
Pass
Fail

Chemical Indicator Classifications: What Technicians Need to Know

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LEARNING OBJECTIVES

1. Review chemical indicator designs and applications
2. Discuss the International Organization for Standardization's chemical indicator classifications
3. Examine the U.S. Food and Drug Administration's approach to chemical indicators and compare it to the International Organization for Standardization's approach

Chemical indicators (CIs) are an important part of a sterilization quality control testing program. CIs are used in conjunction with physical monitors and biological indicators (BIs) to provide critical information on the quality of a sterilization process. This information is necessary to ensure that all instruments are safe and ready for patient use.

Objective 1: Review chemical indicator designs and applications

CIs are defined as a "test system that reveals change in one or more pre-specified process variables based on a chemical or physical change resulting from exposure to a process."[1] CIs respond to certain specified critical variables in the sterilization process, and their response is chemical or physical as opposed to biological (such as a BI response). There are two main types of CI technology. The first is a reactive ink chemistry that changes color after exposure to the process (e.g., cream-colored ink darkens after exposure). The second is a chemical tablet enclosed within the indicator that melts under certain process conditions, and the liquid chemical then travels down a window to reach a pass/fail line. Some designs incorporate both concepts: a sterilant penetrates a restricted access and causes a color change as the sterilant travels down the window.

CIs have three primary applications. The first are external or exposure indicators. These color-change indicators are visible from the outside of a package or container and are intended to provide fast visual evidence that the package has been exposed to the sterilization process. The second applications are special tests such as Bowie-Dick test packs. The third applications are pack or internal indicators. These CIs are placed inside packages or containers and

provide information on the physical conditions inside the package, where the instruments are located. The CI performance requirements are different for each application.

CIs are segmented into different classifications to better describe their specific applications and performance requirements. The three primary CI applications (external indicators, special tests and internal indicators) are quite different and require different CI performance characteristics. CIs are classified by two different organizations: the International Organization for Standardization (ISO) and the U.S. Food and Drug Administration (FDA). These organizations have different charters and objectives and classify CIs differently. It is useful to understand the two organizations' CI classifications, so it is easier to understand CI labeling and instructions for use (IFU).

Objective 2: Discuss the International Organization for Standardization's chemical indicator classifications

ISO is dedicated to standardization to promote global trade and equitable financial growth. ISO connects the national standards bodies of 165 countries, and ISO's standardization work is carried out by approximately 265 technical committees that cover subject areas ranging from dentistry to freight containers to photography. ISO Technical Committee 198 (TC198) is focused on the sterilization of healthcare products. Within this Technical Committee are 13 working groups comprised of international experts who develop standards for specific subject areas (such as moist heat sterilization and sterilization packaging). ISO TC198 Working Group 6 is responsible for all international standards related to CIs.[2] The standard that establishes the ISO CI classifications is ISO 11140-1.[3]

Type	Name	Description
1	Process indicators	Provide visual evidence of exposure to the process
2	Indicators for specific tests	Special tests, such as Bowie-Dick tests
3	Single critical process variable indicators	Respond to one critical process variable
4	Multicritical process variable indicators	Respond to two or more critical process variables
5	Integrating indicators	Respond to all critical process variables. Stated values must be related to theoretical biological indicator. Multiple stated values are required across the entire sterilization temperature range.
6	Emulating indicators	Respond to all critical process variables. Single stated value based on the specified cycle.

Figure 1: ISO chemical indicator types[3]

The U.S. national version of this standard is ANSI/AAMI/ISO 11140-1; this version is identical in content to ISO 11140-1 and describes labeling and performance requirements for CIs. It is generally considered a manufacturer's standard, but familiarity with its content is useful for Sterile Processing (SP) professionals to help understand CI labeling and the performance capabilities of each type of CI.

CIs that meet the requirements of the ISO standard are typically labeled as compliant with the standard. Compliant CIs should be used whenever possible, because they provide a level of assurance that the chosen indicator's performance is appropriate and based on international norms. It should be noted, however, that CI manufacturers self-certify compliance to the standard; there is no international regulatory organization that independently verifies compliance. Some manufacturers will choose to hire a third-party organization (called a "notified body") to verify their compliance claims.

ANSI/AAMI/ISO 11140-1 establishes six types of CIs. They are numbered Types 1 through 6, but there is no hierarchical implication to the numbering system (i.e., six is not better than one; they are simply different categories). The six types of CIs and their descriptions are provided in **Figure 1**.

It should be noted that Type 3 indicators still appear in the standard but are not commonly used because the other internal indicators (Types 4, 5 and 6) provide more information and are readily available. It should also be noted that not all indicator types are described or specified for all sterilization processes.

