

White Paper

Published: March 2019

Type 1 Radiation Chemical Process Indicators: Comparison of Leading Market Products for Stability and Compliance to ISO 11140-1

Summary

This White Paper explores the characteristics of four commercial brands of adhesive Type 1 Radiation (Gamma and E-beam) Chemical Process Indicators (CPIs) related to their chemical stability performance against ISO 11140-1 ultraviolet (UV) standards and stability under storage. CPIs evaluated in this paper were tested for exposure to ultraviolet (UV) radiation at 254 nm per ISO 11140-1:4014, and periods of indirect and direct sunlight (UV/Visible light) to assess stability during storage. The class of products selected for the study represent common Type 1, point of use radiation CPIs, commonly used in irradiation facilities for products used in medical and surgical fields, and other applications where sterilization by irradiation is common, and cost effective verification can be performed by facility staff. All products evaluated were of similar intended use and chemical composition, including self-adhesive, circular (approx. 12.7 mm diameter), with chemical indicator transition (i.e. yellow initial color/ orange, red signal color) at exposures of 10 kGy of gamma/E-beam/beta radiation. Of the products tested, criteria were only met for Type 1 radiation CPIs manufactured by True Indicating LLC, Product: CRYR-1, and ETIGAM B.V., Product: 2.01, for compliance to ISO 11140-1:2014 UV testing, as well as, stability under storage for conditions outlined in this paper.

Introduction

Infections related to contamination of pharmaceuticals, medical devices, surgical tools, and materials, are a major threat to medical and manufacturing facilities around the globe. Proper sterilization of these materials, and cost effective ways to monitor the quality of irradiation processes, including CPIs, is an invaluable tool for the safety and health of patients (1).

Radiation sterilization, including gamma and E-beam technologies are frequently used in the pharmaceutical and medical industry as a terminal sterilization method to kill and eliminate microorganisms prior to use. As compared to other sterilization methods, these are often safe, effective procedures that can be used in high throughput manufacturing and health care facilities, and do not raise temperatures of target materials (2-4).

Radiation CPIs are essential for monitoring sterilization exposure of materials used in healthcare and manufacturing environments, and allow a quick, visual check to ensure irradiation. Type 1 radiation CPIs, which are point of use, self-adhesive “stickers”, are commonly used in for ease of application and costs. These CPIs contain a chemical indicator that produces a visible color change indicting that materials have been sufficiently exposed to gamma or beta radiation. Furthermore, it serves as a quality check to differentiate between processed and non-processed materials in medical and industrial settings.

Type 1 radiation CPI specifications and testing requirements are governed by international standard ANSI/AAMI/ISO 11140-1:2014 Sterilization of health care products – Chemical Indicators- Part 1:General Requirements for Type 1 Chemical Process Indicators. Type 1 CPIs must comply to these standards, and testing requirements, in order to maintain third party compliance (5).

Stability of CPIs during storage remains a major concern for sterilization processing facilities, because CPIs are typically placed on materials prior to being sent for irradiation; the materials are stored in warehouse settings where overhead lighting is generally fluorescent and may include sky lights. Due to the CPIs used, it is important that they remain shelf stable

and that the initial color (i.e. indicative of “unexposed”) does not transition into the final signal color (i.e. indicative of “exposed”) during storage. Even slight variations in color change during storage, can potentially impact quality assessments related to proper processing, or render the indicators unusable and ineffective. Testing procedures that are compliant to international standards such as ISO are performed in controlled laboratory environments, whereas, realistic storage conditions in processing facilities, often have multiple factors involved that could impact stability of CPIs. These factors include intentional, or unintentional storage by personnel, on bench tops, warehouses, warehouse racks, that often allows exposure to indirect and direct sunlight that can trigger unwanted transitions to final signal colors.

This paper and study, helps to assess both the stability under controlled conditions as defined per ANSI/AAMI/ISO 11140-1:2014, as well as the stability under uncontrolled conditions of direct and indirect sunlight that may occur during processing and storage in manufacturing and healthcare facilities for Type 1 Radiation CPIs. In order to assess the criteria, the CPIs of four companies were tested in identical fashion, per the conditions outline in this paper.

