Designation: F3211 – 17

Standard Guide for Fatigue-to-Fracture (FtF) Methodology for Cardiovascular Medical Devices[1]

This standard is issued under the fixed designation F3211; the number immediately following the designation indicates the year of original adoption or, in the case of revision, the year of last revision. A number in parentheses indicates the year of last reapproval. A superscript epsilon (ε) indicates an editorial change since the last revision or reapproval.

1. Scope

1.1 This guide is intended to provide an experimental methodology to assess and determine the structural fatigue life of implantable cardiovascular medical devices.

1.2 This guide is also intended to provide methodologies to determine statistical bounds on fatigue life at *in vivo* use conditions using measured fatigue life derived in whole or in part from hyper-physiological testing to fracture.

1.3 This guide may be used to assess or characterize device durability during design development and for testing to device product specifications.

1.4 Fretting, wear, creep-fatigue, and absorbable materials are outside the scope of this guide, though elements of this guide may be applicable.

1.5 As a guide, this document provides direction but does not recommend a specific course of action. It is intended to increase the awareness of information and approaches. This guide is not a test method. This guide does not establish a standard practice to follow in all cases.

1.6 This guide is meant as a complement to other regulatory and device-specific guidance documents or standards and it does not supersede the recommendations or requirements of such documents.

1.7 *This standard does not purport to address all of the safety concerns, if any, associated with its use. It is the responsibility of the user of this standard to establish appropriate safety, health and environmental practices and determine the applicability of regulatory limitations prior to use.*

1.8 *This international standard was developed in accordance with internationally recognized principles on standardization established in the Decision on Principles for the Development of International Standards, Guides and Recommendations issued by the World Trade Organization Technical Barriers to Trade (TBT) Committee.*

2. Referenced Documents

2.1 *ASTM Standards:*[2]

E178 Practice for Dealing With Outlying Observations

E456 Terminology Relating to Quality and Statistics

E468 Practice for Presentation of Constant Amplitude Fatigue Test Results for Metallic Materials

E739 Practice for Statistical Analysis of Linear or Linearized Stress-Life (***S-N***) and Strain-Life (ε-***N***) Fatigue Data

E1823 Terminology Relating to Fatigue and Fracture Testing

F2477 Test Methods for***in vitro*** Pulsatile Durability Testing of Vascular Stents

F2942 Guide for***in vitro*** Axial, Bending, and Torsional Durability Testing of Vascular Stents

F3172 Guide for Design Verification Device Size and Sample Size Selection for Endovascular Devices

2.2 *ISO Standards:*[3]

ISO 5840-x Cardiovascular implants -- Cardiac valve prostheses -- Part 1: General requirements, Part 2: Surgically implanted heart valve substitutes, Part 3: Heart valve substitutes implanted by transcatheter techniques

ISO 12107 Metallic materials - Fatigue testing - Statistical planning and analysis of data

ISO 25539-x Cardiovascular implants -- Endovascular devices -- Part 1: Endovascular prostheses, Part 2: Vascular stents, Part 3: Vena cava filters

2.3 *Regulatory Guidance:*

Guidance for Industry: Q9 Quality Risk Management, FDA, 2006[4]

3. Terminology

3.1 *Definitions of Terms Specific to This Standard:*

3.1.1 *acceptance criteria*—specific numerical limits or ranges or other conditions identified prior to testing that

[1] This test method is under the jurisdiction of ASTM Committee F04 on Medical and Surgical Materials and Devices and is the direct responsibility of Subcommittee F04.30 on Cardiovascular Standards.

Current edition approved Sept. 1, 2017. Published September 2017. DOI: 10.1520/F3211-17.

[2] For referenced ASTM standards, visit the ASTM website, www.astm.org, or contact ASTM Customer Service at service@astm.org. For *Annual Book of ASTM Standards* volume information, refer to the standard's Document Summary page on the ASTM website.

[3] Available from International Organization of Standards, http://www.ISO.org/ISO/store.htm

[4] Accessed June 23, 2016 (http://www.fda.gov/downloads/Drugs/.../Guidances/ucm073511.pdf).

establish the required results to support a conclusion, a decision, or meet a specification.

3.1.2 *amplitude*—one-half of the difference between the maximum and minimum measurements of the cyclic waveform.