The ISO standard describes the three main applications for CIs (as previously addressed in this lesson). That is, CIs may be used to visually differentiate processed and unprocessed items, they may be used in special tests such as the Bowie-Dick, or they may be used inside individual load items to evaluate process variables and parameters at the point of placement.[3]

Each type of CI has performance requirements specified in the standard. Learning some CI terminology can help technicians understand how the performance of each type is specified in the standard. The first important term is "stated value" (SV), which is defined as "value or values of a critical variable at which an indicator is designed to reach its endpoint."[1] Reaching its end point

Exposure Time	Temperature	Expected Result
2 minutes	121°C	Fail
10 minutes	121°C	Pass
0.3 minutes	134°C	Fail
2 minutes	134°C	Pass
30 minutes	140°C	Fail

Figure 2: Type 1 process indicator requirements (steam)[3]

Type	Test Point	Time	Temperature
4	1	SV	SV
4	2	-25%	-2°C
5	1	SV	SV
5	2	-15%	-1°C
6	1	SV	SV
6	2	-6%	-1°C

Figure 3: Internal indicator performance requirements (steam)[3] In Figure 3, test point 1 is the pass condition, and test point 2 is the fail condition. Fail conditions are created by reducing the critical variable values to reduce the effectiveness of the process and create a process failure.

means showing a "pass" result, so the SV is the sterilization exposure conditions where the indicator must show a pass result. For example, if a steam CI has an SV of 132°C for three minutes, it means the CI must show a pass result when exposed to saturated steam at 132°C for three minutes in a laboratory test sterilizer. The SV(s) for a CI must be listed on the product labeling to be compliant with the standard.

Another important term is "critical process variable," which identifies the elements of a sterilization process that have direct impact on the lethality (or killing power) of the process. For example, the critical process variables for steam sterilization are exposure time, temperature and steam saturation. Any change in these variables (e.g., reduced exposure time or temperature) will affect the process. An example of a non-critical variable for steam sterilization is pressure. Pressure change alone will not affect the lethality of the process.

In general, the ISO standard defines the sterilization conditions where the indicator must show a pass result (the CI reaches its end-point color or travels past the pass/fail line) and conditions where the indicator must show a fail result. In this way, the standard defines the level of challenge the indicator must present to the sterilization process. *Note: Type 2–specific test indicators have a separate set of ISO standards that specify their requirement.*

There is a difference in how performance requirements are specified for Type 1 process indicators (external indicators to verify exposure) and Type 3, 4, 5 and 6 indicators (intended for use inside packages). Type 1 indicators have a prescribed set of pass/fail conditions, while the internal indicators require the use of SV. This is because Type 1 indicators are only intended to verify exposure to the process and differentiate processed from unprocessed items, whereas internal indicators are expected to provide information on the quality of the process by evaluating the critical process variables.

Figure 2 provides an example of how process indicator performance is specified for steam sterilization. For comparison, **Figure 3** shows how steam internal indicator performance is specified.

Note: Since Type 1 indicators are not intended to evaluate the quality of the process, there is no link to SVs in their requirements.

Internal indicators evaluate the quality of the sterilization process by responding to the critical process variables. Type 3 and 4 indicators are only required to respond to one variable or one or more variables, respectively. Type 5 integrating indicators for steam sterilization are required to respond to all of the critical process variables and must also have three SVs specified across the range of sterilization process temperatures. This means that they must have a SV at 121°C, one at 135°C and at least one at a temperature in between (if three SVs are used, the third is usually at 128°C). These SVs should be at least as challenging as the performance of a theoretical BI across the full sterilization range. Type 6 emulating indicators are also required to respond to all critical process variables, but they only have a single SV that must reflect the specific process in which it is used. In other words, Type 6 indicators are cycle specific.

It should be noted that ISO 11140-1 does not define or provide performance requirements for Type 5 and 6 CIs for vaporized hydrogen peroxide (VH2O2) sterilization processes. Type 4 multicritical process variable indicators,

therefore, provide the highest level of information for VH2O2 processes.

Objective 3: Examine the U.S. Food and Drug Administration's approach to chemical indicators and compare it to the International Organization for Standardization's approach

The FDA is a federal organization with broad regulatory responsibilities focused on protecting the health and safety of the public. As part of its responsibility, the FDA regulates medical devices. CIs are considered Class II medical devices and are subject to FDA regulation.

This regulation includes a requirement that a CI manufacturer submit a premarket submission for FDA review before the manufacturer can sell the CI to healthcare facilities. This notification document is called a "510(k)" (named for the clause in the Food and Drug Act that defines this process) and contains testing data and labeling information that will be reviewed by the FDA. If the 510(k) document supports the CI as safe and effective, the FDA will "clear" it and allow for commercial distribution. The FDA uses product codes to categorize medical devices for their internal systems, including 510(k). For example, the product code for BIs is "FRC," and the product code for standard CIs is "JOJ."