Materials and Methods

Materials

The following Type 1 Radiation CPIs were selected and purchased directly from the company or retail locations for purposes of this study: Product: CPI-R01, Crosstex International, Inc., Rush, NY (USA); Product: 2.01, Etigam B.V, APELDOORN, Netherlands; Product: CRYR-1, True Indicating LLC, Toledo, OH (USA); Product: P8101, GEX Corporation, Centennial, CO (USA). All products evaluated were of similar intended use and requirements including self-adhesive, circular of similar size (approx. 12.7 mm diameter), designed to demonstrate exposure at a minimum of 10 kGy of gamma/E-beam/beta radiation, and transitions from yellow to red on exposure to radiation above 10 kGy. All products were evaluated within their assigned expiration date or shelf life and, tightly sealed in original packaging, stored in dark, and according to requirements and conditions as stated by

each manufacturer.

Methods

Ultraviolet (UV) testing at 254nm

UV radiation testing was performed per ANSI/AAMI/ISO 11140-1:2014 Sterilization of health care products – Chemical indicators – Part 1: General requirements_section 8.5, using UVP UVGL-58, 6W UV Lamp, from Analytikjena (Upland, CA), at 254 nm for 120 min (± 5 min). All CPIs were tested simultaneously, positioned side by side, in strips of 10 consecutive indicators, with indicator side facing upward, adhered to manufacturing supplied backing material. This test was used to assess ISO compliance, additional requirements for ISO testing such as ionizing radiation are also required to meet standard and are not evaluated in this study.

Stability Testing – Direct Sunlight

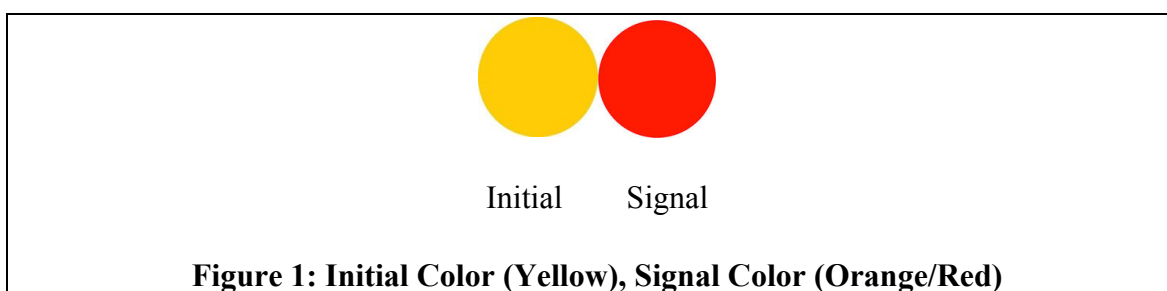
CPIs were exposed to direct sunlight at EPA UV Index #3 (5), at 41.5570° N, 83.6272° W, for a period of 30 minutes (± 1 min) and 8 hours (± 5 min). All CPIs were tested simultaneously, positioned side by side, in strips of 10 consecutive indicators, with indicator side facing upward, adhered to manufacturing supplied backing material.

Stability Testing – Indirect Sunlight

CPIs were exposed to indirect sunlight at EPA UV Index #3 (5), at 41.5570° N, 83.6272° W, to simulate potential warehouse conditions for a period of 30 days (± 1 day). Site location contained 2 overhead polycarbonate sky lights, each measuring 15 in. x 21 in., spaced 6 ft apart. CPIs were placed on a rack between the skylights, approximately 8 ft from ceiling receiving indirect sunlight at approximately 45° from each skylight. Passive indirect light from side windows, open doors, and overhead lights were present during the course of study at intermittent periods due to movement of employees, however, all conditions were identical for all CPIs tested. All CPIs were tested simultaneously, positioned side by side, in strips of 10 consecutive indicators, with indicator side facing upward, adhered to manufacturing supplied backing material.

Criteria for Study

Visible color change criteria for chemical indicators was compared to specifications listed by manufacturer or development of orange or red signal color from initial color of yellow as outline in **Figure 1**. Results were compared to control materials (see Materials section for storage conditions). All CPIs were tested simultaneously under identical conditions. Passing results (Meets Criteria) indicate that the CPIs remained initial yellow color as compared to control, and failing results (Does not Meet Criteria) indicate orange/red signal color development as outline in **Figure 1**.











