Regulatory Basis:
FDA Quality Systems Regulations

Reference: FDA CFR - Code of Federal Regulations Title 21

General Discussion
This document offers a risk assessment approach to document a critical instrument calibration interval change request.

Non-Critical Instruments
Calibration frequencies for non-critical instruments, if any, can be adjusted by the maintenance team as appropriate based on instrument history and other factors. This practice has no impact to non-critical instrument interval change opportunities.

Critical Instruments
Calibration frequencies for critical instruments may be adjusted as necessary based on calibration data or other information that may support a change. Before extending calibration intervals, review the calibration history of the instrument based on the table below. Consider the results of the calibrations [e.g., Return to Service (RTS) limit exceeded, etc.] in the listed time window when modifying frequency.

Interval Change	**Consecutive # of Most Recently Completed Calibrations (w/o adjustment)**
From Weekly to Monthly	12
From Monthly to Quarterly	12
From Quarterly to Semi-Annually	18
From Semi-Annually to Annually	4

The interval change table above, which should be based on instrument history, is the primary method of determining opportunities for calibration interval changes.

Consideration should be given to the level of risk before making changes in calibration interval. For instruments that are considered to be minimal risk, an informal concise assessment is appropriate.

Where service requirements or other information indicates substantial risk associated with failure of a critical instrument, a more formal risk analysis can be used to confirm the calibration interval change.

The calibration risk evaluation should consider how a deviation reporting involving the instrument might affect release of the product lots in question. The extent to which the instrument would impact the product is a good indicator of risk. A more conservative extension of the calibration interval can then be made, if appropriate.

Recommendations & Rationale for Recommendations
Risk Assessment Tool -Failure Mode and Effects Analysis (FMEA) is the tool of choice that is recommended for calibration interval change analysis. Its use enables identification of potential failure modes and assignment of numerical ranking using probability, severity and detectability of the risk

Table I

Probability of Instrument Failure [MTBF = mean time between failures]

	Risk Level → Numeric Ranking →	Low (1)	Medium (2)	High (3)
History	This Instrument (The intent is to use history as an indicator of probability)	Have more than 2 years of records, history shows low rate of calibration OOT (MTBF > 24 months)	Have less than 2 years of records, history shows low rate of calibration OOT	Have no historical records, or records show MTBF < 24 months
	Identical Instrument (make and model)	Have 3 or more identical instruments (MTBF > 24 months)	Have 1 or 2 identical instruments (MTBF > 24 months)	Have no identical instruments to benchmark
	Similar Instruments (The concept is to determine if there are instruments of similar design and functionality utilized in the intended environment that may yield performance data for use as a predictor, i.e. show low risk based on demonstrated reliability)	Have several (e.g. 10) similar (in type, technology, range) instruments in similar environments (MTBF > 24 months)	Have a few similar instruments in similar environments (MTBF > 24 months);	Have no similar instruments in similar environments
Environmental	Temperature and Humidity (both operating and storage conditions)	Temperature and humidity are stable and are always within manufacturer's recommended range	Temperature and humidity vary, but always stay within manufacturer's range	Temperature and humidity are not known or may exceed manufacturer's range
	Power line / Electrical Disturbances	Instrument is non-electric	Instrument is battery powered or well-filtered and protected from power disturbances and lightning	Instrument is located in an electrically "noisy" environment, or may be susceptible to sags, surges, spikes, and severe electro-magnetic interference (EMI)
	Dust / Dirt / Chemical / Wash down	Instrument is located in a clean, dry, area that does not get washed down	Instrument is in a protected cabinet, or removed for area wash down, light dust, and no chemical exposure	Instrument is in an exposed, dirty environment subjected to frequent wash downs, or chemical exposure
	Vibration and shock	Instrument is permanently mounted in a stable environment	Instrument is portable and moved frequently, or may be exposed to occasional vibration or shock	Instrument is subjected to severe shock and vibration
	Physical Damage	Instrument is kept in a segregated or protected area	Instrument is located in a moderate traffic area and potentially susceptible to contact with equipment or personnel in transit	Instrument is located in a high traffic area and susceptible to contact with equipment or personnel in transit
Range of Use	Range of inputs the instrument is subjected to	Instrument is operated at a single fixed setting in the middle portion of its designed functional range	Instrument is operated at multiple settings throughout the middle 80% of its functional range	Instrument is operated at multiple settings across the entire functional range or at a fixed setting at the upper or lower limit of the functional range
Age	Infant mortality (start-up failure) or aging components	Instrument has been in service for >3 months but less than 5 years	Instrument has been in service for less than 3 months, or greater than 5 years	Instrument has been in service for over 10 years