The FDA published a guidance document for CI manufacturers that outlines the information and testing data that must be included in the 510(k) submission.[4] This document lists the three CI classifications used by the FDA. These classifications and their descriptions and applications are shown in **Figure 4**.

The FDA uses only three CI classifications, while ISO uses six. Both organizations have a classification for process indicators and air removal (special) tests. The FDA places all internal indicators (ISO Types 3, 4, 5 and 6) into a single classification: CIs. The FDA's test requirements are different than the ISO's. ISO requirements tend to be more specific as the test conditions for both pass and fail tests are defined. Examples of the FDA requirements for steam process indicators are provided in **Figure 5**.

As shown in some of the figures, the ISO requirements are more detailed than the FDA requirements, with

Classification	Description	Intended use
Process indicator	A chemical indicator intended for use with individual units (e.g., packs, containers) to demonstrate that the unit has been exposed to the sterilization process and to distinguish between processed and unprocessed units	This process indicator is intended to be used by a healthcare provider with sterilization wraps, containers, cassettes or pouches to distinguish between processed and unprocessed units.
Chemical integrator	A chemical indicator designed to react to all critical parameters over a specified range of sterilization cycles	This chemical integrator is intended to be used by a healthcare provider to demonstrate that the parameters over a specified range of sterilization cycles have been met in a specified sterilization wrap, container, cassette or pouch.
Air removal test	A chemical indicator to be used in the standard test pack to determine the efficacy of the air removal phase in the steam sterilization process	This air removal indicator is intended to be used by a healthcare provider in a standardized test pack (e.g., Bowie-Dick test pack) to assess the ability of a pre-vacuum sterilizer to remove air and allow steam to penetrate into wrapped goods and porous loads.

Figure 4: CI descriptions and intended use[4]

Steam	Temperature	Time to show a pass result
Yes	121°C	2 minutes to 10 minutes
Yes	132°C–135°C	20 seconds to 2 minutes
No (dry heat)	140°C	No pass at 30 minutes

Figure 5: FDA steam process indicator requirements

Steam	Exposure Time	Temperature	Expected Result
Yes	2 minutes	121°C	Fail
Yes	10 minutes	121°C	Pass
Yes	0.3 minutes	134°C	Fail
Yes	2 minutes	134°C	Pass
No (Dry heat)	30 minutes	140°C	Fail

Figure 6: ISO steam process indicator requirements

specific conditions defined for both pass and fail results. The FDA requires pass/fail results in the 510(k) document, but the agency leaves it to the manufacturer to determine the test parameters.

For steam integrators, the FDA definition of responding to all critical variables will only compare to ISO Type 5 and Type 6 indicators. In this case, the ISO requirements again are more prescriptive. The FDA testing for CIs asks for side-by-side testing with a BI, while ISO Type 5 indicators require SVs that are related to a calculated BI response.

Requirements for CIs for VH2O2 sterilizers are covered under "New Technology Sterilizers" in the FDA guidance document. The FDA does not provide any specific performance criteria for CIs for VH2O2 processes but indicates that the general approach used for steam CIs should be applied. The FDA has also accommodated innovative technologies in this area and recently added product code "QKM" for chemical vapor sterilization multivariable CIs. These indicators monitor one or more critical process variables, such as H2O2 concentration, temperature and exposure time. This new category aligns closely with the ISO Type 4 definition.

Conclusion

CI classifications are useful as they define the capabilities and appropriate use of the wide range of CIs available. ISO and FDA have different roles related to CIs and categorize CIs differently (ISO focuses on providing benchmark performance requirements for international standardization whereas the FDA focuses on the regulatory aspects of safety and efficacy for the U.S.). The FDA reviews all data, claims and labeling as part of its clearance process, while ISO compliance claims are self-certified by the manufacturer. The FDA does not review ISO compliance claims. Understanding the roles and categorizations of ISO and FDA will help the SP team fully understand CI labeling and the information provided by each type of CI.

REFERENCES

1. International Organization for Standardization. *Sterilization of health care products — Vocabulary of terms used in sterilization and related equipment and process standards.* ISO 11139:2018. https://www.iso.org/standard/66262.html.
2. International Organization for Standardization. "Technical Committees." https://www.iso.org/technical-committees.html.
3. International Organization for Standardization. *Sterilization of health care products — Chemical indicators—Part 1: General requirements.* ISO 11140-1:2014. https://www.iso.org/standard/55080.html.
4. U.S. Food and Drug Administration. *Guidance for Industry and FDA Staff: Premarket Notification [510(k)] Submissions for Chemical Indicators*. Document issued on December 19, 2003.