3.1.3 *censor*—data where the cycle count at failure is only partially known. Run-outs (see definition in 3.1.26) are a form of right-censored data. Tests that use periodic inspections to determine the cycles to fracture are interval censored as the cycle of fracture is unknown but bounded between the previous and current inspection cycle counts.

3.1.4 *component*—a test specimen comprised of a subassembly or an individual part of a cardiovascular medical device in its finished form.

3.1.5 *confidence level*—the probability that the true value for a parameter of interest will fall within a numerical interval. The interval is known as the Confidence Interval. Confidence Intervals are used to establish boundaries for the value of a parameter of interest.

NOTE 1—Confidence levels, typically stated as percentages, are typically chosen through a risk analysis.

3.1.6 *coupon*—a test specimen extracted from a cardiovascular medical device or a component in its finished form.

3.1.6.1 *Discussion*—Often a coupon is "clipped" or cut from an as-manufactured device.

3.1.7 *design curve*—the lower confidence bound for a reliability quantile of the fatigue life distribution. For example, the Load versus fatigue life Number of cycles (S-N) curve for p% survival at c% confidence. See Fig. 1.

3.1.8 *design life*—the number of cycles for which the device is designed to remain functional without significant performance degradation.

3.1.9 *device*—a complete cardiovascular medical implant in its final form, or as deployed, that may be used as a test specimen.

3.1.10 *duty cycle*—a time history of loading conditions.
EXAMPLE—For devices deployed into the vasculature of the lower limbs, a duty cycle may be defined by the number of steps per day, the number of stairs per day, and the number of sit/stand cycles per day.

3.1.11 *failure*—permanent deformation or fracture with complete separation that renders the device ineffective or unable to adequately resist load. Other criteria may be used but should be clearly defined.

3.1.12 *failure mode*—a combination of an external load type, a fracture location or locations, and a fracture type. The external load can be single modes such as bending or twisting torques, radial loads, tension-compression axial loads, and so forth, or combinations of such loads. Fracture locations are positions on a device at which fracture occurred such as in a stent connector, stent apex, or stent strut. The fracture type is characterized by the surface morphology and the material cause or causes of the fracture such as tensile overload, transverse shear, mixed-mode, high cycle fatigue, or low cycle fatigue.

3.1.13 *fatigue factor of safety*—the ratio of the Fatigue Strength at a Specified Life with prescribed reliability and confidence levels to the load at the specified use condition. The Fatigue Factor of Safety is specific to a single failure mode.