Results

UV testing at 254nm

Results for UV radiation testing performed per ANSI/AAMI/ISO 11140-1:2014 Sterilization of health care products – Chemical indicators – Part 1: General requirements_section 8.5, meets criteria established under this study for True Indicating LLC, Product: CRYR-1, and ETIGAM B.V., Product: 2.01, indicative of no change in initial color between unexposed CPI control (T=0 min) and test CPIs after 120 minutes (T=120 min) of UV exposure at 254 nm. GEX Corporation, Product: P8101, and Crosstex International Inc., Product: CPI-R01, did not meet criteria established under this study, as test CPIs indicated orange/red signal color development after 120 minutes (T=120 min) versus CPI control (T=0 min) (**Table 1**).

Table 1: UV Test Results at 254 nm ISO 11140-1:2014













Company	Product	T=0 min	T=120 min	Results*
True Indicating LLC	CRYR-1			Met
ETIGAM B.V.	2.01			Met
GEX Corporation	P8101			DNM
Crosstex International, Inc.	CPI-R01			DNM

*Results: Met = Maintained initial color, DNM= Did Not Meet, Orange/Red Signal Color Developed

Stability Testing – Direct Sunlight

Results for direct sunlight testing meets criteria established under this study for True Indicating LLC, Product: CRYR-1, ETIGAM B.V., Product: 2.01, and GEX Corporation, Product: P8101, indicative of no change in initial color between unexposed CPI control (T=0 min) and test CPIs after 30 minutes (T=30 min) and after 8 hours (T=8 hr) for exposure of direct sunlight. Crosstex International Inc., Product: CPI-R01, did not meet criteria established under this study, as test CPIs indicated orange/red signal color development after 30 minutes (T=30 min) and 8 hours (T=8 hr) versus CPI control (T=0 min) (**Table 2**).

Table 2: Stability Direct Sunlight Test Results









Company	Product	T=0 min	T=30 min	T=8 hr	Results*
True Indicating LLC	CRYR-1				Met
ETIGAM B.V.	2.01				Met
GEX Corporation	P8101				Met
Crosstex International, Inc.	CPI-R01				DNM

*Results: Met = Maintained initial color, DNM= Did Not Meet, Orange/Red Signal Color Developed

Stability Testing – Indirect Sunlight

Results for indirect sunlight testing meets criteria established under this study for True Indicating LLC, Product: CRYR-1, ETIGAM B.V., Product: 2.01, and GEX Corporation, Product: P8101, indicative of no change in initial color between unexposed CPI control (T=0 min) and test CPIs after 30 days (T=30 days) for exposure of indirect sunlight. Crosstex International Inc., Product: CPI-R01, did not meet criteria established under this study, as test CPIs indicated orange/red signal color development after 30 days (T=30 days versus CPI control (T=0 min) (**Table 3**).

Table 3: Stability Indirect Sunlight Test Results

Company	Product	T=0 min	T=30 days	Results*
True Indicating LLC	CRYR-1			Met
ETIGAM B.V.	2.01			Met
GEX Corporation	P8101			Met
Crosstex International, Inc.	CPI-R01			DNM

*Results: Met = Maintained initial color, DNM= Did Not Meet, Orange/Red Signal Color Developed

Discussion

Type 1 radiation CPIs play a crucial role for both manufacturing and healthcare processing facilities, in order for personnel to easily distinguish processed and non-processed materials on simple, visual criteria. Modern radiation CPIs, as evaluated in this study, provide cost effective options for high throughput applications and can help aid in quality assessments at the production level.

The scope of this study serves to assess the chemical stability of four common Type 1 radiation CPIs that are available to for purchase and use by healthcare, manufacturing, and processing facilities under the conditions presented. This is not an exhaustive list of all available products, or of all factors that can affect stability, rather we present some scenarios that may affect the stability of Type 1 radiation CPIs. The

scenarios presented here are both plausible and extreme scenarios, that may occur in high throughput facilities during busy production hours and inadvertent storage conditions outside of manufacturers recommendations for storage. As is often the case in stability analysis, it is important to examine worst case scenarios to challenge and investigate possibilities that may occur outside ideal conditions of the laboratory.

Of the products tested, criteria were met for Type 1 radiation CPIs manufactured by True Indicating LLC, Product: CRYR-1, and ETIGAM B.V., Product: 2.01, for compliance to ISO 11140-1:2014 UV, as well as, stability under storage for conditions outlined in this paper. It is important to note that GEX Corporation, Product: P8101, met our criteria for all of the direct and indirect sunlight tests, and may be an option if ISO 11140-1:2014 UV is not required. In addition, other tests such as ionizing radiation, may be required for compliance to ISO 11140-1:2014 and should be requested from manufacturer if needed to evaluate compliance.

References

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