condition upon the system, process, or even the product to which it is associated or used. Immediate detection is determined by whether the system or process utilizing the instrument is automated, or manual, and whether there are other instruments or tell-tale parameters that occur as a direct result of incorrect instrumentation. Refer to **Table III below.** Systems or processes that are equipped with automation features or components that make it easier to detect OOT conditions should have a reduced risk in detectability ranking. Systems that have additional instruments or detectable parameters that are frequently observed/compared will enable timely identification of OOT conditions, thus resulting in lower risk.

Table III: Detectability of Instrument Failure

Table III

Detectability of Instrument Failure

	Risk Level → Numerical Ranking →	Low (1)	Medium (2)	High (3)
Automatic Operation	Automated verification of critical product characteristics/parameters	100% or continuous online inspection/analysis (PAT) of critical attributes/parameters; redundant stage release testing	Periodic online inspection/analysis of critical attributes/parameters redundant stage release testing	No automated online inspection/analysis of critical attributes/parameters, no stage release testing.
Manual Operation	Human interventions or audits to verify resulting product quality	100% or continuous online inspection/verification of critical attributes/parameters; with or without stage release testing	Periodic inspection/verification of critical attributes/parameters; with stage release testing	No inspections/verifications during the process and no stage release testing

- **Risk Acceptance:**
  Once the probability, severity, and detectability of instrument failure are individually assessed and agreement is reached on the risk associated with each instrument, a site should then define the level of risk it is willing to accept. The FMEA ranking criteria can be used to assign numerical ratings and complete the overall risk evaluation. See **Table IV**.

Example #3:

Instrument: Humidity Transmitter

Application: Ambient humidity sensor in a conditioned room. ***This transmitter is an alarm point only***. The Building Management System (BMS) controls the temperature and humidity, and a chart recorder records them, providing very easy detect ability of failure.

Basis for change:

Instrument Type	Inst. Class Critical?Y or N	Associated System	Probability of Occurrence	Severity of failure	Detectability of Failure	Risk Score (Failure Mode)	Recommended Calibration Period (Months) from table:	Basis for Change Calibration Interval: Since it is low probability and easily detected, consider increasing the calibration interval to 24 months.
Humidity Transmitter	**Y**	**Packout Room**	**1**	**3**	**1**	**3 (low)**	**12**	**24 months**

Example #4:

Instrument: O_2 Sensor

Application: Oxygen sensor detecting ***breathable*** concentration of O2 in an area using liquid nitrogen as a coolant. Typically these devices are covered by a LOPA (layers of protection assessment) evaluation to determine the safety factors.

Basis for change:

Instrument Type	Inst. Class Critical?Y or N	Associated System	Probability of Occurrence	Severity of failure	Detectability of Failure	Risk Score (Failure Mode)	Recommended Calibration Period (Months) from table:	Basis for Change Calibration Interval: Since the history of these devices is awful, and the severity is very high (human injury or death), and detect ability presents a high risk, consider decreasing the calibration interval to 3 months and re-engineering the detection system to mitigate the risks of single-unit failure.
O_2 Sensor	**Y**	**Reactor**	**3**	**3**	**3**	**27 (high)**	**6**	**3 months**

Example #5:

Instrument: **RPM Indicator**

Application: Direct drive gearbox from a synchronous motor.

Basis for change:

Instrument Type	Inst. Class Critical?Y or N	Associated System	Probability of Occurrence	Severity of failure	Detectability of Failure	Risk Score (Failure Mode)	Recommended Calibration Period (Months) from table:	Basis for Change Calibration Interval: Overall negligible risk, consider increasing the calibration interval up to 36 months.
RPM Indicator	**Y**	**Reactor**	**1**	**1**	**1**	**1 (low)**	**18**	**36 months**