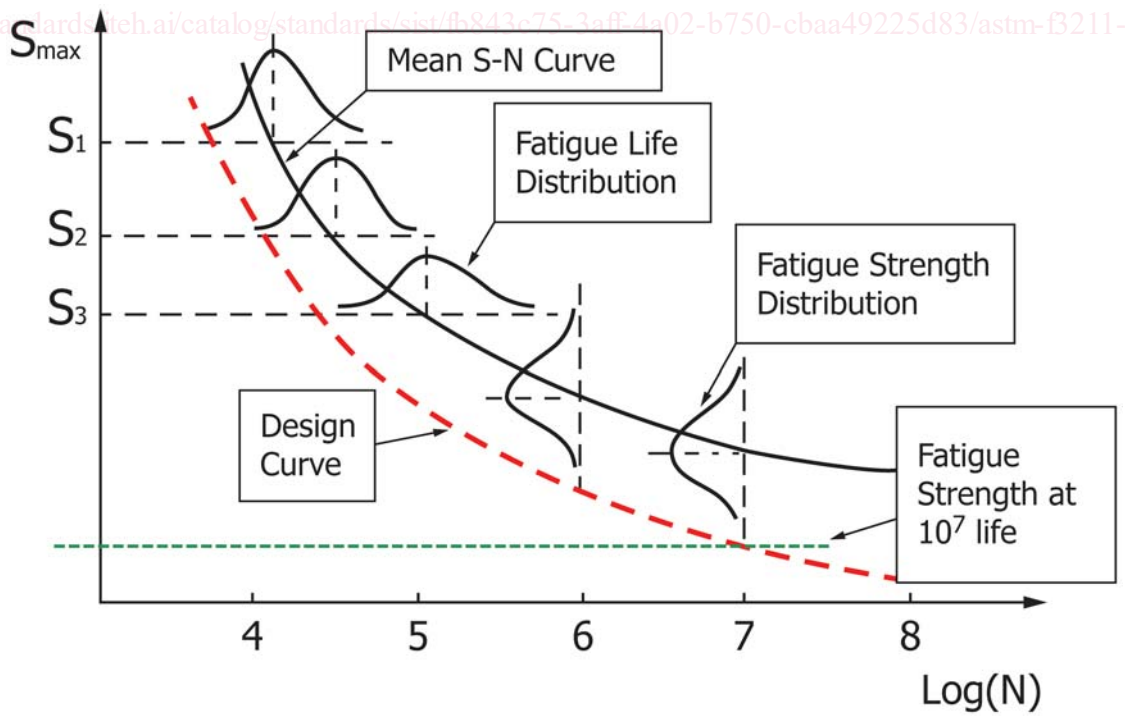

FIG. 1 Fatigue Life Model Depicting Terminology Where S is Load Parameter and N is Fatigue Life, Number of Cycles to Fracture

3.1.13.1 *Discussion*—When mean loads are considered along with the alternating loads, the ratio calculation must be defined and preferably shown on a constant life fatigue diagram.

3.1.13.2 *Discussion*—In communicating a Fatigue Factor of Safety, a clear statement of its intended purpose and the assumptions associated with its calculation is necessary for proper interpretation. For example, a safety factor estimate based on the average amplitude at fracture at the design life relative to the amplitude at the typical use condition will be substantially different from a safety factor based on the 90 % reliability/95 % confidence amplitude at fracture at the design life relative to a conservative estimate of the most challenging use condition amplitude.

3.1.14 *fatigue life model*—a mathematical equation that describes the relationship between fatigue life and loading parameters with prescribed reliability and confidence, statistically derived from experimental fatigue data. See Section 7.2 .

3.1.15 *fatigue strength at a specified life*—the maximum load the test specimen can be expected to survive for a specified number of cycles with a stated confidence and reliability.

3.1.15.1 *Discussion*—The Design Curve at a specified life may be used to show this graphically. See Fig. 1.

3.1.15.2 *Discussion*—The Fatigue Strength is specific to a single failure mode. See Terminology E1823.

3.1.16 *fracture*—complete separation of any device component due to stress with exposure of new surfaces that were previously together.

NOTE 2—A fracture does not necessarily represent a device functional failure.

3.1.17 *FtF*—acronym for Fatigue-to-Fracture.

3.1.18 *hyper-physiological test conditions*—test loads that exceed the expected *in vivo* use conditions.

3.1.19 *load*—used to denote continuous and time-varying forces, stresses, strains, torques, deflections, twists or other parameters that describe the applied fatigue stimuli. Typically these fatigue stimuli are described by a mean value and an alternating value.

NOTE 3—Units and symbols are dependent on the parameter of interest.

3.1.20 *physiological loads*—loads expected on the device during *in vivo* use.

3.1.21 *preconditioning*—simulated use preparation of the specimen prior to testing. See Section 6.12.

3.1.22 *protocol*—a set of instructions that typically defines the specimens, test procedures, analysis procedures, and acceptance criteria.

3.1.23 *quantile*—value such that a fraction of the sample or population is less than or equal to that value. See Terminology E456.

3.1.24 *reliability*——the probability of survival to the specified design life at a given loading condition.

3.1.24.1 *Discussion*—For the purpose of this standard, this is a narrow statistical measure of reliability of the device based on *in vitro* data and modeling. In general, higher reliability in FtF is expected to increase the clinical reliability.

3.1.25 *risk analysis*—(1) a methodical analytical approach to determine and address identified system or component failure modes and their associated causes, based on the probability of occurrence and the severity of their effects on system performance and patient safety; (2) an estimate of the risk associated with identified hazards in accordance with FDA Q9 Quality Risk Management.

3.1.26 *run-out*—no fatigue failure at a specified number of load cycles. See Terminology E1823. This number is typically specified prior to beginning the testing.

3.1.27 *sample size*—the quantity of individual specimens tested. The sample size is typically chosen to establish conformance to a pre-determined specification with appropriate statistical confidence levels.

3.1.28 *load versus life (S-N) curve*—graphical representation of fatigue life data (see Fig. 1). The curve indicates the load versus cycles-to-fracture relationship for a specified probability of survival, for example, the 50^{th}, 90^{th}, or 95^{th} percentile.

