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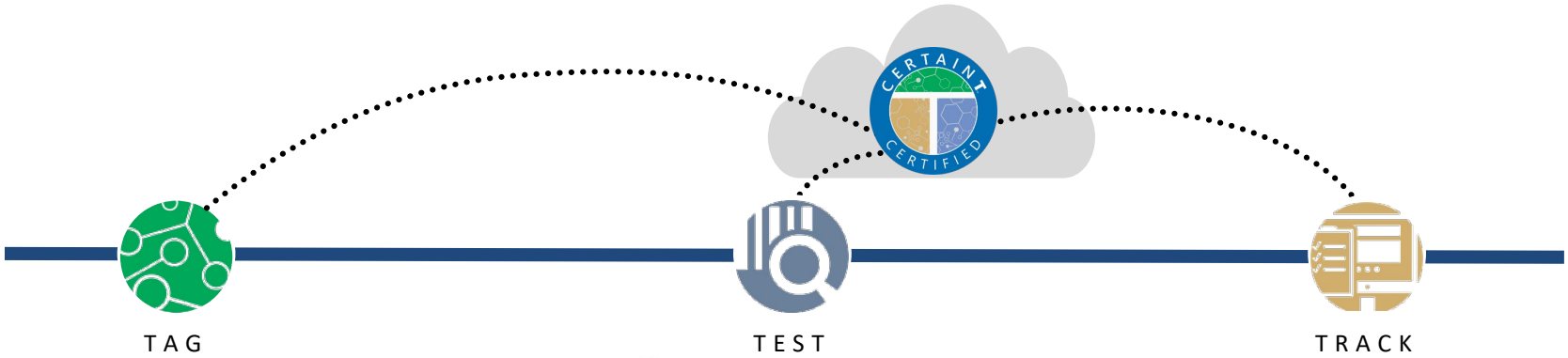
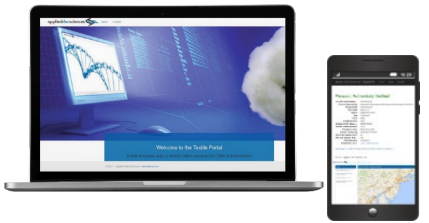
How it's tracked



Application-specific

In-Lab or In-Field



Browser-based desktop or mobile

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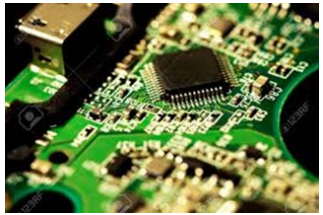
SigNature® molecular taggants
Scale, Variety, Purpose

>250 million pounds
tagged, genotyped cotton;
Costco and Bed, Bath & Beyond

>20 million pounds
tagged recycled polyester;
Walmart.com, Amazon, others

>60,000 tagged
BMW automobiles



>830,000 tagged
microcircuits in circulation
for Defense Logistics Agency

Precommercial scaleups for
excipients, capsules and dietary
supplement ingredients

- **Evidence used in 138 criminal court convictions, 670 sentence years**
- **“Taking the commodity out of cotton” with traceability and evidence**

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Trial at U.S. Pharma manufacturing facility

Tag No Tag

- ✓ 1 part SigNature DNA per 1 trillion parts ink
- ✓ Standard manufacturing process
- ✓ Provides SODF traceability and authenticity

- ✓ Peer-reviewed article

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Research Simulation at King's College, London

- ✓ First report of use of DNA as PCID
- ✓ Simulated illicit drug supply chain evidence

Journals & Books

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ELSEVIER

International Journal of Pharmaceutics
Volume 571, 25 November 2019, 118656

Anti-counterfeiting DNA molecular tagging of pharmaceutical excipients: An evaluation of lactose containing tablets

Mohamad Jamal Altamimi [a, b], Joanna C. Greenwood [c], Kim Wolff [a, d], Michael E. Hogan [c], Ahuti Lakhani [a], Gary P. Martin [a], Paul G. Royall [a]

Show more

https://doi.org/10.1016/j.ijpharm.2019.118656 Get rights and content

- ✓ Peer-reviewed article

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Coatings Co-development Program