NOTE 4—For N, a log scale is commonly used. For loads in stress or strain, either a logarithmic or a linear scale is commonly used. See Terminology E1823. For the purpose of analysis, the S-N curve is commonly modeled using a load-life relationship, for example a Power Law or Coffin-Manson equation.

3.1.29 *strength distribution at life N*—the probability of fracture at the life N as a function of load. The distribution may be computed by integrating the fatigue life distribution at each load from 0 to N.

3.1.30 *surrogate*—a test specimen constructed to represent a device, component, or region of interest of a cardiovascular medical device in its finished form.

3.1.31 *test artifact*—spurious test results attributable to conditions that are not present during *in vivo* use conditions (failure at the grips, for example).

3.1.32 *test specimen*—a test article that is subjected to fatigue loading conditions. A test specimen (also referred to as specimen) may be classified as a *device*, *component*, *coupon*, or *surrogate*.

3.1.33 *test-to-success*—a paradigm for assessing or characterizing the fatigue durability of medical devices whereby specimens are tested at a chosen factor of safety at or near simulated cyclic physiological loads where no fractures are expected. For example, the device "passes" and the test is successful if no devices fail by structural fracture or if all devices maintain sufficient functional integrity. See Test Methods F2477.

3.1.34 *use conditions*—the conditions to which the device will be subject, including the cumulative effects of the final manufacturing state, the process of device delivery and deployment, and the *in vivo* operating environment. See 6.1 and 6.12.

4. Summary of Guide

4.1 The fatigue-to-fracture (FtF) paradigm provides a methodology whereby whole devices, device components, coupons

or surrogates are tested to fracture with hyperphysiological cyclic mechanical loads such as deflections, forces, or torques. In many or all of the tests, the cyclic load should be sufficient to fracture the device in fewer cycles than the desired clinical life. The resulting fatigue data are used to make a statistical estimate of fatigue life and/or generate outputs such as a fatigue safety factor and a fatigue strength distribution at the design life.

4.2 This document provides guidance for test considerations and choices such as determining physiologically relevant test modes, determining load levels, selecting test specimens, defining failure, characterizing and verifying test operation, selecting the test environment, determining an appropriate sample size, setting the test frequency, setting the test duration, preconditioning test specimens, monitoring the test, inspecting for fractures, and documenting test results.

4.3 Prospective test planning procedures are illustrated to generate a credible estimate of durability relative to the *in vivo* use conditions. The planning procedure can be used to generate a test protocol that includes a prospectively chosen statistical model, sample size and test load levels, and rationale for the choices.

4.4 This document provides guidance on statistical interpretation and presentation such as selecting the fatigue life model, calculating confidence bounds, choosing between Frequentist and Bayesian statistical procedures, and avoiding common statistical pitfalls.

5. Significance and Use

5.1 *Use of this Methodology:*

5.1.1 This guide provides a compendium of information on methods to use fracture data, fatigue life models, and statistical techniques to estimate the structural fatigue durability of an implantable medical device under anticipated *in vivo* loading modes. The methodology for high-cycle fatigue assessment relies on hyper-physiological tests intended to cause device fractures. Using the FtF methodology, fractures should not be avoided during testing; instead they provide the information required to statistically assess device longevity under a wide variety of physiological and hyper-physiological test conditions.

5.1.2 Through evaluation of fracture locations, the geometries after fractures, and the use conditions of the device, this guide may be used to help assess device safety.

5.1.3 This guide may be used to help assess differences in fatigue life between different devices or device histories. The effects on fatigue life due to changes to a device's geometry, processing, or material may be assessed using this guide.

5.1.4 Users of this guide must keep in mind that bench tests are simulations of in-use conditions. Adherence to this guide may not guarantee that results translate to individual clinical scenarios. Therefore, in assessing a device's fatigue performance, the results from Fatigue to Fracture testing should be reviewed in combination with other available data, such as animal studies, clinical experience, and computational simulations.

5.2 *Significance of this Methodology:*

5.2.1 While the FtF methodology applies only to bench tests, it can provide insights into device behavior that would not necessarily be apparent in clinical studies that typically focus on patient outcomes. After appropriate boundary conditions such as loadings, fixturing, and materials have been determined, the FtF methodology can provide extensive information on the expected longevity of a device in a period 10 to 1000 times shorter than a real-time clinical study.

5.2.2 FtF is informative in characterizing device behavior over a wide range of loads and cycles. This is especially valuable when the *in vivo* loading mode is understood but the load magnitude and cycle requirements are not well known or when characterizing device performance over a wide range of patient lifetimes, activity levels, and physiological states is desired.

5.2.3 In FtF, test loads greater than the devices' expected use conditions are used. Thus, factors of safety can be measured relative to expected *in vivo* use conditions in both loading/deformation severity and number of cycles.

5.2.4 In FtF, the nature and location of fractures observed as a function of load can help provide insights into the device response to the applied loading. The identified primary and follow-on fracture locations and modes may be used to assess the credibility of device computational models, as well as to evaluate potential impacts on clinical safety and efficacy, especially post-fracture.

5.2.5 The FtF methodology can quickly and reliably assess the impact of changes in processes, materials, or small changes in geometry on *in vitro* fatigue life. These assessments with respect to fracture can be quantified and used as part of validating design changes, demonstrating that the device meets product specifications, or as part of guiding design improvements.

5.2.6 FtF testing can often be completed in a shorter period of time than test-to-success testing since the FtF tests are typically terminated at a smaller number of cycles. Specifically, when extrapolation in cycles is appropriate, comparisons of the loads or the frequency of fracture at a lower number of cycles can provide a useful measure of equivalence.

6. Procedure for Testing

6.1 *Determine Physiological Loads:*

6.1.1 Since the FtF methodology is for bench testing, it is essential that the full range of clinically relevant loading modes and magnitudes be identified or bounded. Guidance documents from regulatory agencies such as the US FDA, guides and standards from organizations such as ASTM or ISO, clinical literature, and medical imaging and observations may provide useful recommendations on applicable types and magnitudes of loads for device fatigue assessment.

6.1.2 For the intended patient population, the manufacturer[5] should identify the use conditions, the design life, the potential of device fracture to produce adverse events, and the intended claims. If particular patient sub-populations present procedural, operating, or lifetime conditions beyond the final product

[5] The term "manufacturer" is used in this guidance to mean "user of this standard".

requirement, a description of those conditions and a rationale for exclusion may be useful. The use of Design Failure Mode and Effects Analysis (DFMEA) and other risk analysis tools in this identification process is encouraged (for example, see Mikulak (**1**)[6] or Teixeira (**2**)).

6.1.3 When determining *in vivo* use conditions, consideration should be given to the types, ranges, and duty cycles of conditions in the intended population. Estimates of *in vivo* fatigue life are strongly dependent on *in vivo* boundary conditions that vary from patient to patient and activity to activity. Imaging or modeling the device's or a well characterized similar device's deformations *in vivo* is encouraged.

6.1.3.1 Limitations on the accuracy and generalizability of *in vivo* measurements should be noted and reported; for example, single-plane x-ray clinical measurements on sedated patients may not accurately represent the geometry or range of actual physiological conditions.

6.2 *Determine Durability Requirements:*

6.2.1 With the intended patient population in mind and the potential hazards associated with durability, the manufacturer should establish the clinical durability requirements such as the device loads and/or the device deformations, the minimum number of cycles to fracture or failure, and the failure criteria.

6.3 *Choose Test Modes:*

6.3.1 The manufacturer should relate the selection of test modes to the known and predicted interactions between the implant site and the implanted device. Fatigue testing should be performed to elicit the anticipated *in vivo* mechanics; for example, a torsion fatigue test is not likely to be informative if *in vivo* bending fatigue is anticipated.

6.3.2 If devices will be exposed to multiple modes of cyclic physiological loads (such as radial compression, bending, torsion, flattening, axial tension/compression, and so forth), consideration should be given to the effects of combined loading. In each case, the manufacturer should relate the magnitudes of each mode tested and the manner in which the loading is combined, or tested in isolation, to represent the *in vivo* use conditions.

6.3.3 If one mode clearly dominates the fatigue life, single-mode testing to fracture to establish a factor of safety combined with analysis of that mode plus the secondary modes may eliminate the need to test one or more of the secondary modes in conjunction with the dominant mode. With appropriate evidence, the manufacturer may choose to exclude loading modes that are not expected to result in fracture or loss of function.