- ✓ Manufacturing process
- ✓ Quality process
- ✓ Value-add feature

Category: Formulation and Quality

M1230-07-44 - Novel Authentication Technology Using Molecular Tags as a PCID in Solid Oral Dosage Forms

Mon, Nov 4 12:30 PM – 1:30 PM

Purpose: The World Health Organization (WHO) performed a review of papers published between 2007-2016 and estimated that 10.5% of medicines are substandard or falsified and could account for $30.5 billion of pharmaceutical sales in low- and middle-income countries.[1] These medicines cover a wide range of treatment categories including cancer medicines, contraceptives, antibiotics, vaccines and other life-saving medicines.[2] The FDA has issued a new guidance to address this issue by incorporating physical or chemical identifiers (PCID) into solid dosage forms.[3] Positive detection of the PCID would help prevent counterfeiting by providing authentication and traceability to individual dosage forms. In this study, an Opadry® complete film coating was incorporated with the SigNature® molecular tag (Applied DNA Sciences, Inc.), a DNA based PCID, to form a fully formulated film coating system that is also a covert authentication platform. This DNA tag functions as a "molecular bar code", enabling identification to a source, as a product type, or other meaningful attribute.

Source: AAPS Conference Abstract

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Schreiner MediPharm Labels

SigNature DNA with Beacon screening tool

Covert in regular and UV light

Appears with decryptant swab and UV light

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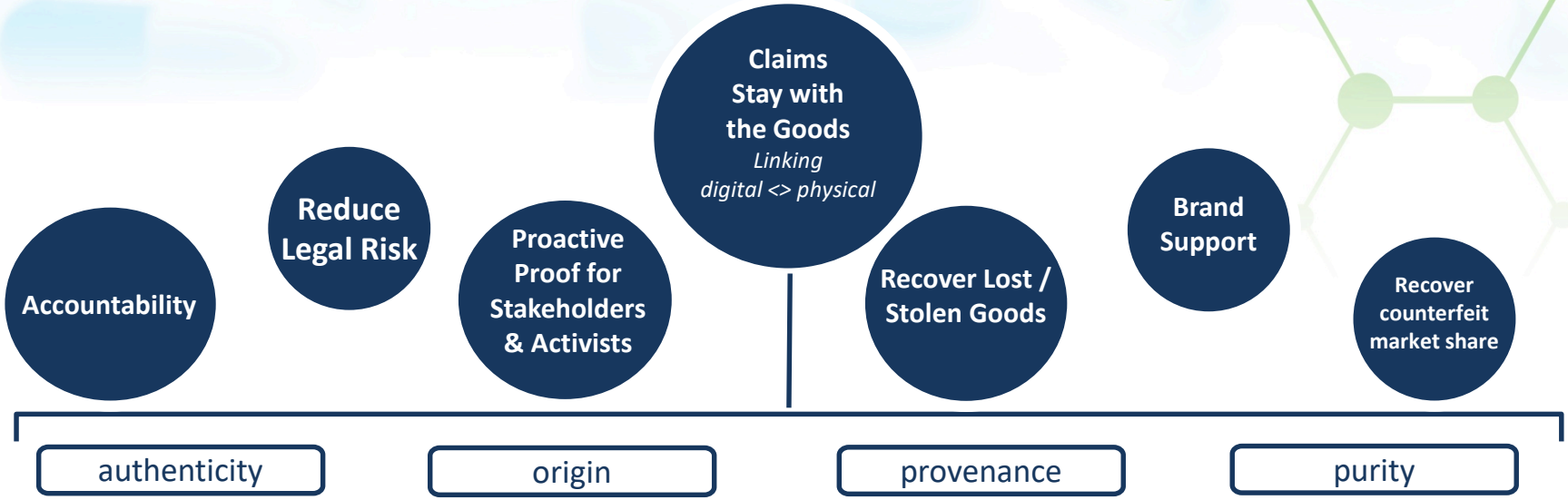
Going Beyond Good Enough: A Benefit for Every Function



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