6.3.4 General guidance to some testing modes is given in Guide F2942, ISO 25539, and ISO 5840.

6.4 *Select Test Specimens:*

6.4.1 Test specimens should be nominal finished devices, appropriate components, coupons extracted from the device or component, or surrogate samples. In order to best reveal unforeseen and characterize known failure modes, preference should be given to testing full devices or the largest subassembly that is practical. Test specimens should be representative of actual clinical components made by the final manufacturing process.

6.4.2 For devices where a single size implant is used over a range of application sizes (vessel diameters, for example), either assess the maximum and minimum use diameters or determine and assess the most challenging use condition based on stress analysis or experimental data. The manufacturer should take into account any interactions between the device and *in vivo* use conditions over the range of application sizes to determine the most challenged device size. See 6.8.4 for one example where vessel diameter may be important.

6.4.3 If devices come in multiple sizes with a common design application, geometric architecture, and materials and processes, then experimental or computational methods may be used to determine the most challenged size and the FtF testing may be confined to that size as a representation for the entire size range.

6.4.4 Select test specimens that are representative of the finished device. Consider test specimen features that may influence the fatigue test results such as surface finish, microstructure (grain size and texture), loading orientation, geometry and dimensions, mechanical properties, cold work, residual stresses, size and distribution of material or process flaws, and preconditioning. Consider these features and any other relevant factors if specimens other than the finished device are to be justified for use in fatigue testing. If a coupon or surrogate is made to facilitate fatigue testing, a numerical model may also be used to demonstrate the similarity in stress distribution between the coupon or surrogate and the actual device under testing conditions.

6.4.5 Though elements of FtF may be applicable, testing of standard test specimens (ASTM "dogbones", for example) or other ideal geometries is considered classical fatigue and can be planned and analyzed using classical methodologies such as in ISO 12107 and Practice E739.

6.4.6 Sample selection procedures should follow good statistical practices to produce a representative sample (see ISO 12107). Randomization in sample selection, such as using a random number generator, is recommended whenever practicable to assure a high degree of independence in the contributions of experimental error to estimates of treatment effects (see Terminology E456).

6.5 *Define Failure in Fatigue:*

6.5.1 A clear definition of the test's acceptance criteria should be established. Typically this is chosen to be consistent with the specific failure mode(s) identified by the FMEA or other risk analysis.

6.5.2 First fracture may be used as the definition of failure. However, depending on the application and type of fracture, the specimen may still be functionally adequate with one or more fractures.

6.5.3 If one or more fractures are acceptable within an individual specimen, the manufacturer should define the criteria and provide supporting evidence to distinguish acceptable from unacceptable fracture(s). However, all acceptable and unacceptable fractures should still be reported and summarized

[6] The boldface numbers in parentheses refer to a list of references at the end of this standard.

in the test report. Recommended post-fracture test procedures are discussed in 6.11.6.

6.5.4 Prescribed acceptance criteria may be established to exclude occurrences of fracture that are artifacts of the test (see 6.15.6).

6.5.5 It may be appropriate to use a failure criterion defined by the loss of acceptable function such as mechanical performance without an actual fracture taking place. For example, cyclic stress-softening could reduce mechanical stiffness to an unacceptable level, or cumulative plastic damage could reduce the diameter to an unacceptable level. If FtF is used in these circumstances, the test report should address whether or not such device behavior is expected, how it is accounted for, and how functional failure is determined and statistically analyzed.

6.6 *Characterize the Test:*

6.6.1 The manufacturer should assess the impact of idealizations and simplifications present in the test setup, operation and test specimens that may impact the results, such as: the boundary conditions[7], machine alignment, machine stability and durability, preconditioning, device alignment, device orientation, device positioning, device non-uniformity, post-fracture behavior, and any pre- and/or post-deployment procedures. The assessment may be used to determine what factors need to be controlled in the test.

NOTE 5—The following characterization activities may be useful:

- Observe the geometry and displacements over the range of test frequencies and amplitudes using high-speed video and image analysis software (if appropriate). Observe the whole specimen, paying attention to potential fracture locations and the apposition between the test specimen and the fixtures used to impose the boundary conditions. When load or strain-rate sensitive fixtures are used, the cycle rate should be sufficiently slow to ensure that the specimens maintain continual apposition to the testing fixtures.
- If test specimens vary substantially in size, stiffness, mass, or other design attributes, it is desirable to observe test operation over the full range of specimens.
- Observe and characterize variations in the applied load (for example displacement, curvature, forces, torques, and so forth) over an appropriate sampling period at various intervals from the beginning to the end of testing. Rapid changes in loads may be indicative of a fracture or a change in deformation mode.
- Force measurements during setup in a deformation controlled test can be useful in assuring that the intended conditions are being imposed on the test specimens.
- Assess the potential for test artifacts to induce fracture, such as stress concentrations associated with rigid grips.
- Assess the potential for force and displacement measurement errors as a result of specimen and fixture geometric tolerances, signal collection and filtering, inertial and frictional effects, and so forth.

6.7 *Verify Test Operation:*

6.7.1 Through dimensional measurements, video and still imagery, strain gages, modeling, and any other appropriate characterization technique, show that the devices are deforming in the intended manner, the loads are as expected, and the counts of cycles are accurate.

6.8 *Select Test Conditions:*

6.8.1 In general, the *in vitro* fatigue properties of a device will be most effectively characterized by testing under a variety of conditions that will induce both fractures and run-outs. The allocation of specimens to hyper-physiological test conditions, where fractures are expected, and Test-to-Success conditions, where no fractures are expected, will depend on considerations of the FMEA or other risk analysis, the raw material behavior, the use environment, and the statistical models to be employed.

6.8.2 The fluctuating loads on a device or test specimen which induce fatigue can vary in type, magnitude, and frequency. For S-N characterization, typically employed in classical fatigue and FtF, constant-type/constant-magnitude/constant-frequency cyclic tests are used (for example see ISO 12107 or Practice E739). For a given test frequency, these test conditions can be described by two parameters: the load amplitude and the mean load. Often, the load level combinations are created by increasing the load amplitude while keeping the mean load constant, the ratio of (load amplitude)/(mean load) constant, or the ratio of (minimum load)/(maximum load) constant. Record the methodology chosen and provide a scientific rationale for its use such as feasibility test data or historical experience.

6.8.3 Given previous material/device fatigue characterization, one load level may be sufficient to compare FtF testing of two similar designs. Also, one load level is typically used in the Test-to-Success approach to demonstrate no or few failures. When less historical data are available, a minimum of two levels are required to demonstrate a transition from majority-fracture condition to majority-run-out conditions. When little pre-existing data are available, or to truly define a transition in regions, such as a plateau from low-cycle to high-cycle fatigue (see Dowling (**3**) for examples), a minimum of three levels is required. In this case, typically two levels are in the shorter life domain to establish an S-N slope for that region and the third level in the majority run-out condition to establish a change in slope. If a fourth test condition, equivalent to Test-to-Success load and cycle life condition is tested, or if the run-out cycle number with super-physiological loads exceeds the design life, then no extrapolation would be required.

6.8.4 The levels should be chosen to incorporate variation in the amplitudes, the mean, or both. The effect of mean load on the fatigue life may differ between low-cycle fatigue and high-cycle fatigue, between force-control and deformation-control fatigue tests (Manson (**4**)), and between materials with residual stresses and those without residual stresses.

NOTE 6—On specific cases:

- In low-cycle deformation-controlled fatigue of devices with materials whose stresses reduce or accumulate plastic damage with cyclic use, initial mean test conditions may have little influence on fatigue life.
- In high-cycle fatigue, in either force- or deformation-control, usually there is little plasticity and correspondingly no or little change in the mean load. Thus mean loads tend to influence high-cycle fatigue life. There may be most-challenging mean conditions; for example in radial fatigue of some self-expanding stents the mean strains are higher in small diameter vessels than in large diameter vessels.
- In load control, devices with stress hardening materials may plastically deform initially, but then stabilize and have good fatigue life. However, devices with strain-softening materials may fail quickly if the deformation magnitude increases from cycle to cycle.
- The presence of residual stress in low-yield stress materials tested under low-cycle fatigue conditions tends to have minimal impact on fatigue life because cyclic plasticity will tend to reduce the levels of

[7] Boundary Conditions refers to loading or deformation conditions imposed on the test sample, geometric constraints that control the force and moment, or deformations at locations where the test article interacts with the testing fixtures.